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Multiple Myeloma (Part 1) – Update on Epidemiology, Diagnostic Criteria, Systemic Treatment and Prognosis

Mieloma múltiplo (Parte 1) – Atualização sobre epidemiologia, critérios diagnósticos, tratamento sistêmico e prognóstico

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Abstract

Multiple myeloma (MM) is a hematological malignancy characterized by unregulated and clonal proliferation of plasma cells in the bone marrow; these cells produce and secrete an anomalous monoclonal immunoglobulin, or a fragment of this, called M protein. The clinical manifestations of MM result from the proliferation of these plasmocytes, the excessive production of monoclonal immunoglobulin and the suppression of normal humoral immunity, leading to hypercalcemia, bone destruction, renal failure, suppression of hematopoiesis and humoral immunity, increasing the risk for the development of infections. The increase in life expectancy of the world population led to a concomitant increase in the prevalence of MM, a pathology that usually affects the elderly population. The aim of this review is to update the reader on epidemiology, diagnostic criteria, differential diagnosis with other monoclonal gammopathies, systemic treatment and prognosis of MM.

Keywords
- epidemiology
- monoclonal gammopathy of undetermined significance
- multiple myeloma
- smoldering multiple myeloma
- plasmacytoma
- prognosis

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Resumo

O mieloma múltiplo (MM) constitui neoplasia maligna de origem hematológica caracterizada pela proliferação desregulada e clonal de plasmócitos na medula óssea; estas células produzem e secretam imunoglobulina monoclonal anômala, ou um fragmento desta, denominado proteína M. As manifestações clínicas do MM decorrem da proliferação destes plasmócitos, da produção excessiva de imunoglobulina monoclonal e da supressão da imunidade humoral normal, levando à hipercalcemia, destruição óssea, insuficiência renal, supressão da hematopoiese e da imunidade humoral, aumentando o risco para o desenvolvimento de infecções. O aumento na expectativa de vida da população mundial levou a concomitante incremento na prevalência do MM, patologia que habitualmente acomete a população idosa. O objetivo desta revisão é atualizar o leitor sobre a epidemiologia, critérios diagnósticos, diagnóstico diferencial com outras gamopatias monoclonais, tratamento sistêmico e prognóstico do MM.

Palavras-chave
- epidemiologia
- gamopatia monoclonal de significância indeterminada
- mieloma múltiplo
- mieloma múltiplo latente
- plasmocitoma
- prognóstico

Introduction

Normal plasma cells originate in the bone marrow and are an important part of the immune system, especially because they produce antibodies that help fight infections and other diseases.[1–3]

Multiple myeloma (MM), also called Kähler's disease, myelomatosis, and plasmacytic myeloma,[1] is a malignant neoplasm of hematological origin characterized by dysregulated and clonal proliferation of plasma cells in the bone marrow.[1,2,4–8] These cells produce and secrete anomalous monoclonal immunoglobulin, or a fragment thereof, called M protein,[1,3,6–10] comprising a heavy [(IgG γ, IgA α, IgM μ, IgD δ, or IgE ε] and a light (*kappa*-κ and *lambda*-λ) chain classes.[9]

MM was first described in the literature by William Macintyre (1850), who recognized proteinuria in samples obtained from a patient who had excruciating pain in the chest and thoracolumbar region for about a year.[9,11] These samples were previously sent (1848) to Henry Bence Jones, a renowned chemical pathologist, who analyzed them in detail, confirming the discovery.[9,11] The disease, however, was not recognized until 1889, when Otto Kähler published the eight-year follow-up (1879-1887) of a 46-year-old patient who presented typical findings of this pathology (bone pain, albuminuria, anemia, severe kyphosis, recurrent bronchial infections and loss of height) – Kähler recognized that the protein identified in the patient's urine had the same characteristics described by Bence Jones.[11]

MM clinical manifestations result from neoplastic plasma cells proliferation, excessive production of monoclonal immunoglobulin and normal humoral immunity suppression.[1,9,10] The pathophysiological consequences of the disease's progression include: hypercalcemia,[5,12] bone destruction (►**Figs. 1** and **2**),[1,4,5,9,10,12] renal failure,[4,12] suppression of hematopoiesis[4,10,12] and humoral immunity,[9] increasing the risk for the development of infections.[4,9,10,12] Approximately 1% to 2% of patients have extramedullary disease at diagnosis, while 8% develop this condition in the course of the disease.[12]

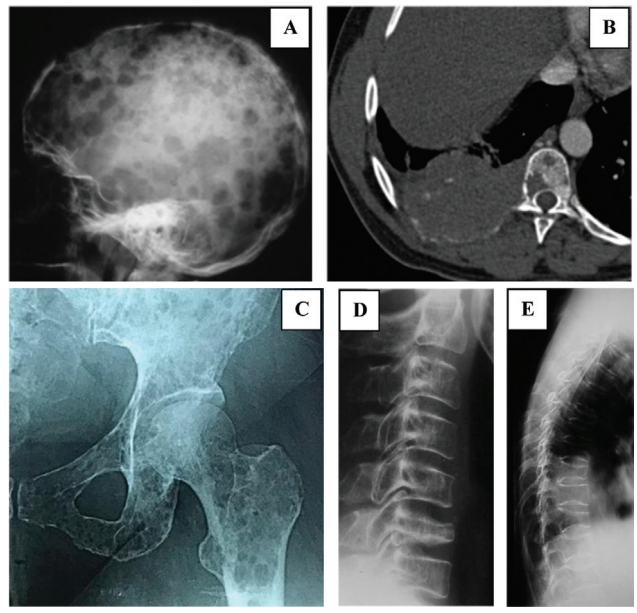


Fig. 1 (**A–E**) Main anatomical locations of MM. (**A**) skull; (**B**) costal arches; (**C**) femur; and (**D, E**) spine.

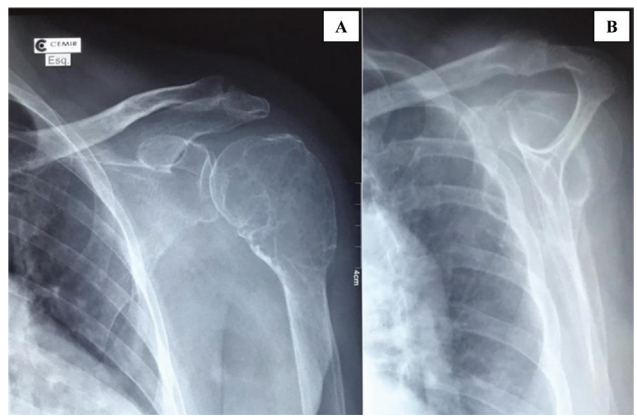


Fig. 2 (**A, B**) Female patient, 68 years old, afro-descendant, with MM, presenting bone lesion in the proximal segment of the left humerus.

The increase in life expectancy of the world population led to a concomitant increase in the prevalence of multiple myeloma, a pathology that usually affects the elderly population.

The objective of this review is to update the reader on the epidemiology, diagnostic criteria, differential diagnosis with other monoclonal gammopathies, systemic treatment and prognosis of MM.

Epidemiology

MM corresponds to 1% of all malignant neoplasms.[3,4,9,12] Its incidence increases with age and reaches its maximum during the seventh decade of life.[9] It is the second malignant neoplasm of hematological origin in order of frequency (inferior only to lymphomas),[4,10] corresponding to approximately 10% of the total number of cases,[2,10,12] and it is also the most common primary malignant bone tumor (47%).[13] In the United States, based on data obtained between the years of 2017 and 2019, it has been estimated that approximately 0.8% of men and women will be diagnosed with MM at some point in their lives.[14]

MM is most often diagnosed among people aged 65 to 74 years;[14] very few cases occur in individuals under the age of 40.[3] In the United States, according to data obtained between 2015 and 2019, the median age of patients at diagnosis was 69 years. It is slightly more common in men than in women and twice as frequent in Afro-descendants, when compared to Caucasians,[3,4,9–12] being less frequent in Asian populations[10] - studies conducted in Brazil, however, point to a higher prevalence in females and in white individuals.[4,15]

In the United States, the annual incidence of MM was 7.1 per 100,000 men and women between the years 2015 and 2019[14]–every year, more than 32,000 new cases are diagnosed,[12] with an estimated 34,470 cases in 2022. In 2019, there were 159,787 MM carriers in that country.[14] Between the years 2015 and 2019 the percentage of deaths from MM was higher among people aged 75 to 84 years (median of 75 years); the annual mortality rate was 3.2 per 100,000 men and women – almost 13,000 patients die annually due to this disease,[12] with an estimate for 12,640 deaths in 2022, That's 2.1 percent of all cancer-related deaths estimated for this year in that nation.[14]

Diagnostic Criteria

If MM is suspected, the presence of M protein should be investigated by laboratory tests such as protein electrophoresis, immunofixation, and serum *free light chains* (FLC).[5] Approximately 2% of patients have non-secretive disease and, therefore, evidence of M protein may be undetectable on these tests.[12]

Bone marrow studies performed at the time of initial diagnosis should include *fluorescent hybridization in situ* (FISH) to detect possible trisomies t(11;14), t(4;14), t(14;16), t(6;14), t(14;20), and del(17p). Conventional karyotyping can be used to detect hypodiploidy and deletion,[13] but if FISH studies are performed, their additional value in initial risk stratification is limited. The *genetic expression profile* (GEP), if available, may provide additional prognostic value.[12]

Diagnosis requires $\geq$10% clonal plasma cells in the bone marrow or a biopsy showing plasmocytoma associated with evidence of one or more *MM-defining events (multiple myeloma defining events*, MDE): CRAB (hypercalcemia, renal dysfunction, anemia, and/or lytic bone lesions), features related to plasma cell disorder, as well as three specific biomarkers: clonal plasmocytosis in the bone marrow $\geq$60%, proportion of involved/uninvolved CLF $\geq$100 (provided that the CLC involved is $\geq$100 mg/L), or $>$1 focal lesion detected on magnetic resonance imaging (MRI).[12]

The criteria reviewed (2015) by the International Myeloma Working Group (IMWG) for the diagnosis of MM and related disorders (monoclonal gammopathies) are shown in ►**Table 1**.

Other monoclonal gammopathies

Almost all patients with MM evolve from an asymptomatic premalignant stage called *monoclonal gammopathy of undetermined significance* (MGUS) (►**Table 1**),[4,6,12] which is the most common monoclonal gammopathy,16 present in more than 3% of the population over 50 years of age,[10,12,16] and in more than 5% from the age of 70 years. [10,16] It is about twice as prevalent in afro-descendants as in caucasians.[12] Approximately 25% of patients with MGUS develop MM, amyloidosis, macroglobulinemia or other lymphoproliferative diseases,[10,16] with an actuarial rate of 16% up to 10 years, 33% up to 20 years and 45% up to 25 years.[16] The predominant M protein is IgG γ (55.5%), followed by IgM μ (20%), IgA α (10%), biclonal (8%), light chain (6%) and IgD δ ($<$0.5%)[11,16] - the concentration of M protein, the type of immunoglobulin, medullary plasma cell infiltration greater than 5% and the presence of monoclonal light chain in the urine can be used in risk stratification in MGUS.[10,16] MGUS progresses to MM or related malignancy at a rate of 1% per year.[10,12,16] As this pathology is asymptomatic, it is believed that $>$50% of the individuals diagnosed were already carriers of this condition more than 10 years before its diagnosis.[12] Its variants of presentation, according to the diagnostic criteria (►**Table 1**), are: non-IgM MGUS, IgM MGUS and MGUS light chain.

In some patients, a more advanced, intermediate, asymptomatic premalignant stage, known as *smoldering multiple myeloma (*SMM), may occur (►**Table 1**).[6,12] SMM progresses to MM at a rate of approximately 10% per year for the first five years after diagnosis, 3% per year for the following five years, and, thereafter, 1.5% per year. This progression ratio is influenced by the underlying cytogenetic profile: patients with t(4;14), del(17p) and gain(1q) translocation have a higher risk of progression from MGUS or SMM to MM.[12]

Solitary plasmocytoma (SP) (►**Table 1**) is an uncommon type of plasmacytic dyscrasia,[17,18]representing approximately 2-5% of all monoclonal gammopathies.[17,18] It is characterized by localized proliferation of neoplastic plasma cells,[16–18] with no evidence of other skeletal lesions on imaging, absence of MM-related signs and symptoms, and morphologically normal bone marrow biopsy (solitary

Table 1 International Myeloma Working Group (IMWG) criteria for the MM diagnosis and other monoclonal gammopathies

Disorder	Definition of the Disease
Monoclonal gammopathy of undetermined significance (Non-IgM MGUS)	All 3 criteria must be met: • Serum monoclonal protein (Non-IgM) <3 g/dl; • Clonal plasma cells in the bone marrow <10%;[a] • Absence of target organ damage, such as hypercalcemia, renal failure, anemia, or bone lesions (CRAB) that can be attributed to proliferative plasma cell disorder.
Latent Multiple Myeloma (SMM)	Both criteria must be met: • Serum monoclonal protein (IgG or IgA) ≥3 g/dl, or monoclonal urinary protein >500 mg in 24 hours and/or 10%-60% of clonal plasma cells in the bone marrow; • Absence of events defining myeloma or amyloidosis.

Multiple Myeloma (MM)	Both criteria must be met:
	• Clonal plasma cells in the bone marrow <10% or bone or extramedullary plasmocytoma confirmed by biopsy;
	• Any one or more of the events that define myeloma:
	  • Evidence of target organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
	  ➢ Hypercalcemia: serum calcium >0.25 mmol/l (>1 mg/dl) higher than the upper limit of normal or >2.75 mmol/l (>11 mg/dl);
	  ➢ Renal failure: *creatinine clearance* <40 ml per minute or serum creatinine >177 mmol/l (>2 mg/dl);
	  ➢ Anemia: hemoglobin value >2 g/dl below the lower limit of normal, or a hemoglobin value <10 g/dl;
	  ➢ Bone lesions: one or more osteolytic lesions on skeletal radiographs, computed tomography (CT), or positron emission tomography-CT (PET-CT).
	  • Percentage of clonal plasma cells in the bone marrow ≥60%;
	  • Free serum light chain ratio (FLC) involved/uninvolved ≥100 (the level of free light chain involved should be ≥100 mg/l);
	  • >1 focal lesion on magnetic resonance imaging (MRI) studies (at least 5 mm in size).

Monoclonal gammopathy of undetermined significance IgM (IgM MGUS)	All 3 criteria must be met: • IgM monoclonal serum protein <3 g/dl; • Lymphoplasmocytic infiltration of the bone marrow <10% • No evidence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, or hepatosplenomegaly that can be attributed to the underlying lymphoproliferative disorder.
Light Chain MGUS	All criteria must be met: • Abnormal FLC proportion (<0.26 or >1.65); • Increased level of appropriate light chain involved (increased *kappa* FLC in patients with a ratio >1.65 and increased lambda FLC in patients with a ratio <0.26); • There is no expression of heavy chain immunoglobulin in immunofixation; • Absence of damage to target organs that can be attributed to the proliferative disorder of plasma cells; • Clonal plasma cells in the bone marrow <10%; • Monoclonal urinary protein <500 mg/24 hours.
Solitary Plasmocytoma	All 4 criteria must be met: • Biopsy showing solitary lesion in bone or soft tissues, with evidence of clonal plasma cells; • Normal bone marrow, no evidence of clonal plasma cells; • Normal investigation of the skeleton, MRI (or CT) of the spine and pelvis (except for the primary solitary lesion); • Absence of target organ damage such as hypercalcemia, renal failure, anemia, or bone lesions (CRAB) that can be attributed to lymphoplasmocyte proliferative disorder.
Solitary Plasmocytoma with Minimal Medullary Involvement[b]	All 4 criteria must be met: • Biopsy showing solitary lesion in bone or soft tissues, with evidence of clonal plasma cells; • Clonal plasma cells in the bone marrow <10%; • Normal investigation of the skeleton, MRI (or CT) of the spine and pelvis (except for the primary solitary lesion); • Absence of target organ damage such as hypercalcemia, renal failure, anemia, or bone lesions (CRAB) that can be attributed to lymphoplasmocyte proliferative disorder.

[a]Bone marrow biopsy may be delayed in patients with low-risk MGUS (IgG, M protein <15 g/l, with normal free light chain ratio) in whom there are no MM-related clinical features.

[b]Solitary plasmocytoma with 10% or more clonal plasma cells is considered as MM.

Fonte: Traduzido a partir de Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification, and management. Am J Hematol. 2020;95 (5):548-567.

plasmocytoma variant) or with very low plasmacytic clonal infiltration (<10%, solitary plasmocytoma variant with minimal medullary involvement) (►**Table 1**).[17,18] SP can be subdivided into two entities: bone SP and soft tissue SP (extramedullary).[16–18] The incidence of bone SP is approximately 40% higher than that of extramedullary SP.[17,18] Bone SP occurs more frequently in the axial skeleton,[16,19] being twice as frequent in the spine than in other sites, besides constituting the most common malignant primary tumor in this location (30% of all cases),[19] while extramedullary SP is more frequently observed in the head and neck.[16–19] The variants have a very different clinical course and prognosis, particularly regarding the progression to MM, being worse in bone SP.[17] The median age at SP diagnosis (55-60 years) is significantly lower than that observed in patients with MM; and the distribution by gender shows male predominance, ranging from 1.2 to 2:1.[17,19] SP has a higher incidence in afrodescendants, being about 30% more frequent than in Caucasians, and has a lower incidence in the Asian population.[18]

Confirmation of the presence of the monoclonal protein is essential to differentiate monoclonal gammopathies from polyclonal gammopathies since the former are neoplastic or potentially neoplastic entities while the latter result from inflammatory or infectious processes.[19]

Systemic Treatment

It is important to understand that MM is treatable, but not curable. Treatment plans vary and are tailor-made for each individual – basic parameters such as the patient's age, pattern of disease progression, prognosis, and patient preference should be applied in this planning.

Autologous stem cell transplantation (TACT) is the first treatment option in MM. From the perspective of treatment and prognosis, MM patients are stratified into three groups: (1) those newly diagnosed and eligible for TACT, (2) those newly diagnosed and not eligible for TACT, and (3) those with relapsed and/or refractory MM.[9]

For patients eligible for TACT, the first step in treatment is the introduction of a triple cocktail including chemotherapy, proteasome inhibitor, and corticosteroids (e.g., bortezomib, lenalidomide, and dexamethasone).[9] Patients are treated with three to four cycles of induction therapy prior to stem cell collection.[12] The stem cells are then collected through central venous access, and then high-dose chemotherapy is initiated.[9] Patients can immediately undergo TACT or resume induction therapy, delaying TCAT until the first relapse. There are many options for initial therapy - these regimens can also be used at the time of relapse. In general, dexamethasone at low doses (40 mg once weekly) is preferred in all treatment regimens as it minimizes toxicity.[12]

In patients with newly diagnosed MM and ineligible for TACT due to age or other comorbidities, the treatment plan is to control the side effects of MM and its progression as much as possible.[9] Normally, treatment is performed using a regimen based on the use of a chemotherapeutic agent, such as lenalidomide, which reduces the production of monoclonal proteins, especially in relapses, and bortezomib[9] or daratumumab,[12] as additive therapy to dexamethasone - this combined action results in greater lethality for anomalous plasma cells.[7] Although melphalan-based regimens have been extensively tested in these patients, they are not recommended due to concerns regarding stem cell damage, secondary myelodysplastic syndrome, and leukemia.[12]

Almost all MM patients go through relapses. The duration of remission in these relapses decreases with each regimen. The median progression of disease-free survival and overall survival in patients with relapsed MM, refractory to lenalidomide and bortezomib, were low before the introduction of daratumumab. The choice of treatment regimen in a relapse is complicated and affected by several factors, including relapse time, response to previous therapy, aggressiveness of relapse, and performance status. Patients eligible for TACT should be considered for the procedure if they have never done so, or if they have had excellent duration of remission (36 months or more) with treatment maintenance. In terms of drug therapy, a triple regimen, containing at least two new drugs to which the patient is not refractory, should be considered. Patients previously treated with lenalidomide often relapse when using a regimen containing the same drug - in patients refractory to lenalidomide treatment, one option is to consider pomalidomide-based regimens.[12]

Recently, the Food and Drug Administration (FDA) approved the first chimeric antigen receptor (CAR) T-cell (T-cell) immunotherapy for MM. This is the idecabtagene vicleucel (Abecma) indicated for patients with refractory or relapsed MM after at least four different types of treatment. Abecma targets the B-cell maturation antigen (BCMA) present on the surface of neoplastic cells. Immune system T cells are collected, genetically modified, multiplied and reinfused into the patient, where they bind to BCMA, leading to the death of tumor cells by apoptosis. The main advantage for the patient is the single infusion, which requires a maximum of two weeks of hospitalization; in addition, modified T cells may persist in the patient's body for a long time, recognizing and attacking neoplastic cells if and when there are relapses.

Prognosis

Overall survival in MM, affected by characteristics of the carrier of the pathology, tumor burden, presence of cytogenetic abnormalities and response to therapy, has improved significantly in the last 15 years. The initial impact came from the introduction of thalidomide, bortezomib and lenalidomide. In the last decade, carfilzomib, pomalidomide, panobinostat, ixazomib, elotuzumab, daratumumab, isatuximab and selinexor have been approved for the treatment of relapses, promising to further improve outcomes.[12]

The age of patients with MM is an important factor in the prognostic classification. Patients over 65 years old have a very low survival rate when compared to younger patients.[10] Similar findings are observed in patients with SP aged over 60 years.[18]

Tumor burden in MM has traditionally been assessed using the Durie-Salmon Staging (DSS) and the International Staging System (ISS).[12]

The biological behavior of the disease is related to the molecular subtype of MM and the presence or absence of secondary cytogenetic abnormalities, such as del(17p), gain(1q), or del(1p). In addition to cytogenetic risk factors, two other markers associated with the aggressiveness of the disease are elevated lactic dehydrogenase, and the presence of circulating plasma cells detected in peripheral blood smears (plasmacytic leukemia). Each of the biomarkers used in the diagnosis of MM (clonal plasmocytosis in the bone marrow $\geq$60%, proportion of CLF involved/uninvolved $\geq$100, or $>$1 focal lesion detected on MRI) is associated with a risk of approximately 80% for progression of symptomatic damage in target organs - attention to these criteria allows early diagnosis and initiation of therapy before these damages occur.[12]

Some findings in laboratory tests routinely performed in patients with MM allow us to indicate more active disease: high levels of ß2 microblobulin, low levels of serum albumin, serum creatinine above normal, lactic dehydrogenase above normal, C-reactive protein above normal, hemoglobin below normal and platelet count below normal. Other special tests such as plasma cell labeling index (PCLI) indicating high percentage of plasma cells, iFISH (interphase fluorescence in situ hybridization) demonstrating chromosome 13 absence and/or other cytogenetic abnormalities and evaluation of microvascular bone marrow density (microvascular density, MVD), demonstrating growth of new blood vessels in the bone marrow, also suggest more active disease.

Survival can range from a few months to more than a decade.[10] In the United States, the five-year relative survival rate was 57.9% between 2012 and 2018.[14] According to the American Cancer Society,[2] following the staging system reviewed for MM (2015) by the International Myeloma Working Group (IMWG)[20,21] (►**Table 2**), stage I survival was not determined; in stage II it was 83 months; and in stage III, it was 43 months.

Final Considerations

Multiple myeloma (MM) is a plasma cell neoplasm characterized by abnormal clonal proliferation of plasma cells in the bone marrow, with production of monoclonal

Table 2 R-ISS for MM is an algorithm for risk stratification that has improved prognostic power when compared to the three widely used prognostic indicators that it incorporates: (1) ISS, determined by serum β2-microglobulin and albumin levels; (2) the presence of any one or more of the three specific chromosomal abnormalities [del(17p), and/or t(4;14) translocation, and/or t(14;16) translocation] detected by iFISH; and (3) LDH level. In patients with newly diagnosed MM, R-ISS allows the identification of three distinct myeloma entities, with significantly different survival outcomes

Determination of the patient's ISS stage	
ISS Stage	**Criteria**
I	Serum β2-microglobulin $<$3.5 mg/l Serum albumin $\geq$3.5 g/dl
II	Not ISS I or ISS III Serum β2-microglobulin $\geq$3.5 mg/l, but $<$5.5 mg/l or Serum albumin $<$3.5 g/dl
III	Serum β2-microglobulin $\geq$5.5 mg/l
Determination of risk according to chromosomal abnormalities detected by iFISH.	
Risk	Criteria
Standard Risk	Chromosomal abnormalities without high risk
High Risk	Presence of del(17p), and/or t(4;14) translocation, and/or t(14,16) translocation
Determination of the risk according to the level of lactic dehydrogenase (LDH)	
Risk	Criteria
Standard Risk	Normal serum LDH, $<$ the upper limit of normal as defined by the laboratory
High Risk	High serum LDH, $>$ the upper limit of normal as defined by the laboratory
Identification of the patient's R-ISS stage, according to the criteria determined above	
R-ISS Stage	Criteria
I	ISS stage I and standard risk for chromosomal abnormalities by iFISH and normal DHL
II	Not R-ISS I or R-ISS III
III	ISS stage III and/or high risk for chromosomal abnormalities by iFISH or high DHL

Abbreviation: LDH, lactic dehydrogenase; iFISH, interphase fluorescence in situ hybridization; ISS, International Staging System; MM, multiple myeloma; R-ISS, Revised International Staging System.
Source: Translated and adapted from Managing Myeloma [Internet]. Medicom Worldwide, Inc. Links; c2020. Revised International Staging System for Multiple Myeloma [cited 2020 Mar 12]. Available from: https://www.managingmyeloma.com/tools/revised-international-staging-system-for-multiple-myeloma?task=download.file&format=raw&dlid=1042.

immunoglobulins, associated with organic dysfunctions. It represents 1% of all malignant neoplasms, and usually affects the elderly population, around the age of 70. Overall survival in MM is affected by characteristics of the carrier of the pathology (especially age, worse >65 years), tumor burden, presence of cytogenetic abnormalities and response to therapy, which has improved significantly in the last 15 years. An adequate understanding of the diagnostic criteria and the appropriate treatment for each patient with MM is very important to obtain the maximum possible control over the side effects of the disease and its progression.

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The authors declare no conflicts of interest.

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Multiple Myeloma (Part 2) – Update on The Approach to Bone Disease

Mieloma múltiplo (Parte 2) – Atualização sobre a abordagem da doença óssea

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Abstract

The increase in life expectancy of the world population has led to a concomitant increase in the prevalence of multiple myeloma (MM), a disease that usually affects the elderly population. Bone lesions are frequent in patients with this condition, demanding an early approach, from drug treatment, through radiotherapy to orthopedic surgery (prophylactic or therapeutic) with the objective of preventing or delaying the occurrence of fracture, or, when this event has already occurred, treat it through stabilization or replacement (lesions located in the appendicular skeleton) and/or promote stabilization and spinal cord decompression (lesions located in the axial skeleton), providing rapid pain relief, return to ambulation and resocialization, returning quality of life to patients. The aim of this review is to update the reader on the findings of pathophysiology, clinical, laboratory and imaging, differential diagnosis and therapeutic approach of multiple myeloma multiple myeloma bone disease (MMBD).

Keywords
- Diphosphonates
- Fractures Spontaneous
- Multiple myeloma
- Prophylactic Surgical procedures
- Orthopedic procedures
- Radiotherapy

Resumo

O aumento da expectativa de vida da população mundial levou a incremento concomitante na prevalência de mieloma múltiplo (MM), patologia que geralmente afeta a população idosa. Lesões ósseas são frequentes nos portadores desta condição, demandando abordagem precoce, desde o tratamento medicamentoso, passando pela radioterapia até a cirurgia ortopédica (profilática ou terapêutica) com os objetivos de prevenir ou retardar a ocorrência de fratura, ou, quando este evento já ocorreu, tratá-la mediante estabilização ou substituição (lesões situadas no esqueleto apendicular) e/ou promover estabilização e descompressão medular (lesões situadas no esqueleto axial), proporcionando rápido alívio da dor, retorno à deambulação e ressocialização, devolvendo a qualidade de vida aos pacientes. O objetivo desta revisão é atualizar o leitor sobre a fisiopatologia, a clínica, exames

Palavras-chave
- Difosfonatos
- Fraturas espontâneas
- Mieloma múltiplo
- Procedimentos cirúrgicos profiláticos
- Procedimentos ortopédicos
- Radioterapia

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laboratoriais e de imagem, diagnóstico diferencial e abordagem terapêutica da doença óssea no mieloma múltiplo (DOMM).

INTRODUCTION

The main clinical manifestations of multiple myeloma bone disease (MMBD) are related to bone destruction.[1,2] Despite progress in antitumor therapy and more aggressive treatments, the incidence of MMBD is still high. Complications such as diffuse osteopenia, osteolytic lesions, pathological fractures, hypercalcemia and bone pain occur in up to 80% of patients with multiple myeloma (MM) at diagnosis and in more than 90% during the course of the disease,[3] constituting the main causes of morbidity.[1,4,5]

The purpose of this article is to update the reader on the approach to MMBD, with regard to pathophysiology, clinical, laboratory and imaging evaluation, differential diagnosis and treatment.

PATHOPHYSIOLOGY

MMBD is characterized by increased resorption on bone formation[1,3,4,6–8] due to overexpression of the receptor activator of nuclear factor kappa B (RANK), its ligand (RANKL) and osteoprotegerin (OPG), resulting in increased osteoclastic activity,[3] that leads to development of lesions without evidence of typical replacement or repair[6–8] and osteoporosis, bone pain, pathologic fractures, hypercalcemia, and spinal cord compression.[3]

Increased Bone Resorption

In MM, bone destruction is mediated by osteoclasts and not by neoplastic cells. Osteoclasts accumulate on resorptive surfaces adjacent to neoplastic cells, and their number is not increased in areas not involved by the tumor. The increase in osteoclastic activity is mediated by the release of osteoclast activating factors produced by neoplastic cells or medullary stromal cells (BMSCs).[1]

Neoplastic cells adhere to BMSCs through a4b1 integrin, present on their surfaces, to vascular cell adhesion molecule-1, expressed in stromal cells.[9] Adhesion of MM cells to BMSCs and osteoblasts increases the production of RANKL, macrophage colony-stimulating factors, and other cytokines that activate osteoclasts, such as IL-6, IL-11, IL-1β, tumor necrosis factors, and factor of basic fibroblastic growth. At the same time, the production of OPG, which naturally occurs and antagonizes the effects of RANKL, preserving bone integrity, is suppressed[1,9] - there is a decrease in OPG production by stromal cells, induced by neoplastic cells, and OPG sequestration by neoplastic cells, which degrade it in their lysosomes; both mechanisms may contribute to the local and systemic reduction of OPG in patients with MM.[1] The RANKL/OPG ratio is determinant in the regulation of bone resorption. The interactive network of cytokines and hormones involved in bone resorption and anti-resorption converge in the RANKL/OPG system, which acts as a common end effector in the regulation of osteoclastic formation from its bone marrow precursors and subsequent activation.[1]

RANK and RANKL play an important role in the development of osteoclasts - RANK is expressed on the surface of these cells; RANKL is expressed on the surface of osteoblasts and stromal cells, and, by binding to its receptor (RANK), it drives differentiation and activation signals in osteoclastic precursors, promoting bone resorption.[1]

IL-1β is a potent stimulator of osteoclast formation, but its levels in patients with MM are very low. This suggests that IL-1β is probably not a major mediator in MMBD.[1,9]

IL-6 stimulates the development of osteoclasts. The use of anti-IL-6 allowed demonstrating the role of this cytokine in stimulating bone resorption in patients with MM.[1]

Other important factors are MIP-1α and MIP-1β chemokines. There is an overproduction of MIP-1α in the bone marrow and both chemokines are secreted by neoplastic cells, acting on the chemoattractiveness and activation of monocytes. Osteoclastic precursors and stromal cells express receptors for MIP-1α and MIP-1β. The chemokine MIP-1α as well as MIP-1β induce RANKL expression in stromal cells and, consequently, increase bone resorptive activity. In addition to their inductive osteoclastic capacity, these chemokines have relevant biological activities in determining other clinical characteristics present in MM patients, acting as potent modulators of hematopoiesis: MIP-1α inhibits early erythropoiesis and MIP-1β increases apoptosis in pre-B cells by suppressing erythropoiesis, B lymphopoiesis, and immunoglobulin production.[1]

Decreased Bone Formation

Histomorphometric studies and biochemical indicators demonstrate that, although the number and function of osteoclasts are increased in the MM, the determining condition for the presence or absence of lytic lesions is lower osteoblastic activity.[1]

In the early stages of MMBD, bone formation is increased, reflecting the coupling of resorption to formation. However, as the disease progresses, bone formation decreases, with rapid bone loss, suggesting that neoplastic cells initially stimulate osteoblastic function and then inhibit it, or there is cellular toxicity during tumor expansion.[1]

Even when MM is in remission, with no evidence of neoplastic cells in the marrow, bone lesions persist. Treatment with bisphosphonates inhibits resorption without inducing bone repair.

The clinical finding that patients with MM have decreased osteoblastic activity has been confirmed in several in vitro and in vivo studies.[9] However, few inhibitory interactions between osteoblasts and MM have been described. MM cells produce the protein dickkoppf 1 (DKK1), which inhibits

osteoblasts. Indeed, DKK1 overexpression in MM is associated with MMBD.[1] Possible candidates for osteoblast inhibitors in MM include DKK1 and other factors that block the Wnt signaling pathway, along with IL-3 and IL-7.[9]

CLINICAL EXAMINATION

MMBD is the leading cause of MM-related morbidity.[10] Patients often have diffuse bone pain, especially around the sternum and pelvis.

The osteopenic state culminates in pathological fractures[6]; $>50\%$ of patients with MM will have fractures during the course of the disease,[2] mainly in the vertebrae, costal arches, pelvis,[1,6,11] skull,[6] and proximal segments of the humerus and femur[1,12] - MM can be diagnosed in this scenario.[11] Fractures significantly compromise quality of life by association with chronic pain and functional disability.[1] Spinal cord compression occurs in up to 5% of patients, leading to pain, paresthesias and paresis in the lower limbs (LL).[11]

A quarter of MM patients have hypercalcemia, more common in the presence of a larger tumor volume, regardless of the protein status related to serum parathyroid hormone - the reasons for this are still unclear, but this fact may be related to the greater intensity of bone resorption produced by the neoplastic cells, as well as the condition of glomerular filtration. Diagnosis is based on ionic calcium concentration, as serum calcium may be low in concentration due to its binding to albumin. It is a serious and potentially fatal condition,[1] the clinical features of which often depend on calcium concentration: patients may be asymptomatic ($\leq$ 3 mmol/l); presenting symptoms such as xerostomia, anorexia and vomiting, polyuria, polydipsia, depression or confusion (3 to 4 mmol/l); or, have a "hypercalcemic crisis" associated with coma ($\geq$ 4 mmol/l).

LABORATORY EXAMINATIONS

It is important to measure ionic calcium and perform tests of renal function and protein electrophoresis.

A critical and sensitive, but nonspecific, laboratory finding is the red blood cells in *rouleaux*, observed in the peripheral slides of patients with MM.[6]

Markers of bone resorption (pyridinoline, deoxypyridinoline, and N-terminal collagen I telopeptide in urine) are increased, while markers of bone formation, such as osteocalcin and alkaline phosphatase, are decreased.[1]

Bone marrow aspiration or biopsy demonstrates the presence of atypical plasma cells.[5]

IMAGING EXAMS

As the main clinical manifestations of MM are related to MMBD, it is important to evaluate the skeleton using imaging tests,[1] making it possible to: detect lesions at risk of fracture; fractures that have already occurred or spinal cord compression; adjust the therapeutic planning; evaluate the evolution of the pathology; and parameterize the evaluation of the response to systemic treatment.[1,12]

Contrary to what is observed in bone metastases (BM) of carcinoma, bone lesions in MM do not usually show reactional new bone formation.[6,10] Approximately 1-2% of patients have extramedullary disease at diagnosis, and in 8% of cases it develops later in the disease course.[10]

MMBD imaging assessment includes whole body radiographs,[1,4–6] ow-dose whole-body computed tomography (CT),[12] magnetic resonance imaging (MRI),[1,4–6,12] whole-body magnetic resonance imaging (WBMRI)[13–16] and positron emission tomography-computed tomography (PET-CT)[6,12,16,17] (►**Figs. 1A-F**, **2E-F**).

Bone scintigraphy (BS) with 99mTc MDP, routinely requested in the investigation of patients with disseminated bone lesions, despite being highly sensitive in detecting BM of breast and prostate carcinoma, does not have the same sensitivity in MM, as lesions not involved by reactive bone usually do not capture[4,15,16]–BS has low sensitivity in detecting osteolytic lesions (37%-60%),[1,5] except in cases where there are associated fractures. The information provided by the BS is useful, however, in the diagnostic direction, suggesting to indicate more adequate imaging methodologies for the staging of this disease.

The advantages and disadvantages of the different imaging tests in the diagnosis of MMBD are summarized in ►**Table 1**.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes monoclonal gammopathy and associated clinical conditions (monoclonal gammopathy of undetermined significance, latent MM, plasmacytoma, Waldenström's macroglobulinemia), polyclonal gammopathy (collagen diseases, cirrhosis, viral exanthems), BM of carcinoma and cystic fibrous osteitis.[5]

INTERNATIONAL MYELOMA WORKING GROUP (IMWG) RECOMMENDATIONS FOR THE TREATMENT OF MMBD[8]

Treatment with Diphosphonates

Diphosphonates are pyrophosphate analogues that bind to exposed areas of hydroxyapatite crystals during the bone remodeling process. They are potent inhibitors of intracellular farnesyl pyrophosphate synthase, leading to osteoclast apoptosis and prevention of bone loss.

Indications

Diphosphonates (zoledronate or pamidronate) should be administered to all patients with active MM, regardless of the presence or absence (only for zoledronate) of identifiable MMBD in imaging studies.

Zoledronate (ZOL) is also indicated in the treatment of MM-related hypercalcemia and is superior to pamidronate (PAM) in this setting.

Choice of Diphosphonate, Route of Administration and Dosing Schedule

In patients with symptomatic MM, 4 mg intravenous (IV) ZOL given over 15 min every 3-4 weeks. 30 or 90 mg IV PAM given

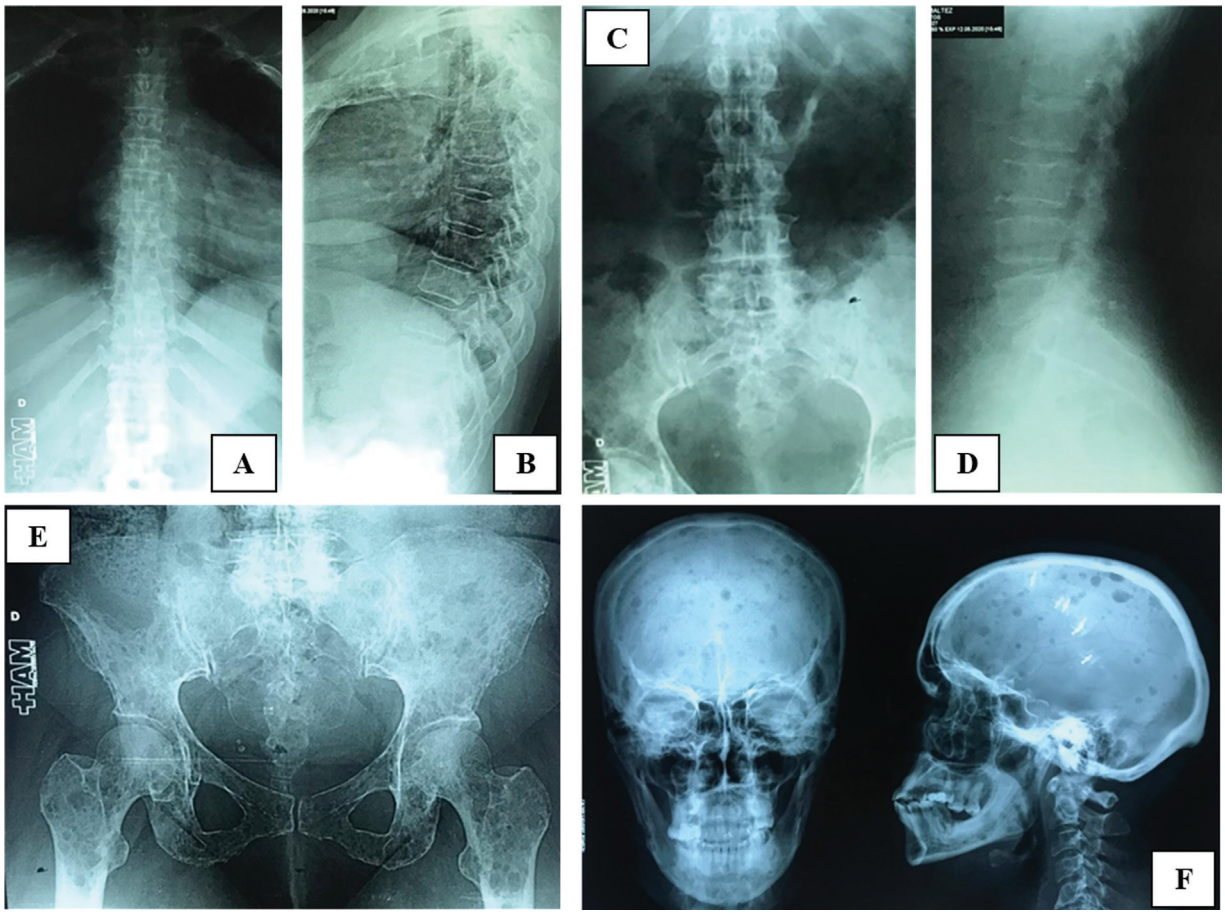


Fig. 1 (**A–F**) Female patient, 49 years old, black, with MM, with multiple bone lesions in the axial and appendicular skeleton.

every 3-4 weeks for 45 min (for 30 mg) or 2 h (for 90 mg) is recommended for prevention of skeletal related events (SRE). Dose adjustments are essential in case of renal impairment, both at diagnosis and during treatment.

In addition to more convenient administration, ZOL is preferred over PAM because of the significant reduction in the mortality rate. ZOL is also preferred over clodronate (CLO) due to its superiority in reducing SRE and improving survival, especially in newly diagnosed patients and patients with multiple MMBD at diagnosis. Compared with placebo or no treatment, only ZOL showed both progression-free survival and overall survival benefits. PAM 90 mg IV monthly is not superior to PAM 30 mg IV monthly for SRE prevention.

In outpatients, administration of IV ZOL is preferred over IV PAM or oral CLO. In patients unable to receive outpatient care, home infusion may be an alternative; in these cases, ZOL is preferable to PAM, due to the shorter infusion time.

Duration of Treatment

ZOL must be administered monthly for at least 12 months. If, after this period, a very good or better partial response is achieved, one may consider decreasing the frequency to every three months or, based on osteoporosis recommendations, every six months or annually, or even discontinuing it. The decision to discontinue ZOL should consider individualized assessment of fracture risk based on gender, age, ethnicity, body mass index, fracture history, smoking, alcohol consumption, bone mineral density, associated systemic disease (other than MM) to secondary osteoporosis, and daily and cumulative dose of glucocorticoid, frequent in continuous anti-myeloma regimens. If, after 12 months, a very good partial response has not been achieved, ZOL should be continued monthly until this occurs; hence, one can decrease the frequency or stop the treatment.

PAM should be administered to patients with MM who have active disease and can be continued at clinical discretion, taking into account patient and disease-related factors.

If discontinued, ZOL or PAM should be restarted on relapse to reduce the risk of new SREs.

Adverse events

Calcium and vitamin D supplementation should be performed in all patients receiving diphosphonates, but only after normalization of calcium concentration, in the case of hypercalcemia. Creatinine *clearance*, serum electrolytes, and urinary albumin (in patients receiving PAM only) should be monitored monthly, with dose adjustments accordingly.

A comprehensive dental examination and any necessary invasive treatment should be performed prior to initiation of therapy. Diphosphonates should be discontinued when osteonecrosis of the jaw is present, unless ongoing treatment is required (MMBD progression or recurrent hypercalcemia).

Table 1 Advantages and disadvantages of different imaging modalities in the diagnosis of MMBD

Imaging Examination	Advantages	Disadvantages
Whole-body radiographs	Cost; readily available; detects skull and limb injuries - findings consist of punch injuries, osteoporosis, or fractures in 75% of patients.	Low sensitivity and positivity; detects lesions only after apparent bone destruction (30 to 50% bone loss); discomfort due to positioning and repetitive exams; the image collection process is slow.
Whole-body low-dose CT	High sensitivity and positivity; allows aspiration biopsy and surgery guided by 3D images; defines radiotherapy planning; demonstrates the measurement of extramedullary lesions, detects bone marrow invasion and osteolysis; allows to evaluate the tumor load; data collection is fast; lower cost than MRI or PET-CT; little discomfort for the patient.	Cost; may miss skull and costal arch injuries; difficult determination of the number of injuries; when lytic bone lesions are not identified, the negative predictive value is low (59%), not excluding the diagnosis, requiring follow-up and complementation with MRI, WBMRI and/or PET-CT.
MRI	There is no exposure to radiation; allows locating and measuring infiltrative lesions in the bone marrow and focal lesions; it allows accurately diagnosing eventual spinal cord compression; the number of lesions may indicate prognosis; displays extramedullary lesions; 3D reconstruction imaging can help with biopsy and planning surgery and radiotherapy.	Cost; lengthy process for data collection; unsuitable for patients with claustrophobia or metal implant wearers; the drug used as a contrast agent is contraindicated in patients with severe renal impairment; bone marrow infiltration may be misdiagnosed as an osteolytic lesion; presence of electric field limitations and motion artifacts.
WBMRI	No ionizing radiation or need for contrast; faster image acquisition than PET/CT; well tolerated; superior spatial resolution; High accuracy in the study of bone marrow, especially when there is no detectable bone destruction on radiographs or CT; more sensitive than PET-CT in detecting bone involvement; better differentiation between therapeutic response and disease progression; provides information with prognostic value (number and extent of lesions, prediction of fracture risk).	Cost; accessibility and availability; time for image acquisition may require sedation; as it is a very sensitive methodology, it may lead to unnecessary tests and biopsies; same contraindications as MRI.
PET-CT	Reflects the activity of the lesions; it allows evaluating the activity of the lesions in the pre and postoperative period; extramedullary lesions can be imaged; it facilitates the evaluation of the prognosis in the pre and postoperative period; the use of new radionuclides makes it possible to identify different diseases.	Cost; accessibility and availability; low resolution in lesions smaller than 0.5 mm; MM insensitive with low fluorodexyglucose activity; limited diagnostic value (false-positive results due to inflammation, infection, fractures, bone remodeling, post-surgical or post-biopsy changes, recent chemotherapy and radiotherapy).

Abbreviations: 3D, three-dimensional; MM, multiple myeloma; PET-CT, positron emission tomography-computed tomography; MRI, magnetic resonance; WBMRI, whole body MRI; CT, computed tomography.
Source: Translated and modified from Committee of Surgeons of the Chinese Myeloma Working Group of the International Myeloma Foundation. Consensus on surgical management of myeloma bone disease. Orthop Surg. 2016;8(3):263-269.

If possible, diphosphonates should be temporarily withheld before and after any tooth extraction or invasive oral procedures, and periprocedural antibiotic prophylaxis should be considered; after that, the treatment can be restarted considering risk-benefit. Patient education is essential in adhering to oral hygiene and supplement consumption, as well as in recognizing and reporting adverse events early.

Treatment with Denosumab

Denosumab is a human monoclonal IgG2 antibody, highly specific against RANKL. This drug mimics the physiological effect of OPG, inhibiting the interaction between RANKL and RANK, decreasing bone resorption.

Indications

Denosumab is recommended in the treatment of newly diagnosed MM and in relapsed or refractory cases with evidence of multiple MMBD. It has an effect equivalent to ZOL in delaying the first SRE after the diagnosis of MM. Denosumab may prolong progression-free survival in patients with newly diagnosed MM who are eligible for autologous stem cell transplantation. Denosumab may be preferable to ZOL in the treatment of patients with MM who have renal dysfunction, and may be considered in the treatment of patients who have a creatinine clearance of less than 30 ml/min under close monitoring. Denosumab can also be given to patients with MM-related hypercalcemia, especially those refractory to ZOL.

Route of Administration, Dosage Schedule and Duration of Treatment

120 mg of denosumab should be administered subcutaneously (SC) at monthly intervals. Home SC injection makes administration of denosumab more convenient than IV administration of diphosphonates. Denosumab should be administered continuously until unacceptable toxicity occurs. De-escalation, pause or discontinuation of the drug can only be considered after 24 months if the patient

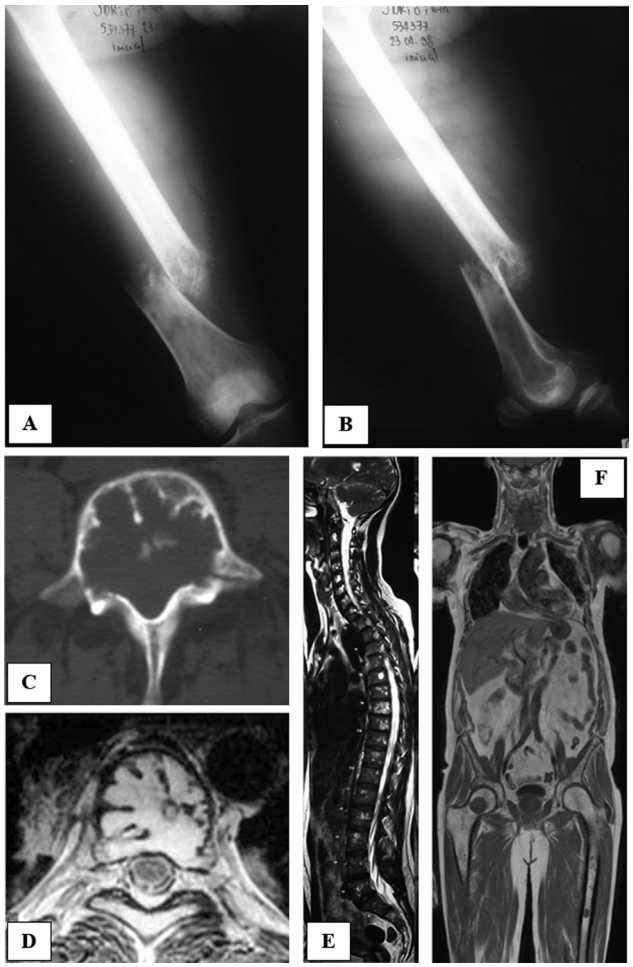


Fig. 2 (**A–F**) (**A, B**) Radiographs in anteroposterior and lateral views of the right femur of a male patient, 67 years old, black, with MM. A pathological fracture of the distal diaphyseal segment of the femur is observed; (**C, D**) CT and MRI of the thoracic spine (axial section) demonstrating osteolysis of the vertebral body (mini brain); (**E,F**) WBMRI demonstrating multiple lesions in vertebral bodies (sagittal section), pelvis, and femur (coronal section).

achieves a very good or better partial response with anti-myeloma treatment. A personalized assessment based on patient characteristics, comorbidities and glucocorticoid use should also guide therapeutic decisions. Until more data is available, a single dose of IV diphosphonate is recommended, at least six months after the last dose of denosumab, to avoid a rebound effect; similarly, the administration of denosumab every six months can be considered.

Adverse Events

Calcium and vitamin D supplementation is recommended for all patients, especially those with renal impairment after normalization of serum calcium concentration, in case of hypercalcemia. Calcium, vitamin D, phosphate and magnesium should be measured regularly to assess the need for supplementation. Oral health should be assessed at baseline and during treatment. Denosumab should be discontinued 30 days prior to invasive dental or oral procedures until healing occurs, at which time it can be restarted.

Radiotherapy

MM cells are radiosensitive and many people with this disease will need radiotherapy at some point, particularly in the treatment of symptomatic bone lesions[1] - radiotherapy is highly effective in relieving pain; up to 90% of patients achieve pain control with this therapeutic approach.[17]

Spinal cord compression occurs in 10% to 20% of patients with MM. In cases where there is no vertebral instability, the use of corticosteroids associated with radiotherapy may prevent permanent neurological deficit.[1]

Radiation therapy may be followed by vertebroplasty/kyphoplasty to ensure vertebral stabilization,[18,19] however, the treatment sequence does not seem to affect the improvement of pain.[19]

The IMWG recommends that radiotherapy should be considered when there is persistent uncontrolled pain, associated with impending or ongoing spinal cord compression, or pathological fractures; in these scenarios, low-dose radiotherapy (above 30 Gy) can be used as a palliative treatment.[8]

Orthopedic Treatment

In general, the orthopedic approach to MMBD is surgical, reserving non-surgical treatment (plastered immobilizations, braces, vests together with drug treatment and/or radiotherapy) for minor injuries that affect the upper limbs (►**Fig. 3A**) and the axial skeleton, accompanied or not by conservatively treatable bone pain not associated with neurological deficits.

More than 90% of patients with MM develop lytic bone lesions that can be surgically treated.[3] The objectives of surgical treatment are: to relieve pain[3,7,8]; maintain function[3,7,8]; improve quality of life[3,7,8] by addressing impending or existing pathological fractures, focal bone lesions associated with refractory pain, medullary and radicular compression, and vertebral instability[3,7,8]; and, (4) need for percutaneous or open biopsy (in 6% of cases, the myelogram is insufficient to establish the diagnosis).[12]

Extensive bone destruction is a surrogate marker of advanced disease and, in general, surgical interventions in these patients may result in a greater number of perioperative complications.[3] Most newly diagnosed patients demand immediate initiation of systemic treatment, impairing immune function. They are usually elderly, many of whom have diabetes and hypertension, in addition to presenting hypercalcemia, anemia, coagulopathies and hypoproteinemia. In particular, care must be taken when correcting anemia; procedures should not be performed until a hemoglobin concentration and platelet count of 10 g/l and 80×10^9/l respectively have been achieved.[13] In this context, multidisciplinary management is considered essential.

Postoperative radiotherapy should be considered,[2,8] especially in long bone fractures, to obtain local control of the disease and prevent failures in procedures involving implants. It is particularly important in those patients who have minimal or no response to systemic treatment.[8]

Staging and prognostic estimation methods that allow categorically defining which patients are eligible for surgical

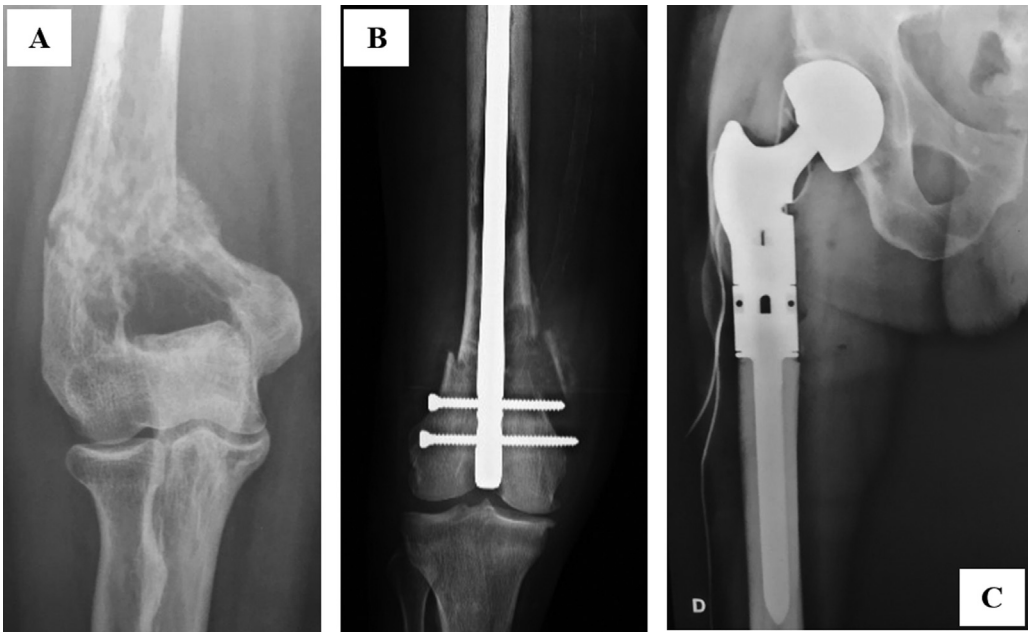


Fig. 3 Orthopedic approach in the treatment of bone lesions associated with MM with imminent or ongoing fracture. (**A**) Nonsurgical treatment of fracture of the distal segment of the right humerus; (**B**) IMN in the treatment of metaphyseal fracture and distal diaphyseal bone lesion in the right femur; (**C**) Modular megaprosthesis in the treatment of an extensive lesion affecting the proximal segment of the right femur.

treatment have not yet been established.[6,12] MM should be staged pre- and postoperatively according to the Revised International Staging System (R-ISS).[6,10,20] Neurological function should be graded using Frankel[12] or American Spinal Injury Association (ASIA) scores, along with assessment of bladder, bowel, and sexual function. Pain should be assessed using the visual analogue scoring system and function using the Karnofsky functional scale[12] or the Eastern Cooperative Oncology Group (ECOG) score.[4] All of these assessment systems are useful for estimating pre- and postoperative therapeutic benefits.[9]

The Committee of Surgeons of the Chinese Myeloma Working Group (CMWG) contraindicates surgical treatment when there is poor clinical condition, intractable cardiac, pulmonary and renal dysfunctions, severe coagulation disorders - which are difficult to control, and severe and uncontrollable infection.[12]

General anesthesia is often the approach of choice because intraspinal blocks and other methods of anesthetic induction are invasive and can lead to bleeding[3,12] and infection.[12] Patients with MMBD are generally in poor physical condition - general anesthesia allows better control of blood pressure, oxygen saturation and respiratory rate.[3,12]

The implants used should preferably be made of titanium alloys or be carbon fiber reinforced as they generate significantly less artifacts than those made of stainless steel. Although titanium alloy implants generate fewer artifacts, the difficulty in properly planning radiotherapy remains, especially in identifying the target and evaluating the amount of dose actually administered to the tissues. Carbon fiber reinforced implants are chemically and biologically stable and allow for even better CT and MRI imaging – these features facilitate monitoring of pathologic fracture healing, local recurrence, progression, and response to treatment,[21] in addition to making it possible to outline an ideal radiotherapy strategy, as the image quality provided during planning reduces discrepancies between late/delivered and measured doses, generating more homogeneous dose distribution[22]; due to their low atomic number and similar radioactive properties to surrounding tissues, they are inert to ionic irradiation and provide minimal disruption to their distribution during radiotherapy.[21]

Pelvic and Periacetabular Injuries

Pelvic and periacetabular involvement in MM has unique characteristics in terms of biomechanics, morbidity, overall survival and prognosis, reflecting on the quality of life of affected individuals.[23] Periacetabular injuries are particularly challenging and are often associated with severe pain, functional disability and pathological fractures; due to load transmission, lesions that show progressive growth can compromise the stability of the pelvic ring.[24]

In MM, pelvic and periacetabular bone involvement occurs in about 6% of cases. The Harrington classification (1981) is widely used in defining the treatment of BM of carcinoma or MM that affect the acetabulum.[25] Group I comprises lesions that present intact subchondral bone; in group II, there is destruction of the medial wall, but demonstrate an intact acetabular roof and lateral wall; in group III, there is destruction of the medial wall, roof and lateral edge of the acetabulum; group IV is defined by the presence of solitary lesions that can be resected en bloc, with anticipation of healing.[24]

Operative treatment is indicated for patients with MM who have periacetabular bone lesions whose non-operative treatment has failed, in pathological/imminent fractures,[24,26] in pelvic collapse, or when the symptoms are intolerable.[24] Expected survival should exceed surgical

recovery time, allowing for a real improvement in quality of life.[24] The surgical approach to these lesions has historically consisted of cementoplasty for contained lesions and Harrington reconstructions for larger and more destructive lesions.[24] In 1981, Harrington described a technique involving the use of threaded Steinmann pins and polymethylmethacrylate for the reconstruction of acetabular defects, associated with cemented total hip arthroplasty, allowing the transmission of load-bearing forces to the intact segment of the pelvis.[24] Due to the limitations of these techniques, new surgical approaches, dictated by the size and location of these lesions, have been created to manage this challenging condition.[26] The use of adjuncts to the Harrington procedure, such as restricted overlays and dual mobility bearings, has reduced historically high rates of prosthetic dislocation.[26] Despite functional improvements and pain control, these procedures are associated with extensive surgical wounds and massive blood loss, leading to the development of percutaneous approaches (including acetabular screw fixation and screw-associated cementoplasty) to minimize surgical morbidity.[24] Antiprotrusion ring with medial wall cementation and acetabular impaction bone graft combined with cementless acetabular components are other well-established methods indicated for contained defects or when acetabular fixation is feasible.[25] Cages and porous tantalum implants are becoming increasingly common in the management of large bone defects and destructive periacetabular injuries.[24] More recently, customized prostheses, developed from the analysis of three-dimensional reconstruction imaging studies, have been used to replace pelvic segments in selected cases.[24]

Spinal injuries

MM is the most common malignancy of the spine,[27] accounting for approximately 15% of all cases.[2] About 70% of patients with MM have spinal injuries,[18] which is the most frequent site for fractures[1] ($>$ 50%)[27]–8 to 10% of patients develop neurological deficits.[2,12,27]

The surgical indication is based on the neurological, oncological, mechanical and systemic (NOMS) decision-making framework, which includes the neurological status (myelopathy, degree of epidural spinal cord compression), radio/chemosensitivity of the tumor, mechanical instability, extension of the systemic disease and comorbidities.[28]

Vertebroplasty and kyphoplasty are indicated for patients with lytic lesions[3] and/or symptomatic compressive vertebral fractures[8] not associated with spinal cord compression.[1,11,12] These procedures provide immediate pain relief and stabilization of the vertebral bodies.[1,12] It is essential to obtain tissue samples during the approach, seeking greater definition or correction in the diagnosis.[12]

Vertebroplasty consists of the percutaneous injection of polymethylmethacrylate (PMMA) into the affected vertebra, under radioscopic control. This procedure allows a significant decrease in pain (up to 97%) but presents a (low) risk of cement leakage and pulmonary embolism.[1]

Kyphoplasty provides vertebral stabilization, pain relief and restoration of vertebral body height. This is possible by inserting a balloon into the affected vertebra which, when inflated, creates a cavity in the vertebral body where PMMA is injected. The frequency of cement leakage is lower with this procedure.[1]

The open approach to the spine is indicated when there is spinal instability, associated or not with spinal cord compression.[3] The procedures are defined according to the number, location and size of the lesions. Approaches include direct anterior, posterior, or combined approaches. The goals of treatment are: removal of as much tumor as possible, decompression, reconstruction and stabilization.[15,16] The implants (titanium alloy or carbon fiber reinforced) are chosen to meet the specific requirements of each procedure, including plates, pedicle screw systems, lateral mass screw fixation systems, artificial vertebral bodies and cages, as well as filling material, such as PMMA and allograft. In addition to facilitating modeling, PMMA has a local adjuvant function, due to the exothermic reaction, which destroys tumor cells - it is therefore the first choice for filling bone defects after tumor removal - autologous bone grafts are not recommended, because they are more prone to resorption.[12]

Combinations of open and minimally invasive surgery are used in the treatment of patients with multiple vertebral injuries, allowing to add advantages presented by both, reducing the need for volume replacement and preventing other complications. Wide or radical resection is unnecessary in the treatment of MM that affects the spine.[12]

Long Bone Injuries

In MM, long bone fractures are relatively less frequent than vertebral fractures, but they usually require hospitalization for early intervention,[6] through fixation or replacement of the affected segment.[1]

Prophylactic surgery has become a reality with the increasingly early diagnosis of MMBD. This approach provides early stability, providing less time for recovery of function when compared to non-surgical treatment.[5] Mirels (1989)[29] developed a risk prediction score for pathological fractures in injuries located in the appendicular skeleton.[6,29–31] This score is based on four characteristics, which are assigned progressive scores from 1 to 3, added at the end: (1) lesion site; (2) nature of the injury; (3) lesion size; and (4) pain (►**Table 2**).[30,31] Based on this score, a recommendation for or against prophylactic surgery is given. Lesions with a score

Table 2 Mirels scoring system

		Score	
Component	*1*	*2*	*3*
Site	Upper limb	Lower limb	Pertrochanteric
Pain	Mild	Moderate	Severe
Lesion	Blastic	Mixed	Lytic
Size	$<$ 1/3 of cortex	1/3–2/3 of cortex	$>$ 2/3 of cortex

Source: Mirels H. Metastatic disease in long bones: a proposed scoring system for diagnosing impending pathologic fractures. Clin Orthop Relat Res. 1989;249:256–264.

equal to or greater than 9 constitute an indication for a surgical approach.[29–31] Lesions with a score of 7 or less can be managed conservatively (observation, radiotherapy and/or pharmacological treatment).[29–31] A score of 8 represents a dilemma - the probability of fracture is only 15%, it is recommended to use clinical judgment for each situation, considering the benefits of prophylactic surgery versus the probability of fracture - more detailed imaging exams allow more accurate access to the dimension of the defect generated by the lesion.[6,29–31]

Pathological fractures of the long bones must be operated on as soon as possible, particularly those in the lower limbs, due to load bearing.[6] Procedures include resection of the affected segment ("expendable" bones), filling with PMMA, internal fixation (screws, plates or intramedullary rods in carbon fiber reinforced or titanium implants)[6,7,11,12,24] or replacement with conventional prostheses[16] or megaprostheses.[1,7,11,15,16]

The choice of surgical procedure depends on the general condition and life expectancy of the patient, previous response to chemotherapy, affected site, number, size and location of lesions and extent of bone invasion.

If there are concomitant lesions in the distal and proximal segments of the same bone, choose long plates or intramedullary nails (IMN). IMN (►**Fig. 3B**) reinforce the affected bone with a definitive, durable and mechanically stable implant, allowing for reduced pain and early discharge.[24,32] Reaming should only be performed when there is good bone quality. The rate of reoperation due to infection, pseudarthrosis or loosening is substantially lower when using IMN, compared to other methods, as it provides greater stability and vascular preservation in bones affected by primary osteoporosis, or secondary to MMBD.[6] Diaphyseal and metaphyseal fractures of the femur and humerus usually require fixation with IMN followed by radiotherapy.

In cases where there is more extensive bone destruction affecting the joint and/or metaphyseal segment of the affected bone,[3] resection with replacement by megaprostheses may be considered (►**Fig. 3C**).[1] Megaprostheses of the proximal segment of the femur provide good functional outcomes, low incidence of complications and better quality of life in the medium term - patients with pathological fracture of the proximal segment of the femur due to MM, confirmed or imminent, treated by resection with replacement, have significantly longer survival.

Although different types of surgeries can provide pain relief and functional improvement in different anatomical locations, the best results, with lower complication rates, are observed in lesions located in the upper extremities[3,12] or diaphyseal segments of long bones.[12]

FINAL CONSIDERATIONS

A proper approach to MMBD is essential for pain control and functional restoration, providing an improvement in quality of life. Therefore, it is necessary to understand the pathophysiology, clinic, laboratory and imaging evaluation, differential diagnosis and treatment associated with this condition.

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Conflict of interests
The authors declare that there are no conflicts of interest.

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Efficacy of Ibuprofen after Total Hip Arthroplasty to Prevent Heterotopic Ossification: Systematic Review and Meta-Analysis*

Eficácia do ibuprofeno após artroplastia total de quadril para prevenção de ossificação heterotópica: Revisão sistemática e metanálise

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Abstract

The objective of this study was to conduct a systematic review and meta-analysis of relevant randomized control trials (RCTs) to determine the role of ibuprofen, as well as the optimum dose and duration of therapy, in preventing the incidence of heterotopic ossification (HO) after primary total hip arthroplasty (THA). A literature search was performed using the PubMed/MEDLINE and Cochrane Library databases for RCTs that compared the use of ibuprofen versus placebo as prophylaxis for HO in patients after THA. The main outcomes for this study were overall occurrence of HO, occurrence according to the Brooker classification, and gastrointestinal complications. A total of 27 potential articles were identified from the database. Eventually, four trials with 1,153 patients were included in the final analysis. When compared with placebo, the use of ibuprofen is associated with a reduction in the incidence of HO at the 3- and 12-month follow-up appointments, as well as the incidence of Brooker II and III HO ($p < 0.05$). However, there was no significant difference between the ibuprofen and placebo groups in terms of treatment discontinuation due to gastrointestinal complications or the incidence of Brooker I and IV HO ($p > 0.05$). The existing data indicates that ibuprofen is safe and efficacious in reducing the total incidence of HO along with Brooker II and III HO at follow-up. However, due to the small number of studies, the conclusions are limited; therefore, more high-quality clinical trials are required to develop guidelines for optimal dose and duration of therapy.

Keywords

- arthroplasty, replacement, hip
- ossification heterotopic
- ibuprofen
- meta-analysis

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Resumo

O objetivo deste estudo foi realizar uma revisão sistemática e metanálise de estudos clínicos randomizados (ECRs) relevantes para determinar o papel do ibuprofeno, sua dose ideal, e a duração do tratamento na prevenção de ossificação heterotópica (OH) após a artroplastia total primária do quadril (ATQ). Uma pesquisa bibliográfica foi feita nos bancos de dados PubMed/MEDLINE e Cochrane Library para a obtenção de ECRs que comparassem o uso de ibuprofeno e de placebo como profilaxia para OH em pacientes submetidos à ATQ. Os principais desfechos deste estudo foram ocorrência geral de OH, classificação de Brooker da OH, e complicações gastrintestinais. No total, 27 artigos foram identificados nos bancos de dados e 4 estudos, com 1.153 pacientes, foram incluídos na análise final. Em comparação ao placebo, o uso de ibuprofeno reduziu a incidência de OH aos 3 e 12 meses de acompanhamento e a incidência de OH Brooker II e III ($p < 0,05$). No entanto, não houve diferença significativa entre os grupos que receberam ibuprofeno e placebo em termos de interrupção do tratamento devido a complicações gastrintestinais ou da incidência de OH Brooker I e IV ($p > 0,05$). Os dados existentes indicam que o ibuprofeno é seguro e eficaz na redução da incidência total de OH e de OH Brooker II e III durante o acompanhamento. No entanto, as conclusões são limitadas devido ao pequeno número de estudos; logo, mais estudos clínicos de alta qualidade são necessários para o desenvolvimento de diretrizes em relação à dose e duração ideal da terapia.

Palavras-chave

- artroplastia de quadril
- ossificação heterotópica
- ibuprofeno
- metanálise

Introduction

Total hip arthroplasty (THA) is widely regarded as one of the most effective and successful procedures in the field of orthopedics.[1] It is a commonly performed surgery for the treatment of osteoarthritis, rheumatoid arthritis, avascular necrosis, developmental dysplasia, and a variety of other hip pathologies. Dislocation of the implant, wounds, or joint infections of the hip, intraoperative and periprosthetic fracture are all common complications after THA.[2,3] Another possible well-recognized complication after THA is heterotopic ossification (HO), which is defined as ectopic bone development in a soft-tissue structure. heterotopic ossification typically presents without clinical manifestations; however, symptomatic cases are clinically characterized by limitations in mobility due to shortened range of motion, severe pain, leg swelling, stiffness, and, in severe but rare cases, complete ankylosis, postoperatively.[4] The Brooker classification system (grades I–IV) is often utilized to evaluate and stratify the severity of HO in patients following THA.[5]

The average incidence of HO occurrence is reported to be at 30%, according to the results of a meta-analysis.[6] In addition to well known risk factors, such as male gender, history of hip surgery, and HO development, the risk of HO incidence is further increased when associated with certain systemic illnesses, such as diffuse idiopathic skeletal hyperostosis, Paget disease, ankylosing spondylitis, and hypertrophic osteoarthropathy.[3,7,8] Along with these factors, the incidence of HO is also dependent on the surgical approach used for THA, with direct lateral and direct anterior approach having a greater risk when compared with the posterior approach.[9,10] Currently, radiation therapy and nonsteroidal antiinflammatory drugs (NSAIDs) are the two accepted methods to prevent the incidence of HO postoperatively.[11] Radiation therapy inhibits HO formation by slowing down the rapidly dividing osteoprogenitor cells and inhibiting the differentiation of mesenchymal cells into mature osteoblasts. However, its use is restricted because it increases the cost of treatment and carries a greater risk of developing soft-tissue neoplasm.[12,13] Meanwhile, NSAIDs work by inhibiting the cyclooxygenase enzyme (COX), which limits the formation of prostaglandins particularly prostaglandin-E_2. Nonsteroidal antiinflammatory drugs have proved to be beneficial in the prevention of HO after THA, and a variety of NSAID drugs are commonly used for HO prophylaxis.[14]

Although ibuprofen, a non-selective NSAID, has been a widely used drug in the prevention of HO, there are no relevant meta-analyses on the use of ibuprofen as a prophylactic agent to prevent HO after THA. The focus of this systematic review and meta-analysis of RCTs is to evaluate the efficacy and safety of ibuprofen for the prophylaxis of HO after hip surgery, specifically primary THA.

Methods

Literature Search

Electronic databases, including the PubMed/MEDLINE and Cochrane Library databases, were searched up to April 26th, 2021, with no restriction on the language of the publications. We formulated a search strategy by combining keywords and MeSH terms using the Boolean AND/OR operator. A detailed PubMed/MEDLINE search strategy is given in (►**Table 1**). Since this article is a meta-analysis of published studies, no ethics committee or institutional review board approval was required for the research. Moreover, the reference lists of the included studies and previously published articles were searched for more relevant studies that met the eligibility

criteria. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed for this systematic review and meta-analysis.[15]

Eligibility Criteria

The eligibility criteria were determined in accordance with the Population, Intervention, Comparator, Outcomes and Study Design (PICOS) principle. 1) Population: patients undergoing primary hip arthroplasty, 2) Intervention: postoperative administration of ibuprofen (any dose and duration of therapy), 3) Comparators: placebo, 4) Outcome: incidence of HO in radiological follow-up, 5) Study Design: RCT. On the contrary, studies were excluded if they were: (1) Studies with incomplete data to perform the analysis, (2) Non-randomized control trials, comparative study, quasi-randomized trials, editorial articles, letter to editor, cohort studies, review article, meta-analyses, expert opinion, conference papers, or books (3) Animals, cadaveric, and in vitro studies (4) Duplicates or overlapping publications by same author or institution.

Data collection and Outcome Measures

Two authors were involved in the following data extraction from each of the included studies: first author's name, year of publication, country of origin of the study, patient demographics, treatment regime for each group, total sample size of the study, and radiological follow-ups. Disagreements were resolved by discussion. The outcomes of this meta-analysis are as follows: overall incidence of HO during follow-up, HO incidence according to the Brooker classification, and treatment discontinuation due to gastrointestinal complications.

Methodological Quality Assessment

Two authors examined the quality of the eligible studies, and, in case of any discrepancies, a third author was referred to. The methodological quality of the studies that met the inclusion criteria was evaluated according to Cochrane Collaboration's tool for assessing risk of bias using the Review Manager, version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014).[16] For the present analysis, each study was evaluated for: allocation, randomization, blinding of participant, blinding of personnel, blinding of assessor, selective reporting, incomplete data, and unknown source of bias.

Statistical analysis

The meta-analysis was conducted using the R version 4.0.3 through RStudio Desktop version 1.4 software (R Foundation for Statistical Computing, Boston, MA, USA). The data was pooled using the DerSimonian-Laird random effects model, risk ratios (RRs) with 95% confidence intervals (CIs) were calculated.[17] Statistical heterogeneity was tested using the chi-squared (x^2) test and I^2 statistic. When $I^2 > 75\%$, it indicated high level of heterogeneity, $I^2 > 50\%$ indicated moderate level of heterogeneity, $I^2 < 50\%$ indicated low level of heterogeneity.[18] Funnel plot was used to detect the existing publication bias. Statistical significance was considered when the p-value < 0.05.

Results

Search Results and Study Characteristics

A summary of the study selection process is presented in (►**Fig. 1**). We identified a total of 27 studies from the initial search of the databases. Following the removal of duplicate studies, an initial screening of articles was conducted based on title and abstract. Eleven articles with full text were selected to be evaluated using the inclusion criteria. Finally, four RCTs were included in the meta-analysis.[19–22]

Study Characteristics

The 4 trials published between 1985 and 2006, represent a total of 1,153 patients with sample sizes ranging from 50 to 902. Three studies were conducted in Sweden, while one was conducted in Australia and New Zealand. The age of

Table 1 Search strategy for PubMed

Search#	Query
#1	heterotopic ossification [MeSH Terms]
#2	heterotopic ossification* [TIAB] OR heterotopic ossify* [TIAB] OR periarticular ossification* [TIAB] OR periarticular ossify* [TIAB] OR ectopic ossification* [TIAB] OR ectopic ossify* [TIAB] OR pathological ossification* [TIAB] OR pathological ossify* [TIAB]
#3	Arthroplasty [MeSH Terms] OR hip arthroplasty [MeSH Terms] hip prosthesis [MeSH Terms] OR hip replacement [MeSH Terms]
#4	hip arthroplasty [TIAB] OR hip replacement*[TIAB] OR hip prosthesis [TIAB] OR hip prosthetic* [TIAB]
#5	Ibuprofen [MeSH Terms]
#6	Ibuprofen [TIAB] OR Advil [ALL] OR Ibutab [ALL] OR Motrin [ALL] OR Brufen [ALL] OR Motrin [ALL]
#7	#1 OR #2
#8	#3 OR #4
#9	#5 OR #6
#10	#7 AND #8 AND #9

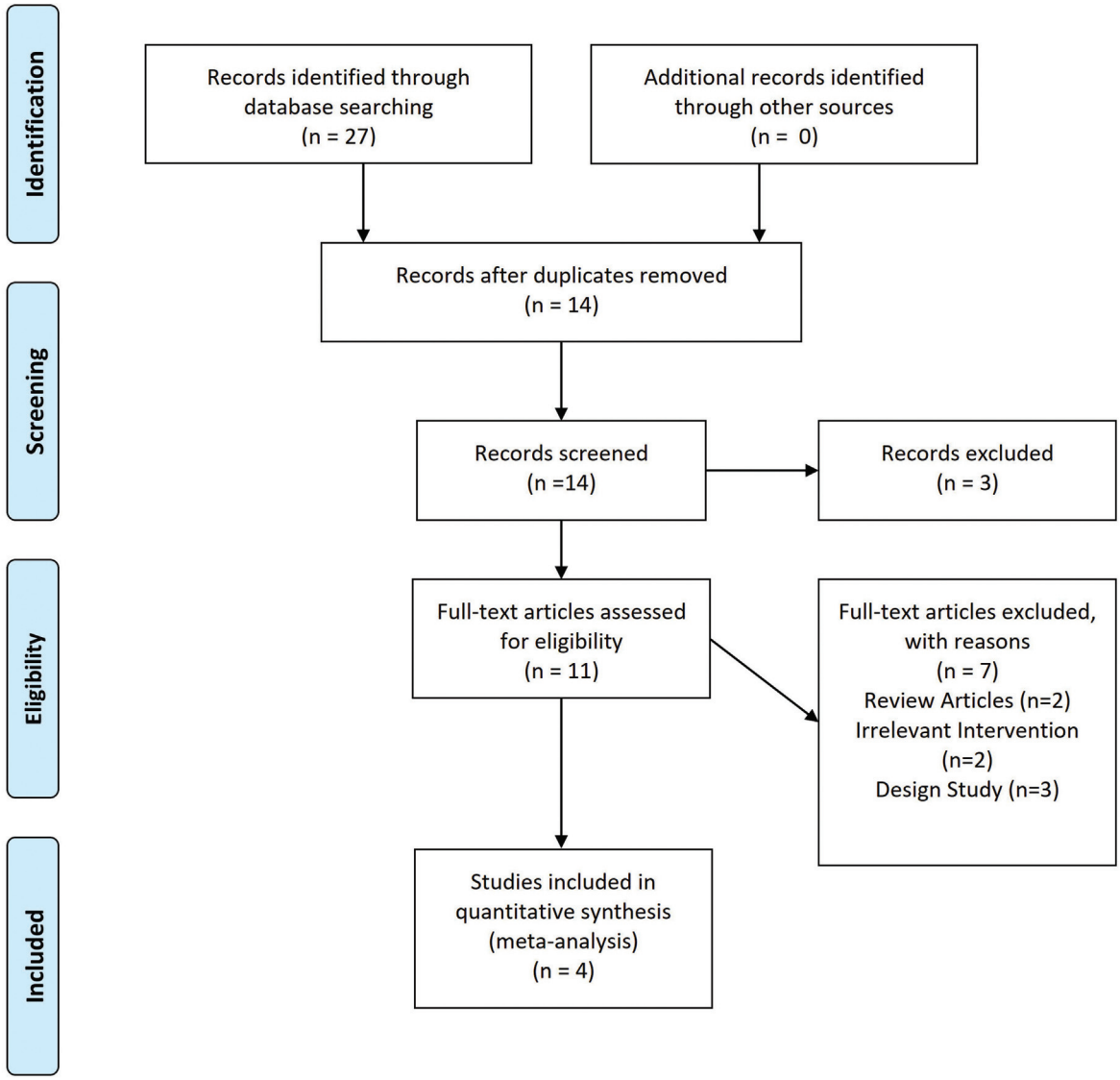


Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews) flow diagram summarizing of the process of selecting relevant clinical studies.

participants of these trials ranged from 66 to 70 years. The daily dose of ibuprofen administered in these trials varied from 1,200 mg to 1,500 mg for a postoperative period of 7 to 92 days. The general characteristics of the included studies are presented in (►**Table 2**).

Results of Meta-Analysis

The Incidence of HO at 3 Months Follow-up

Two studies with 194 participants reported data on the incidence of HO at 3 months follow-up.[20,22]

The reported rate of incidence of HO at 3 months was 13.67% in the ibuprofen group and 43.10% in the control group. The pooled results indicate that the use of ibuprofen was associated with significant reduction in occurrence of HO 3 months after surgery. (RR = 0.33 [95% CI, 0.20–0.54]; $p < 0.01$; $I^2 = 0.0\%$) (►**Fig. 2A**).

The Incidence of HO at 12 Months Follow-up

All studies with 1,153 patients reported data on the incidence of HO at 12 months follow-up.[19–22]

The reported rate of incidence of HO at 12 months was 27.89% in ibuprofen group and 45.85% in control group. There was moderate heterogeneity observed between the included studies ($I^2 = 66\%$). Therefore, a subgroup analysis was performed with respect to daily dose of Ibuprofen administered. According to the results, daily administration of 1,200 mg/day of ibuprofen significantly reduced occurrence of HO at 12 months post-operatively. (RR = 0.53 [95% CI, 0.39–0.74]; $p < 0.01$) (►**Fig. 2B**).

Treatment Discontinuation Due to Gastrointestinal Complications

All four studies with 1,153 patients reported data on treatment discontinuation due to GI complications.[19–22] The

Table 2 The general characteristic of the included studies

Author	Year	Country	Treatment			Duration (days)	Radiological follow-up (months)	Patients			
			Study design	Intervention daily dose (mg)	Control			Male (%)	Mean age (years)	Sample	Dropouts
Elmstedt	1985	Sweden	RCT	Ibuprofen 1,200	Placebo	92	1.4, 3, 6, 12	53	70/70	50	7
Ahrengat	1994	Sweden	RCT	Ibuprofen 1,500	Placebo	10	2, 12	47	70/70	57	10
Persson	1998	Sweden	RCT	Ibuprofen 1,200	Placebo	21[(A)], 7[(B)]	3, 12	N/S	N/S	144	15
Fransen	2006	Australia, New Zealand	RCT	Ibuprofen 1,200	Placebo	14	12	54	66/67	902	49

Abbreviations: RCT, randomized control trial; N/S, not stated.
[A]Ibuprofen for 21 days.
[B]Ibuprofen for 8 days, then 2 weeks of placebo.

reported incidence of treatment discontinuation in ibuprofen group was 11.71% and 7.85% in control group. No statistically significant difference was observed between the two groups (RR = 1.40 [95% CI, 0.97–2.01]; $p = 0.07$; $I^2 = 0\%$) (►**Fig. 2C**).

The Incidence of Brooker I HO

Three studies with 1,103 patients reported data on incidence of Brooker I HO.[19–21] The reported incidence of Brooker I HO in the ibuprofen group was 19.9% and 25.6% in the control group. There was no statistically significant difference observed between the 2 groups in the incidence of Brooker I HO (RR = 0.86 [95% CI, 0.54–1.37]; $p = 0.52$; $I^2 = 49\%$) (►**Fig. 3A**)

The Incidence of Brooker II HO

Three studies with 1,103 patients reported data on the frequency of Booker II HO.[19–21] The reported rate of incidence was 6.71% in the ibuprofen group and 10.7% in the control group. The results suggest there was a statistically significant difference between the 2 treatment groups. The use of ibuprofen was associated with a 36% reduction in the incidence of Brooker II HO (RR = 0.64 [95% CI, 0.43–0.97]; $p = 0.04$; $I^2 = 0\%$) (►**Fig. 3B**).

The Incidence of Brooker III HO

Three studies with 1,103 patients reported data on the incidence of Brooker III HO.[19–21] The reported rate of incidence was 2.37% in the ibuprofen group and 6.69% in the control group. Our analysis of the result indicates that ibuprofen had a statistically significant impact in preventing the development of Brooker III HO postoperatively (RR = 0.38 [95% CI, 0.20–0.73]; $p = < 0.01$; $I^2 = 0$) (►**Fig. 3C**).

The Incidence of Brooker IV HO

Three studies with 1,103 patients reported data on the incidence of Brooker IV HO.[19–21] The reported rate of incidence was 0.39% in the ibuprofen group and 1.72% in the control group. The pooled result indicates that the use of ibuprofen had no significant impact in preventing the development of Brooker IV HO compared with placebo (RR = 0.36 [95% CI, 0.11–1.22]; $p = 0.10$; $I^2 = 0$) (►**Fig. 3D**).

Methodological Quality and Publication Bias Assessment

The methodological quality and risk of bias assessment of the included trials is summarized in (►**Fig. 4A**). All the four included studies were described as RCTs. Three studies reported appropriate methods of randomization, and only one study clearly described the process of allocation concealment. Blinding of participants and personnel was performed in all four studies. The blinding of outcome assessment was not reported clearly in three studies. All the included articles displayed a low risk of bias for the blinding of participants, personnel, incomplete outcome data and selective outcome reporting. Three studies were with unclear risk of bias for other biases. On visual inspection, asymmetry was observed in the funnel plot assessing publication (►**Fig. 4B**). Generally, when the number of studies included a meta-analysis is less than 10 the funnel plot

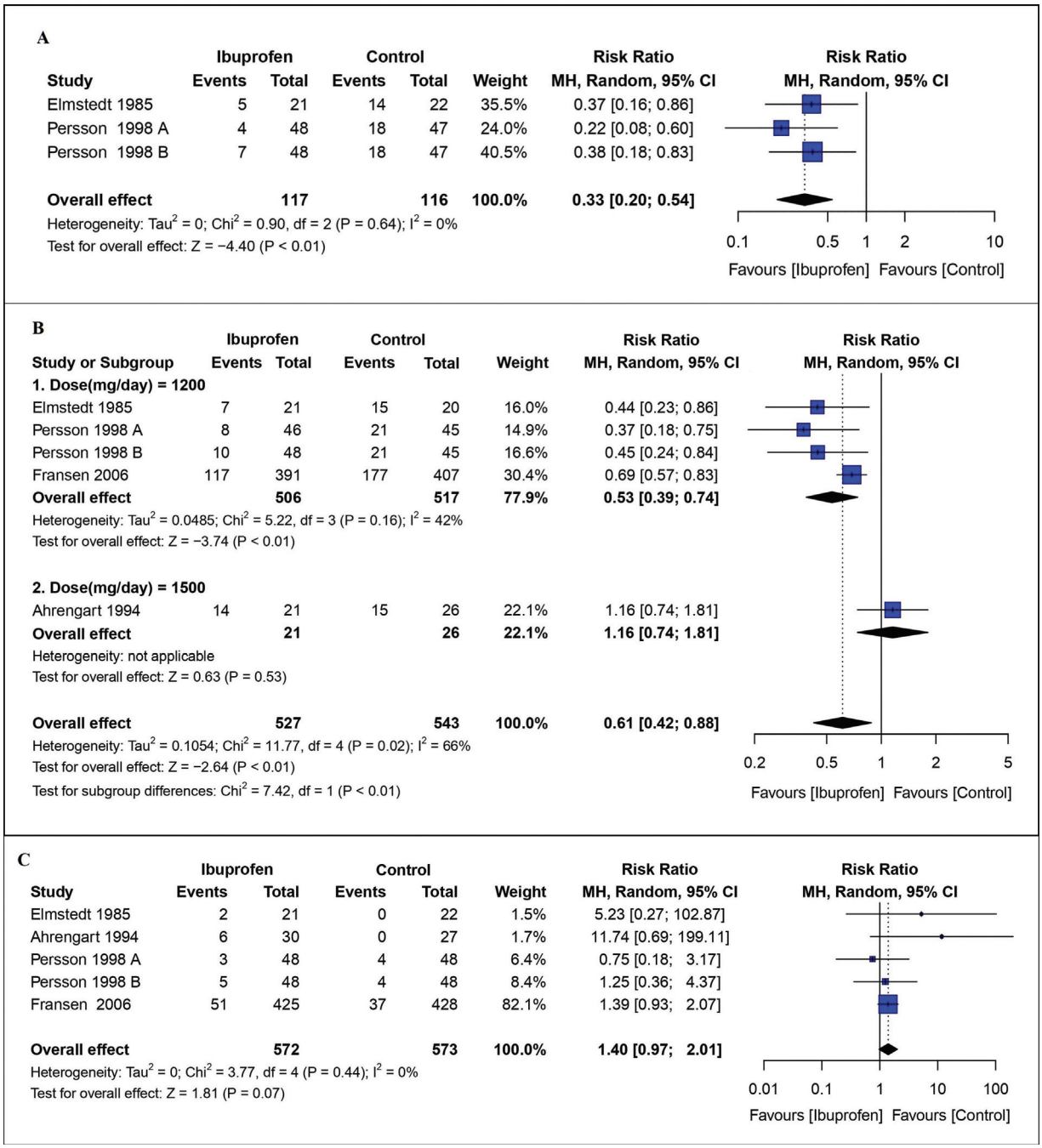


Fig. 2 (A) Forest Plot at 3 months follow-up comparing occurrence of HO between the two groups. (B) Forest Plot at 12 months follow-up comparing occurrence of HO between the two groups. (C) Forest Plot comparing Discontinuation Due to GI side effects between the two groups.

asymmetry is considered non-significant.[23] Since only four studies were included in this meta-analysis, we did not perform the Egger regression test to statistically test for asymmetry.

Discussion

To our knowledge, this is the only meta-analysis performed to date that assesses the effectiveness of ibuprofen versus placebo in preventing HO after primary hip arthroplasty. The main findings indicate ibuprofen was successful in reducing the incidence of HO at the 3 and 12-month follow-ups. Furthermore, no difference was observed in the incidence of treatment discontinuation due to gastrointestinal complications between the two groups. The most common etiology of HO can be due to acquired or non-genetic reasons such as complications of surgery, like arthroplasty, fracture repair, and neurogenic and musculoskeletal trauma; however, rare genetic causes exist as well.[24,25] Similar to fracture healing, HO development occurs by a combination of intramembranous and endochondral ossification, and the pathogenesis of HO is considered to be dependent on these three

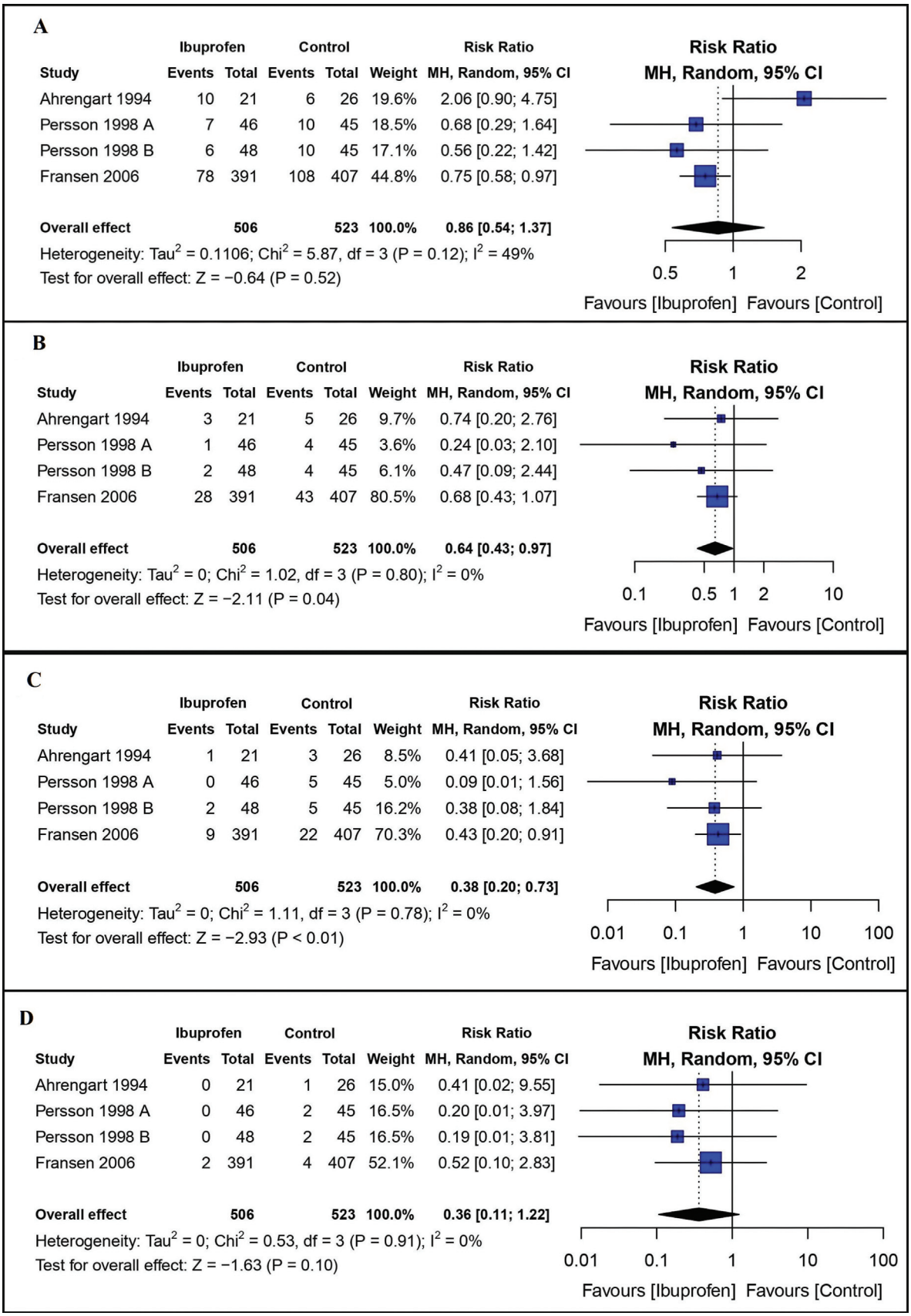


Fig. 3 (**A**) Forest Plot for Incidence of Brooker I HO after surgery between the two groups. (**B**) Forest Plot for Incidence of Brooker II HO after surgery between the two groups. (**C**) Forest Plot for Incidence of Brooker III HO after surgery between the two groups. (**D**) Forest plot for incidence of Brooker IV HO after surgery between the two groups.

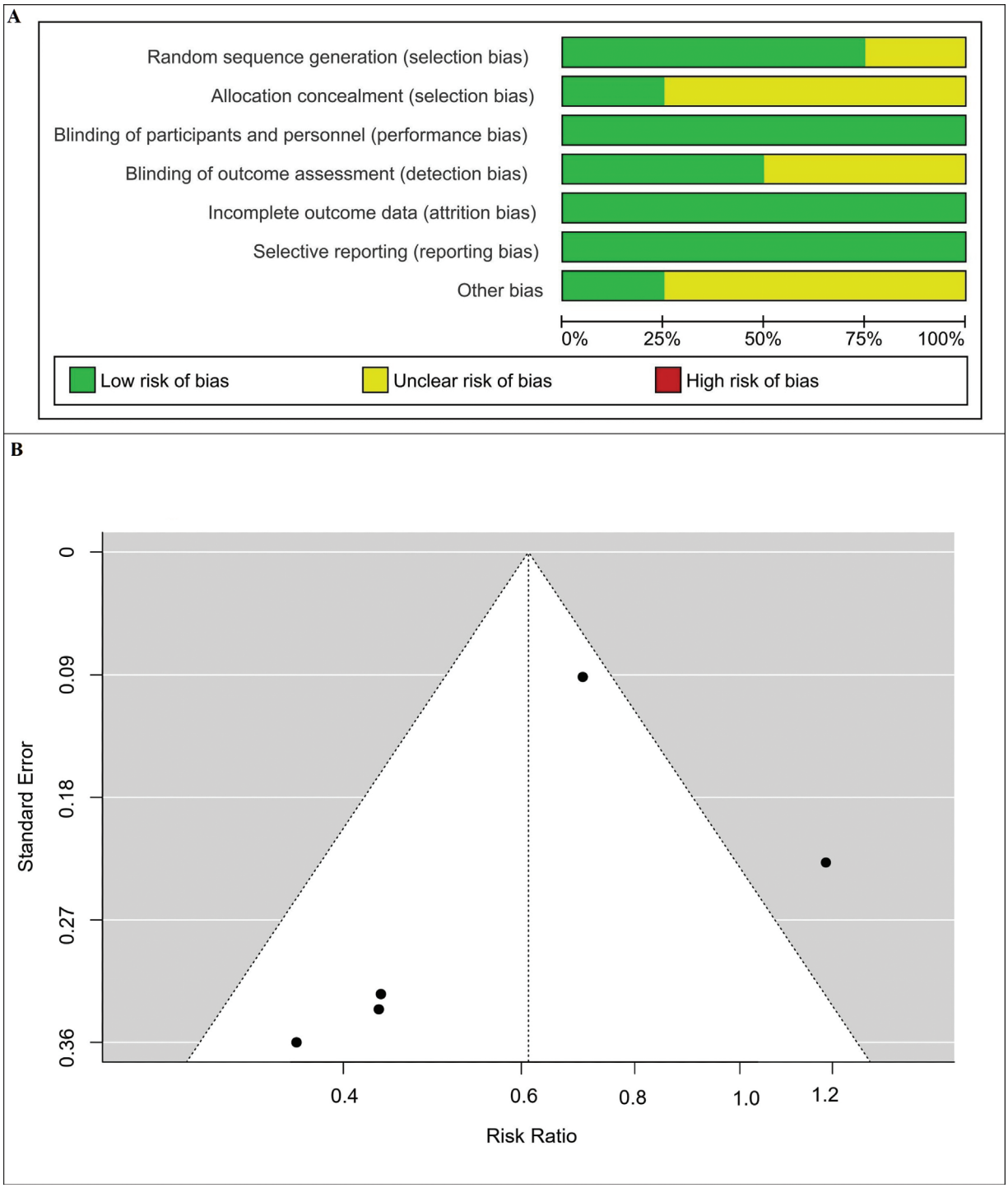


Fig. 4 (**A**) Risk of bias graph: review authors judgements about each risk of bias item presented as percentages across all included studies. (**B**) Funnel plot illustrating publication bias assessment.

factors: inciting stimuli, a conductive environment, and osteogenic precursor cells.[24–26]

Both non-selective NSAIDs (e.g. ibuprofen, indomethacin, diclofenac, naproxen) and selective NSAIDS (e.g. Celecoxib, meloxicam, rofecoxib) are routinely used as prophylaxis for HO post hip surgery.[27–30] A recent meta-analysis by Shapira et al.[11] reported that both non-selective and selective NSAIDs are equally effective in the prevention of HO. In our review, the study by Persson et al.[20] indicates that an ibuprofen course for either 7 days or 21 days postoperatively was equally effective in reducing the incidence of HO. A similar study was conducted on the use of indomethacin prophylaxis for either 3 days, 7 days, or 42 days to prevent HO formation and reported the use indomethacin for a longer period, that is, 42 days, had no positive outcomes but rather increased the incidence of complications, whereas a 7-day treatment had the most beneficial outcomes.[31] Therefore, further investigation is recommended to determine the effectiveness of

shorter course of prophylaxis treatment, which may be helpful in avoiding the undesirable effects of ibuprofen. The use of non-selective NSAIDs have been accompanied by GI symptoms due to blockage of cyclooxygenase-I (COX-I) along with of cyclooxygenase-II (COX-II) enzyme, while selective COX-II inhibitor NSAID have been attributed to decreased gastrointestinal side effects.[32] However, the possible positive outcomes associated with COX-II NSAIDs still warrant caution due to risk of cardiovascular complications as noted by Macfarlane et al.[33] Studies have pointed out that selective NSAID etoricoxib is identified with a tendency to cause blood pressure instability, while rofecoxib has been withdrawn from the market.[34,35] The Cross Trial Safety group performed a meta-analysis on cardiovascular risk of celecoxib and found evidence of dose related risk for cardiovascular events.[36] The decision of whether to administer selective or non-selective NSAID prophylaxis should vary by patient based on preexisting risk factors and the potential for adverse effects.

The Brooker classification is the most common and widely used classification of HO based on anteroposterior (AP) X-Ray of the pelvis.[37] This classification was also used in the studies we examined, except for the study by Elmstedt et al.,[22] which utilized the Rosendahl classification. The Brooker classification assigns four grades to the severity of HO formation following THA. Grade 1 is categorized as small distinct bony regions in the soft tissues surrounding the hip, grade 2 consists of bone exophytes that originate from the pelvis or proximal end of the femur with 1 cm between opposing bone surfaces, while in grade 3, the bone exophytes decrease the separation between opposing bone surfaces to less than 1 cm, and grade 4 is described as bone ankylosis between the pelvis and proximal femur.[37,38] Our analysis indicates that the use ibuprofen had significant reduction in the events of Brooker II and III HO at the final follow-up. Patients with severe HO, such as those with the radiological diagnosis of Brooker III and IV, are of great clinical relevance due to immense pain, limited mobility, and functionality. But there was limited evidence in the included studies to quantify these symptoms using the patient-reported outcome measures such as Harris hip score (HHS), and hip disability and osteoarthritis outcome score (HOOS),[39] making it hard to ascertain the impact of the two treatment groups on functional outcome. Therefore, it is difficult to report if the use of ibuprofen correlates with any improvement in clinical outcomes.

This analysis has the following potential strengths: First, we used a comprehensive methodology in identifying articles from PubMed, Cochrane Library. Second, the study design of the included studies was limited to RCTs, which provides reliable findings. Third, we used subgroup analysis to improve the robustness of our findings. The limitations of this meta-analysis are as follows. First, there were only a few related studies discovered during the literature search. Despite the number of studies found, a significant number of patients were compiled through these studies, with 1,153 patients analyzed in this review. Second, the included RCTs had some potential methodological weaknesses. Third, because the number of included studies was lower than 10, we could not perform the Egger regression test for statistical assessment of funnel plot asymmetry. Finally, no newer studies were discovered during the literature search, the most recent related clinical trial was published in 2006.

Future trials in this area should focus on the methodological design; they need to be double-blinded trials and should clearly report on allocation concealment and method of randomization. Since different doses of ibuprofen ranging from 1,200 mg to 1,500 mg were administered daily over a variety of treatment duration, further studies are needed to investigate for the best dosage and duration of ibuprofen treatment. Additionally, future trials need to comprehensively assess the clinical relevance of HO in patients by utilizing self-reported outcome measures regarding hip function and symptoms.

Conclusion

In conclusion, ibuprofen may be used to prevent HO after THA owing to its significant effect in preventing HO with no increased risk of gastrointestinal complication when compared with placebo.

However, we propose more research is needed to determine the ideal dose and treatment duration for the use of ibuprofen as a prophylactic agent after THA for the prevention of HO.

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Conflict of interests
The authors declare they have no conflict of interests.

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Graft Selection Between Tendon Autograft and Allograft in Anterior Cruciate Ligament Reconstruction Based on the Histological Perspective: A Meta-Analysis

Seleção de enxerto entre autoenxerto e aloenxerto de tendão na reconstrução do ligamento cruzado anterior com base na perspectiva histológica: uma metanálise

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Abstract

Objective: The purpose of this meta-analysis is to compare ligament healing on autograft and allograft in anterior cruciate ligament (ACL) reconstruction.

Methods: The selection of appropriate studies was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We made a statistical analysis using a review manager. Electronic reports were searched using the PubMed, Medline, and Cochrane Library databases. The inclusion criteria were animal studies and cellular histology of both grafts as an outcome.

Results: The initial search revealed 412 potential articles. After duplicates were removed, 246 articles remained. Then, 14 articles were obtained and screened for relevance and eligibility. The relevant articles were searched manually, checking for eligibility and details in order not to miss included reports. Subsequently, 5 studies were included, with a total of 232 samples, reporting the biopsied results with quantitative histology of ligament healing between allograft and autograft. The biopsy samples in those studies were examined under light or electron microscope, to analyze the cellular distribution area and ligamentization stages in each group. Meta-analyses found significant difference between autograft and allograft (Heterogeneity, I2 = 89%;

Keywords
- Adolescent
- Allograft
- Anterior cruciate ligament reconstruction
- Autograft

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Mean Difference, 95% confidence interval [CI] = −34.92, −54.90, −14.93; $p = 0.0006$). There is also a significant difference on both graft in cellular count at over 24 weeks (Heterogeneity, I2 = 26%; Mean Difference, 95% CI = −14.59, −16.24, −12.94; $p < 0.00001$).

Conclusion: In the current meta-analysis, autograft shows a significant difference when compared to allograft, with more cellular accumulation and faster remodeling response on the ligamentization process being noticed in the former. However, a larger clinical trial will be needed to emphasize this literature's result.

Resumo

Objetivo: O objetivo desta metanálise é comparar a cicatrização de ligamentos no autoenxerto e aloenxerto na reconstrução do ligamento cruzado anterior (LCA).

Métodos: A seleção dos estudos adequados foi realizada de acordo com as diretrizes de Relatórios Preferenciais para Revisões Sistemáticas e Metanálises (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses* – PRISMA). Uma análise estatística foi feita usando um gerente de revisão. Os relatórios eletrônicos foram pesquisados usando os bancos de dados PubMed, Medline e Cochrane Library. Os critérios de inclusão foram estudos em animais e a histologia celular de ambos os enxertos como desfecho.

Resultado: A pesquisa inicial revelou 412 artigos potenciais. Após a retirada das duplicatas, restaram 246 artigos. Então, 14 artigos foram obtidos e selecionados pela relevância e elegibilidade. Os artigos relevantes foram pesquisados manualmente, verificando sua elegibilidade e detalhando os estudos para não perder os relatórios incluídos. Posteriormente, foram incluídos 5 estudos, com um total de 232 amostras, relatando os resultados de biópsia com histologia quantitativa de cicatrização de ligamento entre aloenxerto e autoenxerto. As amostras de biópsia nesses estudos foram examinadas sob microscópio leve ou eletrônico, para análise da área de distribuição celular e estágios de ligamentização em cada grupo. As metanálise encontraram diferença significativa entre autoenxerto e aloenxerto (Heterogeneidade, I2 = 89%; Diferença média, 95% intervalo de confiança [IC] = −34,92, −54,90, −14,93; $p = 0{,}0006$). Também há uma diferença significativa nos dois enxertos na contagem celular de mais de 24 semanas (Heterogeneidade, I2 = 26%; Diferença média, 95% IC = −14,59 , −16,24, −12,94; $p < 0{,}00001$).

Conclusão: Na presente metanálise, o autoenxerto mostra resultados significativos quando comparado ao aloenxerto, com mais acúmulo celular e resposta de remodelagem mais rápida no processo de ligamentização sendo observado no primeiro. No entanto, será necessário um estudo clínico maior para enfatizar o resultado desta literatura.

Palavras-chave
- Adolescente
- Aloenxerto
- Autoenxertos
- Reconstrução do ligamento cruzado anterior

Introduction

Injuries to the anterior cruciate ligament (ACL) of the knee are among the most commonly found injuries in young populations. Though it has not been well defined, some literatures estimated the incidence ranged from 30 to 78 per 100.000 people per year.[1] Furthermore, ACL rupture may also cause significant morbidity, where it impairs knee stability and results in difficulty participating in sport activity, as well as increasing the risk of meniscal injury and associated with structure damage. Due to the high incidence of ACL injuries, surgical reconstruction of ACL plays an important role in restoring knee function, especially in the field of Orthopedic Sports Medicine.[2]

Unlike other tissues, such as the medial collateral ligament (MCL), ACL will not heal spontaneously once it is ruptured. The reason is still unclear, but it may be caused by a lack of vascular supply or due to intrinsic failure of the ACL cells to produce new collagen. The main structure of ACL is 90% comprised of collagen type 1, and the remainder 10% is collagen type III, both of which are excreted intracellularly and modified extracellularly; then, they are self-assembled into the microfibrils. The collagen in ACL will be degraded continuously within 300 to 500 days. Beyond the collagen molecules, only 1% of the dry weight ligament is comprised of other molecules, including proteoglycan (chondroitin-4-

sulfate and dermatan sulfate). Fibroblasts are also located in the collagen line, functioning as cell communication to coordinate cellular and metabolic processes, as well as producing and maintaining the extracellular matrix.[3–6]

When the ligament is exposed to extended loading, it will increase in mass and failure load, especially if the load is greater than the sustainable amount, causing partial or complete ligament rupture. Complete ligament rupture requires surgical reconstruction using autograft or allograft. Autograft provides a scaffold similar to the natural composition of the native ligament. Some experimental studies have evaluated the remodeling process of the autograft postoperatively, including cellular changes such as vascular growth and fibroblast proliferation. First, the inflammatory phase will happen from within minutes up until 48 to 72 hours postsurgery; followed by the repairing phase, which initiates fibroblast proliferation signals to rebuild the ligament's tissue matrix. The final phase is remodeling, which can last for years, where the graft begins to resemble normal ligament tissue. Moreover, some scientists believe that ligamentization occurs only in the outer portion of the graft, early revascularization on graft surface will occur within 2 to 4 weeks, and the avascular zone in the mid-substance of the graft remains even after 6 to 12 months. According to some researchers, autograft will begin to appear as "normal" ligament tissue within 9 months. A key advantage on autograft is the absence of foreign body reaction, as the graft was taken from the same body tissue. Regardless of this advantage, autograft is also associated with some morbidity, such as discomfort and decreased range of motion over donor area, which may affect postoperative rehabilitation.[5–7]

Alternatively, allograft is a tissue taken from donor of the same species. There are some advantages for using allograft, such as shorter surgery time and lack of donor-site morbidity. The major disadvantage is the risk of disease transmission.[8] Despite this, some studies consider allograft as the best substitute to autograft.[6]

A standard method to evaluate remodeling process of bone tendon graft healing is a histologic examination of graft tissue.[9,10] Because of the difficulties getting human histologic examination due to research ethics, there are a limited number of experimental studies that directly compared autograft and allograft ligamentization, and some contradiction studies over which one is the best graft option for ACL reconstruction. To advance it further, a thorough analysis of previous experimental studies on the histological process of autograft and allograft should be performed. The aim of this review is to systematically analyze the autograft and allograft healing process based on histological findings.

Materials and Methods

Search Strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11,12] The search for studies was done in the PubMed, Science Direct, and Cochrane Library databases on May 23, 2020, to identify all of the published studies reporting ligament healing based on histological process, comparing autograft and allograft for ACL reconstruction. We extracted the eligibility criteria into keywords of the Boolean Operator. The keywords used were "ligamentization" OR "ligament healing process" OR "re-modelling" AND "autograft-tendon" OR "auto transplant tendon" OR "autologous graft" AND "allograft-tendon" OR "allotransplant tendon" AND "ACL reconstruction" OR "Anterior Cruciate Ligament reconstruction" OR "ACL surgery" OR "Anterior Cruciate Ligament surgery."

All the inherent aspects of each study, including study quality, objective, study selection, data variables, risk of bias assessment, and irrelevant data were analyzed by the first authors. All studies' abstracts and titles were read and selected appropriately by decision of the first author. Duplicate records and irrelevant studies were removed in this phase. Subsequently, the second author decided whether the studies should be further analyzed, as an expert in Orthopedic Sports Surgery. Furthermore, studies that underwent the first screening were evaluated by both authors using the inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

We used the PICO (Population, Intervention, Comparison and Outcome) method. Inclusion criteria were population (animal studies) with the intervention being ACL reconstruction surgery using autograft and allograft. The comparison was cellular healing based on the histological findings between autograft and allograft.

We excluded case reports, case series, review articles, and all articles with level of evidence bigger than II (►**Table 1**). All studies that underwent ACL reconstruction using only autograft or allograft were also excluded.

Adequate study protocols for result verification as well as comprehensible documentation of the remodeling process.

Study Quality Assessments

Authors searched the studies for titles and abstracts based on inclusion criteria. Then, full articles were extracted from all databases that were suitable for the subject. The authors had a meeting and discussed which relevant studies should be included. The quality and content from studies were assessed, and any disagreements were discussed to finalize a highly qualified and eligible study.

All aspects of the studies, including methodological quality, data variables, and risk of bias assessment, were appraised by filling up forms (►**Fig. 1**), which were then collected by the main author. Finally, the authors gathered to discuss any contradicting points.

Statistical Analysis

We measured the results of the meta-analysis using the Review Manager (RevMan. The Nordic Cochrane Center, Cochrane Collaboration. Odense, Denmark) software, version 5.3. The interstudy heterogeneity was computed with the $\chi 2$ test, with results being considered heterogeneous if $I^2 < 50\%$. For the continuous outcome, we used the mean difference (MD) and odds ratio (OR) for dichotomous outcomes. The authors also

Table 1 Studies used in this meta-analysis

Authors	Journal	Country	Procedure Date Range	Study Design	Level of Evidence
Razi et al., 2009	Journal of Orthopaedic Surgery and Research	Iran	2006–2012	Cohort Prospective Study	III
Barber et al., 2014	The Arthroscopy Association of North America	USA	2001–2012	Retrospective Comparative Study	III
Larson et al., 2016	The Arthroscopy Association of North America	USA	2002–2007	Case Series	IV
Li et al., 2012	The American Journal of Sports Medicine	China	NA	Cohort Prospective Study	III
Engelman et al., 2014	The American Journal of Sports Medicine	USA	2005–2009	Case Control Study	III
Sun et al., 2011	The Journal of Arthroscopic and Related Surgery	China	2005–2008	Prospective Comparative Study	II
Tian et al., 2016	The American Jorunal of Sports Medicine	China	2008–2009	Randomized Controlled Trial	II

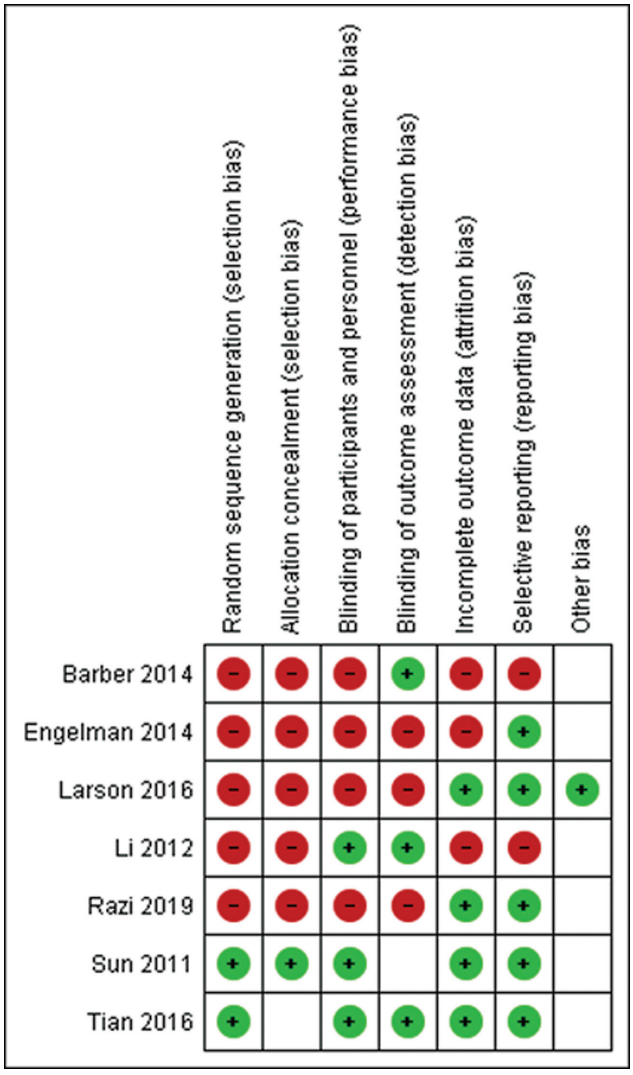


Fig. 1 Flow diagram describing the strategy for conducting this study based on the PRISMA guidelines.

assessed the clinical impact of this meta-analysis review using a trial sequential analysis (TSA) with the statistical software of TSA (Copenhagen Trial Unit. Copenhagen, Denmark), beta version 0.9. The results is considered significant if the Z-curve crosses the boundary of futility.

Result

Search Result

Initial search through PubMed, MEDLINE, and Cochrane Library revealed 412 potential articles. After the duplicates were removed, 246 articles remained. From those, 14 articles were obtained and screened for relevance and eligibility. The relevant articles were searched manually, eligibility was checked, and details were studied in order not to miss included reports. Subsequently, 5 studies were included in this meta-analysis, reporting biopsied results with quantitative histology of ligament healing between allograft and autograft. The 9 excluded studies did not provide ligamentization comparison between allograft and autograft, or ligamentization time frame. At the end of the selection process, 5 studies with animal models were included, as shown in ►**Fig. 2**. The total sample of all studies is 232 animal models.[7,13–16] All of studies were prospective, with designated time points for histology examination..

All articles had varied level of evidence, ranging from level I to II (►**Table 1**). Duration of follow-up started as early as post-operative until a maximum of 54 weeks. The animal models used were mammals such as Merino sheep, goats, and New Zealand rabbit. Each study criteria were listed in ►**Table 2**.

ACL Reconstruction

All included studies had autograft and allograft transplantation groups, with four of them using the flexor tendon as an allograft and autograft. Types of autograft and allograft

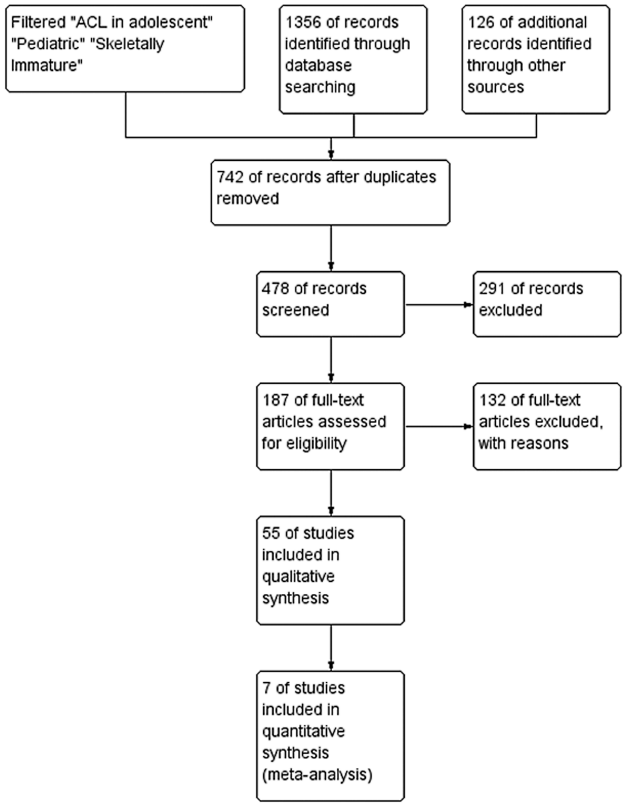


Fig. 2 Risk of bias summary: review of authors' judgements about each risk of bias item for each included study.

preparations were varied. All studies were using graft transplantation with a diameter of 6 to7 mm. Those studies performed both arthrotomy and excised native ACL, followed by ACL reconstruction. Graft fixations also varied from femoral, tibia fixation button, cancellous screw, and Krakow stitches. After the surgical procedure, each animal was immobilized in individual cages.

Graft Examination

Animals were euthanized at fixed time points ranging from 2 to 52 weeks, and the healing process was evaluated by histomorphometry. Only one study evaluated the macroscopic gross on graft treatment, starting from two weeks after surgery, and found accumulation of synovial fluid over the graft insertion.[13] Tissue samples were taken from midsubstance tissue of graft bundle until graft insertion sites; only three studies showed specimen size on biopsy site ranging from free cut at around 7 to 8 µm.[14–16] They also performed H&E staining followed by histologic analysis performed under conventional light and/or high electron microscopes.

Ligamentization Process

To document ligamentization process, all studies evaluated different aspects, such as cellular distribution and morphology, appearance of inflammatory cells, vascularization, extracellular matrix, phases of healing, and length of healing process. The aspects that all of those studies evaluated are cellular distribution of the remodeling graft, phase of healing, and length of healing process. A second look at the arthroscopy and histology evaluation started as early as 2 weeks, up until 54 weeks, as seen in ►**Figs. 1** and **2**.[7,13–16] The initial remodeling changes and degenerative process could be seen at 2 weeks postoperatively. At the peripheral tendon, the regular matrix was replaced with dense connective tissue.[13] At 6 weeks postoperatively, there was cellular proliferation of osteoblasts and newly formed blood vessels, with a marked difference between allograft and autograft, with less cellularity in the first one.[7,14,15] Collagen crimp begins to reorganize toward center of the graft, and the endochondral ossification begins in the bone tendon junction throughout 12 weeks in both graft types.[7] Cellular formation and vascular components will resemble an intact ACL at 48 weeks in autograft. Myofibroblast density will continue to increase up to 52 weeks, when cellular distribution and morphology was improved in each graft.[7,15]

Of the articles included in this research, 4 evaluated that there was less cellular and vascular proliferation in tendon allografts rather than in autografts. Furthermore, 4 of the 5 included studies have been evaluated in different ligamentization stages than those already observed up until 54 weeks.[7,14–16] Only one study had observed within short period until 8 weeks.[13] The 4 other reports have mentioned three different stages of ligamentization with similar characteristics of histologic changes.[7,14–16] Allograft and autograft healing have similar phases and ligamentization time frame, with the exception of cells density, cellular distribution in each phase, and tendon graft vascularization, which will never reach the level of native ACL.[10]

We performed a meta-analysis on the cellular count from 6 to 8 weeks with a statistically significant result between autograft and allograft (Heterogeneity, $I^2 = 89\%$; MD, 95% confidence interval [CI] = −34.92, −54.90, −14.93; $p = 0.0006$). The cellular count at over 24 weeks is also statistically significant between both grafts (Heterogeneity, $I^2 = 26\%$; MD, 95% CI = −14.59, −16.24, −12.94; $p < 0.00001$) (►**Fig. 3**).

Discussion

Nowadays, the allograft has gained more popularity than autograft in ACL reconstruction, since it has decreased surgical time, low donor morbidity, and unaltered patellofemoral tracking.[2] However, there was a debate over the issue of radiated allograft, which uses gamma irradiation and has a greater impact to graft healing. Several studies on the process of allograft healing found it happened similarly to autograft, but with a slower rate of healing. Gulotta et al.[3] found that freezing allograft components during graft preparation will also denature the cell surface components, resulting in a decreased graft immunogenicity and causing hypocellular allograft ligament and limitation of immune response during the initial healing stages.[3,9] Conversely, autograft has some advantages over allograft, including a decrease in the risk of disease transmission during ACL

Table 2 Outcome characteristics of the included studies

Parameters	Razi et al. 2019			Barber et al. 2014			Larson et al. 2016			Li et al. 2012			Engelman et al. 2014		
	Allograft (n = 13)	Autograft (n = 18)	*p*-value	Allograft (n = 28)	Autograft (n = 53)	*p*-value	Allograft (n = 8)	Autograft (n = 22)	*p*-value	Allograft (n = 30)	Autograft (n = 22)	*p*-value	Allograft (n = 38)	Autograft (n = 35)	*p*-value
Primary Outcomes															
Graft Failure	6 (46.2%)	7 (38.9%)		2 (7.1%)	5 (9.4%)	0.85	3 (37.5%)	2 (9%)	0.10	0	0	> 0.99	11 (28.95%)	4 (11.43%)	0.3756
Lachman Test Positive	6 (46.2%)	7 (38.9%)	0.68	3 pt (gr 1 +)	3 pt (gr 1 +)		3 (37.5%)	2 (9%)		6 (20%) gr 1+	4 (18.2%) gr 1+		0	0	
Positive Pivot Shift Test	0	0		2 pt	4 pt		0	0					0	0	
Knee Joint Translation (KT Arthrometer, MRI)	Side to side: -	Side to side: -		Side to side: 0.59 mm (SD = 1.5) < 3 mm: 22 pt 3–5 mm: 3 pt > 5 mm: 0	Side to side: 0.34 mm (SD = 1.9) < 3 mm: 43 pt 3–5 mm: 6 pt > 5 mm: 1	0.58	Mean side to side: 0.4 ± 2.4 mm		<0.01	0.42 ± 0.04 mm	0.43 ± 0.02 mm	0.5908	10.81% pt	15.63% pt	0.5538
IKDC scores	84.3 ± 3.2	85.6 ± 4.4	0.39	1.9–2.9 (pre-post-op) (2.4 ± 0.5)	3.3–3.1 (pre-post-op) (3.2 ± 0.09)	0.32	68.2–91.8 (−27.7–−18.0) 95% CI Mean: 80 ± 11.8		<0.01	92.6 ± 5.9	93.3 ± 5.2	0.644	94 ± 5	88 ± 10	0.4817
Cincinnati Scores				54.6–86.2 (pre-post-op) (70.4 ± 15.8)	39.5–85.1 (pre-post-op) (62.3 ± 22.8)	0.76	75–93.1 (−26.4 (−12.1) 95% CI (94 ± 9.05)		<0.01						
KOOS	78 ± 7.2	75 ± 7.4	> 0.05												
Lysholm Scores				60.3–89.9 (pre-post-op) (75.1 ± 14.8)	44.8–87.0 (pre-post-op) (65.9 ± 21.1)	0.43	79.3–91.5(−20.1 (−6.4) 95% CI (85.4 ± 6.09)		<0.01	93.4 ± 5.2	94.3 ± 5.4	0.543	91.5 ± 6.5	84.5 ± 6.5	0.465
Secondary Outcomes															
Revision surgery	6 pt	7 pt		2 pt	5 pt		3 pt	2 pt		0	0		11 pt	4 pt	
Infection	0	1 pt (5.6)													

Abbreviations: IKDC, International Knee Documentation Committee; MRI, magnetic resonance imaging. **Notes:** *Values in Graft Failures and Lachman Test are reported as number (percentage). Values in IKDC, Cincinnati and Lysholm are reported as median (Interquartile range).

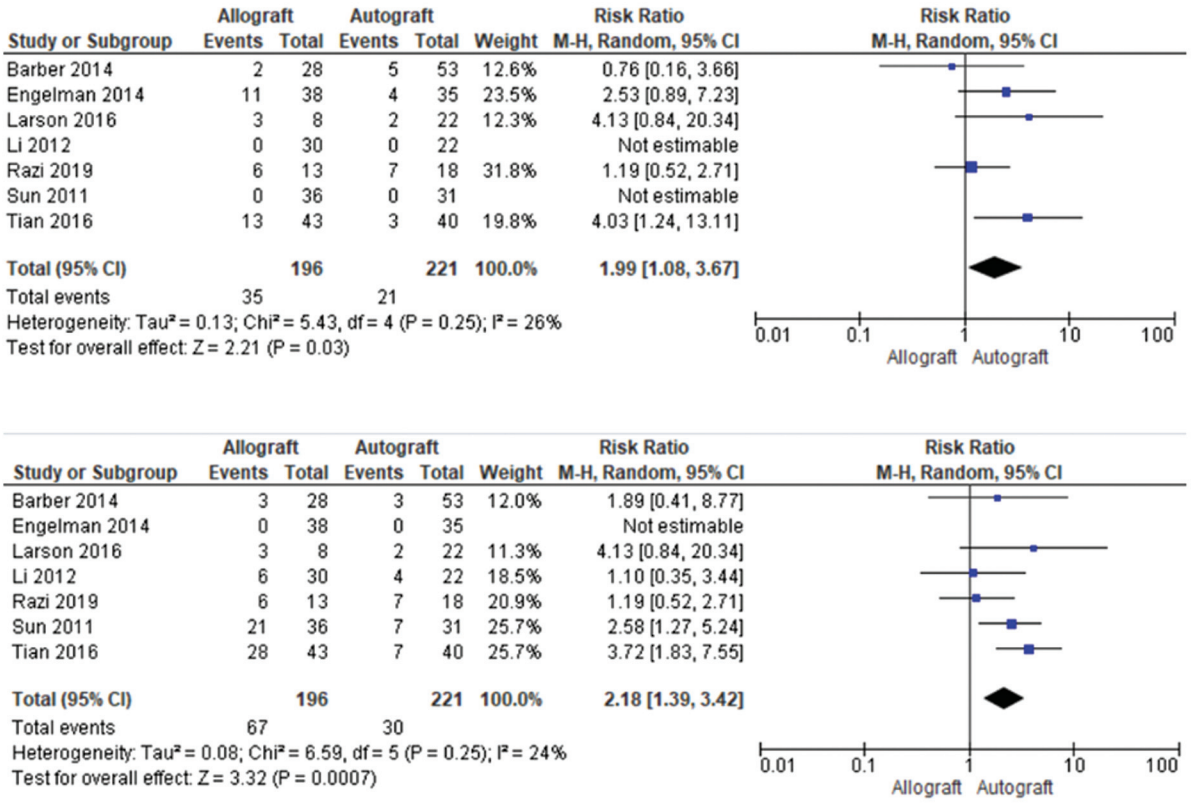


Fig. 3 Comparison: Allograft vs. Autograft; Outcome: Graft Failure, Lachman Test > +1, IKDC Score, Revision Surgery.

reconstruction; some authors also demonstrated that graft incorporation between tendon graft to bone insertion showed a higher rate compared with allograft.[6,13]

According to the included studies, based on cellular distribution, vascularization, and other histology signs of graft maturation, there are three consecutive distinguishable phases of ligamentization. Pauzenberger et al.,[10] in a review based on four studies, found that the initial phase of healing start from 2 up until 12 weeks, followed by remodeling from 12 to 48 weeks, to the final maturation phase, which will be ongoing up until 48 months.[6,10] Primarily using animal models to evaluate ligamentization process in allograft and autograft, Gulotta et al.[3] reveals that the intra-articular healing of both grafts has the same process, from the initial phase until progressive remodeling and maturation, the difference being that allograft relies on bone to tendon healing and heal through fibrovascular tissue with anchoring of formation Sharpey's Fiber and new bone production, first healing of allograft will undergo osteonecrosis over tendon bone graft insertion, followed by incorporation graft to tunnel.[3,10] Several experimental studies also found no differences in ACL reconstruction using allograft or patellar tendon autograft. Conversely, Jackson et al.[14] used patellar goat tendons to demonstrate that there were slower healing rate and less complete incorporation of tendon grafts to an insertion tunnel when compared to autograft. The ACL reconstruction with allograft should be protected from maximum load for a longer period of time.[14,17] Another report has demonstrated myofibroblast formation and collagen crimp; myofibroblast expression was higher, and the restoration and organization of collagen crimp was better in autograft; this process happens in the early healing phase of autograft.[5,7,18] Another study, by Nikolaou et al.,[8] used cryopreserved allograft (−80° C) in canines as a study model and found there was no healing disruption and no effect on the biomechanical properties, so the allograft structures were still similar to autograft. Shino et al.,[19] who used deep freezing allograft (−20° C) in dog models, also found a similar healing process with autograft. Over 30 weeks, allografts will have the same mechanical properties as the previous native ACL, and over 52 weeks the anterior cruciate ligament will be similar to its normal composition.

Furthermore, this review shows the concept of general ligamentization between autograft and allograft proposed in animal models. Ligamentization of graft is a biological continuous and time-dependent process. The difference in graft healing between autograft and allograft is useful to choose the graft technique preoperatively and to determine the rehabilitation period postoperatively. However, there is no consensus in the current review regarding the ligamentization process' time frame, as each study has a different quantitative histology of graft healing.

Parameters	Tian et al. 2016			Sun et al. 2011		
	Allograft (n = 43)	Autograft (n = 40)	*p*-value	Allograft (n = 36)	Autograft (n = 31)	*p*-value
Primary Outcomes						
Graft Failure	(13) 30.2%	(3) 7.5%	0.001	0	0	NA
Lachman Test Positive	Gr 0: 15 (34.9%) Gr I: 16 (37.2%) Gr II: 12 (27.9%) Gr III: 0	Gr 0: 33 (82.5%) Gr I: 4 (10%) Gr II: 3 (7.5%) Gr III: 0	0.001	Gr 0: 29 (80.6%) Gr I: 11 (35.5%) Gr II: 10 (32.3%) Gr III:0	Gr 0: m10 (32.3%) Gr I: 4 (11.1%) Gr II: 3 (8.3%)	0.00011
Positive Pivot Shift Test	Gr 0: 27 (62.5%) Gr I: 11 (25.6%) Gr II: 5 (11.6%) Gr III: 0	Gr 0: 37 (92.5%) Gr I: 3 (7.5%) Gr II: 0 Gr III: 0	0.004	19 (61.3%) gr 0 8 (25.8%) gr 1 4 (12.9%) gr 2	33 (91.7%) gr 0 3 (8.3%) gr 1	0.008
Translation (KT Arthrometer, MRI)	Side to side: 5.5 mm (SD = 1)	Side to side: 2.4 mm (0.7)	0.04	Side to side: 5.6 mm (SD = 3.1) < 3 mm: 10 (32.3%) > 5mm: 10 (32.3%)	Side to side: 2.5 mm (SD = 0.7) < 3 mm: 31 (86.1%) > 5mm: 3 (8.3%)	0.00017
IKDC scores	85 ± 11	89 ± 9	0.0748	83 + 10	87 + 10	0.208
Cincinnati Scores	87 ± 12	90 ± 10	0.2214	85 + 13	88 + 11	0.212
Lysholm Scores	86 ± 9	90 ± 11	0.0727	87 + 11	89 + 8	0.353
Secondary Outcomes						
Revision surgery	0	0		0	0	
Infection				0	0	

Abbreviations: IKDC, International Knee Documentation Committee; MRI, magnetic resonance imaging. **Notes:** *Values in Graft Failures and Lachman Test are reported as number (percentage). Values in IKDC, Cincinnati and Lysholm are reported as median (Interquartile range).

Limitations

The validity of this review is determined by the quality of the included studies, which have a publication range from 1993 to 2012. As different surgical techniques for ACL reconstruction were progressively developed, various animal models have been used, but none of the studies analyzed here used human models. Meanwhile, animals had a higher rate of graft healing compared to humans. However, none of the previous studies in humans have compared ligament healing for each type of graft, as a second invasive procedure was hardly done. Those studies with animal models can be an initial benchmark to compare ligament healing with studies which used bigger populations and humans as a study model. Inter-study heterogeneity with different parameters could interfere with the results, such as various histology study methods and quantitative histology results. Moreover, there is still a limited number of studies which compared ligamentization between allograft and autograft. Further clinical studies are needed to compare the best healing between autograft and allograft, based on histology reviews, to increase the success rate of ACL reconstruction. Those clinical studies seem to be important regarding the failure rate, which has increased.

The healing processes of autograft and allograft were similarly composed, resembling the native ACL as early as 48 weeks in the maturation phase. The major difference of both ligamentization processes is the cellular distribution, which is worse in allograft than autograft. We recommend autograft for ACL reconstruction, because it shows more cellular accumulation and faster remodeling response when compared to allograft, with significant results. Thus, both autograft and allograft healing have similar time duration and three chronological and distinguishable phases, beginning with early inflammatory phase, remodeling phase, and maturation phase. However, larger clinical trials will be needed to emphasize this literature's result.

Conclusion

In ACL reconstruction, both autograft and allograft can be considered as the treatment of choice. However, we concluded that autograft is better than allograft when comparing the healing rates. Furthermore, in autograft, the cellular distribution is different from allograft, in which there is a lower cellular accumulation, meaning autograft has better outcomes with faster remodeling response. Assessment of patients' activity level and postoperative rehabilitation are also important for better outcomes.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Impact of the Suspension of Elective Surgeries for Adolescent Idiopathic Scoliosis during the COVID-19 Pandemic*

Impacto da suspensão das cirurgias eletivas em pacientes com escoliose idiopática do adolescente no período da pandemia de covid-19

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Abstract

Objectives This study evaluated the radiographic progressions of scoliotic curves higher than 40° in patients with adolescent idiopathic scoliosis (AIS). These subjects waited for the surgical procedure while elective surgeries were on hold during the COVID-19 pandemic. In addition to radiographic progressions, this study described the quality of life of these patients.

Methods This study is a retrospective cohort assessing 29 AIS patients with surgical indications registered in the Brazilian public healthcare service. We compared the scoliotic radiographic measurements in two moments: at the beginning of the interruption of elective surgeries due to the COVID-19 pandemic and when these procedures resumed.

Results When comparing the radiographic measurements before and after the suspension of assessments for elective surgeries, we observed a significant increase in main curve angles ($p < 0.001$), with variations ranging from 0 to 68° and a median value of 10°. In secondary curves, we observed an increase in angles from the proximal thoracic ($p < 0.001$) and lumbar ($p = 0.001$) regions. However, the increase in the main thoracic region was not significant ($p = 0.317$).

Conclusion The suspension of elective surgeries for AIS resulted in a significant increase in the radiographic values of patients' spine deformities. This increase harmed the quality of life of these subjects and their families.

Keywords
- adolescent
- scoliosis
- elective surgical procedures
- unified health system

* *Study developed at the Orthopedics and Traumatology Service, Hospital Municipal Universitário de Taubaté, Taubaté, SP, Brazil.*

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Resumo

Objetivos Neste estudo foram avaliadas as progressões radiográficas das curvas escolióticas, acima de 40 graus em pacientes com escoliose idiopática do adolescente (EIA). Os indivíduos analisados aguardavam o procedimento cirúrgico, em período de suspensão das cirurgias eletivas, durante a pandemia de covid-19. Além das progressões radiográficas, nesta pesquisa foi descrita a qualidade de vida destes pacientes.

Métodos O artigo refere-se a um estudo de coorte retrospectivo, que avaliou 29 pacientes com EIA com indicação cirúrgica, todos cadastrados no serviço público de saúde brasileiro. As medidas radiográficas escolióticas dos pacientes foram comparadas em dois momentos: no início do período da interrupção de cirurgias eletivas, devido à pandemia de covid-19, e logo após a liberação destas.

Resultados A partir da comparação das medidas radiográficas entre as avaliações pré e pós suspensão das cirurgias eletivas, observamos o aumento significativo dos valores angulares da curva principal ($p < 0{,}001$), com variações entre 0 e 68°, e mediana de 10°. Em relação às curvas secundárias, observamos um aumento dos valores angulares da região torácica proximal ($p < 0{,}001$) e lombar ($p = 0{,}001$). Entretanto, o aumento da região torácica principal não foi considerado significativo ($p = 0{,}317$).

Conclusão A suspensão das cirurgias eletivas, para a correção da EIA resultou em um aumento significativo no valor radiográfico das deformidades das colunas dos pacientes, fator que promoveu um impacto negativo na qualidade de vida de pacientes e familiares.

Palavras-chave

- adolescente
- escoliose
- procedimentos cirúrgicos eletivos
- sistema único de saúde

Introduction

Adolescent idiopathic scoliosis (AIS) is one of the most frequent spinal diseases, with an incidence ranging from 0.5 to 10% in the world population.[1] The spinal instrumentation and fusion procedure for AIS correction is performed frequently in pediatric orthopedic patients. Nevertheless, only 10% of AIS patients require surgical correction.[2]

The Brazilian Unified Health System (SUS) has difficulties meeting the demand for these major surgeries, which remain restricted to a few regional treatment centers in populous regions. Scoliotic curves higher than 40° with surgical indications constitute severe cases because they progress even after the end of skeletal maturity.[3,4]

Brazil implemented public health measures against the pandemic after the first diagnosis of covid-19 in the country. However, the lack of availability of intensive care unit (ICU) and hospital beds during this period overloaded the healthcare system, leading to restrictions. These factors resulted in the suspension of elective surgical treatments.[5–7]

The excessive delay for scoliosis surgery may require additional procedures, such as an anterior release, for satisfactory spinal curvature correction. Moreover, these subjects may need longer surgeries with a higher risk of complications (increased blood loss, neurological deficits, or unsatisfactory spinal curvature correction).[8]

This study aimed to evaluate the radiographic progression of the scoliotic curve in young patients awaiting surgery in a public hospital in the state of São Paulo, Brazil. The study occurred during the period of suspension of elective surgeries due to the covid-19 pandemic. In addition to the radiographic comparison of scoliotic curves, the patients underwent quality-of-life assessments.

Methods

This retrospective cohort study evaluated 29 patients with AIS (scoliotic curves higher than 40°) with surgical indication, all registered in the Brazilian public health service and awaiting surgery for scoliosis correction.

We evaluated the radiographic evolution of the scoliotic curves from the beginning of elective procedures interruption due to the COVID-19 pandemic until their resumption. In addition, we analyzed the epidemiological data of the sample and other factors associated with the progression of their scoliotic curves. The Research Ethics Committee approved this study under the number 5039.

The scoliotic curve progression evaluation used anteroposterior (AP) and panoramic (P) total spine radiographs in orthostasis. We measured the curve according to the Cobb method[9] before the beginning of the pandemic in Brazil in March 2020. We compared these data with radiographs from the same patients shortly after the return of the elective surgery service in December 2021. The quality-of-life assessment employed the questionnaire proposed by the Scoliosis Research Society (SRS), that is, the Brazilian version of the SRSr-22 questionnaire for AIS.[10,11]

We described categorical variables as absolute frequencies and percentages and numerical variables as mean, standard deviation (SD), median, quartiles, and minimum and maximum values. The Wilcoxon nonparametric tests for paired data compared radiographic measurements. The

Table 1 Data from patients with severe adolescent idiopathic scoliosis awaiting surgical correction (n = 29)

Gender	
Female	25 (86.2%)
Male	4 (13.8%)
Age (years old)	
Mean (SD)	15.8 (2.8)
Median (Q1; Q3)	15.0 (14.0; 17.0)
Minimum and maximum values	11.0; 23.0
Age at menarche (years old) (n = 25)	
Mean (SD)	12.2 (1.3)
Median (Q1; Q3)	12.0 (11.0; 13.0)
Minimum and maximum values	10.0; 15.0
Family member with AIS	
No	23 (79.3%)
Yes	6 (20.7%)
Time between evaluations (months)	
Mean (SD)	23.6 (7.1)
Median (Q1; Q3)	22.0 (18.0; 25.0)
Minimum and maximum values	15.0; 39.0

Abbreviations: AIS, Adolescent idiopathic scoliosis; Q1, first quartile; Q3, third quartile; SD, standard deviation.

analyses were performed using the IBM SPSS Statistics for Windows, Version 24.0 statistical software (IBM Corp., Armonk, NY, USA) considering a significance level of 5%.

Results

The patients' age ranged from 11 to 23 years, with a mean value of 15.8 years (SD = 2.8 years). Twenty-five (86.2%) subjects were female, and 4 (13.8%) were male. A total of 6 (20.7%) patients had a family history of AIS (►**Table 1**).

The interval between radiographic evaluations ranged from 15 to 39 months, with a median time of 22 months (►**Table 1**). The Risser index defined the degree of skeletal maturity of the spine based on an AP pelvic radiograph. Before the elective surgery interruption, we observed the following Risser indices: 0 in 4 (13.8%) patients, 3 in 6 (20.7%) subjects, 4 in 7 (24.1%) patients, and 5 in 12 (41.4%) patients. After resuming elective surgeries, skeletal maturity was as follows: 2 (6.9%) subjects were Risser 3, 6 (20.7%) patients were Risser 4, and 21 (72.4%) patients were Risser 5. ►**Table 2** shows these analyses.

We used the Lenke classification to determine the type of scoliotic curve.[4] The main curve was thoracic (apex = T2–T11/T12 disc) in 24 (82.8%) patients, thoracolumbar (apex = T12–L1) in 2 (6.9%) subjects, and lumbar (apex = L1–L2 disc-L4) in 3 (10.3%) patients.

According to Lenke classification, 9 (31.0%) patients were in the main thoracic type (LENKE 1), 5 (17.2%) were in the double thoracic type (LENKE 2), 11 (37.9%) were in the main double type (LENKE 3), 1 (3.4%) had a triple curve (LENKE 4), and 3 (10.3%) had a rigid lumbar and main thoracic curve (LENKE 6). This sample had no LENKE 5 patients (►**Table 2**).

Table 2 Radiographic features from patients with severe adolescent idiopathic scoliosis awaiting surgical correction (n = 29)

Previous Risser index	
0	4 (13.8%)
3	6 (20.7%)
4	7 (24.1%)
5	12 (41.4%)
Current Risser index	
3	2 (6.9%)
4	6 (20.7%)
5	21 (72.4%)
Curve type/Main curve	
Thoracic (Apex = T2–T11/T12 disc)	24 (82.8%)
Thoracolumbar (Apex = T12-L1)	2 (6.9%)
Lumbar (Apex = L1–L2 disc-L4)	3 (10.3%)
Lenke classification	
Main thoracic	9 (31.0%)
Double thoracic	5 (17.2%)
Main double	11 (37.9%)
Triple curve	1 (3.4%)
Lumbar curve with rigid main thoracic curve	3 (10.3%)
Lumbar modifier	
Type A	7 (24.1%)
Type B	7 (24.1%)
Type C	15 (51.7%)
Sagittal modifier	
Negative	1 (3.4%)
Neutral	25 (86.2%)
Positive	3 (10.3%)
Treatment	
No	24 (82.8%)
Brace	3 (10.3%)
Brace (irregularly used)	2 (6.9%)

Regarding lumbar modifiers, 7 (24.1%) patients were typed A (median vertical sacral line [LSVM] passing between the pedicles of the lumbar apical vertebra), 7 (24.1%) patients were typed B (LSVM touching the pedicle of the apical vertebra), and 15 (51.7%) patients were typed C (LSVM medial to the pedicles of the lumbar apical vertebra).

Regarding the thoracic sagittal modifier, 1 (3.4%) patient had hypokyphosis, 25 (86.2%) subjects had a neutral spine, and 3 (10.3%) patients had thoracic hyperkyphosis (►**Table 2**).

Table 3 Angles from patients with severe adolescent idiopathic scoliosis awaiting surgical correction (n = 29)

Angles	Time		Range	*p* value
	1st evaluation	2nd evaluation	(2nd – 1st evaluation)	
Main curve				
Mean (SD)	60.9 (12.8)	75.0 (18.8)	14.1 (16.4)	< 0.001
Median (Q1; Q3)	60.0 (52.0; 68.0)	75.0 (60.0; 87.0)	10.0 (2.0; 20.0)	
Minimum and maximum values	40.0; 95.0	44.0; 126.0	0.0; 68.0	
Proximal thoracic				
Mean (SD)	25.5 (8.0)	29.6 (10.7)	4.0 (5.4)	< 0.001
Median (Q1; Q3)	28.0 (20.0; 30.0)	30.0 (23.0; 35.0)	3.0 (0.0; 5.0)	
Minimum and maximum values	14.0; 41.0	14.0; 60.0	0.0; 20.0	
Main thoracic (n = 4)				
Mean (SD)	37.5 (12.6)	42.0 (19.7)	4.5 (9.0)	0.317
Median (Q1; Q3)	40.0 (30.0; 45.0)	40.0 (30.0; 54.0)	0.0 (0.0; 9.0)	
Minimum and maximum values	20.0; 50.0	20.0; 68.0	0.0; 18.0	
Lumbar (n = 25)				
Mean (SD)	39.5 (16.3)	46.8 (17.2)	7.3 (9.9)	0.001
Median (Q1; Q3)	30.0 (28.0; 55.0)	45.0 (30.0; 60.0)	5.0 (0.0; 8.0)	
Minimum and maximum values	20.0; 70.0	24.0; 75.0	0.0; 38.0	

Abbreviations: Q1, first quartile; Q3, third quartile; SD, Standard deviation.

In this study, 24 (82.8%) patients had not undergone previous treatment. Three (10.3%) subjects used a brace correctly, and 2 (6.9%) patients used it irregularly (►**Table 2**).

When comparing the radiographic measurements in both evaluations (►**Table 3**, ►**Fig. 1**), we observed a significant increase in the main curve angles ($p < 0.001$), ranging from 0 to 68°, with a median value of 10°. Regarding secondary curves, there was an increase in angles from the proximal thoracic ($p < 0.001$) and lumbar ($p = 0.001$) regions. However, in these cases, the increase in the main thoracic region was not significant ($p = 0.317$). The proximal thoracic region angles ranged from 0 to 20°, with a median value of 3° (1st quartile, 0°, and 3rd quartile, 5°). For the lumbar region, angles ranged from 0 to 38°, with a median value of 5° (1st quartile, 0°, and 3rd quartile, 8°). ►**Table 4** shows individual curves for each patient at both time points.

At the quality of life assessment, the average SRS scores were 16.4 (SD = 4.5) in the function/activity domain, 16.2 (SD = 5.2) in the pain domain, 11.1 (SD = 4.0) in the self--image/appearance domain, 15.1 (SD = 4.5) in the mental health domain, and 7.4 (SD = 1.6) in the treatment satisfaction domain, with a subtotal score of 58.8 (SD = 15.1) and a total score of 66.2 (SD = 15.9). ►**Table 5** shows the information on the quality of life of AIS patients.

Discussion

The main motivation for this study was the concern with the high number of patients waiting for elective surgeries and the potential increase in the angle of their scoliosis curve during the covid-19 pandemic. Our service suspended surgeries requiring postoperative care in intensive care unit (ICU) from March 2020 to December 2021.

Other studies had this same concern since the reduction in the number of elective orthopedic surgeries ranged from 48.5 to 79%.[6,7] However, until now, no study has addressed the interruption of surgeries for deformity corrections, specifically AIS.

This study evaluated patients awaiting AIS correction surgery in a public hospital. The epidemiological data obtained were similar to other Brazilian research of the same nature, consisting of adolescents (11–23 years old), mostly female.[3,12]

In contrast with Lima Junior et al.,[3] the most prevalent Lenke classification was 3, with double main curves predominance. In addition, there were no Lenke 5 curves. The thoracic sagittal and lumbar modifiers were consistent with the literature.[3]

We detected significant increases in the main curve angles, ranging from 0 to 68°, with an average of 14.1°. Similarly, Bressan-Neto et al.[12] observed differences in radiographic parameters, indicating a progression of the scoliotic deformity, when comparing the evaluations at the time of surgical indication and the procedure date. These authors reported an average increase of 18.6° in the Cobb angle of the main deformity.[12]

The excessive delay for scoliosis surgery, especially in public services, was a cause for concern by other authors. Ahn et al.[9] demonstrated that a delay greater than 4 months resulted in the need for additional surgeries, such as anterior release to obtain satisfactory correction of

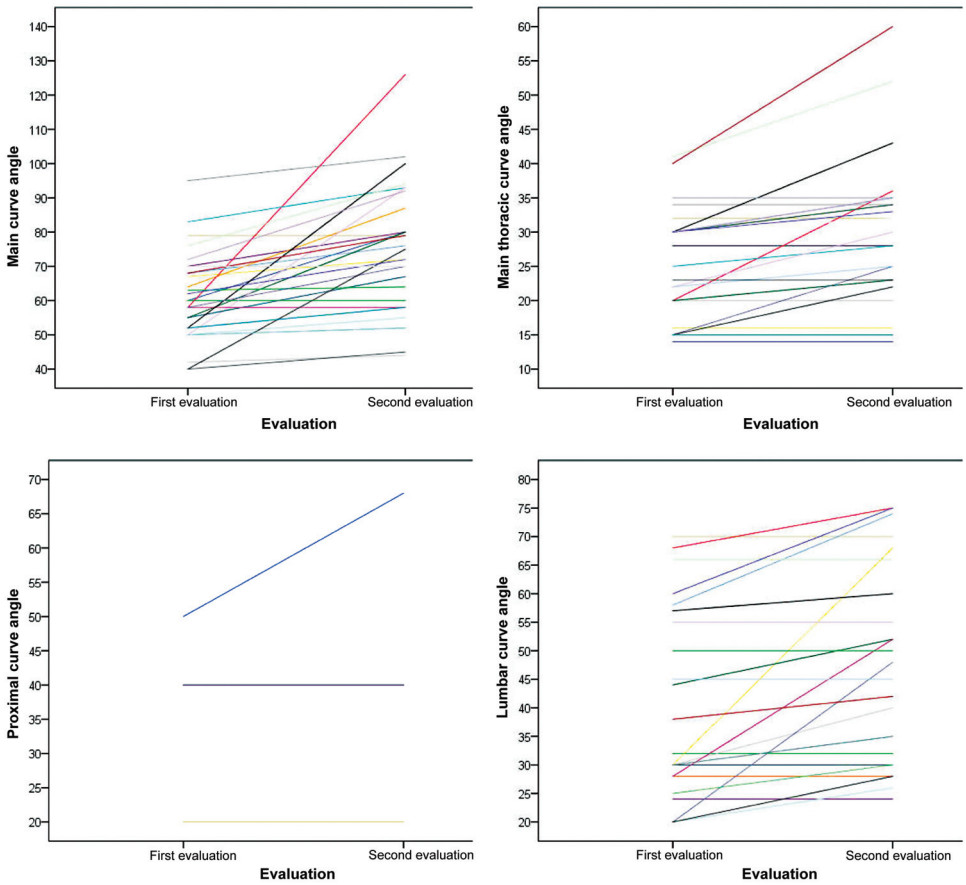


Fig. 1 Angle measurements in both evaluations of patients with severe adolescent idiopathic scoliosis awaiting surgical correction (n = 29).

Table 4 Individual data from the sample

Awaiting list of scoliosis patients									
Number	Gender	Age	Time between evaluations	Curve type/ Main curve	Lenke classifications	Difference in main curve angle	Difference in secondary curve angle	Current Risser index	Previous Risser index
1	F	15	3 years, 3 months	Left lumbar	6CN	T11–L3 = 20°	C7–T4 = 0 / T4–T10 = 18°	5	3
2	F	21	1 year, 10 months	Right thoracic	1C–	T5–T11 = 0	T1–T5 = 0 / T12–L4 = 0	5	5
3	F	16	1 year, 3 months	Right thoracic	1CN	T5–T12 = 0	C7–T5 = 0/ T12–L4 = 0	5	5
4	M	20	2 years	Right thoracic	3CN	T7–T12 = 10°	T2–T7 = 0 / T12–L4 = 0	5	4
5	F	23	2 years, 11 months	Right thoracic	1CN	T6–T12 = 5°	T1–T5 = 0 / T12–L4 = 0	5	5
6	F	13	2 years, 10 months	Right thoracic	4C+	T5–T12 = 68°	T1–T5 = 16° / L1–L5 = 38°	5	0
7	F	15	1 year, 6 months	Right thoracic	3CN	T5–T11= 10°	T1–T5 = 3° / T11–L4= 7°	4	4
8	F	21	2 years, 11 months	Left lumbar	6BN	T12–L4 = 2°	T2–T5 = 0 / T5–T12 = 0	5	5
9	F	15	2 years, 5 months	Right thoracic	1BN	T5–L1 = 8°	T2–T5 = 5° / L1–L5 = 5°	5	4
10	M	15	2 years, 1 month	Right thoracic	1BN	T5–T12 = 25°	T2–T5 = 3° / T12–L5 = 10°	4	0
11	F	15	1 year, 5 months	Right thoracic	3CN	T5–T11 = 23°	T2–T5 = 4° / T11–L4 = 16°	4	3
12	F	11	1 year, 10 months	Right thoracic	3A+	T4–T10 = 43°	T2–T4 = 8° / T10–L5 = 8°	4	3
13	M	17	1 year, 4 months	Right thoracic	2AN	T7–L2 = 12°	T2–T7 = 4° / L2–L5 = 0	5	5
14	M	15	1 year, 9 months	Right thoracic	2BN	T5–T12 = 18°	T1–T5 = 11° / T12–L4 = 0	4	5
15	F	15	1 year, 5 months	Right thoracic	1BN	T9–L3 = 0	T4–T9 = 0 / L3–L5 = 0	5	4
16	F	17	1 year, 11 months	Right thoracic	3CN	T4–T11 = 7°	T1–T4 = 0 / T12–L5 = 0	5	5
17	F	14	2 years, 11 months	Right thoracic	2BN	T6–L2 = 48°	T2–T7 = 13° / L2–L5 = 24°	4	3
18	F	17	1 year, 10 months	Right thoracic	1AN	T6–L1 = 5°	T1– T7 = 0 / L1–L5: 5°	5	5

(*Continued*)

Table 4 (*Continued*)

Awaiting list of scoliosis patients									
Number	Gender	Age	Time between evaluations	Curve type/ Main curve	Lenke classifications	Difference in main curve angle	Difference in secondary curve angle	Current Risser index	Previous Risser index
19	F	14	1 year, 6 months	Right thoracic	3CN	T6–T11: 1°	T1– T5 = 2°/T12–L4 =3°	5	4
20	F	13	1 year, 11 months	Right thoracic	1AN	T6–L1 = 12°	T1–T6 = 10° / T11–L4 = 6°	5	3
21	F	13	1 year, 4 months	Right thoracic	3CN	T3–T10 = 2°	C7–T3 = 0 / T10–L4 = 0	5	4
22	F	13	2 years	Right thoracic	3AN	T4–T12 = 35°	C7–T4 = 7°/ T12–L5 = 28°	3	0
23	F	14	1 year, 6 months	Right thoracic	1AN	T6–T12 = 2°	T1–T6 = 3° / T12–L4 = 5°	5	5
24	F	17	1 year, 8 months	Right thoracic	2AN	T5–T12 = 11°	T2–T6 = 20° / L1–L5 = 8°	5	4
25	F	19	3 years, 1 month	Right thoracic	3BN	T5–T11 = 10°	T1–T5 = 3° / T11–L4 = 0°	5	5
26	F	16	1 year, 7 months	Right thoracic	3CN	T4–T11 = 0	T1–T4 = 0 / T11–L4 = 4°	5	5
27	F	15	1 year ,7 months	Right thoracic	2CN	T10–L3 = 6°	T1–T6= 0 / T6–T10 = 0	5	5
28	F	13	1 year, 7 months	Right thoracic	3C+	T7–T12 = 20°	T1–T7= 5° / T12–L5 = 15°	3	0
29	F	15	1 year, 9 months	Left lumbar	6CN	T12–L3 = 5°	T1–T6= 0 / T6–T12 = 0	5	3

Abbreviations: F, Female; M, male.

Table 5 Scoliosis Research Society (SRS) questionnaire scores for evaluation of the current quality of life of patients with severe adolescent idiopathic scoliosis awaiting surgical correction (n = 27)

Function/activity	
Mean (SD)	16.4 (4.5)
Median (Q1; Q3)	16.0 (14.0; 19.0)
Minimum and maximum values	8.0; 25.0
Pain	
Mean (SD)	16.2 (5.2)
Median (Q1; Q3)	16.0 (11.0; 21.0)
Minimum and maximum values	8.0; 25.0
Self-image/appearance	
Mean (SD)	11.1 (4.0)
Median (Q1; Q3)	9.0 (8.0; 14.0)
Minimum and maximum values	5.0; 21.0
Mental health	
Mean (SD)	15.1 (4.5)
Median (Q1; Q3)	15.0 (12.0; 19.0)
Minimum and maximum values	6.0; 22.0
Subtotal	
Mean (SD)	58.8 (15.1)
Median (Q1; Q3)	60.0 (46.0; 65.0)
Minimum and maximum values	28.0; 89.0
Treatment satisfaction	
Mean (SD)	7.4 (1.6)
Median (Q1; Q3)	8.0 (6.0; 8.0)
Minimum and maximum values	4.0; 10.0
Total	
Mean (SD)	66.2 (15.9)
Median (Q1; Q3)	68.0 (52.0; 73.0)
Minimum and maximum values	32.0; 97.0

Abbreviations: Q1, first quartile; Q3, third quartile; SD, standard deviation.

the curvature of the spine. Moreover, surgeries were longer and had a higher risk of complications. According to this research, the scoliotic curve increased, on average, 14.1° during the surgery suspension period. This increase must be followed-up until the surgical procedure because of the reported complications. In our study, the time between radiographic evaluations ranged from 15 to 40 months, with a median of 22 months. This interval occurred because of health restrictions leading to the suspension of elective surgeries and the decreased availability of hospital beds.

The literature showed a significant drop in the number of referrals of patients to reference services in deformity treatment during the covid-19 pandemic.[13] The restrictions promoted by the public health services result in anxiety and prolonged suffering for patients and families, negatively impacting their quality of life.[8] In our sample, we observed a lower quality of life, with the worst scores related to the self-image and mental health domains.

Conclusions

This study concludes that, during the pandemic, the suspension of surgeries in AIS patients resulted in a significant increase in spine deformities and a negative impact on quality of life. Therefore, it is critical to consider these findings, especially in the current post-covid-19 pandemic period, to improve public health strategies and optimize elective surgeries for AIS correction.

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Conflict of Interests
The authors declare that there is no conflict of interests.

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A Prospective Observational Study on Outcomes of Single Stage Posterior Decompression and Fixation for Dorsolumbar Spine Tuberculosis

Estudo observacional prospectivo sobre os desfechos da descompressão posterior e fixação em estágio único na tuberculose da coluna dorsolombar

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Abstract

Objective To study the results of only posterior decompression and instrumentation in dorsal and dorsolumbar spine tuberculosis.

Methods The patients ($n = 30$) who were included in this study had dorsal or dorsolumbar spine tuberculosis, with or without neurological deficit, and with or without deformity. All 30 patients were managed by only posterior approach decompression and instrumentation. We studied cases for correction and maintenance of deformity at dorsal and dorsolumbar spine, functional outcome by the Oswestry disability index (ODI) and visual analogue scale (VAS) scores, as well as neurological outcome by the Frankel grade.

Results In the current series, 30 patients were operated with single stage posterior decompression and instrumentation, and showed significant improvement in neurological status and functional outcomes, which were accessed by the ODI score, VAS score, and Frankel grade.

Conclusion The posterior (extracavitary) approach provides optimum access to the lateral and anterior aspects of the spinal cord for good decompression. It facilitates early mobilization and avoids problems of prolonged recumbency, provides better functional outcome, and significantly better sagittal plane kyphosis correction.

Keywords

- Koch´s spine
- posterior approach
- Pott´s spine
- spondylodiscitis

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Resumo

Objetivo Estudar os desfechos da descompressão posterior isolada e instrumentação na tuberculose da coluna dorsal e dorsolombar.

Métodos Os pacientes ($n = 30$) incluídos no estudo apresentavam tuberculose na coluna dorsal ou dorsolombar acompanhada ou não por déficit neurológico e/ou deformidade. Todos os 30 pacientes foram tratados apenas por descompressão posterior e instrumentação. Estudamos a correção e manutenção da deformidade na coluna dorsal e dorsolombar, o desfecho funcional segundo o índice de deficiência de Oswestry (ODI, do inglês Oswestry disability index) e a escala visual analógica (EVA), e o desfecho neurológico de acordo com a classificação de Frankel.

Resultados A atual série de 30 pacientes submetidos à descompressão posterior e instrumentação em estágio único apresentou melhora significativa no estado neurológico e desfecho funcional segundo ODI, EVA e classificação de Frankel.

Conclusão A abordagem posterior (extracavitária) permite o acesso ideal aos aspectos laterais e anteriores da medula espinhal para uma boa descompressão. Facilita a mobilização precoce, evita problemas associados ao decúbito prolongado, proporciona melhor desfecho funcional e corrige a cifose no plano sagital de maneira significativamente melhor.

Palavras-chave

- coluna de Koch
- abordagem posterior
- coluna de Pott
- espondilodiscite

Introduction

In India, tuberculosis is a significant infectious cause of death affecting the pulmonary system, but extrapulmonary involvement is also frequently encountered. Skeletal system involvement accounts for 1 to 3% of the cases. The most frequent kind of skeletal tuberculosis (50%) is spinal tuberculosis.[1]

From the pre-antitubercular era to the post-antitubercular era, treatment for tuberculosis of the spine has progressed. Antitubercular medicines, decompression surgeries, and a mid-path regimen are good treatment options.[1]

Due to anatomical and biomechanical differences, the natural history of tuberculosis in the dorsal and lumbar areas may differ from that of other spine regions. Tuberculosis of the dorsal and lumbar regions destroys the anterior (paradiscal and central) column of the spine, resulting in kyphosis, instability, and late-onset paralysis.[2]

Tuberculosis-related kyphosis is an unstable condition that tends to worsen until the entire body fuses anteriorly. The surgical treatment is recommended for failed conservative management, instability, and progressive neurological deficit.

Anterior vertebral bodies and paradiscal spaces are the most typically afflicted. The anterior approach has long been considered the gold standard, as it provides direct access to affected vertebral bodies for debridement and abscess drainage, as well as extensive decompression and defect restoration.[3,4]

Morbidity and problems linked with anterior surgery due to thoracotomy or retroperitoneal exploration are especially common in the thoracic and lumbar regions. Because of the accompanying osteoporosis of vertebrae associated with illness, the anterior fixation is structurally weak, preventing a sufficient and stable fixation.[5,6]

The use of a combined anterior debridement and posterior instrumentation helps to overcome the anterior approach's instability issues.[7,8] It does, however, necessitate two procedures (single or staged) with added morbidity, and it is only recommended for patients with severe deformity.

Extrapleural approaches (posterior) can be used to reach the anterior and lateral column via posterior or posterolateral decompression. The posterior approach provides excellent exposure for spinal cord decompression, allows posterior instrumentation above and below the level of involvement, has less morbid surgery, allows for earlier mobilization, better sagittal-plan deformity correction, and is a more widespread approach.[3,9]

The aim of this prospective study is to analyze the clinical and functional outcomes in term of pain and neurology, in the single stage posterior approach for tuberculosis of dorsolumbar spine among patients operated at our institution.

Materials and Method

This study was conducted at the New Civil Hospital, Surat, India; we studied 30 patients with tuberculosis of dorsal and lumbar spine. All patients were treated with the single stage posterior approach for decompression, fixation, and correction of deformity, as well as fusion for tuberculosis of dorsolumbar spine, from February 2018 to May 2020.

Inclusion Criteria

Age group of 18 to 60 years.
Tuberculosis of dorsal and lumbar spine with instability.
Patients with tuberculosis of dorsolumbar spine with neurological signs which are neither improving nor worsening within 4 weeks of adequate conservative treatment.

Progressive neurological deficit even on adequate treatment or recurrence of neurological signs after improvement.
Rapid onset or late onset paraplegia.

Exclusion Criteria

Multi segmental tuberculosis of the spine.
Age under 18 and age over 60 years.
Tubercular spine with other comorbidities of the spine.
Patient responding to conservative management.

Methods

All patients were selected according to above criteria, preoperative diagnosis was based on magnetic resonance imaging (MRI) of the affected spine, and preoperative abscess aspiration, with sample analysis based on the cartridge-based nucleic acid amplification test (CBNAAT) and computed tomography (CT) guided biopsy. Preoperatively, 14 patients were diagnosed with tubercular infection by CBNAAT performed on ultrasound guided aspiration, and 4 patients by CT guided biopsy. All patients were treated with single stage posterior decompression and fixation. As per sensitivity reports, antithrombotic therapy (ATT) continued postoperatively for 9 to 12 months.

Operative Technique

Under general anesthesia, in prone position via midline incision, the subperiosteal dissection was done two levels above and below the affected vertebrae. After adequate exposure, a pedicle screw was inserted in unaffected vertebrae. A shaft with one side temporarily contorted (according to the deformity) was applied to maintain spinal stability during decompression (posterior and posterolateral) and debridement. Paravertebral and epidural abscess were drained and thorough debridement was done until fresh, bleeding bone was seen. The same procedure was repeated over other side. Harvested samples were sent for biopsy and culture for confirmation. Anterior column reconstruction was done using the minced spinolaminous process mixed with streptomycin powder (1 g). A cage was inserted when the defect was too large. The bilaterally placed contorted shafts and the construct were compressed, thereby achieving deformity correction (►**Fig. 1**–case 1).

The patients are followed up at 3 months, 6 months, and 1 year by the visual analogue pain scale (VAS) and the functional outcome was evaluated by using the postoperative Frankel grading, angle of kyphosis, Oswestry disability index (ODI), and blood investigations at 6 months. During follow-up, the duration of ATT was decided based on the clinical improvement and radiological evidence of disease regression (resolution of abscess and inflammation on follow up MRI, along with evidence of fusion).

Results

The dorsolumbar spine is most commonly affected (46.7%).

The mean surgical time was 3 hours and 20 minutes (range 2h20min – 4h10min).
The average blood loss was 800 ml (400–1500 mL).

The mean preoperative VAS was 7.9 (range 7–10) which improved to 2.1 (range 1–4) on the postoperative period, then to 1.1 on 6 months, and 0.9 on the 1-year follow-up.

The mean preoperative kyphosis in the dorsal and dorsolumbar spine was 27.9 degrees, which was corrected to a mean of 9.5 degrees in the final follow up MRI images, implying better correction and maintenance of kyphosis.

Before surgery, 1 patient was classified with a Frankel grade A, 3 were classified as Grade B, 6 patients were classified grade C, 16 patients were classified as D, and 4 were classified as E (►**Table 1**). After surgery, at the 1-year follow up, 6 patients were with grade C improved to D grade. Out of 16 patients with grade D, 12 improved to grade E and 2 remained the same; only 1 patient with grade A improved to grade C. All 3 patients with grade B improved to grade C (►**Table 2**).

Before surgery, the ODI score of 4 patients was within the range of 0 to 20% (minimal disability); 16 patients were in the 20 to 40% range (moderate disability); 6 patients were in the 40 to 60% range (severe disability); and 4 patients were in the 60 to 80% range (crippled) (►**Table 3**). There was an improvement in the ODI score noted during follow-up assessment, which suggests functional improvement.

Histopathological examination of intraoperative samples of 30 patients suggestive of rifampicin-sensitive tuberculosis and ATT was started (none of the patients were diagnosed with multidrug-resistant tuberculosis). Duration of ATT was decided based on clinical signs of improvement, laboratory investigations, and radiological evidence of disease regression during follow-up.

Complications

There were 3 patients who developed a superficial wound infection, 2 of which were treated with conservative measures and antibiotics for a longer period of time, and 1 patient was taken for debridement.

On the 6th month of follow-up, 1 patient developed loosening of 2 distal screws which was not progressed on the 12th month of follow-up.

On the 9th month of follow-up, 1 of the patients' MRI scans showed signs of delayed fusion, which on 12th month of follow-up showed satisfactory signs of healing.

Discussion

The dorsal region exhibited the highest rate of neurological impairment (30%). The majority of the patients with tuberculosis in the lumbar region had no neurological impairments. This may be due to them having a narrow spinal canal in the dorsal part of the spine and a relatively wide spinal canal space in the lumbar area.

The goals of surgery for tuberculosis of the dorsal and lumbar spine include appropriate decompression, adequate debridement, correction of deformity, and the prevention of kyphosis progression.

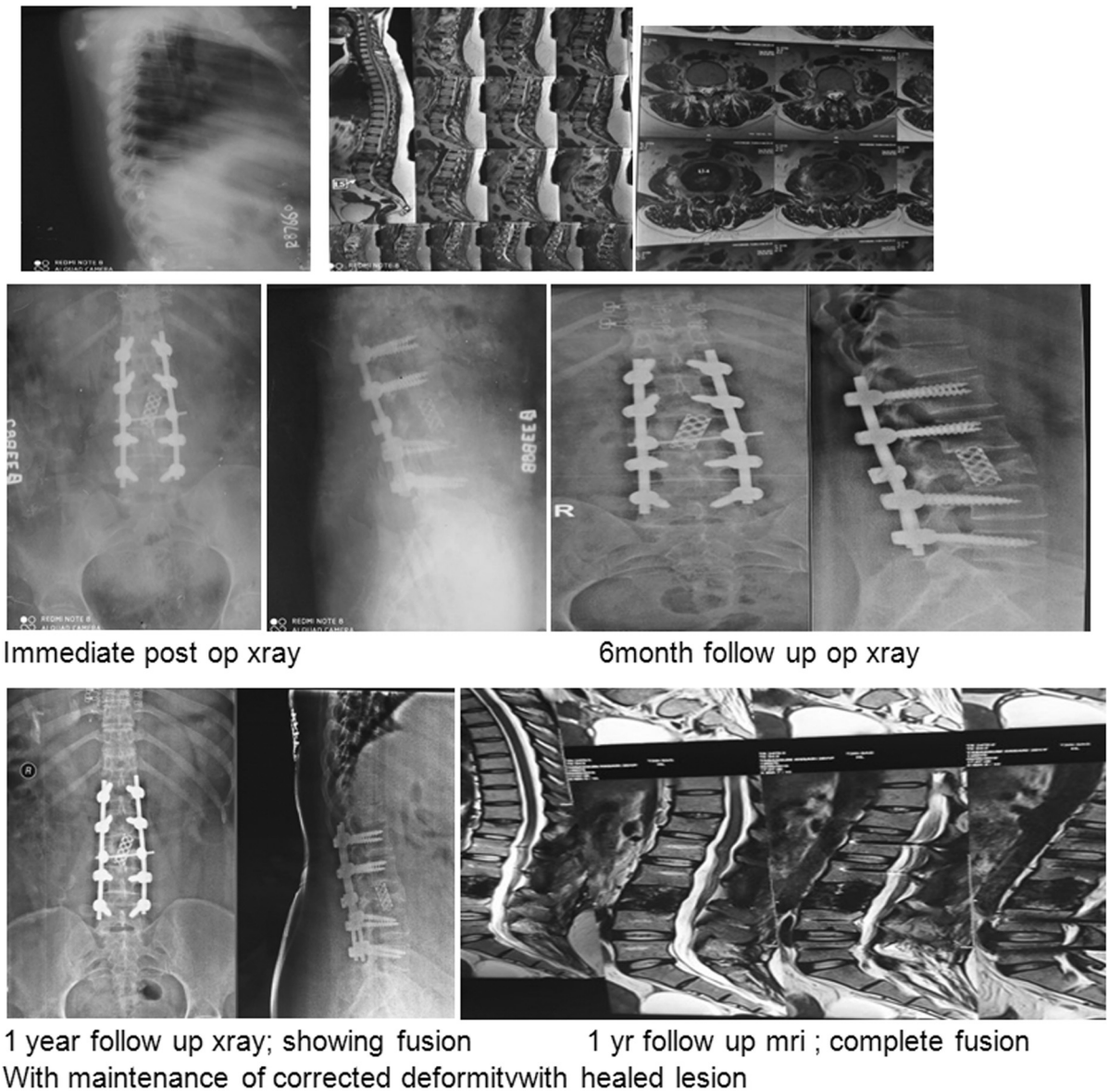


Fig. 1 Case: 28 year female with L2-L3 spondylodiscitis, MRI showing pre- and paravertebral abscess.

The anterior technique is the gold standard for debridement and decompression in spinal tuberculosis. The capacity to directly access the disease for decompression, greater correction of deformity, and ability to place a graft under the compressive load for fusion are the three advantages of the classic anterior technique. However, anterior approach has disadvantages in terms of morbidity and mortality linked with the transpleural and retroperitoneal approaches, such as atelectasis, chest infection, pneumothorax, postoperative ileus, and retrograde ejaculations. In the anterior technique, the structural bone graft does not provide immediate stability, and graft-related complications are more common when the graft crosses more than two disc spaces.[10]

Moon et al. discovered that anterior arthrodesis was unsuccessful in preventing the progression of kyphosis or correcting previous abnormality.[11]

A stable anterior graft provided structural support in only 41% of the patients, according to Rajasekaran and Soundarapandian,[12] while graft failure with residual kyphosis occurred in 59%. As a result, we came to the conclusion that

Table 1 Preoperative Frankel grade presentation

	Frankel grade – preoperative				
	A	B	C	D	E
Number of patients	1	3	6	16	4

Table 2 Postoperative Frankel grade presentation

	Frankel grade – postoperative				
	A	B	C	D	E
Number of patients	0	0	4	10	16

Table 3 Oswestry deficiency index (ODI) score presentation on respective follow-ups

	ODI score at the 6th month follow-up			
	0–20%	**20–40%**	**40–60%**	**60–80%**
Number of patients	10	12	6	2
	ODI score at the 1-year follow-up			
	0–20%	**20–40%**	**40–60%**	**60–80%**
Number of patients	16	10	4	0

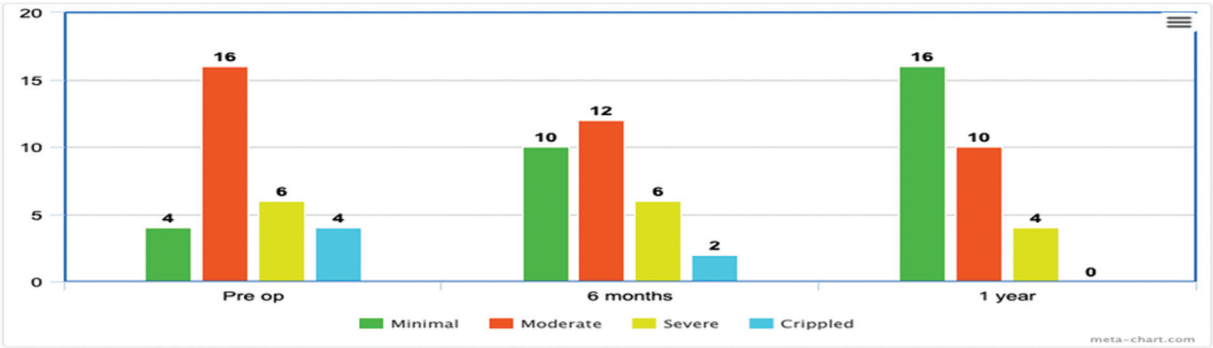


Fig. 2 Graphical representation of ODI score of respective follow-ups.

depending solely on the anterior strut bone graft to prevent vertebral collapse was not enough.[12]

The use of posterior instrumentation has been shown to be very beneficial in reducing graft-related complications and kyphosis development. Because the disease pathology is anterior, the fundamental advantage of posterior instrumentation is that it can give adequate fixation using posterior unaffected vertebrae.[13]

In one or two steps, posterior instrumentation with anterior decompression and fusion can be performed. Although this surgery is more extensive, it has a higher morbidity when conducted in one stage. There is a danger of graft slippage and neurological deterioration while waiting for the second stage of stabilization. When the posterior fixation is done initially, it will simply be in situ stabilization followed by second stage decompression, resulting in minor kyphosis correction.[14]

As reported by Jain et al.,[2] a posterior approach utilizing solely the extrapleural technique is a successful choice. The extrapleural method allows for decompression of the spinal cord under direct vision, and is complemented by a stable posterior fixation that can be extended above and below if necessary. Due to stable posterior instrumentation, early mobilization is possible, avoiding the risks of prolonged recumbency.[8]

In a retrospective analysis of 70 patients with thoracic and lumbar tuberculosis, Garg and Somvanshi[3] compared the clinical, radiological, and functional outcomes of anterior versus posterior debridement and fixation. They found that while the anterior approach is equally good for debridement and stabilization, posterior instrumentation is better for kyphosis correction, and is associated with lesser morbidity and problems.

Shah et al.,[15] in case series of 50 patients with tuberculosis of the dorsal and lumbar spines, used posterior instrumentation to reduce and stabilize the unstable kyphotic zone. The practical consequence was much better in the posteriorly fixed group of patients, with an average Seybold and Bayley score of 14.66 (good).

Zeng et al.[16] used single stage, posterior transpedicular debridement, interbody fusion, and posterior fixation followed by chemotherapy for single-segment thoracic spinal tuberculosis with neurological impairments, which were sufficient.

Islam et al.[17] did an observational, follow-up study of 21 patients and concluded that the posterior approach is a minimum surgical intervention that encourages neurological recovery.

Patidar et al.[18] published a prospective study of 20 patients, which suggested that single stage posterior approach is safe and effective for management of dorsolumbar spine tuberculosis.

In our research, posterior stabilization and reconstruction of the spine by posterior and posterolateral fusion, as well as fusion with cage in certain cases, helped to correct the deformity and prevent its progression.

Conclusion

The posterior technique (extracavitary approach) allows for reasonable access to the lateral and anterior spaces of the cord, allowing for equally effective cord decompression. It's a less morbid method that avoids the complications of thoracotomy and laparotomy.

It allows for early mobilization and eliminates the issues associated with extended recumbency; which results in a better functional outcome as well as a considerable improvement in the sagittal plane's deformity correction.

The posterior approach is chosen due to its familiarity, simplicity, and lower rate of complications.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Lumbopelvic Muscle Mobility and Resistance and their Association with Musculoskeletal Pain in Ballet Dancers

Mobilidade e resistência muscular lombopélvica e associação com dor musculoesquelética em bailarinas

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Abstract

Objective The present study analyzes ankle mobility and lumbopelvic muscle mobility and resistance. In addition, it identifies factors associated with musculoskeletal pain in young ballet dancers.

Methods This is a quantitative, descriptive, cross-sectional study evaluating 14 ballet dancers aged 12 to 16 years old. We used the following instruments: a) Nordic Musculoskeletal Symptom Questionnaire (NSQ) for musculoskeletal pain assessment; b) leg lateral reach test, lumbar lock, and rotation test (for trunk mobility analysis) and lunge test (for ankle mobility evaluation); c) front bridge, lumbar extensor, and lumbar flexor muscles tests to assess lumbopelvic complex resistance.

Results The main complaints reported by ballet dancers were pain in the low back area and in the lower extremities, especially in the knee (57.1%). Those with low back pain had significantly lower lumbar mobility ($p = 0.05$) and lower ankle mobility on both sides ($p \leq 0.05$). Dancers with knee pain presented significantly lower muscular trunk extensor muscle resistance ($p = 0.05$).

Conclusions Our study revealed significant associations between the lumbopelvic complex function and musculoskeletal symptoms, supporting the implementation of preventive strategies.

Keywords
- dancing
- musculoskeletal pain
- low back pain

Study developed at the Universidade Federal do Pampa, Uruguaiana, RS, Brazil.

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Resumo

Objetivo Analisar a mobilidade e a resistência muscular lombopélvica e mobilidade de tornozelo, assim como identificar os fatores associados com dor musculoesquelética em bailarinas jovens.

Métodos Trata-se de um estudo quantitativo, descritivo e transversal que avaliou 14 bailarinas de 12 a 16 anos. Os seguintes instrumentos foram aplicados: a) Questionário Nórdico de Sintomas Osteomusculares (QNSO) para avaliação da dor musculoesquelética; b) *leg lateral reach test, lumbar lock* e *rotation test* (avaliação da mobilidade de tronco) e *lunge test* (avaliação da mobilidade de tornozelo); c) ponte frontal, extensores lombares e flexores lombares para avaliação da resistência do complexo lombopélvico.

Resultados A dor lombar e em membros inferiores, especialmente no joelho (57,1%), foram as principais queixas relatadas pelas bailarinas no presente estudo. As bailarinas avaliadas com dor lombar apresentavam significativamente menor mobilidade lombar ($p = 0,05$) e menor mobilidade de tornozelo em ambos os lados ($p \leq 0,05$). Entre as que apresentavam dores nos joelhos, a resistência muscular de extensores de tronco foi significativamente menor ($p = 0,05$).

Conclusões O presente estudo encontrou associações importantes entre a função do complexo lombopélvico e sintomas musculoesqueléticos e apoia a construção de estratégias preventivas neste contexto.

Palavras-chave

- dança
- dor musculoesquelética
- dor lombar

Introduction

Dance emerged due to the natural human need to express feelings; people danced even before speaking.[1] Although classical ballet originated in Renaissance Italy in the 1500s, it only gained strength in the following century, in France, under Louis XIV.[2] A dancer himself, Louis XIV founded the first ballet school in the world, beginning a technical improvement that led to the recognition of French as the official language of ballet.[3]

Ballet is different from other dance modalities, with specific physical fitness and skills requirements.[4] In addition, it uses "en dehors" (a 180° external rotation of the lower limbs), pointe shoe work, extreme joint ranges, prolonged isometrics, and high-impact repetitive movements, including jumping and twisting, resulting in biomechanics prone to injury.[5]

These features make classical ballet the dance with the highest technical requirements and the highest rate of injuries.[6] Ballet dancers can present several injuries throughout their careers due to biomechanical changes causing functional imbalance and directly affecting the proper maintenance of body structures.[7]

The high physical demand resulting from repetitive spinal flexion, hyperextension, and rotation was associated with high rates of lumbosacral discomfort.[8] This was shown by Smith et al.,[9] who found a 62% prevalence of lumbosacral pain, and by Henn et al.,[10] who reported a 57% rate of low back pain in nonprofessional dancers. Other authors also demonstrated high rates of muscle imbalance and spinal dysfunction in this population.[11] In addition, there is evidence of reduced physical conditioning concerning muscle strength in dancers compared with athletes from other modalities.[12]

These injuries seem conditioned to inefficient lumbopelvic movements, since ballet favors a force imbalance between the anterior and posterior trunk muscles due to an exacerbated agonist contraction of the lumbar region at a disadvantage to the abdominal antagonist group.[8,13] The core acts on the hip-pelvis-lumbar complex, providing strength control and static and dynamic stability; moreover, it is essential for proper trunk and lower limb movements. Therefore, changes in this region can cause long-term functional loss and disability, shortening the career of a ballet dancer.[14]

The present study assessed ankle mobility and lumbopelvic muscle mobility and resistance due to their strong influence on functional and sports demands. It also identified factors associated with musculoskeletal pain in young ballet dancers.

Materials and Methods

Study and sample

This is a quantitative descriptive cross-sectional study with a convenience sample of classical ballet dancers practicing in a studio in 2021. Previously-trained researchers performed the evaluations in June 2021, following all sanitary measures for COVID-19 prevention and control.

We invited 15 nonprofessional ballet dancers to participate in the study. Fourteen agreed to participate voluntarily and met the inclusion criteria. To participate in the study, the dancer had to meet the following criteria: a) female gender; b) age between 12 and 16 years old; and c) to practice ballet for at least 3 years with a minimum frequency of 2 classes per week. We chose this age group and attendance to obtain a minimum practice time. Exclusion criteria were the following: a) orthopedic injury in the previous 3 months; b)

neurological or rheumatic lesions or both attested by a medical report; and c) inability to perform the proposed tests.

We complied with all ethical precepts set forth by Resolution 466/12 of the Brazilian Health Council and the Declaration of Helsinki (2008). The institutional Research Ethics Committee approved the present project under opinion number 4.587.592. The ballet dancers and their legal guardians signed an informed consent form agreeing to participate in the research.

Procedures

Initially, the subjects answered a questionnaire for sample characterization, including age, time of ballet dancing (in years), use of pointe shoes, practice of other physical activity, and history of previous injuries. Then, the Nordic Musculoskeletal Symptom Questionnaire (NSQ), validated for use in Brazil, assessed the incidence of musculoskeletal disorders among the subjects. The NSQ is composed of questions regarding symptoms from all anatomical areas in the previous 12 months and in the 7 days preceding the interview.[15] It is worth mentioning that we only assessed symptoms occurring within 12 months.

The ballet dancers underwent mobility tests (trunk and ankle) and lumbopelvic muscular resistance tests at the dance studio before the beginning of the class so responses would not be influenced. The protocol was as follows:

- Anthropometric assessment: Determination of body mass with an electronic digital scale (Supermedy, with 180-kg capacity, and results given in kilograms) and height (in centimeters) using a measuring tape.
- Trunk mobility assessment with the following tests:
  - Leg lateral reach test: In this test, subjects were in a supine position with their arms at their sides. Then, they performed hip flexion with knee extension on one of the lower limbs, on the side to be tested, and directed it to the contralateral side, rotating the trunk without losing shoulder contact with the ground. The goal was to reach a previously marked measuring tape perpendicular to the popliteal fossa on the contralateral side and keep it at maximum reach for at least 5 seconds. The subjects performed this movement three times on each side (right and left) to determine the average maximum reach distance.[16]
  - Lumbar locked rotation test: In this test, the subjects were in a four bases position with knees and hips in maximum flexion. The elbows were flexed at 90 degrees and then placed in contact with the knees on the ground. Then, one hand was placed on the neck and the thoracic spine was rotated to the same side. We determined maximum rotation with a magnetic-based angle meter (inclinometer, Western) used for precise measurements from 0° to 90° positioned in the thoracic region between T1 and T2 at the end of the left- and right-sided rotation.[17]
- Lunge test: This test assessed ankle dorsiflexion range of motion (ROM). The subjects stood in front of a wall with a measuring tape fixed to the floor. The hands and contralateral foot were in a comfortable position. The second metatarsal of the assessed foot was 10 cm away from the wall. Then, the subject flexed the ipsilateral knee, leaning against the wall and keeping the heel in contact with the floor. If the dancer could rest her knee easily on the wall, the second metatarsal was moved 1 cm backward, and so on, until the ankle was at its maximum dorsiflexion. On average, there were 3 attempts, with 1-minute intervals between them.[18]
- Evaluation of the muscular resistance of the lumbopelvic complex: a smartphone timed all tests, determining the maximum time sustained during exercises. We selected the following tests:
  - Front bridge: We chose this test because it requires both abdominal and lumbar extensor muscle work at the same time, allowing the assessment of muscle strength and synergy. In the prone position, with elbows flexed at 90 degrees, shoulder-width apart, hips elevated from the stretcher, and feet supported only with the fingers, we asked subjects to form a straight line with suspended shoulders, hips, and ankles.[19]
  - Lumbar flexor muscles: We asked the subjects to seat down with hips and knees flexed at 90° and the trunk forming a 60° angle with the stretcher.[19]
  - Lumbar extensor muscles: Subjects were in the prone position, with the lower extremity of the body remaining fixed on the stretcher using a Velcro strip placed under the greater trochanter. The trunk remained elevated with no support, and the arms remained crossed in front of the chest.[19]

Data analysis used descriptive statistical procedures with mean, standard deviation (SD), and absolute and relative frequencies determination. The Pearson test correlated numerical variables. Variables categorization used median values. The Fisher exact test analyzed the association between categorical variables. IBM SPSS Statistics for Windows, version 21.0, performed all tests considering a significance level of 5%.

Results

Fourteen ballet dancers (age: 13.5 ± 1.55 years old) participated in the study. ►**Table 1** summarizes their descriptive data.

In addition to ballet, 9 (64.3%) dancers reported practicing another type of physical activity. Four (28.6%) did weight training, whereas 2 did functional training (14.3%). Most dancers reported a previous injury (57.1%), with ankle sprains (14.3%) and low back pain (14.3%) as the most frequent. Five dancers (35.7%) underwent physical therapy due to these injuries. Four (28.6%) dancers reported using pointe shoes in the previous 12 months of classes.

►**Fig. 1** shows the frequency distribution of musculoskeletal disorders reported by the participants in the last 12 months. Most dancers complained of knee pain (57.1%).

Table 1 Sample characterization and descriptive variables

Variables	Mean value	Standard deviation
Age (years old)	13.5	1.55
Mass (kg)	47.7	6.25
Height (cm)	157.0	4.20
Ballet time (years)	6.7	1.89
Classes per week (days)	2.7	0.46
Lumbar spine mobility, right side (cm)	69.8	5.47
Lumbar spine mobility, left side (cm)	80.7	31.56
Thoracic spine mobility, right side (°)	74.5	4.02
Thoracic spine mobility, left side (°)	72.6	6.31
Ankle mobility, right side (cm)	11.7	1.63
Ankle mobility, left side (cm)	12.0	1.88
Lumbopelvic muscle resistance (seconds)	107.9	37.75
Trunk flexor muscle resistance (seconds)	233.7	217.15
Trunk extensor muscle resistance (seconds)	148.3	47.34

Moreover, 42.9% of the dancers reported pain in the lumbar spine, the hip, and the ankles within the previous year.

The correlation between mobility measures and muscular resistance revealed that lumbar mobility has a significant moderate correlation with lumbopelvic muscle resistance ($r = 0.682$; $p = 0.007$). However, there was an inversely proportional and significant correlation between thoracic mobility and trunk extensor muscle resistance ($r = -0.640$; $p = 0.014$). The analysis of the categorical variables of mobility and muscular resistance showed a single significant association between left ankle mobility and trunk extensor muscle resistance ($p = 0.05$), since 85.7% of the ballet dancers with higher muscle resistance had less mobility in this segment.

►**Table 2** shows the association between mobility and muscular resistance and musculoskeletal disorders at the lumbar spine and in the lower limbs (hip, knee, and ankle). Ballet dancers with low back pain had significantly lower left lumbar mobility ($p = 0.05$), lower right ankle mobility ($p = 0.05$), and lower left ankle mobility ($p < 0.01$). On the other hand, ballet dancers with hip pain presented higher right lumbar mobility ($p = 0.05$), and those with ankle pain had higher left thoracic mobility ($p = 0.05$). Dancers with knee pain presented significantly lower trunk extensor muscle resistance ($p = 0.05$).

Discussion

In the present study, an expressive percentage of ballet dancers reported pain in the lumbar spine and in the lower limbs in the previous year, especially in the knee (57.1%),

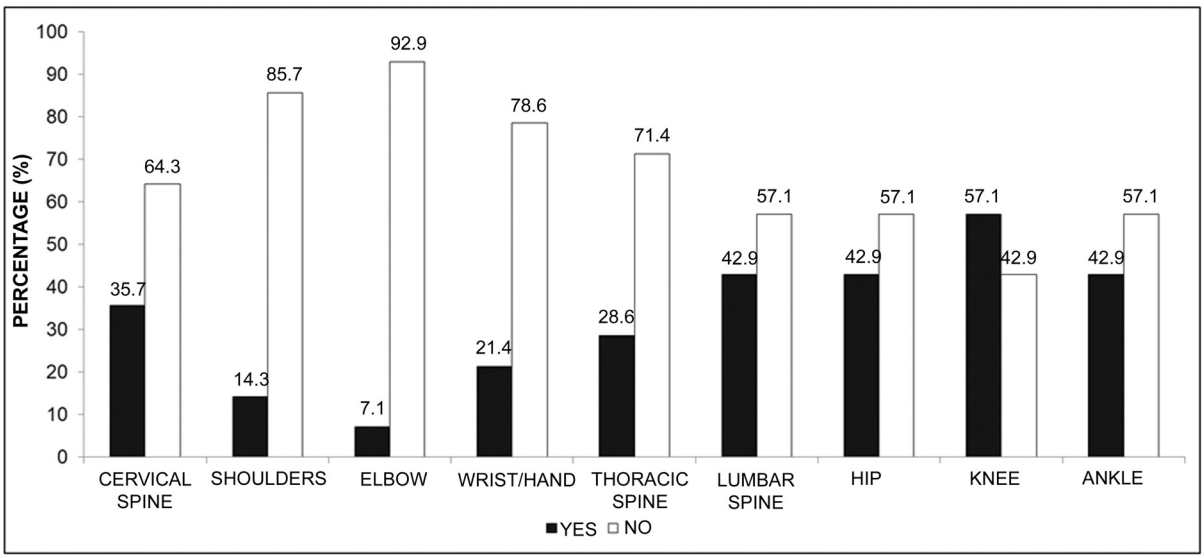


Fig. 1 Frequency distribution of musculoskeletal disorders presented by ballet dancers in the last 12 months.

Table 2 Association between mobility and lumbopelvic resistance variables with the most prevalent musculoskeletal symptoms

Variable	Lumbar spine $n=6$		Hip $n=6$		Knee $n=8$		Ankle $n=6$	
	Yes (%)	*p-value*	Yes (%)	*p-value*	Yes (%)	*p-value*	Yes (%)	*p-value*
Lumbar spine mobility, right side								
Lower mobility	50.0	0.70	16.7	0.05*	37.5	0.29	50.0	0.70
Higher mobility	50.0		83.3		62.5		50.0	
Lumbar spine mobility, left side								
Lower mobility	83.3	0.05*	66.7	0.29	50.0	0.70	33.3	0.29
Higher mobility	16.7		33.3		50.0		66.7	
Thoracic spine mobility, right side								
Lower mobility	33.3	0.59	33.3	0.59	37.5	0.40	0.0	0.07
Higher mobility	66.7		66.7		62.5		100.0	
Thoracic spine mobility, left side								
Lower mobility	50.0	0.70	50.0	0.70	50.0	0.70	16.7	0.05*
Higher mobility	50.0		50.0		50.0		83.3	
Ankle mobility, right side								
Lower mobility	83.3	0.05*	66.7	0.29	62.5	0.29	50.0	0.70
Higher mobility	16.7		33.3		37.5		50.0	
Ankle mobility, left side								
Lower mobility	100.0	< 0.01*	66.7	0.47	50.0	0.47	66.7	0.47
Higher mobility	0.0		33.3		50.0		33.3	
Lumbopelvic muscle resistance								
Lower force	50.0	0.70	66.7	0.29	50.0	0.70	66.7	0.29
Higher force	50.0		33.3		50.0		33.3	
Trunk flexor muscle resistance								
Lower force	50.0	0.70	66.7	0.29	50.0	0.70	50.0	0.70
Higher force	50.0		33.3		50.0		50.0	
Trunk extensor muscle resistance								
Lower force	33.3	0.29	50.0	0.70	75.0	0.05*	50.0	0.70
Higher force	66.7		50.0		25.0		50.0	

followed by the lumbar region, hip, and ankle (all with 42.9%). In addition, ankle sprain and low back pain were the most prevalent previous injuries in these subjects. Our findings corroborate those of Costa et al.,[6] who reported that ankle sprain was the most frequent injury among professional (69.8%) and nonprofessional ballet dancers (42.1%).

Other authors, such as Hendry et al.,[20] have demonstrated that lower limb injuries among adolescent dancers are significantly more frequent in comparison with athletes from different modalities, such as artistic gymnastics, within the same age group. Ratifying these findings, Lampe et al.[21] analyzed the most painful musculoskeletal regions in amateur dancers, reporting the knee, followed by the lumbar spine, as those with a higher incidence of pain. Moreover, Hendry et al.[20] proposed that this results from the excessive use of the lower limbs during classes, in repetitive jumping and landing movements, indicating a causal nexus between these factors, and explaining the high incidence of musculoskeletal symptoms in the lower extremities of dancers.

Another striking aspect is the use of pointe shoes due to their reduced impact absorption capacity.[22] In addition, Bickle et al.[23] suggested an accentuation of the ground reaction force when non-professional ballet dancers wear pointe shoes. Thus, because of the increased postural sway caused by pointe shoes, which is common in younger ballet dancers, their use can contribute to the onset of musculoskeletal pain in the lower limbs.[22] Hendry et al.[20] pointed out that the age group studied is within their peak growth and skeletal maturation, predisposing the development of biomechanical misalignments, in particular dynamic valgus. These misalignments generate predictive injury mechanisms during the execution of the movements required in dance.

Our findings are consistent with those of Swain et al.,[24] who found a high prevalence of low back pain in a sample of ballet dancers > 12 years old. These authors explain that low back

pain may be associated with incorrect technique execution and muscle imbalances in the lumbopelvic region, leading to spinal instability during specific dance movements.

Regarding lumbar spine mobility, we noticed a moderately significant correlation with lumbopelvic resistance. In contrast, other authors demonstrated the importance of lumbopelvic stability for the correct execution of trunk and lower limb movements, especially in athletic activities.[25] Moreover, Bobály et al.[26] associated lumbopelvic strength with greater trunk mobility, improved flexibility, proper postural alignment, correct technique execution, and better performance in young ballet dancers.

Our study revealed that some factors relate to painful lumbar region events in ballet dancers, including lower left lumbar mobility and bilateral reduced ankle mobility. With similar outcomes, Mullerpatan et al.[27] associated low back pain with lower ankle mobility. The same study proposes that the hip, knee, and ankle are interconnected segments, components of a kinetic chain. Therefore, any change in this segment alters the kinematics of the lower limbs, directly influencing lumbopelvic performance.

Furthermore, ballet dancers with knee pain had significantly lower trunk extensor muscle resistance. Chaudhari et al.[28] also detected this association in a study identifying a reduced lumbopelvic stability in young athletes with increased patellofemoral contact pressure during running which could cause joint symptoms and, consequently, pain, such as the patellofemoral pain syndrome. Trompeter et al.[29] reiterate that the stability of the lumbopelvic complex refers to the ability of the body to transfer force control from the proximal segment to the distal components. However, ballet dancers have little central stability, and they may present biomechanical imbalances that indirectly affect the lower limbs. These imbalances impair functional demands and can culminate in musculoskeletal pain or injury.

Our study found some negative associations between trunk extensor muscular resistance and mobility, as the ballet dancers with less resistance in these muscles had greater thoracic and ankle mobility. These findings may be associated with compensatory factors involving extreme ranges of motion, as explained by Chan et al.[30] These authors stated that excessive joint mobility accompanies more fragile tendinous and ligament structures, contributing to a delay in soft tissue responses to the effects of training. This delay impairs the muscle strengthening process and makes the dancer more prone to injuries. Moreover, Steinberg et al.[31] reported that the prevalence of joint hypermobility was significantly higher in dancers compared with their control group, composed of nondancers.

On the other hand, our study found that dancers with hip pain had greater lumbar mobility, whereas those with ankle pain present higher thoracic mobility. Other investigations suggest that young ballet dancers seek to overcome individual limitations and mitigate technical deficiencies through compensations, including increased hip anteflexion angles and excessive lumbar and thoracic mobility.[32] Therefore, excess joint mobility has been associated with movement dysfunction throughout the kinetic chain and with an increased risk of musculoskeletal pain and injury.[33]

Although we obtained relevant findings, some limitations must be highlighted, such as the reduced number of ballet dancers evaluated and the lack of reference values for the tests applied. The latter makes it difficult to discuss the results and perform a more reliable sample comparison.

Conclusion

Based on the results, we can conclude that pain in the lower back and in the lower limbs, especially in the knee, were the main complaints reported by the ballet dancers in our study. Subjects with low back pain presented lower lumbar and ankle mobility, whereas those with knee pain had lower trunk extensor muscle resistance. These findings indicate critical associations between the lumbopelvic complex and lower limb biomechanics.

Therefore, our study draws attention to the implementation of preventive interventions aimed at the lumbopelvic complex to reduce the rate of musculoskeletal pain and injuries in dancers and improve their performance and quality.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Proprioception Analysis following Anterior Cruciate Ligament Reconstruction using Stabilometry: A Prospective, Longitudinal Study

Análise de propriocepção por estabilometria após a reconstrução do ligamento cruzado anterior: Um estudo prospectivo e longitudinal

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Abstract

Objective Commonly used methods for measuring proprioception have resulted in conflicting reports regarding knee proprioception with anterior cruciate ligament (ACL) rupture and the influence of ACL reconstruction.

Methods One hundred subjects (50 patients with radiologically and arthroscopically confirmed unilateral ACL rupture and 50 normal controls) were assessed with regards to proprioception using dynamic single-leg stance postural stabilometry. Instrumented knee ligament laxity and knee outcome scores were also measured. Of the 50 patients in the ACL group, 34 underwent reconstruction and were reassessed postoperatively.

Results There was a significant proprioceptive deficiency in the ACL group compared with their contralateral knee ($p < 0.001$) and to the control group ($p = 0.01$). There was a significant improvement in knee proprioception following ACL reconstruction compared to preoperative findings ($p = 0.003$). There was no correlation between ligament laxity measurements and outcome scores. A significant correlation was found preoperatively between outcome scores and proprioception measurements. This correlation was not found post-operatively. Pre-operative proprioception testing had a significant correlation ($r = 0.46$) with post-operative proprioception ($p = 0.006$).

Keywords
- anterior cruciate ligament
- mechanoreceptors
- proprioception
- stabilometry
- knee ligament laxity
- knee outcome scores

* *Commonly used methods for measuring procarionte have resulted in conflicting reports regarding knee proprioception with anterior cruciate ligament (ACL) rupture and the influence of ACL reconstruction.*

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Conclusion Patients with an ACL rupture had a proprioceptive deficit which improved following ligament reconstruction. Knee outcome scores had a better correlation with proprioception than ligament laxity. Proprioception may be a superior objective measure than ligament laxity in quantifying functional knee deficits and outcomes in patients with ACL ruptures.

Level of Evidence III Therapeutic Study; Prospective Longitudinal Case-Control Study.

Resumo

Objetivo O objetivo deste estudo foi avaliar a propriocepção do joelho por meio de estabilometria em pacientes com ruptura do ligamento cruzado anterior (LCA) antes e depois da reconstrução e correlacionar esses achados a resultados de testes instrumentados de lassidão ligamentar e desfechos clínicos.

Métodos A propriocepção de 100 indivíduos (50 pacientes com ruptura unilateral do LCA confirmada à radiologia e artroscopia e 50 controles normais) foi avaliada por estabilometria postural dinâmica em apoio unipodal. A lassidão ligamentar do joelho instrumentado e suas pontuações de desfechos também foram medidas. Dos 50 pacientes do grupo LCA, 34 foram submetidos à reconstrução e reavaliados no período pós-operatório.

Resultados O grupo LCA apresentou deficiência proprioceptiva significativa em relação ao joelho contralateral ($p < 0{,}001$) e ao grupo controle ($p = 0{,}01$). A propriocepção do joelho melhorou de maneira significativa após a reconstrução do LCA em relação aos achados pré-operatórios ($p = 0{,}003$). Não houve correlação entre as medidas de lassidão ligamentar e as pontuações de desfechos. Além disso, observamos uma correlação significativa entre as pontuações de desfechos e as medidas de propriocepção antes da cirurgia. Essa correlação não foi detectada no período pós-operatório. O teste pré-operatório de propriocepção teve correlação significativa ($r = 0{,}46$) com a propriocepção pós-operatória ($p = 0{,}006$).

Conclusão Os pacientes com ruptura do LCA apresentaram déficit proprioceptivo que melhorou após a reconstrução ligamentar. As pontuações de desfecho do joelho tiveram melhor correlação à propriocepção do que a lassidão ligamentar. A propriocepção pode ser uma medida objetiva superior à lassidão ligamentar na quantificação de déficits funcionais e desfechos do joelho em pacientes com ruptura do LCA.

Nível de Evidência III Estudo Terapêutico; Estudo de Caso-Controle Longitudinal Prospectivo.

Palavras-chave
- ligamento cruzado anterior
- mecanorreceptores
- propriocepção

Introduction

The central nervous system receives a collective neural input from peripheral receptors found within joints, ligaments, tendons, muscles, and skin.[1–4] The anterior cruciate ligament (ACL) contains mechanoreceptors and free nerve endings. The latter are more abundant and function as nociceptors, reacting to joint inflammation and pain stimuli. The mechanoreceptors found in the ACL include Pacinian corpuscles (quick adapting receptors activated by compression and mediate kinesthesia), Ruffini endings, and Golgi tendon organs (slow adapting receptors activated by stretch and mediate joint position sense).[4–6] These receptors signal potentially harmful deformations of the ligaments and knee joint via proprioceptive feedback which constitutes the afferent arc input. Protective reflexes intended to resist the injurious movements, such as reflex muscular stabilization, are initiated via efferent responses (Hilton's law).[6]

In addition to its proprioceptive role, the ACL is the primary restraint to anterior tibial translation and a major secondary restraint to internal rotation, thereby contributing to the normal kinematics of the knee.[7–10] Rupture of the ACL can lead to mechanical instability resulting in pathological displacement of the tibia relative to the femur. This may give rise to progressive instability, which can result in meniscal tears and early arthritis.[11–13] ACL reconstruction can be performed in order to restore mechanical knee stability. Following reconstruction, there are some patients who have a persistent laxity on clinical examination but, nonetheless, return to their preinjury level of activities.

Table 1 Demographics of subjects

	ACL group (n = 50)	Control group (n = 50)
Mean age (yrs) (SD)	30 (9)	25 (5)
Male: female	36:14	35:15
Injured knee (right: left)	24:26	—
Mean height (m) (SD)	1.72 (0.1)	1.75 (0.1)
Mean weight (kg) (SD)	78.1 (14.4)	76.1 (14.4)
Mean BMI* (kg/m^2) (SD)	26.2 (3.8)	24.6 (3.4)

Abbreviations: ACL, anterior cruciate ligament; BMI, body mass index; SD, standard deviation.

There are also some patients who have a clinically stable knee postoperatively but remain unsatisfied and continue to perceive a feeling of instability in their knee. Proprioception testing may be a superior end-point of quantifying a successful outcome following ACL reconstruction than clinically observed ligament laxity testing.

We conducted a prospective longitudinal study analyzing knee proprioception using dynamic single-leg stance postural stabilometry. The primary aim of the study was to evaluate if a proprioceptive deficit exists in patients with ACL ruptures, either compared to their contralateral knee or to normal controls. The secondary aim of the study was to investigate if there was an improvement following ACL reconstruction if a preoperative proprioceptive deficit was present. The tertiary aim of the study was to assess if a correlation existed between proprioceptive function, instrumented ligament laxity testing, and clinical outcome measures.

Materials and Methods

Full approval was received for the study from the Research Ethics Committee and the Research Governance Committee. All subjects signed informed consent forms to participate. This therapeutic study is a prospective longitudinal case-control study which formed part of the first author's doctorate thesis.

There was a total of 100 subjects recruited to the study. ►**Table 1** shows their demographic details. The mean time from injury to clinic review for the ACL group was 63 weeks (SD = 59). ►**Fig. 1** shows the mechanism of injury of the ACL group. An ACL rupture was diagnosed by clinical history and examination as well as magnetic resonance imaging (MRI) scan of the injured knee for all patients in the ACL group. The diagnosis was confirmed at the time of knee arthroscopy. The patients in the ACL group had a normal contralateral knee confirmed by clinical history and examination. ►**Fig. 2** illustrates the flow of the patients in the ACL group through the study. Four patients with delayed surgical intervention postponed their operation for personal reasons (i.e., work or university commitments). One patient was recruited to the ACL group and underwent all the assessments except for the proprioception analysis as the equipment was unavailable at the time of the patient's attendance. However, the data for the remaining assessments that they did undergo are still included in the relevant

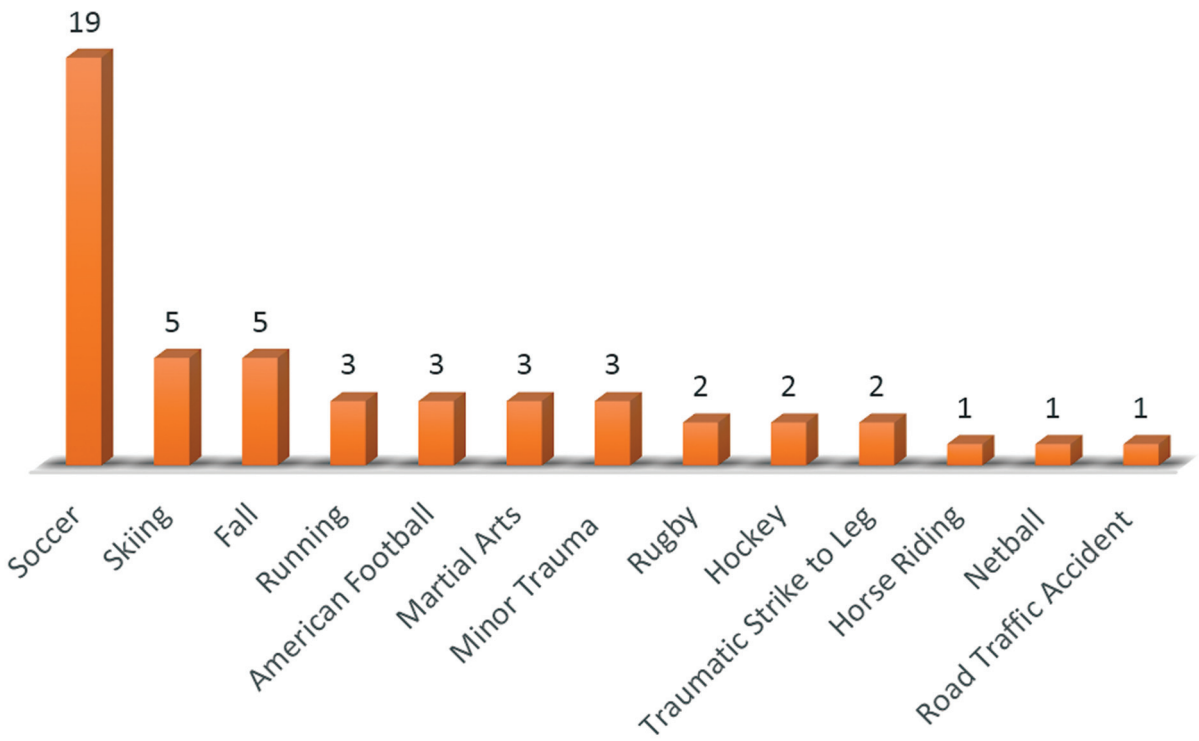


Fig. 1 Mechanism of injury ACL group (n = 50),

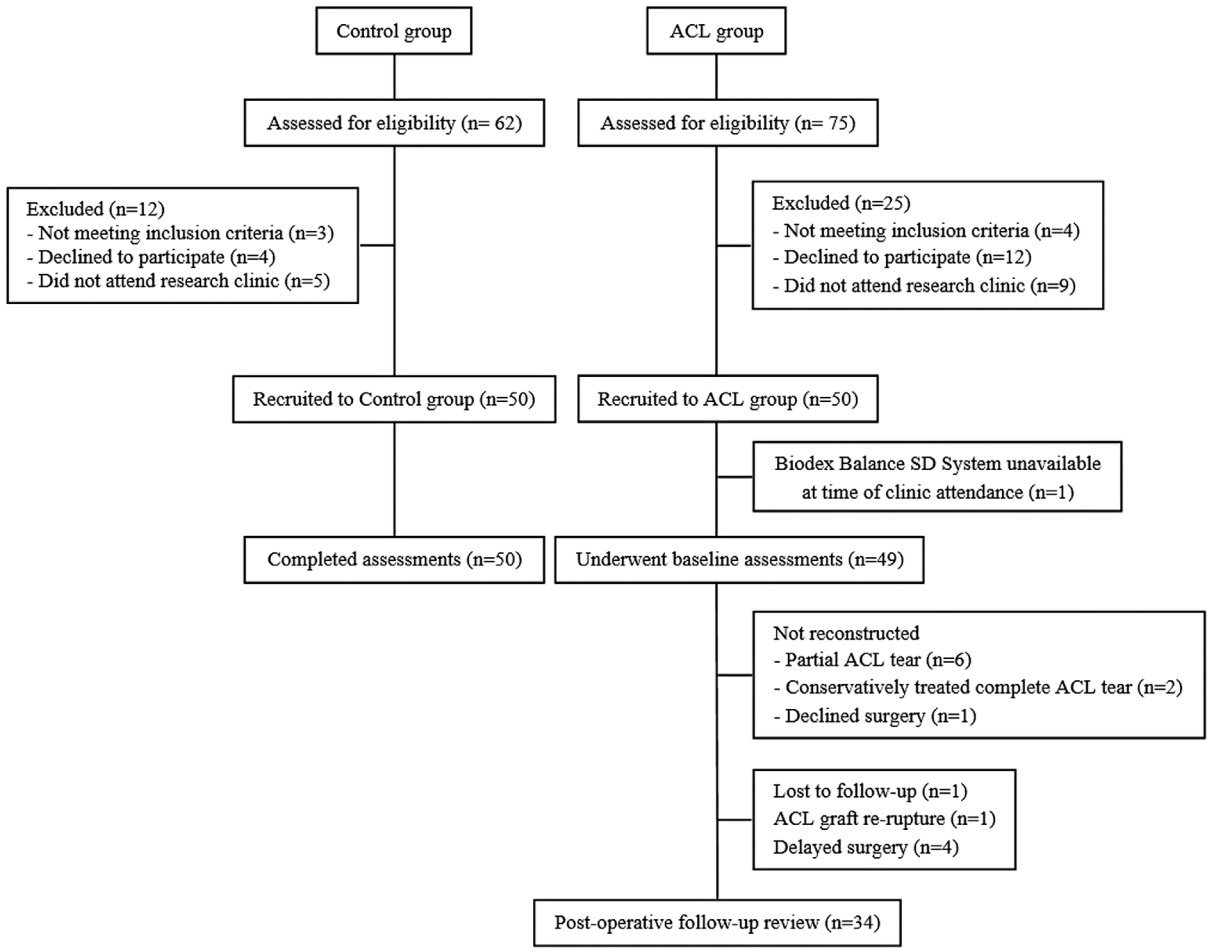


Fig. 2 Flow of subjects through the study.

sections. Of the 34 patients who underwent ACL reconstruction, 25 had an ipsilateral middle third bone-patella tendon-bone autograft, and 9 had an ipsilateral quadrupled hamstring autograft. At the time of surgery in the ACL group, 11 patients were found to have a concomitant medial meniscal tear, 8 patients had a lateral meniscal tear, and 11 subjects had both a medial and a lateral meniscal tear. All patients with concurrent meniscal tears also underwent a partial meniscectomy. None of the patients had significant associated articular cartilage lesions. The mean time to follow-up was 14 weeks (SD = 4) following surgery.

►**Fig. 2** illustrates the flow of the subjects in the control group through the study. All the participants in the control group had normal knees confirmed by clinical history and examination of both knees as well as an MRI scan of one knee. The control group data was also used as the normal controls in other published studies.[14,15]

Subjects who were 16 to 45 years of age were included. Participants were excluded from the study if there was a concomitant posterior cruciate ligament (PCL), medial collateral ligament (MCL) or lateral collateral ligament (LCL) tear of the knee, significant history of ankle or hip pathology, lumbar spine symptoms (including radiculopathy in either limb), neurological or vestibular disease, diabetes, or regular



Fig. 3 The Rolimeter knee arthrometer **(A)** Lachman test **(B)** Anterior drawer test.

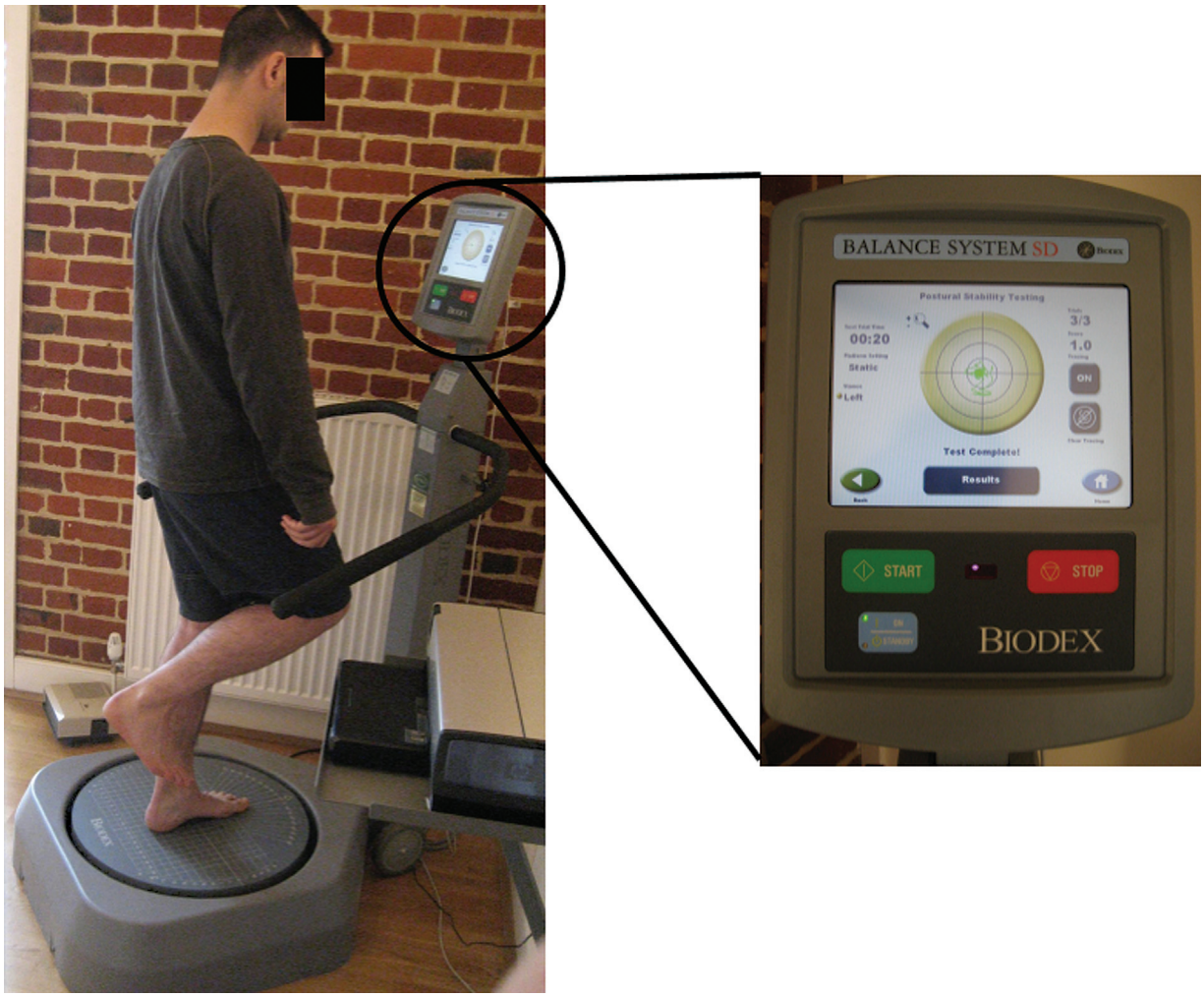


Fig. 4 Single-leg stance postural stability testing using the Biodex Balance SD System.

use of opiate analgesics. In addition, subjects were excluded from the control group if there was a significant history of any knee pathology.

The Rolimeter knee arthrometer (Aircast Incorporated, Summit, NJ, USA) was used to measure quantitatively the anterior displacement of the tibia relative to the femur of both knees in both groups. The maximum manual instrumented test was used to measure ligament laxity in both the Lachman test (20° knee flexion) and the anterior drawer test (90° knee flexion) (►**Fig. 3**). The registered anterior displacement (in mm) was used for statistical analysis.

All subjects of both groups were assessed using the Tegner activity score[16] and the Lysholm knee score.[16]

The Biodex Balance SD System (Biodex Medical Systems Incorporated, Shirley, NY, USA) was used to quantitatively measure postural stability (►**Fig. 4**). It has been validated for its use in assessing dynamic single-leg postural stability.[17–19] Stabilometry is an accepted method of measuring proprioception in the ACL deficient knee.[20,21] The Biodex Balance SD System consists of a multiaxial moveable platform which computes an output in the form of an overall stability index (OSI). A low score indicates that the subject has good postural stability (and, therefore, good proprioception), and a high score reflects poorer stability and proprioception. Each leg in all the participants (in bare feet) was assessed 3 times for a duration of 20 seconds for each test period. The computer output for each leg was calculated from the average of the three tests. The mean OSI result was used as the quantitative measure of proprioception for the purpose of statistical analyses.

Statistical Analysis

A *post-hoc* power calculation for this study was derived from the results of the longitudinal within-group analysis of the ACL group injured knee log (OSI) (primary outcome) as detailed in ►**Table 4**. The sample size of 34 subjects based on a conventional type I error of 5% with a within-group mean difference of 0.23 and a within-group standard deviation of 0.40 yielded a statistical power calculation of 90.2% for this study. All data variables for both groups displayed a normal distribution (verified by both plotted histograms and the Shapiro-Wilks test) except for the OSI measurements (negatively skewed distribution). Data transformation was

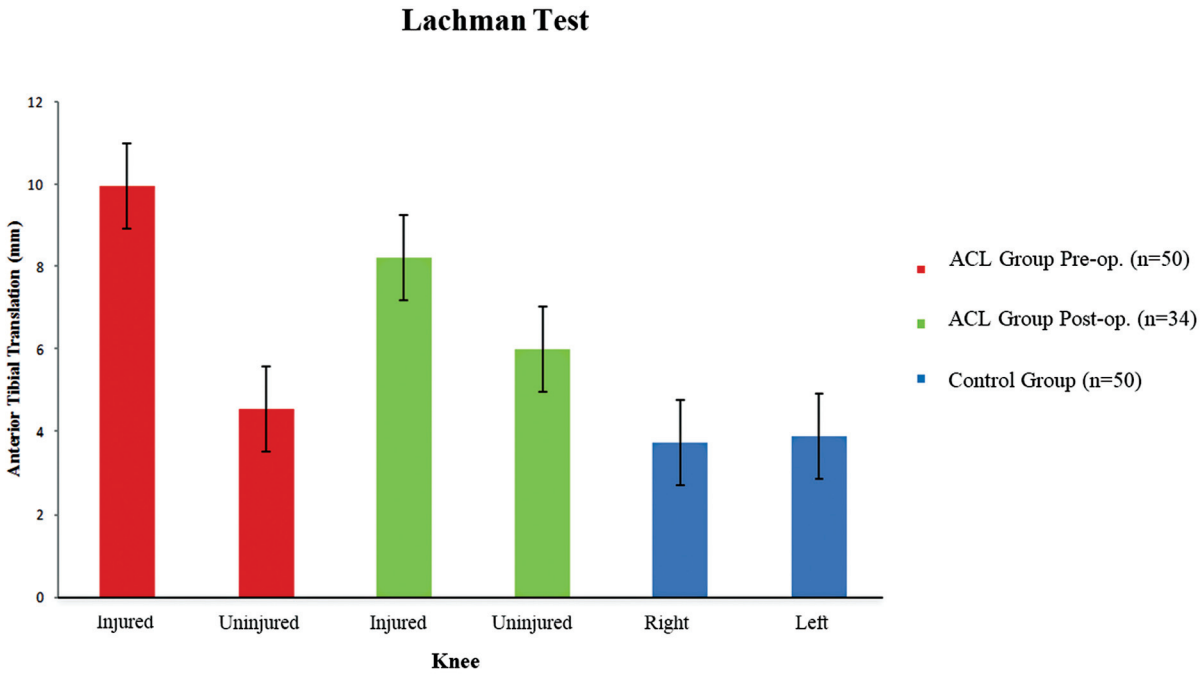


Fig. 5 Instrumented ligament laxity measurement for the Lachman test displaying means and standard errors.

implemented using the natural logarithm following which the log (OSI) data demonstrated a normal distribution and was used for the purposes of statistical calculations using the appropriate parametric tests. The level of statistical significance was set at $p < 0.05$. Statistical analysis was performed using the SPSS for Windows, version 25.0 (IBM Corp.,

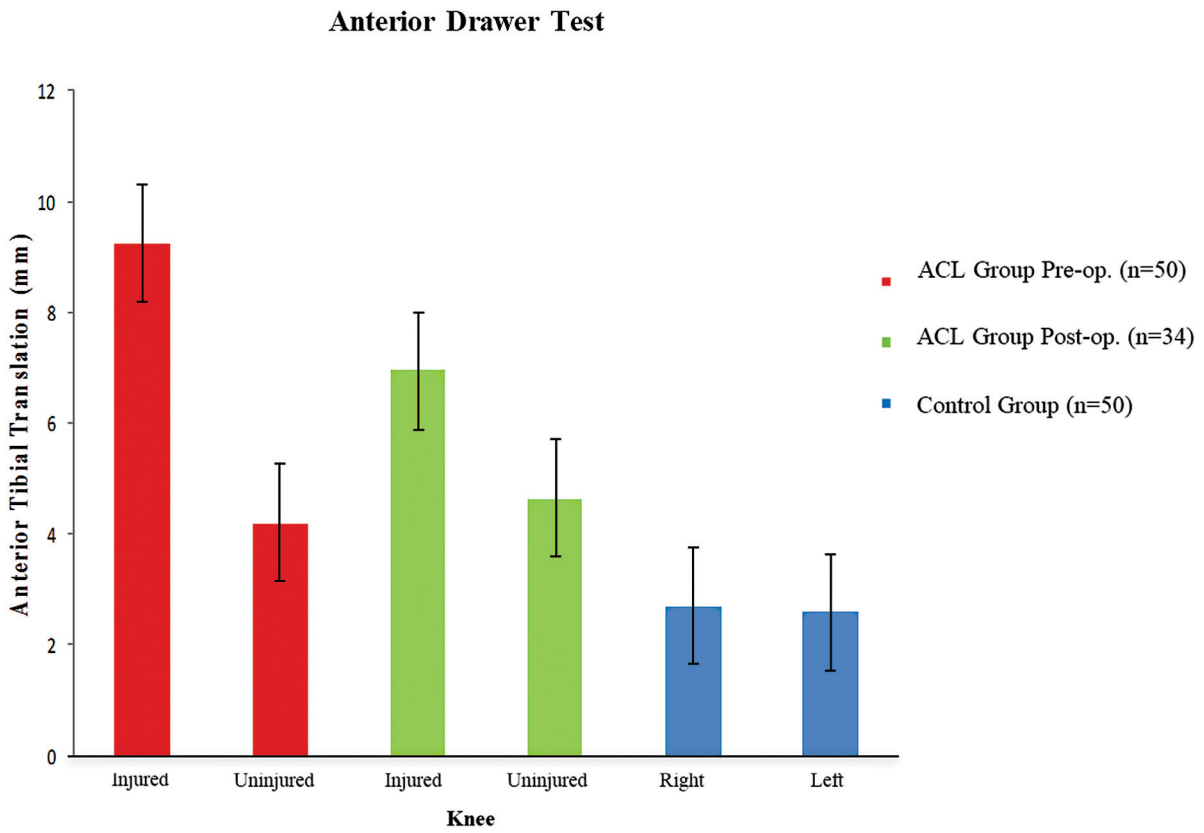


Fig. 6 Instrumented ligament laxity measurement for the anterior drawer test displaying means and standard errors.

Table 2 Statistical analysis of instrumented ligament laxity measurements

	Uninjured knee[a]	Control group[b]	Injured knee postop[a]
	p-value (95%CI)	*p*-value (95%CI)	*p*-value (95%CI)
Lachman			
Injured knee preop.	< 0.001* (4.6, 6.2)	< 0.001* (5.2, 7.3)	< 0.001* (1.0, 2.5)
Injured knee postop.	< 0.001* (1.4, 3.1)	< 0.001* (3.7, 5.4)	—
Anterior Drawer			
Injured knee preop.	< 0.001* (4.3, 5.8)	< 0.001* (5.4, 7.8)	0.001* (0.9, 3.3)
Injured knee postop.	< 0.001* (1.5, 3.1)	< 0.001* (3.4, 5.2)	—

Abbreviation: 95% CI, 95% confidence interval.
[a]Within-group comparison; paired Student *t*-test
[b]Between-group comparison; independent-sample Student *t*-test
*Statistically significant at <0.05 level

Table 3 ACL group knee outcome scores

	Preoperative	Postoperative	*p*-value[a] (95% CI)
	Mean (SD)	Mean (SD)	
Lysholm	71.7 (12.8)	85.3 (10.5)	< 0.001 (8,18–19,18)
Tegner	3.3 (1.2)	4.1 (0.2)	0.006 (0,23–1,28)
	Preinjury	Postoperative	
Tegner	6.7 (1.3)	4.1 (0.2)	< 0.001 (2,11–3,31)

Abbreviations: 95% CI, 95% confidence interval; SD, standard deviation.
[a]Within-group comparison; paired Student *t*-test
*Statistically significant at $p < 0.05$ level

Armonk, NY, USA). The power calculation was performed using the Minitab statistical software version 19 (Minitab LLC, State College, PA, USA).

Results

►**Figs. 5** and **6** illustrate the findings of the instrumented ligament laxity measurements of both the Lachman test and the anterior drawer test respectively, and ►**Table 2** shows the results of their statistical analyses. There was no significant difference between the right and left knees of the control group for either the Lachman test ($p = 0.53$; 95% CI -0.50, 0.26) or the anterior drawer test ($p = 0.32$; 95% CI -0.10, 0.30). There was a significant difference of both tests when comparing the injured knee of the ACL group preoperatively to their uninjured knee and that of the control group. Following surgery, the injured knee of the ACL group showed a significant improvement compared to preoperative findings but still had a significant difference compared to their uninjured knee and the control group.

►**Table 3** shows the results of the knee outcome scores for the ACL group. There was a significant improvement postoperatively of both the Tegner activity score and the Lysholm score. A significant difference persisted between the preinjury and postoperative Tegner activity scores.

►**Table 4** shows the proprioception measurements for the ACL and the control groups. The results of their statistical analyses are shown in ►**Table 5**. There was no significant difference found between the right and left knees of the control group ($p = 0.42$; 95% CI -0.04, 0.10). There was no significant difference found of the uninjured knee in the ACL group between preoperative and postoperative results ($p = 0.28$; 95% CI -0.05, 0.19). There was a statistically

Table 4 Means and standard deviations of stabilometry measurements (log [OSI])

Group	Mean (SD)
ACL group preoperatively (n = 49)	
Injured knee	0.70 (0.45)
Uninjured knee	0.46 (0.35)
ACL Group postoperatively (n = 34)	
Injured knee	0.47 (0.40)
Uninjured knee	0.42 (0.39)
Control group (n = 50)	
Right knee	0.49 (0.35)
Left knee	0.52 (0.34)

Abbreviations: OSI, overall stability index; SD, standard deviation.

Table 5 Statistical analysis of stabilometry measurements (log [OSI])

	Uninjured knee[a]	Control group[b]	Injured knee postop[a]
	p-value (95%CI)	*p*-value (95%CI)	*p*-value (95%CI)
Injured knee preop.	< 0.001* (0.14, 0.34)	0.01* (0.05, 0.38)	0.003* (0.10, 0.42)
Uninjured knee	—	0.73 (-0.16, 0.12)	—
Injured knee postop.	0.25 (-0.03, 0.13)	0.85 (-0.18, 0.15)	—

Abbreviations: 95% CI, 95% confidence interval; OSI, overall stability index.
[a]Within-group comparison; paired Student *t*-test
[b]Between-group comparison; independent-sample Student *t*-test
*Statistically significant at $p < 0.05$ level

Table 6 Correlations between knee outcome scores, stabilometry and instrumented ligament laxity measurements of the injured knee of the ACL group

	*Pre*operative			*Post*operative		
	Log (OSI)	Lachman	Anterior drawer	log (OSI)	Lachman	Anterior drawer
	r / *p*-value[a]	r / *p*-value[a]	r / *p*-value[a]	r / *p*-value[a]	r / *p*-value[a]	r / *p*-value[a]
	95% CI	95% CI	95% CI	95% CI	95% CI	95% CI
Lachman	0.07 / 0.630	——	——	-0.24 / 0.180	——	——
	(-0.22, 0.34)			(-0.53, 0.11)		
Anterior drawer	-0.07 / 0.640	——	——	0.09 / 0.620	——	——
	(-0.34, 0.22)			(-0.26, 0.42)		
Tegner	-0.42 / 0.003*	0.02 / 0.890	0.13 / 0.370	-0.12 / 0.500	-0.19 / 0.2900	-0.15 / 0.4200
	(-0.63, -0.16)	(-0.27, 0.30)	(-0.16, 0.40)	(-0.44, 0.23)	(-0.50, 0.16)	(-0.46, 0.20)
Lysholm	-0.35 / 0.016*	-0.25 / 0.090	-0.20 / 0.180	-0.09 / 0.610	-0.22 / 0.230	-0.02 / 0.920
	(-0.58, -0.07)	(-0.50, 0.04)	(-0.46, 0.09)	(-0.42, 0.26)	(-0.52, 0.13)	(-0.36, 0.32)

Abbreviations: 95% CI, 95% confidence interval; OSI, overall stability index.
[a]Pearson product moment correlation analyses.
*Statistically significant at $p < 0.05$ level.

significant difference between the injured knee of the ACL group preoperatively when compared to their uninjured knee and also to the control group. There was no significant difference found between the uninjured knees of the ACL and the control groups. There was a statistically significant improvement in proprioception of the injured knee in the ACL group compared to preoperative findings following ACL reconstruction, to the extent that no significant difference was found between their operated knee and either their uninjured knee or the control group.

►**Table 6** shows the results of the Pearson correlation analyses between knee outcome scores, stabilometry and ligament laxity measurements of the injured knee of the ACL group. Preoperatively, proprioception measurements had a significant (inversely proportional) correlation with both knee outcome scores. A higher knee outcome score (i.e., better function) was associated with a lower log (OSI) score (i.e., good proprioception). There was no significant correlation between ligament laxity measurements and proprioception. Postoperatively, there were no statistically significant correlations between any of these variables.

►**Fig. 7** illustrates the scatterplot of the Pearson correlation analyses comparing pre and postoperative proprioception measurements of the injured knee of the ACL group. A significant (directly proportional) correlation was found demonstrating that low preoperative log (OSI) scores were associated with low postoperative log (OSI) scores.

Discussion

The results of this study found that there is a significant proprioceptive deficit as measured by dynamic single-leg postural stabilometry in patients with an ACL rupture as compared to their contralateral uninjured knee and to normal controls. ACL reconstruction significantly improved proprioception to the level of normal controls. We found no significant difference in proprioception between the uninjured knee of the ACL group and that of the control group. Clinical outcome measures were found to have a better correlation with proprioception than with instrumented ligament laxity testing.

Beard et al.[22] defined proprioception into three components; joint position sense (static awareness of joint position in space), kinesthesia (detection of joint movement and

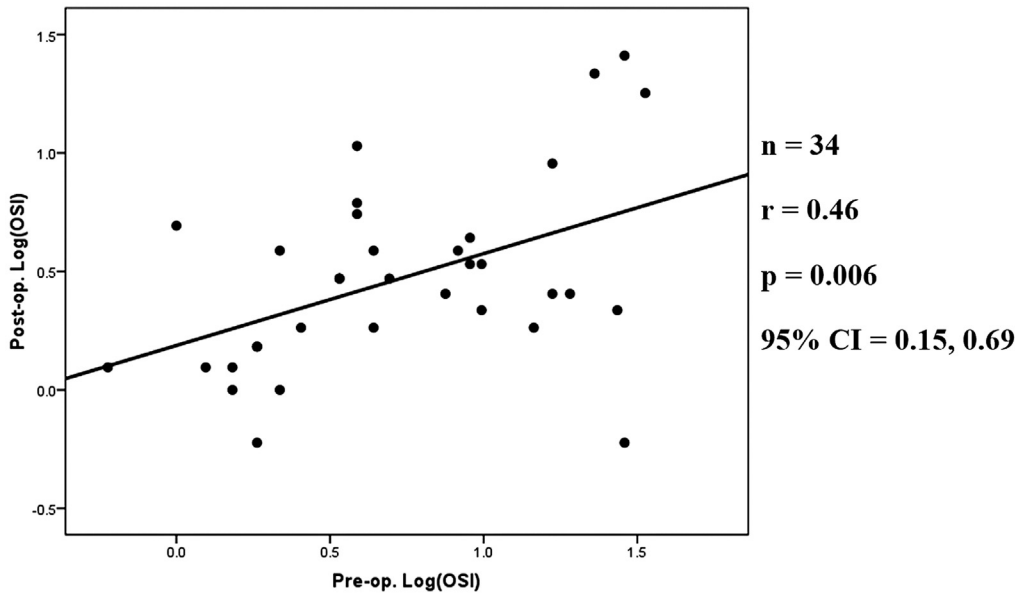


Fig. 7 Pearson product moment correlation analysis of proprioception measurements of the injured knee of the ACL group before and after reconstruction.

acceleration), and the efferent closed-loop reflex which regulates muscle stiffness. The complex interactions between the afferent sensory and the efferent motor pathways are collectively referred to as the sensorimotor system.[20] The present study measured proprioception using dynamic single-leg postural stabilometry, which assesses both the afferent and the efferent neuromuscular pathways.[23] This has the advantage of assessing proprioception whilst the subjects are balancing upright and is a more dynamic technique than the joint position sense (JPS) or threshold to detection of passive movement (TDPM) testing methods, in which the subjects are in the seated position.

The present study found a significant improvement of proprioceptive function at an average of 14 weeks (approximately 3 months) following surgery. In other studies, Iwasa et al.[24] showed that proprioception did not recover fully until 18 months after reconstruction, Fremerey et al.[2] showed that proprioceptive recovery occurred 6 months after surgery while Reider et al.[4] demonstrated an improvement of TDPM as compared to preoperative values as early as 6 weeks following reconstruction. Graft reinnervation alone is unlikely to explain a proprioceptive improvement as soon as 3 months after surgery in the present study. A more probable explanation would be that ACL reconstruction provides a static restraint and, thereby, improves the abnormal relationship between the femur and the tibia (i.e., abnormal knee kinematics) that exists in the ACL deficient knee. This, in turn, reduces the abnormal neural output from the joint capsule and the remaining ligaments and intraarticular structures of the knee.[4,24]

There was a significant improvement in ligament laxity measurements following ACL reconstruction, but a significant difference remained as compared to their contralateral uninjured knee and to normal controls. The present study found a significant improvement of both validated knee outcome scores when the ACL group were reassessed 3 months following surgery. Preoperatively, proprioception measurements were found to have a significant correlation with both knees' outcome scores. There was no significant correlation between the proprioception results and the instrumented ligament laxity measurements. Ligament laxity had no correlation with either of the knee outcome scores. This shows that proprioception is a better objective measure of knee impairment and perceived functional stability than ligament laxity testing. Barrett[11] demonstrated that proprioception measured using JPS testing methods correlated well with functional outcome and patient satisfaction and poorly with clinical ligament testing.

However, postoperatively, proprioception had no significant correlation with any of the outcome scores or ligament laxity measurements. An explanation for this is that the outcome scores ask questions relating not only to activities of daily living, which the patients may return to relatively early after surgery (such as walking and returning to work), but also to running, sprinting, activities which involve cutting movements, and return to competitive sport. Following an ACL reconstruction, patients undergo a structured rehabilitation program which involves a gradual increase in activity levels. Indeed, returning to full contact sport is prohibited until 9 months after surgery, in the study's host. These aspects will have a bearing on the answers that subjects can give to certain items in the outcome scores. Furthermore, a significant difference between the preinjury and postoperative Tegner activity score was noted. Therefore, a correlation may indeed exist between postoperative proprioception and the knee outcome scores, but the analyses may have been obscured by the activity limiting restrictions which were imposed on the patients at the early stages following their surgery. A correlation analysis performed 9 months or later after surgery may have yielded a different result.

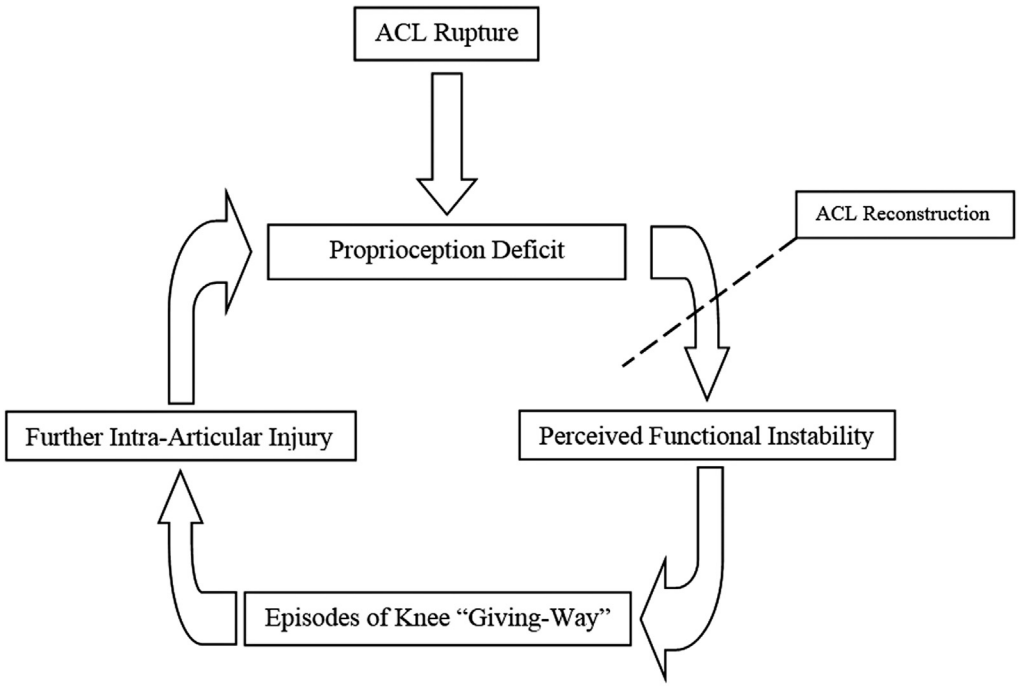


Fig. 8 The knee injury cycle. ACL reconstruction aims to improve proprioception and thereby interrupt the cycle.

There was a significant correlation between pre and postoperative proprioception measurements. This relationship can help inform the surgeon that patients with an ACL rupture and a good level of proprioceptive function prior to surgery are likely to have a good functional outcome following an ACL reconstruction. Conversely, a patient with a poor level of proprioceptive function prior to surgery is less likely to have as good a postoperative functional outcome. The contrary can also be argued, that patients who have a good level of proprioception following an ACL rupture maybe better candidates for conservative treatment. The secondary stabilizers in their knee maybe sufficient to allow satisfactory progress with a structured rehabilitation program back to a premorbid level of sporting activity. Similarly, patients who have poor preoperative proprioceptive acuity may require reconstructive surgery in order to protect the remaining intact structures of the knee which are providing a degree of proprioceptive input and prevent any further decline in this respect. ►**Fig. 8** summarizes the concept of proprioceptive deficits leading to further knee injuries and the impact that an ACL reconstruction has in preventing further functional decline.

The weaknesses of this study include the length of time for the follow-up review following surgery (approximately 3 months) and the number of subjects (16 patients) in the ACL group that did not return for their postoperative assessment. There is also the possibility that the structured rehabilitation program undertaken by the subjects postoperatively may have played a significant role in the proprioceptive improvement.

Conclusion

The present study showed a significant proprioceptive deficit as measured by dynamic single-leg postural stabilometry in patients with an ACL rupture that improved following ligament reconstruction. The proprioceptive acuity of the uninjured contralateral knee was similar to that of normal controls and is, therefore, an adequate comparator for proprioception. Knee outcome scores had a better correlation with proprioception analysis than instrumented ligament laxity measurements.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Simultaneous Bilateral Total Knee Arthroplasty May be Safe

A artroplastia total de joelhos bilateral simultânea pode ser segura

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Abstract

Objectives This study aims to analyze the safety of a simultaneous bilateral total knee arthroplasty (SBTKA) and to investigate patients' satisfaction with the procedure performed concomitantly.

Methods In a prospective study, we evaluated 45 patients undergoing SBTKA performed by two surgical teams. The mean age of the patients was 66.9 years; 33 subjects were female (73.3%) and 12 (26.6%) were male. We followed a protocol of intra- and postoperatively measures to ensure the safety of this procedure. We evaluated the surgery time and blood loss by hematocrit (Ht) and hemoglobin (Hb) levels on the first postoperative day, the percentage of patients who received a transfusion of packed red blood cells, and the number of required units. We also recorded perioperative complications, and, at the end of 3 months, we asked patients about their preference between the simultaneous or staged procedure.

Results The mean surgery time was 169 minutes. In the postoperative period, there was an average decrease of 28.2% in Htc and 27.0% in Hgb. A total of 16 patients (35.5%) received a transfusion of packed red blood cells (mean, 1.75 units per patient requiring a transfusion). There were 12 minor complications (26.6%) and 2 major complications (4.4%); furthermore, no patient had a clinical diagnosis of deep vein thrombosis, and there were no deaths.

Keywords
- arthroplasty, replacement, knee
- patient satisfaction
- knee

This study was developed at the Department of Surgery, Faculdade de Ciências Médicas e da Saúde de Sorocaba, Pontifícia Universidade Católica de São Paulo, Sorocaba, SP, Brazil.

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Conclusions: The SBTKA procedure may be considered safe if performed in selected patients and with a care protocol to prevent complications. This type of procedure was unanimously approved by patients.

Resumo

Objetivos Os objetivos deste estudo foram analisar a segurança da artroplastia total bilateral de joelho simultânea (ATJBS) e investigar a satisfação dos pacientes com o procedimento realizado de forma concomitante.

Métodos Em um estudo prospectivo, avaliamos 45 pacientes submetidos à ATJBS feita por duas equipes cirúrgicas. A idade média dos pacientes foi 66,9 anos, sendo 33 do gênero feminino (73,3%) e 12 (26,6%) do gênero masculino. No período intra- e pós-operatório foi seguido um protocolo de medidas visando a segurança do procedimento. Avaliamos o tempo de cirurgia, a perda sanguínea pelo hematócrito (Ht) e hemoglobina (Hb), obtidos no primeiro dia de pós-operatório, a porcentagem de pacientes que receberam transfusão de concentrado de hemácias e quantidade de unidades que foram necessárias. Verificamos as complicações no período perioperatório e, ao final de 3 meses, inquirimos aos pacientes sobre a preferência entre o procedimento simultâneo ou estagiado.

Resultados O tempo médio de cirurgia foi de 169 minutos; no pós-operatório houve um decréscimo médio de 28,2% do Ht e de 27,0% da Hb. Ao todo, 16 pacientes (35,5%) receberam transfusão de concentrado de hemácias (média de 1,75 unidades por paciente que precisou de reposição). Tivemos 12 complicações menores (26,6%) e 2 complicações maiores (4,4%); além disso, nenhum paciente teve o diagnóstico clínico de trombose venosa profunda e não houve mortes.

Conclusões A ATJBS pode ser considerada um procedimento seguro, se realizada em pacientes selecionados e com um protocolo de cuidados para prevenir complicações. Esse procedimento teve a aprovação unânime dos pacientes.

Palavras-chave
- artroplastia do joelho
- satisfação do paciente
- joelho

Introduction

Osteoarthritis features an abnormal remodeling of joint tissues triggered by inflammatory mediators.[1] Recently, a metanalysis included 88 studies and 10,081,952 participants. The authors estimated that, in 2020, there were 654.1 million subjects over 40 years old with knee arthrosis and that the global prevalence of the disease was 16%. Additionally, these authors reported an incidence of 203 cases per 10,000 people/year and a higher frequency among females. They also highlighted the impact of osteoarthritis on global health.[2]

Total knee arthroplasty (TKA) is usually recommended for patients over 60 years old with severe arthrosis in more than one compartment to improve pain and function. However, Wallace et al.[3] reported that 42% of people from the postindustrial cycle had bilateral knee osteoarthritis. If both knees of a patient are affected, TKA can be performed in stages or simultaneously. Warren et al.[4] analyzed information from a national database and concluded that patients undergoing simultaneous bilateral TKA (SBTKA) were at increased risk for every complication compared to unilateral TKA regardless of their health status.

Nevertheless, many surgical procedures reported as simultaneous are actually consecutive, that is to say, the surgery is performed by a single surgeon under the same anesthesia, initially on one knee and then on the contralateral side.[5–7] Consecutive procedures virtually double the surgery and anesthesia times, and such doubling has consequences. Furthermore, some authors used spinal anesthesia,[5] whereas others preferred epidural[7] or general anesthesia;[6] some used a pneumatic tourniquet,[6,7] and others did not.[5]

The technique of TKA with two surgical teams working simultaneously allows the performance of both procedures in the time equivalent to one surgery and under the same amount of anesthesia. Additionally, the patient undergoes only one hospitalization and anesthesia, which can reduce costs,[8–12] and a single physical therapy rehabilitation protocol. This study aimed to evaluate the safety of SBTKA performed by two surgical teams based on clinical parameters, laboratory tests, and any reported complications, as well as to determine patients' satisfaction with the simultaneous procedure.

Material and Methods

The Ethics Committee from our institution authorized this research under the number 36680920.6.0000.5373. Included patients signed an informed consent form. In a prospective study, we evaluated 45 subjects who underwent bilateral

TKA performed simultaneously by two teams between April 2014 and October 2021. Of the 45 patients, 33 were women (73.3%), and 12 (26.6%) were men. Their mean age was 66.9 years old, ranging from 48 to 81, with a standard deviation (SD) value of ± 6.3.

This study included patients with gonarthrosis grades IV and V, as per the Keyes et al.[13] classification. We informed the patients that each knee would be operated on by a surgeon and that the team's senior surgeon would supervise the contralateral procedure. All subjects underwent the following standardized preoperative tests: electrocardiogram, echocardiogram, anteroposterior chest x-ray, complete blood count, coagulation profile, blood sugar levels in fasting, A1c hemoglobin (Hb) levels, blood nitrogen urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), sodium, potassium, and 25-OH vitamin D levels, protein electrophoresis, ABO and Rh typing, and urinalysis. The maximum allowed blood sugar level for surgery was 137 mg/dL;[14] for A1c Hb, the maximum allowed level was 7%.[7] The ABO and Rh blood typing assessed the risk of class-related thromboembolism.[15] Immediately after the initial visit, we advised smokers to stop smoking, as the risk of infections in arthroplasty is 1.8 times greater in this population.[16] However, we are not certain if they followed our recommendation.

Preoperatively, a cardiologist and an anesthesiologist evaluated all patients to assess their surgical risk per the American Society of Anesthesiologists (ASA) criteria. Healthy patients were ASA I; those with controlled mild systemic diseases were ASA II; and subjects with systemic disease and functional limitation were ASA III.

All patients received 2 g of intravascular cefazolin as prophylactic antibiotic therapy immediately before surgery. Anesthesia was spinal. The surgical team was composed of two surgeons, two assistants, and two scrub nurses, who performed all procedures using two sets of instruments. We placed the patients in a supine position at the operating table, with the lower limbs in 45° abduction, to ensure a better space for the surgical teams (►**Fig. 1**). We did not use a pneumatic tourniquet.

Patients received 1 g tranexamic acid at the beginning and end of the procedure. Before cementation, we injected a solution containing bupivacaine, morphine, epinephrine, ketorolac, and methylprednisolone into the posterior, medial, and lateral joint capsule, and the medial and lateral subcutaneous tissue of each knee. Additionally, we used 1.0 g of powdered vancomycin on each joint. Surgery time was the interval from the incision beginning to the last skin suture. No patient required a suction drain or urinary catheter.

The day after surgery, hematocrit (Ht) and Hb levels were measured, and a Hb value lower than 8 g/dL was a criterion for transfusion.[17] We recommended early movement and use of compression stockings for approximately 21 days as mechanical prophylaxis; as well as 300 mg of acetyl salicylic acid every 12 hours for 15 days as pharmacological prophylaxis against deep vein thrombosis (DVT).[18] Pharmacological prophylaxis continued for 3 months at a 100 mg/day dose; we also prescribed a gastric protective agent for 30 days.



Fig. 1 Patient positioning at the operating room. Subject in supine position with lower extremities in 45° abduction.

Immediate deambulation was allowed with a walker and full support under the supervision of a physical therapist. Routine hospital discharge occurred in 3 days. Assessment of immediate results considered the following parameters: age, gender, surgery time, Ht and Hb levels before surgery and on the first day after the procedure, need for blood transfusion and administered amount, admission to the intensive care unit (ICU) or not, perioperative complications, and length of hospital stay. All patients were reassessed 2 weeks after surgery for suture removal and to check for potential effusions, erythema, healing problems, and rehabilitation progress. Clinical signs, including erythema, calf stiffness, and pain during ankle dorsiflexion, determined the presence or absence of DVT.

Routinely, all subjects had a new clinical evaluation at 1, 2, and 3 months after surgery. Then, we asked all patients what they would choose if they could go back in time: if they'd have surgery on both knees simultaneously or on one knee at a time.

Statistical Analysis

The Shapiro-Wilks test assessed data normality. The Student t-test determined whether the postoperative drop in Ht and Hb levels were related to the gender of the patients. The Pearson correlation coefficient defined a potential correlation between the postoperative decrease in Ht and Hb levels with the surgery duration and patient's age. The significance level was 5% for all tests.

Results

Among the study's population, 43 patients were ASA II (95.5%), 1 patient was ASA I (2.2%), and 1 was ASA III (2.2%). The mean surgery time was 169 minutes (range, 105–270, SD ± 35.8 minutes). The mean preoperative Hb level was 13.7 mg/dL (range, 11.6–16.1, SD ± 1.2 mg/dL);

the day after the procedure, this level was 10.0 mg/dL (range, 8.1–13.2, SD ± 1.2 mg/dL), indicating a mean drop of 27.0%. The mean pre- and postoperative Ht levels were 41.8% (range, 32.8–47.0, SD ± 3.3%) and 30.0% (range, 23–39.1, SD ± 4.2%), respectively, indicating a mean decrease of 28.2%. The Ht levels of 1 of the 45 patients (2.2%) were not determined before or after surgery. Also, 16 patients (35.5%) received a transfusion of packed red blood cells, an average of 1.75 units per patient requiring a transfusion.

The mean length of stay was 3.3 days (minimum of 3 and maximum of 5 days, SD ± 0.5 day). A single patient went to the ICU. Regarding minor perioperative complications, 1 patient had a whole-body allergy (2.5%), 5 subjects (11.1%) presented postoperative erythema that could indicate a superficial infection. These patients received broad-spectrum antibiotic agents with a 100% resolution rate. Six patients (13.3%) required manual expression of the hematoma. All patients received broad-spectrum antibiotic agents with a 100% resolution rate.

Major complications included a patient with a type B (partial) right medial femoral condyle fracture according to the AO classification. The fracture occurred during the cementation impaction of the prosthesis due to osteoporotic bone. Its treatment involved two 6.5 mm cancellous screws. Another patient, who was 70 years old and ASA III due to a previous acute myocardial infarction, presented symptoms of hypovolemia during the postoperative period. she remained in the ICU for 3 days, where she received three units of packed red blood cells for clinical stabilization.

No patient had clinical signs of DVT, and there were no signs of deep infection. No one died during this period. There was no statistically significant difference between genders regarding the postoperative drop in Ht ($p = 0.88$) and Hb levels ($p = 0.131$) (►**Table 1**). Additionally, there was no significant correlation between surgery duration and the postoperative decrease in Ht ($r = 0.21$; $p = 0.166$) and Hb levels ($r = 0.07$; $p = 0.65$), nor between patients' age and the postoperative decline in Ht ($r = -0.115$; $p = 0.454$) and Hb levels ($r = -0.042$; $p = 0.786$) (►**Table 2**). Finally, 3 months after the procedures, when asked, all patients reported that they would opt for its simultaneous performance.

Table 2 Postoperative hematocrit and hemoglobin levels drop regarding surgery time and patients' age

		Ht drop	Hb drop
Surgery time	r	0.07	0.21
	p	0.65	0.166
	n	44	45
Age	r	-0.042	-0.115
	p	0.786	0.454
	n	44	45

Abbreviations: Hb, hemoglobin; Ht, hematocrit; r, ratio coefficient value; n, number of patients.
Source: Research institution.

Discussion

The main finding of our study is that SBTKA performed by two teams in a single surgical time, with single anesthesia, can be considered a safe procedure provided protective measures are implemented. Moreover, all patients preferred an SBTKA compared to a staged procedure.

We selected spinal anesthesia because it associates with a reduced general complications rate and requires fewer healthcare resources.[19] We did not use a tourniquet on lower limbs to reduce the risk of venous thromboembolism[20] and the hemodynamic changes resulting from a partial blockage to the blood flow in two extremities.

The administration of tranexamic acid in bilateral TKA reportedly results in lower blood transfusion rates with no increase in the risk of thromboembolic events.[21] Chalmers et al.[7] demonstrated that using a suction drain in TKA doubles the risk of transfusion and do not recommend it. These measures aim to reduce the need for blood replacement. In patients undergoing total hip and knee arthroplasty, the probability of developing superficial and deep wound infections is significantly higher among those receiving blood transfusions compared to those who do not.[22]

Post-TKA pain increases postoperative morbidity, complicates physical therapy, and decreases patient satisfaction and recovery. Therefore, we administer intraarticular injections[23] at the end of the procedure to reduce pain, improve movement and, as a result, minimize the probability of DVT development.

We used intraarticular vancomycin powder to reduce the risk of periprosthetic infections.[24] Subjects undergoing spinal anesthesia may not require a urinary catheter.[25] Acetylsalicylic acid administration at a dose of 100 mg/day occurred for 3 months to prevent infarction since ischemic heart disease is the main cause of death in the first 90 days after arthroplasty. Additionally, we prescribed a gastric protective agent for 30 days because digestive disorders can result in death after arthroplasties.[26]

Table 1 Postoperative hematocrit and hemoglobin levels reduction according to gender

Variable	N	Gender	Min	Max	Mean	SD	*p*
Hb drop	12	M	0.9	7.9	3.84	2.19	0.88
	33	F	1.2	6.0	3.74	1.24	
Ht drop	12	M	6.8	22.0	13.31	4.56	0.131
	32	F	2.6	18.0	11.16	3.96	

Abbreviations: Hb, hemoglobin; Ht, hematocrit; Min, minimum value; Max, maximum value; N, number of patients; SD, standard deviation.
Source: Research institution.

Putnis et al.[5] reported that the risk of major complications is associated with an ASA classification $\geq$ III. In fact, in our study, the only case with complications requiring ICU admission was an ASA III patient. We found few articles regarding bilateral TKAs performed in a truly simultaneous way.

For Haddad et al.,[8] SBTKA seems a safe procedure, with no increased surgical risks. These authors observed one peroneal nerve palsy, a deep infection, and 21 clinical complications. They recommended careful patient selection and avoiding the procedure in older patients with significant comorbidities.

On the other hand, García et al. reported that the group undergoing consecutive bilateral TKA (CBTKA) had better outcomes with no increased surgical risk or major complications. They observed the occurrence of thrombophlebitis and superficial infection.[9] However, their sample had only 18 patients. Blood loss was very similar between simultaneous and consecutive procedures (667 and 645 cm^3, respectively). Costs and surgery and anesthesia times were lower in SBTKAs, and their only disadvantage was pain.

For Wyles et al.,[10] SBTKA can be a lower-cost option with fewer complications. Additionally, the use of the operating room was more efficient compared to CBTKA. There were no revision procedures or deaths 3 months after surgery. Within this period, there was a single perioperative clinical complication (1.2%). Gill et al.[12] published a study based on medical data from the Australian arthroplasties registry obtained from 11/1/2008 to 6/30/2016; they concluded that SBTKA may be superior to the staged procedure, since patients reported less joint pain and better function, with similar complication profiles. However, they observed that superficial infections were twice as common in the staged group.

In another article, Gill et al.[27] evaluated data from the Australian Orthopedic Association National Joint Replacement Registry from 9/1/1999 to 12/31/2018. These authors said that the revision rate was lower in patients undergoing SBTKA compared to CBTKA (6.4 vs. 6.9%, respectively), and that deaths within 30 days were infrequent (0.21% in SBTKA and 0.13% in CBTKA).

Uzer et al.[28] reported that SBTKA with two surgeons is a safe method, having lower complication rates compared with CBTKA, and that experienced teams can perform it safely. They observed a 3.2% complication rate, including a peroneal nerve palsy, an acute renal failure, a superficial infection, and a change in mental status. They recommended peri- and postoperative care to decrease the risk of bleeding, particularly in patients undergoing SBTKA.

►**Table 3** compares our materials and results with those from other authors. In general, samples were similar regarding age, the predominance of female patients, ASA classification, Hb level drop, percentage of transfused patients, and length of hospital stay. Our surgical time was longer probably because we measured it from the incision to suture completion.

When asked if they would prefer a simultaneous or staged procedure at 3 months after the surgery, 100% of the patients answered that they would opt for the former.

Table 3 Simultaneous bilateral total knee arthroplasty data according to different authors

	Number of cases	Mean age (years)	Females (%)	ASA Classification	Anesthesia	Surgery time (minutes)	Hb drop (%)	Transfusion (%)	Length of stay (days)	ICU patients (%)
Haddad et al., 2015	69	65.8	68	I – 3 II – 48 III –18	General	141	29.5	36	9	4.34
García et al., 2017	18	71	66	NI	NI	NI	NI	NI	NI	NI
Wyles et al., 2019	42	61	57	III and IV – 19%	NI	101	NI	NI	3	NI
Gill et al., 2020	122	70.6	62.3	I – 7 II – 81 III and IV – 33	NI	135	NI	53	5	NI
Uzer et al., 2020	121	68	89	I – 14 II – 85 III – 24	General	120	NI	NI	3	NI
Our data, 2022	45	66.9	73.3	I – 1 II – 43 III – 1	Spinal	169	27	35	3.3	2.22

Abbreviations: ASA, American Society of Anesthesiologists; Hb, hemoglobin; ICU, intensive care unit; NI, not informed.
Source: Research institution.

Putnis et al.[5] noted that when asking TKA patients if they would like to have the same procedure or a staged surgery, 73% answered definitely yes, and 22% said probably yes in favor of SBTKA.

The lack of a control group is the main limitation of our research. Other weaknesses are the 3-month follow-up and the fact that we did not assess postoperative function. However, our goal was to analyze clinical parameters and laboratory tests in the first trimester after surgery. Another potential limitation would be the lack of direct measurement of blood loss, but we did not use a suction drain; therefore, we determined blood loss based on the decrease in Ht and Hb levels.

Conclusion

The SBTKA procedure can be considered safe in selected patients, when performed concurrently by two trained teams and with a healthcare protocol to prevent complications. Patients in our study unanimously approved this procedure.

Conflict of Interests
The authors have no conflict of interests to declare.

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Assessment of the Risk Factors Related to the Length of Hospital Stay and Postoperative Complications in Patients Undergoing Primary Total Knee Arthroplasty

Avaliação dos fatores de risco relacionados ao tempo de internação e às complicações pós-operatórias em pacientes submetidos a artroplastia total primária do joelho

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Abstract

Objective To assess the risk factors involving longer hospital stays and early postoperative complications (first 30 days after surgery) in patients undergoing total knee arthroplasty (TKA).

Materials and Methods A cross-sectional study was conducted with collection of data of patients who underwent TKA in a private hospital between 2015 and 2019. The following data were collected: age, gender, body mass index, and clinical comorbidities. We also collected intraoperative data such as the grade on the classification of the American Society of Anesthesiologists (ASA), the duration of the surgery, the length of stay, the postoperative complications, and readmission within 30 days. Statistical models were used to investigate the possible risk factors associated with longer hospital stays and postoperative complications.

Results There was evidence of an increase in the length of hospital stay in older patients, with higher grades on the ASA classification or who suffered postoperative complications. For each increase in 1 year of age, we expect the length of stay to be multiplied by 1.008 (95% confidence interval [95%CI]: 1.004 to 1.012; $p < 0{,}001$). In patients who were ASA grade III, the time is expected to be multiplied by 1.297 (95%CI:

Keywords
- arthroplasty, replacement, knee
- outcome assessment
- postoperative complications
- length of stay

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1.083 to 1.554; $p = 0{,}005$) when compared with grade-I patients. In patients who suffered postoperative complications, the time is expected to be multiplied by 1.505 (95%CI: 1.332 to 1.700; $p < 0.001$) compared with patients without complications.
Conclusion The present study demonstrated that, in patients who underwent primary TKA, preoperative characteristics such as older age and ASA grade $\geq$ III, as well as the development of postoperative complications, independently predict the increase in the length of hospital stay.

Resumo

Objetivo Avaliar os fatores de risco relacionados a um tempo de internação mais longo e às complicações pós-operatórias precoces (primeiros 30 dias após a cirurgia) em pacientes submetidos a artroplastia total do joelho (ATJ).
Materiais e Métodos Este é um estudo transversal com coleta de dados de pacientes submetidos a ATJ em um hospital privado entre 2015 e 2019. Os seguintes dados foram coletados: idade, gênero, índice de massa corporal, e comorbidades clínicas. Também coletamos dados intraoperatórios, como o grau na classificação da American Society of Anesthesiologists (ASA) e a duração da cirurgia, além do tempo de internação, as complicações pós-operatórias, e a readmissão em 30 dias. Os possíveis fatores de risco associados a um tempo de internação mais longo e às taxas de complicações pós-operatórias foram investigados por meio de modelos estatísticos.
Resultados Os pacientes mais velhos, com graus mais elevados na classificação da ASA ou que sofreram complicações pós-operatórias, ficaram internados por mais tempo. Para cada aumento em um ano de idade, esperamos que o tempo de internação seja multiplicado por 1,008 (intervalo de confiança de 95% [IC95%]: 1,004 a 1,012; $p < 0{,}001$). Em pacientes de grau III na classificação da ASA, espera-se que o tempo seja multiplicado por 1,297 (IC95%: 1,083 a 1,554; $p = 0{,}005$) em comparação com pacientes de grau I. Em pacientes com complicações pós-operatórias, espera-se que o tempo seja multiplicado por 1,505 (IC95%: 1,332 a 1,700; $p < 0{,}001$) em comparação com pacientes sem complicações.
Conclusão Este estudo demonstrou que, em pacientes submetidos a ATJ primária, características pré-operatórias, como idade avançada e grau $\geq$ III na classificação da ASA, e o desenvolvimento de complicações pós-operatórias predizem o aumento do tempo de internação hospitalar de forma independente.

Palavras-chave
- artroplastia do joelho
- avaliação dos resultados
- complicações pós-operatórias
- tempo de internação

Introduction

Total knee arthroplasty (TKA) is an orthopedic procedure that can successfully reduce pain, restore function, and improve the quality of life of patients with osteoarthritis of the knee. The mean age of patients undergoing TKA is 71 years old, and in advanced degrees of osteoarthritis, the procedure is considered the gold-standard treatment.[1–4] The demand for TKA has grown rapidly all over the world. The data available suggest that 650,674 primary TKAs were performed in 2017 in the United States, and this number is expected to grow by 673% to 3.48 million procedures by 2030.[4,5]

The main complications of the procedure are deep vein thrombosis, surgical wound infection, joint stiffness, aseptic loosening of the prosthesis, and periprosthetic fractures, among others.[6,7] All of these can dramatically affect the outcomes of the procedure and increase the healthcare costs, leading to greater patient disability and even death.[8]

There is not much epidemiological information on the risk factors associated with early complications after primary TKA, readmission within the first 30 days, and hospital length of stay (LOS). Some studies even propose risk predictive models; however, few of these use intraoperative variables.[9–11] Though not a substitute for clinician expertise, these models are a valuable adjunct as they can help orthopedists assess a patient's expected risk based on similar patients.

The present study aims to assess the risk factors for longer hospital LOS and early postoperative complications (first 30 days after surgery) in patients undergoing primary TKA.

Materials and Methods

Data Collection

The present study was sent to and approved by the institutional Ethics in Research Committee (CAAE- 39446720.6.0000.0071).

All data were analyzed anonymously so that there was no personal identification of the patients included.

We conducted a cross-sectional study with retrospective data of patients undergoing primary TKA between 2015 and 2019 at a single institution. The following data were collected: age, gender, body mass index (BMI), comorbidities, grade on the classification of the American Society of Anesthesiologists (ASA), duration of surgery, postoperative complications, and 30-day readmission.

Early operative complications were any events within 30 days after the procedure that altered the normal postoperative course, requiring any type of intervention or acceptance of functional loss by the patient. All patients underwent standardized rehabilitation programs.

The inclusion criteria were patients undergoing primary TKA between 2015 and 2019 who were included in the institutional database. The exclusion criteria were revision TKAs, bilateral TKAs, and unicompartmental TKAs.

Statistical Analysis

The data were expressed as absolute and relative frequencies for the categorical variables, and as means, standard deviations (SDs), medians, interquartile ranges, and minimum and maximum values for the numerical variables.

For the analysis of the association of the LOS with variables of interest, we used generalized mixed models, contemplating the dependence regarding surgeries performed on the same patient, with Gamma distribution due to the asymmetric distribution observed. The model results were also expressed as mean values and estimated odds ratios and their respective 95% confidence intervals (95%CIs).

The associations of the occurrence of postoperative complications within 30 days with the variables of interest were investigated using mixed models with binomial distribution, considering the dependence regarding surgeries performed on the same patient. The model results were also expressed as mean values and estimated odds ratios, and their respective 95%CIs.

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Statistics for Windows, SPSS Inc., Chicago, IL, United States), software, version 17.0. Values of $p > 0.05$ were considered statistically significant.

Results

A total of 527 primary TKAs in 485 patients were included in the study sample. Two surgeries were performed in patients diagnosed with osteonecrosis, and three, in patients diagnosed with osteoarthritis secondary to rheumatoid arthritis or fracture sequelae. The others were diagnosed with primary osteoarthritis. We observed that 42 patients underwent bilateral TKAs at different times during the study period.

The sample was composed of 348 (66.0%) women and 179 (34.0%) men, with ages ranging from 36 to 93 years and a mean of 70.3 ± 8.9 years. The patients weighed between 43 kg and 160 kg, with a mean of 79.8 ± 15.4 kg, and the BMI ranged from 16.8 kg/m^2 to 46.7 kg/m^2, with a mean of 29.1 ± 4.7kg/m^2.

The LOS ranged from 1 to 28 days. Immediately after surgery, 128 (24.3%) patients went to the semi-intensive care unit and 93 (17.6%), to the intensive care unit. In the postoperative period, 3 patients (0.6%) required readmission within 30 days due to the surgical site infection (2 patients) and deep vein thrombosis (1 patient) (►**Table 1**).

Considering the occurrence of any early postoperative complications, 39 (7.4%) patients had some type of complication (surgical site or systemic infection, dislocation, and venous or pulmonary thromboembolism), 472 (89.6%) did not have any complication, and 16 (3.0%) patients were not classified due to insufficient information.

Table 1 Demographic, intraoperative, and postoperative data

	Mean ± standard deviation	n (%)
Gender		
Female		348 (66.0%)
Male		179 (34.0%)
Age (years)	70.3 ± 8.9	
Body mass index (kg/m^2)	29.1 ± 4.7	
Comorbidities		
Arterial hypertension		234 (44.4%)
Diabetes mellitus		85 (16.1%)
Behavioral disorders		70 (13.3%)
Smoking		18 (3.4%)
Previous cancer diagnosis		34 (6.5%)
Heart disease		59 (11.2%)
Grade on the ASA classification		
I		41 (7.8%)
II		438 (83.1%)
III		35 (6.6%)
IV		1 (0.2%)
No Information		12 (2.3%)
Operative time (hours)	2.5 ± 0.7	
Length of stay (days)	4.4 ± 2.4	
Postoperative complications		
No		472 (89.6%)
Yes		39 (7.4%)
No information		16 (3.0%)
Readmission within 30 days		
No		524 (99.4%)
Yes		3 (0.6%)

Abbreviation: ASA, American Society Anesthesiologists.

Association of the Length of Stay with the Variables of Interest

There was evidence of a significant association between the patient's age and the LOS (►**Table 2**), and for each increase in 1 year in age, we expect the LOS to be multiplied by 1.008 (95%CI: 1.004 to 1.012; $p < 0.001$). In an attempt to better understand this relationship, patients were classified according to age group in decades, and the age groups with little representation were placed in the same category. There was evidence of an increase in the LOS in the age group of patients 80 years or older compared with those aged up to 59 years, in which the time is expected to be multiplied by 1.257 (95%CI: 1.082 to 1.460; $p = 0.003$) in the older age group. There was no evidence of differences regarding patients aged up to 59 years compared with groups aged 60 to 69 years ($p = 0.382$) and 70 to 79 years ($p = 0.359$).

There was also evidence of an association between the LOS and the grade on the ASA classification, and, for ASA grade-III patients, the time is expected to be multiplied by 1.297 (95%CI: 1.083 to 1.554; $p = 0.005$) when compared with ASA grade-I patients, but there is no evidence of differences between ASA grade-II and grade-I patients ($p = 0.849$). Finally, we also found evidence of increased LOS in patients who developed postoperative complications compared with those who did not, and, in this case, the time is expected to be multiplied by 1.505 (95%CI:1.332 to 1.700; $p < 0.001$) in the group with complications.

Associations of the Occurrence of Postoperative Complications with the Variables of Interest

No evidence was found of an association of the occurrence of postoperative complications with any of the variables analyzed. The analysis of this association is shown in ►**Table 3**.

Discussion

The most interesting finding of the present study was that some preoperative characteristics of patients undergoing TKA, including age over 80 years and grade $\geq$ III on the ASA classification, as well as the development of postoperative complications, can be considered predictors of increased hospital LOS. This analysis can be used to stratify the risk of candidates for primary TKA preoperatively. Adequate stratification of patients assists in preoperative planning and in establishing expectations for patients and their families. Understanding which risk factors can influence complications and increase the LOS for patients undergoing major surgeries such as TKA is of fundamental importance to reduce the risks involved in the procedure, as well as to reduce the operating cost and optimize health resources. In 2017, Molloy et al.[12] found an increase in the cost of hospitalization of patients undergoing TKA and total hip arthroplasty in an American national database from 2002 to 2013, despite a reduction in the LOS from 4.06 days to 2.97 days. This cost could have increased more had there not been such a reduction in the average LOS.

Several studies[12–16] have been performed on the incidence of postoperative complications and mortality after primary TKA. However, the authors of these studies tend to combine complications from primary prostheses with revision prostheses, or to associate knee and hip procedures in the same study to assess risk factors. Thus, the benefits of applying these findings to patients undergoing primary TKA may be limited.

The identification of factors that interfere with the LOS of patients undergoing arthroplasties has been the focus of recent studies. In a 2019 study, Roger et al.,[17] analyzing TKA and total hip arthroplasty, found female gender, age, and the presence of diabetes as independent variables for increased LOS. Sarpong et al.,[18] in a retrospective study of the American National Surgical Quality Improvement Program database from 2006 to 2016, found a reduction in the LOS throughout the decades, and an association with shorter LOS in patients who were younger, male, and had low BMI and fewer comorbidities. Foni et al.[19] demonstrated that the focus on early rehabilitation of patients undergoing TKA can also contribute to shorter LOS without compromising the patients' health. Characteristics like female gender, higher grade on the ASA classification, high BMI, laboratory alterations related to malnutrition and systemic inflammation, and comorbidities such as smoking, diabetes, and lung diseases, have been reported and corroborated by other studies as predictors of increased hospital LOS.[20,21]

The Cleveland Clinic Orthopaedic Arthroplasty Group[22] performed a prospective cohort study in 2019 with 4,509 patients undergoing primary TKA with a follow-up of 1.5 years and found that, despite patient-related factors such as age, gender, and comorbidities being predictive of increased hospital LOS after TKA, the main predictors of LOS 24 hours after TKA were either procedure- or structure-related factors, including the hospital and the surgeon. In a systematic review conducted in 2019, March et al.[23] showed that the patient's worse psychological state in the preoperative period can also influence the LOS. In the present study, older patients ($>$ 80 years) or those with higher grades ($\geq$ III) on the ASA classification were found to be more likely to have increased LOS compared with younger patients or those with lower grades on the ASA classification.

Although many studies analyze variables that may interfere with the LOS, few studies seek to identify risk factors for early complications related to TKA. Some studies[24–26] have found an association with complications in patients with increased BMI, heart disease, neurological disease, preoperative low back pain, blood transfusion, male gender, smoking, and arthritis in a joint other than the knee. However, most of these studies analyzed arthroplasties in general, without differentiating TKA from total hip arthroplasty, or even looked for an association with a specific complication, disregarding other general complications. In the present study, no associations regarding increased incidence of postoperative complications were

Table 2 Association regarding the length of stay and the variables of interest

	Lenght of stay[#] (95%CI)	Odds ratio (95%CI)	*p*-value
Gender			
Female	4.17 (3.98–4.36)	1.053 (0.975–1.138)	0.191
Male	3.96 (3.72–4.22)	1.00	—
Age	—	1.008 (1.004–1.012)	< **0.001**
Age by subgroup			
≤ 59 years	3.96 (3.53–4.45)	1.00	—
60 to 69 years	3.73 (3.51–3.98)	0.943 (0.826–1.076)	0.382
70 to 79 years	4.20 (3.98–4.44)	1.062 (0.934–1.206)	0.359
≥ 80 years	4.98 (4.53–5.47)	1.257 (1.082–1.460)	**0.003**
BMI (kg/m^2)	—	0.996 (0.988–1.004)	0.352
BMI by subgroup			
Low weight/Normal weight	4.14 (3.81–4.51)	1.00	—
Overweight	4.19 (3.95–4.44)	1.011 (0.912–1.120)	0.835
Grade-1 obesity	3.92 (3.67–4.19)	0.946 (0.850–1.053)	0.307
Grade-2 obesity	3.89 (3.41–4.45)	0.939 (0.802–1.100)	0.435
Arterial hypertension			
No	4.04 (3.85–4.24)	1.00	—
Yes	4.16 (3.94–4.39)	1.029 (0.957–1.106)	0.434
Diabetes mellitus			
No	4.05 (3.90–4.22)	1.00	—
Yes	4.29 (3.93–4.69)	1.059 (0.961–1.167)	0.246
Behavioral disorders			
No	4.08 (3.92–4.24)	1.00	—
Yes	4.19 (3.80–4.63)	1.029 (0.926–1.144)	0.597
Smoking			
No	4.10 (3.95–4.26)	1.00	—
Yes	4.11 (3.38–5.00)	1.002 (0.822–1.222)	0.982
Previous cancer diagnosis			
No	4.09 (3.94–4.25)	1.00	—
Yes	4.13 (3.60–4.75)	1.011 (0.875–1.167)	0.883
Heart disease			
No	4.06 (3.91–4.22)	1.00	—
Yes	4.38 (3.94–4.88)	1.080 (0.964–1.209)	0.185
Grade on the ASA classification			
I	3.96 (3.50–4.48)	1.00	—
II	4.01 (3.85–4.17)	1.013 (0.890–1.152)	0.849
III	5.14 (4.49–5.88)	1.297 (1.083–1.554)	**0.005**
Operative time (hours)	—	1.045 (0.992–1.102)	0.098
Postoperative complications			
No	3.90 (3.76–4.04)	1.00	—
Yes	5.86 (5.21–6.60)	1.505 (1.332–1.700)	< **0.001**

Abbreviations: 95%CI, 95% confidence interval; ASA, American Society of Anesthesiologists; BMI, Body mass index.
Note: [#]Average time estimated by the model.

Table 3 Association regarding the occurrence of postoperative complications and the variables of interest

	Proportion of patients with postoperative complications[#] (95%CI)	Odds ratio (95%CI)	*p*-value
Gender			
Female	7.2% (4.9%–10.5%)	0.688 (0.360–1.313)	0.256
Male	10.1% (6.4%–15.6%)	1.00	—
Age	—	1.000 (0.965–1.036)	0.998
Age by subgroup			
$\leq$ 59 years	11.4% (5.2%–23.2%)	1.00	—
60 to 69 years	5.9% (3.2%–10.7%)	0.486 (0.167–1.413)	0.185
70 to 79 years	8.1% (5.2%–12.5%)	0.684 (0.258–1.813)	0.444
$\geq$ 80 years	11.7% (6.0%–21.7%)	1.026 (0.334–3.153)	0.965
BMI (kg/m^2)	—	0.992 (0.925–1.064)	0.830
BMI by subgroup			
Low weight/Normal weight	9.0% (4.6%–16.9%)	1.00	—
Overweight	8.8% (5.6%–13.6%)	0.975 (0.410–2.316)	0.954
Grade-1 obesity	5.7% (3.0%–10.7%)	0.609 (0.226–1.638)	0.325
Grade-2 obesity	11.0% (4.2%–25.7%)	1.239 (0.352–4.354)	0.738
Arterial hypertension			
No	7.7% (5.1%–11.4%)	1.00	—
Yes	8.7% (5.7%–13.1%)	1.146 (0.606–2.167)	0.674
Diabetes mellitus			
No	7.6% (5.5%–10.6%)	1.00	—
Yes	10.7% (5.7%–19.3%)	1.459 (0.672–3.170)	0.339
Behavioral disorders			
No	7.9% (5.8%–10.9%)	1.00	—
Yes	9.3% (4.3%–18.9%)	1.183 (0.482–2.899)	0.714
Smoking			
No	8.2% (6.1%–11.0%)	1.00	—
Yes	6.7% (1.1%–32.6%)	0.803 (0.116–5.557)	0.824
Previous cancer diagnosis			
No	8.2% (6.1%–11.1%)	1.00	—
Yes	6.7% (1.8%–21.6%)	0.800 (0.200–3.205)	0.752
Heart Disease			
No	8.0% (5.8%–10.9%)	1.00	—
yes	9.2% (4.0%–20.1%)	1.174 (0.446–3.091)	0.745
Grade on the ASA classification			
I	8.2% (2.7%–21.9%)	1.00	—
II	7.3% (5.1%–10.1%)	0.879 (0.263–2.936)	0.834
III	20.6% (10.1%–37.4%)	2.920 (0.707–12.068)	0.138
Operative time	—	1.517 (0.987–2.331)	0.057

Abbreviations: 95%CI, 95% confidence interval; ASA, American Society of Anesthesiologists; BMI, Body mass index.
Note: [#]Average time estimated by the model.

found in relation to any variable analyzed. However, an interesting finding was that postoperative complications can increase the hospital LOS. Patients who develop complications after TKA require more hospital resources, and there is also an increase in the costs due to the longer hospital stay; therefore, these patients should be monitored to prevent such occurrences. As the present study was performed in a reference center in Latin America, we had few events of complications during the study period; in addition, the profile of the cases in the present study consists mostly of patients without comorbidities or with well-controlled comorbidities, with a low number of smokers, for example, something that may have influenced this finding.

The present study is not without limitations. First, it is a retrospective analysis of a database. Thus, some clinical information, such as operative details, blood transfusion, and rehabilitation protocol, was not completely available. Furthermore, the present study was performed in a private hospital, and this may have implications for the generalization of our findings. Finally, the data reflect the work of a small number of surgeons, and the observed pattern of care may only represent orthopedic practices in a given healthcare system. On the other hand, the present study has important clinical relevance as it provides information to the orthopedic community that can refine the understanding of the risk factors related to increased hospital LOS in patients undergoing primary TKA.

Conclusions

The present study demonstrated that preoperative characteristics such as age $>$ 80 years, grade $\geq$ III on the ASA classification, and the development of postoperative complications are considered predictors of increased hospital LOS. Among these factors, the presence of postoperative complications demonstrated the greatest risk for prolonged LOS.

Conflict of Interests
The authors have no conflict of interests to declare.

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Microbiological Profile of Periprosthetic Knee Infections in a Brazilian Unified Health System Hospital Specialized in Highly Complex Orthopedic Surgeries*

Perfil microbiológico das infecções periprotéticas do joelho em um hospital do Sistema Único de Saúde especializado em cirurgias ortopédicas de alta complexidade

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Abstract

Objective We studied the microbiological profile of periprosthetic knee infections treated in a Brazilian tertiary hospital.

Methods The study included all patients undergoing revision surgery for total knee arthroplasty (RTKA) between November 2019 and December 2021, with a diagnosis of periprosthetic infection confirmed per the 2018 International Consensus Meeting (ICM) criteria.

Results Sixty-two patients had a periprosthetic joint infection (PJI) per the 2018 ICM criteria. Cultures were monomicrobial in 79% and polymicrobial in 21% of cases. The most frequent bacterium in microbiological tissue and synovial fluid cultures was *Staphylococcus aureus*, observed in 26% of PJI patients. Periprosthetic joint infection with negative cultures occurred in 23% of patients.

Conclusion Our results show the following: i) a high prevalence of *Staphylococcus* as an etiological agent for knee PJI; ii) a high incidence of polymicrobial infections in early

Keywords
- arthroplasty, replacement, knee
- postoperative complications
- intraarticular injections
- prosthesis-related infections

* *Study developed at Instituto Nacional de Traumatologia e Ortopedia (INTO), Rio de Janeiro, Brazil.*

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infections; iii) the occurrence of PJI with negative cultures in approximately one fourth of the subjects.

Resumo

Objetivo Identificar o perfil microbiológico das infecções periprotéticas do joelho tratadas em um hospital terciário brasileiro.

Métodos Todos os pacientes submetidos à cirurgia de revisão de artroplastia total do joelho (RATJ), no período compreendido entre novembro de 2019 e dezembro de 2021, e que tiveram o diagnóstico de infecção periprotética confirmado de acordo com critérios do *International Consensus Meeting* (ICM) 2018, foram incluídos no estudo.

Resultados Sessenta e dois pacientes foram diagnosticados com infecção periprotética (IAP) pelos critérios do *International Consensus Meeting* 2018. Culturas monomicrobianas foram identificadas em 79% e polimicrobianas em 21% dos casos. A bactéria mais frequentemente identificada nas culturas microbiológicas de tecidos e líquido sinovial foi o *Staphylococcus aureus,* presente em 26% dos pacientes com infecção periprotética. Infecções periprotéticas com culturas negativas ocorreram em 23% dos pacientes.

Conclusão Nossos resultados evidenciam: i) alta prevalência de bactérias do gênero *Staphylococcus* como causadores da IAP do joelho; ii) a alta incidência de infecções polimicrobianas nas infecções precoces e iii) IAP com culturas negativas ocorre em, aproximadamente, um quarto dos pacientes.

Palavras-chave
- artroplastia do joelho
- complicações pós-operatórias
- injeções intra-articulares
- infecções relacionadas à prótese

Introduction

Periprosthetic joint infection (PJI) represents a severe complication, with an incidence ranging from 1 to 4% after primary arthroplasties. However, this incidence can get up to 5 to 15% in high-risk patients and those undergoing revision surgery. Thus, in many series, PJI is the most significant cause for revision in modern knee arthroplasty.[1–3]

Early diagnosis and pathogen identification are critical for proper treatment and infection eradication. Nevertheless, PJI diagnosis is difficult because of its different clinical presentations and the lack of a single clinical test to confirm or rule out this complication. Thus, since 2011, several societies have proposed criteria to standardize PJI diagnosis.[4–6]

These criteria allow diagnostic confirmation of PJI, even in patients with negative microbiological cultures. However, pathogen identification remains a fundamental principle for treating these infections.[5,7] Thus, this study aims to characterize the microbiological profile of periprosthetic knee infections treated in a Brazilian tertiary hospital.

Material and methods

Study subjects

This study included all patients undergoing revision surgery for total knee arthroplasty (RTKA) from November 2019 to December 2021 with a diagnosis of periprosthetic infection confirmed per the 2018 International Consensus Meeting (ICM) criteria. The Research Ethics Committee approved this research under number 20309419.0.0000.5273. Patients confirmed their participation in the study by signing an informed consent form.

►**Table 1** shows exclusion criteria.

The application of exclusion criteria resulted in a final sample of 62 patients diagnosed with a periprosthetic knee infection.

Surgical procedure and biological sampling

On the day before surgery, we collected peripheral blood from all patients for routine preoperative serological tests, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and D-dimer.

All patients underwent spinal anesthesia with a peripheral nerve block. We performed all procedures under ischemia with the pneumatic cuff inflated 100 mm Hg above the systolic blood pressure.

After limb exsanguination and surgical drapes placement, we performed an arthrocentesis with a 20G needle to get

Table 1 Exclusion criteria

Exclusion criteria
- Refusal to sign the informed consent form
- Revision of an unicompartmental arthroplasty
- Reimplants in patients with spacers (second time)
- Impossibility to sample synovial fluid
- Insufficient information to confirm or rule out an infectious diagnosis
- Use of antibiotic agents within 15 days before the surgery
- Patients with other active bacterial infectious diseases
- Patients with acquired immunodeficiency syndrome

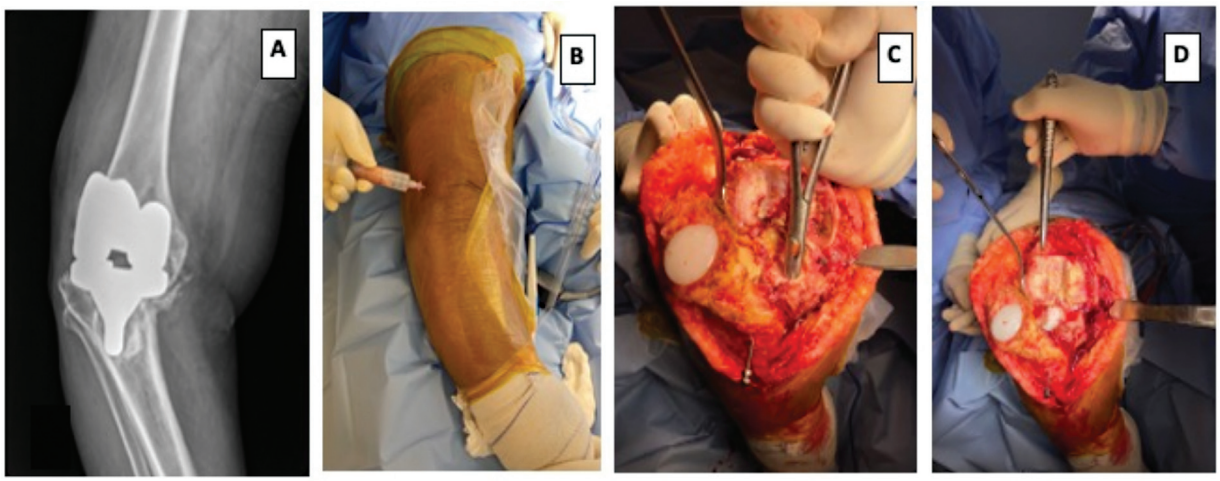


Fig. 1 Surgical procedure and biological material sampling. (A) Anterior-posterior radiograph of the right knee showing failure of the total knee arthroplasty; (B) Arthrocentesis after sterile drapes placement and before the surgical incision to avoid synovial fluid contamination with blood, (C) Periprosthetic bone tissue sampling for microbiological analysis, (D) Periprosthetic membrane sampling for histopathological analysis.

synovial fluid (SF) samples. The lack of surgical access or additional local anesthetic block minimized any chance of SF contamination by blood or other agents (►**Fig. 1**). If SF sampling was not feasible, we performed a second attempt by direct visualization after the medial parapatellar surgical approach.

We placed 1 to 2 mL aliquots of SF in vacuum blood collection tubes containing ethylenediaminetetraacetic acid (EDTA). These samples went immediately to the laboratory for a total white cell count and determination of the percentage of polymorphonuclear cells in an Abbott Cell Dyn 3700 SL equipment (Abbott Laboratories, Chicago, IL, USA).

We inoculated 3 to 5 mL aliquots of SF into aerobic blood culture tubes and, if possible, the same amount into anaerobic blood culture tubes. Blood culture tubes were sent immediately for microbiological culture. All samples were cultured for 14 days.

After removing the prosthetic components, we collected the following samples for microbiological analysis: three samples of femoral bone tissue, three samples of tibial bone tissue, and a fragment of the periprosthetic membrane. If the obtention of a periprosthetic membrane fragment was not feasible, we collected a peri-implant soft-tissue sample. For histopathological analysis, we sampled the periprosthetic membranes from the femur and tibia. Antibiotic therapy started only after collecting all biological samples.

We placed the bone fragments in sterile tubes with 1 mL of 0.9% saline solution. The samples went immediately to the laboratory for microbiological cultures. All samples were cultured for 14 days.

For the histopathological examination, we collected one or two periprosthetic membrane fragments and stored them in flasks containing 10% formalin solution. Membrane classification followed the parameters proposed by Morawietz et al.[8]

Diagnostic definition and group allotment

The following 2018 ICM criteria confirmed PJI diagnosis: i) growth of the same pathogen in two or more periprosthetic tissue cultures, or ii) presence of a fistula. These major criteria are enough for diagnostic confirmation. In addition, a score equal to or greater than 6 confirmed infections per the proposed algorithm (►**Table 2**).

Statistical analysis

Quantitative data, depicted as mean, standard deviation (SD), median, minimum, and maximum values, underwent descriptive analysis. The analysis of categorical variables, expressed as frequencies and percentages, used the chi-squared or Fisher exact test when necessary. We performed all analyses with the Med Calc and GraphPad Prism (GraphPad Software Inc., La Jolla, CA, USA) software. Significance was set at a $p > 0.05$ level.

Results

Study population

Based on clinical data and laboratory tests, we evaluated 84 patients who underwent RTKA for PJI diagnosis per the 2018 ICM criteria. In total, we included 62 patients with PJI in the study. ►**Table 3** summarizes the demographic data from these patients.

►**Fig. 2** shows the temporal evaluation (30 days) from infected patients.

Pathogen identification

The microbiological cultures showed positive results, allowing pathogen identification in 77% (48 patients) of the cases. Cultures were monomicrobial in 79% and polymicrobial in 21% of the subjects. Periprosthetic joint infection with negative cultures occurred in 23% of patients.

We identified gram-negative agents in 24% of the cultures. Considering only monomicrobial infections, 86% of the

Table 2 Criteria to diagnose a knee periprosthetic infection

Major criteria (at least one positive)				**Decision**
Two cultures positive for the same organism				Infected
Fistulae				
Preoperative diagnosis	**Minor criteria**		**Score**	**Decision**
	Serum	Elevated CRP or D-dimer	2	≥ 6 infected
		Elevated ESR	1	
	Synovial fluid	Elevated leukocyte count or positive leukocyte esterase	3	2–5 Potentially infected*
		Positive alpha-defensin	3	0–1 not infected
		Elevated neutrophil %	2	
		Elevated CRP	1	
Intraoperative diagnosis	**Inconclusive preoperative criteria or lack of synovial fluid**		Score	Decision
	Preoperative score		–	≥ 6 infected
	Positive histopathological analysis		3	4-5 potentially infected
	Presence of pus		3	
	One positive culture		2	≤ 3 not infected

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

patients presented gram-positive agents alone and 14% had exclusively gram-negative agents. The most frequent agent in cultures of periprosthetic tissues and SF samples was *Staphylococcus aureus*, present in 26% of patients with PJI. ►**Fig. 3** reveals the bacteria identified at cultures from PJI patients and their rates.

When evaluating only patients with positive microbiological cultures, we found out that polymicrobial infections were significantly more frequent in early infections, that is, occurring up to 3 months after surgery, compared with intermediate or late infections ($p = 0.02$) (►**Fig. 4**). The distribution of PJI patients with negative cultures was similar in acute, intermediate, and chronic infections.

Table 3 Demographics distribution

Variable	Infection
N	62
Gender, *n (%)*	
Female	23 (37%)
Male	39 (63%)
Age (years), *mean (±standard deviation)*	68.9 (±8.7)
BMI (kg/m^2), *mean (±standard deviation)*	27.4 (±9.9)
Diabetes, *n (%)*	12 (19%)
Inflammatory disease, *n (%)*	11 (18%)
Previous implant, *n (%)*	
Primary prosthesis	38 (61%)
Revision	18 (29%)
Rate of events characterizing infection, *n (%)*	
Fistulae	16 (25%)
≥ 2 positive cultures	46 (74%)
Time between prosthesis implant and revision, *n (%)*	
≤ 3 months	23 (37%)
3–12 months	9 (15%)
> 12 months	30 (48%)

Abbreviations: n, Number of patients; BMI, body mass index.

Discussion

Although the risk of periprosthetic infection after knee arthroplasty is low, the exponential boost in the amount of

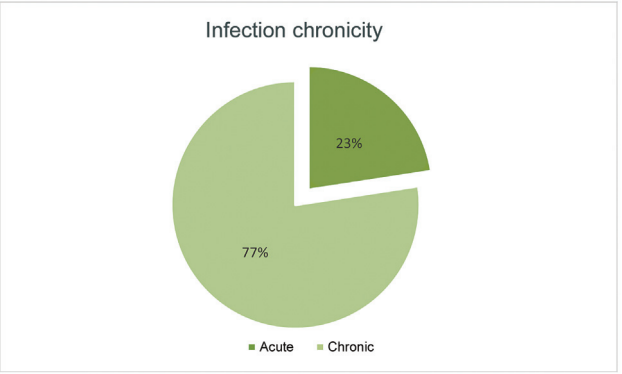


Fig. 2 Distribution of patients with acute or chronic periprosthetic infection.
Cronicidade da infecção = Infection chronicity
Aguda = Acute
Crônica = Chronic

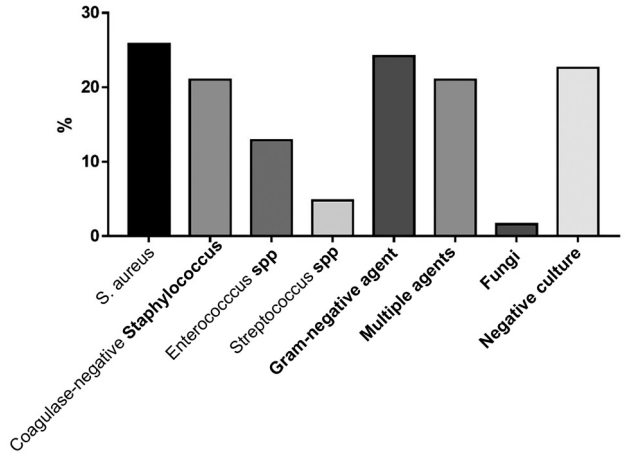


Fig. 3 Distribution of culture-identified pathogens.
S. aureus = *S. aureus*
Staphylococcus coagulase negative = Coagulase-negative *Staphylococcus*
Enterococccus spp = *Enterococccus* spp
Streptococcus spp = *Streptococcus* spp
Gram negativas = Gram-negative agent
Polimicrobianas = Multiple agents
Fungos = Fungi
Cultura negativa = Negative culture

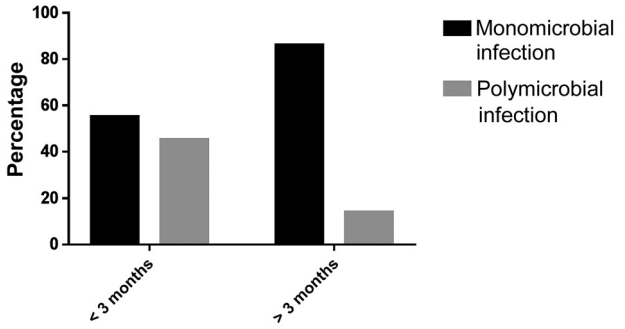


Fig. 4 Frequency of monomicrobial or polymicrobial infections regarding the time between the previous surgery and the revision surgery for total knee replacement.
Percentual = Percentage
< 3 meses = < 3 months
> 3 meses = > 3 months
Monomicrobiana = Monomicrobial infection
Polimicrobiana = Polymicrobial infection

TKAs performed annually makes this complication a significant and increasingly frequent problem.

The 2018 ICM criteria for periprosthetic infection diagnosis allow its confirmation even in the absence of positive cultures. However, pathogen identification remains a fundamental principle for the proper diagnosis and treatment of bacterial diseases, including determining the most appropriate antibiotic agent. A significant issue with microbiological assays is their sensitivity since cultures fail to identify the etiological agent in 5 to 45% of periprosthetic infections.[9–11] Negative cultures pose a critical challenge for treating periprosthetic infections since the lack of pathogen identification leads to the empirical use of antimicrobial agents, which may not be active against the actual infectious organism. In addition, they are associated with a 4.5-fold higher risk of reinfection when compared with cases with positive cultures.[12–14] Our findings show the microbiological profile of periprosthetic knee infections treated in a Brazilian tertiary hospital specialized in highly complex orthopedic surgery.

In our series, the most frequently identified pathogen was *S. aureus*, followed by coagulase-negative *Staphylococcus*. This finding is consistent with other series, in which these pathogens accounted for 50 to 60% of cases.[15,16] Polymicrobial infections totaled 21% of the cases, especially early infections. Cobo et al.[17] had similar results, with an incidence of 32% of polymicrobial infections in subjects with early PJI. Other studies corroborate this finding, suggesting that this higher frequency of polymicrobial infections in early infections may reflect the inoculation of multiple organisms during surgery or contiguous dissemination from the surgical incision.[15,18,19]

For Tan et al.,[10] the incidence of suspected culture-negative periprosthetic infection was 22%. However, according to the Musculoskeletal Infection Society (MSIS) diagnostic criteria, the incidence of infections with negative cultures was 6.4%. Per the 2018 ICM criteria, the actual rate of periprosthetic infection with negative cultures ranges from 7 to 15%.[11] These findings reinforce the importance of differentiating whether periprosthetic infections with negative cultures are actually sterile or a false-negative result, that is, a failure to identify the organism infecting an implant.[11]

The main factors contributing to a negative culture are the following: (1) administration of antibiotic therapy before culture sampling, (2) using a culture medium inadequate for atypical or biofilm-encapsulated agents, (3) improper sample handling and transportation, (4) inadequate incubation time (especially for rare and indolent agents), (5) a limited number of samples or inadequate tissue collection, (6) delay in transportation to the laboratory, (7) infection by a low virulence organism.[9–11] It is important to emphasize that, unlike in other areas of microbiological diagnosis, there are no standardized culture methods for PJI diagnosis. The 2018 ICM recommends the collection of at least three and ideally five or more peri-implant tissue samples during revision surgeries, in addition to the synovial fluid sample. However, there is no consensus on the type of solid tissue most suitable for conventional cultures. Thus, further studies standardizing culture methods are required to optimize the efficiency of this test.[18]

Approximately one fourth of our patients had a negative biological culture. In these subjects, infection diagnosis was based on other tests from the ICM diagnostic criteria. Studies indicate that surgeons often minimize PJI and perform incomplete assessments for diagnosis confirmation.[20] In addition, we know that many of these tests are unavailable in Brazilian public hospitals. However, given this scenario, we emphasize the importance of adopting a careful routine to evaluate patients with a persistent exudative wound or a hot, swollen, or painful joint to rule out or confirm PJI

diagnosis. This routine would allow for an early diagnosis and more effective treatment.

Limitations of this study include the lack of evaluation of the antibiotic resistance profile of the identified bacteria and the fact that it occurred during the pandemic, which may have impacted the profile of patients treated at our institute.

Conclusion

Our results show i) a high prevalence of *Staphylococcus* spp. as causes of knee PJI, ii) a high incidence of polymicrobial infections in early cases, and iii) the occurrence of PJI with negative culture in approximately one fourth of the patients.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Endoscopic Release of the Ulnar Nerve at the Elbow: Technique Description and Case Series

Liberação endoscópica do nervo ulnar no cotovelo: Descrição da técnica e série de casos

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Abstract

Objective The endoscopic release of the ulnar nerve reproduces a simple (*in situ*) procedure with smaller incisions, less soft tissue damage, and higher preservation of nerve vascularization. Endoscopy allows the clear visualization of the entire path of the nerve and surrounding noble structures. Moreover, it reveals any signs of compression and allows a safe release of 10 cm distally or proximally to the medial epicondyle.

Methods A retrospective survey revealed that 15 subjects (1 with a bilateral injury) underwent an ulnar nerve compression release at the elbow using the endoscopic technique with Agee (Micro-Aire Sugical Instruments, Charlottesville, VA, EUA) equipment from January 2016 to January 2020.

Results Symptoms of ulnar nerve compression improved in all patients; on average, they resumed their work activities in 26.5 days. There was no recurrence or need for another procedure. In addition, there were no severe procedure-related complications, such as infection and nerve or vascular injury. One patient had transient paresthesia of the sensory branches to the forearm, with complete functional recovery in 8 weeks.

Conclusion Our study shows that the endoscopic release of the ulnar nerve at the elbow with the Agee equipment is a safe, reliable technique with good outcomes.

Keywords
- ulnar nerve
- cubital tunnel syndrome
- nerve compression syndromes
- elbow
- paresthesia
- minimally invasive surgical procedures

Resumo

Objetivo A liberação endoscópica do nervo ulnar permite reproduzir uma liberação simples (*in situ*), mas através de incisões menores e com menor lesão de partes moles e

Work developed in the Departamento de Ortopedia e Traumatologia do Hospital Santa Casa de Misericórdia de Porto Alegre, RS, Brazil.

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uma maior preservação da vascularização do nervo. A visualização clara através da endoscopia permite observar todo o trajeto do nervo e das estruturas nobres circundantes, mostrando os sinais de compressão, possibilitando realizar a liberação de forma segura em um trajeto de 10 cm nos sentidos distal e proximal ao epicôndilo medial.

Método Foram encontrados, de forma retrospectiva, no período entre janeiro de 2016 e janeiro de 2020, 15 pacientes (sendo 1 com lesão bilateral) submetidos a liberação da compressão do nervo ulnar no cotovelo pela técnica endoscópica com equipamento de Agee (Micro-Aire Sugical Instruments, Charlottesville, VA, EUA).

Resultados Todos os pacientes tiveram melhora dos sintomas de compressão do nervo ulnar e o período de retorno ao trabalho foi de em média 26,5 dias. Não houve recidivas e não houve a necessidade de outro procedimento. Também não houve complicações graves decorrentes do procedimento, como infecção, lesão nervosa ou vascular. Em um paciente, houve parestesia transitória dos ramos sensitivos para o antebraço, com retorno completo da função em 8 semanas.

Conclusão Os resultados mostram que a liberação endoscópica do nervo ulnar no cotovelo com o equipamento de Agee é uma técnica segura, confiável e com bons resultados.

Palavras-chave
- nervo ulnar
- síndrome do túnel ulnar
- síndromes de compressão nervosa
- cotovelo
- parestesia
- procedimentos cirúrgicos minimamente invasivos

Introduction

Ulnar nerve compression at the elbow level is the second most frequent compressive neuropathy in the upper limb after carpal tunnel syndrome,[1–4] with an incidence of 25 cases per 100,000 inhabitants, being twice as common in men.[5] The most common symptom is paresthesia at the ulnar border of the hand and forearm. In addition, the subject may complain of pain in the medial region of the elbow irradiating to the forearm, weakness in the intrinsic muscles of the hand, and decreased pinch strength. The most severe and long-term cases may result in atrophy of the intrinsic musculature of the hand, especially of the first dorsal interosseous muscle.[3,4]

The superficial position of the ulnar nerve in the cubital tunnel and the increased tension and traction at elbow flexion account for its susceptibility to this compressive neuropathy. In most patients, the condition is idiopathic. However, it is critical to rule out potential lesions, including osteophytes, post-traumatic cubitus valgus, soft tissue tumors, post-traumatic contractures, and subluxation of the ulnar nerve at the medial epicondyle.[2,4]

The most frequent compression site is within the cubital tunnel, formed by the medial epicondyle and the proximal ulna and covered by the Osborne arcuate ligament. In the proximal portion, the area of higher compression is the arcade of Struthers, located ~ 10 cm proximally to the medial epicondyle. In the distal region, the deep fascia, or the area between the two heads of the flexor carpi ulnar may compress the ulnar nerve. Potential compression sites often range from 8 cm proximally to 5 cm distally to the medial epicondyle (►**Fig. 1A**).[3,6]

Conservative treatment failure indicates the need for surgical release of the ulnar nerve. The endoscopic release

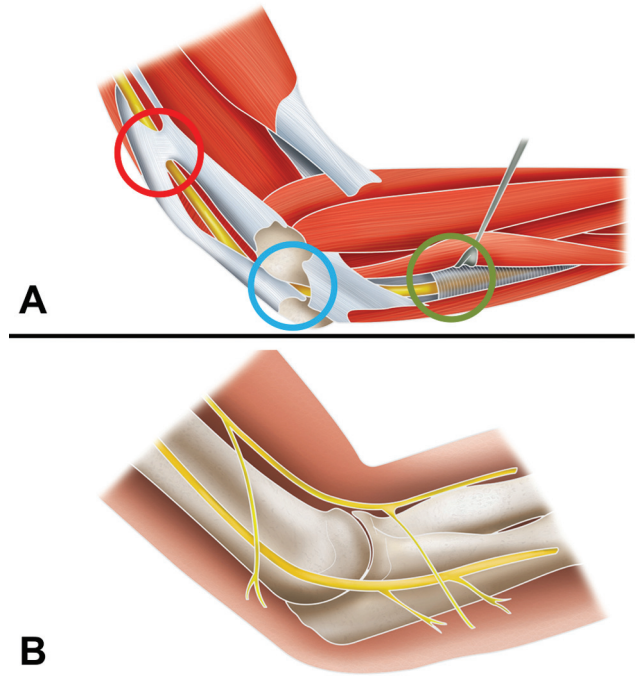


Fig. 1 Anatomy of the medial region of the elbow showing the most frequent sites of ulnar nerve compression. The main ulnar nerve compression sites include the arcade of Struthers (red circle) proximally, the cubital tunnel (blue circle) centrally, and the deep fascia or area between the two heads of the flexor carpi ulnaris (green circle) distally. Locations range from ~ 8 cm proximally to 5 cm distally to the medial epicondyle (**A**). Anatomy of the ulnar and medial cutaneous nerves of the forearm showing their superficial sensory branches passing obliquely at the elbow. Their protection is critical during the endoscopic release of the ulnar nerve (**B**). Source: Instituto da Mão.

Table 1 McGowan classification of cubital tunnel syndrome

Grade 0	No symptoms
Grade 1	Minimal symptoms with paresthesia and dysesthesia. No weakness or atrophy of the intrinsic musculature supplied by the ulnar nerve.
Grade 2	Moderate symptoms with weakness and atrophy of the intrinsic musculature supplied by the ulnar nerve. Preservation of some motor function.
Grade 3	Severe symptoms with paralysis of the intrinsic musculature supplied by the ulnar nerve. Marked hand weakness.

of the ulnar nerve reproduces a simple (in situ) procedure with smaller incisions, less soft tissue damage, and higher preservation of nerve vascularization. Endoscopy allows the clear visualization of the entire path of the nerve and surrounding noble structures. Moreover, it reveals any signs of compression and allows a safe release 10 cm distally or proximally to the medial epicondyle. Different studies and meta-analyses have concluded that simple (in situ) cubital decompression is comparable to the classically proposed anterior transposition but with fewer complications.[7–9]

Endoscopic surgery is contraindicated in subjects with space-occupying lesions, previous ulnar decompression (or transposition), severe elbow stiffness requiring treatment, symptomatic subluxation of the cubital nerve, and previous trauma with scar adhesion.[10,11]

The present study describes the technique and outcomes of a series of patients with ulnar nerve compression at the elbow surgically treated with an endoscopic release using the Agee (Micro-Aire Surgical Instruments, Charlottesville, VA, USA) equipment.[12,13]

Materials and Methods

A retrospective survey revealed that 17 patients underwent an endoscopic ulnar nerve release at the elbow (LENUC, in the Portuguese acronym) between January 2016 and January 2020. The lack of adequate follow-up led to the exclusion of two patients. Therefore, we analyzed 15 patients. One subject had bilateral injuries, and the surgical treatment of each elbow occurred at different times. In total, we assessed 16 elbows for a minimum follow-up period of 9 months after surgery. The ethics committee of our hospital authorized the present study.

After history and physical examination suggested an ulnar nerve compression at the elbow, all patients had the diagnosis confirmed by electroneuromyography. Preoperatively, the modified classification proposed by McGowan[10] determined the degrees of disease severity (►**Table 1**).

We referred for LENUC patients with no improvement after 3 months of consistent conservative treatment with anti-inflammatory medication, physical therapy, and night orthotics use. We excluded patients with a history of fractures in the affected elbow, joint stiffness with a referral for arthrolysis, and those with associated cervical radiculopathy. We included only adult patients ($>$ 18 years old), with no restriction regarding the upper age limit.

Outcomes included clinical aspects and potential complications resulting from surgery. The evaluation used the modified Wilson et al. scale (►**Table 2**) and the Bishop scoring system (►**Table 3**).[2,10] In addition, we determined the time required to return to physical, daily, and professional activities. The same surgeon performed the procedure in all patients using the technique described below.

Endoscopic Ulnar Nerve Release Technique using Agee

Agee was designed for the endoscopic release of carpal tunnel syndrome and was adapted for the treatment of cubital tunnel syndrome.[12,13]

The patients were positioned in dorsal decubitus, with the upper limb supported on a hand table. We performed regional block anesthesia and sedation and placed a pneumatic tourniquet. Initially, the elbow was flexed, with external rotation of the shoulder, for an easier approach to the medial portion of the elbow. Less experienced surgeons may use a dermographic pen to mark the medial epicondyle, the olecranon, and the entire course of the ulnar nerve, which is immediately posterior to the medial epicondyle.

The 1.5- to 2-cm incision was oblique and located 1 cm proximal to the retroepitrochlear canal (►**Fig. 2**). We carefully dissected the area using this mini approach until

Table 2 Wilson and Krout criteria for postoperative outcome evaluation of patients with ulnar nerve compression at the elbow

Outcome	Description
Excellent	No pain on the incision site, with minimal sensitive or motor abnormalities.
Good	Improvement of compressive symptoms but with occasional sensitive abnormalities.
Regular	Improvement but with persistent sensitive or motor abnormalities, which are minor compared with the preoperative period.
Poor	No improvement or worsening of symptoms.

Table 3 Bishop scoring system

Evaluation	Score
Patient satisfaction	
Satisfied	2
Satisfied with restrictions	1
Not satisfied	0
Improvement	
Improvement	2
No alteration	1
Worsening	0
Intensity of residual symptoms (pain, paresthesia, weakness)	
Asymptomatic	3
Occasional	2
Moderate	1
Intense	0
Professional activity	
Working or able to resume work	1
Not working	0
Intensity of labor	
Limited	0
Unlimited	1
Grip and pinch strength	
$\geq$ 80% on both sides	2
$\geq$ 80% on one side	1
$<$ 80% on both sides	0
Static sensitivity and two-point discrimination	
Normal ($\geq$ 5mm)	1
Abnormal ($<$ 5mm)	0
	Total 12
Score	
Excellent	10–12
Good	7–9
Regular	4–6
Poor	1–3

reaching the deep fascia and the ulnar nerve. After localizing and protecting the ulnar nerve, we created a space between the deep fascia and the subcutaneous cellular tissue using Metzenbaum scissors. Differently from carpal tunnel syndrome release, here the medial cutaneous nerve of the forearm and its branches pass through the subcutaneous space around the cubital tunnel. So, we needed to create a space both inside the cubital tunnel and between the fascia and the subcutaneous tissue to protect sensory nerve branches (►**Fig. 1B**).

First, we proceeded to the proximal release of the ulnar nerve. We introduced the cannula into the space between the ulnar nerve and the fascia, advancing carefully without forcing the entry or injuring the nerve. At the same time, we placed a long soft tissue retractor between the superficial part of the fascia and the subcutaneous tissue to avoid damage to the superficial sensory nerve branches and vessels during the release (►**Fig. 3**). After cannula, it was easy to see the fascial fibers covering the cubital tunnel with the blade between the nerve and the fascia. Next, we activated the trigger, projecting the 3.5-mm blade into the device tip. Then, a retrograde movement of the pistol held by the surgeon sectioned the ligament. A single, continuous movement is usually enough to open the ligament in its entirety. Even so, we must check if the entire ligament was released because the pistol may need triggering again (►**Fig. 4**).

We performed the exact same procedure at the proximal path for distal release. Initially, using retractors, we created a space between the nerve and the roof of the cubital tunnel. We introduced the cannula superficial to the nerve and deep to the fascia; with the superficial soft tissue retractor, we created a space between the (deep) fascia and the (superficial) subcutaneous cellular tissue. Then, we confirmed the absence of nerve branches and superficial vessels at the release site. We introduced the cannula with the optics and located the distal course of the ulnar nerve. Next, under direct visualization of the fascia, we opened the distal portion of the fascia when we were sure that the nerve was totally below the cannula. Occasionally, blunt dissection with scissors may be required to put the cannula below the fascia, removing potential nerve adhesions that may hinder the introduction and advancement of the device. Then, we removed the cannula and viewed the tissues with the help of the retractors, leaving space for introducing the optics that show the path of the released nerve, both proximal and distal to the medial epicondyle. The ease of following the path of the ulnar nerve with both proximal and distal optics, with no compression points, confirmed its complete release. Any potential compression point can be treated with scissors, completing the release under endoscopic view.

We released the tourniquet and proceeded to hemostasis before closing the incision with sutures and an elastic compressive dressing. This surgery is usually performed on an outpatient basis. The patient is encouraged to keep the hand elevated and to mobilize the fingers. Gentle active mobilization of the elbow is allowed starting on the 1st postoperative day. We recommended putting ice over the surgical site. The first dressing change occurred 3 to 5 days after surgery, when a Band-Aid (Johnson & Johnson, New Brunswick, NJ, USA). replaced the elastic immobilization. As a general rule, joint mobility was complete within 1 week. We removed the sutures 10 to 12 days after surgery. We instructed the patient to avoid physical exertion for 2 weeks and allowed work activities according to their tolerance. We educated our patients that discomfort in the medial region of the elbow is common for 2 to 3 months after the procedure.

Results

We analyzed 16 operated elbows (15 patients; 7 female and 9 males) with LENUC, followed prospectively, following them

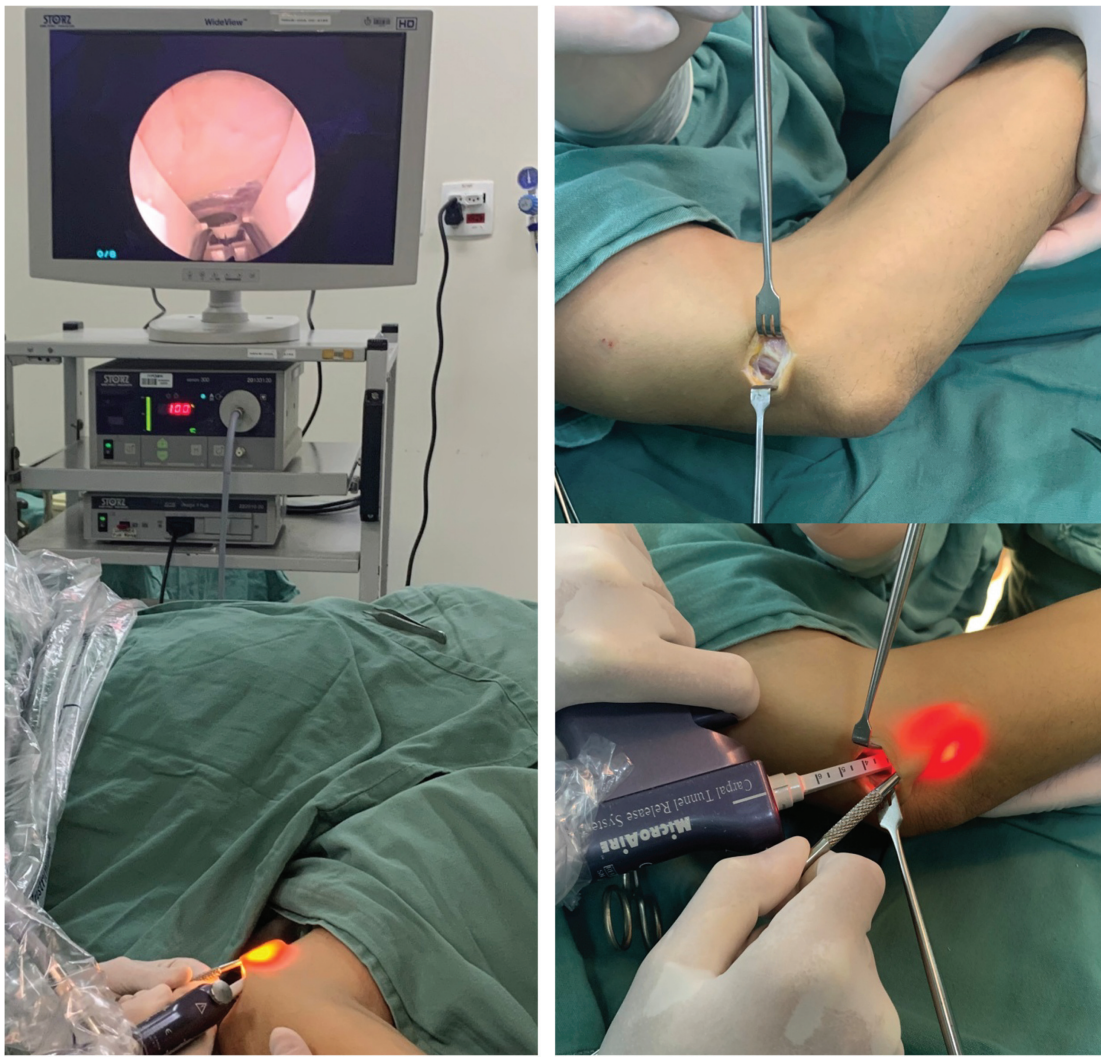


Fig. 2 The 1.5- to 2-cm incision was oblique and located 1 cm proximal to the retroepitrochlear canal (**A**). We carefully dissected the area using this mini approach until reaching the deep fascia and the ulnar nerve. Release of the ulnar nerve began proximally (**B**), extending to the distal region (**C**). Source: Instituto da Mão.

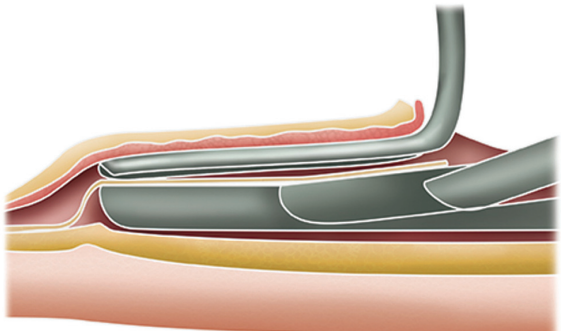


Fig. 3 Schematic drawing of the relationship between the anatomical structures and the instruments used for the procedure. From top to bottom, a long soft tissue retractor pulled the skin apart, revealing the fascia underneath. The retractor protected the superficial sensory branches of the ulnar nerve. We introduced the cannula immediately below the fascia to section it, decompressing the nerve. The bottom of the cannula protected the ulnar nerve throughout the procedure. At the end of the surgery, it can be visualized by directing it to the opposite side.

up from surgery until the patients resumed work and sports activities (►**Table 4**). We operated on seven right elbows and nine left elbows. The age at surgery ranged from 26 to 66 years old, and the mean age was 45.81 years old. The condition was present for 6 to 24 months, with a mean period of 11.87 months. All patients underwent electroneuromyography, which showed moderate compression in nine patients and severe compression in seven subjects. Clinically, 11 patients were type II and 5 were type III according to the classification by McGowan.

The mean follow-up time was 17.25 months, ranging from 9 to 36 months. According to the Wilson et al. scale, outcomes were excellent in 11 patients, good in 4 patients, and regular in 1 subject. All patients presented improved ulnar nerve compression symptoms, and the mean time until return to work was 26.56 days, ranging from 10 to 60 days.

There were no recurrences or need for another procedure. In addition, there were no severe procedure-related complications, such as infection, nerve, or vascular injury. One

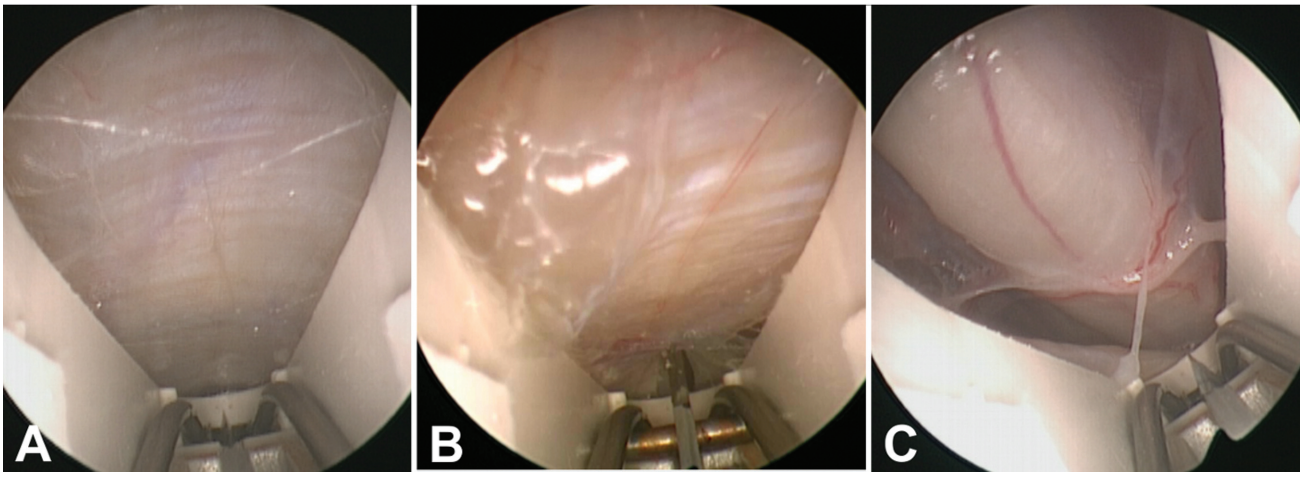


Fig. 4 Endoscopic view of the fascia fibers closing the cubital tunnel (**A**). The trigger was pulled, projecting the 3.5-mm blade into the device tip. A retrograde movement of the pistol held by the surgeon sectioned the ligament. A single, continuous movement is usually enough to open the ligament in its entirety (**B**). Confirmation of nerve release throughout its course (**C**). Source: Instituto da Mão.

Table 4 Patient series and postoperative outcomes

Elbows	Gender	Age (years old)	Side	Onset (months)	ENMG	McGowan	Wilson & Krout	Resume working (days)	Follow-up (months)	Bishop
1	Male	34	Left	8	Moderate	2	Excellent	30	12	Excellent
2	Female	49	Left	12	Moderate	2	Excellent	15	24	Excellent
3	Male	39	Right	18	Severe	2	Good	60	18	Good
4	Male	33	Left	6	Moderate	2	Excellent	15	12	Excellent
5	Male	66	Left	24	Severe	3	Good	30	12	Regular
6	Male	26	Right	12	Severe	2	Excellent	20	18	Excellent
7	Female	52	Left	8	Moderate	3	Excellent	15	24	Excellent
8	Male	44	Left	9	Moderate	2	Excellent	30	18	Excellent
9	Female	52	Right	9	Moderate	2	Excellent	45	24	Excellent
10	Female	53	Left	15	Moderate	2	Excellent	30	36	Excellent
11	Male	38	Right	18	Severe	3	Good	15	9	Excellent
12	Male	47	Left	12	Moderate	3	Excellent	10	12	Excellent
13	Female	60	Left	12	Severe	2	Regular	30	18	Regular
14	Male	41	Right	12	Moderate	3	Good	45	18	Good
15	Female	51	Right	6	Severe	2	Excellent	20	12	Excellent
16	Female	48	Right	9	Severe	2	Excellent	15	9	Excellent

Abbreviation: ENMG, electroneuromyography.

patient had transient paresthesia of the sensory branches to the forearm, with complete functional recovery in 8 weeks.

Discussion

The management of ulnar compressive neuropathy in the elbow must be nonsurgical in patients with a mild injury (McGowan type I) of short duration.[14,15] We refer patients with conservative treatment failure or more advanced lesions (McGowan types II and III) to surgery. Several techniques were described, but there is no consensus on which is the best.[10,16,17] From a didactic point of view, these techniques include in situ ulnar nerve decompression or medial epicondylectomy and those for anterior transposition of the nerve and its positioning at the subcutaneous, intramuscular, and submuscular tissues. Most of these techniques have good outcomes with a low rate of complications.[3,18–20]

Dellon[21] performed a meta-analysis of 50 articles with $>$2,000 patients and different surgical techniques. They concluded that most surgeries have satisfactory outcomes in 90% of patients with minimal compression symptoms. In prospective studies, Gervasio et al.,[22] Biggs et al.,[23] and

Bartels et al.[24] showed that the in situ release of the ulnar nerve is at least as effective as its submuscular or subcutaneous transposition. This realization led to the recent development of increasingly less invasive techniques with satisfactory outcomes.

Tsai et al.[25] was the first to propose an endoscopy-assisted technique in 1989. Subsequently, other authors described several similar techniques.[12,26–28]

The latest published reviews state that the open technique and endoscopic surgery had similar clinical outcomes, patient satisfaction levels, and relapse rates.[29] However, endoscopic ulnar nerve release offers several benefits over open surgery, including lower morbidity in the surgical area, minimal risk of injury to adjacent noble structures, a significant reduction in complication rates, faster recovery, and better aesthetic results with greater patient satisfaction due to the smaller incision.[29]

None of our patients required a second procedure for a new release because our technique reached very proximal and distal levels, preventing the formation of potential compression points. In addition, there were reports of injuries at cutaneous sensory nerves.

The endoscopic procedure is more expensive than the traditional open surgery, which may be a limitation in some circumstances. However, an earlier return to work activities may compensate for this higher cost.[4]

One author (Carratalá V.) has published two articles with a series of patients with ulnar nerve compression at the elbow treated with the technique described by Cobb et al.[26] using the Endoscopic Cubital Tunnel Release System (Endorelease system, Integra LifeSciences, Plainsboro, NJ, USA) and a standard 4-mm optic. These papers report good outcomes consistent with our series conducted with the Agee device.[10,11,26]

The use of endoscopic ulnar nerve release techniques at the elbow through a minimal incision is increasing, and most published articles show a significant benefit to the patient.[1] However, like most publications, our study is limited by the lack of control groups due to the small sample size and nonstandardized outcome measures.

Conclusions

Our study provides consistent data that the endoscopic release of the cubital tunnel with ulnar nerve decompression is a safe, reliable technique with good outcomes. It has a high rate of patient satisfaction, fast improvement, and aesthetic advantages. We emphasize, however, that this technique requires previous training with arthroscopic procedures.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Use of Smartphones as a Risk Factor for the Development of Morbidities in the Wrist and Fingers*

Uso de smartphones como fator de risco para o desenvolvimento de morbidades no punho e nos dedos

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Abstract

Objective To investigate the long-term use of smartphones as a risk factor for the development of morbidities in the wrist and fingers.

Methods The present is a descriptive, exploratory study with a quantitative approach based on injury prevalence among one hundred smartphone users of a private university in the state of Pernambuco, Northeastern Brazil. We applied a semi-structured questionnaire and the Boston Carpal Tunnel Questionnaire (BCTQ), as well as the Visual Analog Scale (VAS) and the Finkelstein, Phalen, reverse Phalen, and Tinel signal tests on the wrist.

Results The average of the sample was of 22.73 years, with a prevalence of single, right-handed female participants. Most of them had been using smartphones for 5 to 10 years, and 85% reported discomfort in the wrist and fingers while using the device, with numbness as the most prevalent symptom. Most clinical tests were negative, and the Finklestein test showed greater positivity. The BCTQ is composed of a symptom severity scale (S scale) and a functional status scale (F scale): the overall score on the S scale was of 1.61, indicating mild to moderate symptoms, and the F scale revealed that the symptoms did not affect functionality.

Conclusion There was a significant correlation between the length of use of smartphones and discomfort in the wrist and fingers; as such, smartphones are a risk factor for the development of morbidities.

Keywords
- mobile phones
- wrist trauma
- hand trauma
- cumulative trauma disorders

* *Study developed at Faculdade de Integração do Sertão (FIS), Serra Talhada, PE, Brazil.*

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Resumo

Objetivo Investigar o uso de *smartphones* em longo prazo como fator de risco para o desenvolvimento de morbidades no nível do punho e dos dedos.

Métodos Realizou-se um estudo descritivo, exploratório, de abordagem quantitativa, para a obtenção de medidas de prevalência com cem acadêmicos usuários de *smartphones* de uma faculdade privada localizada no sertão de Pernambuco. Foram aplicados um questionário semiestruturado e o Questionário de Síndrome do Túnel do Carpo de Boston (Boston Carpal Tunnel Questionnaire, BCTQ, na sigla em inglês), além da Escala Visual Analógica (EVA) e dos testes de Finkesltein, Phalen, Phalen reverso, e sinal de Tinel no punho.

Resultados A idade média da amostra foi de 22,73 anos, com prevalência de solteiros, de destros, e do sexo feminino. O tempo de uso do *smartphone* indicado pela maioria dos participantes era entre 5 e 10 anos, e 85% da amostra relatou já ter sentido desconforto no punho e nos dedos durante o uso do aparelho, sendo a dormência o sintoma mais prevalente. Com relação aos testes clínicos, houve prevalência de resultados negativos, e o de Finklestein apresentou maior positividade. Quanto ao BCTQ, dividido em duas escalas, uma de gravidade dos sintomas (escala G) e uma de estado funcional (escala F), a média geral das pontuações foi de 1,61 na escala G, o que indica sintomas de leve a moderados, já a escala F revelou que os sintomas não afetavam a funcionalidade.

Conclusão Foi possível observar uma correlação significativa entre o tempo de uso dos *smartphones* e a presença de desconforto no punho e nos dedos, o que indica que se trata de um fator de risco para o desenvolvimento de morbidades.

Palavras-chave

- telefones celulares
- traumatismos do punho
- traumatismos da mão
- transtornos traumáticos cumulativos

Introduction

The 19th century witnessed the advent of new information and communication technologies; by the late 1870s, the first telephones caused a revolution in culture and communication. However, the real revolution occurred in the 21st century with social/digital networks and mobile technologies. A clear example is the smartphone, which currently surpasses notebook computers as a tool for internet access, communication, and work; it also aggregates functions from several other devices.[1,2]

According to the Brazilian National Telecommunications Agency (Agência Nacional de Telecomunicações, ANATEL, in the Portuguese acronym),[3] Brazil had approximately 236 million cell phones in March 2018; this is a high figure compared to the number of inhabitants, of about 209.1 million per the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística, IBGE, in the Portuguese acronym).[4] Cell phones are a valuable invention with several features that make daily life easier. However, while it provides benefits, it can also lead to physical harm, as shown by Guterres et al.,[5] who evaluated musculoskeletal complaints in every region of the body among smartphone users and found the neck (49.4%) as the area most frequently involved, followed by the wrists and hands (37.9%).

Anatomically, the wrist is considered one of the most complex joints in the body. It performs flexion, extension, ulnar deviation, radial deviation, and circumduction movements. The hand is the distal end of the upper limb, and it is considered the most important functional part of the upper appendicular skeleton. The carpometacarpal joints consist of the second row of the carpal bones and metacarpal bones. The metacarpophalangeal joints, formed by the metacarpal bones and the proximal phalanges, perform flexion, extension, hyperextension, adduction, and abduction movements. Lastly, the interphalangeal joints are located between the phalanges and enable flexion and extension movements.[6,7]

The thumb is the first digit, and it presents the highest level of functionality. Its carpometacarpal joint consists of the trapezium and the base of the first metacarpal bone, and it enables flexion, extension, adduction, abduction, opposition, reposition, and circumduction of the thumb. Although the thumbs are highly mobile, their design does not enable the heavy lifting required to handle a smartphone; as such, the level of effort may vary depending on the mode and speed of typing.[8]

The highest prevalence of upper-limb symptoms resulting from repetitive efforts occurs in the hands. These symptoms are due to repetitive movement, vibration, use of hand tools, high forces, and inadequate postures, which cause discomfort, feeling of heaviness, pain, numbness, tingling, and decreased functionality and strength.[9] Among these disorders, De Quervain tenosynovitis and carpal tunnel syndrome prevail.[10]

Although the association between repetitive movements and musculoskeletal morbidities is a fact, few studies in the literature report these conditions with the use of smartphones. It is possible to prevent or delay these physical health issues by using smartphones in moderation and correctly; the population and healthcare professionals must know

these risks to formulate preventive strategies and measures. Thus, the present study aims to investigate the long-term use of smartphones as a risk factor for the development of wrist and fingers conditions.

Materials and Methods

The present is a descriptive, exploratory study with a quantitative approach to assess the prevalence of injuries among smartphone users. The research was conducted at a college, and the sample consisted of one hundred students. The Research Ethics Committee approved the study under opinion number 2,889,152 before data collection.

The subjects included were enrolled at the college during the research period, had been using smartphones for more than 5 years, and were 21 to 30 years old. The excluded subjects were those performing any paid activity other than their college studies, or those who had a previous diagnosis of rheumatic diseases.

After presenting the study to the participants, they signed an informed consent form before data collection, which occurred in three stages. The first stage was the application of a semi-structured questionnaire (►**Appendix A, Supplementary material**), available on-line only[11] consisting of closed questions with a single alternative to be checked, except when otherwise stated. This questionnaire enabled the collection of data pertaining to the sociodemographic profile and routine cell phone use of the participants. The presence of pain on evaluation was verified using the visual analog scale (VAS).

The second stage consisted of the application of the Boston Carpal Tunnel Questionnaire (BCTQ) to quantify six critical domains: pain, paresthesia, numbness, weakness, nocturnal symptoms, and global functional status. This questionnaire has two scales, one for the severity of symptoms (S scale) and one for functional status (F scale). The S scale contains 11 multiple-choice questions with scores from 1 to 5, in which 1 represents the absence of symptoms and 5, severe symptoms. The score is an average of these 11 individual items. The F scale addresses 8 usual activities, with scores from 1 to 5 points, in which 1 represents no difficulty, and 5 indicates that the subject cannot perform the activity. Its total score is the average value of these eight items.

The sample data were descriptively analyzed and tabulated using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, United States) software, version 22.0, to determine the means, minimum, maximum, standard deviation (SD), and percentage distribution per the specificity of each variable. The Chi-squared test evaluated the significance between the variables with a 95% confidence interval (95%CI; $p < 0.05$). The results are shown in tables.

Results

►**Table 1** shows the sociodemographic profile of the research participants. The average age of the students was of 22.73 years (SD: ± 2.296). Regarding gender, there was a prevalence of females (69%). In addition, right-handed subjects were predominant (89%).

Table 1 Sociodemographic profile of the students

Variables	Categories	n	%	Average	Standard deviation
Age		–	–	22.73 years	± 2.296
Gender	Female	69	69	–	
	Male	31	31		–
Dominant hand	Right	89	89	–	
	Left	11	11		–

Table 2 Data on smartphone use (N = 100)

Variables	Categories	n	%
Time of use	5–10 years	57	57
	10–15 years	33	33
	More than 15 years	10	10
Time of daily use	More than 10 hours	28	28
	5–8 hours	28	28
	8–10 hours	19	19
	Other	25	25
Pauses during use	Up to 20 minutes	33	33
	30 minutes to 1 hour	27	27
	No pauses	22	22
	Other	18	18
Main activity performed	Typing	84	84
	Talking	8	8
	Other	8	8

►**Table 2** reveals that most students (57%) had been using smartphones for 5 to 10 years; 33% reported taking breaks of up to 20 minutes during use, and only 22% reported not doing so. As for daily time distribution, 28% used the smartphone for more than 10 hours, and 84% reported typing as the main activity performed.

►**Table 3** describes the most frequent way of handling and typing. A total of 51% of the subjects held the device only with their right hand, and 71% typed using both hands.

►**Table 4** shows a positive correlation between the time of use and discomfort ($p = 0.000$). Out of the 28 students reporting cell phone use for more than 10 hours a day, 89.3% mentioned some episode of discomfort during use, as well as in all other time variables. This confirms that the daily use of smartphones can cause wrist and finger soreness, regardless of the number of years that the device has been used, as even those who had been using them for shorter periods reported discomfort.

Table 3 Smartphone handling (N = 100)

Variables	Categories	n	%
How the smartphone is held	With the right hand	51	51
	With both hands	45	45
	With the left hand	4	4
How one types	With both hands	71	71
	With a single hand	29	29

Table 4 Awareness on risks and symptoms related to smartphone use (N = 100)

Variables	Categories		n	%
Have you ever felt any discomfort during use?	Yes		85	85
	No		15	15
Where?	Wrist		54	26.3
	Thumb		49	23.9
	Hand		28	13.7
	Forearm		20	9.8
	Other		54	26.3
Symptom	Numbness		43	30.7
	Tingling		34	24.3
	Pain		30	21.4
	Other		33	23.6
Visual Analog Scale	With pain – 24% (n = 24)	Moderate	13	54.2
		Mild	11	45.8
	No pain	–	76	76

When asked if they had ever felt any discomfort in the upper limbs while using a smartphone, 85% of the subjects answered yes. The most affected regions were the wrist (26.3%) and the thumb (23.9%). Regarding the characteristics of these symptoms, 30.7% reported numbness, 24.3%, tingling, and 21.4%, pain. Only 24% of the sample reported pain on the VAS assessment; among them, 54.2% described moderate symptoms.

Participants self-reported numbness and tingling as the most common discomfort, especially in the wrist, thumb, and hand. These findings may indicate carpal tunnel syndrome and De Quervain tenosynovitis, or a predisposition for their development.

►**Table 5** shows the overall mean score on the S scale of the BCTQ and the mean values per symptomatology. The overall mean score was of 1.61 (SD: ± 0.485), indicating mild symptoms, since 1 and 2 respectively refer to no and few symptoms. When analyzing each individual symptom, the highest mean score, of 1.68 (SD: ± 0.657), was for tingling, followed by pain (1.65; SD: ± 0.560), weakness (1.59; SD: ± 0.727), and difficulty picking up objects (1.11; SD: ± 0.423).

Table 5 Average scores on the symptom severity scale (S scale) of the Boston Carpal Tunnel Questionnaire

Variable	Mean	Standard deviation
Overall average on the S scale	1.61	± 0.485
Average tingling score	1.68	± 0.657
Average pain score	1.65	± 0.560
Average weakness score	1.59	± 0.727
Average difficulty picking up objects	1.11	± 0.423

Table 6 Average scores on the functional status scale (F scale) of the Boston Carpal Tunnel Questionnaire

Variable	Mean	Standard deviation
Overall average on the F scale	1.43	± 0.493
Ability to carry grocery bags	1.63	± 0.816
Ability to hold the telephone	1.61	± 0.827
Ability to perform household work	1.60	± 0.912
Ability to open a glass jar	1.50	± 0.870
Ability to write	1.49	± 0.771
Ability to hold a book during reading	1.40	± 0.663
Ability to button up clothes	1.14	± 0.348
Ability to shower and get dressed	1.08	± 0.338

The average score on the S scale regarding difficulty picking up objects was of 1.11 (SD: ± 0.423). This value had a positive correlation with the overall average score on the F scale ($p = 0.000$), showing virtually no difficulty in picking up objects. This finding confirms that symptoms do not affect the quality of life of participants probably because their condition is mild.

Lastly, the F scale of the BCTQ, shown in ►**Table 6**, assessed how much these symptoms affect activities of daily living. In addition, we calculated the mean scores for each task; the highest value referred to the ability to carry grocery bags (1.63; SD: ± 0. 85), and the lowest value, to the ability to shower and get dressed (1.08; SD: ± 0.34).

Discussion

The average age of the participants was of 22.73 years, which is consistent with other studies on the use of smartphones by university students, including the one by Xie et al.,[12] in which the average age was of 23.9 years. The prevalence of females in the present study corroborates the research by Taufiq et al.,[13] who evaluated the association between De Quervain

tenosynovitis and excessive typing on smartphones among 137 medical students, 80% of whom were female. Ali et al.[14] observed that out, of 300 students, 94% were right-handed, corroborating the present study. The literature does not specify why most people are right-handed, but there is a potential association with genetic, anatomical, and cultural factors.[15]

Pereira et al.[16] conducted an online survey with one hundred subjects to assess the relationship between smartphone use and carpal tunnel syndrome; they found out that half of the sample had been using smartphones for more than five years, confirming our data. As for taking breaks, 58% of the participants did not do it during smartphone use. This data does not corroborate our research, since the percentage of those who did not take breaks was lower.

As for the distribution of daily time, Guterres et al.[5] found that most subjects (22%) use smartphones for more than 10 hours, confirming our results. Eapen et al.[17] verified the prevalence of cumulative trauma in the upper limbs from cell phone users and observed that 96.5% of respondents used the phone to type text messages.

In an observational study on typing postures and styles, Gold et al.[18] observed that 46.1% of the subjects held the smartphone with both hands and 36.2%, with the right hand; in addition, 82.3% typed using the thumb, corroborating our findings.

Xie et al.[12] performed an electromyographic study and found that the upper limbs had increased activity when typing with only one hand, requiring greater amplitude and more repetitive movements of the thumb. These authors[12] suggested that smartphones should be held with both hands, using both thumbs to prevent muscle overload and morbidities.

Studies on smartphone handling show that we must limit the daily use of these devices to avoid morbidities in the upper limbs. In addition, we must use both hands and both thumbs to hold the smartphone, take frequent breaks, avoid typing at high speed, and support the forearms while typing.[14,19] In the present study, the time of daily use was consistent with the results found by Oliveira,[20] in which 72.11% of subjects using the device for more than 10 hours had discomfort, and there was discomfort regardless of the time of daily use.

Regarding discomfort in the upper limbs with the use of smartphones, our findings corroborate those of the research by Oliveira,[20] in which 71.2% of college students reported discomfort in the wrist and fingers. Eapen et al.[17] reported that 53% of subjects complained of discomfort in the thumbs, and 13%, in the wrists. In addition, these authors state[17] that several symptoms were related to repetitive strain injuries, especially pain, followed by discomfort and tingling. They also observed a high prevalence of pain (61.7%). Thus, our data is consistent with the main types of symptoms presented; however, pain was the third most frequent symptom in the present study, but the literature indicates it as the main symptom.

Oliveira[20] reported that 71.15% of the participants complained of pain, mostly classified as moderate (75.2%), which corroborates the level of pain found in the present study. The overall mean score obtained by Oliveira[20] was of 1.82, which is also considered mild. Regarding individual symptoms, pain prevailed, with the highest average (2.04), followed by tingling (average score: 1.72), weakness (average score: 1.64), and difficulty picking up objects (average score: 1.31). These figures do not corroborate the most prevalent symptom, but are similar to the average values, ranges, and least prevalent symptom.

Comparing the difficulty picking up objects found in the present study and the same finding by Oliveira,[20] which was of of 1.31 on average, one can observe that they were similar, since both samples presented mild difficulty. The scores on the F scale of the BCTQ are consistent with those of the literature, which shows that symptoms do not affect the functionality and activities of daily living of participants, such as in the study by Pereira et al.,[16] who reported that subjects had no major issues or difficulty when handling a smartphone.

Conclusion

Given the aforementioned data, we conclude that there is a significant association between the time of daily smartphone use and the presence of discomfort; smartphones are a risk factor for the development of wrist and finger morbidities. Furthermore, we suggest further studies to investigate not only subjective symptoms, but also physical capacity quantitatively, as well as the muscle biomechanics of typing. This will enable the development of more specific preventive measures, which are critical because the incidence of smartphone-associated repetitive strain injuries tends to rise.

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Conflict of Interests
The authors have no conflict of interests to declare.

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The Impact of COVID-19 on the Timing of Rotator Cuff Repair and Method of Postoperative Follow-up

Impacto da COVID-19 no momento de reparo do manguito rotador e método de acompanhamento pós-operatório

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Abstract

Objective Rotator cuff repair (RCR) is one of the most common arthroscopic procedures. Our investigation aims to quantify the impact that the COVID-19 pandemic had on RCR, specifically on patients with acute, traumatic injuries.

Methods Institutional records were queried to identify patients who underwent arthroscopic RCR between March 1st to October 31st of both 2019 and 2020. Patient demographic, preoperative, perioperative, and postoperative data were collected from electronic medical records. Inferential statistics were used to analyze data.

Results Totals of 72 and of 60 patients were identified in 2019 and in 2020, respectively. Patients in 2019 experienced shorter lengths of time from MRI to surgery (62.7 ± 70.5 days versus 115.7 ± 151.0 days; $p = 0.01$). Magnetic resonance imaging (MRI) scans showed a smaller average degree of retraction in 2019 (2.1 ± 1.3 cm versus 2.6 ± 1.2 cm; $p = 0.05$) but no difference in anterior to posterior tear size between years (1.6 ± 1.0 cm versus 1.8 ± 1.0 cm; $p = 0.17$). Less patients in 2019 had a telehealth postoperative consultation with their operating surgeon compared with 2020 (0.0% versus 10.0%; $p = 0.009$). No significant changes in complications (0.0% versus 0.0%; $p > 0.999$), readmission (0.0% versus 0.0%; $p > 0.999$), or revision rates (5.6% versus 0.0%; $p = 0.13$) were observed.

Conclusion From 2019 to 2020, there were no significant differences in patient demographics or major comorbidities. Our data suggests that even though the time from MRI to surgery was delayed in 2020 and telemedicine appointments were

Keywords
- COVID-19
- operative time
- perioperative period
- rotator cuff
- shoulder

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necessary, RCR was still performed in a timely manner and with no significant changes in early complications.
Level of Evidence III.

Resumo

Objetivo O reparo do manguito rotador (RMR) é um dos procedimentos artroscópicos mais comuns. Nossa pesquisa visa quantificar o impacto da pandemia de COVID-19 sobre o RMR, especificamente em pacientes com lesões agudas e traumáticas.
Métodos Os prontuários institucionais foram consultados para identificação de pacientes submetidos ao RMR artroscópico entre 1° de março e 31 de outubro de 2019 e de 2020. Dados demográficos, pré-operatórios, perioperatórios e pós-operatórios dos pacientes foram coletados de prontuários eletrônicos. Os dados foram analisados por estatística inferencial.
Resultados Totais de 72 e de 60 pacientes foram identificados em 2019 e 2020, respectivamente. Os pacientes de 2019 apresentaram menor intervalo entre a ressonância magnética (RM) e a cirurgia (62,7 ± 70,5 dias *versus* 115,7 ± 151,0 dias; $p = 0,01$). Os exames de RM mostraram menor grau médio de retração em 2019 (2,1 ± 1,3 cm *versus* 2,6 ± 1,2 cm; $p = 0,05$), mas nenhuma diferença foi observada na extensão anteroposterior da laceração entre os anos (1,6 ± 1,0 cm *versus* 1,8 ± 1,0 cm; $p = 0,17$). Em 2019, o número de pacientes atendidos por seus cirurgiões em consultas pós-operatórias por telemedicina foi menor em comparação com 2020 (0,0% *versus* 10,0%; $p = 0,009$). Não foram observadas alterações significativas nas taxas de complicação (0,0% *versus* 0,0%; $p > 0,999$), de readmissão (0,0% *versus* 0,0%; $p > 0,999$) ou de revisão (5,6% *versus* 0,0%; $p = 0,13$).
Conclusão Não houve diferenças significativas nos dados demográficos dos pacientes ou nas principais comorbidades entre 2019 e 2020. Nossos dados sugerem que, embora o intervalo entre a RM e a cirurgia tenha sido maior em 2020 e tenha havido necessidade de consultas por telemedicina, o RMR ainda foi realizado em tempo hábil e sem alterações significativas nas complicações precoces.
Nível de Evidência III.

Palavras-chave
- COVID-19
- duração da cirurgia
- período perioperatório
- manguito rotador
- ombro

Introduction

Rotator cuff tears are one of the most common causes of shoulder pain in adults and can contribute to significant dysfunction and shoulder pain. The degree of dysfunction noted – specifically with acute, traumatic tears – generally leads patients to present for orthopedic evaluation in a short time frame.[1] However, during the 2019 novel coronavirus disease (COVID-19) pandemic, health systems were forced to allocate medical resources and personnel to combat the rapidly spreading illness. The first case of COVID-19 was reported in the state of New York, USA, on March 1, 2020. To curb spread and preserve resources, the surgeon general issued a statement advising hospitals throughout the nation to halt elective procedures on March 14, 2020. This moratorium on elective procedures was lifted in New York City on June 8, 2020, but it took an additional period of months before elective procedures began to return to numbers resembling their prepandemic levels.

Even after elective surgical procedures resumed, patients remained hesitant to present for evaluation or treatment of shoulder injuries. There was a significant decline in public interest for rotator cuff surgery during the period of the pandemic, with a 53.32% decline in Google search volume during this period.[2] Previous investigations have identified that only between 27 and 56.8% of patients would be willing to undergo an elective procedure at the earliest available time.[3,4]

With patient hesitancy to obtain elective surgery, there was a potential for delayed care for rotator cuff pathology, a risk factor that has been linked to worse outcomes.[5,6] There is a risk for increased tear size, progression of muscle atrophy, and increased risk of revision surgery with delayed treatment of rotator cuff tears.[7–10] Given this risk for worsening outcome with delay, it has been recommended that rotator cuff repair (RCR) – specifically for acute tears – be given consideration to be prioritized over other, potentially less time-sensitive, elective procedures.[11,12]

The goals of our investigation are to evaluate for any differences in demographics in patients undergoing rotator cuff surgery immediately following the COVID-19 outbreak

in 2020 compared with the same period from 2019 and to evaluate the extent to which rotator cuff surgeries were delayed (from onset of symptoms or time of magnetic resonance imaging [MRI] to time of surgery). We hypothesize that patients undergoing rotator cuff surgery in 2020 will be younger, more likely to have an acute injury, and have a larger delay in treatment for an acute injury compared with the previous nonpandemic year.

Materials and Methods

Patient Cohort

Our institutional review board approved the present study. Institutional records were queried to identify patients who underwent arthroscopic RCR based on Current Procedural Terminology (CPT) code 29827 between March 1 and October 31 of both 2019 and 2020. These procedures were performed at a single institution by two attending surgeons.

Data Collection

Electronic medical records for identified patients were queried for demographic data, MRI findings, and physical exam data. These data include preoperative, perioperative, and postoperative characteristics of patients undergoing RCR. Range of motion for forward elevation and external rotation were collected from the initial physical exam of the patients with their respective operating surgeon. Patient operative reports were reviewed to identify the type of rotator cuff repair and the number of anchors used during repair. Patients who were miscoded and did not undergo RCR upon review of operative reports were excluded from the analysis. For each patient, MRI imaging was reviewed to determine the Goutallier score, the degree of tear retraction, and the anterior-to-posterior extent of tear. Subanalyses were also performed by comparing the subset of patients who sustained traumatic injuries in 2019 versus the same group in 2020.

Statistical Analysis

Data were compared between the 2019 and 2020 cohorts. Descriptive and comparative statistics for patient demographics, as well as preoperative, perioperative, and postoperative data, were analyzed for all patients. Univariate analysis of categorical data was performed using the chi-squared test or the Fisher exact test when appropriate. Continuous data were analyzed using the 2-sample *t*-test or the Mann-Whitney U test depending on the normality of the sample. Normality was determined using the Kolmogorov-Smirnov test. To compare variance between the two groups, the F-test for equality of variance was used. Statistical significance was set to a p-value < 0.05.

Results

Demographics

The present study identified 132 patients, 72 in 2019 and 60 and 2020, who underwent RCR. There was no difference in gender (48.6 male versus 58.3% male; $p = 0.27$), mean age at surgery (61.0 ± 9.4 years versus 60.5 ± 10.2 years; $p = 0.78$), or body mass index (BMI) (28.1 ± 5.3 versus 29.9 ± 7.0; $p = 0.27$). American Society of Anesthesiologists (ASA) scores ($p = 0.31$), smoking status ($p = 0.68$), and history of diabetes (6.9 versus 15.0%, $p = 0.12$) and hypertension (48.6 versus 56.7%; $p = 0.29$) were also similar between years. The distribution of insurance providers for these patients was also consistent ($p = 0.63$) (►**Table 1**). After the end of the moratorium on elective procedures on June 8, 2020, 38 patients in the 2019 cohort underwent RCR, compared with 46 patients in the 2020 cohort.

Preoperative Characteristics

More subjects in the 2019 cohort had a history of surgery on the same shoulder than in 2020 (11.1 versus 1.7%; $p = 0.04$). There was also a trend toward more subjects in the 2019 cohort being treated for acute injuries (38.9 versus 25.0%; $p = 0.09$) but this was not significant in our sample. No significant difference was found for the number of traumatic injuries treated between years (68.1 versus 75.0%; $p = 0.35$). Additionally, no difference was found between years for the length of time from pain or injury onset to surgery for traumatic injury patients (360.6 ± 938.5 days versus 259.4 ± 304.0 days; $p = 0.47$) or atraumatic injury patients (436.3 ± 388.1 days versus 478.7 ± 426.7 days; $p = 0.66$). For preoperative therapy, a similar number of patients attempted physical therapy (63.2% versus 55.0%; $p = 0.35$) and received a corticosteroid injection in the office prior to attempting operative management (25.0 versus 28.3%; $p = 0.67$). For patients who did receive corticosteroid injections, there was a trend toward 2019 patients experiencing longer times from injection to surgery (342.9 ± 376.4 days versus 157.8 ± 89.2 days; $p = 0.10$). For the preoperative physical exam, there was no difference in range of motion for both forward elevation ($158.0° \pm 38.6°$ versus $158.3° \pm 29.3°$; $p = 0.47$) and external rotation ($51.6° \pm 13.1°$ versus $50.5° \pm 14.7°$; $p = 0.63$) (►**Table 2**).

Radiographic Findings and Intraoperative Characteristics

Patients in 2019 experienced significantly shorter lengths of time from MRI to surgery (62.7 ± 70.5 days versus 115.7 ± 151.0 days; $p = 0.01$). There was no difference between 2019 and 2020 in the amount of rotator cuff tears that progressed from partial tear as read on MRI to full tear as determined by intraoperative evaluation (12.5 versus 15.0%; $p = 0.68$) or the amount of full rotator cuff tears at surgery (84.7 versus 81.7%; $p = 0.64$). There was no difference in Goutallier scores for supraspinatus (0.5 ± 0.7 versus 0.8 ± 1.0; $p = 0.17$) or infraspinatus (0.5 ± 0.8 versus 0.6 ± 0.8; $p = 0.25$). The 2019 cohort demonstrated smaller degrees of retraction for their rotator cuff tears (2.1 ± 1.3 cm versus 2.6 ± 1.2 cm; $p = 0.05$) but there was no significant difference in size on the anterior-to-posterior measurement (1.6 ± 1.0 cm versus 1.8 ± 1.0 cm; $p = 0.17$). There was no difference in the number of massive (> 4 cm) rotator cuff tears between the 2 years (7.0 versus 7.5%; $p = 0.91$). Reviewing the operative reports, there was a trend toward a greater proportion of single-row repairs being performed in 2019 (72.7 versus 56.0%; $p = 0.06$) but there

Table 1 Patient demographics (2019: $n = 72$; 2020: $n = 60$)

Characteristic	2019	2020	*p-value*
Age at surgery (years old)	61.0 ± 9.4	60.5 ± 10.2	0.78
Gender			
Male	35 (48.6%)	35 (58.3%)	0.27
Female	37 (51.4%)	25 (41.7%)	
BMI	28.1 ± 5.3	29.9 ± 7.0	0.27
ASA Score			0.31
1–2	56 (77.8%)	42 (70.0%)	
3–4	16 (22.2%)	18 (30.0%)	
Insurance Provider			0.63
Medicare	16 (22.2%)	18 (30.0%)	
Medicaid	7 (9.7%)	3 (5.0%)	
Private	37 (51.4%)	26 (43.3%)	
Workers compensation	11 (15.3%)	12 (20.0%)	
Self-paid	1 (1.4%)	1 (1.7%)	
Diabetes			0.12
Yes	5 (6.9%)	9 (15.0%)	
No	67 (93.1%)	51 (85.0%)	
Hypertension			0.29
Yes	35 (48.6%)	34 (56.7%)	
No	37 (51.4%)	26 (43.3%)	
Smoking history			0.68
Responses (*n*)	70	60	
Never	44 (62.9%)	42 (70.0%)	
Former	18 (25.7%)	13 (21.7%)	
Current	8 (11.4%)	5 (8.3%)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.

was no difference in the number of anchors used between 2019 and 2020 for either single-row repair (1.4 ± 0.8 versus 2.2 ± 1.5; $p = 0.61$) or double-row repair (2.6 ± 1.5 versus 2.5 ± 1.7; $p = 0.53$) (►**Table 3**).

Perioperative Characteristics

There was no significant difference in the duration of the surgical procedure between 2019 and 2020 (80.0 ± 28.2 minutes versus 86.7 ± 34.1 minutes; $p = 0.32$) or length of stay in the recovery unit on the day of their procedure (8.1 ± 3.0 hours versus 7.4 ± 1.9 hours; $p = 0.12$). Additionally, no patient in either group experienced any intraoperative complication (►**Table 4**).

Postoperative Characteristics

Significantly more subjects in 2020 had a virtual/telehealth postoperative visit with their operating surgeon compared with 2019 (0.0 versus 10.0%; $p = 0.009$). There was also a trend toward 2020 patients experiencing longer lengths of time and more variability in the time between their surgery date and postoperative visit (12.0 ± 4.7 days versus 16.7 ± 17.5 days; $p = 0.19$). There was no significant difference in participation in physical therapy between the two cohorts (2019: 98.5 versus 2020: 90.4%; $p = 0.08$). There was no difference in readmission rates (0.0 versus 0.0%; $p > 0.999$) or in patients needing revision surgery on the same shoulder (5.6 versus 0.0%; $p = 0.13$) (►**Table 5**).

Subanalysis of Patients with Traumatic Injury

Subjects in the 2019 and 2020 cohorts who sustained an identifiable traumatic injury to their rotator cuff were further analyzed. In the 2019 cohort, 57.1% of the traumatic injuries occurred in males compared with 60% in the 2020 cohort ($p = 0.836$). There was still no significant difference in the length of time from injury to surgery in 2019 and 2020 (360.6 ± 938.5 days versus 259.4 ± 304.0 days; $p = 0.47$). Additionally, patients in 2019 still experienced shorter lengths of time from MRI to surgery (56.7 ± 47.3 days versus 80.9 ± 75.8 days; $p = 0.04$). When comparing the variance in time from the onset of symptoms between cohorts, there was a significantly greater variance in the 2019 cohort compared with the 2020 cohort ($p < 0.001$).

Table 2 Patient preoperative characteristics (2019: $n = 72$; 2020: $n = 60$)

Characteristic	2019	2020	*p-value*
Prior shoulder surgery			0.04
Yes	8 (11.1%)	1 (1.7%)	
No	64 (88.9%)	59 (98.3%)	
Chronic versus acute injury			0.09
Chronic (> 3 months from injury to surgery)	44 (61.1%)	45 (75.0%)	
Acute (< 3 months from injury to surgery)	28 (38.9%)	15 (25.0%)	
Traumatic versus atraumatic injury			0.35
Traumatic	49 (68.1%)	45 (75.0%)	
Atraumatic	23 (31.9%)	15 (25.0%)	
Average time from injury to surgery (days)			
Traumatic	360.6 ± 938.5	259.4 ± 304.0	0.47
Atraumatic	436.3 ± 388.1	478.7 ± 426.7	0.66
Attempted physical therapy prior to surgery			0.35
Responses (*n*)	68	60	
Yes	43 (63.2%)	33 (55.0%)	
No	25 (36.8%)	27 (45.0%)	
Received corticosteroid injection			0.67
Yes	18 (25.0%)	17 (28.3%)	
No	54 (75.0%)	43 (71.7%)	
Average time from injection to surgery (days)	342.9 ± 376.4	157.8 ± 89.2	0.10
Preoperative forward elevation	158.0° ± 38.6°	158.3° ± 29.3°	0.47
Preoperative external rotation	51.6° ± 13.1°	50.5° ± 14.7°	0.63

Discussion

These findings suggest that the COVID-19 pandemic caused a delay in time to surgery for patients following rotator cuff tear. Patients in 2019 were more likely to have had a previous surgery on their shoulder, but there were no other significant differences between the 2019 and 2020 cohorts. After the moratorium on elective procedures, more patients underwent RCR surgery in 2020 compared with 2019. This is despite previous literature that demonstrated a 53.32% decrease in Google search trends for "rotator cuff surgery" during and around the COVID-19 pandemic.[2]

Mall et al.[1] described that acute, traumatic rotator cuff tears are more likely to occur in generally young, male patients. Previously, Moverman et al.[4] found that male patients were more likely to feel comfortable pursuing elective surgery during the early stages of the COVID-19 pandemic. However, we found no significant difference in the gender distribution in traumatic rotator cuff tears or time from injury to surgery between the 2019 and 2020 cohorts. Additionally, it is likely that the mean difference in time from MRI to surgery between the 2 groups (53 days) can be partially explained by the duration of the moratorium on elective surgery (86 days).

The current literature on the increased risk for retear or worse outcomes in patients who undergo delayed repair of their rotator cuff tear is controversial. Kwong et al.[13] reported in a systematic review that approximately one-third of symptomatic, full-thickness rotator cuff tears progress by ≥ 5 mm by 37.8 months, at a rate of ∼ 1% per month. Fu et al.[8] demonstrated an increased rate of retear in the delayed reconstruction group (> 12 months) compared with both the early (< 6 weeks) and routine (6 weeks to 12 months) groups. However, these data were obtained from a large national database and only evaluated the time from the date of the initial diagnosis – nontraumatic event – to the date of surgery. Another report on a series of 20 patients undergoing surgery within 6 months of injury demonstrated improved patient-reported outcomes scores compared with an age- and gender-matched cohort who underwent surgery at between 6 and 18 months after injury.[7] In contrast, Petersen et al.[10] reported no significant influence on the outcome for any size rotator cuff tear in a series of 36 patients if repaired within 4 months of the injury; however, massive tears repaired after 4 months had inferior outcomes. Patel et al.[9] demonstrated a shorter time to recovery and less need for allograft augmentation in large tears for subjects in an early repair group, but there was no significant difference in outcomes at the mid-term follow-up (a median of 30 months postoperatively). In their systematic review, Mall et al.[1] did not demonstrate any consensus in the literature on improved outcomes with early repair of rotator cuff tears. Our data did

Table 3 Operative Report and Magnetic Resonance Imaging data (2019: $n = 72$; 2020: $n = 60$)

Characteristic	2019	2020	*p-value*
Time from MRI to surgery (days)	62.7 ± 70.5	115.7 ± 151.0	0.01
Partial tear at MRI to full tear at surgery			0.68
Yes	9 (12.5%)	9 (15.0%)	
No	63 (87.5%)	51 (85.0%)	
Type of rotator cuff tear at surgery			0.64
Full	61 (84.7%)	49 (81.7%)	
Partial	11 (15.3%)	11 (18.3%)	
Average supraspinatus Goutallier scores	0.5 ± 0.7	0.8 ± 1.0	0.17
Supraspinatus Goutallier scores			0.12
0–1	56 (90.3%)	45 (80.4%)	
2–3	6 (9.7%)	11 (19.6%)	
Average infraspinatus Goutallier scores	0.5 ± 0.8	0.6 ± 0.8	0.25
Infraspinatus Goutallier scores			0.35
0–1	53 (85.5%)	51 (91.1%)	
2–3	9 (14.5%)	5 (8.9%)	
Average degree of retraction (cm)	2.1 ± 1.3	2.6 ± 1.2	0.05
Average tear size (cm)	1.6 ± 1.0	1.8 ± 1.0	0.17
Massive rotator cuff tears at MRI			0.91
MRI read (*n*)	57	53	
Yes	4 (7.0%)	4 (7.5%)	
No	53 (93.0%)	49 (92.5%)	
Type of Rotator Cuff repair			0.06
Single Row	48 (72.7%)	28 (56.0%)	
Double	18 (27.3%)	22 (44.0%)	
Average Number of Anchors used			
Single-row repair	1.4 ± 0.8	2.2 ± 1.5	0.61
Double-row repair	2.6 ± 1.5	2.5 ± 1.7	0.53

Table 4 Perioperative characteristics of the patients (2019: $n = 72$; 2020: $n = 60$)

Characteristic	2019	2020	*p-value*
Duration of surgery (minutes)	80.0 ± 28.2	86.7 ± 34.1	0.32
Length of stay (hours)	8.1 ± 3.0	7.4 ± 1.9	0.12
Blood transfusion			1.0
Yes	0 (0.0%)	0 (0.0%)	
No	72 (100.0%)	60 (100.0%)	
Surgical complications			1.0
Yes	0 (0.0%)	0 (0.0%)	
No	72 (100.0%)	60 (100.0%)	

demonstrate significantly more retracted tears in the 2020 cohort, but there was no difference in the number of anchors required for arthroscopic repair between the 2 cohorts.

Elective surgery during the COVID-19 pandemic was strongly influenced by several factors, including ethical considerations, resource limitations, and patient willingness to undergo surgery during a pandemic.[6,11,14] In a report on oncological orthopedic patients, the delays in surgical management caused by COVID-19 demonstrated major morbidity.[5] There have been no reports to date on the impact in delays in surgical management on orthopedic sports medicine patients. One evidence-based guideline suggested that

Table 5 Postoperative characteristics of the patients (2019: $n = 72$; 2020: $n = 60$)

Characteristic	2019	2020	*p-value*
Postoperative visit method			0.009
Telehealth visit	0 (0.0%)	6 (10.0%)	
In-person office visit	69 (100%)	54 (90.0%)	
Time from surgery to postoperative visit (days)	12.0 ± 4.7	16.7 ± 17.5	0.19
Performed physical therapy			0.08
Responses (*n*)	67	52	
Yes	66 (98.5%)	47 (90.4%)	
No	1 (1.5%)	5 (9.6%)	
Readmission			1.0
Yes	0 (0.0%)	0 (0.0%)	
No	72 (100.0%)	60 (100.0%)	
Revision surgery			0.13
Yes	4 (5.6%)	0 (0.0%)	
No	68 (94.4%)	60 (100.0%)	

acute, traumatic rotator cuff injuries should be treated in a time-sensitive manner while chronic, degenerative injuries should be treated as not time-sensitive surgeries.[11] Specifically for massive tears, evidence suggests that repair in a timely fashion can improve outcomes and reduce morbidity.[10,12,15]

During the COVID-19 pandemic, a significant number of patients participated in telehealth consultations rather than in-person consultations for their immediate postoperative appointment. This was offered at several institutions worldwide, including our own.[14] The goal of these visits was to reduce the number of potential exposures and infections in our community while encouraging appropriate stewardship of healthcare resources. Early reports demonstrated no significant impact on patient-reported outcomes for shoulder surgery patients who underwent telemedicine follow-up postoperatively.[16] We found no immediate increase in postoperative complications in patients who underwent telemedicine follow-up postoperatively; however, only a relatively small proportion of patients (10%) selected this option. The potential for expanding the role of telemedicine without compromising the quality of patient care has been suggested as an area of impact and potential improvement in a postpandemic healthcare environment.[17]

Regarding the limitations of the present study, we only collected immediate and short-term data for patients in the 2020 cohort and cannot compare longer-term outcomes and complications between cohorts. Additionally, our institution represents a specific subset of the global pandemic experience; while our investigation represents a region of significant impact, we have a well-developed healthcare system with the benefits of significant resources and administrative support in aiding a return to normal after COVID-19. Our hope is that the lessons learned during the current pandemic can help guide future approaches to disasters that require rationing of healthcare resources. Future investigations should aim to quantify if the changes surrounding the pandemic led to any intermediate or long-term changes in patient outcomes.

Conclusion

There were no significant differences in patient demographics during the COVID-19 pandemic. Delays in surgical management of acute, traumatic tears from the time of diagnosis via MRI were noted, but the delay from time of injury was not significantly different between the 2019 and 2020 cohorts. Our data suggests that these injuries were still able to be treated in a timely fashion during the pandemic, and the utilization of postoperative telemedicine visits did not lead to any significant changes in early complications.

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Conflict of Interests
Cagle, P. J., – Stryker: Consultant
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Translation and Cultural Adaptation to Portuguese of the Long Head of Biceps Tendon Score*

Tradução e adaptação cultural à língua portuguesa do Long Head Biceps Score

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Abstract

Objective To translate and culturally adapt the Long Head of Biceps Tendon (LHB) score into Brazilian Portuguese.

Methods The process involved translations by professionals fluent in the target language, followed by independent back translations. Next, a committee compared the original and translated versions, pretested the final version, and concluded it.

Results We translated and adapted the questionnaire according to the proposed methodology. In the first version in Portuguese (VP1) there was divergence regarding the translation of twelve terms. Compared to the original version, the back translation of VP1 presented eight diverging terms. A committee prepared a second version in Portuguese (VP2) and applied it to a pretest group consisting of 30 participants. Finally, we conceived the third version in Portuguese, called LHB-pt.

Conclusion The translation and cultural adaptation into Brazilian Portuguese of the LBH score was successfully accomplished.

Keywords
- LHB score
- tenodesis
- tenotomy
- long head biceps tendon

* *Study developed at the Shoulder Surgery Service of Hospital Ortopédico BH (Belo Horizonte, Minas Gerais, Brazil) and the Department of Orthopedics and Traumatology of Universidade Federal de São Paulo (São Paulo, São Paulo, Brazil).*

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Resumo

Objetivo Realizar a tradução e adaptação cultural à língua portuguesa do Long Head of Biceps Tendon (LHB).

Métodos O processo envolveu a produção de traduções por indivíduos com domínio da língua-alvo, retrotraduções de maneira independente, criação de um comitê para comparar as versões original e traduzida, realização de pré-teste com a versão final, e elaboração da versão final.

Resultados O questionário foi traduzido e adaptado conforme a metodologia proposta. Na primeira versão em português (VP1), houve divergências na tradução de doze termos. A retrotradução da VP1 apresentou, quando comparada à versão original, divergência em oito termos. A segunda versão em português (VP2), elaborada por um comitê, foi aplicada a um grupo pré-teste constituído por 30 participantes, e ao final chegou-se à terceira versão em português, denominada LHB-pt.

Conclusão A tradução e adaptação do LHB foram concluídas com sucesso.

Palavras-chave

- LHB score
- tenodese
- tenotomia
- tendão da cabeça longa do bíceps

Introduction

Injuries to the tendon of the long head of the biceps are a significant cause of shoulder pain,[1] especially on the anterior surface, with potential irradiation along its course through the arm.[2] The symptoms usually result from instability, inflammation, or local trauma.[3] The incidence of pain ranges from 36% to 83%, and it is higher according to the severity of associated rotator cuff injuries.[4,5]

Several clinical tests aid in the diagnosis. The Speed test,[6] which is widely accepted and used in the academic environment, has high sensitivity (90%) and low specificity (13.8%).[7]

Complete rupture of the LHB fibers causes a cosmetic deformity known as Popeye sign, which is an increase in the volume of the distal region of the arm, on the anterior surface, resulting from the distal migration of the muscle belly. In a systematic review[8] of 699 tenotomies, the authors reported that this deformity occurs in 43% of the cases. According to the Brazilian literature,[9–12] its incidence ranges from 8.3% to 59.1%. Several factors influence the identification of this sign, including age, the experience of the evaluator, and obesity (especially when the patient has a body mass index [BMI] $> 30\,kg/m^2$).[9,10,13] The Popeye sign is a critical outcome in studies assessing the treatment of biceps injuries.

The biceps brachii acts in forearm supination and elbow flexion; in addition, it makes a small contribution to shoulder flexion.[14] Electroneuromyographic studies[15] have shown that the muscle belly of the long head of the biceps contributes to the dynamic stabilization of the glenohumeral joint, especially during flexion and abduction. A retrospective isokinetic evaluation study[16] involving tenotomized patients with a 7-year follow-up showed 7% of loss in maximal forearm flexion strength and 9.1% of loss in maximal forearm supination strength. Other authors[17] have observed a higher loss of supination strength due to complete tendon rupture. The Brazilian literature has also reported these changes; however, the loss of strength was not higher in patients with more evident Popeye sign.[18]

The wide variety of outcomes associated with this structure has led to the development of the Long Head of Biceps Tendon (LHB) score,[19] which is a functional, specific questionnaire applied by an examiner comparing both shoulders. The LHB score consists of three large domains with different scores: the first one refers to signs and symptoms, the second, to the identification of the Popeye sign, and the third, to the assessment of elbow flexion strength.

In the present study, we describe the process of translation and cultural adaptation of the LHB score into Brazilian Portuguese.

Materials and Methods

The institutional ethics committee analyzed and approved the study. We informed the developers of the score about our intention to translate it, and they consented to it.

Translation and cultural adaptation

The translation into Portuguese and cultural adaptation of the LHB score followed the guidelines proposed by Guillemin.[20] The process included five steps: 1) translation by professionals fluent in the target language; 2) independent back translations; 3) creation of a committee to compare the original and translated versions; 4) pretest of the final version to determine its equivalence with the original test; and 5) adaptation of the weight of the scores per the cultural context.

The translation was made by two translators, native Portuguese speakers and fluent in English. Then, the researchers compared these two versions to generate a consensual first version in Portuguese (VP1). The terms *patient name*, *date of examination*, and *date of birth*" were excluded from the translation as they are not part of the score.

The back translation started following the completion of the VP1. After choosing the terms for the VP1, the researchers designed the LHB form using the same graphic and image standards as those of the original score. A third translator, a native English speaker fluent in Portuguese,

also blinded to the study, evaluated the VP1 and made the back translation.

The professionals who prepared the VP1 and the one who did the back translation were unaware of the purpose of the study.

The third step was the creation of a committee, consisting of three translators, three researchers, and three orthopedists who specialized in shoulder surgery, which compared the original version, the VP1, and the back translation. Based on this analysis, the terminology used in the second Portuguese version (VP2) was determined by consensus. The committee assessed semantic (word meaning), idiomatic (idioms and colloquialisms), and conceptual (concept validity) equivalences through practical experience.

The pretest stage began after the completion of the first three steps. Then, the principal investigator recruited 30 male and female Brazilian subjects, aged 18 to 80 years, who presented partial or subtotal rupture of the long head of the biceps tendon, superior labrum anterior to posterior (SLAP) injuries, or bicipital tendon instability with pulley or rotator cuff injury. They underwent arthroscopic surgical treatment and were followed up for at least one year. We excluded patients with calcified tendinitis, glenohumeral

Table 1 Divergences between translators and specialists in the development of the first version in Portuguese (VP1)

Item	Original	Translator A	Translator B	VP1
Pain/Cramps*	Pain/Cramps (max. 50 points)	Dor/Cãibras (máx. 50 pontos)	Dor/Cólica (Máximo 50 pontos)	Dor/Cãibras (máx. 50 pontos)
Severe*	Severe	Severa	Severa	Grave
None	None	Nenhuma	Nenhuma	Nenhuma
LHB – pain	LHB – pain	Dor LHB	Dor LHB	Dor na cabeça longa do bíceps
Right side	Right side	Lado direito	Lado direito	Lado direito
Left side	Left side	Lado esquerdo	Lado esquerdo	Lado esquerdo
Tenderness*	Tenderness over the bicipital grove	Maciez ao redor do sulco bicipital	Sensibilidade no sulco bicipital	Sensibilidade no sulco bicipital
Speed-test*	Speed-test	Teste de velocidade	Teste rápido	Teste de Speed
Cramps*	Cramps	Cãibras	Cólicas	Cãibras
At rest*	At rest	Em repouso	Sem esforço	Em repouso
On exertion*	On exertion	Em esforço	Com esforço	Em esforço
None	None	Nenhuma	Nenhuma	Nenhuma
Cosmesis*	Cosmesis (max. 30 points)	Cosmética (máx.30 pontos)	Cosmese (máximo 30 pontos)	Estética
Patient-dependent deformity*	Patient-dependent deformity	Percepção do paciente em relação à deformidade	Deformidade do paciente dependente	Percepção do paciente em relação à deformidade
None	None	Nenhuma	Nenhuma	Nenhuma
Mild*	Mild	Fraca	Suave	Leve
Moderate	Moderate	Moderada	Moderada	Moderada
Severe*	Severe	Severa	Severa	Grave
Examiner-dependent deformity*	Examiner-dependent deformity	Percepção do examinador em relação à deformidade	Deformidade do examinador dependente	Percepção do examinador em relação à deformidade
Elbow flexion strength	Elbow flexion strength (max. 20 points)	Força de flexão do cotovelo (máx. 20 pontos)	Força de flexão do cotovelo (máximo 20 pontos)	Força de flexão do cotovelo (máx. 20 pontos)
Affected side	Affected side	Lado afetado	Lado afetado	Lado afetado
Opposite side	Opposite side	Lado oposto	Lado oposto	Lado oposto
Total	Total	Total	Total	Total

Abbreviations: LHB, long head of the biceps; max., maximum; máx., máximo.
Notw* Terms in which divergences were observed between the translators, and/or divergences with the VP1 developed by the researchers.

arthrosis, or associated neurological injury. The exclusion criteria were patients with deafness, aphasia, or any cognitive deficit that directly limited their understanding of the test.

The selected patients filled out an informed consent form (ICF) before the pretest. Then, the principal investigator read VP2 aloud. If any of the terms were not understood by the participant, the researcher could explain the meaning in their own words. Then, the participant could suggest a new word which, in their opinion, provided a clearer definition in Brazilian Portuguese. We reformulated items with a non-understanding rate of 15% or more using the definitions proposed by the participants to develop the third Portuguese version (VP3).

Results

►**Table 1** shows the terms presented by translators A and B, as well as the VP1. In the first step of the process, twelve cases of divergence were observed.

►**Table 2** shows the back translation, in which eight cases of divergence in the translation were observed regarding the original version. This table also describes the terms chosen by the committee for the VP2.

►**Table 3** presents the descriptive analysis of the group submitted to the pre-test. The sample was mainly composed of female patients with an average age of 62.3 years; the right side was the most affected. The postoperative follow-up ranged from 1 to 6 years.

Table 2 Summary of divergences between translators and specialists in the development of the second version in Portuguese (VP2)

Original version	VP1	Back translation	VP2
Pain/Cramps (max. 50 points)*	Dor/Cãibras (máx. 50 pontos)	Pain/Cramps (max. 50 points)	Dor/Desconforto muscular (máx. 50 pontos)
Severe*	Grave	Severe	Intensa
None	Nenhuma	No pain**	Nenhuma
LHB – pain	Dor na cabeça longa do bíceps	Pain on the biceps brachii long head**	Dor na cabeça longa do bíceps
Right side	Lado direito	Right side	Lado direito
Left side	Lado esquerdo	Left side	Lado esquerdo
Tenderness over the bicipital grove*	Sensibilidade no sulco bicipital	Sensitivity in the bicipital groove**	Dolorimento no sulco bicipital
Speed-test	Teste de Speed	Speed-test	Teste de Speed
Cramps*	Cãibras	Cramps	Desconforto muscular
At rest	Em repouso	At rest	Em repouso
On exertion*	Em esforço	With effort**	Ao esforço
None	Nenhuma	None	Nenhuma
Cosmesis (max. 30 points)*	Estética (máx. 30 pontos)	Aesthetics (max. 30 points)**	Aspecto estético (máx. 30 pontos)
Patient-dependent deformity*	Percepção do paciente em relação à deformidade	Perception of the patient in relation to the deformity**	Percepção da deformidade pelo paciente
None	Nenhuma	None	Nenhuma
Mild*	Leve	Slight**	Discreta
Moderate	Moderada	Moderate	Moderada
Severe	Grave	Severe	Grave
Examiner-dependent deformity*	Percepção do examinador em relação à deformidade	Perception of the examiner in relation to the deformity**	Percepção da deformidade pelo examinador
Elbow flexion strength (max. 20 points)	Força de flexão do cotovelo (máx. 20 pontos)	Elbow flexion strength (max. 20 points)	Força de flexão do cotovelo (máx. 20 pontos)
Affected side	Lado afetado	Affected side	Lado afetado
Opposite side	Lado oposto	Opposite side	Lado oposto
Total	Total	Total	Total

Abbreviations: LHB, long head of the biceps; max., maximum; máx., máximo; VP1, first version in Portuguese.
Notes:* Terms modified by the committee. ** Terms in which divergences were observed between the original version and the back translation.

Table 3 Characteristics of the sample to whom the pretest was applied

Gender	n
Male	12
Female	18
Age (years)	
Minimum	45
Maximum	79
Dominant side	
Right	29
Left	01
Laterality	
Right	16
Left	14
Shoulder procedure	
Arthroscopic repair of the rotator cuff	30
Biceps procedure	
Tenotomy	19
Tenodesis	11

At the end of this stage, the final version of the Brazilian Portuguese translation of the LHB score, called LHB-pt was concluded (►**Fig. 1**).



Fig. 1 LHB-pt.

Discussion

The most significant result of the present work is that the LHB-pt score will be made available for public use. This score is a practical tool with great potential in studies involving the long head of the biceps tendon.

Several authors have demonstrated that general scores to assess shoulder function, such as the Constant-Murley score, are not helpful in the follow-up of patients with conditions affecting the long head of the biceps tendon. In addition, these scores do not enable the detection of differences between bicipital tenotomy and tenodesis.[21–24] In a comparative functional assessment using the LHB score, Schiebel et al.[25] could observe differences among patients undergoing distinct bicipital tenodesis techniques.

The LHB score is more specific for this type of assessment because it includes outcomes that several authors deem fundamental.[8–10,21–24,26–28] However, its accuracy is limited because there may be an overlap with symptoms from rotator cuff injury. Therefore, the LHB score is not useful to screen for lesions before surgery.[19]

In a study regarding the translation and cultural adaptation of the LHB score into Turkish, the authors[29] assessed its reproducibility, validity, and reliability. They[29] concluded that the questionnaire was reproducible (interclass coefficient: 0.940; $p < 0.001$), valid (Cronbach alpha: 0.640), and reliable, as it remained stable throughout the testing and retesting processes. Although we did not evaluate the properties of the test, we believe that we may extrapolate these findings to the LHB-pt.

Some modifications occurred after the analysis of the VP1 and the back translation by the expert committee. The committee changed the term *dor/cãibra* (*pain/cramp*) to *dor/desconforto muscular* (*pain/muscle discomfort*) due to the belief that *cãibra* defines a very intense muscle discomfort in the Brazilian sociocultural context. As the score intends to identify the intensity of muscle discomfort, it would not be proper to use a term that culturally already defines it as intense. However, during the pretest, 14 patients (46%) suggested replacing *desconforto muscular* with *cãibra*. Thus, researchers decided to use *cãibra* in the final version of the score.

We changed the term *grave* (*severe*) to *intensa* (*intense*). The latter is better associated with the degree of muscle pain and discomfort, whereas *grave* can indicate a subjective worsening of the patient's condition, with no quantitative evaluation.

In addition, we changed *sensibilidade no sulco bicipital* (*bicipital sulcus tenderness*) to *dolorimento no sulco bicipital* (*bicipital sulcus soreness*). This change occurred because *sensibilidade* (*tenderness*), in the Brazilian context, is more related to a sensory ability, be it tactile, thermal, or related to pain. The committee believes the score does not intend to

identify the sensory capacity of the bicipital sulcus but rather the sensation of pain on local palpation. Therefore, we opted for the term *dolorimento* (*soreness*).

We suggested some modifications to adapt to the syntactic context of Brazilian Portuguese. Therefore, *em esforço* (*on exertion*) was altered to *ao esforço*. Likewise, the terms *percepção do paciente em relação à deformidade* (*patient-dependent deformity*) and *percepção do examinador em relação à deformidade* (*examiner-dependent deformity*) were respectively altered to *percepção da deformidade pelo paciente* and *percepção da deformidade pelo examinador*.

The term *estética* (*cosmesis*) was altered to *aspecto estético*, a more didactic way for the patient to understand that this item evaluates the physical features of the affected site. The committee chose to use the terms *nenhuma* (*none*), *discreta* (*mild*), *moderada* (*moderate*), and *grave* (*severe*) to assess the degree of deformity perceived by the patient. Among these terms, only *discreta* was not included in the VP1 and was chosen for the VP2. This occurred because the committee believed that a potential change in cosmesis would be better graded as *discreta* instead of *leve* (the usual translation for *mild*).

It is worth mentioning that the first question of the tool refers to pain in the long head of the biceps. While applying the test, evaluators may have doubts on how to measure pain. Scheibel et al.[25] say that this parameter should be assessed as the perception of spontaneous pain in the anterior aspect of the shoulder. There was no change in this methodology when we adapted and translated the score. It is also important to clarify that, according to the developers of the score,[19] a dynamometer must determine elbow flexion strength, and this measurement must be repeated three times. The mean flexion strength of the affected limb is compared with that of the healthy contralateral limb. The percentage results are scored from 0 to 20 points. Strength higher than 91% results in 20 points; from 90% to 81%, 16 points; from 80% to 71%, 12 points; from 70% to 61%, 8 points; and from 60% to 51%, 4 points. Strength below 50% receives no points.

We believe that the objective nature of the answers associated with direct questions facilitates the use of the LHB score in the clinical practice. Despite the great diversity of regionalisms and barbarisms in Brazil, the questionnaire is easy to understand. Moreover, it has great applicability in studies that assess the long head of the biceps tendon.

The limitations of the present study include the lack of assessment of the reproducibility and reliability of the test. We believe that future publications may identify these properties.

Conclusion

The translation and cultural adaptation of the LHB score into Brazilian Portuguese, which generated the LHB-pt, were successfully accomplished.

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Conflict of interests
The authors have no conflict of interests to declare.

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Genetic Polymorphisms in *COL1A2* gene and the Risk of Tendinopathy: Case-Control Study

Polimorfismos genéticos no gene COL1A2 e o risco de tendinopatia: Estudo de caso-controle

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Abstract

Objective To evaluate the influence of polymorphisms on genes encoding type I collagen and the genetic susceptibility of tendinopathy.

Methodology Case-control study involving 242 Brazilian athletes from different sports modalities (55 cases of tendinopathy and 187 controls). The polymorphisms *COL1A1* (rs1107946) and *COL1A2* (rs412777, rs42524, and rs2621215) were analyzed by the TaqMan system. Odds ratio (OR) with their 95% confidence intervals (CIs) were calculated using a nonconditional logistic regression model.

Results The mean age was 24.0 ± 5.6 years old and 65.3% were men. Of the 55 cases of tendinopathy, 25.4% had > 1 affected tendon, the most frequent being patellar (56.3%), rotator cuff (30.9%) and elbow or hand flexors (30.9%). Age and amount of time of sports practice were associated with a higher chance of presenting tendinopathy (5 and 8 times, respectively). The frequency of variant alleles in control and case patients, respectively, was: *COL1A1* rs1107946 24.0 and 29.6%; *COL1A2* rs412777 36.1 and 27.8%; rs42524 17.5 and 25.9%; and rs2621215 21.3 and 27.8%. After adjusting for

Keywords
- athletes
- tendinopathy
- collagen type 1
- polymorphism, genetic

The multicenter work was developed at the Universidade do Estado do Rio de Janeiro (UERJ-ZO), Fundação Oswaldo Cruz (Fiocruz), and Instituto Nacional de Traumatologia e Ortopedia Jamil Haddad (INTO), Rio de Janeiro, RJ, Brazil.

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confounding factors (age and years of sports practice), *COL1A2* rs42524 and rs2621215 polymorphisms were associated with increased risk of tendinopathy (OR = 5.5; 95% CI = 1.2–24.6 and OR = 3.9; IC95% = 1.1–13.5, respectively). The haplotype *COL1A2 CGT* was associated with low risk for disease development (OR = 0.5; 95%CI = 0.3–0.9). **Conclusion** Age (≥ 25 years old), time of sports practice (≥ 6 years) and polymorphisms in the *COL1A2* gene increased the risk of developing tendinopathy.

Resumo

Objetivo Avaliar a influência de polimorfismos nos genes que codificam o colágeno tipo I e a suscetibilidade genética da tendinopatia.
Metodologia Estudo caso-controle envolvendo 242 atletas brasileiros de diferentes modalidades esportivas (55 casos de tendinopatia e 187 controles). Os polimorfismos *COL1A1* (rs1107946) e *COL1A2* (rs412777, rs42524 e rs2621215) foram analisados pelo sistema TaqMan. As razões de chance (OR) com seus intervalos de confiança (IC) de 95% foram calculadas usando um modelo de regressão logística não-condicional.
Resultados A média de idade foi de 24,0 ± 5,6 anos e 65,3% eram homens. Dos 55 casos de tendinopatia, 25,4% apresentaram mais de um tendão acometido, sendo os mais frequentes o patelar (56,3%), o manguito rotador (30,9%) e o do cotovelo ou flexores das mãos (30,9%). A idade e o tempo de prática esportiva foram associados a uma maior chance de apresentar tendinopatia (5 e 8 vezes, respectivamente). A frequência dos alelos variantes nos controles e casos, respectivamente, foi: *COL1A1* rs1107946 24,0 e 29,6%; *COL1A2* rs412777 36,1 e 27,8%; rs42524 17,5 e 25,9%; e rs2621215 21,3 e 27,8%. Após ajuste pelos fatores de confundimento (idade e anos de práticas esportiva), os polimorfismos *COL1A2* rs42524 e rs2621215 foram associados a um risco aumentado de tendinopatia (OR = 5,5; IC95% = 1,2–24,6 e OR = 3,9; IC95% = 1,1–13,5, respectivamente). O haplótipo *COL1A2 CGT* foi associado a um baixo risco para desenvolvimento da doença (OR = 0,5; IC95% = 0,3–0,9).
Conclusão A idade (≥ 25 anos), o tempo de prática esportiva (≥ 6 anos) e polimorfismos no gene *COL1A2* aumentaram o risco de desenvolvimento da tendinopatia.

Palavras-chave
- atletas
- tendinopatia
- colágeno tipo 1
- polimorfismo genético

Introduction

Tendinopathy is a multifactorial tendon disease, representing 1 to 6% of musculoskeletal injuries in the general population and 20 to 50% in athletes.[1,2] Initially, there is a physiological change in the tendon tissue, which may worsen with continuous stress or failures in the healing process, causing inflammation, pain, and even tissue degeneration.[2–4] The prevalence of the disease varies between the different parts of the body and according to age, sex, and occupation.[2] In athletes, the affected tendons vary according to sports modality, but mainly affect the Achilles tendon, the patellar tendon, rotator cuff tendons and tendons that originate from the lateral epicondyle.[1,2,5] The interaction between mechanical and biological factors is associated with the development of tendinopathies.[2–4,6]

Tendons are composed of a dense extracellular matrix (ECM) with low cellularity, but with high content of structural proteins, mainly type I collagen, a protein with heterotrimer morphology, composed of two α1 chains and one α2.[2,4] This structure offers the tendon tissue unique mechanical properties in terms of elasticity and tension, allowing the transmission of load between muscle and bone, promoting joint movement. The musculotendinous and osteotendinous junctions have specific histological characteristics.[7,8] The α1 chains are encoded by the *COL1A1* gene, located on chromosome 17, and the α2 chain is encoded by the *COL1A2* gene, and is located on chromosome 7.[4,9] It has been observed that the reduction in gene transcription of *COL1A1* and *COL1A2* in mice altered the properties of tendon strength, elasticity, tension, and healing.[10]

Recent studies have shown the influence of single nucleotide polymorphism (SNP) on the susceptibility of tendinopathy.[2,3,6,11] Genetic polymorphism is characterized by the substitution, deletion, or insertion of nucleotides in DNA tape, occurring in > 1% of the population, which may result in changes in the expression or functionality of gene products, determining individual characteristics, including susceptibility to certain diseases and response to some medications. The possible combinations of two alleles that characterize an SNP can form three possibilities of genotypes (heterozygous, wild homozygous or variant), which may or may not differ in phenotypes.[12] The combination of strongly correlated alleles

on the same chromosome is generally inherited as a unit, called haplotypes, because there is no genetic recombination between sites.[13]

COL1A1 and *COL1A2* genes are polymorphic and may alter the expression or biological function of type 1 collagen.[9,11,14] The SNPs *COL1A1* rs1800012 ($C > A$) and rs1107946 ($G > T$), present in the promoter region, were associated with soft tissue injuries of the musculoskeletal system in South African athletes of various sports modalities and in a cohort of nonathletes from the United Kingdom.[9,15] To date, no study has evaluated the influence of SNPs of the *COL1A2* gene on tendinopathy. Thus, the aim of the present study was to evaluate the contribution of SNPs *COL1A1* rs1107946 and *COL1A2* rs412777, rs42524 and rs2621215 as factors associated with genetic susceptibility of tendinopathy in Brazilian athletes.

Methodology

A retrospective observational case-control study was conducted with 242 Brazilian athletes, approved by the Human Research Ethics Committee of a tertiary hospital of the Brazilian Unified Public Health System (number 81225817.0.0000.5273). All participants signed the Informed Consent Form (TCLE, in the Portuguese acronym) and self-completed a questionnaire previously validated by experts in the area, available online in a previous study.[1] At the end of data collection, a trained observer verified and confirmed with each athlete the information. The database was filled out by a trained researcher, with double verification by two other different researchers, to ensure the veracity of the information entered in the database.

The inclusion criteria were federated athletes aged between 18 and 45 years old and of different sports modalities, who were recruited from February 2018 to November 2019. Athletes with no data on musculoskeletal injury and/or who had no biological material collected were excluded.

►**Fig. 1** shows the flowchart of the 242 athletes included in the study; 187 athletes with no history of injury in the musculoskeletal system (control group) and 55 athletes reported clinically diagnosed tendinopathy (case group), confirmed with magnetic resonance imaging (MRI). All diagnoses of tendinopathy were evaluated by two specialized orthopedic surgeons, as described in previous studies, referring to the selection criterion of cases of tendinopathy.[3,6]

Genomic DNA was obtained from an oral mucosa sample collected by sterile and isolated swab with the QIAmp DNA Mini Kit extraction kit (Qiagen, Hilden, Germany), following the recommendations of the manufacturer. The analyses of the SNPs of interest were performed by the real-time polymerase chain reaction (RT-PCR) technique, using validated allelic discrimination assays using TaqMan system (Thermo Fisher Scientific, Waltham, MA, USA) as described in the literature.[16] The TaqMan system for allelic discrimination consists of a set of primers and oligonucleotide probes designed specifically for each target SNP. The 2 probes are marked with different fluorescence, allowing the identification of the two possible alleles (*COL1A1* rs1107946 $G > T$ and *COL1A2* rs412777 $A > C$, rs42524 $G > C$ and rs2621215 $T > G$) present in the sample of the individual. The fluorescence intensity is captured by the equipment, discriminating the genotype of each individual (►**Fig. 2**). To ensure the quality control of the analysis, for each SNP, two standardized positive controls of each genotype were used, in addition to two negative controls, as described in the literature.[6]

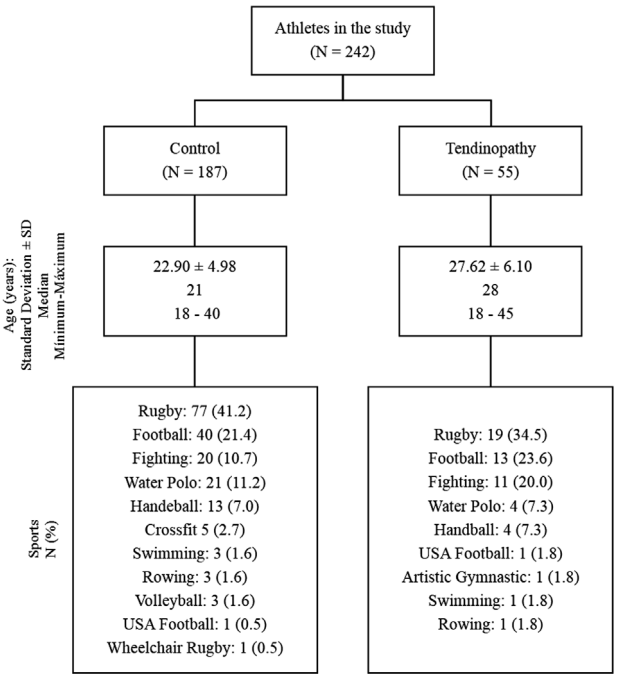


Fig. 1 Flowchart of the participants included in the study.

The sample size was used in the Epi Info 7 program, version 7.1.3. (http://wwwn.cdc.gov/epiinfo/html/downloads.htm) to detect differences between groups (case and control), assuming a ratio between cases and controls of 1:3 and odds ratio (OR) of 2.5 with a power of 0.8 and 5% of type I error.

The normal distribution of continuous variables in the studied population was verified by the Shapiro-Wilk test. Comparisons of continuous variables between tendinopathy cases and control groups were performed using the Student t-test, and they were presented as ± standard deviation (SD). Categorical variables, as well as the distribution frequencies of genotypes and alleles between the two groups were expressed in percentage and determined by the chi-squared test ($\chi 2$) or by the Fisher exact test, when applicable.

The frequencies of alleles and genotypes of *COL1A1* and *COL1A2* SNPs were determined by direct counting of alleles, and then the Hardy-Weinberg balance (HWE) was calculated. Haplotype patterns and binding imbalance coefficients (D' is the degree of imbalance in the module and R2 is the degree of correlation) were inferred using the Haploview program, as described in the literature.[16,17] The binding imbalance describes the combinations of alleles that occur in a sample due to the formation of haplotypes, calculated from the frequency of the individual alleles.[13] The combined analysis

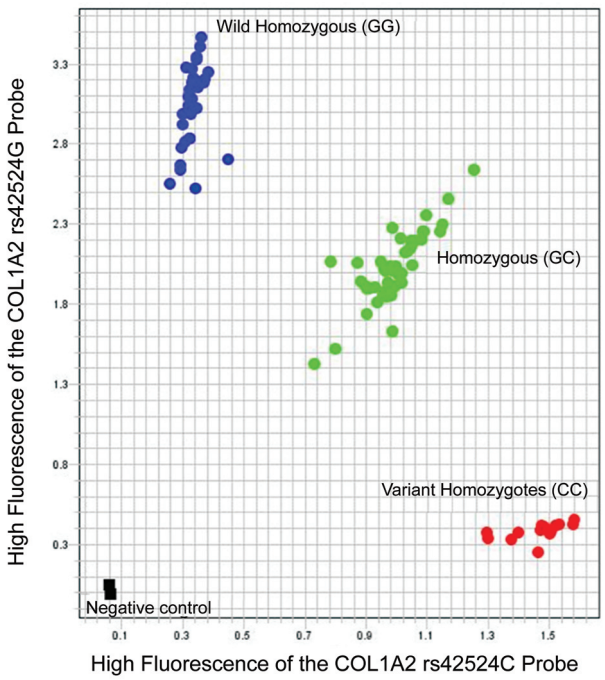


Fig. 2 Analysis of polymorphisms by real-time PCR using the Taqman system. **Label:** Example of discrimination of genotypes of *COL1A2* rs42524*G* > *C* polymorphism. The blue circles, which present high fluorescence of the *COL1A2* rs42524*G* probe, are the patients with wild homozygous genotype (*GG*). The red circles, which present high fluorescence of the *COL1A2* rs42524*C* probe are the variant homozygotes (*CC*) and the green circles are heterozygotes (*CG*), because they present fluorescence of both probes. Black squares are negative controls (water), which should not present PCR amplification and, consequently, fluorescence.

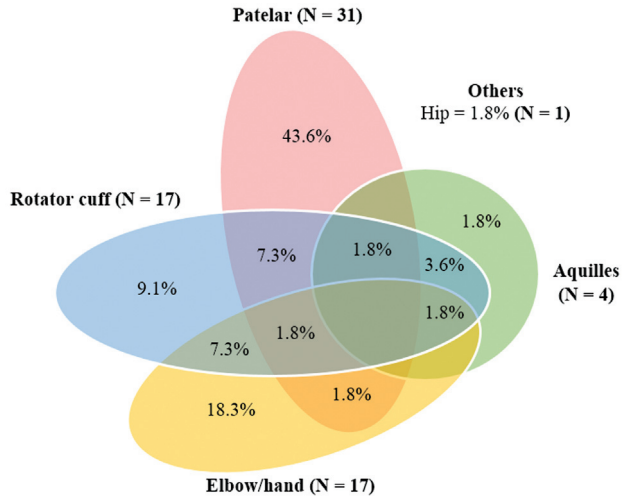


Fig. 3 Distribution of sites affected by the disease. **Label:** Of the athletes who reported more than one site of tendinopathy, 7.3% ($n = 4$) had rotator cuff and elbow/hand tendons, 7.3% ($n = 4$) were in the patellar and rotator cuff, 3.6% ($n = 2$) in the Achilles cuff and rotator cuff, 1.8% ($n = 1$) in the Achilles and elbow/hand, 1.8% ($n = 1$) in the patellar, rotator cuff, and elbow/hand, and 1.8% ($n = 1$) in the patellar, rotator, and Achilles cuff.

of alleles (haplotypes) is possibly clinically more relevant than the individual analysis of each isolated SNP.[17]

The magnitude of the association between the presence of polymorphisms and tendinopathy was estimated by Odds Ratio (OR), with their respective 95% confidence intervals (95%CIs), using a binary logistic regression model. The construction of the final model was based on the degree of statistical significance in the univariate analysis and on the biological importance of the variables studied, attributing an input significance level < 0.25 ($p \leq 0.25$) and remaining with an output level of 0.05 ($p \leq 0.05$). All statistical analyses were performed using the IBM SPSS Statistics for Windows version 20.0 (IBM Corp., Armonk, NY, USA).

Results

Of the 55 tendinopathy cases, 31 (56.3%) reported patellar tendon disease, 17 (30.9%) in rotator cuff tendons, 17 (30.9%) in the elbow or hand flexors, 4 (7.3%) in the Achilles tendon, and 1 (1.8%) in the middle gluteus tendon (►**Fig. 3**). In addition, 14 (25.4%) athletes reported > 1 tendon affected by the disease.

The mean age of the 242 athletes was 24.0 ± 5.6 years old (18 to 45 years old), the mean body weight was 74.7 ± 16.3 Kg (48 to 128 Kg), the mean height was 1.7 ± 0.1 m (1.51–2.05), the mean body mass index (BMI) was 24.7 ± 3.5 Kg/m^2 (17.5 to 41.8 Kg/m^2), the mean years of sports practice were 9.5 ± 6.1 (1 to 34), and the mean hours per training week was 13.0 ± 7.7 (1 to 42). The demographic, clinical, sports and training tendinopathy variables and controls are found in ►**Table 1**. The variables were evaluated to identify the possible confounding factors in the analysis of association between SNPs and tendinopathy. After applying the nonconditioned logistic regression model, only age and years of practice remained associated with the risk of tendinopathy in the studied population (Table 1).

The success rate of the genetic analysis was 98.8% for SNP *COL1A1* (rs1107946), 99.2% for *COL1A2* rs42524, 97.9% for rs412777 and rs2621215. The genotypic distributions of all SNPs were in HWE, indicating that the frequencies of alleles remained unchanged throughout the generations. The frequencies of the smallest variant allele of the studied SNPs are shown in ►**Fig. 4**, in which there was no significant difference in the distribution between the tendinopathy and control groups. After adjusting for confounding factors (age, sports modality, and years of sports practice), variant genotypes *COL1A2* rs42524 *CC* and *COL1A2* rs2621215 *GG* were associated with increased risk (approximately 5.5 and 4 times, respectively) of tendinopathy (►**Table 2**).

Eight *COL1A2* (rs412777, rs42524, rs2621215) SNPs haplotypes were inferred and the frequency of the *COL1A2 AGT* wild haplotype was 48.4 and 50.9% in controls and tendinopathy cases, respectively (►**Fig. 5**). After adjustment for confounding variables, variant *COL1A2 CGT* haplotype was negatively associated with tendinopathy (OR = 0.48; 95%CI = 0.25–0.93).

Discussion

Tendinopathy is a musculoskeletal system disorder very common in sports, with a prevalence of 10 to 50%, with

Table 1 Epidemiological and clinical analysis of the individuals included in the study ($n = 242$)

Variables	Control ($n = 187$)	Tendinopathy ($n = 55$)	*p-value*[a]	Adjusted OR (95%CI)[b]
Age (years old)	***n* (%)**			
≤ 20	84 (44.9)	7 (12.7)	< **0.001**	1[c]
21 to 24	46 (24.6)	10 (18.2)		2.63 (0.92–7.54)
25 to 29	33 (17.7)	18 (32.7)		5.53 (2.06–14.86)
≥ 30	24 (12.8)	20 (36.4)		5.16 (1.79–14.83)
Gender				
Female	63 (33.7)	21 (38.2)	0.54	1[c]
Male	124 (66.3)	34 (61.8)		0.64 (0.31–1.32)
Weight (Kg)				
≤ 64.00	49 (26.2)	12 (21.8)	0.53	1[c]
64.01 to 73.50	48 (25.7)	12 (21.8)		0.93 (0.34–2.56)
73.51 to 83.50	43 (23.0)	18 (32.7)		1.65 (0.65–4.21)
> 83.50	47 (25.1)	13 (23.7)		0.85 (0.32–2.26)
Height (m)				
≤ 1.67	50 (26.7)	17 (30.9)	0.67	1[c]
1.67 to 1.74	46 (24.6)	10 (18.2)		0.47 (0.17–1.27)
1.75 to 1.80	42 (22.5)	15 (27.3)		1.11 (0.45–2.77)
> 1.80	49 (26.2)	13 (23.6)		0.69 (0.27–1.77)
Alcohol consumption				
No	82 (43.9)	20 (36.4)	0.32	1[c]
Yes	105 (56.1)	35 (63.6)		1.19 (0.59–2.38)
Smoking				
No	177 (94.7)	53 (96.4)	0.61	1[c]
Yes	10 (5.3)	2 (3.6)		0.43 (0.08–2.30)
Years of sports				
≤ 5	69 (36.9)	3 (5.5)	**0.001**	1[c]
6 to 10	60 (32.1)	17 (30.9)		8.62 (2.30–32.25)
11 to 15	40 (21.4)	16 (29.1)		10.72 (2.82–40.77)
> 15	18 (9.6)	19 (34.5)		11.00 (2.78–43.53)
Weekly training hours				
≤ 8	62 (32.8)	14 (25.5)	0.27	1[c]
9 to 12	56 (30.2)	13 (23.6)		0.83 (0.32–2.13)
13 to 18	37 (19.8)	13 (23.6)		1.30 (0.49–3.43)
> 18	32 (17.2)	15 (27.3)		1.42 (0.53–3.83)

[a]p-value calculated by Fisher's χ^2 or exact test, when necessary; [b]OR = *Odds ratio,* odds ratio adjusted for age, years of training; CI = 95% confidence interval; [c]reference group.

the affected tendon varying according to the sports modality of the athlete.[1,2] The patellar tendon is among the most vulnerable and frequent to suffer excessive use injuries in the lower limbs.[1,18] In the present study, ~ 60% of the athletes reported patellar tendon disease, being more frequent in rugby, soccer, and football. The increase in tension and mechanical load during knee flexion generates cellular changes, with degeneration of collagen fibril that decreases the structural properties of the tissue.[19] Rotator cuff and elbow or hand flexors tendinopathies were the most frequent (~ 62%) in the upper limbs, especially in rowing, artistic gymnastics, swimming, wrestling sports and, water polo. The shoulder is widely used in sports that require greater demand and strength of the upper limbs, such as throwing movements in water polo and in attack and defense exercises required in combat sports.[1,20]

Age and time of sports practice were associated with the risk of the presence of tendinopathy, according to other

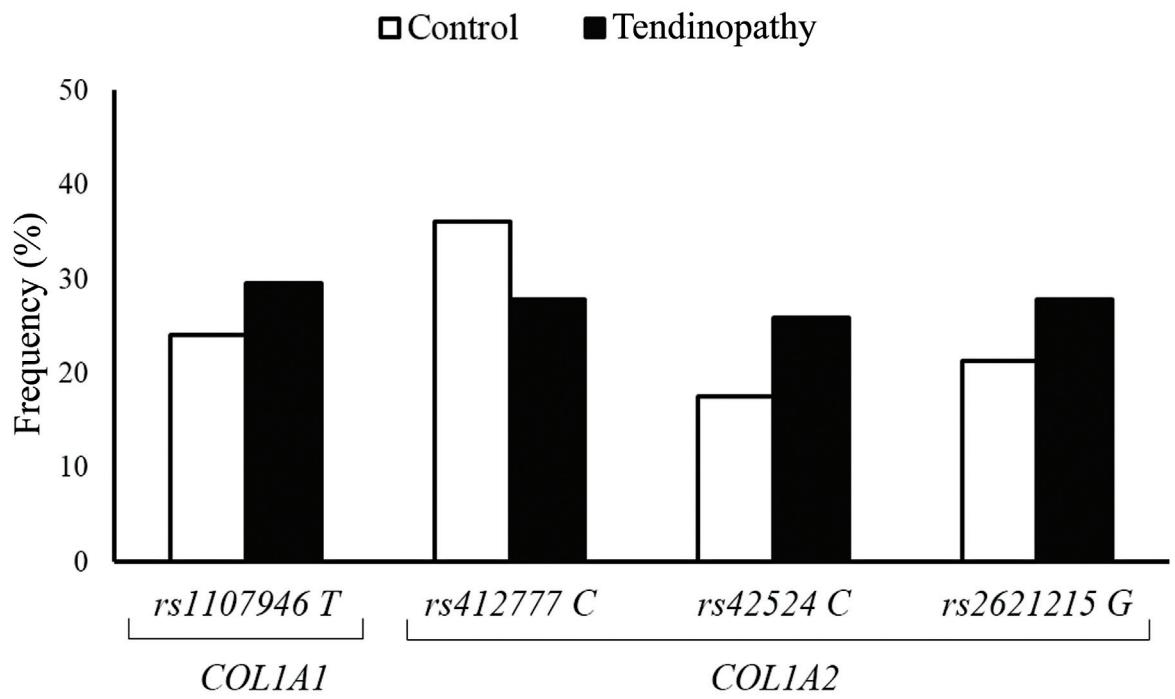


Fig. 4 Distribution of the allelic frequency of *COL1A1* and *COL1A2* polymorphisms in the studied population ($n = 242$). **Label:** There was no significant difference between the groups.

Table 2 Analysis of the association of *COL1A1* and *COL1A2* polymorphisms with the development of tendinopathy

Variables	Control ($n = 187$)	Tendinopathy ($n = 55$)	*p-value*[a]	Adjusted OR (95%CI)[b]
COL1A1 rs1107946[d]	*n* (%)			
GG	110 (59.5)	29 (53.7)	0.13	1[c]
GT	61 (33.0)	18 (33.3)		1.22 (0.57–2.61)
TT	14 (7.5)	7 (13.0)		2.60 (0.83–8.13)
COL1A2 rs412777[e]				
AA	75 (41.0)	28 (51.9)	0.27	1[c]
AC	84 (45.9)	22 (40.7)		0.70 (0.34–1.44)
CC	24 (13.1)	4 (7.4)		0.33 (0.09–1.16)
rs42524[f]				
GG	125 (67.2)	32 (59.3)	**0.03**	1[c]
GC	57 (30.6)	16 (29.6)		1.21 (0.57–2.55)
CC	4 (2.2)	6 (11.1)		**5.47 (1.22–24.58)**
rs2621215[e]				
TT	113 (61.7)	30 (55.6)	0.16	1[c]
TG	62 (33.9)	18 (33.3)		1.24 (0.59–2.62)
GG	8 (4.4)	6 (11.1)		**3.91 (1.13–13.48)**

[a]p-value calculated by the Fisher χ^2 or exact test, when necessary; [b]OR = *Odds ratio*, odds ratio adjusted for age, years of training; CI = 95% confidence interval; [c]reference group; [d]Information obtained from 239 athletes (185 controls and 54 cases of tendinopathy); [e]Information obtained from 237 athletes (183 controls and 54 cases of tendinopathy); [f]Information obtained from 240 athletes (186 controls and 54 cases of tendinopathy).

studies in the literature.[1,2] Advancing age can cause tendon aging, causing a change in tendon vascularization and, consequently, forming a less rigid structure vulnerable to undergoing tissue stress.[21] The present study found that older athletes, > 25 years old, and with > 10 years of sports practice were strongly associated with tendinopathy in Brazilian athletes (about 5 and 11 times, respectively), which corroborates a previous study, which observed an 8 times

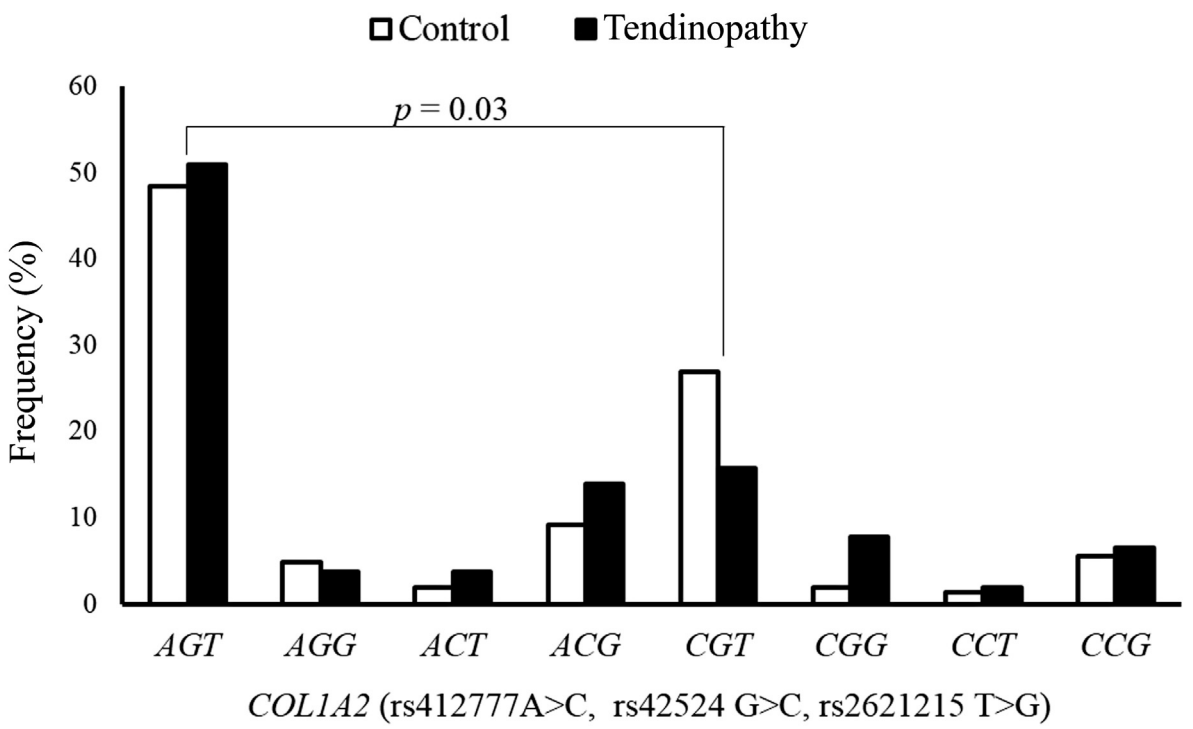


Fig. 5 Distribution of haplotypic frequency of *COL1A2* polymorphisms in the studied population ($n = 242$). **Label:** Eight *COL1A2* haplotypes, involving polymorphisms rs412777, rs42524, rs2621215, were found in the studied population. There was a significant frequency distribution difference of the AGT and *CGT haplotypes*.

risk associated with tendinopathy in the patellar tendon, rotator cuff and Achilles in Brazilian volleyball athletes > 24 years old and > 15 years of sports practice.[3] Also, the prevalence of the disease was observed in 17% of adult athletes compared with 5.6% in adolescents.[22] In addition, intense exposure to volume and frequency of training can cause recurrent tendon injuries, with an incidence of 0.12 injuries/1,000 hours of training or competition time.[23] Different training models, such as jump load and repetitive movements, may increase the risk of developing tendon injury.[2]

Genetic variations have been presented as intrinsic risk factors associated with the development of tendinopathy.[2,4,11,24] The gene-environment interaction of some modifiable risk factors, especially in athletes, related to the intensity and volume of training or competitions, and not modifiable, such as the genetic profile of the athlete, may result in a synergistic effect on the manifestation of tendon injury.[25] A systematic review study involving 17 studies on the influence of genes linked to collagen structure and tendon homeostasis observed the relevance of the contribution of polymorphisms in genes encoding collagen with susceptibility to Achilles tendinopathy.[26] Patients with shoulder instability, for example, have lower expression of *COL5A1*.[27]

The injured tendons have higher collagen expression of types I and III.[9,15] Considering type I collagen, *COL1A1* rs1107946 $G > T$ polymorphism is related to differences in transcriptional activity of the gene, in which the G allele presents higher transcription efficiency when compared to the T-allele.[28] Ficek et al.[15] observed that the *COL1A1 GT* (rs1107946-rs1800012) haplotype is associated with a lower risk of rupture of the anterior cruciate ligament in a group of professional football players, but did not find an association with tendinopathy, as observed in the present study, in which *COL1A1* rs1107946 SNP was not associated with the risk of tendinopathy. To date, there is no report of studies evaluating the influence of the *COL1A2* gene on the etiology of tendinopathy, making the present study a pioneer in describing the risk association of variant genotypes *COL1A2* rs42524 *CC* and rs2621215 *GG* with susceptibility to the disease. Recently, Perini et al. observed that variant genotypes *COL1A2* rs42524 *CC* and *COL1A2* rs2621215 *GG* presented a chance of ~ 5 times for noncontact rupture of the anterior cruciate ligament.[16] The substitution of the amino-acid alanine by proline (Ala > Pro) of *COL1A2* rs42524 $G > C$ SNP promotes a change in the stability of the triple collagen helix.[14] *COL1A2* rs2621215 $T > G$ SNP may interact with other functional polymorphisms and affect the removal of introns from this gene causing damage to collagen structure.[29] Thus, the presence of variant alleles *COL1A2* rs42524 *C* and rs2621215 *G* may produce a less flexible collagen, making it more vulnerable to tissue stress.

COL1A2 CGT haplotype, formed only by the variant allele of SNP rs412777*C*, and the other wild two (rs42524*G* and rs2621215*T*), presented a protective factor for the development of tendinopathy. The exchange of the nucleotide adenine by cytosine in exon 25 does not promote the exchange of the aminoacid proline at position 392 of the α2 chain of type

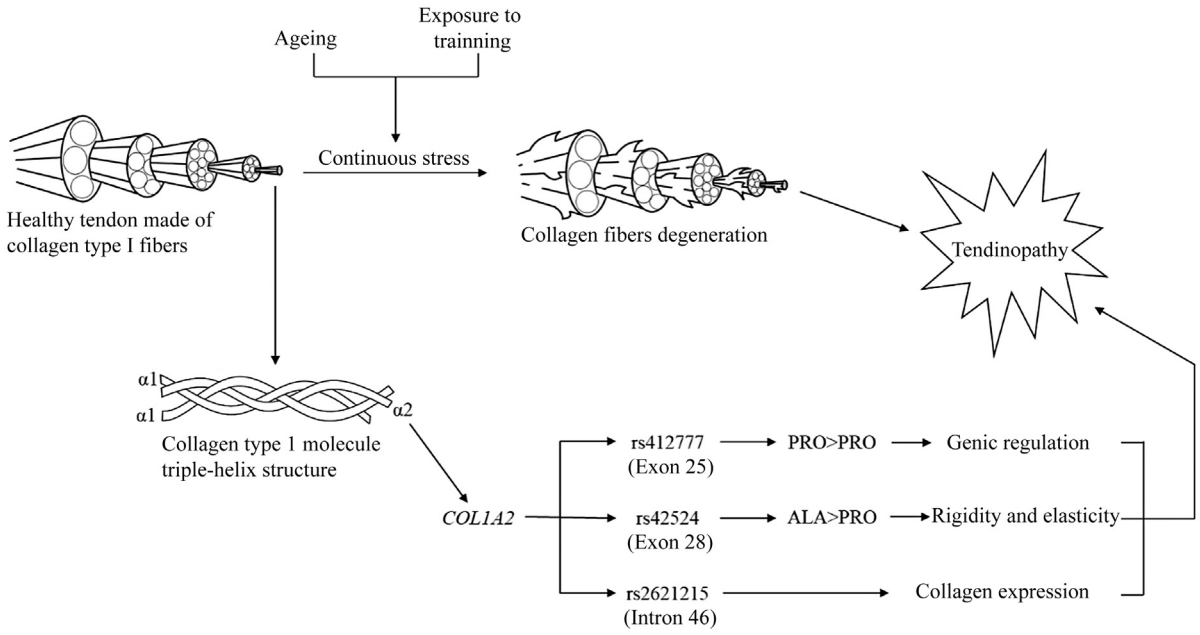


Fig. 6 Hypothesis of mechanism of the development of tendinopathy in the presence of intrinsic factors (age and polymorphisms of *COL1A1* and *COL1A2*) and extrinsic (years of sports training).

1 collagen. The mechanisms by which the different *COL1A2* gene polymorphisms affect its expression and/or function are not yet fully known. However, SNP rs412777 may be in imbalance in connection with a functional mutation and may influence gene expression and interfere with the mechanism of removal of introns and union of the exons, which are fundamental for protein formation.[30]

Finally, based on the results found, a mechanism of hypothesis of the gene-environment interaction between the age of the athlete, the time of practice in sport and the contribution of *COL1A2* SNPs (rs412777, rs42524, rs2621215) in the development of tendinopathy was suggested. Factors such as aging and mechanical stress can contribute to increased demand or irregular distribution of the tensile load, causing tissue changes.[2] Type 1 collagen fibers present differences between individuals due to the presence of polymorphisms in the genes (*COL1A1* and *COL1A2*), which encode the protein.[9,14,15] *COL1A2* SNPs can influence gene expression, increasing stiffness and decreasing tissue elasticity.[14,30] Thus, we suggest that gene-environment interaction (*COL1A2* SNPs added to aging and high exposure to training) can contribute synergistically to the development of tendinopathy in athletes (►**Fig. 6**).

This is a pioneering and innovative study, which can contribute to the biotechnological and clinical advancement in personalized medicine; however, the sample size of the tendinopathy group of cases was the main limitation of the study, not allowing stratified analysis of the disease in tendons with different biomechanical activities. Moreover, the present study did not differentiate insubstantial tendinopathies from those of insertional ones or that occur at the myotendinous junction, which should be a reason for investigation in future analytical studies because they are diseases of a diverse clinical spectrum. However, we have the science that even with differences in anatomical sites, all tendons are composed of type 1 collagen. We also have a variety of sports modalities, which differ in the type of training, biomechanical demands and, consequently, in the tendons affected by the disease. However, the possible confounding variables were inserted in the logistic regression model to evaluate the real influence of SNPs on the development of tendinopathy. Thus, the results of the present study may contribute as a database for future studies in order to build a database with different populations so that it is possible to identify modifiable and nonmodifiable risk factors associated with the development of tendinopathy. Individualized programs of injury prevention using genetic information can contribute to the promotion of the health and well-being of individuals, besides being useful diagnostic tools in the clinical practice of the orthopedist.

Conclusion

Athletes > 25 years old, with > 6 years of sports practice, with genotypes *COL1A2* rs42524 *CC* and rs2621215 *GG* have a higher risk of developing tendinopathy, while the *COL1A2 CGT* variant haplotype presented a protective effect on the development of the disease.

Contribution of the Authors

The authors contributed individually and significantly to the development of this article: Perini J. A., Lopes R. L., and Goes R. A. participated in the conception and design of the study. Perini J. A., Lopes R. L., and Goes R. A. gathered the data and developed the database. Perini J. A., Lopes R. L., Pereira C. G., and Wainchtock V. S. carried out the

experiments and statistical analyses. Perini J. A., Lopes R. L., Amaral M. V. G., and Miranda V. A. R. performed data analysis and interpretation. Perini J. A., Lopes R. L., Pereira C. G., and Wainchtock V. S. wrote the manuscript. Guimarães J. A. M. and Amaral M. V. G. performed the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Conflict of Interests
The authors have is no conflict of interests to declare.

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Adhesive Capsulitis' Patients Report Improvement in Functionality Trough International Classification of Functioning, Disability and Health Checklist and Dash After Suprascapular Nerve Blocks*

Pacientes com capsulite adesiva relatam melhora da funcionalidade pela Classificação Internacional de Funcionalidade, Incapacidade e Saúde e DASH após bloqueios do nervo supraescapular

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Abstract

Objective To evaluate the functionality in patients with adhesive capsulitis undergoing suprascapular nerve block (SSNB).

Methods A before-and-after clinical prospective study in a single center was conducted with patients with secondary adhesive capsulitis treated with four nerve blocks based on anatomical limits. The sample was non-probabilistic, and it was obtained after a routine appointment at a specialized outpatient clinic. The instruments used for evaluation were the International Classification of Functioning, Disability and Health (ICF) and the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire, which were applied at baseline (T_0), one week after the fourth SSNB (T_4), and three months after the first SSNB (T_{12}). The paired *t*-test was used to compare the means of the ICF checklist items and DASH in the different: T_0xT_4; T_4xT_{12}; and T_0xT_{12}). The probability of rejecting the null hypothesis was 5%.

Keywords
- adhesive capsulitis
- nerve block
- International Classification of Functioning, disability and health
- shoulder
- patient reported outcome measures

* *Work developed at the School of Medicine of Universidade Federal de Goiás, Goiânia, GO, Brazil.*

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Results The sample was composed of 25 individuals with a mean age of 58.16 years; 16 of them were female. The duration of the pain symptoms ranged from 2 to 16 months, with a mean of 5.92 months. The ICF checklist showed that all domains had already improved in $T_{4,}$ except for the environmental factors, which only improved at 03 months ($p = 0.037$). The patients reported improvements in shoulder function in T_4, which increased more in T_{12}, at the end of data collection ($p = 0.019$).

Conclusion The SSNB technique is effective in patients with adhesive capsulitis after 4 weeks of application, with improvements in individual's functionality lasting for 12 weeks.

Resumo

Objetivo Avaliar a funcionalidade em pacientes com capsulite adesiva submetidos a bloqueio do nervo supraescapular (BNSE).

Métodos Um estudo clínico prospectivo do tipo antes e depois foi realizado em um único centro com pacientes com capsulite adesiva secundária tratados com quatro bloqueios baseados em limites anatômicos. A amostra foi não probabilística, tendo sido obtida após consulta de rotina em ambulatório especializado. Os instrumentos utilizados para avaliação foram a Classificação Internacional de Funcionalidade, Incapacidade e Saúde (CIF) e o questionário de Disfunções do Braço, Ombro e Mão (DASH), que foram aplicados antes da intervenção intervenção (T_0), uma semana após o quarto BNSE (T_4), e três meses após o primeiro BNSE (T_{12}). As médias dos itens da CIF e do DASH nos diferentes tempos (T_0 x T_4; T_4 x T_{12}; e T_0 x T_{12}) foram comparadas por meio do teste *t* pareado. A probabilidade de rejeitar a hipótese nula foi de 5%.

Resultados A amostra foi composta por 25 indivíduos com média de idade de 58,16 anos; 16 eram mulheres. Os sintomas dolorosos ocorreram por 2 a 16 meses, com média de 5,92 meses. A CIF mostrou que todos os domínios já haviam melhorado em $T_{4,}$ à exceção dos fatores ambientais, que só melhoraram aos 3 meses ($p = 0,037$). Os pacientes relataram melhora na função do ombro em T_4 e mais ainda em T_{12}, no final da coleta de dados ($p = 0,019$).

Conclusão A técnica de BNSE é eficaz em pacientes com capsulite adesiva após 4 semanas de aplicação, com melhora da funcionalidade e sua manutenção por até 12 semanas.

Palavras-chave
- capsulite adesiva
- bloqueio nervoso
- Classificação Internacional de Funcionalidade, incapacidade e saúde
- ombro
- medidas de resultados relatados pelo paciente

Introduction

Adhesive capsulitis (AC) is a disabling shoulder disease with a prevalence of 2% to 5% among the general population that most commonly affects females between 40 and 70 years of age.[1,2] Its clinical features are pain and stiffness;[1,3,4] it often presents bilaterally, and does not affect the same shoulder twice. Adhesive capsulitis can present in the primary (idiopathic) form or be secondary to previous surgery, trauma, immobilization, and systemic alterations such as diabetes mellitus and hypothyroidism.[1,3–6] The non-surgical approach is mandatory, and suprascapular nerve block (SSNB) is one therapeutic option with satisfactory results.[7,8]

This condition is limiting and negatively impacts the function and structure of the affected person's body.[8] The International Classification of Functioning, Disability and Health (ICF) was developed by the World Health Organization (WHO) in 2001 so that the individual can describe their current state of health-disease-functionality-care.[9–11] Due to its multifaceted nature, the ICF contributes to the assessment of different health conditions; however, its use has been restricted to rehabilitation professionals.[12,13]

The use of the ICF checklist in the clinical practice can provide important information to be raised in patient care, with a unified and standardized language based on different constructs and domains.[14–16] Another widely used instrument in studies on uppers limb diseases is the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire, but it is only applied to evaluate the function and symptoms of this part of the body during the performance of certain activities.[17]

There is an increasing support for the use of patient-reported outcomes to determine the quality of the treatment and of the therapeutic conduct. These outcomes are obtained through validated questionnaires that are filled out by the patients according to their perceptions of their health status, disability and level of impairment. These questionnaires also enable the comparison of outcomes before and after

procedures to evaluate the efficacy of a clinical intervention from the patients' perspective. A combination of two types of patient-reported outcome measures is often used.[18]

To date, studies on AC with the simultaneous use of the ICF checklist and the DASH have not been found. This investigation would enable the mapping of the functionality construct regarding the aspects affected by AC as well as the individual as a the aim of the present study was to evaluate, through the ICF and DASH simultaneously, the functionality of patients with AC submitted to SSNB. We hypothesize that those affected will experience an improvement in both patient-reported outcome measures after the treatment.

Materials and Methods

Location of the Study and Study Design

The present is a prospective study, of the before-and-after type, performed in a single center at a tertiary private hospital from March 2019 to July 2020. It was approved by the institutional Ethics in Research Committee on February 29, 2019, under protocol 08599119.1.0000.8058. All subjects signed the Informed Consent Form.

Participants

The finite proportion sample calculation was used considering a significance level of 5%, a test power of 80% and a margin of error of 5%. The sample size obtained was 25 participants. The sample, which was non-probabilistic and consecutive, was obtained after routine appointments at a specialized outpatient clinic.

The eligible cases of AC were those which had constant pain for more than four weeks and limited active and passive range of motion in every direction, such as: anterior elevation, external rotation in 0°/90° of abduction, and internal rotation in adduction. The imaging diagnosis showed local disuse osteopenia on radiographs and volume restriction of axillary recess, as well as thickening of coracohumeral ligament, on magnetic resonance imaging.

Patients who had secondary AC were included in the study due to the following factors established by Zuckerman and Rokito:[4] previous surgery, trauma, prolonged immobilization, rotator cuff tear, calcareous tendinitis, as well as diabetes mellitus, neuropathies and hypo- or hyperthyroidism.

Patients with glenohumeral arthrosis, blocked shoulder dislocation, humeral head necrosis, malunion of the proximal humerus, and primary AC were excluded.

Data Collection

Data was collected through the following steps: 1) presentation of the research proposal and signing of the Free and Informed Consent Term; 2) application of the sociodemographic and clinical questionnaire; and 3) application of the patient-reported outcome measures (ICF checklist and DASH). All of these steps were performed by the same researcher (SRN), who was not in charge of performing the SSNB.

The four SSNBs, based on anatomical limits, were performed by the same shoulder specialist (MRF) in a prepared room in weekly intervals (►**Figs. 1**, **2**, **3**).[19] The AC patient

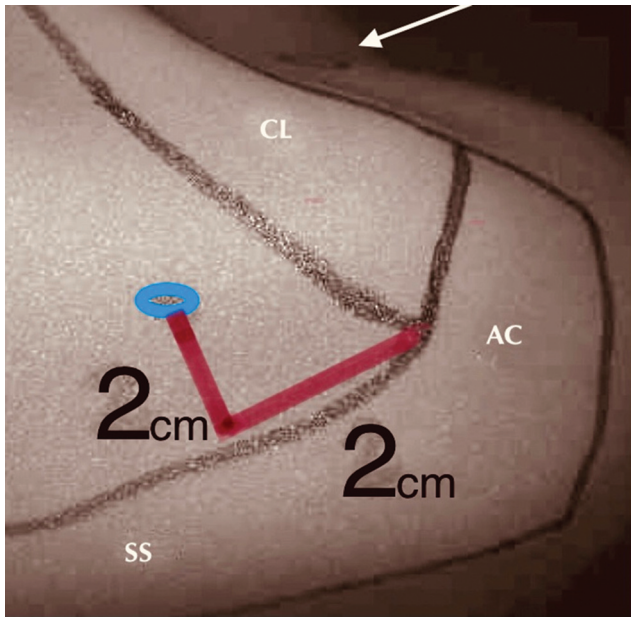


Fig. 1 Lateral and indirect technique of suprascapular nerve block based on anatomical limits. Posterior and superior shoulder view; blue circle: the needle is inserted perpendicularly to the skin in the craniocaudal direction, 2 cm from the medial acromial border and 2 cm from the upper margin of the scapular spine. White arrow: coracoid process. Abbreviations: CL, clavicle; AC, acromion; SS, scapular spine.



Fig. 2 Posterior shoulder view during suprascapular nerve block. Abbreviations: AC, acromion; SS: scapular spine.

was placed in a sitting position with the affected upper limb at 0° of abduction, and the region of the shoulder was sterilized with 70% alcohol before the injection. A syringe with an 18-gauge venipuncture catheter (Abocath; Bio-Med Healthcare Products, Haryana, India) was used with 10 mL of bupivacaine at 0.5% associated with 1:200.000 epinephrine (Neocaine, Cristália, Itapira, Brazil).

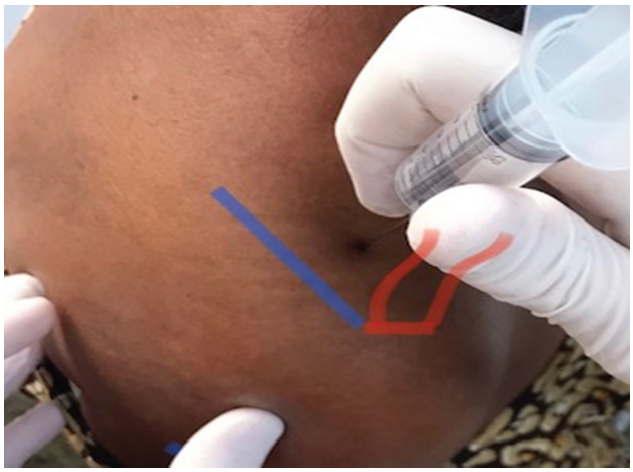


Fig. 3 Superior shoulder view during suprascapular nerve block. Blue line: superior border of scapular spine; red lines: distal clavicle.

All patients were evaluated through the ICF checklist and DASH at baseline (T_0), one week after the fourth SSNB (T_4), and three months after the first SSNB (T_{12}) (►**Fig. 4**).

Instruments

All 54 categories of the ICF checklist were used, and 11 of them concern body functions, 2 concern body structures, 17 are on activity and participation – performance, 17 are on activity and participation – capacity, and 7 involve environmental factors.[20] We used the RAW Scale formula, which has a score form 0 to 100, with qualifiers graded from 0 to 4 to determine the magnitude of the disability: 0% to 4% – none (0); 5% to 24% – slight (1); 25% to 29% – moderate (2); 50% to 95% – serious (3); and 96% to 100% – complete (4). The lower the value, the better the individual's functionality.[15,20]

The DASH evaluates upper limb disabilities over time through 30 questions about symptoms and the performance of specific activities, and it can be applied before and after procedures. Its score goes up to 100 (the higher the score, the greater the disability).[17,21]

Outcomes/Independent Variables

The outcomes were the functionality of individuals and of the upper limb according to the ICF checklist and the DASH. The independent variables were: age (in years); gender (male/female); ethnicity (white/black/brown); level of schooling ($<$ or $\geq$ eight formal years); monthly income (in multiples of the minimum wage); religion (yes/no); duration of pain (months); affected side (right/left); dominance (right-handed/left-handed).

Data Analysis

The categorical variables were presented as frequencies and percentages, while the continuous variables, as mean, standard deviation, maximum and minimum values.

The Kolmogorov-Smirnov test was used to verify the distribution of sample data. The Cronbach alpha coefficient was calculated to verify the internal consistency and reliability of the ICF and DASH at T_0, T_4, and T_{12}. The Chi-squared test was used to verify the homogeneity of the sample. The paired *t*-test was used to compare the means of the ICF checklist items and DASH in the different periods: T_0xT_4, T_4xT_{12}, and T_0xT_{12}. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS for Windows, IBM Corp., Armonk, NY, United States) software, version 20.0. The probability of rejecting the null hypothesis was 5%.

Results

The number of patients with AC who were recruited was 52; however, 9 had primary CA, 13 with secondary CA did not want to undergo the SSNB, 3 with secondary CA did not have time to participate, and 2 did not return with the test results requested. So, the final sample was composed of 25 participants with AC.

The sociodemographic and clinical data of the sample are summarized in ►**Table 1**. The mean age was of 58.16 years, and the duration of the pain symptoms ranged from 2 to 16 months, with a mean of 5.92 months.

►**Table 2** shows the reliability and internal consistency analysis of the ICF and DASH at T_0, T_4, and T_{12}, with a Cronbach alpha > 0.80.

►**Table 3** shows the results of the mean, standard deviation, maximum and minimum values of the ICF checklist domains, as well as the DASH scores at T_0, T_4, and T_{12}.

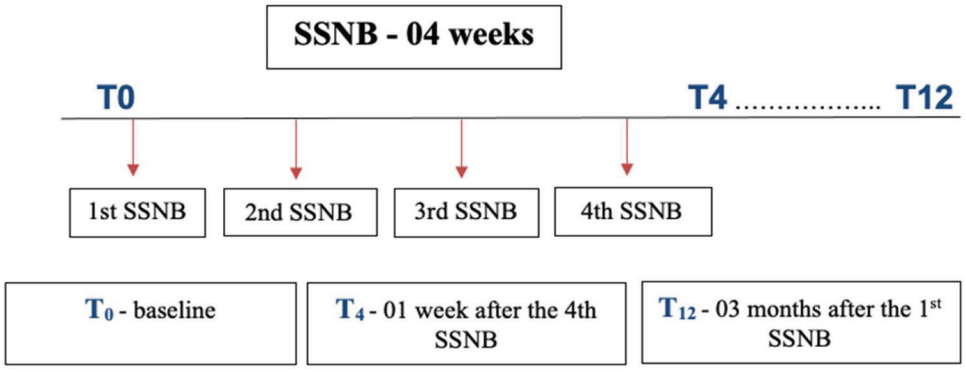


Fig. 4 Flowchart of assessment of the adhesive capsulitis patients through the ICF checklist and the DASH during the three months of the study. Abbreviations: SSNB, suprascapular nerve block; T, injection time; ICF, International Classification of Functioning, Disability and Health; DASH, Disabilities of the Arm, Shoulder and Hand questionnaire.

Table 1 Sociodemographic and clinical data of adhesive capsulitis patients ($n = 25$)

Variables	n	%	p^*
Gender			
Female	16	64.0	
Male	9	36.0	0.162
Age			
$\leq$ 60 years old	15	60.0	
$>$ 60 years old	10	40.0	0.317
Monthly income			
1 to 2 minimum wages	7	28.0	
3 to 4 minimum wages	8	32.0	0.756
$\geq$ 5 minimum wages	10	40.0	
Ethnicity			
White	17	68.0	
Black	2	8.0	**0.001**
Brown	6	24.0	
Religion			
Yes	24	96.0	
No	1	4.0	**0.000**
Level of schooling			
$<$ 8 years	4	16.0	
$\geq$ 8 years	21	84.0	**0.001**
Affected side			
Right	17	68.0	
Left	8	32.0	0.072
Dominance			
Left-handed	2	8.0	
Right-handed	23	92.0	**0.000**
Duration of pain			
2 to 6 months	12	48.0	
$>$ 6 months	13	52.0	0.841

Note: *Chi-squared test.

Table 2 Cronbach reliability coefficient regarding the ICF checklist and DASH at T_0, T_4, and T_{12} ($n = 25$)

	Cronbach alpha	Number of items
ICF at T_0	0.91	54
ICF at T_4	0.87	54
ICF at T_{12}	0.85	54
DASH at T_0	0.87	30
DAHS at T_4	0.96	30
DASH at T_{12}	0.94	30

Abbreviations: DASH, Disabilities of the Arm, Shoulder and Hand questionnaire; ICF, International Classification of Functioning, Disability and Health; T_0, baseline; T_4, one week after the fourth suprascapular nerve block (SSNB); T_{12}, three months after the first SSNB.

The analysis of the general classification of the ICF Checklist enabled us to verify that, at the beginning of the study (T_0), the individuals had functional disability, which restricted and limited their activities. At T_{12}, they presented lower values in terms of the extent of the disability, represented by the ICF qualifiers, mainly in the categories of performance and capacity, when compared with the beginning of treatment. Likewise, the DASH scores decreased, which expresses an improvement in upper limb function.

►**Table 4** shows the t-paired test analysis comparing the mean scores on the ICF checklist and DASH at T_0, T_4, and T_{12}. The score on the ICF checklist showed improvement in all domains as early as T_4, except for the environmental factors, which only improved at 03 months ($p = 0.037$). In the evaluation of the DASH, the patients had already reported an improvement in shoulder function at T_4 ($p = 0.019$), which improved even more at the end of data collection (T_{12}).

Discussion

The functionality of AC patients improved after four weeks (T_4) of SSNB injections (one per week) according to the two patient-reported outcome measures used: the ICF checklist and the DASH. This improvement continued until three months after the beginning of the treatment (T_{12}). The single ICF domain that improve only in T_{12} was environmental factors.

We need to know more about the health status of people with AC. The data collected in the present study contributed to the assessment of the treatment, and they can point to a new perspective regarding the assessment of functionality in the field of orthopedics.[22] The results of the present study showed that the ICF checklist and the DASH enable the identification of the level of impairment of the individual and of the upper limb before the procedure, as well as the clinical evolution after it.

Studies[23,24] on other health conditions that used the ICF checklist highlighted the value of this tool.[23,24] Magalhães et al.[23] evaluated work-related repetitive stress disorders/musculoskeletal disorders, and found that, the ICF enabled the identification of the clinical and social aspects experienced by patients during rehabilitation and their return to work. Silveira et al.[25] evaluated individuals with Parkinson disease, and the results demonstrated that the ICF seems to have good ability and sensitivity to address aspects of functionality regarding this disease.

Access to information about functionality has been a priority in the treatment of certain diseases, and the ICF is a tool with great applicability to guide these functionality processes.[26] Therefore, there is a need to check the importance of including the ICF in the clinical measures, as it considers the biopsychosocial context in which the individual is inserted. In the present study, all ICF domains had already improved in the outcome studied at T_4, except for the "environmental factors."

Table 3 Mean, standard deviation, maximum and minimum values of the ICF checklist and DASH scores at T_0, T_4, and T_{12} ($n = 25$)

	n	Mean	SD	Min.	Max.
ICF checklist					
T_0					
Body functions	25	46.82	7.65	31.82	59.09
Body structures	25	62.50	8.84	50	75
Activity and participation –performance	25	38.53	14.96	1.47	64.71
Activity and participation – capacity	25	42.59	12.41	16.18	64.71
Environmental factors	25	57.71	9.26	39.29	75
T_4					
Body functions	19	32.06	9.90	11.36	52.27
Body structures	19	50.00	12.50	37.5	75
Activity and participation – performance	19	9.91	9.67	1.47	35.29
Activity and participation – capacity	19	25.77	9.55	5.88	39.71
Environmental factors	19	55.45	7.28	35.71	64.29
T_{12}					
Body functions	19	19.02	9.62	6.82	36.36
Body structures	19	50.66	11.39	25	62.50
Activity and participation – performance	19	8.90	8.64	1.47	32.35
Activity and participation – capacity	19	22.68	8.21	4.41	33.82
Environmental factors	19	54.89	7.92	35.71	67.86
DASH					
DASH at T_0	25	50.68	11.18	28	67
DASH at T_4	19	42.37	16.88	5	70
DASH at T_{12}	19	29.58	13.33	7	51

Abbreviations: DASH, Disabilities of the Arm, Shoulder and Hand questionnaire; ICF, International Classification of Functioning, Disability and Health; Max., maximum; Min., minimum; SD, standard deviation; T_0, baseline; T_4, one week after the fourth suprascapular nerve block (SSNB); T_{12}, three months after the first SSNB.

These "environmental factors" are composed of the physical, social and environmental actions through which people live and lead their activities.[9,12,15] In the present study, the results showed that the environmental factors did not represent barriers (negative) or facilitators (positive) before T_{12}, and that the lived experience did not interfere with the disease nor impacted the individual's functionality. It is important to know that this domain still lacks clarity about the scope of the personal factors, and if it really represents an influence on the individual's specific functionality.[10,12,26]

Jung et al.[27] compared the efficacy of SSNB and intra-articular corticosteroid injection in two intervention groups

Table 4 Comparative analysis of the ICF checklist and DASH scores mean values at T_0, T_4, and T_{12} ($n = 25$)

	T_0 X T_4	T_4 X T_{12}	T_0 XT_{12}
	p^*	p^*	p^*
ICF Checklist			
Body functions	**0.000**	**0.000**	**0.000**
Body structures	**0.000**	0.841	**0.000**
Activity and participation – performance	**0.000**	**0.005**	**0.000**
Activity and participation – capacity	**0.000**	**0.000**	**0.000**
Environmental factors	0.134	0.547	**0.037**
DASH	**0.019**	**0.003**	**0.000**

Abbreviations: ICF, International Classification of Functioning, Disability and Health; DASH, Disabilities of the Arm, Shoulder and Hand questionnaire; T_0, baseline; T_4, one week after the fourth suprascapular nerve block (SSNB); T_{12}, three months after the first SSNB.
Note: *Paired *t*-test.

during a two-month evaluation, and they concluded that the association of interventions significantly improved the pain and functional outcomes of the patients. In the present study, the parameters that indicate significant improvement were observed in the first month of treatment with the SSNBs (T_4), which was confirmed by the DASH and the ICF checklist.

The strategy used in the present study was composed of four injections of SSNB in seven-day intervals over the course of four weeks; however, Mortada et al.[28] compared single and multiple blocks (nine injections) in three weeks, and they highlighted that this number of injections yielded better results than a single one. In the present study, improvement in shoulder function was observed with fewer applications until 12 weeks, which corroborates the findings by Haque et al.,[29] who recommended the SSNB as the initial procedure of choice in patients with AC. The guidance by ultrasound[28] or anatomical limits[8] is effective regarding the SSNB, with comparable results.[30]

The use of the DASH to assess upper limb disabilities before and after the treatment is satisfactory, as it is easy to apply, and enables the monitoring of the patient in the clinical setting.[21] A wide variety of available outcome tools, including the DASH, demonstrate acceptable levels of measurement properties, and are appropriate for virtually every patient with a shoulder disorder.[22]

The limitations of the present study include the lack of a control group submitted to another intervention for comparison. Some risk factors were not analyzed, neither were the comorbidities and other methods of treatment. The non-probabilistic sampling, of the consecutive type, may have imposed a selection bias, not enabling all patients to participate in the study. Moreover, we do not know if more severe AC patients had worse results.

However, the strengths of the study are the validated instruments (with good internal consistency that have been translated into Brazilian Portuguese, which enables the comparison across different cultures); the longitudinal clinical design with follow up; the well-defined eligibility criteria, and the absence of similar studies in the literature. All patients were submitted to x-rays and magnetic resonance, as well as to a complete clinical evaluation performed by the same shoulder specialist who performed the SSNB, who was not the same researcher who collected the data.

The simultaneous application of the DASH and ICF tools (patient reported outcome measures) in AC patients is the novelty of the present study. The correlation of these two instruments applied in AC patients is under analysis to be published in the near future, which will enable us to understand if they complement each other or not.

Conclusion

According to the ICF and DASH, the SSNBs improve the functionality of AC patients. This improvement lasted up to three months after the beginning of procedure. The single ICF domain that only improved at T_{12} was "environmental factors".

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Conflict of Interests
The authors have no conflict of interests to declare.

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Comparative Analysis of TNF-alpha, TNF-R1, and TNF-R2 in Patients with Low-impact Fractures Due to Osteoporosis

Análise comparativa de TNF-alfa, TNF-R1 e TNF-R2 em pacientes com fraturas de baixo impacto decorrentes de osteoporose

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Abstract

Objective To analyze the serum levels of TNF-alpha and its TNF-R1 and TNF-R2 receptors in the blood of patients with low-impact fractures due to osteoporosis, comparing between genders and with healthy patients.

Methods The present study was conducted with a blood sample of 62 patients, divided into patients with osteoporosis and healthy patients. The results were obtained using the ELISA method. Cytokine concentrations were determined based on the absorbance values obtained.

Results Serum TNF-alpha levels were undetectable in female patients, while in males they were found only in one patient, with no significant difference. Similar results were found in the analyses of TNF-R1 and TNF-R2 levels, a significant increase in levels of TNF-alpha receptors in the groups of patients with osteoporosis compared with the control group in both sexes. There was no significant difference between the sexes in the dosage of both receptors within the group with osteoporosis. There was also a positive and significant correlation in the levels of TNF-R1 and TNF-R2 only in women.

Conclusion The significant increase in TNF-R1 and TNF-R2 levels in women with osteoporosis suggest that the release and expression of these receptors may be contributing differently to the development of osteoporosis in men and women.

Keywords
- osteoporosis
- tumor necrosis factor-alpha
- receptors, tumor necrosis factor

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Resumo

Objetivo Analisar os níveis séricos de TNF-alfa e de seus receptores TNF-R1 e TNF-R2 no sangue de pacientes com fraturas de baixo impacto, decorrentes de osteoporose, comparando entre os sexos e com pacientes saudáveis.

Métodos O estudo foi realizado com amostra de sangue de 62 pacientes, divididos em pacientes com osteoporose e pacientes saudáveis. Os resultados foram obtidos através do método de ELISA. As concentrações de citocinas foram determinadas com base nos valores de absorbância obtidos.

Resultados Os níveis séricos de TNF-alfa foram indetectáveis nos pacientes do sexo feminino, enquanto no masculino encontrou-se somente em um paciente, não havendo diferença significativa. Encontrou-se resultados semelhantes nas análises dos níveis de TNF-R1 e TNF-R2, aumento significativo nos níveis dos receptores de TNF-alfa nos grupos de pacientes com osteoporose em comparação com o grupo controle, em ambos os sexos. Não houve diferença significativa entre os sexos na dosagem de ambos os receptores dentro do grupo com osteoporose. Houve ainda correlação positiva e significativa nos níveis de TNF-R1 e TNF-R2 apenas nas mulheres.

Conclusão O aumento significativo nos níveis de TNF-R1 e TNF-R2 em mulheres com osteoporose sugerem que a liberação e expressão destes receptores pode estar contribuindo de maneira distinta no desenvolvimento da osteoporose em homens e mulheres.

Palavras-chave

- osteoporose
- fator de necrose tumoral alfa
- receptores do fator de necrose tumoral

Introduction

Osteoporosis is a systemic disease characterized by decreased bone mass with deterioration of the skeletal microarchitecture, leading to bone fragility and increasing the propensity to fractures.[1]

Bone metabolism is active throughout life, and renewal is a constant process in which osteoclast pulls out the mineral component and osteoblast resets it.[2] The normal skeletal maturation process involves the accumulation of bone mass up to about 30 years of age. From then on, there is a physiological loss of about 0.3% each year, initiating the osteopenia process, with decreased bone mineral density, weakening, and increased bone trabeculations. Osteoporosis can affect both men and women, and may occur in any region, with the main bones being the ones in the hip joint, the wrist, the spine, and the ribs. The weakening caused by low bone density is related to most low-impact fractures in the elderly.[3]

Several components of the innate and adaptive immune response have been related to the modulation of osteoclast and osteoblast activity, thus leading to direct changes in the bone matrix.[4] Several signaling pathways were identified as contributors to the interaction between osteoblasts and osteoclasts, including RANK, NF-Kb receptor activator, and its ligand (RANK-L).[5–7]

The connection of RANK-L to its receptor, RANK, provides the signal to conduct the development of osteoclasts from hematopoietic progenitor cells, in addition to activating mature osteoclasts. Osteoprotegerin, also known as an osteoclastogenesis inhibitor, is the TNF-alpha receptor-related protein (alpha tumor necrosis factor) that controls the development and function of osteoclasts. It is responsible for the negative regulation between RANK-L and its receptor, therefore inhibits bone resorption by osteoclasts.[8,9]

TNF-alpha is a potent cytokine, which exerts a variety of biological effects, and can perform a pleiotrophic role in the immune response, inflammation, in addition to controlling cell proliferation, differentiation and apoptosis.[10,11] Tumor necrosis factor alpha acts on osteoclastogenesis through a mechanism involving the activation of NF-kB.[12,13] In addition, TNF-alpha acts by directly stimulating macrophages to differentiate into osteoclasts by an independent mechanism of RANK-L.[14,15]

Currently, it is known that TNF-alpha binds to 2 cell surface receptors, type 1 receptor (TNF-R1), also known as p55, and type 2 receptor (TNF-R2) or p75 sections, each receptor being responsible for mediating distinct intracellular signals.[16]

Both TNF-R1 and TNF-R2 are highly expressed in osteoclast precursors.[17] When activated by TNF-alpha, the type 1 receptor stimulates osteoclastogenesis by activating NF-Kb and inhibits the osteoblasts differentiation.[18,19] On the other hand, type 2 receptor activation showed osteoclastogenesis suppression in *in vitro* experiments.[17]

The present study aims to evaluate the levels of TNF-alpha and its receptors, TNF-R1 and TNF-R2, in elderly patients with low-impact fractures due to osteoporosis, comparing and analyzing the values between men and women and with patients in the control group.

Materials and Methods

All procedures of the present study were approved by the Research Ethics Committee of the University under protocol (CAAE) number: 51827515.4.0000.5145 and opinion number

Table 1 Distribution of study groups by gender

Group	Number	Average age (years old)	Standard error	*p-value*
Control woman	11	40.9	3.1	0.83
Control man	17	42.6	3.2	
Osteoporosis woman	21	80.1	2.1	0.14
Osteoporosis man	13	78.9	2.6	

1,375,317, and all participants signed a Free and Informed Consent Form, after clarification.

Peripheral blood samples were collected from 62 patients, 21 women and 13 men, with low-impact fractures due to osteoporosis, and 11 women and 17 men who presented high-impact trauma fractures, forming patients in the control group (►**Table 1**).

The collection was conducted in the orthopedic center of our institution. Patients with bone diseases, fractures not related to osteoporosis, immunosuppressed patients, patients with malignant neoplasms and those who did not agree to participate in the study were excluded.

ELISA For Measuring Sly Cytokines

Tumor necrosis factor alpha (TNF-alpha) and tumor necrosis factor receptor types 1 and 2 (TNFR1 and TNFR2) were evaluated by enzyme immunoabsorption assay (ELISA). Plates of 96 high-affinity bonding wells (Nunc, Roskilde, Denmark) were sensitized with monoclonal antibodies specific to each cytokine investigated (BD Biosciences, San Jose, CA, USA) under the conditions recommended by the carbonate-bicarbonate buffer manufacturer (pH 9.5) and were incubated overnight at 4°C. After incubation, the contents of the wells were discarded and the plates were blocked with 200 µL per phosphate buffer well containing 2% buffered saline solution with bovine serum phosphate/albumin (PBS-BSA) (Sigma, St. Louis, MO, USA) for 4 hours at room temperature. Bovine serum phosphate/albumin was then discarded and lines 1 to 10 were filled with diluted serum samples 1:2 in 1% of PBS-BSA for a total volume of 100 µL per well. Serial dilutions of recombinant cytokines were used to elaborate the standard curve. The plates were incubated overnight at 4°C and then rinsed 4 times with PBS solution containing Tween at 0.05% (Sigma, St. Louis, MO, USA). Next, biotin-conjugated antibodies (BD Biosciences, San Jose, CA, USA) specific to each cytokine investigated were added to wells diluted with PBS-BSA at 1% at the concentration indicated by the manufacturer for a total of 100 µL per well. The plates were incubated for 4 hours at 37°C, rinsed with 0.05% PBS Tween, treated with 100 µL per strepavidin well conjugated with peroxidase and then incubated for 3 hours at 37°C. Finally, the plates were rinsed with 0.05% PBS-Tween. A total of 100 µL of tetramethylbenzidine (TMB) development buffer was added per well under light and at room temperature; the reaction was interrupted by the addition of 50 µL of sulfuric acid. The results were obtained by measuring absorbance at 450 nm using an automatic ELISA reader (Enspire, Perkin Elmer, USA). Cytokine concentrations were determined based on linear regression using absorbance values obtained from recombinant cytokine curves and are expressed in pg/ml. The sensitivity of the method ranged from 10 to 18 pg/ml.

Statistical analysis

Statistical analysis was performed in GraphPad Prism 7.0 and Statview (Abaccus, USA) software. The normality of quantitative variables was investigated using the Kolmogorov-Smirnov test and the Shapiro-Wilk test. The Student t-test was used to analyze clinical parameters such as age. Cytokine levels were analyzed by the Mann-Whitney test. The significance level was established at 5% ($p < 0.05$) in all quantitative tests.

Results

Tumor necrosis factor alpha serum levels were undetectable in all female patients. In the male group, it was detected in only one patient. The median was zero in both groups, with no significant difference (Mann-Whitney; $p = 0.38$) (data not shown).

Tumor necrosis factor-R1 serum levels ranged from 1,209 to 4,918 pg/ml (median of 2,720 pg/ml) in the group of women with osteoporosis. In men with osteoporosis, levels ranged from 1,257 to 4,273 pg/ml (median of 2,680 pg/ml). There was no significant difference between the groups of patients with osteoporosis when analyzed by gender (Mann-Whitney; $p = 0.74$). In the control group, TNF-R1 serum levels ranged from 369 to 2,000 pg/ml (median of 689 pg/ml) in the group of women. In men, levels ranged from 198 to 2,417 pg/ml (median of 608 pg/ml). Tumor necrosis factor-R1 levels showed a significant increase in the osteoporosis group compared with the control group in both females and males ($p < 0.0001$) (►**Fig. 1**).

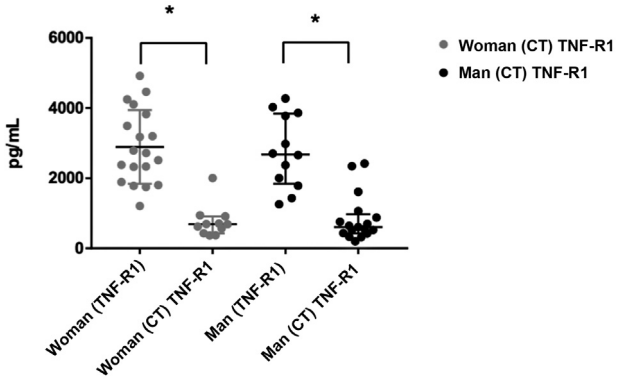


Fig. 1 Comparison of TNF-R1 serum levels between study groups in patients of both sexes.

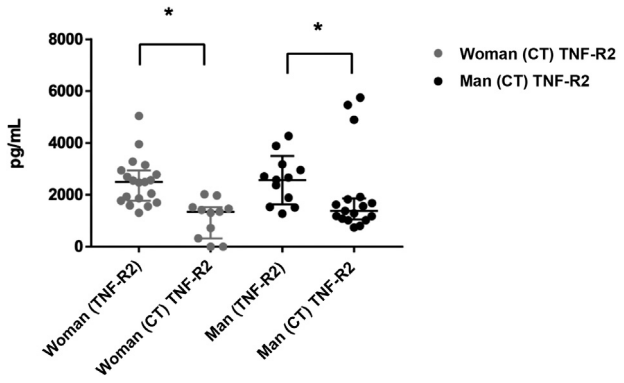


Fig. 2 Comparison of TNF-R2 serum levels between study groups in patients of both sexes.

Tumor necrosis factor-R2 serum levels had similar results, ranging from 1,313 to 5,042 pg/ml (median of 2,495 pg/ml) in the group of women with osteoporosis. In men with osteoporosis, the levels ranged from 1,276 to 4,271 pg/ml (median of 2,618 pg/ml). There was no significant difference between the groups of patients with osteoporosis when analyzed by gender (Mann-Whitney; $p = 0.85$). In the control group, TNF-R2 serum levels ranged from undetectable to 2,023 pg/ml (median of 1,350 pg/ml) in the group of women. In men, the levels ranged from 744 to 5,753 pg/ml (median of 1,380 pg/ml). Tumor necrosis factor-R2 levels showed a significant increase in the osteoporosis group compared with the control group in both females and males ($p < 0.0001$ and 0.033, respectively) (►**Fig. 2**).

As a significant increase in TNF-R1 and TNF-R2 was observed in men and women with osteoporosis, we tested whether there would be a correlation between TNF-R1 and TNF-R2 serum levels in osteoporosis, both in males and females. The results presented in ►**Figs. 3** and **4** show that there is a positive and significant correlation only in females (Sperman; $p = 0.049$).

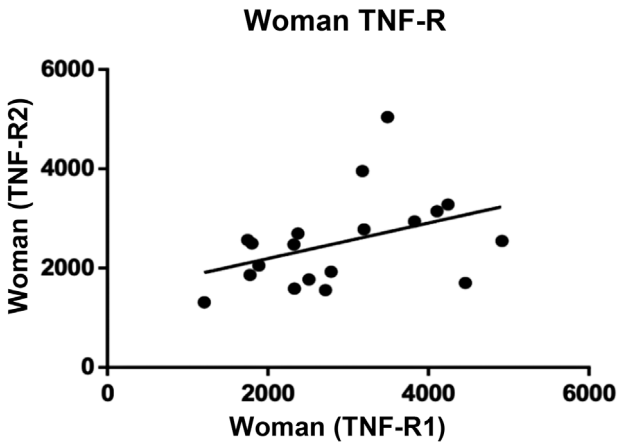


Fig. 3 Correlation between TNF-R1 and TNF-R2 serum levels in women with osteoporosis.

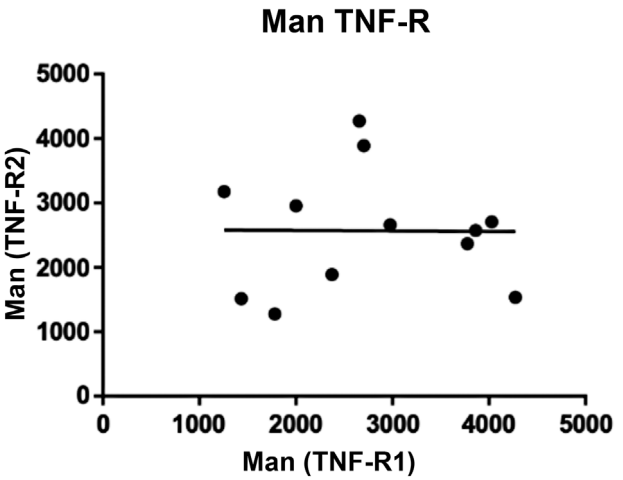


Fig. 4 Correlation between TNF-R1 and TNF-R2 serum levels in men with osteoporosis.

Discussion

Osteoporosis develops from an imbalance in bone remodeling, which results from both hormonal changes and immunological factors. In the present study, we analyzed the presence of TNF-alpha, a potent cytokine in the inflammatory role, and its receptors, TNF-R1 and TNF-R2, in patients with osteoporosis and in the control group, also comparing between genders.

The results showed significant differences in the amount of TNF-R1 and TNF-R2 receptors. Women with osteoporosis have high levels of TNF-R1 and TNF-R2 receptors when compared with women in the control group. Similarly, men with osteoporosis have high levels of TNF-R1 and TNF-R2 receptors when compared with men in the control group.

Studies show that the increase in proinflammatory cytokines, such as TNF-alpha, may be directly related to aging, and inappropriate production of this cytokine or sustained activation of its signaling pathways are factors related to the development of osteoporosis.[20,21] However, as well as the present study, other authors have demonstrated no association between changes in TNF-alpha levels between normal women and men and those with osteoporosis.[22,23]

In the present study, we also evaluated the serum levels of TNF-alpha receptors. The evaluation of soluble forms of TNF-alpha receptors should be evaluated,[24] since the dosage of circulating levels of TNF-alpha based on bone mass status is inconsistent and controversial.[22,23] Studies show that the activation of TNF-R1 leads to increased osteoclastogenesis and decreased differentiation of osteoblasts.[21]

In the present study, serum levels of TNF-alpha, TNF-R1, and TNF-R2 receptors were analyzed. We found a significant increase when comparing TNF-R1 levels in women and men with osteoporosis with those in the control group, corroborating that there is a relationship between the physiopathogenesis of osteoporosis and the effects of TNF-R1 activation. Similarly, we showed a significant increase in TNF-R2 serum levels in patients with osteoporosis, both in the male and female groups. The activation of TNF-R2 has been described

as suppressive of osteoclastogenesis.[25] Our data show that TNF-alpha was not detected in the serum of patients with osteoporosis and that serum levels of their TNF-R1 and TNF-R2 receptors are increased when compared with the control group. Signaling of these receptors is associated with modulation of osteogenesis and, if stimulated inadequately, it may result in bone homeostasis imbalance as demonstrated in studies that observed imbalance in bone deposition, in the occurrence of weakened differentiations of osteoblasts and adipocytes.[26]

An interesting finding was the fact that there is a positive and significant correlation between the levels of TNF-R1 and TNF-R2 only in women, suggesting that the two receptors are released homogeneously only in females.

Conclusion

The present study demonstrates a significant increase in TNF-alpha, TNF-R1, and TNF-R2 receptors in patients with osteoporosis in men and women. In females, serum levels of these receptors present a significant and positive correlation, while this correlation was not observed in males. These data suggest that the expression and release of these receptors may be contributing differently to the development of osteoporosis in men and women.

Conflict of Interests
The authors have no conflicts of interest to declare.

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Biomechanical Gait Analysis in Patients with Osteonecrosis of the Femoral Head

Análise biomecânica da marcha de pacientes com osteonecrose da cabeça do fêmur

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Abstract

Objectives Although osteonecrosis of the femoral head is a prevalent condition, its effects on gait parameters have not been thoroughly studied and are not well-established in the current literature. The primary aim of the present study is to describe gait in patients with a diagnosis of osteonecrosis.

Methods This is a cross-sectional study. Nine patients diagnosed with osteonecrosis of the femoral head who were regularly followed-up at an outpatient clinic were selected for the present study and underwent gait analysis using Vicon Motion Capture Systems. Spatiotemporal data was obtained, and joint angles were calculated using an Euler angle coordinate system. Distal coordinate systems were used to calculate joint moments and force plates to obtain ground reaction forces.

Results Patients with osteonecrosis presented with slower velocity (0.54 m/s $\pm$ 0.19) and smaller cadence (83.01 steps/min $\pm$ 13.23) than healthy patients. The pelvic obliquity range of motion was of 10.12° $\pm$ 3.03 and rotation was of 18.23° $\pm$ 9.17. The mean hip flexion was of 9.48° $\pm$ 3.40. Ground reaction forces showed reduced braking and propelling forces. Joint moments were reduced for flexion and adduction (0.42 Nm/kg $\pm$ 0.2 and 0.30 Nm/kg $\pm$ 0.11, respectively) but the abduction moment was increased (0.42 Nm/kg $\pm$ 0.18).

Conclusions The present study showed that osteonecrosis of the femoral head presents compensatory gait mechanisms, with increased pelvic motion and decreased knee flexion to protect the hip joint. Decreased moments for hip flexion and adduction were also identified and muscle weakness for those groups may be correlated to the disease.

Keywords

- arthroplasty, replacement, hip
- biomechanical phenomena
- femur head necrosis
- gait analysis

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Resumo

Objetivos Embora a osteonecrose da cabeça do fêmur seja uma lesão prevalente, seus efeitos sobre os parâmetros da marcha não foram minuciosamente estudados e não estão bem estabelecidos na literatura atual. O objetivo principal do presente estudo é descrever a marcha em pacientes com osteonecrose.

Métodos Trata-se de um estudo transversal. Nove pacientes com diagnóstico de osteonecrose da cabeça do fêmur, sob acompanhamento regular em ambulatório, foram selecionados para o presente estudo e submetidos à análise da marcha com Vicon Motion Capture Systems. Os dados espaciais e temporais foram obtidos e os ângulos articulares foram calculados com o sistema de coordenadas angulares de Euler. Sistemas de coordenadas distais e plataformas de força foram utilizados para o cálculo de momentos articulares e de forças de reação ao solo, respectivamente.

Resultados Os pacientes com osteonecrose apresentaram menor velocidade (0,54 m/s $\pm$ 0,19) e menor cadência (83,01 passos/minuto $\pm$ 13,23) do que pacientes saudáveis. As amplitudes de movimento de obliquidade e rotação pélvica foram de 10,12° $\pm$ 3,03 e 18,23° $\pm$ 9,17, respectivamente. A média de flexão do quadril foi de 9,48° $\pm$ 3,40. O estudo das forças de reação ao solo revelou redução das forças de frenagem e propulsão. Os momentos articulares de flexão e adução caíram (0,42 Nm/kg $\pm$ 0,2 e 0,30 Nm/kg $\pm$ 0,11), mas o momento de abdução aumentou (0,42 Nm/kg $\pm$ 0,18).

Conclusões O presente estudo mostrou que a osteonecrose da cabeça do fêmur é associada a mecanismos compensatórios da marcha, com aumento da movimentação pélvica e diminuição da flexão do joelho para proteção da articulação do quadril. A redução dos momentos de flexão e adução do quadril também foi identificada e a fraqueza destes grupos musculares pode estar correlacionada à doença.

Palavras-chave

- artroplastia de quadril
- fenômenos biomecânicos
- necrose da cabeça do fêmur
- análise da marcha

Introduction

Osteonecrosis of the femoral head (ONFH) is a disease caused by the disruption of the blood supply to the femoral head, culminating in medullary bone tissue death and, subsequently, evolving to subchondral bone collapse and femoral head deformity.[1–9] It is a debilitating, progressive condition, with the potential for causing degenerative hip disease and functional loss.[1,2,10] The condition affects patients aged between 30 and 50 years old,[7,9] with an incidence of 10,000 to 20,000 cases per year in the USA,[7,10] and is responsible for 10% of all total hip arthroplasties (THAs) performed in the USA.[3]

Although the pathogenesis of ONFH is unclear,[4] it is considered a multifactorial disease in which both genetic and environmental factors play a role in its outcome.[5] Ischemia can arise from endothelial damage, thrombosis, increased intraosseous pressure, cytotoxic effects from medications such as corticosteroids, increasing osteocyte apoptosis, and traumatic events.[3] Considering its etiology, ONFH can be idiopathic, traumatic, and nontraumatic. Osteonecrosis due to trauma is generally related to femoral neck fractures, hip dislocations, or repetitive microtraumas. The nontraumatic risk factors can be cortisone therapy, alcohol abuse, blood dyscrasias (sickle cell disease, Factor V Leiden mutation, decreased protein C or S, increased blood lipoprotein), systemic lupus erythematosus, Gaucher disease, Caisson disease, and some less commonly documented factors such as human immunodeficiency virus infection.[4,6,9]

Patients are often asymptomatic in the early stages, progressing to pain in the groin or in the gluteal sulcus and decreased hip range of motion (RoM), particularly for internal rotation.[4,6,9] Early diagnosis is essential to prevent the progression to collapse. Radiographs are the first imaging methods obtained; however, these may be normal. If there is clinical suspicion with unaltered radiographs, a magnetic resonance imaging (MRI) exam should be performed since it is up to 100% sensitive for the diagnosis of ONFH.[2,3]

After the diagnosis, staging is used to define treatment. The Ficat and Arlet classification is the most widely used system in clinical settings. Radiographical signs are used to stage between 0 to IV in the Ficat and Arlet system.[11] The Steinberg classification system also uses radiographic criteria to classify mild, moderate, or severe stages according to the percentage of the femoral head affected. The Association Research Circulation Osseous (ARCO) system includes scintigraphy, MRI, and computed tomography (CT) scan findings that help to determine the position and total area of necrosis.[10,12]

Treatment choice is based on staging. Nonoperative treatments include oral medications (primarily bisphosphonates), hyperbaric chamber, extracorporeal shockwave therapy, and pulsed electromagnetic fields.[8,9] Operative treatment alternatives include core decompression, osteotomies, bone grafting, and THA. Hip arthroplasties are

preferred due to their high success rate; however, there is a higher risk of aseptic loosening and infection in younger patients.[7,8]

Biomechanical gait analysis is one of the most reliable forms of assessing kinetic and kinematic gait parameters,[13] producing adequate and detailed data for evaluating patients with gait impairment diseases, their functional conditions, and compensatory mechanisms.[14]

Despite the high incidence, economic burden, and severe functional impairments of the disease, there is a paucity of studies evaluating its effect on gait parameters. The present cross-sectional study aimed to assess and describe gait parameters of patients with a diagnosis of ONFH, to compare this function with the existing literature on gait analysis of conditions with similar degenerative outcomes, as well as to describe a possible compensatory mechanism for identified gait deficits.

Methods

Participants

This was a cross-sectional study. It was approved by the Research Ethics Committee (47578621.0.0000.5404) of the institution. Nine patients who decided to participate were previously diagnosed with ONFH and were regularly followed-up at the Adult Hip Pathologies Outpatient Clinic at the clinical hospital were included. Patients who had previously undergone definitive surgical procedures to treat ONFH; had other pathologies such as neurological, syndromic, orthopedic, or lower limb deformities that could affect gait; had undergone previous procedures that affected gait; or had a recent lower limb trauma were excluded from the study. All participants gave their informed written consent for the present study.

Gait Analysis

Before gait analysis, a data collection form containing age, gender, and Ficat and Arlet and ARCO classifications were filled out according to clinical data, patient medical chart, and the most recent patient imaging in the hospital imaging system. The classifications were reviewed by the authors. Body mass was measured using a balance scale and was converted to Newtons for normalization.

Gait analysis was performed using a 12-camera (Vero) Vicon motion capture system (Vicon, Oxford, United Kingdom) at 120 Hz for both kinetic and kinematic data, and two AMTI force plates built in a fixed 10-m-long walkway (Advanced Mechanical Technology Inc., Watertown, MA, USA) for ground reaction forces (GRFs). Three-dimensional (3D) reconstruction and data analysis were performed using The Motion Monitor xGen system (Innovative Sports Training Inc., Chicago, IL, USA). Seven four-marker sensor clusters were positioned in the sacrum, the right and left thighs, the right and left shanks, and the right and left foots of each participant, for segment selection. A stylus was used to digitize anatomical landmarks for the 3D reconstruction (►**Fig. 1**), segment, and joint center identification. The participants were then asked to walk at a comfortable pace over the walkway for 30 seconds and data were collected from 10 to 20 gait cycles for each patient. One value for each variable was collected every 10 milliseconds.

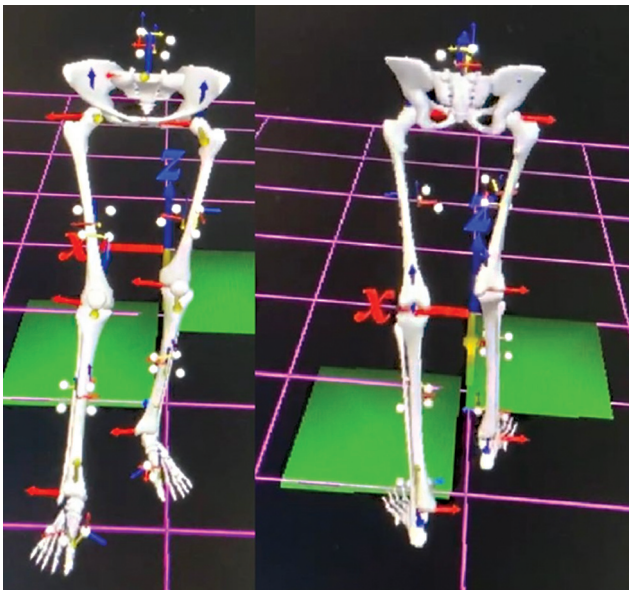


Fig. 1 Three-dimensional animation of gait during one trial with The Motion Monitor xGen system (Innovative Sports Training Inc., Chicago, IL, USA).

Joint centers and body segments were identified with The Motion Monitor (Innovative Sports Training Inc., Chicago, IL, USA) and segment mass and inertia were calculated using nonlinear regression equations. Euler angles were used to calculate joint angles, through a distal coordinate system, in a flexion-extension, abduction-adduction, and internal-external rotation sequence. Pelvic, hip, knee, and ankle angles data were collected bilaterally; however, only the affected limb was analyzed. The moment was calculated using inverse dynamics and was expressed in the distal segment coordinate system; division normalization was used for both moment and force data. The authors used an internal perspective to evaluate kinetic data and interpret gait function.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA). All data were evaluated for normality. One-sample *t*-tests were used to compare characteristics of peak values found in the literature for healthy participants.[14–16] Significance was established at $p < 0.05$.

Results

Nine participants who fulfilled the eligibility criteria were included in the present study, of which 66.7% ($n = 6$) had bilateral hip disease and 33.3% ($n = 3$) had unilateral hip disease. So, a total of 15 hips were analyzed. Six patients were men, and the mean age of all patients was 44.11 years old (± 14.8; $p = 0.101$). The average weight was 76.1 ± 17.6 kg, and the mean height was 166.6 ± 6.7 cm. The Ficat and Arlet classification was stage IV for 13 of the evaluated hips, stage

Table 1 Spatiotemporal linear kinematics of gait in patients with a diagnosis of osteonecrosis of the femoral head

	Reference*[14]	Mean	SD	*p-value*
Gait Velocity (m/s)	1.32	0.54	0.19	< 0.01
Cadence (steps/min)	99	83.01	18.23	0.015
Stride length (m)	1.21	0.78	0.24	< 0.01
Stride frequency (Hz)		0.69	0.15	
Cycle duration (s)	1.22	1.51	0.35	0.019

Abbreviation: SD, standard deviation.
*Reference for normal gait parameters found in the literature.

III for 1, and stage II for 1 hip evaluated. The ARCO classification was 4 for 13 of the hips, 3A for 1, and 1 for 1 hip. In sum, there was a significant preponderance of hips evaluated post femoral head collapse, which accounts for Ficat and Arlet stage IV and ARCO stage 4.

Kinematic data were analyzed linearly for gait speed, cadence, stride length, stride frequency and cycle duration, and angularly for joint angles. Results for kinematic analysis are assembled in ►**Tables 1**, **2** and **3**. Linear kinematics are presented in mean and standard deviation (S|D), and joint angles are described in mean, RoM, and SD for every joint movement.

Briefly, gait velocity was 0.54 ± 0.19 with a cadence of 83.01 ± 13.23. Pelvic obliquity reached a RoM of 10.12 ± 3.03 and rotation of 18.23 ± 9.17. Hip flexion mean was 9.48 ± 3.40 and RoM of 23.62 ± 7.56.

Kinetic data were analyzed for GRFs and joint moment. The GRFs were normalized for body weight (BW) and moment for body mass (kg).[13,17] The GRFs are presented in ►**Fig. 2**, and joint moment data are presented in ►**Table 4**.

Discussion

Gait analysis is a helpful tool in evaluating patient functionality in osteomuscular diseases. Thus, physicians can assess a daily activity that can greatly impair quality of life, as well as invest in immediate nonoperative measures that can improve pain, functionality, and, eventually, surgical outcomes. Although several systems exist to evaluate hip performance,[18] they are dependent on patient self-evaluation and on physical examination and often lack objectivity.

Osteonecrosis of the femoral head is a fairly incident condition that can arise from several etiologies; however, very few studies evaluate its effect on gait, perhaps due to its similar clinical outcomes to hip osteoarthritis (OA). The present study described gait kinetics and kinematics and compared results with the relevant literature both in participants with ONFH and asymptomatic, healthy individuals.

Our study found smaller values of gait speed, cadence, and stride length, and larger cycle duration compared with those found by Cho et al.[19] in 39 participants with ONFH before

Table 2 Pelvic angular kinematics of gait in patients with a diagnosis of osteonecrosis of the femoral head with unilateral and bilateral disease and in the subject group overall

			Reference*[15]	Angle	SD	*p-value*
Unilateral	Pelvic Tilt	Mean	11.4	40.66	19.88	0.63
	Obliquity	Mean	0.1	5.56	4.64	0.89
		RoM	10.3	10.29	4.44	0.49
	Rotation	Mean	0	10.28	5.18	0.03
		RoM	12.5	15.70	5.94	0.22
Bilateral	Pelvic Tilt	Mean	11.4	35.13	16.34	0.08
	Obliquity	Mean	0.1	4.04	2.26	0.04
		RoM	10.3	10.04	5.20	0.45
	Rotation	Mean	0	11.70	9.66	0.02
		RoM	12.5	19.5	10.7	0.85
Overall	Pelvic Tilt	Mean	11.4	32.60	17.9	< 0.01
	Obliquity	Mean	0.10	4.55	4.68	< 0.01
		RoM	10.3	10.12	3.03	0.45
	Rotation	Mean	0	11.23	8.1	< 0.01
		RoM	12.5	18.23	9.17	0.05

Abbreviations: RoM, range of motion; SD, standard deviation.
*Reference for normal gait parameters found in the literature.

Table 3 Hip, knee and ankle angular kinematics of gait in patients with a diagnosis of osteonecrosis of the femoral head

			Reference*[15]	Angle	SD	*p-value*
Hip	Flexion	Mean	16.4	9.48	3.40	< 0.01
		RoM	43.6	23.62	7.56	< 0.01
	Extension	Mean	−7.4	7.29	3.66	< 0.01
		RoM	42.0	18.24	8.45	< 0.01
	Abduction	Mean	−8.0	5.04	2.50	< 0.01
		RoM	14.0	13.35	7.86	0.40
	Adduction	Mean	−0.4	4.01	2.14	< 0.01
		RoM	14.0	10.16	4.29	< 0.01
	Internal Rotation	Mean	0.7	5.29	2.58	< 0.01
		RoM	0.9	12.39	5.28	< 0.01
	External Rotaion	Mean	0.7	7.54	1.58	< 0.01
		RoM	0.9	17.36	3.47	< 0.01
Knee	Flexion	Mean	20.6	16.21	2.58	< 0.01
		RoM	61.2	51.9	6.69	0.02
Ankle	Dorsiflexion	Mean	29.4	4.31	1.62	0.004
		RoM	6.2	24.67	9.17	0.08
	Plantar Flexion	Mean	−29.4	5.05	1.51	0.026
		RoM	−6.2	25	6.61	0.041

Abbreviations: RoM, range of motion; SD, standard deviation.
*Reference for normal gait parameters found in the literature.

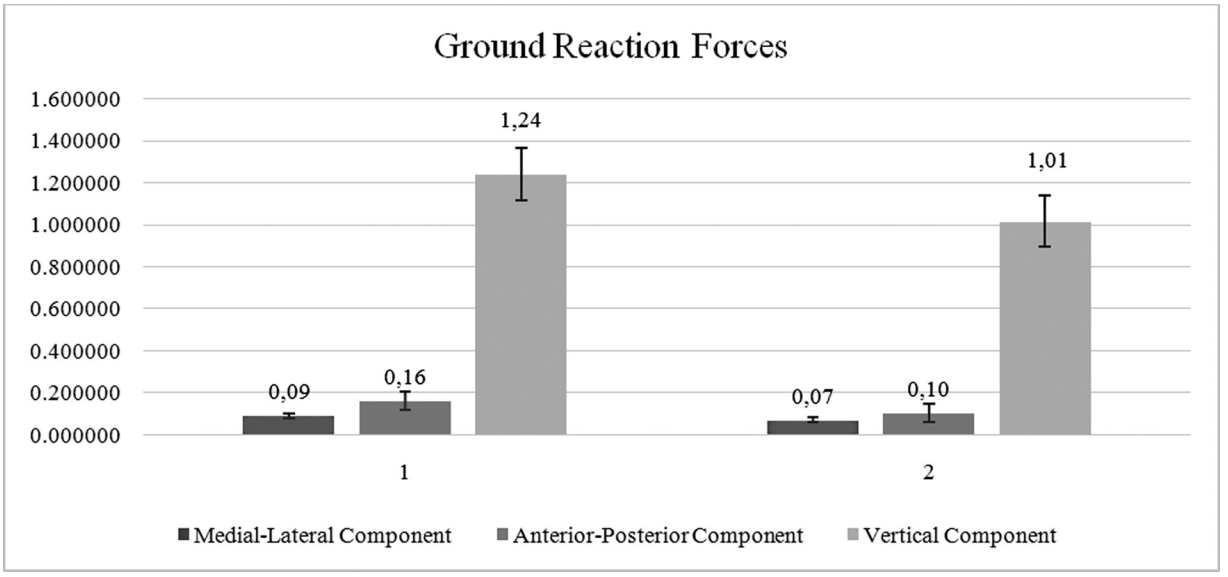


Fig. 2 Means and standard deviations for ground reaction forces (GRFs) (N/BW) in patients with osteonecrosis of the femoral head. 1. Average mean GRF in the second peak stance. 2. Average mean GRF in the first peak stance. Standard deviation for medial-lateral (ML) component of 0.01 ($p = 0.29$), anteroposterior (AP) component of 0.04 ($p = 0.015$) and vertical (V) component of 0.12 ($p = 0.34$).

THA. All spatiotemporal data were compared with those found by Holden et al.,[14] showing significantly minor averages for both distance and temporal parameters in healthy individuals. While those results were expected in comparison with physically fit participants, differences found between both ONFH groups may arise from the disease severity in patients analyzed in the present study. Slower velocity is commonly found in degenerative hip conditions with decreased joint RoM and pain.

Overall, the pelvic angular parameters were abnormally different to those found in healthy participants by Otayek et al.,[15] particularly regarding pelvic mean upwards obliquity and in mean and RoM for rotation. However, these parameters were similar to those observed in the ONFH group by

Table 4 Joint moments in patients with osteonecrosis of the femoral head

		Reference*[16]	Mean	SD	*p-value*
Hip flexion / Extension moment (Nm/kg)	Loading response	0.92	0.42	0.20	< 0.01
	Terminal stance	0.65	0.51	0.20	0.06
	Terminal Swing		0.34	0.09	
Hip abduction / Adduction moment (Nm/kg)	Initial single support	0.24	0.42	0.18	< 0.01
	Middle single support		0.28	0.09	
	Terminal single support	0.83	0.30	0.11	< 0.01

Abbreviation: SD, standard deviation.
*Reference for normal gait parameters found in the literature.

Cho et al.,[19] which may signify a compensatory mechanism to minimize the effects of decreased hip RoM in gait. When comparing groups of patients with ONFH, those with unilateral disease have isolated increased mean pelvic rotation, whereas those with bilateral hips affection have an increase in both mean pelvic obliquity and mean pelvic rotation.

In another study,[19] hip mean flexion and RoM were greater in patients with ONFH, as well as in healthy participants.[15,20] Our study found significantly greater mean hip extension, abduction, and adduction, although, for the latter two, the RoM was smaller than in the unaffected hips in other studies; however, for abduction RoM, that was insignificant.[15] As for rotation, our study found greater mean internal and external rotation in patients than those observed by Otayek et al.[15] in unaffected individuals, but similar values to those observed by Cho et al.[19] in other participants with ONFH and in a healthy control group. Limited hip motion is often associated with ONFH, particularly after femoral head collapse and initially for internal rotation. Although the evaluated group in the present study comprised most patients with an advanced degenerative disease, which could limit RoM on its own, limited hip angular values might also arise from patient pain.[4]

Knee mean flexion and range were slightly reduced when compared with kinematics in physically fit participants. Ankle dorsiflexion and plantarflexion were also slightly decreased; however, it is insignificant for ankle dorsiflexion RoM.[15,20] As reported by Bejek et al.,[21] when evaluating participants with OA, increased pelvic movement and reduced knee joint motion could mean an adjusting mechanism to maintain overall speed and stride length, as well as to protect the affected hip joint from excess motion and subsequent pain.

In kinetic data, GRFs were evaluated for stance phases of gait. Participants presented with a bimodal aspect of stance. The average impact peak (first peak) neared the BW of the participants, showing little muscle component in generating this reaction force, which is to be expected. The average active peak (second peak) was above BW at a 1.24 Nm/BW, translating to push-off during gait. The detected values were significantly similar to those found by Nilsson et al. during walking at slow speed in healthy participants, indicating effective muscle activity during push-off.[16] There was no significant difference in medial-lateral GRF in comparison with normal hips. Braking and propulsive GRF translate to the anteroposterior component obtained from the force plates. The braking and propulsive second peaks were significantly smaller than the value observed in healthy individuals.[16] These values may be a consequence of the slower gait speed observed, since propulsive force is in direct proportion to gait velocity and is consistent with a tendency of preserving the hip joint.

The hip joint moment was analyzed in all affected hips. Flexion moments in loading response and terminal swing, as well as abduction moments for all single support phases, were smaller than those found by Cho et al. in other participants with ONFH.[19] As previously mentioned, this may be due to the higher severity of the evaluated cases in the present study, although the gravity classifications are not disclosed in the aforementioned article, neither are the normalization methods. Regarding healthy participants, all data were smaller for flexion moment. There was no significant difference in maximum extension moment, which occurs during terminal stance, from that found by Moisio et al.[17] There is a significant muscle weakness for flexion, particularly the rectus femoris and the iliacus, which participate most actively during gait, especially in loading response and swing phases.[22] In contrast, the hip extension moment is quite similar to the ONFH group evaluated by Cho et al.,[19] but it was slightly decreased when compared with healthy individuals.[17] Regarding abduction moment, which was higher than what was found by Moisio et al.,[17] the present study shows a good function for the gluteus medius, which acts during the initial single support phases of gait.[22] In contrast, adduction moment was significantly reduced when compared with normal hip motion.[17] A stronger abduction strength may arise in patients with ONFH from the necessity to stabilize the pelvis during gait, since it is apparent that pelvic motion may be one of the main compensatory mechanisms in ONFH gait.

Conclusion

Overall, ONFH participants showed significantly slower time-distance parameters in comparison with healthy individuals. In angular kinematics, joint angles are generally decreased for ONFH hip mean and RoM; compensatory mechanisms appeared to be present. There was an increased

pelvic movement for both obliquity and rotation, and decreased knee flexion, which appeared to decrease hip motion and reduce pain in order to maintain spatiotemporal parameters. The observed GRFs were compatible with a bimodal vertical GRF in healthy participants. Braking and propulsive forces were significantly smaller and might be related to a slower walking speed. In the present study, the patients were found to have increased muscle weakness for hip flexor and adductor muscles; however, increased abduction strength in single support phases was observed when compared with unaffected participants.

The present study focused primarily on patients with ONFH post femoral head collapse and further studies could focus on a more varied group of disease stages. Future studies could also evaluate gait parameters before and after nonoperative and operative treatments.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Pipkin Type-II Femoral Head Fracture: A Biomechanical Evaluation by the Finite-Element Method*

Fratura da cabeça femoral de tipo II de Pipkin: Avaliação biomecânica pelo método de elementos finitos

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Abstract

Objective To evaluate the biomechanical capacity of two forms of fixation for Pipkin type-II fractures, describing the vertical fracture deviation, the maximum and minimum principal stresses, and the Von Mises equivalent stress in the syntheses used.

Materials and Methods Two internal fasteners were developed to treat Pipkin type-II fractures through finite elements: a 3.5-mm cortical screw and a Herbert screw. Under the same conditions, the vertical fracture deviation, the maximum and minimum principal stresses, and the Von Mises equivalent stress in the syntheses used were evaluated.

Results The vertical displacements evaluated were of 1.5 mm and 0.5 mm. The maximum principal stress values obtained in the upper region of the femoral neck were of 9.7 KPa and 1.3 Kpa, and the minimum principal stress values obtained in the lower region of the femoral neck were of -8.7 KPa and -9.3 KPa. Finally, the peak values for Von Mises stress were of 7.2 GPa and 2.0 GPa for the fixation models with the use of the 3.5-mm cortical screw and the Herbert screw respectively.

Keywords
- femoral head
- hip fractures
- bone screws

* *Work developed at Instituto de Pesquisa e Ensino, Hospital Ortopédico e Medicina Especializada (IPE-HOME), Brasília, Distrito Federal, Brazil.*

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Conclusion The fixation system with the Herbert screw generated the best results in terms of reduction of vertical displacement, distribution of the maximum principal stress, and the peak Von Mises equivalent stress, demonstrating mechanical superiority compared to that of the 3.5-mm cortical screw in the treatment of Pipkin type-II fractures.

Resumo

Objetivo Avaliar a capacidade biomecânica de duas formas de fixação de fraturas tipo II de Pipkin descrevendo o desvio da fratura no sentido vertical, as tensões máxima e mínima principais, e a tensão equivalente de Von Mises nas sínteses utilizadas.

Materiais e Métodos Dois fixadores internos foram desenvolvidos para tratar a fratura tipo II de Pipkin por meio de elementos finitos: parafuso cortical de 3,5 mm e parafuso de Herbert. Sob as mesmas condições, foram avaliados o desvio da fratura no sentido vertical, as tensões máxima e mínima principais, e a tensão equivalente de Von Mises nas sínteses utilizadas.

Resultados Os deslocamentos verticais avaliados foram de 1,5 mm e 0,5 mm. Os valores de tensão máxima obtidos na região superior do colo femoral foram de 9,7 KPa e 1,3 KPa, e os valores de tensão mínima obtidos na região inferior do colo femoral foram de -8,7KPa e -9,3 KPa. Por fim, os valores de pico da tensão equivalente de Von Mises foram de 7,2 GPa e 2,0 GPa para os modelos de fixação com o uso do parafuso cortical de 3,5 mm e do parafuso de Herbert, respectivamente.

Conclusão O sistema de fixação com parafuso de Herbert gerou os melhores resultados em termos de redução do deslocamento vertical, distribuição da tensão máxima e do pico da tensão equivalente de Von Mises, o que demonstra sua superioridade mecânica comparada à do parafuso cortical de 3,5 mm no tratamento da fratura tipo II de Pipkin.

Palavras-chave
- cabeça do fêmur
- fraturas do quadril
- parafusos ósseos

Introduction

Despite their rare incidence (ranging from 8% to 26%) compared to that of other proximal or articular hip lesions, femoral head fractures, described in 1869,[1] have great clinical and scientific importance due to their surgical complexity and predisposition to the development of severe dysfunctions.[2] With an etiology linked to automobile accidents with high energy impact, they are usually accompanied by posterior hip displacements (ranging from 5% to 15%).[3,4] The conservative approach to treatment does not present good results, so open reduction and internal fixation is the main recommendation.[3,5] Surgical planning is dependent on the severity of the lesion, and it is initially guided by the Pipkin classification (from types I to IV)[1–6] (►**Fig. 1**).[7]

Type-II lesions present great controversy regarding approach and fixation models, with little scientific research.[2,3,8–11] Previous studies (case reports and retrospective analyses) show favorable results with the use of cortical screws of minifragment (measuring between 2.0 mm and 2.4 mm)[9] and Herbert screws.[8,10] On the other hand, despite their differentiated compression capacity compared to that of other syntheses and their wide clinical use, 3-mm canulated screws have been associated with a greater predisposition to develop osteoarthritis.[12]

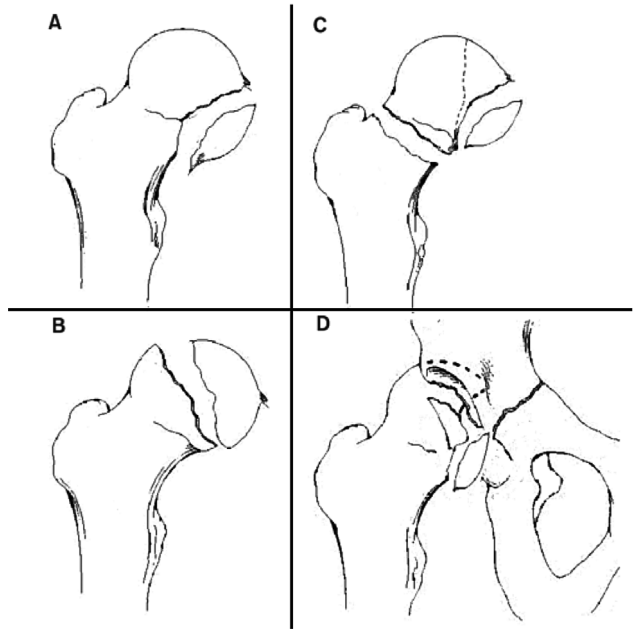


Fig. 1 The Pipkin classification. (**A**) Type I: fracture of the femoral head inferior to the central fovea. (**B**) Type II: fracture extended superiorly to the central fovea. (**C**) Type III: any fracture of the femoral head with associated femoral neck fracture. (**D**) Type IV: any fracture of the femoral head with associated acetabular fracture.[7]

The scientific foundation for the direction and surgical clinical planning of Pipkin type-II fractures is composed of case reports and longitudinal studies. The lack of mechanical tests based on validated methodologies makes it difficult to practice a solid evidence-based medicine, a tangible fact due to its low frequency. As far as we know, the biomechanical investigation of the treatment of Pipkin type-II fractures through the finite-element method (FEM) has so far been neglected. The possibility of performing complex biomechanical studies that enable the visualization of the mechanical performance of the synthesis and fracture under analysis demonstrates the potential and explains the use of the FEM.[13,14]

Thus, we aimed to evaluate the biomechanical ability of two forms of fixation of Pipkin type-II fractures (3.5 mm cortical screw and Herbert screw), describing the vertical fracture deviation, the maximum and minimum principal stresses, and the Von Mises equivalent stress in the syntheses used. The present is the first FEM biomechanical report comparing two treatments for Pipkin type-II fractures.

Materials and Methods

Dimensional Characteristics and Bolt Insertion Technique

The Herbert screw was formatted with a larger diameter of its threads, of 4.3 mm and 5.3 mm, distal and proximal respectively, and 3.3 mm in diameter in its body (threadless area). The 3.5-mm cortical screw, on the other hand, carefully respected the dimensional similarities for each structural part, sold by Depuy-Synthes (Raynham, MA, United States) (►**Figs. 2C** and **D**).

Analysis though the Finite-Element Method (FEM)

Tomographic images of a medium-sized synthetic femur (Sawbones, Vashon Island, WA, United States, fourth generation, model 3403-103, of 10 pounds per cubic foot (PCF) on the left side were used for the analyses.

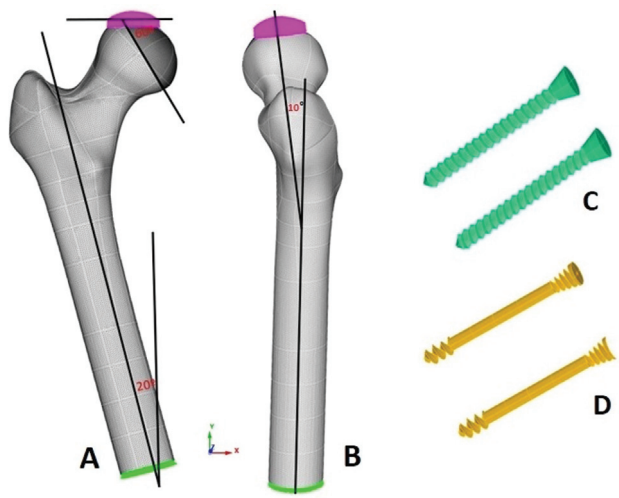


Fig. 2 Conditions and contours of the tests. (**A**) Frontal view. (**B**) Lateral view of a model representing a Pipkin type-II femoral head fracture and the position during the essay. Green area at the base of the femur: fixation point. Pink area on the femoral head: loading area. (**C**) 3.5-mm cortical screw. (**D**) Herbert screw.

In the study through the FEM, the materials used are divided according to their characteristics into ductile and non-ductile. Metallic materials, for example, the synthesis, belong to the ductile group, and their tension is measured by Von Mises equivalent stress test. However, the von Mises equivalent stress is not used in bone analysis, since bones belong to the non-ductile group of materials, and the maximum and minimum principal stresses are more suited for their evaluation.

We will now describe in detail the variables for the analysis of the von Mises equivalent stress and of the maximum and minimum principal stresses.

Von Mises equivalent stress: the stress of materials with metallic characteristics is measured by the Von Mises equivalent stress test, which consists of a magnitude proportional to the distortion energy used in failure tests of ductile materials in which the failure of the material is predicted, regardless of the stress/strain status, which means that the traction and compression stresses are considered equal and treated in the same way.

Maximum principal stress: for the analysis of the maximum principal stress, there is the traction force composed of load that corresponds to pulling the solid, and this type of forces presents positive values, so the traction force is composed of a load that intends to stretch or extend the solid.

Minimum principal stress: for the analysis of the minimum principal stress, the compression force is composed of load that corresponds to compressing the solid, and this type of force is conceptually represented by negative values, just to inform the opposite direction of its application in relation to the maximum principal stress.

Developing the Biocad

The three-dimensional (3D) virtual models of each system (bone, synthesis) were developed using the Rhinoceros (Robert McNeel & Associates, Seattle, WA, United States) software, version 6, and the FEM analysis was performed in the Altair SimLab (HyperWorks, Troy, MI, United States) software using the Altair Optistruct solver.

Based on the models of synthetic bones, tomographic images of the bone were obtained and saved following in the Digital Imaging and Communications in Medicine (DICOM) protocol. We used the 16-channel Emotion tomograph (Siemens Healthineers, Erlangen, Germany) with a resolution of 512 × 512 and a distance of 1.0 mm between cuts. The DICOM file was imported to the InVesalius (Software livre do Centro de Tecnologia da Informação Renato Archer, Campinas, SP, Brasil) software for the 3D reconstruction of the anatomical structure. Based on a set of two-dimensional imagesd obtained through computed tomography equipment, the software enables the development of 3D virtual models of the regions of interest of the system imported there (►**Fig. 2**). After the 3D reconstruction of the DICOM images, the software enables the creation of 3D files in the format called stereo lithography or standard triangle language (STL).

File Conversion

In the InVesalius software, all the slices were imported to obtain the STL file with the images that would be used in the process of obtaining the 3D solid, and with this there is the option of multiplanar generation that shows the sagittal, coronal, and axial views, and the volume. The development of the 3D surface is based on the volume, in which one may select the regions of interest using masks and/or filters, which cause the file to be hidden or portrayed according to the algorithm in question, thus generating the 3D surface.

Simulation

The FEM was used for the simulations of the stability of the different assemblies. First, the files were imported to the Altair Simlab software, with the identification of each part of the digital models.

Material Properties

To perform the simulations, one must know and define the properties of the materials of each part of the digital models, which are the cortical bone, the trabecular bone, and the steel alloy. The properties of the materials used for the simulations are the modulus of elasticity and the Poisson coefficient (►**Table 1**).

Boundary Conditions

To define the boundary conditions, a load of 6,000 N was applied to the upper region of the femoral head in the direction of the Z axis. No load was applied to the X and Y axis. Loading was performed with the positioning of 20° of posterior inclination and 0° in the axial axis, maintaining the physiological 10° of anteversion of the femoral neck. Subsequently, the movement restriction regions (fixed) were delimited, marked in all directions of the X, Y, and Z axes, of displacement and rotation. These restrictions are to ensure that the system has a perfect alignment without displacement and/or rotation (►**Figs. 2A** and **B**).

After the control of the meshes of each part, care should always be taken to preserve the size of the element, so that there are no contact issues between different parts (femur and synthesis) in the simulations. The element adopted for mesh formation was tetrahedral. The number of nodes was also established.

Table 1 Properties of the materials used in the present study

Material	Properties	
	Modulus of Elasticity and (MPa)	Poisson coefficient (v)
Cortical bone	17	0.26
Trabecular bone	1.7	0.26
Syntheses (steel)	193	0.33

Source: Markus, AT, Miguel LFF. Simulation of human humerus fracture using the discrete elements method. Computational Mechanics 2008;45:3411-3422.

Analysis Criteria

The displacement of the models and the specific displacement of each fragment were analyzed through the FEM. For the analysis of the stress in the non-ductile materials (bone and fracture), we used the variables maximum principal stress (traction) and minimum principal stress (compression). For the ductile (metallic) materials, the stress analyzed was the Von Mises equivalent stress.

The variables maximum and minimum principal stresses and Von Mises equivalent stress are principles of matter presented in the form of tension. The unit of measurement for stress is the Pascal (Pa), and the stress forces are measured in megapascals (MPA) and gigapascals (GPa).

The results were expressed as absolute values and percentiles through following the equation: higher value $\times$ X = lower value $\times$ 100 (simple rule of 3), and the final percentile value equals 100–X.

Results

Description of the Vertical Fracture Displacement in the Different Fixation Models

The vertical displacements evaluated were of 1.5 mm and 0.5 mm for the fixation models using the 3.5-mm cortical screw and Herbert screw respectively (►**Fig. 3**).

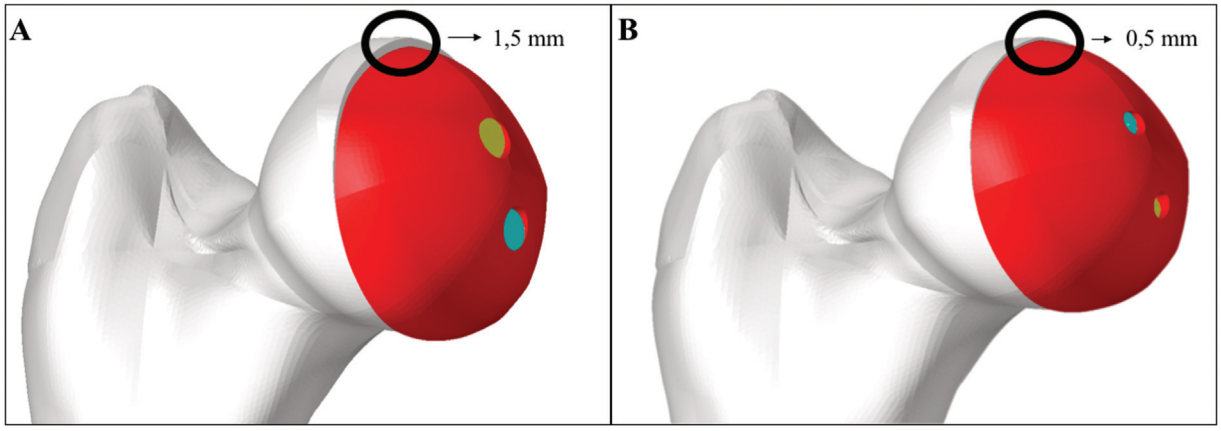


Fig. 3 Description of the vertical displacement of the fracture with the different fixation models. (**A**) 3.5-mm cortical screw (displacement: 1.5 mm). (**B**) Herbert screw (displacement: 0.5 mm).

We observed that the Herbert screw reduced the vertical displacement at a rate of ~ 66.6% in Pipkin type-II femoral head fractures.

Distribution of Maximum (Traction) and Minimum (Compression) Principal Stresses in Fractures in the Different Fixation Models

The values for the maximum principal stress obtained in the upper region of the femoral neck, adjacent to the fracture, were of 9.7 KPa and 1.3 KPa for the fixation models with the use of the 3.5-mm cortical screw and Herbert screw respectively (►**Figs. 4A** and **B**), representing a reduction of 87% in the local tension and a better distribution with the use of Herbert screw.

The values for the minimum principal stress obtained in the lower region of the femoral neck, adjacent to the fracture, were of -8.7 KPa and -9.3 KPa for the fixation models with the use of the 3.5-mm cortical screw and Herbert screw respectively (►**Figs. 4C** and **D**), representing an increase of 6.4% in the local tension with comparable distribution using the Herbert screw.

Distribution of the Peak Von Mises Equivalent Stress in the Different Fixation Models

The peak values for the Von Mises equivalent stress were of 7.2 GPa and 2.0 Gpa for the fixation models with the use the 3.5-mm cortical screw and Herbert screw respectively. The reduction observed with the Herbert screw was of approximately 72.2%. Moreover, the synthesis models presented their largest area of tension in the fracture line, a site that represents a greater concern in the synthesis fracture (►**Fig. 5**).

Discussion

Fractures of the femoral head have historically been associated with controversial results that depend on the synthesis used. Internal fixation must ensure stability, preferably with compression between the fracture fragment and the rest of the femoral head.[3] Because it is a rare fracture, experimental or computational mechanical essays are extremely important, for they provide data that assist in the outcomes of the patients. The FEM has been proven to be an efficient methodology for biomechanical research in the field of bone fractures.[14,15]

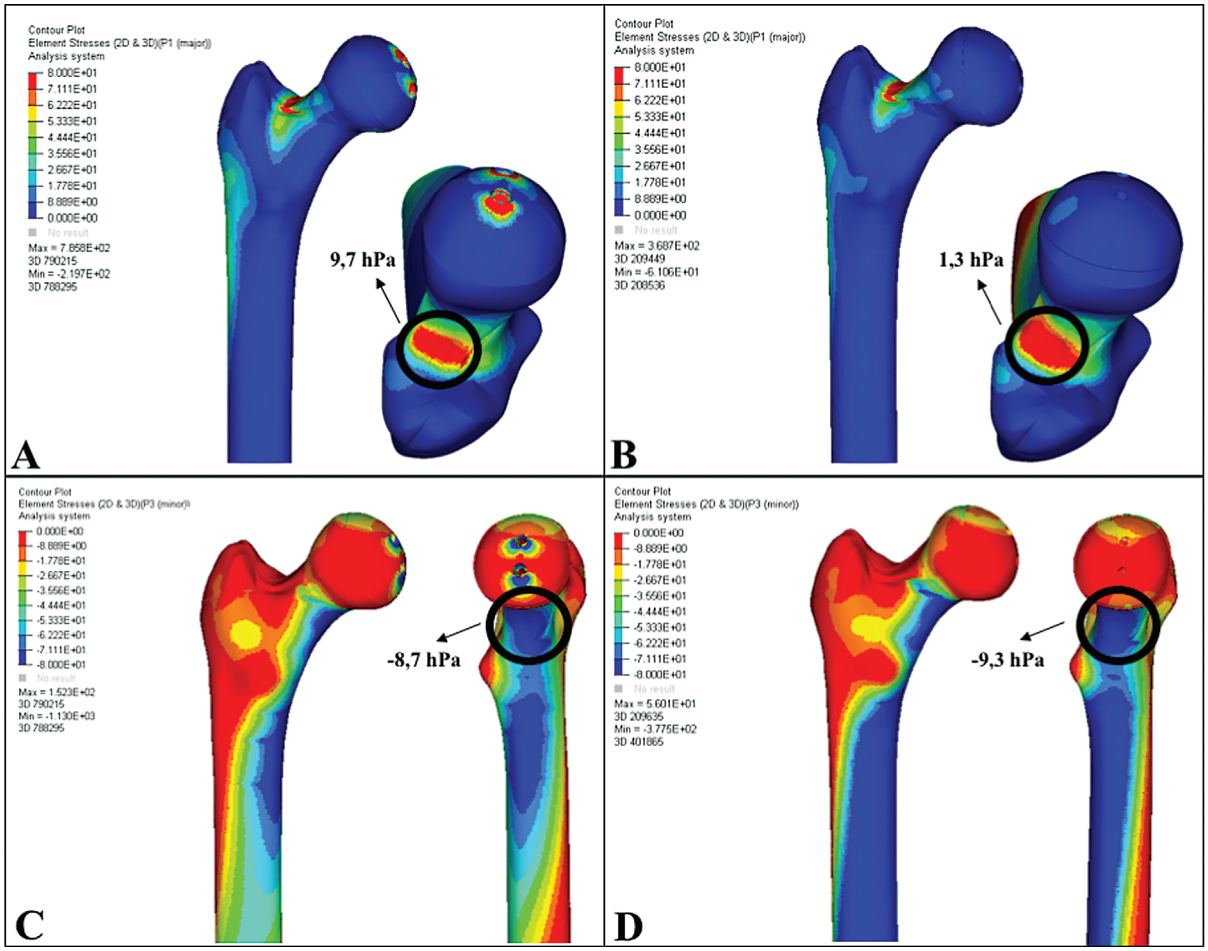


Fig. 4 Distribution of the maximum principal stress in fractures with the different fixation models. (**A**) 3.5-mm cortical screw: 9.7 KPa. (**B**) Herbert screw: 1.3 KPa. Distribution of the minimum principal stress in fractures with the different fixation models. (**C**) 3.5-mm cortical screw: -8.7 KPa. (**D**) Herbert screw: -9.3 KPa.

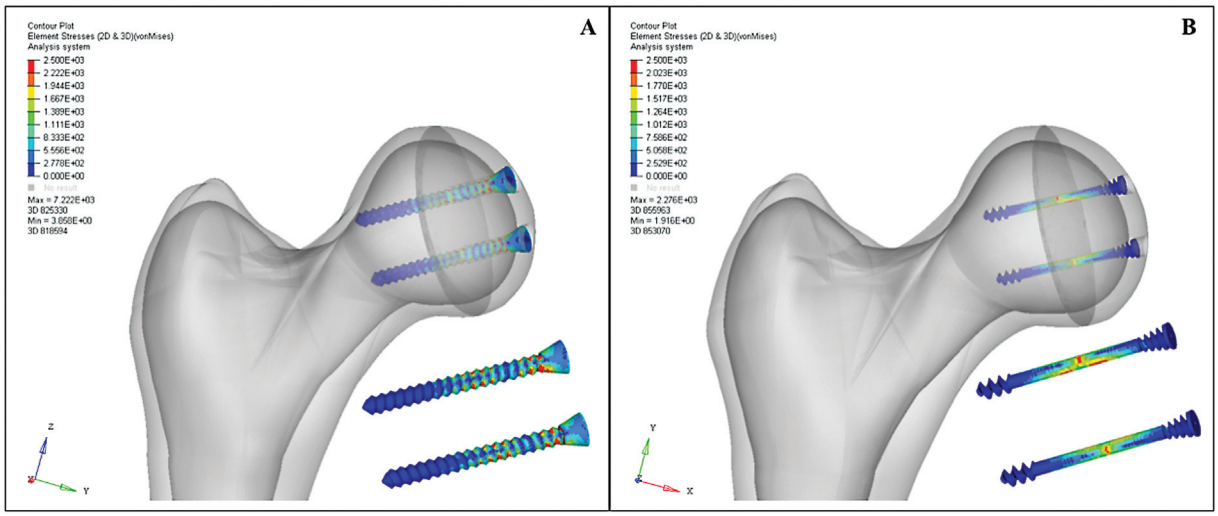


Fig. 5 Distribution of the peak Von Mises equivalent stress in the different fixation models. (**A**) 3.5-mm cortical screw: 7.2GPa. (**B**) Herbert screw: 2.0 GPa.

Thus, through the FEM, we evaluated the vertical dsplacement of the fracture, the maximum and minimum principal stresses, and the Von Mises equivalent stress of 2 syntheses (3.5-mm cortical screw and Herbert screw) widely used in the treatment of Pipkin type-II fractures. As far as we know, the present is the first FEM model in Pipkin type-II fractures, and the first study comparing treatments using biomechanical methods. Our results show the superiority of the Herbert screw, which causes a reduction decrease in the vertical displacement and the distribution of the maximum principal stress and the peak of the Von Mises equivalent stress.

The search for syntheses that promote adequate internal fixation, enabling early mobilization and thus contributing to good clinical results was the focus of previous clinical research, which pointed in the same direction as the biomechanical results of the present study, demonstrating the positive effects of the Herbert screw on Pipkin type-II fractures. In 1988, Murray et al.[10] performed open reduction and internal fixation with the Herbert screw in an osteochondral fracture of the femoral head. After twelve months, the results showed an excellent hip function and no radiographic evidence of avascular necrosis. More recently, Zaizi et al.[8] reported good results with the treatment of Pipkin type-II fractures using anatomical reduction and internal fixation by means of two Herbert screws, after two years of follow-up. Wang et al.,[11] in a prospective analysis of three patients treated using Herbert screws, reported results of satisfactory hip function assessed by the modified Merle d'Aubigné score.

Despite the numerous clinical difficulties regarding the treatment of fractures in load-bearing joints, the possibility of compression inherent to the characteristic of the differences in the threads (distal and proximal) of the Herbert screw, and that for this it needs to have a larger diameter in relation to the 3.5-mm screw, we were able to experimentally confirm its biomechanical advantage.[10] Furthermore, our results suggest that the ability to distribute stress and decrease fracture dislocation are relevant factors to understand the mechanical effectiveness of the Herbert screw. One of the indirect objectives of the present study was to qualitatively analyze the close relationship between synthesis material and bone structure using the interfragment compression technique. The close contact of the Herbert screw due to the lack of need for a smooth tunnel in its technique (unlike the 3.5-mm screw) seems to be a hypothesis for its better biomechanical results, and it may also make a difference in terms of fracture stability in the reabsorption phase of the fractured edges. Future studies need to improve the methodology to perform a more accurate evaluation and determination of this clinical hypothesis (►**Fig. 6**).

The present is the first study to use the FEM to compare different fixation methods, analyzing complex biomechanical variables (peak Von Mises equivalent stress and compression and traction distribution in fractures) in Pipkin type-II fractures. The present study has certain limitations that should be highlighted. The lack of effects of muscle and ligament on fracture stability, bone quality and possible individual differences in terms of gender, ethnicity, age, and previous diseases were not taken into account during the analyses. These limitations should be evaluated in future clinical manuscripts.

Conclusion

The fixation system with the Herbert screw yielded the best results in terms of reduction of the vertical displacement, distribution of the maximum principal stress and peak Von Mises equivalent stress, demonstrating its mechanical superiority compared to the 3.5-mm cortical screw in the treatment of Pipkin type-II fractures.

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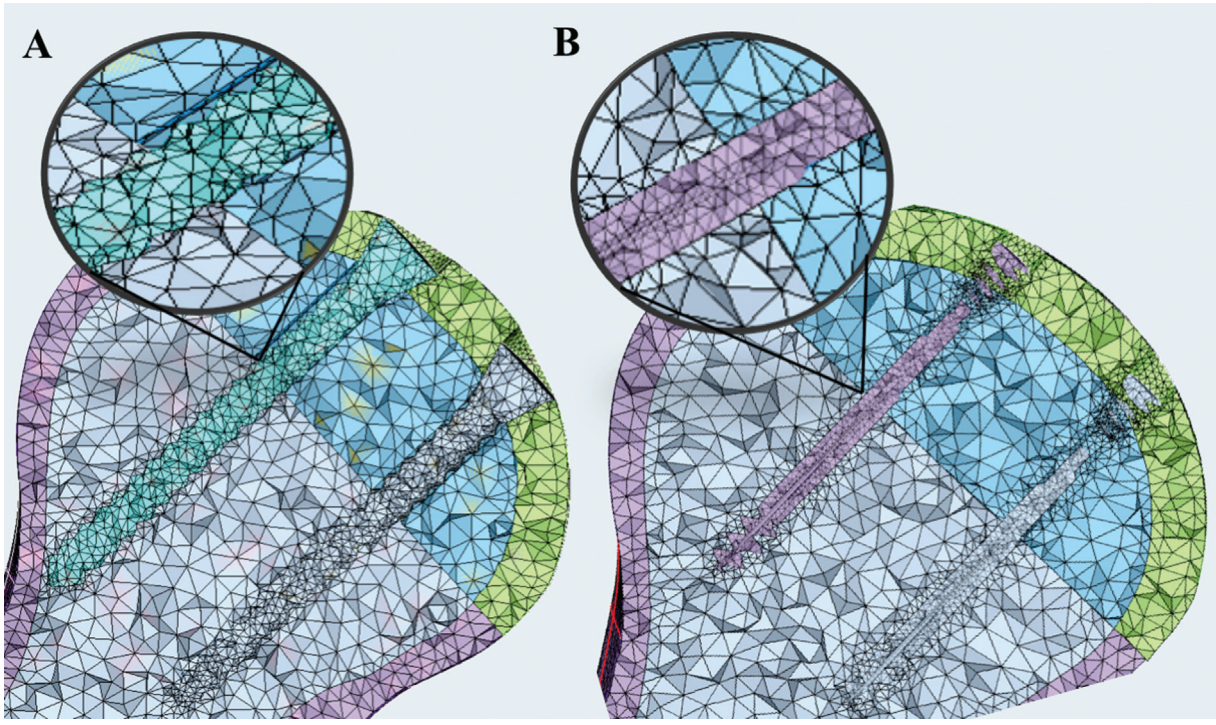


Fig. 6 Qualitative analysis of the relationship between synthesis material and bone structure. (**A**) close relationship between the Herbert screw and bone structure. (**B**) The need for a smooth tunnel in the interfragment compression technique with the 3.5-mm cortical screw does not yield the same degree of relationship observed between synthesis and bone structure with the Herbert screw.

Conflict of Interests
The authors have no conflict of interests to declare.

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Perception of Patients on the Waiting List for Total Hip Arthroplasty on the Resumption of Elective Surgeries during the COVID-19 Pandemic

Percepção dos pacientes em lista de espera para artroplastia total do quadril sobre a retomada das cirurgias eletivas durante a pandemia COVID-19

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Abstract

Objective To analyze the profile and perception of patients on the waiting list for total hip arthroplasty (THA) about performing elective surgeries during the COVID-19 pandemic.

Methods From July to November 2021, patients on the THA waiting list were interviewed during outpatient consultations. To compare the groups regarding categorical variables, the Chi-square test or Fisher's exact test was applied, and for quantitative variables the Mann-Whitney test was applied. The results were calculated using the Statistica program version 7.

Results 39 patients answered the questionnaire. The mean age was 58.95 years, with 53.85% male. Approximately 60% expressed concern about contracting or transmitting COVID-19 to their family members after hospitalization for THA. 58.9% of patients felt hampered by the delay in scheduling elective surgeries during the pandemic. 23% lost or had a family member who lost their job during the pandemic, with a statistical difference for the group under 60 years old ($p = 0.04$).

Conclusion Most patients were concerned about becoming infected and exposing family members to COVID-19 after surgery and noted damage due to suspensions and delay in scheduling elective surgeries. The economic impact of the pandemic was revealed by the rate of 23% of respondents who lost or had a family member who lost their job during the pandemic, being higher in patients under 60 years of age ($p = 0.04$).

Keywords

- COVID-19
- elective surgical procedures
- arthroplasty, replacement, hip
- patient perception of surgery

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Resumo

Objetivo Analisar o perfil e a percepção dos pacientes em lista de espera para artroplastia total do quadril (ATQ) sobre a realização das cirurgias eletivas durante a pandemia pela COVID-19.

Métodos De julho a novembro de 2021, foram entrevistados pacientes em lista de espera para ATQ durante consultas ambulatoriais. Para comparar os grupos com relação às variáveis categóricas foi aplicado o Teste Qui-quadrado ou Teste exato de Fisher e para as variáveis quantitativas foi aplicado o teste de Mann-Whitney. Os resultados foram calculados utilizando o programa Statistica versão 7.

Resultados 39 pacientes responderam ao questionário. A média de idade foi de 58,95 anos, sendo 53,85% do sexo masculino. Aproximadamente, 60% manifestaram preocupação em contrair ou transmitir COVID-19 aos seus familiares após internação hospitalar para ATQ. 58,9% dos pacientes sentiram prejudicados pelo atraso no agendamento das cirurgias eletivas durante a pandemia. 23% perderam ou tiveram algum familiar que perdeu o emprego durante a pandemia, havendo diferença estatística para o grupo com menos de 60 anos ($p = 0,04$).

Conclusão A maioria dos pacientes sentiram preocupação em infectar-se e expor familiares à COVID-19 após a cirurgia e notaram prejuízo pelas suspensões e atraso no agendamento de cirurgias eletivas. O impacto econômico da pandemia revelou-se pela taxa de 23% de entrevistados que perderam ou tiveram algum familiar que perdeu seu emprego durante a pandemia, sendo maior nos pacientes menores de 60 anos ($p = 0,04$).

Palavras-chave

- COVID-19
- procedimentos cirúrgicos eletivos
- Artroplastia de quadril
- percepção do paciente sobre a cirurgia

Introduction

Since March 2020, the new coronavirus (COVID-19) pandemic began to interfere with the functioning of the publicly funded health care system – Sistema Único de Saúde (SUS) – in Brazil. With the increase in the occupation of beds in intensive care units, state and municipal governments and public and private health managers have chosen to suspend elective surgeries. This was one of the measures taken to contain transmission, reduce hospitalizations and make beds available for critically ill patients with COVID-19. The economic and social impact of restrictions on elective orthopedic hip surgeries and the perception of patients regarding the resumption of surgeries remain poorly studied in our country.

There is no study in Brazil that estimates the damage resulting from the stoppage of elective surgeries in the country. However, data from the American Hospital Association estimate that, in that country, losses to hospitals and health services could reach the mark of 202 billion dollars.[1] More than half of Americans reported a decrease in income since the pandemic began, and the unemployment rate has risen sharply.[2]

The social impact of suspending surgeries is directly related to the reduction in patients' quality of life. 100 patients awaiting orthopedic surgery, of whom 70 were scheduled for primary arthroplasty or revision arthroplasty of the hip or knee were interviewed at University College London Hospital. Their results indicated that approximately 90% would like to undergo the procedure as soon as possible.[3] This reflects the deterioration in the quality of life of patients living with osteoarthritis of the knee and hip.[4] Among patients on the waiting list for total hip arthroplasty (THA), it was observed that 33% consider their quality of life worse than death, in addition to there being an association between time on the waiting list and loss of quality of life.[5]

The patients' perception of the possibility of resuming activities is an important factor that requires further studies. In the United States, there are data demonstrating that men would be more interested in performing elective surgeries more quickly than women, after the removal of restrictions due to COVID-19. And most respondents are concerned about contracting the virus while hospitalized for surgery, as well as exposing their family members to the virus.[6]

Due to the scarcity of data that may reflect the local reality on the effects of postponing elective surgeries and patients' expectations, this study sought to study the profile of patients on the waiting list for total hip arthroplasty and their perception of the pandemic and the impact it has on their lives.

Material and methods

This study was approved by the Research Ethics Committee of our Institution and inserted in the Brazil Platform (CAAE-47957921.7.0000.0020) and the informed consent form was provided and signed by the research participants.

From July to November 2021, thirty-nine patients on the waiting list for total hip arthroplasty (THA) at a university hospital were assessed using a questionnaire prior to surgery. The questionnaire was applied during an outpatient consultation by a specialist in hip surgery (Appendix 1).

Patients over 18 years of age with an indication for THA were included. Patients awaiting THA surgery due to fracture of the proximal femur were excluded from the study.

The collected data were summarized with the preparation of frequency tables and contingency tables. To compare the groups with regard to categorical variables, the Chi-square test or Fisher's exact test was applied, for quantitative variables the Mann-Whitney test was applied. The results were calculated using the Statistica program version 7.

Results

A total of 39 patients answered the questionnaire. The patients were, on average, 58.95 years old (ranging from 26 to 93 years old), with just over half being male (53.85%). More than 75% of patients had an income of less than three minimum wages per family member. ►**Table 1** represents the demographic profile of the studied sample.

Approximately 60% of patients expressed concern about contracting COVID-19 or exposing their family to the coronavirus after hospitalization for THA. There was no difference between groups by age or sex regarding concern about COVID-19 infection during hospitalization for surgery. The presence of comorbidities also did not influence the responses ($p = 0.29$). There was a statistical difference between the proportion of vaccinated individuals between age groups, being greater in patients over 60 years of age ($p = 0.004$). However, complete vaccination did not confer less concern about COVID-19 infection ($p = 0.24$).

Patients were asked about their perception of the severity of the symptoms they could manifest in case of COVID-19 infection (no symptoms, with mild symptoms, with moderate symptoms without risk of death and moderate with risk of death). More than 70% of respondents believe that if they become infected with COVID-19, they will only experience mild symptoms. Considering patients over 60 years old, the belief that they would only have mild symptoms was 68.75%. There was no significant difference in responses when comparing age groups ($p = 0.45$).

Table 1 Demographic profile of the sample

Characteristics	N	%
Sex		
Male	21	53.85
Female	18	46.15
Age range (years)		
18-39	2	6.02
40-49	6	15.38
50-59	15	38.46
60-69	5	12.82
>70	11	28.21
Civil status		
Married	28	71.79
Single	3	7.69
Widower	5	12.82
Divorced	3	7.69
Race		
White	34	87.18
Black	3	7.69
Brown/Mestizos	2	5.13
Minimum wages per person in the family		
Up to 1	16	41.03
1-3	14	35.90
3-6	4	10.26
6-10	4	10.26
>10	1	2.56
Number of people living in the same household		
1	4	10.26%
2	15	38.46%
3	13	33.33%
4 or more	7	17.95%
Lives with or cares for people over 60		
No	31	81.58%
Yes	7	18.42%
Works or lives with someone who works in essential services		
No	26	66.67%
Yes	13	33.33%
Job loss in the pandemic (patient or family member)		
No	30	76.92%
Yes	9	23.08%
Receive sick pay		
No	29	74.36%
Yes	10	25.64%
Complete immunization for COVID		
No	21	53.85%
Yes	18	46.15%
Comorbidities		
Obesity	12	30.77%
Diabetes Mellitus	11	28.21%
Systemic Arterial Hypertension	26	66.67%
Smoking	5	12.82%
Alcoholism	1	2.56%

Font: Authors' data.

Nearly 75% stated that their pain score is 8 or more and that they had been waiting for total hip replacement surgery for more than 12 months. Approximately 60% of respondents feel harmed by the delay in surgery.

More than 80% of the participants stated that they would feel comfortable with undergoing the surgery within one month, after approval of elective surgeries by the competent bodies.

They were asked which place or situation in the hospital they were most concerned about the risk of being contaminated by COVID-19. More than 60% of the participants stated that admission and the waiting room are the most worrisome environments, with the hospitalization room and post-operative recovery area in second place, contact with the assistant teams in third and, lastly, the operating room.

When asked whether the risk of contamination is higher or lower during hospitalization compared to daily activities, about 40% responded that there is a higher risk in the hospital. The risk was considered lower in the hospital environment for 39% and equal for 21%. There was no significant difference between age groups regarding this proportion ($p = 0.55$).

More than 23% of respondents lost their jobs during the pandemic or had a family member who became unemployed. There was a significant difference between age groups ($p = 0.04$), with younger people (less than 60 years old) presenting significantly more cases of job loss. On the other hand, the younger group benefited from income supplementation through government programs such as sick pay ($p = 0.002$).

More than 85% of respondents would like the first outpatient consultation after surgery to be face-to-face, while the rest would opt for telemedicine. There was no significant difference between the age groups regarding this proportion ($p = 0.28$).

Discussion

The average age of the studied population, 58.95 years, was within the expected range, considering the prevalence of coxarthrosis in the adult population. The hypotheses that the presence of more comorbidities, incomplete vaccination for COVID-19, higher age group and female gender would be associated with greater fear of contracting COVID-19 when hospitalized for total hip arthroplasty was not confirmed after statistical analysis.

Females were more concerned about the risk of COVID-19 infection (64.71% versus 52.38% of males) and 58.82% of females were afraid of exposing their family members to the COVID-19 virus after the hospitalization. Although we did not find statistical significance for this difference between genders in our population, the findings confirm the results of another study in which this concern is more prevalent in women.[6] The average of patients who are concerned about contracting COVID-19 during hospitalization (57.9%) is similar to data from surveys carried out in other countries, where the rate was 61% and 53%.[3,6,7]

It was expected that patients over 60 years of age would be more concerned about contracting COVID-19 or fear of developing more severe symptoms due to general knowledge about the epidemiology of the disease. However, there was no significant difference in responses when comparing the age groups ($p = 0.45$). 68.75% of the elderly believe that if they were infected, they would evolve with the mild form of the disease, which did not differ significantly from respondents aged less than 60 years (72.73%).

There was no statistically significant difference when patients answered whether they considered the hospital a place with a higher risk of exposure and contamination to COVID-19 when compared to daily activities. This finding may reflect the diversity of the population's exposure level, considering that patients who are more restricted to the home environment, who do not use public transport or do not work outside the home, would be less exposed. On the other hand, patients with a routine of more contact with other people at work, with neighbors, family members would be more likely to become infected and considered the hospital to be safer. Assessing this perception of patients was important because in periods when the government is free to perform the procedure, most patients who canceled their surgery mentioned concerns about contracting COVID-19 as the main reason. Therefore, patients who consider the hospital as a place with a higher risk of transmitting COVID-19 are subject to canceling their surgeries.[7]

Most patients (58.9%) felt that the delay in having their total hip arthroplasty surgery had been delayed. This finding reinforces the loss of quality of life that patients with hip arthrosis suffer.[4]

Ho et al.[7] found an association between patients' agreement to undergo elective orthopedic surgery and the perception that their situation was serious or getting worse. In our study, we did not find an association between greater pain intensity and the prevalence of agreeing to undergo surgery in less than 30 days after the application of the questionnaire. Considering that trust in hospitals and in the health system is a necessary factor to undergo elective surgery,[7] it is possible that the caution in waiting more than 30 days for the procedure was due to the understanding that the collapse of public health, in the country, did not provide the ideal time for hospitalization. During the study, the country suffered from a lack of infirmary and intensive care beds in public and private hospitals.

After the first wave of COVID-19 in England, the desire of patients to have their total hip replacement performed during the pandemic was evaluated. 94.7% of patients wanted to undergo surgery as soon as possible.[3] On the other hand, our study showed that 81.58% of patients wanted to undergo surgery in less than 30 days. The difference found can be explained by several factors. The questionnaires applied in our study were initially applied when there was still a ban on elective surgeries due to the large number of new cases, deaths and hospitalizations due to COVID-19 in the country. It is also possible that the difference is due to the fact that we do not have the same perioperative care protocol that could reduce intra-hospital contamination, such as the requirement of negative PCR tests for COVID-19 and preoperative isolation lasting 14 days; in addition to not informing that the hospital was being considered a "COVID-free zone",

in which suspected or confirmed cases of COVID-19 were not seen or treated.

At our institution, patients undergoing hip arthroplasty are hospitalized and most are discharged on the second postoperative day. In other services there is the possibility of hospital discharge within 24 hours. It is possible to suggest that the estimate of staying longer in the hospital, where there may be patients hospitalized for COVID-19, in the postoperative period may negatively influence the desire to operate as soon as possible due to the fear of being contaminated or becoming ill during hospitalization.

In the second and third quarters of 2021, unemployment in Brazil reached rates of 14.9 and 14.2%, according to data from the Brazilian Institute of Geography and Statistics (IBGE).[8] The economic impact was mainly reflected in the 23.08% of patients who lost their jobs or family members during the pandemic, especially for the group under 60 years old ($p = 0.04$).

Despite the fear of contracting COVID-19, 85% of patients would like the first postoperative consultation to be face-to-face instead of telemedicine. The data may be related to the difficulty of accessing the internet and lack of the ability to make effective use of electronic devices. Even if there were no such difficulties, it is possible that the desire to have the physical examination, assessment of the surgical wound and removal of stitches performed in the first postoperative consultation led most to prefer a face-to-face consultation.

Conclusion

The study evaluated the perception of patients on the waiting list for total hip arthroplasty during the COVID-19 pandemic. Most patients felt hampered by cancellations and delays of elective surgeries and concerns about becoming infected or exposing family members to COVID-19 after surgery. The economic impact of the pandemic was revealed by the rate of 23% of respondents who lost or had a family member who lost their jobs during the pandemic, being higher in patients younger than 60 years ($p = 0.04$).

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Conflict of interests
The authors declare no conflict of interest.

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Appendix 1–Questionnaire: Perception of patients on the waiting list for elective surgeries at the University Hospital Cajuru

Name:
Age:
How old are you?
a) between 18 and 30 years old
b) between 30 and 39 years old
c) between 40 and 49 years old
d) between 50 and 59 years old
e) between 60 and 69 years old
f) 70 year old or more

Sex:
a) Male
b) Female
c) Prefer not to answer

In which health macro-region do you live in the State of Paraná?
a) East (includes the metropolitan region of Curitiba and Paranaguá)
b) Campos Gerais (includes Ponta Grossa, Irati, União da Vitória, Telêmaco Borba)
c) Center-South (includes Guarapuava and Pato Branco)
d) West (includes Francisco Beltrão, Foz do Iguaçu, Cascavel, Toledo
e) Northwest (includes Campo Mourão, Umuarama, Cianorte, Paranavaí, Maringá)
f) North (Apucarana, Londrina, Cornélio Procópio, Jacarezinho, Ivaiporã)
g) Another state

What is your Civil Status?
a) Single
b) Married
c) Divorced
d) Widowed

What ethnic group do you identify with?
a) White
b) Black
c) Yellow
d) Indigenous
e) Brown/Mestizo

Adding your income with the income of the people who live with you, what is, approximately, the monthly family income per person?
a) Up to 1 minimum wage (up to R$ 1100.00)
b) From 1 to 3 minimum wages (from R$ 1100.01 to R$ 3300.00)
c) From 3 to 6 minimum wages (from R$ 3300.01 to R$ 6600.00)
d) From 6 to 10 minimum wages (from R$ 6600.01 to 11000.10)
e) More than 10 minimum wages (above BRL 11,000.10)

Is the main source of family income due to your work?
a) Yes
b) No

How many people live in the same household as you?
a) I live alone
b) 2
c) 3
d) 4 or more

Do you live with or care for people over 60?
a) Yes
b) No

Do you or someone who lives with you work in services considered essential?
a) Yes
b) No

Have you or anyone in your family lost their job during the pandemic?
a) Yes
b) No

Do you receive sick pay?
a) Yes
b) No

Are you immunized for COVID with the vaccine (at least three weeks after the second dose of vaccine for two-dose vaccines)?
a) Yes
b) No

How often do you need someone to help you read or interpret your doctor's instructions, pamphlets, or other written materials?
a) Never
b) Rarely
c) Sometimes
d) Most of the time
e) Always

In general, would you say your health is:
a) Excellent
b) Very good
c) Good
d) Bad
e) Very bad

Check below if you have any of the health problems listed below (more than one answer can be ticked):
a) Systemic Arterial Hypertension (High Blood Pressure)
b) Diabetes mellitus
c) Smoking
d) Alcoholism
e) Obesity (body mass index greater than 30)

Which surgery are you waiting for
a) Total hip arthroplasty
b) Revision of total hip arthroplasty

Do you have an indication for surgery on one side only or on both hips?
a) One side only
b) On both sides

From zero to 10, with zero being no pain and 10 being excessive pain, what grade would you give to your pain?
How do you feel about the delay of your surgery?
a) Very impaired
b) Slightly impaired
c) I do not feel harmed or benefited
d) Little benefited
e) Much benefited

How long have you been waiting to perform the surgery?
a) Less than 6 months
b) Between 6 months and 1 year
c) Between 1 and 2 years
d) More than 2 years

The surgery will be performed by:
a) Sistema único de saúde (SUS) – publicly funded health care system
b) Health plan
c) Private

How worried are you about getting infected by the coronavirus?
a) I'm not worried
b) Very little worried
c) I'm a little worried
d) I am very worried

How concerned are you about the risk of exposing your family to COVID-19 after your surgery?
a) I'm not worried
b) Very little worried
c) I'm a little worried
d) I am very worried

The biggest concern of contracting COVID-19 is due to (choose one answer):
a) Yourself
b) Your spouse
c) Family
d) I do not feel worried about contracting COVID-19

Do you believe that if you have COVID-19 infection you will have serious symptoms?
a) No symptoms
b) Mild symptoms
c) More severe symptoms but without risk of death
d) Severe symptoms at risk of death

Once the resumption of elective surgeries is cleared, when would you feel comfortable undergoing the proposed surgery?
a) 1 month
b) Between 1 and 3 months
c) Between 3 and 6 months
d) More than 6 months

If there was the possibility of having your surgery performed earlier, during the pandemic period, would you hire a health plan or have the surgery privately if you had financial conditions?
a) Yes
b) No
c) Not applicable (my surgery will be by health plan or private)

Even if your surgery is performed via a health plan or private, there may be some delay in authorizing your surgery. Would you be willing to pay an extra fee to have your surgery performed sooner?
a) Yes
b) No
c) Not applicable (my surgery will be done by SUS)

What part of the surgery process are you most concerned about getting COVID-19?
a) Admission and waiting room
b) Operating room

c) Post-surgical recovery area and hospitalization room
d) Contact with the assistant teams

Do you believe that the risk of you contracting Covid 19 in the hospital during hospitalization is?
a) Much higher than in my day-to-day activities
b) A little higher than in my day-to-day activities
c) Same as the risk in my day-to-day activities
d) Less than in my day-to-day activities
e) Much lower than in my day-to-day activities

How would you prefer the first outpatient visit after surgery to be?
a) In person
b) Telemedicine (consultation via video call)

To be filled by the doctor:
If the patient is awaiting primary Total Hip Arthroplasty surgery, what is the classification of arthrosis according to Tonnis?
a) Grade 0–No signs of osteoarthritis
b) Grade I – Increased sclerosis, slight decrease in joint space, without loss/slight loss of sphericity of the femoral head
c) Grade II – Small cysts, moderate decrease in joint space, moderate loss of head sphericity
d) Grade III – Cysts of large dimensions, marked reduction of joint space, marked deformity of the head.

If the patient is waiting for a Hip Arthroplasty Revision surgery, what is the reason for the indication?
a) Periprosthetic fracture
b) Femoral osteolysis
c) Acetabular osteolysis
d) Femoral and acetabular osteolysis
e) Infection
f) Wear of the tribological pair
g) Recurrent dislocation
h) Others

Osseointegration and Success in Hip Arthroplasty Acetabular Revision Using Structured Homologous Graft: Average 9.6 Years Follow-up

Osteointegração e sucesso em revisão acetabular de artroplastia total de quadril com enxerto estrutural homólogo: seguimento médio de 9,6 anos

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Abstract

Objective To evaluate the clinical and radiographic results and survival of the acetabular revision surgery of total hip arthroplasty with cemented implant without the use of reinforcement ring, associated with structural homologous bone grafting.

Methods A total of 40 patients (44 hips) operated from 1995 to 2015 were retrospectively analyzed. Radiographs were evaluated according to the classification of the acetabular bone defect, graft shape, and the presence of osseointegration. Cases were considered as failures when the migration of the implant was >5 mm in any direction, and/or the progression of radiolucency lines around the acetabular component were >2 mm. We verified the association of radiographic findings with cases of failure using statistical tests and analyzed survival using the Kaplan-Meier curve.

Results Of the 44 hips, 45.5% of the acetabular defects were Paprosky type 3A and 50% were 3B. In 65% of the hips, the graft configuration was classified as Prieto type 1 and in 31% as type 2. No radiographic evidence of osseointegration was observed in

Keywords
- arthroplasty, replacement, hip
- grafting bone
- cross-sectional studies
- osseointegration
- transplantation, homologous, reoperation.
- osteointegration

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13.6% of the cases. We observed 9 (20.5%) reconstruction failures. A correlation was observed between reconstruction failure and the absence of radiographic signs of graft osseointegration.

Conclusion We observed good clinic and radiographic results, with survival of 79.54% in a mean follow-up of 9.65 years. Also, there was an association between absence of radiographic signs of osseointegration of the structural graft and failure in this series of patients with large bone defects. The failures did not correlate with the severity of the acetabular bone defect, thickness, or graft configuration.

Resumo

Objetivo Avaliar os resultados clínicos, radiográficos e a sobrevida da cirurgia de revisão acetabular de artroplastia total de quadril com implante cimentado sem uso de anel de reforço, associado à enxertia óssea homóloga estrutural.

Métodos Um total de 40 pacientes (44 quadris) operados de 1995 a 2015 foram analisados retrospectivamente. As radiografias foram avaliadas de acordo com a classificação do defeito ósseo acetabular, o formato do enxerto e à presença de osteointegração. Foram considerados casos de insucesso a migração do implante >5 mm em qualquer direção e/ou a progressão de linhas de radioluscência em torno do componente acetabular >2mm. Verificamos a associação dos achados radiográficos com os casos de falha utilizando testes estatísticos e analisamos a sobrevida utilizando a curva de Kaplan-Meier.

Resultados Dos 44 quadris, 45,5% dos defeitos acetabulares eram Paprosky tipo 3A e 50%, 3B. Em 65% dos quadris, a configuração do enxerto foi classificada como tipo 1 de Prieto e em 31% como tipo 2. Não foi observada evidência radiográfica de osteointegração em 13,6% dos casos. Observamos 9 (20,5%) falhas de reconstrução. Foi observada correlação entre falha da reconstrução com a ausência de sinais radiográficos de osteointegração do enxerto.

Conclusão Observamos bons resultados clínicos e radiográficos, com sobrevida de 79,54% em seguimento médio de 9,65 anos. Também houve associação entre ausência de sinais radiográficos de osteointegração do enxerto estrutural e falha nesta série de pacientes com grandes defeitos ósseos. As falhas não se correlacionaram com a severidade do defeito ósseo acetabular, espessura ou configuração do enxerto.

Palavras-chave
- artroplastia de quadril
- enxerto ósseo
- estudos transversais
- osteointegração
- transplante homólogo
- reoperação

Introduction

Acetabular reconstruction surgery during total hip arthroplasty revision (THAR) is a complex procedure. Loosening of the implant after arthroplasty is one of the most frequent complications in the long term, leading to bone loss.[1] The main objectives of acetabular reconstruction surgery are to obtain implant stability by restoring the hip anatomy with positioning of the component as close as possible to the center of joint rotation.[2]

There are several forms of treatment of large acetabular bone defects in THAR: placement of implant with high hip center of rotation (High Hip Center), use of large diameter implants (Jumbo cup), use of structural homologous bone graft (with or without reinforcement ring), impaction of fragmented homologous bone graft (with or without reinforcement ring), in addition to the use of enlargements in trabecular metal.[3] However, the most appropriate treatment remains undefined.[4,5]

Our service started the use of homologous graft in THAR in the 1980s, with the subsequent publication of the results.[6–8] The analysis of our cases and the result of the literature allows the verification of homologous bone graft consolidation with possible osseointegration in most cases, allowing a stable reconstruction.[2,5] The use of bone graft makes it possible to restore the center of hip rotation, obtain implant stability, restore the acetabular integrity and bone stock, facilitating future revisions.[9] With the stability of the graft in reconstruction, it is possible to provide conditions for revascularization and osseointegration to the host bone.[9] The disadvantages that can be found with this technique are the potential resorption of the graft and the nonunion to the host bone.[10,11]

The aim of the present study is to evaluate the clinical and radiographic results and survival of acetabular reconstruction surgery with cemented implant without the use of reinforcement ring, associated with structural homologous bone grafting.

Materials and Methods

Between January 1995 and August 2015, 318 patients were submitted to THAR by 2 surgeons from the same medical team (Roos B. D. e Roos M. V.). Of these, 71 were submitted to THAR with the use of cemented acetabular implant without reinforcement ring associated with structural homologous bone grafting. Thirty-one patients were excluded due to loss of follow-up, follow-up < 24 months, or for presenting incomplete medical records or exams. Forty patients were analyzed (44 hips) in a retrospective study (►**Table 1**).

The decision to use the technique evaluated in the present study was the preoperative radiographic finding of segmental or combined acetabular bone defects, in addition to large

Table 1 Clinical and demographic characteristics of cases (operated hips)

	Preoperative				Immediate postoperative		Late postoperative period	
#	Gender	Operated side	Age (Years)	ATK type	Date of surgery	Type of revision	Last follow-up (years + months)	Failure
1	Female	Left	40	Cemented	31/01/2007	Cemented	11y + 11m	No
2	Female	Right	46	Hybrid	12/05/2003	Cemented	8y + 4m	No
3	Female	Right	42	Girdlestone	13/11/2002	Cemented	14y + 11m	No
4	Male	Right	43	Cemented	21/02/2003	Cemented	9y + 1m	No
5	Female	Left	77	Cemented	16/07/2001	Cemented	4y + 2m	No
6	Female	Right	47	Not cemented	08/11/2006	Cemented	10y + 10m	No
7	Male	Right	67	Cemented	05/08/2002	Cemented	14y + 6m	No
8	Female	Right	72	Not cemented	17/09/2003	Reverse hybrid	11y + 10m	Yes
9a	Female	Right	64	Spacer	19/09/2005	Cemented	7y + 6m	Yes
10a	Female	Right	72	Cemented	13/05/2013	Cemented	7y + 10m	Yes
11	Female	Right	76	Partial	04/02/1997	Cemented	8y	No
12	Female	Left	57	Not cemented	20/11/2000	Cemented	15y + 4m	No
13	Male	Right	67	Cemented	02/08/2004	Cemented	6y + 1m	No
14	Female	Right	71	Cemented	07/11/2005	Cemented	4y + 9m	No
15b	Male	Right	42	Cemented	17/03/1998	Cemented	16y + 10m	No
16b	Male	Left	51	Cemented	14/05/2007	Cemented	7y + 8m	No
17	Male	Right	69	Not cemented	10/05/2001	Cemented	4y + 4m	No
18	Female	Right	78	Cemented	31/01/1995	Cemented	18y + 9m	No
19	Male	Right	72	Cemented	17/01/2008	Cemented	10y + 11m	Yes
20	Female	Right	43	Not cemented	24/06/2003	Cemented	14y + 2m	No
21	Male	Left	47	Cemented	19/11/1996	Cemented	16y + 7m	No
22	Female	Left	57	Not cemented	13/09/2000	Cemented	14y + 1m	Yes
23	Male	Left	59	Cemented	13/04/1999	Cemented	8y + 10m	No
24	Female	Right	72	Cemented	22/11/2006	Cemented	7y + 7m	No
25	Female	Left	65	Not cemented	06/09/2004	Cemented	4y + 0m	No
26	Female	Left	38	Not cemented	14/03/2003	Cemented	15y + 0m	No
27	Female	Left	62	Not cemented	19/05/2005	Cemented	13y + 8m	No
28c	Female	Right	38	Cemented	27/10/2005	Cemented	2y + 1m	Yes
29c	Female	Right	45	Cemented	30/07/2012	Cemented	7y + 2m	Yes
30	Male	Right	77	Cemented	25/10/2002	Cemented	6y + 6m	No
31	Female	Right	73	Not cemented	05/12/2007	Cemented	10y + 6m	No
32	Female	Left	61	Not cemented	21/12/1998	Cemented	12y + 3m	No
33	Female	Left	66	Cemented	25/10/2005	Cemented	13y + 5m	No
34	Female	Left	56	Not cemented	13/10/2004	Cemented	12y + 9m	No
35	Female	Left	41	Not cemented	03/07/2000	Cemented	16y + 3m	No

(*Continued*)

Table 1 (*Continued*)

	Preoperative				Immediate postoperative		Late postoperative period	
#	Gender	Operated side	Age (Years)	ATK type	Date of surgery	Type of revision	Last follow-up (years + months)	Failure
36	Female	Right	70	Cemented	19/06/2007	Cemented	12y + 5m	No
37d	Male	Left	56	Cemented	27/09/1997	Cemented	6y + 10m	Yes
38d	Male	Left	63	Cemented	27/08/2004	Cemented	15y + 9m	No
39	Female	Right	70	Not cemented	10/08/2015	Reverse hybrid	3y + 2m	No
40	Female	Right	46	Not cemented	15/07/2015	Reverse hybrid	4y + 0m	No
41	Female	Right	63	Cemented	21/07/2015	Reverse hybrid	3a + 1m	Yes
42	Female	Right	64	Cemented	19/05/2015	Reverse hybrid	2a + 1m	No
43	Male	Right	69	Cemented	12/02/2015	Reverse hybrid	2a + 1m	No
44	Male	Left	59	Girdlestone	01/10/2014	Reverse hybrid	2a + 0m	No

Abbreviations: m, months; y, years.
Letters a, b and c indicate the same patient, but different surgery.

cavitary defects, with or without pelvic discontinuity (D'Antonio Classification[12]). The study was initiated after approval by the Ethics Committee of our institution.

Clinical Evaluation

Late pre- and postoperative clinical evaluation was performed in all patients using the Harris Hip Score (HHS) hip evaluation score.[13]

Radiographic Evaluation

Standardized radiographs of the pelvis were performed preoperatively, in the immediate postoperative period, and in the follow-up exams at 6 weeks, 3 months, 6 months, and, afterwards, annually.

The classification of the acetabular bone defect was preoperatively evaluated using the Paprosky[14] and D'Antonio methods,[12] in addition to the size of the defect in millimeters.[6]

On immediate postoperative radiography, the percentage of coverage of the acetabular component by the structural graft and the measurement in millimeters of the largest craniocaudal thickness of the graft were evaluated. To describe the configuration of the structural graft in the acetabulum, we used the description published by Prieto et al.,[2] which defined it in three types: Type 1, buttress configuration or "flying buttress"; Type 2, dome support; and, Type 3, on base or "footing".

On later postoperative radiography, osseointegration of the graft was classified as described in another publication, which became known as the "Coon criterion".[15] Type 1 was defined as total continuity of the bone trabeculate at the interface between the host bone and the graft (total osseointegration); Type 2, as partial continuity of the bone trabeculate at the interface between the host bone and the graft (partial osseointegration); Type 3, as absence of continuity of the bone trabeculate at the interface between the host bone and the graft (absence of osseointegration); and Type 4 as impossibility of visualization of the graft due to the presence of prosthetic components (screens, reinforcement rings, etc.).

In serial radiographs, the presence of progressive radiolucent lines around the acetabular component, and signs of graft resorption and osteolysis were evaluated, according to the acetabular zones determined by DeLee et al.[16]

The migration of the acetabular component was measured in radiographs obtained in the immediate postoperative period compared to the later one, through parameters defined by Knight et al.,[17] having as reference points the teardrop of both hips, the Köhler line, and the hip rotation center.

The reconstruction was considered a failure when there was loosening of the implant with migration >5 mm in any direction, and/or the progression of radiolucent lines around the acetabular component >2 mm wide. The cases of failure were compared with the others (success) seeking correlation with the classification of the bone defect according to Paprosky et al.[14] and D'Antonio et al.,[12] the size of the bone defect in millimeters,[6] the largest thickness of the graft in millimeters, the percentage of implant coverage by the graft, osseointegration of the graft,[15] the presence of graft resorption and osteolysis, in addition to its configuration.[18]

To avoid inter- and intra-observer errors, the measurements were performed by one team member and reviewed by another. In case there was disagreement, a new evaluation was performed by a third member of the team, and then a consensus was reached.

Surgical Technique

We used the modified Hardinge anterolateral surgical approach in all cases. Initially, the acetabular component is removed; later, debris and fibrous tissue are cleaned from the cavity, using curettes and acetabular cutters, to reach a surface that is cruent and able to receive the graft. Then, the removal of the femoral stem is performed when necessary.

The graft is prepared and washed with saline, block graft was used on the acetabular ceiling associated or not with a

chopped graft. After cleaning the acetabulum, a bed is prepared with impacted chopped graft at the site that will receive the bone block, so that there are no "dead zones" that allow the formation of fibrous tissue or cysts, hindering the consolidation and possible integration of the block.

The fixation of the structural graft in the host bone is through 3.5 mm spongy screws with partial thread, at a 45° angle and in variable number according to the size and number of bone blocks used. After fixing the graft, the cavity is milled until it reaches the ideal size. After complementary filling of the existing defects, the acetabular component is placed, cemented or not, and at least one anchorage is performed, made superiorly with a 10 mm drill, necessarily reaching the host bone, and another made in the ischium through the host bone, impacted graft, or bone block (depending on the size of the existing cavity). We used an iodopovidone solution with saline solution throughout the transoperative period.

Postoperative Management

Mechanical thromboembolic prophylaxis was used in the immediate postoperative period, prophylactic oral anticoagulation for 30 days and antibiotic prophylaxis with vancomycin and ceftriaxone. In addition, one gram of ceftazidime is added to each dose of bone cement used. A radiographic evaluation is performed 6 weeks after the surgical procedure, from that moment on, full support with a crutch is allowed as an accessory element of balance.

Statistical Analysis

Statistical analysis was performed to establish comparisons between pre- and postoperative measurements in relation to clinical and radiological data and criteria, using the Student *t* test, the chi-squared test, the Mann-Whitney test, or the Fischer exact test. The Shapiro Wilk normality test was used. Survival analysis of the acetabular component was performed using the Kaplan-Meier method with radiographic data. A significant value was considered when $p < 0.05$, with 95% confidence interval (CI). IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) was used for data analysis.

Results

Forty patients (44 hips), with a mean follow-up of 9.65 years (2 to 18.75 years) were evaluated. In 39 initial patients of the series (88.66%), a conventional cemented acetabular component (noncrosslinked) was used.

Regarding clinical results, the mean preoperative Harris Hip Score (HHS)[13] was 48.8 points, and in the late postoperative period it was 82. Comparatively, a statistically significant difference was observed ($p \leq 0.001$).

Of the 44 operated cases, 20 acetabular defects (45.5%) were classified as Paprosky type 3A[14] and 22 (50%) as type 3B. According to the classification by D'Antonio,[12] 39 combined defects (88.6%) were observed. The size of the bone defect in millimeters[6] was on average 62.48 mm. The radiographic characteristics of the patients are described in ►**Table 2**.

The percentage of mean coverage of the implant cemented by the graft was 77% (43 to 100%), and in 41 cases (93.18%) > 50% coverage was evidenced. The largest craniocaudal thickness of the graft was on average 2.2 mm (1.2 to 4.6 mm). In 29 hips (65%), the graft configuration was classified as Prieto type 1 (footing), and in 14 (31%) as type 2 (dome support).

Postoperatively, no radiographic evidence of osseointegration was observed in 6 (13.6%) cases (Coon 3[15]). In 14 hips (26%), partial graft reabsorption was observed, all in DeLee zone 1.[16] In 8 cases (18.2%), the presence of osteolysis was evidenced, all in DeLee zone 3.[16]

Progressive radiolucency lines > 2 mm wide were observed around the acetabular implant in 9 cases. Of these, in 8 cases, migration > 5 mm was evidenced. According to the radiographic criteria established, 9 cases (20.5) were considered reconstruction failures. Five (11.5%) of these patients were resubmitted to revision surgery, one of whom had an infection. Of the 9 cases of failure, no osseointegration of the graft was observed in 6 cases (►**Figs. 1** and **2**).

Using radiographic criteria to define failure, we found a 79.54% survival rate in a mean follow-up of 9.65 years. When the criterion was used for a new surgery to review the acetabular component for any reason, survival was 88.63%. As complications, we observed 4 cases (9.09%) of instability and 1 (2.27%) of infection.

The survival of the reconstruction was evaluated through the Kaplan-Meier curve, being 92.1% in 5 years and 78.3% in 10 years, when the radiographic parameters of failure were used. The 5- and 10-year survival free of new acetabular component revision surgery for any reason as an outcome was 94.4 and 83.2%, respectively (►**Fig. 3**).

A correlation was observed between migration and reconstruction failure, with the absence of radiographic signs of graft osseointegration ($p < 0.01$). There were 5 cases with complications: 4 with instability (9.09%) and 1 (2.27%) with infection.

Discussion

In the present study, most patients had large acetabular defects; 90.9% of the defects were classified as Type III or IV of D'Antonio and 95.5% as Paprosky type 3A or 3B. A correlation was observed between reconstruction failure and absence of radiographic signs of graft osseointegration ($p < 0.01$). Patients with radiographic signs of failure showed significantly worse postoperative scores than the other patients.

Acetabular reconstruction in the presence of severe acetabular bone deficiency is a challenging scenario in hip revision surgery. Acetabular reconstruction techniques using structural bone graft allow restoring the center of hip rotation, obtaining implant stability, with the possibility of restoration of bone stock, facilitating future revisions.[18]

Acetabular reconstruction using a structural homologous graft in THAR presents controversial results in the literature.[11,18,19] Prieto et al.[2] found 94% survival in noncemented implants with high porosity metal associated with the use of structural allograft in 5 years of follow-up. Brown et al., using

Table 2 Radiographic characteristics of patients

Features		Total ($n = 44$)	Failure ($n = 9$)	Success ($n = 35$)	*p-value*
Failure in osseointegration		62.48 (± 8.26)	65.67 (± 10.95)	61.66 (± 7.39)	0.226ǂ
Acetabular defect (Paprosky)	2a	1 (2.3%)	0 (0.0%)	1 (100.0%)	0.239Δ
	2b	1 (2.3%)	1 (100.0%)	0 (0.0%)	
	3a	20 (45.5%)	4 (20.0%)	16 (80.0%)	
	3b	22 (50.0%)	4 (18.2%)	18 (81.8%)	
Acetabular defect (D'Antonio)	I	1 (2.3%)	0 (0.0%)	1 (100.0%)	0.178Δ
	Ii	3 (6.8%)	0 (0.0%)	3 (100.0%)	
	Iii	39 (88.6%)	8 (20.5%)	31 (79.5%)	
	Iv	1 (2.3%)	1 (100.0%)	0 (0.0%)	
Coverage (%)		0.77 (± 0.16)	0.76 (± 0.16)	0.78 (± 0.17)	0.748ǂ
Increased graft thickness		2.20 (± 0.71)	2.30 (± 0.99)	2.17 (± 0.64)	0.907ǂ
Graft configuration (Prieto)	I (flying buttress)	29 (65.9%)	7 (24.1%)	22 (75.9%)	0.662Δ
	II (dome support)	14 (31.8%)	2 (14.3%)	12 (85.7%)	
	III (footing)	1 (2.3%)	0 (0.0%)	1 (100.0%)	
Osseointegration (Coon)	1 (total)	27 (61.4%)	3 (11.1%)	24 (88.9%)	≤0.001Δ
	2 (partial)	11 (25%)	0 (0.0%)	11 (100.0%)	
	3 (away)	6 (13.6%)	6 (100.0%)	0 (0.0%)	
Migration (≥ 2 mm)		9 (20.5%)	0 (0.0%)	35 (100.0%)	≤0.001¥
Absorption (DeLee Zone I)		14 (31.8%)	5 (55.6%)	9 (25.7%)	0.117¥
Osteolysis (DeLee Zone III)		8 (18.2%)	2 (22.2%)	6 (17.1%)	0.659¥
Migration		8 (18.2%)	8 (88.9%)	0 (0.0%)	≤0.001¥
Reoperation		8 (18.2%)	6 (66.7%)	2 (5.7%)	≤0.001¥
Revision		4 (9.1%)	4 (9.1%)	0 (0.0%)	≤0.001¥

ǂWhitney U's t-test; *Student's t-test; ¥ Fisher's Exact Test; Δ Chi-squared test.

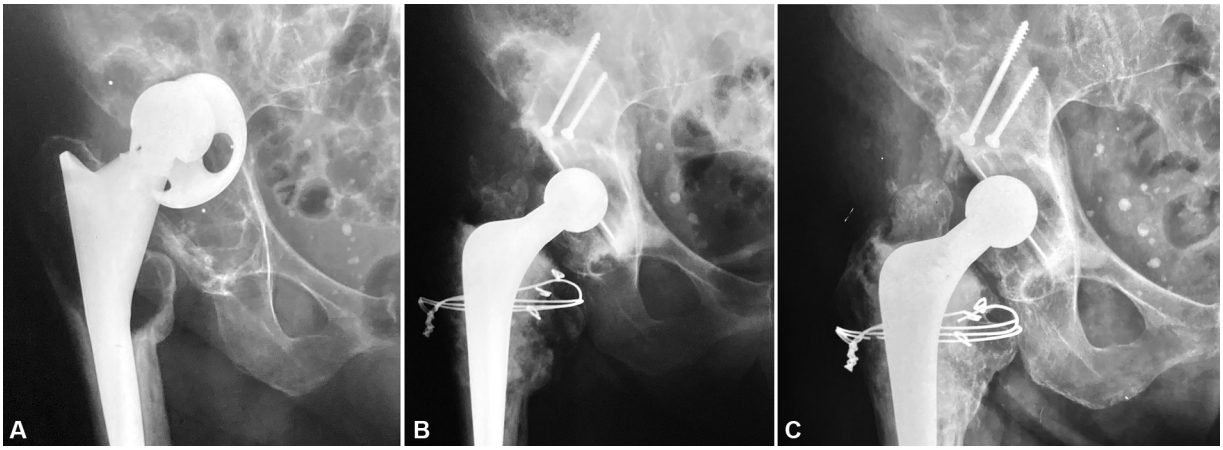


Fig. 1 Radiographs of a 73-year-old female patient who had her right hip operated. A) preoperative radiography showing noncemented total hip arthroplasty with combined defect (D'Antonio); Paprosky 3B, measuring 82 mm; B) immediate postoperative radiography presenting acetabular reconstruction with structural graft and cemented acetabular component; C) postoperative radiography at 10 years and 6 months after acetabular reconstruction without signs of release.

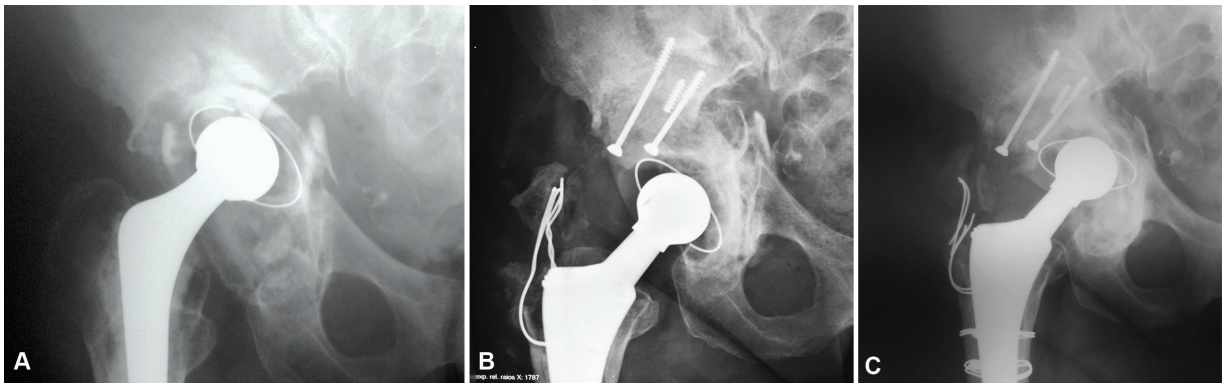


Fig. 2 Radiographs of a 63-year-old female patient who had her right hip operated. A) preoperative radiography showing cemented total hip arthroplasty with pelvic discontinuity; Paprosky 3B, measuring 80 mm; B) immediate postoperative radiography presenting acetabular reconstruction with structural graft and cemented acetabular component; C) postoperative radiography at 3 years and 1 month after acetabular reconstruction with signs of loosening.

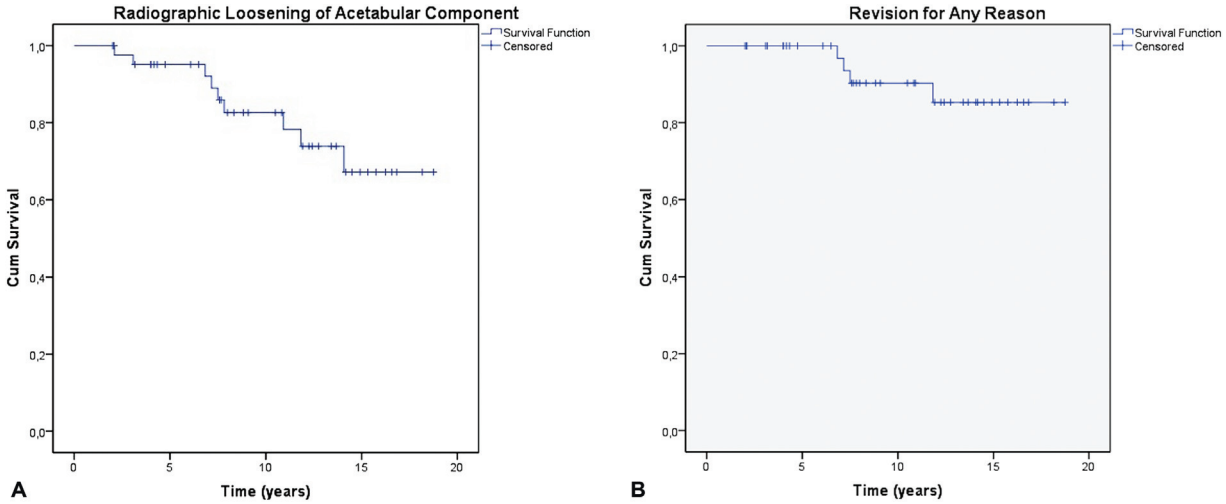


Fig. 3 Kaplan-Meier curves for reconstruction survival without revision for: (A) acetabular loosening (92.1% in 5 years, 78.3% in 10 years, and 67.5% in 15 years) or (B) any cause (94.4% in 5 years and 83.2% in 10 and 15 years).

structural allograft of distal femur associated with noncemented implant, observed 72% survival in 21 years of mean follow-up.[20] Garbuz et al.[21] evaluated 33 cases of acetabular reconstruction with structural graft supporting > 50% of the implant, in a mean follow-up of 7 years. A 45% failure was observed, which occurred mainly in cases in which no reinforcement ring was used.

Butscheidt et al.,[5] analyzed 13 structural homologous grafts after death by radiography, computed tomography (CT), histology, and electron microscopy. The distance between the current allograft and the host bone, and the distance between the original allograft and the host bone were evaluated. The study observed adequate osseointegration of all grafts along most of the interface between the graft and the host bone. The eventual nonosseointegration in some points did not lead to graft collapse within 22 years of follow-up.[5]

The literature indicates a higher incidence of reconstruction failure when using a structural graft with > 50% acetabular implant coverage, which we did not evidence in the present series even without the use of reinforcement ring.[10,11,22] The patient with the longest follow-up time (18.75 years) has no signs of release or failure so far (►**Fig. 4**).

Total hip arthroplasty revision in the presence of severe acetabular defects is more challenging and may have worse results. In the present study, with the analysis of the treatment of large bone defects, however, we did not observe a correlation between reconstruction failure and severity of the acetabular bone defect, graft thickness or configuration.

Our study has some limitations. We observed a good time of mean follow-up of the patients (9.65 years); however, we had a considerable loss of follow-up, which made it impossible to find more conclusions. Moreover, as the series of patients is old and there was no local availability of acetabular implant cemented with crosslinked polyethylene, it should be considered that the use of conventional polyethylene in most cases may have compromised the survival of reconstruction due to early wear. We suggest future research to evaluate the osseointegration of the structural graft using only one type of cemented prosthetic implant, aiming to reduce confounding factors.

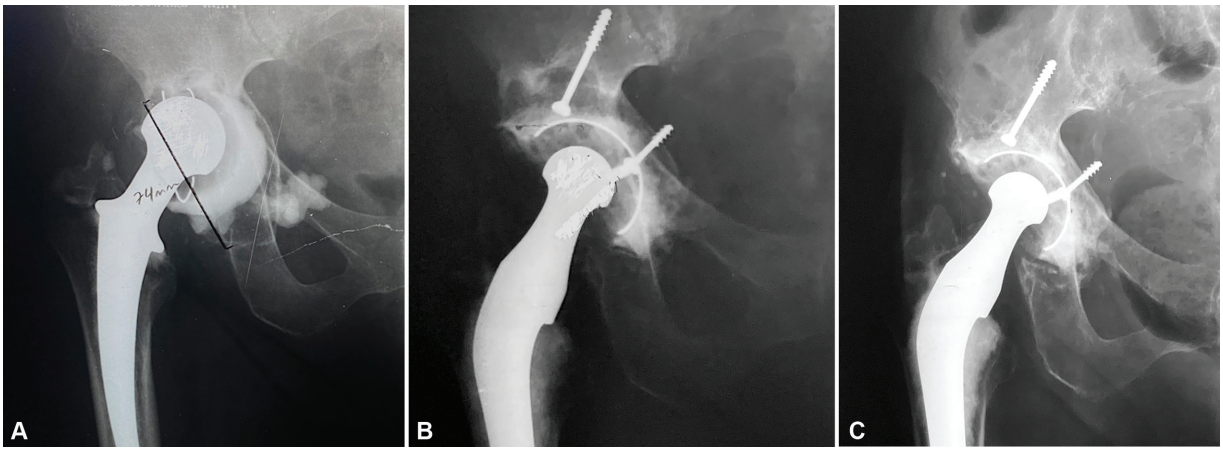


Fig. 4 Radiographs of a 74-year-old female patient who had her right hip operated. A) preoperative radiography showing cemented total hip arthroplasty with combined defect (D'Antonio); Paprosky 3A, measuring 74 mm; B) immediate postoperative radiography presenting acetabular reconstruction with structural graft and cemented acetabular component; C) postoperative radiography at 18 years and 9 months after acetabular reconstruction without signs of loosening.

Conclusion

We observed good clinic and radiographic results, with survival of 79.54% in a mean follow-up of 9.65 years. There was an association between absence of radiographic signs of osseointegration of the structural graft and failure of acetabular THAR in the present series of patients with large bone defects. The failures did not correlate with the severity of the acetabular bone defect, thickness, or graft configuration.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Fracture in Humeroradial Synostosis: Description of Two Clinical Cases*

Fratura em sinostose rádio-umeral: Descrição de dois casos clínicos

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Abstract

Synostosis is a generic term to indicate the union of two originally separated bones. At the elbow, humeroradial or longitudinal synostosis causes significant disability, which varies depending on hand function, elbow positioning, adjacent joints mobility and contralateral limb function. It is estimated that, to date, a little more than 150 patients have been described with this deformity, which is more common in subjects with deficient ulnar formation or affected by conditions such as Antley-Bixler and Hermann syndromes. The lack of the elbow joint, with the formation of a longer bone due to humerus-radius fusion, results in stiffness. As such, it is assumed that fractures in this topography are not uncommon. However, since synostosis is rare, this lesion was only described twice in the literature. We report two patients with a fracture of the single bone formed by a humeroradial synostosis and Bayne type-IV ulnar formation failure. Both patients were treated surgically with success. We emphasize the need for adequate treatment to not compromise the daily activities of patients who are adapted to their deformity, thus avoiding worsening the function of a previously affected limb.

Keywords
- synostosis/surgery
- radius/abnormalities
- congenital abnormalities
- syndrome
- ulna/abnormalities

Resumo

Sinostose é um termo genérico utilizado para indicar a união de dois ossos originalmente separados. No cotovelo, a sinostose rádio-umeral ou longitudinal causa importante incapacidade, que varia a depender da função da mão, da posição do

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cotovelo, da mobilidade das articulações adjacentes e da função do membro contralateral. Estima-se que um pouco mais de 150 pacientes foram descritos até hoje com essa deformidade, sendo mais frequente em portadores de deficiência de formação ulnar ou podendo fazer parte de síndromes como de Antley-Bixler e de Hermann. Devido à rigidez causada pela ausência da articulação do cotovelo, que resulta na formação de um osso mais longo com a fusão do úmero no rádio, presume-se que fratura nessa topografia não seja incomum. No entanto, pela raridade dessa patologia, tal lesão apresenta apenas duas descrições prévias na literatura. Relatamos os casos de dois pacientes com fratura do osso único formado pela sinostose entre o úmero e o rádio portadores de falha de formação ulnar do tipo IV de Bayne. Ambos os pacientes foram tratados de forma cirúrgica e evoluíram bem. Salientamos a necessidade do tratamento adequado para não comprometer as atividades da vida de um paciente já adaptado à deformidade, evitando piorar a função de um membro já alterado.

Palavras-chave
- sinostose/cirurgia
- rádio/anormalidades
- anormalidades congênitas
- síndrome
- ulna/anormalidades

Introduction

Synostosis is a generic term used to indicate the union of two generally separated bones. At the elbow, proximal radioulnar synostosis (PRUS; transverse synostosis) must be differentiated from humeroradial synostosis (HRS; longitudinal synostosis). Proximal radioulnar synostosis is less rare and disabling, and it may occur alone or combined with some syndromes, such as trisomy 13 and 21.[1] Elbow flexion and extension is normal, but pronosupination is blocked. This movement can be compensated by shoulder and wrist rotation and surgical treatment is successful in selected patients.[1]

Humeroradial synostosis is rarer, and it occurs in patients with postaxial longitudinal formation failure (PALFF), also called ulnar deficiency. These lesions may also be associated with conditions such as Antley-Bixler and Hermann syndromes.[2–7] This anomaly prevents elbow flexion and extension, resulting in variable disability, depending on hand function, elbow positioning, adjacent joints mobility and contralateral limb function. Ulnar deficiency resulting from HRS is classified as Bayne type IV. Bilateral involvement of upper limbs is not uncommon (20%), as well as other skeletal deformities, including congenital short femur, congenital scoliosis, developmental dysplasia of the hip, phocomelia,

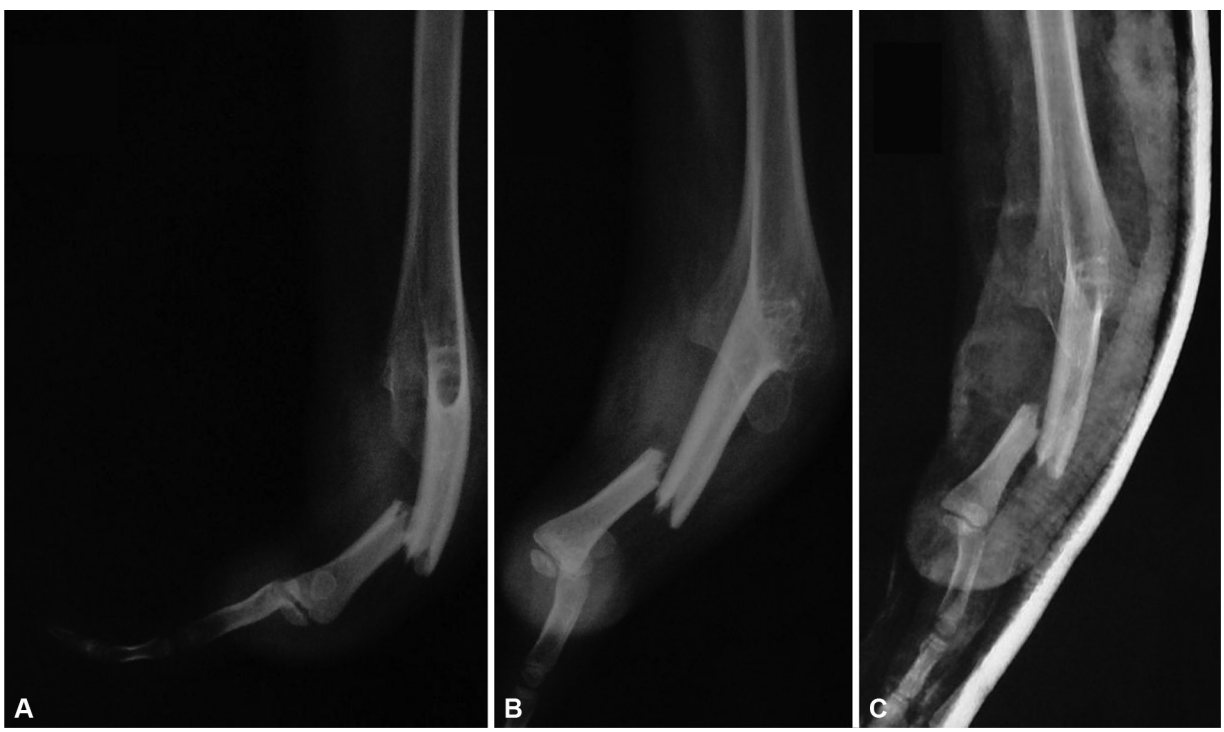


Fig. 1 An 11-year-old boy with humeroradial synostosis fell to the ground and sustained a trauma to the right upper limb. Radiographs revealed a fracture of the single bone formed by a proximal radioulnar synostosis, immediately distal to the synostosis site (A), with angulation and bone shortening even after an attempted reduction (B and C).

fibular hemimelia, and congenital clubfoot.[8–10] In these patients, treatment aims to improve hand function and positioning, especially for those with the classic "hand on flank" position due to an exaggerated internal rotation of the upper extremity, resulting in hand rotation towards the gluteal region.[1,8] Surgery for mobility recovery at a synostosis site is often unsuccessful.[1,4]

The lack of the elbow joint, with the formation of a longer bone due to humerus-radius fusion, results in stiffness. As such, it is assumed that fractures in this topography are not uncommon. However, synostosis is rare, and this lesion was only described twice in the literature.[2,3]

We report two patients with a fracture at the single bone formed by a humeroradial synostosis and Bayne type-IV ulnar formation failure. Both patients were treated surgically with success. We emphasize the need for adequate treatment to not compromise the daily activities of patients who are adapted to their deformity, thus avoiding worsening of the function of a previously affected limb.

Case reports

We treated an 11-year-old boy with a severe, isolated congenital malformation in the upper limbs. The boy is the only child of a family with no history of congenital disorders. His mother said that she had no complications during pregnancy, such as illness or exposure to radiation, medications, alcohol, or drugs. She also said that there is no history of consanguineous marriages in the family. The patient had been followed up since birth at our pediatric hand surgery service. He

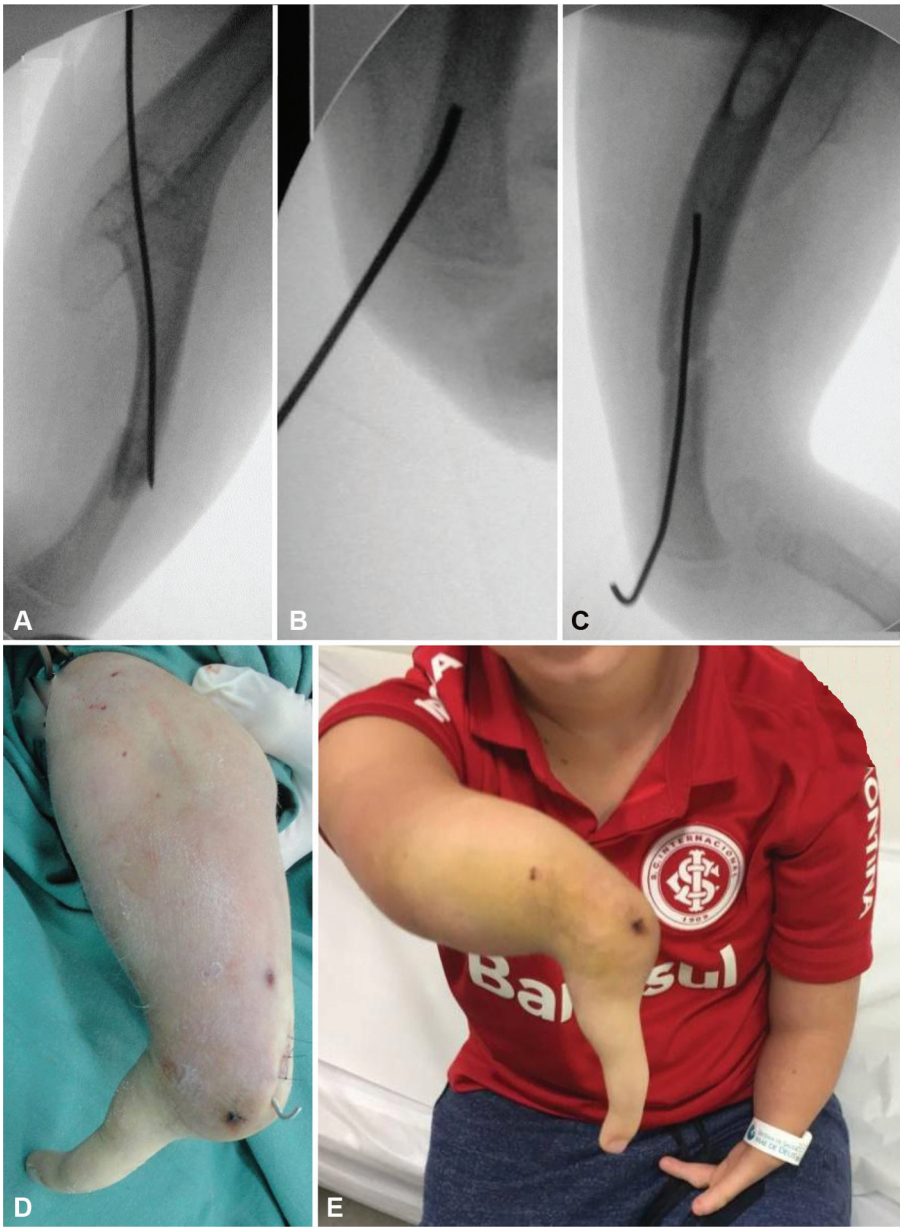


Fig. 2 Initial, unsuccessful attempt of fracture fixation with anterograde intramedullary wire through the synostosis site (A). A retrograde, percutaneous intramedullary fixation was performed (B, C, and D). The patient was followed up once a month for the first 6 months and, 3 years after the surgery, he had no pain and reported preinjury functional levels (E).

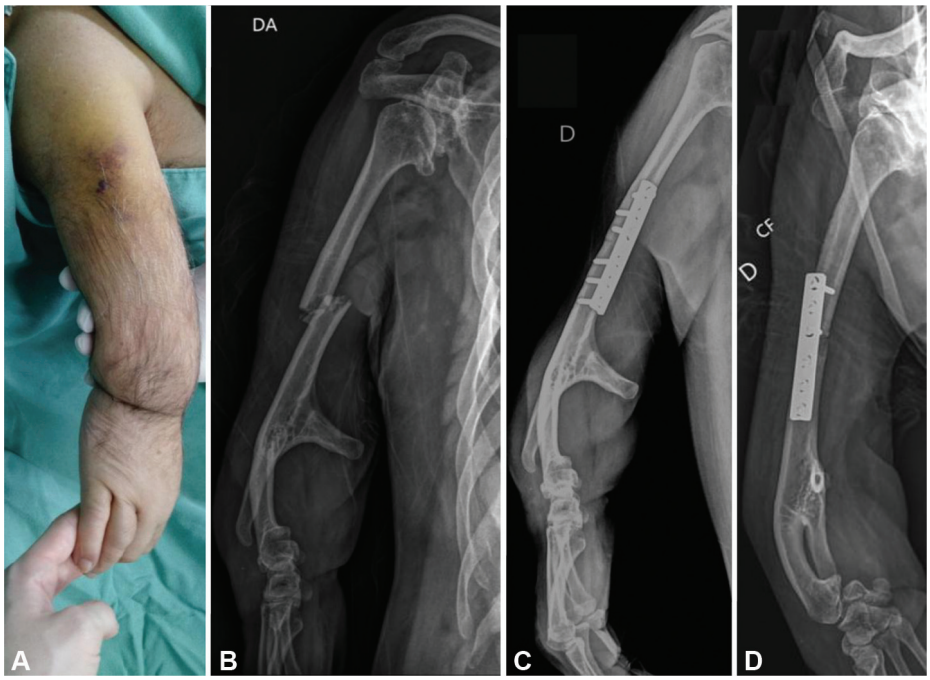


Fig. 3 A 62-year-old patient with humeroradial synostosis fell from a ladder and sustained right upper limb trauma, with local deformity and pain (A). Radiographs show a fracture proximal to synostosis and degenerative shoulder and wrist arthrosis (B). As definitive treatment, fracture was fixed using a plate and screws (C and D).



Fig. 4 Two years after the surgery, the patient had a stable limb, with no pain, and reported preinjury functional levels (A, B, C, and D).

presents bilateral PALFF, with humeroradial synostosis (Bayne type IV), only one finger in the right hand, and finger agenesis with syndactyly of the second and third fingers of the left hand (Bayne type III), previously submitted to surgical correction. We were called to the emergency room to assess the patient, who presented with pain and deformity in his right arm after falling from a bicycle. The physical exam revealed deformity and angulation in the lower third of the upper limb, with no vascular or neurological deficit, in addition to the congenital condition. Initial radiographs showed a fracture of the single bone formed by HRS, immediately distal to the synostosis site (►**Fig. 1**). An axillar-palmar plastered splint was placed in an attempt of fracture reduction. Surgical treatment was indicated due to the considerable fracture deviation and performed under general anesthesia. Initially, the fracture was fixed using an anterograde intramedullary wire. However, local anatomical changes prevented medullary channeling, so we decided for a percutaneous retrograde intramedullary fixation. After radioscopic confirmation of fracture reduction, the patient was immobilized with a plaster cast. In the following days, the patient did not present any procedure-related complications, such as nerve or vascular injury (►**Fig. 2**). Radiographic control and plaster splint change were performed at weekly visits. Twenty days after surgery, the plaster cast was removed, a sling was indicated, and light wrist and shoulder movements were encouraged. The wires were removed 8 weeks after the surgery, when radiographs revealed signs of fracture consolidation. The patient was followed up in monthly visits for the first 6 months, and then evaluated every 6 months. Physical activities and contact sports were allowed 4 months after the surgery. In a late evaluation, 3 years after the surgery, the patient did not present pain or functional deficits. Radiographs showed complete fracture healing, with no intercurrences.

The second patient treated by our team was a 62-year-old-man with right-sided, isolated PALFF, HRS (Bayen type IV), and thumb agenesis. He is the second child in a family with no history of congenital changes, and his mother (who is deceased) had no complications during pregnancy. He arrived at our hospital with right upper limb trauma after falling from a ladder. On examination, he presented deformity and angulation in the upper third of the upper limb, with no vascular or neurological deficits. Radiographs showed a fracture on the single bone formed by the HRS, proximal to the synostosis. There was also evidence of shoulder and wrist osteoarthritis (►**Fig. 3**). At the first visit, a provisional axillar-palmar plastered splint was provided for fracture alignment. Definitive treatment was plate fixation under brachial plexus block, in an approach equivalent to the standard anterolateral approach for anatomically normal humerus. The only relevant anatomical change in this procedure was humeral size, which was considerably hypoplastic. The patient had no early or late procedure-related complications. He was not immobilized after surgery, opting for a sling. Prior to the procedure, we offered the patient the possibility of elbow extension and extreme internal rotation correction, but he declined it because he considered himself well-adapted to his condition, with a functional limb. The patient was followed-up in weekly visits, and radiographs revealed signs of fracture consolidation at 6 weeks. Next, the patient was followed-up once a month for the first 6 months, and then every 6 months. Daily life activities and sports were allowed 4 months after the surgery. In a late evaluation, 2 years after the surgery, the patient had no pain or functional deficits (►**Fig. 4**).

Discussion

Fractures on the single bone formed by HRS are probably not rare. The longer bone resulting from the lack of the elbow joint mechanically predisposes the limb to this injury. However, since patients with HRS are scarce, there are only two cases of abnormal limb fractures described in the literature. Both reports focus much more on the patient's underlying condition, the context of the syndrome and facial changes, with little regard for bone damage and treatment.

Elbow deformities in patients with PALFF are so characteristic that one of the first classifications[10] was based on elbow synostosis and radial head dislocation. Further classification systems, including Ogden, Riordan, Swanson and Miller apud Cole and Manske, focused more on ulna and hand deformities.[10] Currently, the most accepted system is the modified Bayne classification, based on Ogden,[10] which divides changes into four types and includes elbow and forearm deformities.[1,10] (►**Table 1**).

The incidence of HRS is unknow. In 1955, Card and Strachman[11] reported the 35th case in the literature. Years later, Swanson et al.[9] and Buck-Gramcko apud McIntyre et al.[5] published two series with 47 and 20 subjects, respectively. It is estimated that 150 cases were described in the literature.[6] In the PALFF series, the incidence of HRS ranges from 20 to 53%, and it is worth noting that the incidence of PALFF is 4 to 10 times lower compared to its preaxial (radial) counterpart.[1,10] No surgery is indicated for patients with good hand positioning and semiflexed elbow. Surgical attempts to obtain movement at a synostosis site are invariably unsuccessful.[1,4] Tabrizi et al.[4] reported complete recurrence of synostosis after an attempt of bone bar resection and fat interposition to improve hand positioning. In some patients with HRS, the upper limb is in an exaggerated

Table 1 Bayne classification, based on Ogden, dividing longitudinal postaxial formation failures of the upper limb into four types, according to severity and elbow involvement

Bayne classification for postaxial longitudinal formation failures.
Type I. Hypoplastic ulna, with proximal and distal epiphyses.
Type II. Partial absence of the ulna, with failure in the distal region (most frequent type).
Type III. Total absence of the ulna.
Type IV. Absence of the ulna with humeroradial synostosis (rarer type).

internal rotation, with the hand turned to the back, the so-called "hand on flank" posture. This is extremely disabling, and Miller and James recommended external rotary osteotomy of the humerus for these patients.[1,8]

McIntyre et al.[5] classified HRSs into two types. Type I is the most common HRS, with a three-times higher frequency; it is a sporadic deformity, associated with PALFF, digital hypoplasia and extended elbow. In type II, synostosis has a familial character, and it is associated with syndromic conditions; the elbow is fixed in flexion and there are no hand changes. Our two patients present type-I HRS, and we believe the extended elbow increased the risk of injury and fractures due to a greater susceptibility to trauma and the increased lever arm generated by a long, straight bone.

We believe that other congenital skeletal changes associated with HRS, such as double or bifid scapula, may be an attempt to increase limb mobility, compensating for the stiffed elbow. These patients would present a lower risk of fracture at the synostosis site. As such, we think that one of the factors resulting in the fracture sustained by our second patient, in addition to the severity of the trauma, is wrist and shoulder arthrosis, leading to greater rigidity of the entire upper limb.

Patients with HRS usually present other skeletal changes and, like most subjects with congenital deformities, have some degree of adaptation.[1] Therefore, any change in limb anatomy and positioning, especially in adults, may hinder their daily life activities. In both our patients, we preferred surgical treatment to restore the original anatomy and avoid further limb deformity and shortening, also with less immobilization time. For patients with severe internal rotation of the limb and a fracture, surgical treatment can be a good opportunity to correct a rotational deformity.

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Conflict of Interests
The authors have no conflict of interests to declare.

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Ultrasound-Guided WALANT Technique in Carpal Tunnel Decompression Surgery*

Técnica WALANT guiada por ultrassom na cirurgia de descompressão do túnel do carpo

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Abstract

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy in the human body. Its symptoms result from compression of the median nerve in the carpus. The treatment can be conservative, with medications and/or infiltrations that alleviate the symptoms, or surgical, which is more effective, with decompression of the median nerve by surgical section of the flexor retinaculum of the carpus. The anesthetic technique varies according to the anesthesia method: sedation, venous locoregional anesthesia and, more recently, wide-awake local anesthesia no tourniquet (WALANT), which can be performed by the surgeons themselves. The WALANT technique uses local anesthesia with a vasoconstrictor, and does not require the use of a tourniquet on the upper limb nor sedation. The median nerve block in ultrasound-guided WALANT provides better accuracy to the technique, with greater patient safety; in the present article, its use in the performance of carpal tunnel decompression is described, and the literature is reviewed.

Keywords
- carpal tunnel syndrome
- ultrasonography, interventional
- anesthesia, local

Resumo

A síndrome do túnel do carpo (STC) é a neuropatia compressiva mais comum do corpo humano. Seus sintomas decorrem da compressão do nervo mediano no carpo. O tratamento pode ser incruento, com medicações e/ou infiltrações que amenizam os sintomas, ou cruento, mais eficaz, com a descompressão do nervo mediano pela seção cirúrgica do retináculo dos flexores do carpo. A técnica anestésica varia de acordo com o serviço de anestesia: sedação, anestesia locorregional venosa e, mais recentemente, a anestesia local com o paciente acordado e sem torniquete (*wide-awake local*

Palavras-chave
- síndrome do túnel carpal
- ultrassonografia de intervenção
- anestesia local

* *Study developed at the School of Medicine, Universidade de Araraquara/UNIARA, Araraquara, São Paulo, Brazil.*

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anesthesia no tourniquet, WALANT), que pode ser realizada pelo próprio cirurgião. Por utilizar anestesia local com vasoconstritor, essa técnica dispensa o uso de torniquete no membro superior e a necessidade de sedação. O bloqueio do nervo mediano na WALANT guiada por ultrassonografia confere melhor precisão à técnica, e mais segurança ao paciente, e, neste artigo seu uso na realização da descompressão do túnel do carpo é descrito, e a literatura, revisada.

Introduction

Carpal tunnel syndrome (CTS) is the most frequent compression syndrome in the human body, and it is defined as compression of the median nerve in the carpus. Its estimated prevalence is of 5% of the population, with a predominance among women between the fourth and sixth decades of life.[1]

The median nerve and nine flexor tendons superficially delimited by the flexor retinaculum (FR) are contained in the osteofibrous tunnel.[1] The sensory territory of the median nerve in the hand corresponds to the volar skin of the thumb, second, third and radial half of the fourth finger, which explains the symptoms of paresthesia in the more radial territory of the palm.[1]

The conservative treatment of CTS consists of the administration of analgesic medications, anti-inflammatory drugs and neuropathic pain modulators, corticoid infiltration, and the use of wrist orthosis to improve the symptoms of the patient.[2] The surgical treatment consists of the surgical section of the FR. Retinaculotomy improves the symptom of paresthesia by decompressing and decreasing the intratunnel pressure of the median nerve in the carpus.[2] The technique can be open, mini-open or endoscopic.[2,3]

Anesthesia can be general, locoregional or local. Local anesthesia consists of blocking the median nerve at the wrist and at the surgical incision site, and the association of adrenaline and lidocaine can be used to reduce intraoperative bleeding, and to eliminate the use of the tourniquet in the arm and the need for patient sedation.

This last technique is known as wide-awake local anesthesia no tourniquet (WALANT), which is a surgery with the patient awake, under local anesthesia, and without tourniquet.[2,4,5] The administration of epinephrine proves to be advantageous, as tourniquets and sedation for the patient are not required. It enables a faster onset of action and longer-lasting anesthetic effect, a surgical field with minimal bleeding, a lower dose of anesthetic to be administered to achieve pain control, lower cost, shorter preoperative time, and lower chances of complications, especially in elderly patients.[4,6] The technique was introduced by Lalonde and Martin (apud Kang et al.[6]), who demonstrated that it is a safe method in patients of any age, and capable of preventing bleeding in the surgical field without using a tourniquet. Recently, the surgical indications of this type of anesthesia have expanded beyond the treatment of CTS, and it is used in wrist surgeries, hand tenoplasty and neurolysis, for example.[5]

The introduction of the local anesthetic can be even more accurate when the introduction of the needle is guided by musculoskeletal ultrasound (US), which enables the identification, evaluation and diagnosis of lesions, in addition to the visualization of the needle and of the site of infiltration in real time. It provides effectiveness and accuracy to the procedure, and safety, agility and comfort to the patient.[7,8]

Local anesthesia with a vasoconstrictor in US-guided CTS surgery consists of the injection of perineural anesthetic with circumferential distribution, which provides a higher rate of sensory block,[7] and the volar subdermal injection of the carpus, corresponding to the surgical incision, in order to avoid bleeding.[5,7–9] The real-time guidance provided by US improves the accuracy of the injection site, makes nerve block a faster process, and enables the administration a lower dose of anesthetic, with a lower risk of developing systemic toxicity. The surgical treatment of CTS proves to be an ideal modality for therapeutic injections guided by US.[9]

Materials and Methods

A volunteer patient underwent carpal tunnel decompression surgery after failure of the conservative treatment. This patient was operated on by the specialist orthopedic surgeon who is one of the authors of the present article. Prior to the surgical procedure, the patient was properly informed about the US-guided local anesthesia procedures and the surgery itself. Participation as a volunteer was confirmed after the patient signed the free and informed consent form. The present study was approved by the institutional Ethics in Research Committee under opinion number 4.304.166.

Technique Description

The US-guided WALANT technique for carpal tunnel decompression consists of two steps. The first step is the circumferential anesthetic block of the median nerve proximally to the carpal tunnel, and the second step is the infusion of the same solution in the subdermal region in the projection of the volar surgical incision in the carpus. A portable wireless ultrasound device with a linear probe and 7.5 MHz to 10 MHz of frequency (Mobissom, São Paulo, SP, Brazil), was used, which is suitable for visualizing musculoskeletal anatomical structures in the wrist and hand, which, in turn, are necessary for the preoperative block. The images are transmitted via bluetooth to an iPad (Apple, Cupertino, CA, US).

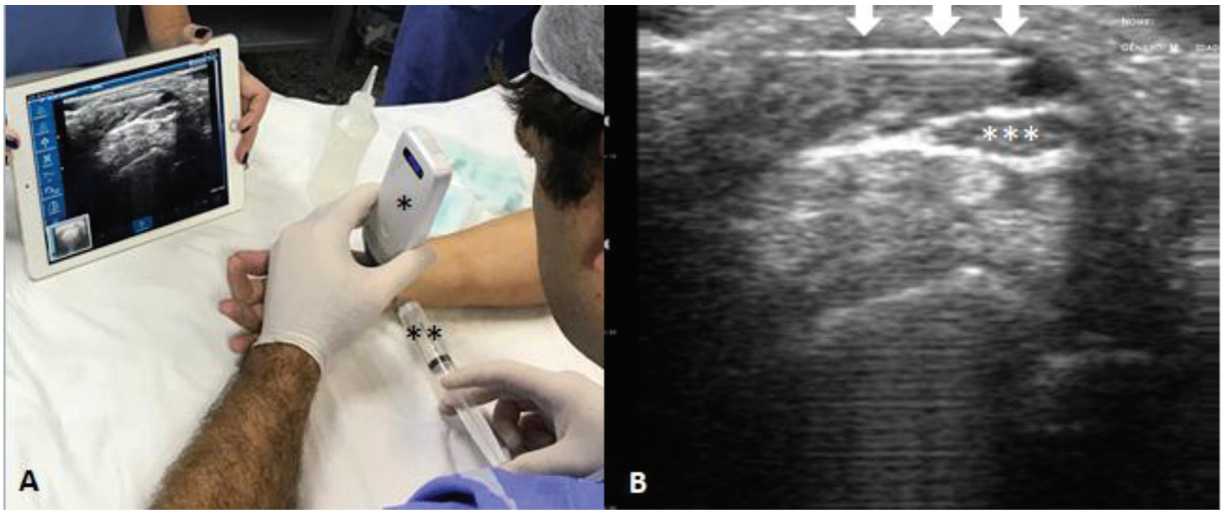


Fig. 1 (**A**) Right upper limb of the patient in supine on the hand table. A portable ultrasound with a linear probe* (Mobissom) is positioned across the wrist, with real-time identification of the median nerve*** in the image transmitted to an iPad (Apple). A gray disposable hypodermic needle, measuring 25 mm x 0.70 mm and attached to a 20-ml syringe containing xylocaine solution at 1% with vasoconstrictor** is introduced in the ulnoradial direction to the perineurium of the median nerve, according to white arrows (**B**). Circumferentially, ~ 6 ml to 10 ml are infused around the median nerve.

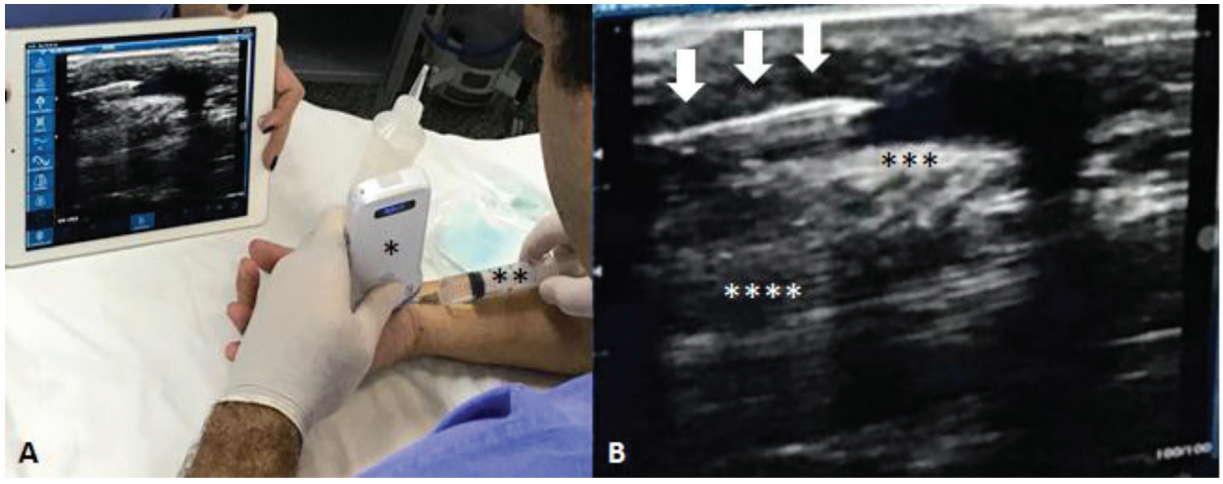


Fig. 2 (**A**) Right upper limb of the patient in supine position on the hand table. A portable ultrasound with a linear probre* (Mobissom) is positioned volarly and longitudinally on the carpus, in the projection of the surgical incision. A gray hypodermic needle,measuring 25 mm x 0.70 mm and attached to a 20-ml syringe,** is introduced through the wrist crease and distally directed between the dermis and the flexor retinaculum (FR). With the ultrasound image transmitted to an iPad (Apple) (**B**), the needle (white arrows) is positioned between the dermis and the FR,*** and a volume of ~ 10 ml of xylocaine solution at 1% with vasoconstrictor is injected. In image B, the deep median nerve to the FR is also observed, longitudinally.****

With the patient in dorsal decubitus position and the upper limb on a hand table, after degermation and antisepsis, the US linear transducer is placed transversely on the wrist, and the median nerve is identified. A total of 10 ml of 2% xylocaine with vasoconstrictor is diluted with 10 ml of 0.9% saline, obtaining a volume of 20 ml of 1% xylocaine. From the anesthetic solution obtained, 6 ml to 10 ml are used in the first step, and the remainder is used in the subdermal region of the surgical incision, through a gray hypodermic needle measuring 25 mm x 0.70 mm, which can be visualized on US, as shown in ►**Figs. 1B** and **2B**.

In the first stage, the median nerve is blocked circumferentially proximally to the carpal tunnel after insertion of the radial needle to the plane shown with a transverse linear probe in the wrist, as shown in ►**Fig. 1A**. As the tip of the needle is positioned adjacent to the nerve, content aspiration is recommended to certify that the region's vessels are not injured, and then the anesthetic is injected above and below the nerve.

In the second stage of the block, as shown in ►**Fig. 2**, the US transducer is placed longitudinally on the carpus, in the projection of the surgical access. The space between the subcutaneous tissue and the FR is identified. With an entry point in the volar crease of the wrist, in a distal and longitudinal direction, the needle is introduced into the visualized space, and ~ 10 ml of the anesthetic solution are injected. This volume is sufficient to promote vasoconstriction and provide a surgical field without bleeding. After

5 to 10 minutes, the time needed to prepare the surgical fields and to put on the medical garments, the surgical procedure itself can be performed.

Discussion

Traditionally, surgery to decompress the median nerve in patients with CTS is performed using a tourniquet. Due to the need for sedation of the patient, it has disadvantages such as a longer surgical time, higher costs, and the possible complications of sedation, especially in elderly patients with comorbidities. The WALANT technique, through the association of xylocaine and adrenaline, enables a safe surgery, without the need of tourniquet placement and patient sedation. The use of US enables the refinement of the technique.

Kang et al.[6], in a study aiming at comparing pain relief and the effectiveness of the WALANT technique in 20 patients undergoing CTS surgery, detected a significantly lower result on the visual analogue scale (VAS) for pain when compared to traditional locoregional anesthesia techniques within the first 24 hours of the postoperative period. They also found lower opioid consumption due to less postoperative pain.

In a study by Liebmann et al.[8] aiming at identifying the feasibility of US-guided radial, ulnar and median nerve block in the forearm of patients admitted to the hospital emergency department, a mean reduction of 5.0 in the VAS was evidenced 15 minutes after the procedure. During the study, the time needed for a complete nerve block was also measured, starting with the initiation of US and ending with the total nerve block, resulting in an average time of three minutes.

In another study, de Freitas Novais Junior et al,[4] observed 41 patients who underwent hand surgery under the technique of local anesthesia with an association of lidocaine and adrenaline at a concentration of 1:100,000. The bleeding observed during surgery was minimal in 32 patients, moderate in 6, and classified as severe in 3, 2 of whom were being treated for chronic kidney disease. In none of the cases it was necessary to stop the surgery due to bleeding. There were no cases of necrosis, hematoma, or any postoperative complications.[4]

In a study by Barros et al.,[10] the authors concluded that the WALANT technique in the surgical treatment of CTS is effective and safe. The study demonstrated a significant improvement in postoperative pain, and 75% of patients reported that the procedure is equivalent to or better than venipuncture, showing satisfaction with the technique and its effectiveness. Sardenberg et al.[11] concluded that wrist, hand and finger surgeries can be safely performed with the WALANT technique, after an evaluation of 488 operated patients, without any adverse outcome.

As for the surgical costs of CTS surgery performed in traditional surgical centers in hospitals in Canada, Leblanc et al.[12] concluded that it is four times more expensive and less efficient (less than half) compared to WALANT surgery performed in a small procedure room. The update article by Pires Neto et al.[5] corroborates the conclusion.

As in hand surgery, in which the use of an anesthetic with a vasoconstrictor is no longer a myth that causes ischemia, musculoskeletal US has changed some dogmas in orthopedics, with an increasing number of interventional and therapeutic possibilities. The use of US in the WALANT technique for the surgical treatment of CTS is an example of this evolution, which provides accuracy and effectiveness to the technique, and safety and comfort to the patient.

Final considerations

In carpal tunnel decompression surgery, US to perform the WALANT technique enables the refinement of the anesthetic technique, with greater accuracy, effectiveness, and patient safety.

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Conflict of interests

The authors have no conflict of interests to declare.

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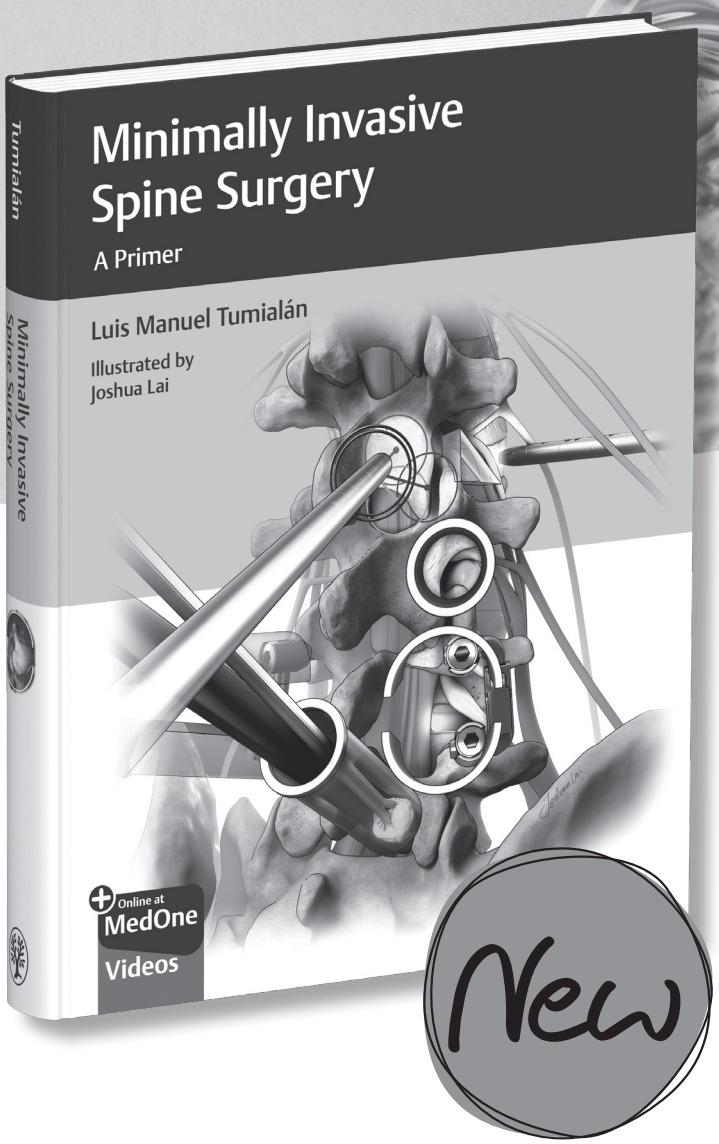
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