



Original Article

Is there a relationship between the neutrophil/lymphocyte ratio and bilaterality in patients with coxarthrosis?☆



Gustavo Göhringer de Almeida Barbosa*, Fabricio Cardozo Vicente, Miguel Antonio Razia Fagundes, Lauro Manoel Etchepare Dornelles, Marcelo Reuwsaat Guimarães, Cristiano Valter Diesel

Hospital da Beneficência Portuguesa de Porto Alegre, Porto Alegre, RS, Brazil

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ABSTRACT

Objective: The objective of this study was to evaluate the relationship between the neutrophil/lymphocyte ratio and the presence of signs of arthrosis in both hips in patients followed at this medical center.

Methods: This was a cross-sectional, retrospective study through the analysis of medical records and database review of patients over 18 years of age with hip arthrosis, followed at the outpatient clinic of this hospital.

Results: Regarding the analysis of the Mann-Whitney test to correlate the neutrophil/lymphocyte ratio and laterality, a bi-lateral test result of $p = 0.036$ was obtained, thus demonstrating a significant difference between the observed groups. When we analyzed the absolute values of neutrophils and lymphocytes, the authors obtained results of $p = 0.14$ and $p = 0.24$. Therefore, it was not possible to observe statistically significant differences between the absolute values in the two groups.

Conclusion: Considering the interactions between the inflammatory mechanisms in osteoarthritis and the fact that the interaction between neutrophils and lymphocytes has differences in relation to the laterality of the coxarthrosis, it is hypothesized that the inflammatory etiology of unilateral and bilateral osteoarthritis could have different dynamics. However, more in-depth studies with flow cytometry are needed to assess the possible impact of these differences in the inflammatory mechanisms observed in this study.

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☆ Study conducted at Hospital da Beneficência Portuguesa de Porto Alegre, Porto Alegre, RS, Brazil.

* Corresponding author.

E-mail: gustavogab@hotmail.com (G.G. Barbosa).

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Existe relação entre a razão neutrófilo/linfócito e a bilateralidade para artrose de quadril?

R E S U M O

Palavras-chave:

Osteoartrose
Inflamação
Neutrófilos
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Objetivo: Avaliar a relação entre a razão neutrófilo/linfócito e a presença de sinais de artrose em ambos os quadris em pacientes acompanhados neste serviço.

Métodos: Estudo transversal, retrospectivo, que usou análise de prontuários e revisão de banco de dados de pacientes maiores de 18 anos com diagnóstico de artrose de quadril acompanhados no ambulatório deste hospital.

Resultado: Com relação à análise do teste de Mann-Whitney para correlacionar a razão neutrófilo/linfócito e a lateralidade, observou-se um resultado de teste bilateral de 0,036, evidenciou desse modo a diferença entre os grupos. Quando os valores absolutos de neutrófilos e linfócitos foram analisados, observaram-se $p = 0,14$ e $p = 0,24$, não foi possível observar diferenças estatisticamente significativas entre os valores absolutos nos dois grupos.

Conclusões: Considerando-se as interações entre os mecanismos inflamatórios na osteoartrose e o fato de que a interação entre os neutrófilos e os linfócitos tem diferenças com relação à lateralidade da coxartrose, é possível levantar a hipótese de que a etiologia inflamatória da osteoartrose unilateral e da bilateral tem dinâmicas diferentes. Entretanto, são necessários estudos mais aprofundados, com citometria de fluxo, para avaliar o impacto com relação às diferenças nos mecanismos inflamatórios observados nesse estudo.

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Introduction

Osteoarthritis (OA) is characterized by joint degeneration with subchondral and periosteal lesions. Several factors may be involved in the progression of joint degeneration, such as obesity, repetitive task injuries, joint trauma, genetic alterations, metabolic and muscular diseases, infections, and coagulation disorders such as hemophilia.^{1,2} OA is often described as a noninflammatory condition. However, new studies have shown that the progress of joint degeneration is correlated with the production of inflammation factors and with the release of cartilage-degrading enzymes.³ There is an increasing interest in establishing the role of inflammation in OA evolution since it is often associated with low-grade synovitis. At the cellular level, the infiltration of macrophages and perivascular T and B lymphocytes has been observed both at early and in more advanced OA. In patients with early OA, there is an increase in the expression of CD4+ and CD68+ cells in the synovium and an increased expression of inflammatory mediators.⁴⁻⁶ Neutrophils and lymphocytes are protagonists in the inflammatory process. The neutrophil/lymphocyte ratio (NLR) is calculated by dividing the absolute neutrophil count by the lymphocyte count obtained from a complete peripheral blood count.⁷ NLR is a very cheap and easy to obtain clinical marker and is used as an indicator of inflammatory processes in several clinical conditions, such as ankylosing spondylitis, sarcoidosis, and lung and colorectal cancer.⁸⁻¹² The importance of NLR in the diagnosis and follow-up of OA progression is not precisely known. This study was aimed at evaluating the relationship between NLR and the presence of signs of OA in both hips in patients followed-up at this medical facility.

Material and methods

This is a cross-sectional, retrospective study that reviewed the medical records and database of patients over 18 years diagnosed with hip arthrosis who were followed-up at the outpatient clinic of this hospital. A total of 132 patients were selected, and 113 were eligible for this study. This study was approved by the Research Ethics Committee under CAAE No. 63313416.6.0000.5530.

The presence of OA was defined by radiographic analysis; the study included patients older than 18 years with any radiological alteration greater than grade 2 in the Kelgren and Lawrence¹³ score (Table 1) in either of their hips. Patients with rheumatologic or autoimmune diseases, coagulopathy, using a corticoid, or with chronic infection or a known chronic inflammatory state were excluded.

Patients were divided into two groups: the unilateral group, in which only one of the hips presented radiological alterations greater than grade I, and the bilateral group, in which both sides presented radiological alterations greater than grade II. Regarding the blood cell count variables, the most recent hemogram was evaluated, from which the data to measure the NLR was extracted.

Table 1 – Kellgren and Lawrence classification.¹³

Grade	Definition
I	Joint space (<3 mm)
II	Joint space obliteration
III	Mild bone friction (0-5 mm)
IV	Moderate bone friction (5-10 mm)
V	Severe bone friction (>10 mm)

Table 2 – Characteristics of the sample.

Population distribution by age, gender, and laterality	
Mean age	63.9 ($\sigma \pm 9.6$)
Gender	
Male	58 (51.3%)
Female	51 (48.7%)
Laterality	
Unilateral	16 (14.2%)
Bilateral	97 (85.8%)

Statistical analysis

Descriptive data, such as age and gender, were summarized as mean and simple frequencies. The Mann–Whitney test was used to assess the correlation between the NLR and bilaterality. Student's t-test was used to analyze the existence of a relationship between absolute neutrophil and lymphocyte values and bilaterality. All analyses were performed with SPSS software version 22.0. *p*-Values <0.05 were considered statistically significant.

Due to the lack of previous data in the literature, the sample size was calculated as aiming at observing a two-fold difference between the means of the groups. To detect a difference in NLR values, the study's power was set at 95% and the level of significance at 0.05; at least 12 patients were required per group.

Results

A total of 132 patients with hip OA were considered. Of these, ten were excluded due to comorbidities. Regarding the losses, nine patients were excluded due to insufficient data for analysis; 113 patients met the inclusion criteria and were eligible for the study.

The mean age of the study participants was 63.9 years, with a standard deviation of 9.6 years. Gender distribution was also balanced: 58 men (51.3%) and 51 women (48.7%; [Table 2](#)). Of the

Table 3 – Descriptive statistics of the neutrophil/lymphocyte ratio, neutrophil count, and lymphocytes count in the unilateral group.

Neutrophil/lymphocyte ratio		
NLR		
Median	5.22	Var = 4.8
Minimum	1.32	
Maximum	17.74	
Neutrophils		
Mean	7015.4 ($\sigma \pm 2585$)	
Minimum	3010	
Maximum	12,719	
Lymphocytes		
Mean	1709 ($\sigma \pm 1.007$)	
Minimum	474	
Maximum	3690	

Kolmogorov-Smirnov's test was used to assess the normality of the sample.

113 patient included in the study, 16 (14.2%) presented unilateral OA and 97 (85.8%) were included in the bilateral OA group.

The median NLR in the unilateral group was 5.22. In the bilateral group, the median was 2.64. The absolute mean values of neutrophils and lymphocytes and their standard deviations were 7015.4 ($\sigma \pm 2585$) and 1709 ($\sigma \pm 1007$) in the unilateral group, respectively, and 5925.6 ($\sigma \pm 3146$) and 2054.2 ($\sigma \pm 928$) in the bilateral group ([Tables 3 and 4](#)).

In the Mann–Whitney test to correlate NLR and laterality, a bilateral test result of 0.036 was observed, demonstrating a statistically significant difference between the observed groups ([Table 5](#)).

When analyzing the absolute values of neutrophils and lymphocytes, the tests presented $p=0.14$ and $p=0.24$; it was not possible to observe statistically significant differences between the absolute values in the two groups ([Table 5](#)).

Table 4 – Descriptive statistics of the neutrophil/lymphocyte ratio, neutrophil count, and lymphocytes count in the bilateral group.

Neutrophil/lymphocyte ratio		
NLR		
Median	2.64	Var = 2.8
Minimum	0.83	
Maximum	17.2	
Neutrophils		
Mean	5925.6 ($\sigma \pm 3.146$)	
Minimum	2040	
Maximum	24,212	
Lymphocytes		
Mean	2054.2 ($\sigma \pm 928$)	
Minimum	465	
Maximum	5923	

Kolmogorov-Smirnov's test was used to assess the normality of the sample.

Table 5 – NLR, neutrophil count and lymphocyte count, and laterality.

Comparison between groups		
NLR and laterality	U = 521	Bilateral testing: 0.036
Neutrophils and laterality	$\bar{x} = 1089 \sigma \pm 721$	Bilateral testing: 0.14
Lymphocytes and laterality	$\bar{x} = 345 \sigma \pm 721$	Bilateral testing: 0.24

Discussion

To date, the inflammatory mechanisms associated with hip OA are still not well established. In contrast to other rheumatologic diseases, such as gout, psoriasis, and rheumatoid arthritis, the crucial role played by inflammation in osteoarthritis has only recently been observed. The presence of an inflammatory component is noteworthy, in light of symptoms such as joint pain, edema, and stiffness.¹⁴

The disease onset is characterized by cartilage damage and chondrocyte death. Progressively, OA evolves to a subchondral lesion, causing an imbalance in the osteoclast bone resorption dynamics and in bone remodeling by osteoblasts.¹⁵

Chondrocytes maintain the components of the cartilaginous matrix under low turnover conditions. In OA, exposure to alterations in the joint microenvironment, such as mechanical stress, inflammatory cytokines, and oxidative stress, promotes the activation of chondrocytes and other synovial cells and joint tissues.¹⁶

In a recent study that analyzed the occurrence of cells of inflammatory origin in the synovial fluid of patients with OA, a preponderance of lymphocytes of the NK lineage was observed.¹⁷

In contrast to peripheral NK cells, the NK cells from synovial fluid expressed different phenotypes, with considerable potential to produce pro-inflammatory molecules, especially granzyme A, a proinflammatory molecule recently identified in animal studies.¹⁸

These data suggest that, in patients with OA, the peculiar dynamics between inflammatory cells are of etiological importance. However, the literature does not present data on the dynamics of inflammatory cells in patients with unilateral and bilateral OA.

The present study observed differences in the NLR in the peripheral blood of patients with unilateral and bilateral OA. In the unilateral group, the median was 5.22, while in the bilateral group the median was 2.64; the difference between them was considered statistically significant ($p = 0.03$). In the group with unilateral involvement, the median was almost twice the value of the bilateral group.

Conclusion

Considering the interactions between the inflammatory mechanisms in OA and the fact that the interaction between neutrophils and lymphocytes shows differences regarding the laterality of coxarthrosis, it can be hypothesized that the inflammatory responses of unilateral and bilateral OA have different dynamics. Moreover, the fact that the samples were collected in only one moment of time does not allow to draw conclusions about whether the observed difference is a cause

or consequence of OA laterality. Therefore, more in-depth studies are required, with several samples collected over time, associated with measurements of other inflammatory markers and the use of flow cytometric analysis techniques to evaluate the impact of the differences in the inflammatory mechanisms observed in this study.

Conflicts of interest

The authors declare no conflicts of interest.

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