CLINICAL STUDY

Can neutrophil-to-lymphocyte, platelet-to-lymphocyte and monocyte-to-lymphocyte ratios be useful to the diagnosis of aseptic loosening after total knee arthroplasty?

Bozgeyik B[1], Tekin SB[2], Mert A[3]

Kadirli State Hospital Department of Orthopedic Surgery Osmaniye, Turkey.
bahribozgeyik@gmail.com

ABSTRACT
BACKGROUND: The aim of this study is to determine the role of hematological parameters – neutrophil/lymphocyte, platelet/lymphocyte, and monocyte/lymphocyte ratios – in the diagnosis of aseptic loosening after total knee arthroplasty.
METHODS: This study retrospectively analyzed the data of 244 patients who had primary total knee arthroplasty and 66 patients with aseptic loosening developed after total knee arthroplasty. The white blood cell counts, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, monocyte/lymphocyte ratio and c-reactive protein levels in both groups were determined using the results of venous blood samples collected during preoperative preparation and compared between the groups.
RESULTS: Our study findings reveal that the monocyte/lymphocyte ratio of the group with aseptic loosening was statistically significantly different from that of the patient group who had primary total knee arthroplasty ($p = 0.02$). Furthermore, although c-reactive protein levels are not high enough to suggest systemic inflammation, the difference between the groups is statistically significant ($p = 0.01$).
CONCLUSIONS: No hematological parameter that could be used in the diagnosis of aseptic loosening has been defined in the literature so far. This study demonstrated that the monocyte/lymphocyte ratio could be a helpful parameter in the diagnosis of aseptic loosening *(Tab. 1, Fig. 1, Ref. 28).* Text in PDF *www.elis.sk*
KEY WORDS: knee, arthroplasty, revision, monocyte, neutrophil.

Introduction

Total knee arthroplasty is an effective surgical option for the treatment of osteoarthritis (1). After this satisfactory surgical procedure some complications may occur. An example is the loosening that develops following total knee arthroplasty. Aseptic loosening is one of the most common conditions requiring revision after total knee arthroplasty (2, 3). Loosening that occurs in the early period after prosthesis implantation is usually associated with inadequate fixation, while the loosening that occurs in the following years is associated with bone resorption (4). This clinical condition can sometimes be difficult to diagnose until the migration of prosthetic components is observed (5, 6). Radiography is insufficient for the diagnosis of loosening in the early stages, and it is more sensitive to the malposition of the prosthetic components and in detection of fractures (7, 8). Bone scintigraphy with technetium helps the diagnosis but it is not specific to aseptic loosening (6, 9).

Given that the diagnosis is mostly based on clinical observation, the difficulty in establishing the diagnosis indicates a necessity of auxiliary diagnostic tools. Therefore, the present study investigated the diagnostic assistance of biochemical parameters. In addition, the selection of eligible patients is critical to establishing the diagnosis of aseptic loosening and the requirement of revision arthroplasty (10).

To the best of our knowledge, the effect of hematological parameters on the diagnosis of aseptic loosening has not been described in the literature so far. Our aim is to examine the diagnostic value of hematological parameters, namely neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR), and monocyte/lymphocyte (MLR) ratios, in aseptic loosening.

Materials and methods

This study retrospectively analyzed the data of patients who presented with the diagnosis of knee osteoarthritis and had undergone primary total knee arthroplasty between January 2005 and January 2020, as well as the data of patients who had undergone revision after total knee arthroplasty due to aseptic loosening diagnosed at follow-up after primary total knee arthroplasty. Our study was approved by the ethics committee and planned in accordance with the Declaration of Helsinki.

[1]Kadirli State Hospital Department of Orthopedic Surgery Osmaniye, Turkey, [2]25 Aralik State Hospital Department of Orthopedic Surgery Gaziantep, Turkey, and [3]Ömer Halis Demir University Hospital Department of Orthopedic Surgery Nigde, Turkey

Address for correspondence: B. Bozgeyik, küçük kizilhisar district gedikardi area 72/B-40, Poste code: 27470 Şahinbey, Gaziantep, Turkey. Phone: 05079711156

Tab. 1. Demographic data of group 1 and group 2 and comparison between groups.

		Group 1	Group 2	p
	No	66	244	
Gender	Male	18 (27%)	44 (18%)	0.24
	Female	48 (73%)	200 (82%)	
	Age	65.51 (49–79)	66.9 (48–90)	0.37
Side	Right	40 (60%)	164 (67%)	0.70
	Left	26 (40%)	80 (33%)	
Comorbidity	None	48 (73%)	168 (68%)	0.418
	1	18 (27%)	64 (27%)	
	≥2	0	12 (5%)	
	CRP	0.78 (0.05–3.9)	0.49 (0.03–3.6)	0.01
	White blood cells	7927 (3800–11400)	7863 (3800–14100)	0.868
Hematological parameters	NLR	2.14 (0.85–3.9)	1.95 (0.43–5.27)	0.26
	PLR	131.57 (67.37–271)	120.77 (39.48–319)	0.25
	MLR	0.28 (0.12–0.5)	0.22 (0.07–0.5)	0.02

The study sample included 310 patients comprising 244 patients who had undergone primary total knee arthroplasty with the diagnosis of osteoarthritis and had accessible follow-up data, and 66 patients who had undergone revision after total knee arthroplasty due to the results of bone scintigraphy with technetium that were compatible with aseptic loosening while having no growth in their intraoperative microbiological culture samples. Aseptic loosening was diagnosed with bone-scan scintigraphy with technetium and x-rays. Excluded were patients scheduled for revision after total knee arthroplasty with the diagnosis of periprosthetic infection incompatible with aseptic relaxation, patients with c-reactive protein (CRP) levels suggestive of infection, patients diagnosed with autoimmune disease, patients under follow-up with the diagnosis of malignancy or those receiving immunosuppressive agents, and patients whose postoperative culture samples were positive for bacterial growth. All patients were operated by one surgeon.

The study patients were evaluated as part of one of two groups. The analyzed variables included age, gender, operated side, presence and number of comorbidities, white blood cell count, CRP levels, and neutrophil, lymphocyte, monocyte, and platelet counts from venous blood samples collected during preoperative preparation, as well as NLR, PLR, and MLR. Furthermore, the time from primary total knee arthroplasty to aseptic loosening was ascertained.

Patients and care

All patients were operated under spinal anesthesia. A tourniquet was used in all operations. Cefazolin sodium was administered for prophylaxis 30–60 minutes before applying the tourniquet and its administration continued intravenously for one postoperative day. In addition, patients were mobilized with full weight-bearing on postoperative day 1. Low molecular-weight heparin (0.4 IU) was being administered subcutaneously for prophylaxis for one month.

Statistical analysis

Descriptive statistics of the study data were presented as mean and standard deviation for numerical variables and frequency and percentage for categorical variables. For statistical analysis between groups one-way ANOVA test followed by the post-hoc Dunn's test. A further ROC analysis was conducted for MLR to analyze the area under the curve as well as sensitivity and specificity. Analyses were conducted using SPSS Version 22.0. The level of p <0.05 was considered significant.

Results

Out of 310 study patients, 66 patients who had undergone revision after total knee arthroplasty with the diagnosis of aseptic loosening were evaluated as part of group 1, and 244 patients who had undergone primary total knee arthroplasty were part of group 2. There were 248 (80 %) women and 62 (20 %) men among 310 patients, and their mean age was 66.61 (48–90) years. The mean time from primary total knee arthroplasty to aseptic loosening was 76.72 (12–180) months. The comparison of data between the groups revealed no statistically significant differences in gender, operated side, age, comorbidity, and white blood cell count. When CRP levels were compared between the groups, the group with aseptic loosening was found to have a statistically significant change (p=0.01). In addition, there was a statistically significant inter-group difference in MLR, one of the hematological parameters (p=0.02). There was no statistically significant inter-group difference in NLR and PLR (p >0.05) (Tab. 1).
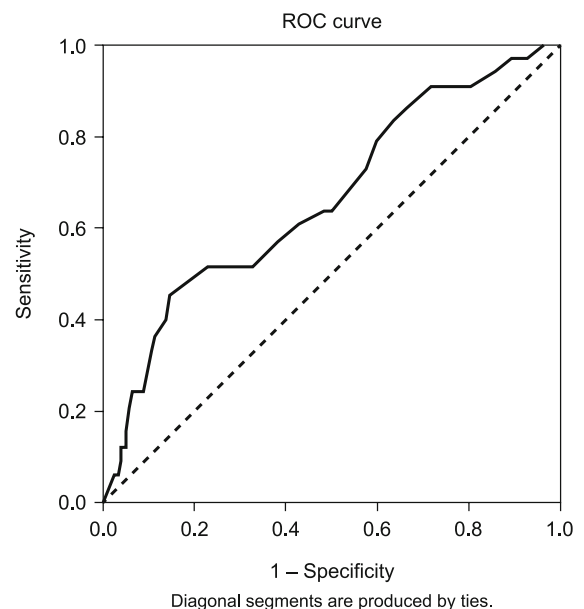
Fig. 1. ROC analysis curves for MLR. AUC = 0.66; sensitivity 77 %, specificity 74 %. ROC – receiver operating characteristic, AUC – area under curve, MLR – monosit/lymphocyte ratio.

The ROC analysis for MLR identified a cut-off value of 0.23 (sensitivity 77 % and specificity 74 %) (Fig. 1).

Discussion

The present study examined the diagnostic value of hematological parameters in patients with aseptic loosening, which is one of the potential complications following total knee arthroplasty. Our findings showed a significant relationship between MLR, one of the parameters, and aseptic loosening (p = 0.02). To the best of our knowledge, this is the first study to analyze the hematological parameters used in the diagnosis of aseptic loosening.

Although the pathophysiology of aseptic loosening has not been fully clarified, research indicates the presence of macrophages and giant cells in the femoral cortex in the samples from the periprosthetic osteolysis site. It has been further shown that there is an appearance compatible with the histology of foreign body reaction and rheumatoid arthritis around the prosthesis (11). Maloney et al demonstrated that the periprosthetic chronic inflammation damaged the prosthesis-bone relationship (12). Glant et al established findings supporting this theory (13). All these findings suggest that aseptic loosening is an intraarticular inflammatory response (14–17). As a result, it was believed that there would be an increase in the blood levels of inflammatory parameters.

The review of the literature reveals several studies on the relationship between the hematological parameters, NLR, PLR, and MLR and malignancies, chronic diseases, obesity, and systemic inflammation (18–24). Gao et al investigated the relationship between NLR, PLR, and MLR and the development of knee osteoarthritis on 119 patients, and established a statistically significant relationship when compared with control groups. The authors found MLR to have a higher diagnostic value than the other two parameters did (25). Shi et al found PLR to be associated with the development of knee osteoarthritis. Büyükavci et al demonstrated the relationship between NLR and the development of osteoarthritis (26).

The study by Trimula et al conducted on 538 patients regarding the development of periprosthetic joint infection after total knee arthroplasty concluded that TLR was a statistically significant parameter (27). In addition, Zhao et al pointed out that NLR and PLR were closely associated with early periprosthetic joint infection (28). These studies showed the relationship between hematological parameters and systemic inflammation. When we reviewed the literature, we did not find any study on the relationship between NLR, PLR, and MLR, i.e., hematological parameters, and the development of aseptic loosening. In our study, we established a significant relationship between the hematological parameter MLR and aseptic loosening. We believe that the use of this parameter in the diagnosis of aseptic loosening would be useful in determining the clinical diagnosis. Furthermore, our study is important in determining the cut-off value for this parameter.

Our study has some limitations. First, it is a retrospective study. However, the impact on the hematological data following the surgery was not examined. In addition, although the number of patients appears limited, it is believed to be sufficient to homogenize both groups.

Conclusion

Aseptic loosening is a process associated with chronic inflammation. MLR can be used to help initiating the diagnosis after total knee arthroplasty and the diagnosis can be then finalized with other auxiliary diagnostic methods.

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