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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

# Can Inflammatory Markers Measured before Total Knee Replacement be an Early Indicator of Revision?

## Total Diz Protezi Öncesi Ölçülen İnflamatuar Belirteçler Revizyonun Erken Belirteci Olabilir Mi ?

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## ABSTRACT

**Aim**: Knee replacement is one of the most commonly performed orthopedic surgeries today. Various prognostic markers are being investigated to reduce the revision rate. In this study, inflammatory markers measured from preoperative blood were evaluated in terms of revision.

**Material and Method**: 100 patients who underwent Total Knee prosthesis between January 2017 and December 2021 (50 revisions and 50 non-revisions) were included in the study. Systemic immune-inflammatory index (SII), neutrophil-lymphocyte ratio(NLR), lymphocyte-monocyte ratio(LMR) and platelet-lymphocyte ratios(PLR) calculated from the hemograms taken before the first surgery of these patients; were evaluated comparatively between those with and without revision surgery.

**Results**: The mean age of the patients was 63.98±9.30 (38-80) in patients who underwent revision, and 65.64±9.45 (46-87) in patients who did not undergo revision. There was no significant difference in age and gender distribution between the revised and non-revisioned groups (p>0.05). No significant difference was observed in the number of neutrophils, lymphocytes, and monocytes between the revised and non-revisioned groups (p>0.05). There was no significant difference in SII, NLR, LMR and PLR values between the revised and non-revisioned groups (p>0.05)

**Conclusion**: SII, NLR, LMR and PLR calculated from the preoperative hemogram taken before total prosthesis surgery, and no significant relationship was found between revision of the knee prosthesis.

**Keywords**: total knee arthroplasty, Systemic immune-inflammatory index, revision, neutrophil-lymphocyte ratio

## ÖZ

**Amaç**: Diz protezi günümüzde en sık uygulanan ortopedik ameliyatlardan biridir. Revizyona gitme oranını düşürmek için çeşitli prognostik belirteçler araştırılmaktadır. Bu çalışmada da ameliyat öncesi alınan kanlardan ölçülen inflamatuar belirteçlerin revizyona gitme açısından değerlendirmesi yapılmıştır.

**Gereç ve Yöntem**: Çalışmaya Ocak 2017-Aralık 2021 tarihleri arasında Total Diz protezi yapılan 100 hasta(50 revizyona giden 50 revizyona gitmeyen) dahil edilmiştir. Bu hastaların ilk ameliyatları öncesi alınan hemogramlarından hesaplanan Sistemik immün-inflamatuar indeks (SII), nötrofil lenfosit oranı(NLR), lenfosit monosit oranı(LMR) ve platelet lenfosit oranları (PLR); revizyon ameliyatı olan ve olmayanlar arasında karşılaştırmalı olarak değerlendirilmiştir.

**Bulgular**: Hastaların yaş ortalaması revizyon yapılan hastalarda 63,98±9.30(38-80), revizyon yapılmayan hastalarda ise 65,64±9.45(46-87) olarak bulundu. Revizyon yapılan ve yapılmayan grup arasında yaş ve cinsiyet dağılımı anlamlı farklılık gözlenmedi(p>0.05). Revizyon yapılan ve yapılmayan grup arasında nötrofil, lenfosit, monosit sayısında anlamlı farklılık gözlenmedi(p>0.05). Revizyon yapılan ve yapılmayan grup arasında SII, NLR, LMR ve PLR değerlerinde anlamlı farklılık gözlenmedi(p>0.05)

**Sonuç**: Total protez ameliyatı öncesi alınan preop hemogramdan hesaplanan Sistemik immün-inflamatuar indeks (SII), nötrofil lenfosit oranı, lenfosit monosit oranı ve platelet lenfosit oranı ile diz protezinin revizyona gitmesi arasında anlamlı bir ilişki bulunamamıştır.

**Anahtar Kelimeler:** total diz artroplastisi, Sistemik immün-inflamatuar indeks, revizyon, nötrofil-lenfosit oranı

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## INTRODUCTION

The knee joint is the largest joint of the human body and has complex movements. The joint most affected by degenerative diseases like osteoarthritis is the knee. Osteoarthritis (OA) is the most common disease of the musculoskeletal system (2). OA; It is a complex disease that causes degeneration of joint components through a combination of structural, mechanical and biological pathways (3). There are many factors in the etiology, and it is the result of the interaction of systemic and local factors (4,5).

The history of total knee arthroplasty, which has been successfully applied for many years in the treatment of knee joint osteoarthritis (gonarthrosis), dates back to the middle of the 19th century. In addition to clinical and functional positive results, loosening due to long years of use of the prosthesis is an absolute result. The need for revision knee arthroplasty arises as a result of the instability that develops due to the decrease in the adhesion between the bone and the prosthesis (6).There are many factors in the loosening of knee arthroplasty components. Overuse, obesity, implant design, surgical technique and infection are some of these factors (6). Miller et al. reported that the first step of the mechanism that causes prosthesis loosening is micro-movements between the prosthesis and bone(7). Other mechanisms are osteolysis, component collapse, inflammatory response to microparticles formed as a result of polyethylene insert abrasion, and inflammation that develops in infective conditions (7).The basic mechanism underlying osteolysis, which is the first condition for the development of non-septic loosening, is the biological response to microparticles formed as a result of prosthesis wear. As a result of phagocytosis of these particles in the joint by macrophages, it initiates the inflammatory process. It has been shown that mediators such as IL-1, IL-6, TNF, PGE2 and metalloproteinase are secreted in the inflammatory process (9-11).

It has been shown that inflammation markers such as C-reactive protein (CRP), IL-6 and TNF-α, which are widely used, are significant in the prognosis of OA and the level of pain due to arthrosis (12,13). On the other hand, parameters such as systemic immune-inflammatory index (SII), neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio and platelet-lymphocyte ratio are practical and innovative biomarkers that are developing in cancer and inflammatory diseases(14).

In this study, we aimed to examine whether the Systemic immune-inflammatory index (SII), neutrophil lymphocyte ratio, lymphocyte monocyte ratio and platelet lymphocyte ratio measured before knee replacement surgery can be used as a prognostic marker for revision.

## MATERIAL AND METHOD

This study was approved by the local ethics committee and complies with the Helsinki Declaration. The informed consent was waived due to the retrospective nature of the study and the assessment utilized anonymous research findings.

In this study, the data of 164 patients who applied to the Orthopedics and Traumatology outpatient clinic with the complaint of pain between January 2017 and December 2021 were retrospectively analyzed. 42 patients who were found to have septic loosening as a result of the examinations were excluded from the study.

Twenty-two patients with known autoimmune disease, acute and chronic infectious disease, systemic inflammatory disease, current immunosuppressive drug use, anti-inflammatory drug use in the last 15 days, chronic liver disease, history of malignancy, and disease causing coagulation disorder were excluded. As a result of physical examination and imaging, 50 patients who were diagnosed with aseptic loosening in knee prosthesis, underwent revision total knee arthroplasty and had at least 1 year of regular follow-up were selected. Fiftypatients undergoing total knee arthroplasty and not undergoing revision knee arthroplasty were selected as the control group. As a result, a total of 100 patients were included in the study. It was observed that total knee prosthesis was applied in various brands and models in line with the physician's preference in the patients. All of the patients were selected from those who had a total knee prosthesis that PCL-Substituting Knee Prosthesis

Neutrophil, lymphocyte, platelet and monocyte values obtained from CBC tests performed within 10 days before surgery in the included patients were used. Systemic Inflammatory Index (SII)(Neutrophil *Platelet/Lymphocyte), Neutrophil-Lymphocyte ratio (NLR), Lymphocyte-Monocyte ratio (LMR) and Platelet-Lymphocyte ratio (PLR) parameters were calculated.

### Statistical analysis

IBM SPSS version 26.0 software program (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Mean, standard deviation, minimum and maximum values were used in the descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov-Smirnov test. Mann-Whitney U test and independent sample test were used in the analysis of quantitative independent data. Chi-square test was used in the analysis of qualitative independent data, and Fischer test was used when the chi-square test conditions were not met. A P value of $<0.05$ was considered statistically significant.

## RESULTS

The study included 100 patients, 50 revisions (41 Female, 9 Male) and 50 non-revision (41 Female, 9 Male) patients between 2017-2021.

The mean age of the patients was 63.98±9.30 (38-80) in patients who underwent revision, and 65.64±9.45 (46-87) in patients who did not undergo revision.

There was no significant difference in age and gender distribution between the revised and non-revisioned groups (p>0.05).

No significant difference was observed in the number of neutrophils, lymphocytes, and monocytes between the revised and non-revisioned groups (p>0.05). There was no significant difference in SII, NLR, LMR and PLR values between the revised and non-revisioned groups (p>0.05) (**Table 1**).

## DISCUSSION

A hemogram is a laboratory evaluation performed before almost all surgeries. It is frequently used for many evaluations because it is both cheap and easy to access (14). It has been shown in many studies that there is a correlation between the proportional relationship between the blood markers in the hemogram and the prognosis of some diseases (15-18). No relationship was found between the indicators and revision.

Recent studies have shown that the SII value calculated by peripheral lymphocyte, neutrophil and platelet counts is a good index for demonstrating local immune response and systemic inflammation. SII is an index of inflammation that is easy to calculate and can be reproduced from CBC results. It has been found to be significant in the prediction of prognosis and in patient follow-up in conditions such as various malignancies (hepatocellular cancer, esophageal cancer, small cell lung cancer), cardiogenic shock, adult Still's disease, ankylosing spondylitis (15-20).

Although there are many studies on the cancer prognosis of emerging and innovative biomarkers with parameters such as systemic immune-inflammatory index (SII), neutrophil lymphocyte ratio, lymphocyte monocyte ratio and platelet lymphocyte ratio (14), no significant difference was observed in our study in terms of the prognosis of total knee prosthesis (p>0.05).

It has been found that these parameters, which have significant results as inflammatory markers in many malignant and inflammatory diseases, do not give significant results as early markers of knee replacement revision. This may be because the inflammation that develops in aseptic knee arthroplasty is not at a level to affect systemic blood parameters. Also, the small number of patients in the study may have affected the statistical analysis. In addition, patients with autoimmune diseases, a history of acute and chronic infections, systemic inflammatory diseases, a history of malignancy and coagulation disorders were not included in the study. However, a similar trial was conducted in this group of patients and it was likely that a statistically significant change in the parameters studied could be detected.

Our study had several limitations. Our study included only a limited number of patients and is single centered. Future multicenter studies with higher patient numbers will provide more accurate information.

## CONCLUSION

No significant correlation was found between the Systemic immune-inflammatory index (SII), neutrophil lymphocyte ratio, lymphocyte monocyte ratio and platelet lymphocyte ratio calculated from the preop hemogram taken before the total prosthesis surgery and revision of the knee prosthesis.

**Table 1. Relationship with demographic data and hematological parameters of patients**

| Descriptive Statistics | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Revised | | | Non-revised | | | p |
| | Mean±SD | Minimum | Maximum | Mean±SD | Minimum | Maximum | |
| NEU | 4,50±1.8 | 2,31 | 10,86 | 4,87±2.13 | 1,90 | 12,90 | 0,23 |
| LYM | 2,01±0.73 | 0,70 | 3,84 | 2,19±0.77 | 0,50 | 4,30 | 0,19 |
| MONO | 0,47±0.17 | 0,02 | 0,93 | 0,48±0.18 | 0,20 | 1,30 | 0.7 |
| SII | 732,50±629.91 | 257,83 | 3173,63 | 687,01±553.02 | 163,00 | 3168,00 | 0,98 |
| NLR | 2,62±1.98 | 1,17 | 11,63 | 2,90±3.58 | 0,98 | 24,00 | 0,63 |
| LMR | 8,01±26.58 | 1,20 | 192,00 | 4,90±1.91 | 1,08 | 10,75 | 0,13 |
| PLR | 156,47±89.55 | 61,39 | 590,14 | 133,61±48.93 | 66,25 | 271,33 | 0,29 |
| AGE | 63,98±9.30 | 38 | 80 | 65,64±9.45 | 46 | 87 | 0,55 |
| Gender | | Female 41<br>Male 9 | | | Female 41<br>Male 9 | | 1.00 |

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** This study was approved by the local ethics committee and complies with the Helsinki Declaration.

**Informed Consent**: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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