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# The Effect of Femoral Nerve Block on the Neutrophil-to-Lymphocyte Ratio in Total Knee Arthroplasty

Total Diz Artroplastilerinde Femoral Sinir Bloğunun Nötrofil Lenfosit Oranı Üzerine Etkisi

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**Informed Consent:** The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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**Abstract:** This study investigated whether femoral nerve block (FNB) reduces postoperative systemic inflammation, as measured by the neutrophil-to-lymphocyte ratio (NLR), in patients undergoing total knee arthroplasty (TKA) under spinal anesthesia. It was hypothesized that FNB would mitigate the inflammatory response by alleviating pain and surgical stress. In this retrospective cohort study, data from 199 patients who underwent unilateral TKA between January 1 and December 1, 2024, were analyzed. Patients were divided into two groups: Group F (n=97), who received spinal anesthesia combined with femoral nerve block (FNB), and Group C (n=102), who received spinal anesthesia with standard analgesia only. Preoperative and 24-hour postoperative NLR values were obtained from complete blood counts. Statistical analysis was performed using IBM SPSS Statistics 26.0. The independent samples t-test or Mann-Whitney U test was used, depending on data distribution. Baseline NLR values were similar between groups (Group C: 1.85, Group F: 2.08; p=0.255). Postoperatively, NLR increased significantly in both groups; however, the increase was significantly lower in Group F (Group C: 9.15 vs. Group F: 5.58; p<0.001). The percentage increase in NLR was 356.58% in Group C and 170.99% in Group F (p<0.001), indicating a markedly attenuated inflammatory response in patients receiving FNB. FNB significantly reduces the postoperative rise in NLR in patients undergoing TKA under spinal anesthesia. This effect may result from both superior pain control and the anti-inflammatory properties of local anesthetics. These findings suggest that FNB may enhance recovery beyond analgesia by modulating the surgical stress response.

**Keywords:** Total knee arthroplasty, femoral nerve block, neutrophil-to-lymphocyte ratio, inflammation, spinal anesthesia.

**Özet:** Bu çalışma, spinal anestezi altında total diz artroplastisi (TDA) uygulanan hastalarda femoral sinir bloğunun (FSB) nötrofil lenfosit oranı (NLR) üzerindeki etkisini incelemeyi hedeflemiştir. NLR, cerrahi sonrası sistemik inflamasyonun bir göstergesi olarak kullanılmıştır. FSB'nin postoperatif ağrı ve stres yanıtını azaltarak inflamasyonu hafifleteceği ve NLR'de düşüş sağlayacağı iddia edilmektedir. Yöntemler: Retrospektif kohort analizi, 1 Ocak 2024 - 1 Aralık 2024 tarihleri arasında tek taraflı TDA geçiren 199 hasta. Grup F (n=97): Spinal anestezi + FSB uygulanan hastalar, Grup K (n=102): Sadece spinal anestezi ile standart analjezi alan hastalar. Preoperatif ve postoperatif 24. saatte NLR değerleri tam kan sayımından hesaplandı. İstatistiksel analizler için IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, ABD) yazılımı kullanıldı. Grupların karşılaştırılmasında; verilerin dağılımına göre bağımsız örneklem t testi veya Mann-Whitney U testi kullanıldı. Preoperatif NLR gruplar arasında benzerdi (Grup K: 1.85, Grup F: 2.08, p=0.255). Postoperatif NLR: Grup K'da 9.15'e yükselirken Grup F'de 5.58 olarak kaldı (p<o,001).NLR artış oranı Grup K'da %356.58 iken Grup F'de %170.99 (p<0.001) olarak bulundu. FSB uygulanan hastalarda NLR artışı anlamlı derecede daha azdı, bu da inflamasyonun baskılandığını göstermektedir. Femoral sinir bloğu, TDA sonrası cerrahi stres ve inflamasyonu azaltarak NLR'de belirgin bir düşüş sağlayabilir. Bu etki, FSB'nin etkili ağrı kontrolü ile stres yanıtını sınırlaması ve lokal anesteziklerin antienflamatuar özelliklerinden kaynaklanabilir. Bulgular, FSB'nin analjezik faydasının ötesinde iyileşme sürecini olumlu etkileyebileceğini düşündürmektedir.

**Anahtar Kelimeler:** Total diz artroplastisi, femoral sinir bloğu, nötrofil lenfosit oranı, inflamasyon, spinal anestezi

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## 1. Introduction

Total knee arthroplasty (TKA) is a widely performed surgical intervention used to restore joint function and alleviate pain when severe knee joint damage cannot be managed with conservative treatments. Despite its effectiveness, patients often experience moderate to severe pain in the early postoperative period, which can negatively impact rehabilitation, patient satisfaction, and overall surgical outcomes. Although opioids have long been a mainstay in perioperative pain management due to their strong analgesic properties, their use is linked to several side effects, including nausea, respiratory depression, urinary retention, and the risk of dependency. As a result, multimodal analgesia—an approach that integrates multiple techniques and medications to optimize pain control— has become the preferred strategy for managing perioperative pain in TKA (1,2). This approach includes preemptive analgesia, central neuraxial blocks (such as spinal anesthesia), peripheral nerve blocks, patient-controlled analgesia, local infiltration, and combinations of opioid and non-opioid medications. Together, these methods aim to enhance pain relief, support faster recovery, and minimize opioid requirements (1).

A key component of multimodal analgesia, femoral nerve block (FNB), is a regional anesthesia technique frequently employed in knee surgeries. Temporary blockade of the femoral nerve using local anesthetics effectively reduces surgical pain, particularly in the anterior knee region, thereby decreasing opioid requirements and their associated side effects (3,4). In recent years, regional anesthesia techniques have gained attention not only for their analgesic effects but also for their influence on surgical stress and inflammation. Some experimental and clinical studies suggest that peripheral nerve blocks may modulate the inflammatory response to surgery. For instance, in an animal model, peripheral nerve block was shown to enhance acute inflammatory responses to surgical incision (5). Conversely, continuous peripheral block techniques have been reported to reduce inflammatory markers (6,7), highlighting the potential of peripheral nerve blocks to influence inflammation and immune response.

The neutrophil-to-lymphocyte ratio (NLR), a simple and widely available laboratory marker, is calculated from complete blood count data and reflects the ratio of neutrophils to lymphocytes. First described by Zahorec in 2001, NLR is considered an indicator of systemic inflammation and stress, reflecting the balance between neutrophilia and lymphopenia (8). In response to major surgery, trauma, sepsis, or shock, neutrophil counts typically increase while lymphocyte counts decrease, resulting in an elevated NLR. NLR has demonstrated prognostic and predictive value in various clinical contexts, including cardiovascular risk assessment, tumor burden and prognosis in cancer, and diagnosis and prognosis in sepsis and infections (9-14). In healthy adults, the average NLR has been reported to be approximately 1.65, with a 95% confidence interval ranging from 0.78 to 3.53 (15).

Postoperative pain is closely associated with tissue injury and inflammation. Experimental studies have shown that systemic inflammation increases pain sensitivity and lowers the pain threshold in humans (16). Moreover, severe acute pain can exacerbate stress responses and suppress immune function, negatively impacting recovery (7). Therefore, effective control of postoperative pain is essential for both patient comfort and reduction of the surgical stress response. In this context, the femoral nerve block administered after TKA may not only relieve pain but also attenuate the inflammatory response induced by surgery.

The present study aimed to investigate the effect of femoral nerve block on NLR as a marker of postoperative inflammation in patients undergoing TKA. We compared postoperative NLR values between patients who received femoral nerve block and those who did not, all of whom underwent spinal anesthesia. Our hypothesis was that femoral nerve block would reduce systemic inflammatory response by mitigating postoperative pain and stress, leading to a significant decrease in NLR values.

## 2. Materials and Methods

**Study Design and Sample**: This retrospective study was based on data collected from patients who underwent unilateral total knee arthroplasty (TKA) in the Orthopedics Department of our hospital between January 1 and December 1, 2024. Ethical approval from the institutional review board and necessary institutional permissions were obtained (Decision No:

2024/012). The inclusion criteria consisted of patients aged between 18 and 80 years who underwent elective primary TKA under spinal anesthesia. Patients were excluded if they had malignancy, sepsis, underwent emergency surgery, experienced thromboembolic events, had multiple trauma, severe respiratory failure, or a history of pneumonia. A total of 199 patients who met the inclusion criteria were enrolled in the study.

### Data Collection

Demographic data, anesthesia and surgical records, and laboratory findings were retrospectively reviewed from the hospital's electronic medical records. For each patient, preoperative neutrophil and lymphocyte counts, along with NLR values, were recorded based on blood tests performed at hospital admission. Similarly, neutrophil, lymphocyte, and NLR values within the first 24 postoperative hours were noted. In accordance with the institutional protocol, all patients who received spinal anesthesia as the primary anesthetic technique had been administered hyperbaric bupivacaine. In patients who underwent a single-shot femoral nerve block, the procedure had also been performed in line with the institutional protocol—immediately after the completion of surgery, while the patient was still on the operating table, under sterile conditions and with ultrasound guidance, using 20 mL of 0.25% bupivacaine. Based on the analgesic method, patients were divided into two groups: those who received a femoral nerve block after spinal anesthesia (Group F) and those who received standard analgesia without a femoral block (Group C).

### Statistical Analysis

Sample size was determined based on a power analysis targeting 80% power and 5% alpha error to detect a significant difference. Statistical analysis was performed using IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA). Normality of distribution for continuous variables was assessed with the Kolmogorov-Smirnov test. Data were expressed as mean ± standard deviation for normally distributed variables and as median (25th-75th percentile) for non-normally distributed variables. Categorical variables were presented as frequencies and percentages. The independent samples t-test or Mann-Whitney U test was used for between-group comparisons of continuous variables, depending on distribution. Categorical variables were analyzed using Pearson’s chi-square test or Fisher’s exact test. A p-value <0.05 was considered statistically significant.

## 3. Results

In this retrospective study, a total of 218 patients were evaluated. Nineteen patients who did not meet the eligibility criteria or had incomplete data were excluded from the study. The remaining 199 patients were included and divided into two groups based on the anesthesia technique used: 102 patients who received spinal anesthesia alone were assigned to Group C, while 97 patients who received spinal anesthesia combined with a femoral nerve block were assigned to Group F (Figure 1).

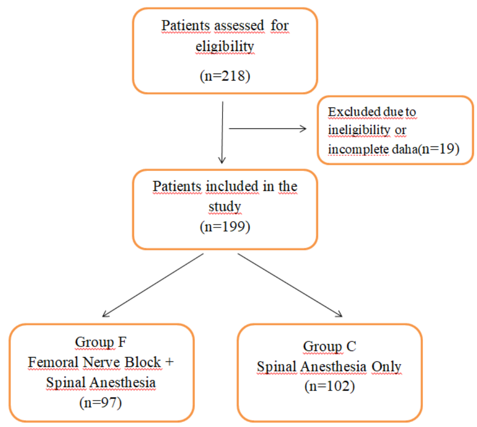


**Figure 1.** Study flowchart

The average age of the patients was around 65 years, and 74% of the study population were female. There were no statistically significant differences between Group F (n = 97) and Group C (n = 102) regarding age, gender distribution, ASA classification, or comorbid conditions such as diabetes and hypertension (all p-values > 0.05; Table 1).

**Table 1.** Demographic Characteristics of the Patients

| Characteristic | Group C (n=102) | Group F (n=97) | p value |
|---|---|---|---|
| **Age (years)** | 64 ± 7 | 65 ± 8 | 0.717ǂ |
| **Sex** | | | 0.780* |
| **Female** | 75 (73.5%) | 73 (75.3%) | |
| **Male** | 27 (26.5%) | 24 (24.7%) | |
| **ASA Classification** | | | 0.111* |
| **ASA I** | 16 (15.7%) | 24 (24.7%) | |
| **ASA II** | 86 (84.3%) | 73 (75.3%) | |
| **Coronary artery disease** | 4 (3.9%) | 5 (5.2%) | 0.743** |
| **Respiratory disease** | 8 (7.8%) | 11 (11.3%) | 0.401* |
| **Hypertension** | 54 (52.9%) | 39 (40.2%) | 0.072* |
| **Diabetes mellitus** | 29 (28.4%) | 19 (19.6%) | 0.145* |

*Data are presented as mean ± standard deviation or n (%). ASA: American Society of Anesthesiologists physical status classification.*
ǂ *Independent samples t-test*
** Chi-square test*
*** Fisher's exact test*

Preoperative and postoperative NLR values are presented in Table 2. There was no significant difference in preoperative NLR values between the groups (p=0.255). However, at 24 hours postoperatively, the median NLR in Group C increased markedly to 9.15 (5.99–13.12), while in Group F it remained lower at 5.58 (3.89–7.58), a statistically significant difference (p<0.001).

**Table 2.** Neutrophil-to-Lymphocyte Parameters of the Patients

| Neutrophil/Lymphocyte Ratio | Group C (n=102) | Group F (n=97) | p value |
|---|---|---|---|
| **Preoperative** | 1.85 (1.5–2.66) | 2.08 (1.58–2.67) | 0.255 |
| **Postoperative (24th hr)** | 9.15 (5.99–13.12) | 5.58 (3.89–7.58) | <0.001 |
| **Percentage Change (%)** | 356.58 (190.57–626.23) | 170.99 (59.47–300.27) | <0.001 |

Data are presented as median (25th–75th percentile). Mann-Whitney U test was used. Percentage change = 100 × (Postoperative – Preoperative) / Preoperative Although both groups exhibited increased NLR values postoperatively compared to baseline, the rate of increase was significantly higher in the control group. The median percentage increase in NLR was 356.6% (190.6–626.2) in Group C and 171.0% (59.5–300.3) in Group F ($p<0.001$). These findings suggest that patients who did not receive FNB experienced approximately twice the increase in NLR compared to those who did (Figure 2).

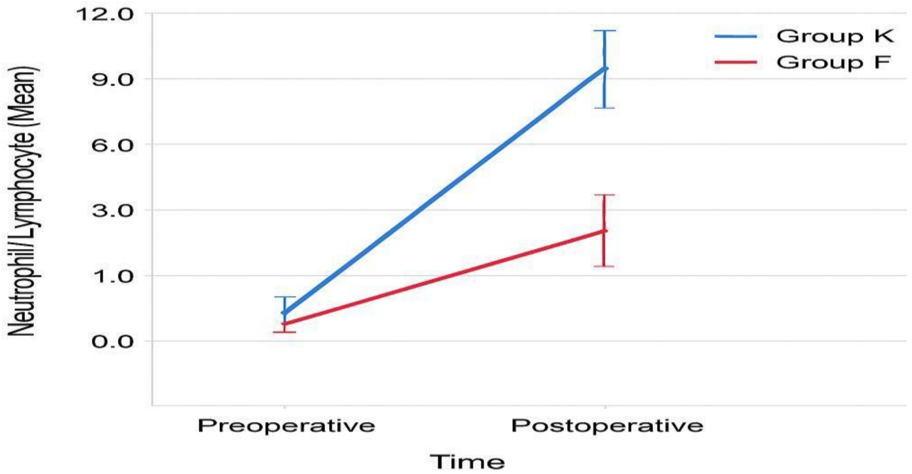


**Figure 2.** Neutrophil-to-Lymphocyte Parameters Over Time.

## 4. Discussion

This study demonstrated that the addition of femoral nerve block in patients undergoing TKA under spinal anesthesia significantly reduced postoperative NLR values, a marker of systemic inflammation. Patients who received FNB had notably lower postoperative NLR compared to those who did not, indicating that while spinal anesthesia alone partially suppresses surgical stress, additional peripheral nerve block further limits NLR elevation. Our findings suggest that femoral nerve block, in addition to its analgesic effect, may help mitigate the inflammatory response to surgery.

Surgical trauma triggers a cascade of immunological changes. Neutrophil counts increase rapidly due to lysosomal enzyme release, bone marrow mobilization, and delayed apoptosis, while lymphocyte counts decline due to migration to peripheral tissues and apoptosis (8). This concurrent neutrophilia and lymphopenia lead to a marked rise in NLR within the first 24 hours postoperatively. In major surgeries, neutrophil percentages may exceed 80% and lymphocytes drop below 10% (8). Elevated NLR correlates with the severity of surgical stress and clinical outcomes. HigherNLR values areassociated with more severe surgical trauma or sepsis, reflecting the intensity of the stress response (8,17). In our study, the control group exhibited nearly a four-fold increase in NLR following TKA, confirming a substantial systemic inflammatory response. In contrast, the FNB group had only a two-fold increase, suggesting reduced surgical stress.

The preoperative NLR values observed in both groups (Group C: ~1.85, Group F: ~2.08) were consistent with reference ranges reported in the literature. In a study by Forget et al., the normal NLR range in healthy adults was reported as 0.78–3.53, with an average of approximately 1.65 (15). Both groups in our study were within this normal range preoperatively, indicating comparable baseline inflammatory status. Postoperatively, while NLR increased in both groups, Group C exceeded the normal range substantially, reaching a median value of 9, whereas Group F showed a more moderate increase with a median of 5.6. NLR values above 5 are generally considered indicative of significant systemic inflammation (13, 14). Thus, patients in the control group appeared to experience a higher inflammatory burden compared to those who received FNB.

Anesthetic technique is known to influence surgical stress and inflammatory responses. General anesthesia (GA) may provoke a strong neuroendocrine stress response due to intubation, surgical awareness, and systemic drug effects, whereas regional techniques like spinal anesthesia (SA) may attenuate inflammatory responses by limiting afferent signaling to the medulla and reducing sympathetic activity (18). In a study by Hadimoğlu et al. on cesarean deliveries, patients under GA exhibited significantly higher levels of IL-6 and NLR compared to those under SA (16). Similarly, a recent retrospective study by Bengü Köksal et al. showed that patients undergoing upper extremity surgery under general anesthesia had significantly higher postoperative NLR values (mean 6.12) than those who received infraclavicular peripheral nerve block (mean 3.82) (7). The authors emphasized that better analgesia and reduced opioid use in the nerve block group may positively influence immune response. They proposed that the superior pain control and anti-inflammatory effects of local anesthetics help suppress excessive inflammatory responses to surgery (7). These findings support the notion that regional anesthesia techniques, whether central or peripheral, can help reduce systemic inflammation.

Our study adds a novel perspective to the existing literature by demonstrating the additional anti-inflammatory benefit of peripheral nerve block when used in conjunction with spinal anesthesia. Previous studies comparing GA with SA or GA with peripheral nerve block had shown reduced NLR with regional techniques (7,16,18). In our study, all patients received SA, which already limits surgical stress, yet the addition of FNB further reduced NLR. This finding underscores the value of combining effective analgesic methods such as FNB with regional anesthesia to attenuate the inflammatory response. Lower pain scores and reduced intraoperative/postoperative opioid requirements in the FNB group may have contributed to lower stress hormone and pro-inflammatory cytokine levels. Moreover, local anesthetics are known to have anti-inflammatory effects by modulating neutrophil and macrophage activity in addition to blocking nerve conduction. These mechanisms likely underlie the reduced neutrophilic response and lymphopenia observed in patients who received FNB.

### Limitations

Our study had some limitations. Firstly, inflammation was assessed solely using the neutrophil-to-lymphocyte ratio (NLR); other inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), were not included in the evaluation. Incorporating these additional markers might have offered a more comprehensive view of the inflammatory response. However, there is substantial evidence in the literature supporting the link between NLR and systemic inflammation, and our results were interpreted within this framework. Secondly, due to the retrospective nature of the study, precise documentation of sensory block durations related to spinal and femoral blocks, as well as quantitative pain scores (e.g, VAS), was not consistently available. However, the analgesic effect of the femoral nerve block was evaluated based on clinical observations, institutional standards, and supported by findings from previous literature.

## 5. Conclusion

In patients undergoing total knee arthroplasty under spinal anesthesia, the addition of femoral nerve block was associated with a significant reduction in postoperative NLR levels, a hematological marker of surgical stress. Through effective pain control and attenuation of the inflammatory response, peripheral nerve blocks may contribute positively to recovery in patients undergoing major orthopedic surgery.

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