

# Does the pre-operative neutrophil-lymphocyte ratio have a predictive value in detecting infection in type 3 open tibia diaphysis fractures?

✉ Tahsin Sami Çolak, M.D., ✉ Ahmet Fevzi Kekeç, M.D.

Department of Orthopaedics and Traumatology, Necmettin Erbakan University Meram Faculty of Medicine, Konya-Turkey

## ABSTRACT

**BACKGROUND:** This retrospective study was aimed to investigate whether the pre-operative neutrophil-lymphocyte (N/L) ratio has a predictive value in terms of evaluating the development of infection in patients with type 3 open fractures of the tibia diaphysis.

**METHODS:** A total of 72 patients with type 3 open tibia fractures who consulted to the emergency service at the Necmettin Erbakan University Meram Faculty of Medicine, during the period between 2015 and 2020 were retrospectively examined. A total of 39 patients who underwent external fixator in the first treatment were included in the study. The information pertaining to the patients such as the patient demographic data, type of injury, wound cultures, and N/L rates during the pre-operative period were recorded. Patients were divided into two groups based on the presence of infection: Group 1 (12 patients) consisted of patients who had infection, and Group 2 (27 patients) consisted of patients who had no infection.

**RESULTS:** 34 (87.2%) of the patients were male and 5 (12.8%) were women. The mean age of these patients was  $43.18 \pm 18.67$  (19–80). Infection was detected in 12 (30.8%) out of 39 patients. Of these patients, 9 (75%) were monomicrobial, and 3 (25%) were polymicrobial. The most common mechanism of the injury was gunshot injury in 16 (41%) of all patients. However, there was no significant difference between the groups in terms of mechanism of injury ( $p=0.445$ ). When all patients were examined in terms of N/L rates and presence of infection, there was no significant difference between Group 1 and Group 2 ( $p=0.976$ ).

**CONCLUSION:** Although N/L ratio of the blood in the pre-operative period has a predictive value for chronic diseases, we believe that it has no predictive value for detecting infection in patients with type 3 acute open tibia fractures.

**Keywords:** Infection; neutrophil-lymphocyte ratio; open tibia fracture.

## INTRODUCTION

Although new generation treatment protocols have been developed, open fractures are one of the orthopedic emergencies that challenge clinicians today, as it has always been the case in the past. Open fractures are most commonly seen in the tibia due to possible exposure to trauma and low soft tissue covering.<sup>[1,2]</sup> Open fractures are classified into three main types according to the Gustilo–Anderson classification. Type 3 open fractures with injuries which are greater than 10 cm, accompanied by separation of the periosteum and soft-tissue defects pose a great risk of infection.<sup>[3]</sup> Development

of infections may lead to a number of difficulties and complications which are hard to treat such as insufficient soft-tissue covering, exposed bone structures, non-unions, and osteomyelitis that can cause loss of limb in the long-term.<sup>[4]</sup> Therefore, having an early indicator to identify patients who may be infected in the early preoperative period will be useful to prevent possible complications.<sup>[5–7]</sup>

A number of laboratory parameters (C-reactive protein, sedimentation, white sphere, neutrophil percentage, neutrophil-lymphocyte (N/L) ratio) with predictive values are reported for many diseases.<sup>[8–13]</sup> The fact that these parameters are

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Address for correspondence: Tahsin Sami Çolak, M.D.

Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi, Ortopedi ve Travmatoloji Anabilim Dalı, Konya, Turkey

Tel: +90 332 - 223 67 68 E-mail: drtahsincolak@gmail.com

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easily accessible and cost-effective, as well as being useful for patient follow-up gives an advantage to the clinician. There are studies in the literature which state that these parameters can be also useful in predetermining possible bone infections in different groups of patients.<sup>[14–16]</sup>

The N/L ratio is attained by dividing the total number of neutrophils by the total number of lymphocytes in the blood count. It has been indicated by many publications that the N/L ratio can be an easily estimated parameter in indicating systemic inflammation.<sup>[9,10]</sup> It is known that the N/L ratio increases in cases of malignancies and many other situations such as postoperative mortality after hip fracture and myocardial infarction.<sup>[11–13]</sup> In addition, it is reported that the N/L ratio can also be used in orthopedic infectious patient groups such as osteomyelitis, diabetes-related infection, and peripheral artery disease.<sup>[15,16]</sup> As far as we know, there is no study conducted previously in the literature that investigated the relationship between infection that can develop at an early stage in patients with open tibia fractures and pre-operative laboratory parameters.

In this study, the aim is to investigate whether the N/L ratio determined in the pre-operative period has a predictive value in terms of evaluating the development of infection in patients with type 3 open fractures of the tibial diaphysis.

## MATERIALS AND METHODS

A total of 72 patients with type 3 open tibia fractures who consulted to the emergency service at Necmettin Erbakan

University Meram Faculty of Medicine between 2015 and 2020 were retrospectively examined. To create a standard group of patients and to avoid affecting the results of the study, a set of exclusion criteria is defined which is composed of agricultural injuries, pathological fractures, additional organ injuries and vascular nerve injury, additional bone pathologies, and non-diaphysis fractures. In addition, to form a homogeneous group, patients who underwent external fixator in their first treatment were included in the study. A total of 39 patients who underwent external fixator in the first treatment were included in the study. Patients' age, gender, the type of injury, whether there is reproduction in their cultures or not, and the N/L rates during the pre-operative period were retrospectively reviewed from the hospital records. In addition, the causative microorganisms in patients with reproduction in their culture were recorded. Patients were divided into two groups based on the presence of infection: Group 1 (12 patients) consisted of patients who had infection and Group 2 (27 patients) consisted of patients who had no infection.

The results were statistically analyzed using SPSS 22 (IBM Corp., Armonk, NY, USA). Average values were expressed as mean±standard deviation. Mechanism of injury and presence of infection were examined using Chi-square test. The statistical distribution of the N/L ratio was performed using the Mann-Whitney U-test. The value of  $p < 0.05$  was considered statistically significant.

## RESULTS

About 34 (87.2%) of the patients were male, and 5 (12.8%)

**Table 1.** Patients' demographic data

	All patients	Group 1	Group 2
Gender, n (%)			
Female	5 (12.8)	3 (25)	2 (7.4)
Male	34 (87.2)	9 (75)	25 (92.6)
Mean age	43.18±18.67 (19–80)	38.08±17.21 (20–67)	45.44±19.15 (19–80)

**Table 2.** Patients' mechanisms of injury GSI, IVTA, OVTA, WA, FFH

Type of injury	All patients n (%)	Group 1 n (%)	Group 2 n (%)	p-value
GSI	16 (41)	6 (50)	10 (37)	0.445
IVTA	7 (17.9)	3 (25)	4 (14.8)	
OVTA	7 (17.9)	–	7 (25.9)	
WA	6 (15.4)	1 (8.3)	4 (14.8)	
FFH	3 (7.7)	2 (16.7)	2 (7.4)	

GSI: Gunshot injury; IVTA: Intra-vehicle traffic accident; OVTA: out of vehicle traffic accident; WA: Work accident; FFH: Fall from height.

**Table 3.** Patients' N/L ratios

	All patients n (%)	Group 1 n (%)	Group 2 n (%)	p-value
N/L ratio	8.85±6.05 (0.49–24.19)	9.1±6.1 (1.26–21.81)	8.75±6.15 (0.49–24.19)	0.976

N/L: Neutrophil-lymphocyte.

of them were women. The mean age of these patients was 43.18±18.67 (19–80). Infection was detected in 12 (30.8%) out of 39 patients. Of these patients, 9 (75%) were monomicrobial, 3 (25%) were polymicrobial. Demographic data of patients are summarized in Table 1.

The most common mechanism of injury was gunshot injury in 16 (41%) of all patients; in 6 (50%) of the patients who had infection and in 10 (37%) of the patients who had non-infection. However, there was no significant difference between the groups in terms of injury mechanism ( $p=0.445$ ) (Table 2). When all patients were examined in terms of N/L rates and presence of infection, there was no significant difference between Group 1 and Group 2 ( $p=0.976$ ) (Table 3).

## DISCUSSION

To the best of our knowledge, the relationship between the N/L ratio and the infection which may develop at an early stage in emergency situations such as open fractures has not been previously studied in the literature. In our study, we discovered that the N/L ratio in the blood in the pre-operative period did not have a predictive value in terms of detecting infection in patients with acute type 3 open tibia fractures. In the study conducted by Yapıcı et al.<sup>[15]</sup> they state that the N/L ratio has a predictive value in diabetes-induced infection and osteomyelitis. Demirdal et al.<sup>[16]</sup> report in their study that the N/L ratio has a predictive value in peripheral artery disease and in patients who need amputation due to diabetes-induced infection. Therefore, the N/L ratio was shown as an infection indicator in these studies. However, the selected patients had chronic diseases and long-term infection. Since patients in our study were in the acute period, we did not obtain similar results which were obtained and presented in the literature. We believe that the motive behind this is caused by the difference between acute and chronic infection.

In fact, the N/L ratio can be interpreted as an indirect indicator of a patient's immune response. It has been reported in systematic meta-analyses and many studies that high N/L ratio can be used as an indicator of poor prognosis, especially in cancer patients.<sup>[17–20]</sup> It can be explained by the increase in the N/L ratio as metastasis' increasing the number of neutrophils through various cytokines and chemokines and suppressing the number of lymphocytes.<sup>[21]</sup> Besides, the N/L ratio has been proven to have a predictive value not only in

cancer patients, but also in a number of diseases presenting with inflammation.<sup>[8,9]</sup> Therefore, when a patient has other diseases, this might produce false-positive results regardless of the disease studied.<sup>[14]</sup> Sigmund et al.<sup>[14]</sup> put forward that although the sensitivity of such parameters checked in the blood is relatively high, their specificity is low. It should be kept in mind that similar parameters are not specific to a disease but may increase in many different systemic conditions (such as pneumonia, urinary tract infection, and multiple trauma conditions) or chronic diseases (such as cancer and autoimmune diseases).<sup>[14,15]</sup> We believe that the fact that there is no significant difference between the groups with and without infection in terms of the N/L ratio in our study may be related to this.

Infections that may develop after an open tibia fracture can be divided into two as superficial infection or deep infection.<sup>[22]</sup> In addition to this, infections occur as monomicrobial or polymicrobial in terms of their causative agent. In our study, we encountered 3 cases with polymicrobial factors, and when they were evaluated among themselves, we found out no significant relationship between the N/L ratio and the polymicrobial aspect of the infection. Again, Sigmund et al.<sup>[14]</sup> put forward in their study that inflammation biomarkers routinely looked for in patients with fractures cannot be used for the presence or exclusion of infection, but it would be correct to take increased serum values into account in patients with fracture-related infection. Based on the results of our study, we believe that infection cannot be predetermined by looking at a single laboratory value in patients with open tibia fractures.

In a systemic review conducted by Dickson et al.,<sup>[22]</sup> it is reported that infection development after circular external fixator applied to patients with type 3 open tibia fractures is statistically detected that they are significantly less compared to other techniques (plate, nail, monolateral external fixator, reamed and unreamed nails). In the study conducted by Webb et al.,<sup>[23]</sup> they evaluated surgical technique and infection development and identified infection in 15.4% of the patients who were treated with nailing procedure and in up to 40% of the patients who were treated with external fixator. Naique et al.<sup>[24]</sup> reported in their study that the different results obtained in the development of infection after an open tibia fracture are due to differences in open fracture type, mechanism of injury, integrity of soft tissue, type, and timing of

surgery performed at the early stages and also age. However, to obtain more homogeneous data in our study, we excluded cases treated with other techniques in terms of surgical technique and included only those cases who were treated with external fixator. Therefore, we could not compare the applied surgical techniques with each other in terms of infection development. In our study, the incidence of infection was 30.8%. This suggests that we obtained parallel results which were obtained and presented in the literature.<sup>[23]</sup>

In addition, Decruz et al.<sup>[25]</sup> reported in their study that open fractures of the tibia diaphysis are mostly caused by traffic accidents (57.1%). Similarly, Weiss et al.<sup>[26]</sup> reported in their study that this type of fractures occurs most frequently after a traffic accident (43%). In our study, we also identified the most common mechanism of injury as gunshot injury. In our study, when the injury mechanism and infection development were examined, we found that the injury mechanism did not make a significant difference in the development of infection.

Undoubtedly, our study had some limitations. First of all, our study was a retrospective study. We set many exclusion criteria, considering that we could obtain more homogeneous data. This relatively reduced the number of our patients. We believe that more specific data can be obtained through prospective studies with proper planning and with a greater number of patients.

## Conclusion

In conclusion, as far as we are concerned, our study is the first study questioning the usability of pre-operative N/L ratio as an infection indicator in type 3 open fractures. Our study showed that the pre-operative N/L ratio in type 3 open fractures does not have a predictive value for a possible infection.

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**Conflict of Interest:** None declared.

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## ORJİNAL ÇALIŞMA - ÖZ

### Ameliyat öncesi nötrofil-lenfosit oranının Tip 3 tibia diafiz açık kırıklarında enfeksiyon açısından prediktif değeri var mıdır ?

Dr. Tahsin Sami Çolak, Dr. Ahmet Fevzi Kekeç

Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi, Ortopedi ve Travmatoloji Anabilim Dalı, Konya

**AMAÇ:** Bu geriye dönük çalışmada tibia diafiz tip 3 açık kırıklı hastalarda ameliyat öncesi dönemdeki nötrofil-lenfosit (N/L) oranının enfeksiyon gelişiminin değerlendirilmesi açısından prediktif değeri olup olmadığının araştırılması amaçlanmıştır.

**GEREÇ VE YÖNTEM:** 2015–2020 yılları arasında Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi acil servisine başvuran tibia tip 3 açık kırıklı 72 hasta geriye dönük olarak tarandı. İlk tedavisinde eksternal fiksator yapılan toplam 39 hasta çalışmaya alındı. Hastaların demografik verileri, yaralanma şekli, kültürlerinde üreme olup olmaması ve ameliyat öncesi dönemdeki N/L oranları kayıt edildi. Hastalar enfeksiyon varlığına göre enfeksiyon olanlar: grup 1 (12 hasta), enfeksiyon olmayanlar: grup 2 (27 hasta) olarak iki gruba ayrıldı.

**BULGULAR:** Tüm hastaların 34'ü (%87.2) erkek beşi (%12.8) kadındı. Bu hastaların yaş ortalaması  $43.18 \pm 18.67$  (19–80) idi. Toplam 39 hastadan 12'sinde (%30.8) enfeksiyon tespit edildi. Hastaların dokuzu (%75) monomikrobiyal üçü (%25) polimikrobiyalı. Tüm hastaların 16'sında (%41), enfeksiyon olanların altısında (%50) ve enfeksiyon olmayanların 10'unda (%37) en sık yaralanma mekanizması ateşli silah yaralanmasıydı. Ancak gruplar arasında yaralanma mekanizması açısından anlamlı bir fark bulunmadı ( $p=0.445$ ). Tüm hastalar N/L oranları ile enfeksiyon varlığı açısından incelendiğinde grup 1 ve grup 2 arasında anlamlı fark tespit edilmedi ( $p=0.976$ ).

**TARTIŞMA:** Ameliyat öncesi dönemdeki kanda hesaplanan N/L oranının kronik hastalıklarda prediktif değeri olmasına karşın akut tibia tip 3 açık kırıklı hastalarda enfeksiyon varlığı açısından prediktif değerinin olmadığı kanaatindeyiz.

**Anahtar sözcükler:** Enfeksiyon; nötrofil-lenfosit oranı; tibia açık kırık.

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