

# Can ratio of neutrophil-to-lymphocyte count and erythrocyte sedimentation rate in diabetic foot infecti on predict osteomyelitis and/or amputation?

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## Abstract

The aim of this study was to search for any relations between the neutrophil-to-lymphocyte ratio (NLR) and the development of osteomyelitis and the need for amputation in patients with diabetic foot infection (DFI). All data included DFI patients who were hospitalized in our Infectious Diseases Clinic between 2012 and 2015 and who were classified according to International Classification Disease Code System. 75 patients were analyzed in the study. The DFI patients were stratified into 3 groups of whom had amputation procedure, whom had only debridement/drainage procedure and whom had any surgery procedure. Sidac post hoc analysis was used to perform the effects of NLR, C-reactive protein, erythrocyte sedimentation rate and glycosylated hemoglobin on the surgery procedure status. The DFI patients were also stratified into two another separate group for another analysis to search for the effect of NLR values on the development of osteomyelitis. The mean value of NLR in the amputated patients' group (15.7±10.3) was significantly higher than those with debridement procedure (9.9±5.6) and those without any surgery (6.0±2.8) (P=0.001). NLR values were also found significantly higher in patients with osteomyelitis in the second analysis (P=0.004). In this study, the NLR was found to have a predictive value on the development of osteomyelitis and on the progression to amputation in patients with DFI.

## Introduction

Irritation, inflammation, ischemia, neuropathy and infections are important factors in diabetic foot pathophysiology.<sup>1,2</sup> Studies

showed that changes in the amount of lymphocytes and neutrophils play an important role in inflammation and infection.<sup>3,4</sup> NLR is cheap and it can easily be calculated by using the peripheral blood count. The NLR which is an indicator of immune response and systematic inflammation, has a prognostic effect on many diseases including coronary artery disease<sup>5,6</sup> and cancer.<sup>7,8</sup> In the literature, few studies showed that NLR was meaningful for the diagnosis of diabetes and for the prediction of development of diabetic complications.<sup>9,10</sup> Whether or not NLR can predict the prognosis in diabetic foot infection is unclear. Therefore, the aim of this study was to investigate any relations between the NLR and the development of osteomyelitis and the need for amputation in patients with DFI.

## Materials and Methods

All data included DFI patients who were hospitalized in our Infectious Diseases Clinic between 2012 and 2015 and who were classified according to International Classification Disease (ICD-10) Code System. 25 patients whom had amputation procedure, 25 patients whom had only debridement/drainage procedure, and 25 patients whom had any surgery procedure were included in the study. Imaging methods, physical examination and/or laboratory methods were used to put the diagnosis of DFI. Totally, 75 patients were analyzed in this study. NLR, CRP, ESR and HbA1c values of the all patients were obtained from the medical records. Variance analysis and Sidak post hoc analysis were used to perform the effects of NLR, CRP, ESR and HbA1c on the surgery procedure status.

The DFI patients were also stratified into two another separate group for another analysis to search for the effect of NLR values on the development of osteomyelitis. We used the same 75 patients for both of the two different analysis. The groups for this second analysis were stratified as the patients with osteomyelitis and the patients without osteomyelitis.

Statistical analysis was performed by using SPSS software version 22.0 (IBM, USA). P value <0.05 was accepted as significant.

## Results

A total of 75 patients [males: 54 (72%) females: 21 (28%)] were included in the study. Seventy two percent of the patients

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were male and the mean age of the all patients was 60.9±11.6 years. 100% (n=25) of the all patients whom had amputation had osteomyelitis, 68% (n=17) of the all patients whom had only debridement/ drainage procedure had osteomyelitis, and 44% (n=11) of the all patients whom had any surgery procedure had osteomyelitis. The mean values of NLR, CRP, ESR and HbA1c on admission were 10.60±8.0, 151.57±98.9 mg/L, 78.5±25.6 mm/h and 9.3±2.3 %, respectively.

The mean value of NLR in the amputated patients' group (15.7±10.3) was significantly higher than those with debridement procedure (9.9±5.6) and those without any surgery (6.0±2.8)(P=0.001). Mean CRP values of amputated patients (182± 94.9) and patients with only debridement procedure (171.6±99.5) were higher than patients without any surgery procedure (100.9±85.3) (P=0.006). And mean ESR values of amputated patients (93.5±19.1) and patients with only debridement procedure (80.0±16.2) were higher than patients without any surgery procedure (62.1±29.4) (P=0.001). On the other side, no significant difference were found among the HbA1c levels of the three group patients (9.5±2.6), (10.0±2.6) (9.0±2.8), respectively; P=0.425) (Table 1).

The initial NLR and ESR values were found significantly higher in patients with osteomyelitis (P=0.004, P=0.001, respectively) (Table 2).

**Table 1. Neutrophil-to-lymphocyte ratio, C-reactive protein, erythrocyte sedimentation rate and glycosylated hemoglobin values of the patients according to surgery procedure groups.**

Mean values	No-surgery, Group 1 (n <sub>1</sub> =25)	Debridement/drainage, Group 2 (n <sub>2</sub> =25)	Amputation, Group 3 (n <sub>3</sub> =25)	P-value	Post-hoc
NLR	6.0±2.8	9.980±5.6	15.7±10.3	0.001	3>2.1
CRP (mg/L)	100.9±85.3	171.6±99.5	182.1±94.9	0.006	3.2>1
ESR (mm/h)	62.1±29.4	80.0±16.2	93.5±19.1	0.001	3.2>1
Hb1Ac (%)	9.5±2.6	10.0±2.6	9.0±2.8	0.425	

NLR: Neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb1Ac: glycosylated hemoglobin.

**Table 2. Neutrophil-to-lymphocyte ratio and erythrocyte sedimentation rate values of patients with and without osteomyelitis.**

Mean values on admission	Osteomyelitis absent (n <sub>1</sub> =22)	Osteomyelitis present (n <sub>2</sub> =53)	P-value
NLR	6.0±3.7	12.3±8.6	0.004
ESR (mm/h)	51.9± 18.3	89.6±19.3	0.001

NLR: Neutrophil-to-lymphocyte ratio; ESR: Erythrocyte sedimentation rate.

## Discussion

DFI are serious problems in patients with diabetes, about 10% to 25% of patients with diabetes develop a foot ulcer and 60% of them are infected.<sup>11</sup> Diabetic foot ulcers are the most common reasons for the hospitalizations and for the operations in patient with diabetes.<sup>12,13</sup> Operations of diabetic patients lead to losses in both manpower and economy.<sup>12,13</sup> DFI are classified as mild, moderate and severe according to the 2012 Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections.<sup>14</sup> Inflammatory markers such as CRP, ESR, procalcitonin could help to distinguish uninfected ulcers from infected ones. Especially ESR is an important laboratory marker in the diagnosis of DFO.<sup>15</sup> It is well known that ESR levels higher than 70 mm/h is one of the most powerful laboratory finding in the diagnosis of DFO. Van Asten *et al.* evaluated 24 DFO patients and found the mean initial ESR value as 78 mm/h.<sup>16</sup> Ertugrul *et al.* reported that ESR ≥65 mm/h together with a wound size ≥2 cm<sup>2</sup> were significant threshold levels for the diagnosis of DFO.<sup>17</sup> In our study, the mean value of ESR was found as 89 mm/h. The ESR values of the patients with osteomyelitis were found significantly higher than the ESR values of the patients without osteomyelitis. Our findings were similar to the literature.<sup>16,17</sup>

Clinicians like to establish predictive factors for prognosis. In the last years, several investigators searched about NLR to use NLR in the diagnosis and in the prognosis of different infectious diseases such as

brucellosis, tuberculosis, inactive hepatitis B.<sup>18-20</sup> Loonen *et al.* reported that NLR could be used as a predictor for bloodstream infections in the emergency care units.<sup>21</sup> Also, NLR was shown as a significant inflammatory marker in determining the severity, prognosis and differential diagnosis of bacterial pneumonia.<sup>22,23</sup> Kahramanca *et al.* reported significantly higher NLR values in patients who required more than one debridement than in patients who required only one debridement.<sup>24</sup> NLR might also be valuable for determining the prognosis of Fournier's gangrene.<sup>24</sup> Lou *et al.* showed that post-treatment neutrophil-lymphocyte ratio independently predicts amputation in critical limb ischemia without operation.<sup>25</sup> We showed that NLR was significantly higher in patients with osteomyelitis. We also found that high NLR value was independent risk factor for progression to amputation. Our results comply with the literature.<sup>24,25</sup> Lastly, NLR level might be a predictive biomarker for determining progression to amputation. Further studies are needed in this area to have an exact decision on establishing NLR as a prognostic factor.

## Conclusions

Neutrophil-to-lymphocyte ratio value could be used as a cheap and simple biomarker to predict the development of osteomyelitis and/or amputation risk in patients with DFI. It may also be established as a prognostic factor with further studies.

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