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Preoperative PLR and NLR values as predictors of mortality in diabetic foot amputations.

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Abstract

Background: The incidence of lower extremity complications associated with diabetes mellitus has been increasing as the number of patients with diabetes rises. Amputation is the most critical complication. The aim of this study was to elucidate the correlations of the preoperative platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) with wound complications, re-amputations, and mortality.

Materials and methods: This study included 258 patients who underwent lower extremity amputations due to diabetes (152 with below-knee amputations and 106 with above-knee amputations). The preoperative PLR, NLR, and hemoglobin concentration were calculated. Postoperative deaths were classified as those that occurred within the first 6 months (Group I), from 6 months to 1 year (Group II), from 1 to 3 years (Group III), and beyond 3 years (Group IV). Age, sex, re-amputation, and wound complications were investigated.

Results: The amputation level and mortality rate were significantly correlated (p=0.017). No significant difference was found among Groups I to IV in either the haemoglobin concentration (9.4, 10.1, 10.1, and 10.7 g/dl, respectively; p=0.709) or PLR (247.7, 222.3, 229.4, and 195.0, respectively; p=0.678). The NLR was significantly higher in Group I (9.2) than in Groups II to IV (5.5, 6.3, and 5.6, respectively; p=0.012).

Conclusion: Patients with a high preoperative NLR and above-knee amputation due to diabetes had a higher mortality rate. The PLR is not a suitable prognostic marker for patients undergoing amputation due to diabetes.

Keywords: Diabetes mellitus, Amputation, Mortality, Platelet/Lymphocyte ratio, Neutrophil/Lymphocyte ratio.

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Introduction

Diabetes mellitus (DM) is most frequently seen in people with a poor socioeconomic status. This chronic disease severely impairs the patient's comfort level. Approximately 10% of the general population is affected by DM and its complications [1]. Especially in its later stages, DM leads to peripheral neuropathy, vasculopathy, and foot deformities. Treatment-resistant chronic ulcers, arthropathies, and osteomyelitis develop secondary to these neurovascular pathologies [2]. In the early stages of the disease, treatment with wound care, debridement, and tissue flaps may be curative; in the later stages, however, amputation is the only salvage therapy. The general health status of the patient, vasculature of the extremity, and presence of chronic wounds and infection must be considered when determining the amputation level. However, predicting the optimal amputation level and associated prognosis is challenging for physicians. Many studies have evaluated the amputation frequency and mortality in patients with DM [3]. Although the platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) are useful and frequently used laboratory parameters in many fields of study, few studies have evaluated their clinical use in patients with diabetic foot [4]. Measurement of these ratios is a cost-effective method with which to predict the prognosis of oncologic and cardiac patients in terms of mortality and morbidity [5,6]. In the present study, we evaluated the correlation of a high preoperative PLR and NLR with wound complications, re-amputation, and mortality in patients with DM.

Materials and Methods

Patients with tibial or femoral amputation due to DM were enrolled in the study from April 2005 to December 2012. Data were collected on age, sex, amputation level (above-knee, below-knee), wound complications, and the need for re-amputation. Postoperative deaths were confirmed using the local data system. The preoperative hemoglobin concentration, platelet count, lymphocyte count, neutrophil count, PLR, and NLR were calculated. Postoperative deaths were classified as those that occurred within the first 6 months (Group I), from 6 months to 1 year (Group II), from 1 to 3 years (Group III), and beyond 3 years (Group IV). The PLR, NLR, and hemoglobin

concentration were compared between patients who died (Groups I-III) and those who survived (Group IV).

Statistical analysis

Data processing and statistical analysis were carried out using SPSS v.23 (IBM Corp., Armonk, NY, USA). The normality of the data was analyzed with the Shapiro-Wilk test. An independent-sample t test and one-way analysis of variance were used to compare normally distributed parameters. The Kruskal-Wallis test was used to compare data that were not normally distributed. Pearson's chi-squared test was used for the categorical data analysis. The results are presented as arithmetic mean ± standard deviation, median (minimum-maximum), frequency, and percentage. A p value of <0.05 was considered statistically significant.

Results

In total, 258 patients were included in the study (167 male, 91 female). The mean age of the male patients was 60.2 years (range, 38-92 years), and the mean age of the female patients was 68.6 years (range, 40-91 years). The 258 amputations comprised 152 below-knee and 106 above-knee amputations. Eight of the below-knee amputations required re-amputation, and 12 developed wound complications. Five of the above-knee amputations required re-amputation, and nine developed wound complications. There was no significant difference in re-amputation or wound complications between patients who underwent below-knee and above-knee amputations (p=0.746). There was a significant difference in the mortality rate between patients who underwent below-knee and above-knee amputations (Table 1). Although the hemoglobin concentrations were lower in Group I, there was no statistically significant difference (Table 2). The PLR was lowest in Group IV, but there was no statistically significant difference among the groups (Table 3). The NLR was significantly higher in Group I than in the other groups (Table 4). Patients with a high NLR had a higher risk of mortality in the first 6 months after amputation.

Table 1. *Association between survival and amputation level.*

	Patients who survived (n)	Patients who died (n)	p value*
Below-knee amputation (n)	85	67	0.017
Above-knee amputation (n)	37	69	

*p values of <0.05 were considered statistically significant.

Table 2. *Preoperative hemoglobin concentrations according to time of postoperative death.*

	Patients (n)	Haemoglobin (g/dl)	p value*
Group I	94	9.4 ± 2.2[b]	0.709
Group II	28	10.1 ± 1.8[b]	
Group III	14	10.1 ± 1.0[b]	
Group IV	122	10.7 ± 1.8[b]	

Postoperative deaths were classified as those that occurred within the first 6 months (Group I), from 6 months to 1 year (Group II), from 1 to 3 years (Group III), and beyond 3 years (Group IV).

Haemoglobin is presented as mean ± standard error of the mean.

*p values of <0.05 were considered statistically significant.

[b]No significant difference.

Table 3. *Preoperative platelet/lymphocyte ratio according to time of postoperative death.*

	Patients (n)	PLR	p value*
Group I	94	247.7 (12.6-776.9)[b]	0.678
Group II	28	222.3 (55.9-677.1)[b]	
Group III	14	229.4 (129.8-816.9)[b]	
Group IV	122	195.0 (0.8-1185.2)[b]	

Postoperative deaths were classified as those that occurred within the first 6 months (Group I), from 6 months to 1 year (Group II), from 1 to 3 years (Group III), and beyond 3 years (Group IV).
PLR, platelet/lymphocyte ratio. PLR is presented as median (range).
*p values of <0.05 were considered statistically significant.

[b]No significant difference.

Table 4. *Preoperative neutrophil/lymphocyte ratio according to time of postoperative death.*

	NLR	p value*
Group I	9.2 (0.9-36)[a]	0.012
Group II	5.5 (1.3-17.1)[b]	
Group III	6.3 (2.9-15.5)[b]	
Group IV	5.6 (0.0-29.2)[b]	

Postoperative deaths were classified as those that occurred within the first 6 months (Group I), from 6 months to 1 year (Group II), from 1 to 3 years (Group III), and beyond 3 years (Group IV).
NLR, neutrophil/lymphocyte ratio. NLR is presented as median (range).
*p values of <0.05 were considered statistically significant.
[b]No significant difference.

Discussion

DM is a chronic disease with an increasing incidence. With this increase in incidence, the numbers of complications such as chronic wound ulcers, infection, and gangrene are also rising. Peripheral neuropathy is a key complication that leads to diabetic ulcers and osteomyelitis and contributes to unsuccessful treatment. Patients with neuropathy develop motor, sensory, and autonomic dysfunction [7]. These complications in patients with DM must be assessed by a multidisciplinary team comprising an endocrinologist, infection disease specialist, plastic surgeon, cardiovascular surgeon, and orthopedic surgeon [8]. In patients with DM, sores or ulcers in the foot region start as small wounds and then move toward the proximal aspect of the extremity causing serious health problems. Approximately 70% of the health costs in these patients are associated with wound healing problems after amputation, home care, and rehabilitation

expenses [9]. Therefore, the treatment of every patient must be personalized to save time and determine the optimal level of amputation; both are important in terms of cost.

Many different predictive factors for successful ulcer healing and amputation have been investigated in patients with DM [10]. Ai et al. [11] reported that higher cystatin C concentrations were associated with ulcer healing problems. Diabetic foot ulcers and related major and minor complications can be prevented by angioplasty revascularization [12]. Diabetic foot problems and amputation are mostly seen in male patients. Alvarsson et al. [13] found that the mean age of male patients at the time of DM-related amputation was 10 years younger than that of female patients and that re-amputation was more frequently required in male patients. The results of the present study support these data; 167 of 258 patients were male and their mean age was 60.2 years, which was younger than that of the female patients. This may be explained by the heavier physical workload, higher rate of smoking, and lower sociocultural levels among men than women. Therefore, physicians may need to exercise greater caution against diabetic foot problems and implement alternative methods of wound care and treatment in male patients.

Debridement and free flaps are the preferred treatment methods for acute and superficial ulcers, whereas amputation is more appropriate in the presence of deep ulcers, infection, and vascular dysfunction. Distal-level amputation will provide better functional capacity; however, the risks of wound complications and re-amputation are higher at this level of amputation [14]. In the present study, we found no significant correlation of the amputation level with wound complications or re-amputation. Other factors such as the general health status of the patient and vascular status of the extremity are also considered when determining the optimal level of amputation; thus, determining the ideal level of amputation may be difficult. Lepantalo et al. [15] reported a 72% success rate after knee-level amputation with rapid recovery of the amputation stump and emphasized the importance of early mobilization. There is a significant difference in mortality between patients with DM who do and do not undergo amputation, and higher-level amputations are associated with increased mortality rates. The present study, comparison of patients who underwent below-knee versus above-knee amputation revealed that above-knee amputation was associated with a higher mortality rate. However, this mortality rate may be independent of the level of amputation and may instead be related to the overall progression of the disease.

The present study revealed a correlation of the preoperative PLR and NLR with mortality. The PLR in Groups I, II, and III (patients who died) was higher than that in Group IV, but no significant difference was noted. Surgical and medical therapy should be administered more carefully for patients with a high PLR. Some studies have indicated that high platelet counts may trigger vascular occlusion and deep vein thrombosis, subsequently leading to thrombus formation. Lower extremity venous congestion may lead to venous ulcers and wound complications. High platelet numbers can cause a relatively high PLR, which may lead to venous congestion in the lower extremities. The height of the PLR may lead to venous ulcers and wound complications in patients with DM. An elevated PLR is also known to increase the incidence of pulmonary embolism and cardiac pathologies [16]. The NLR is another marker used to determine the prognosis of and mortality associated with certain diseases. A high NLR in patients with type II DM is associated with a high risk of coronary artery disease [17]. A high NLR is also correlated with a poor prognosis in patients with hip fractures and bone metastasis [17,18]. In this study, the association between the NLR and mortality was also compared. The NLR was higher in patients who died within the first 6 months than in patients who died later. The NLR is a relatively acute-phase reactant and may serve as a new indicator with which to predict early mortality. This is the first study to predict the prognosis of diabetic amputations using the PLR and NLR. However, a major limitation is the fact that we did not account for other risk factors in our comparison of the PLR and NLR.

Statement of human and animal rights

The study protocol was approved by the Institutional Human Ethics Committee of the Ondokuz Mayıs University.

Conclusion

In patients with DM, the preoperative PLR and NLR can be used as prognostic markers when predicting the need for lower extremity amputation and risk of wound complications, re-amputation, and mortality.

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