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*Research Article*

# Analysis of the factors affecting mortality after non-traumatic major lower extremity amputations

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ABSTRACT

***Objective:*** The aim of this study was to evaluate the prognostic factors affecting mortality after major lower extremity amputations in patients with diabetes mellitus and peripheral vascular disease.

***Methods:*** For this retrospective study, 484 patients (345 male, 139 female) who were previously diagnosed with diabetes mellitus and peripheral vascular disease and underwent first-time nontraumatic major lower extremity amputations between January 2008 and January 2021 were included. The mean age of the patients was 64.2 ± 13.8 (20-114). In 32.4% of patients, peripheral vascular disease was the underlying cause, whereas diabetes mellitus was responsible for the etiology in 67.6% of patients. About 68.8% of patients had below-knee amputations, whereas 2.9% had bilateral below-knee amputations, 27.1% had above-knee amputations, and 1.2% had hip disarticulation performed. Gender, age, amputation level, amputation etiologies, Charlson comorbidity index, need for blood transfusion, and laboratory findings such as hemoglobin, platelet, albumin, erythrocyte sedimentation rate, C-reactive protein, sodium, potassium, and neutrophil to lymphocyte ratio levels were recorded preoperatively and at the time of discharge. Patients were grouped as died ≤1 month, ≤3 months, ≤6 months, and ≤12 months or alive.

***Results:*** Advanced age, female gender, high Charlson comorbidity index, blood transfusion requirement, proximal amputation level, preoperative low platelet, preoperative low albumin, and parameters such as low hemoglobin, low erythrocyte sedimentation rate, high sodium, low platelet, low albumin, high C-reactive protein, and high neutrophil to lymphocyte ratio at time of discharge were seen to have a statistically significant effect on mortality at 1 month, 3 months, 6 months, and 12 months postoperatively. Preoperative high C-reactive protein had a statistically significant effect on mortality at 1 and 3 months postoperatively, whereas low C-reactive protein had a statistically significant effect on mortality at 6 months postoperatively. High potassium at the time of discharge was associated with mortality at 6 and 12 months postoperatively.

***Conclusion:*** This study has shown us that mortality rates are affected by modifiable parameters at the time of discharge such as hemoglobin, sodium, potassium, platelet, and albumin, and normalization of these parameters before discharge could reduce the rates of mortality in the postoperative period.

***Level of Evidence:*** Level IV, Prognostic Study

## Introduction

Peripheral vascular disease (PVD), diabetes mellitus (DM), trauma, and malignant tumors are the main indications for lower extremity amputations.[1] Peripheral vascular disease and DM, which are among the etiological factors that cause amputation, are also important because the only problem in both diseases is not in the extremity but the whole body involved. The vast majority of these patients have other accompanying diseases.[1,2] In this patient group, approximately one-fifth of the patients die in the first month, and approximately half in the first year, especially after major amputation.[3-5]

It is known that factors such as advanced age, proximal amputation level, chronic renal disease, cerebrovascular disease, and cardiovascular disease are very important in early and late mortality after major amputation.[6] Neutrophil to lymphocyte (N/L) ratio, which is an indicator of the increase in inflammation in the body, is used to predict mortality in many diseases.[7,8] Studies investigating the relationship between the N/L ratio and post-amputation mortality have been reported in the literature in recent years.[8-13] Most of these studies were performed after amputation in patients with PVD.[8-11,13] The literature data on the effect of N/L ratio on mortality after amputation due to diabetes are very limited. In addition, the number of patients included in these studies is generally 400 or less.

This study aimed to analyze the effect of the possible risk factors including the N/L ratio on short-term (1, 3, 6, and 12 months) mortality after major lower extremity amputations in patients with DM and PVD.

## Materials and Methods

This retrospectively designed study was approved by the local ethical committee (date: February 22, 2021, number: 2021/02-08). The information of patients who underwent lower extremity amputation in a single tertiary care hospital between January 2008 and January 2021 was obtained from the system

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where the surgery data were recorded. More detailed information about patients who underwent amputation was obtained from the hospital registry system. Patients who underwent lower extremity amputation for the first time and were diagnosed with PVD or DM were included in the study. Patients who underwent amputation at the ankle and distal level, who underwent amputation due to tumor, chronic osteomyelitis, or trauma, who underwent second lower extremity amputation in the same center, and whose laboratory data were missing were excluded from the study. Of 925 patients who underwent lower extremity amputation, 382 were excluded because they were at the ankle and lower level. Twenty-two patients were excluded because they were amputated twice and 4 patients were excluded because they were amputated 3 times. Six patients were excluded because of insufficient data, and 27 patients were amputated due to trauma, tumor, or chronic osteomyelitis. As a result, 484 patients were included in the study.

Variables such as gender, age, amputation level, amputation etiologies, Charlson comorbidity index (CCI),[13] and need for blood transfusion were investigated from the file information of the patients. As laboratory data, hemoglobin (Hb), platelet, albumin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), sodium (Na), potassium (K), and N/L ratio levels before the operation and at the discharge were recorded.

The state mortality system was used to investigate whether patients were alive or dead. If the patients died, the death dates were recorded. Postoperative survival durations (in months) of deceased and surviving patients were also examined. After these evaluations, patients were grouped as died ≤1 month, ≤3 months, ≤6 months, and ≤12 months or alive'.

**Statistical analysis**

The statistical package for Social Sciences version 24 (IBM SPSS Corp, Armonk, NY, USA) was used for the statistical analysis. The Shapiro–Wilk test was used to evaluate the normality of groups. For the normally distributed continuous data, the *t*-test was used. If the distribution of data was not normal, the Mann–Whitney *U*-test was used to compare the groups. Categorical data were analyzed by using the Fisher's exact or chi-squared tests. As the Chi-squared test was found to be significant, subgroup analyses were performed with Bonferroni-corrected 2-proportion *z*-test. Binary logistic regression analysis was performed including the variables with a *P*-value ≤ .20 to evaluate the important factors in first, third, sixth, and twelfth month of mortality. MedCalc Statistical Software version 15.8 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2015) was used for the receiver operating characteristic (ROC) curve analysis for N/L ratio levels before the operation and at the time of discharge. Kaplan–Meier survival curve was created for survival estimates. A *P*-value below .05 was accepted as statistically significant.

**HIGHLIGHTS**

- Peripheral vascular disease, diabetes mellitus are two of the main indications for lower extremity amputations, which is associated with a high mortaliy rate. This study aimed to analyze the effect of the possible risk factors including the neutrophil to lymphocyte (N/L) ratio on short-term mortality after major lower extremity amputations in patients with DM and PVD.
- The results showed that high N/L ratio at the time of discharge is an important indicator for estimating mortality in patients with a major lower extremity amputation. Female gender was associated with higher mortality in this population. Additionally, a 70% mortality was seen in the long-term follow-up in patients who had major lower extremity amputation.
- The results indicate that patients with a high N/L ratio at discharge should be more followed-up more closely. Taking precautionary measures for their comorbidities can be effective in reducing mortality rates.

## Results

One hundred thirty-nine of the patients were female (28.7%). The mean age of the patients was 64.2 ± 13.8 (20-114) years, the mean mortality time was 13.7 ± 23.1 (0-111.4) months, and the mean survival time was 61.1 ± 44 (0.03-146.7) months. The mean age of female patients who underwent amputation [69.2 ± 15.7 (20-114)] was statistically significantly higher than that of males [62.1 ± 12.4 (27-98)] ($P < .001$). Below-knee amputation was performed in 333 patients (68.8%), bilateral below-knee in 14 patients (2.9%), above-knee amputation in 131 patients (27.1%), and hip disarticulation in 6 patients (1.2%). While PVD was the cause of amputation in 157 (32.4%) patients, the etiology was DM in 327 (67.6%) patients who underwent amputation. Of the patients, 93 (19.2%) died within the first month, 141 (29.1%) died within the first 3 months, 157 (32.4%) died within the first 6 months, and 184 (38%) died within the first year. The mortality rate in the study population, regardless of the duration, was 69.4% (336 patients). Kaplan–Meier survival curve is shown in Figure 1.

Advanced age ($P < .001$), female gender ($P = .002$), high CCI ($P < .001$), blood transfusion requirement ($P = .034$), and proximal amputation level ($P < .001$) were statistically significantly effective on the first month of mortality. Laboratory findings that are statistically significant in the first month of mortality were low platelet ($P < .001$), low albumin ($P < .001$), high CRP ($P = .04$), and low N/L ratio ($P = .001$) levels for the preoperative period and low Hb ($P < .001$), high ESR ($P < .001$), high Na ($P < .001$), low platelet ($P < .001$), low albumin ($P < .001$), high CRP ($P < .001$), and high N/L ratio ($P < .001$) levels for the discharge period (Table 1).

Advanced age ($P < .001$), female gender ($P < .001$), proximal amputation level ($P < .001$), high CCI ($P < .001$), and blood transfusion requirement ($P = .003$) were statistically significantly effective on the first 3 months of mortality. Laboratory findings that are statistically significant in the first 3 months of mortality were low platelet ($P < .001$), low albumin ($P < .001$), and high CRP ($P = .035$) levels for the preoperative period and low Hb ($P < .001$), low ESR ($P < .001$), high Na ($P < .001$), low platelet count ($P < .001$), low albumin ($P < .001$), high CRP ($P < .001$), and high N/L ratio ($P < .001$) levels for the discharge period (Table 1).

Advanced age ($P < .001$), female gender ($P < .001$), proximal amputation level ($P < .001$), high CCI ($P < .001$), and blood transfusion requirement ($P = .002$) were statistically significant on the first 6 months of mortality. Laboratory findings that are statistically significant in the first 6 months of mortality were low platelet ($P < .001$), low albumin ($P < .001$), and low CRP ($P = 0.037$) levels for the preoperative period and low Hb ($P < .001$), low ESR ($P < .001$), high Na ($P < .001$), high K ($P = .006$), low platelet ($P < .001$), low albumin ($P < .001$), high CRP ($P < .001$), and high N/L ratio ($P < .001$) levels for the discharge period (Table 2).

Advanced age ($P < .001$), female gender ($P < .001$), proximal amputation level ($P = .003$), high CCI ($P < .001$), and blood transfusion requirement ($P = .017$) were statistically significantly effective on the first 12 months of mortality. Laboratory findings that are statistically significant in the first 12 months of mortality were low platelet

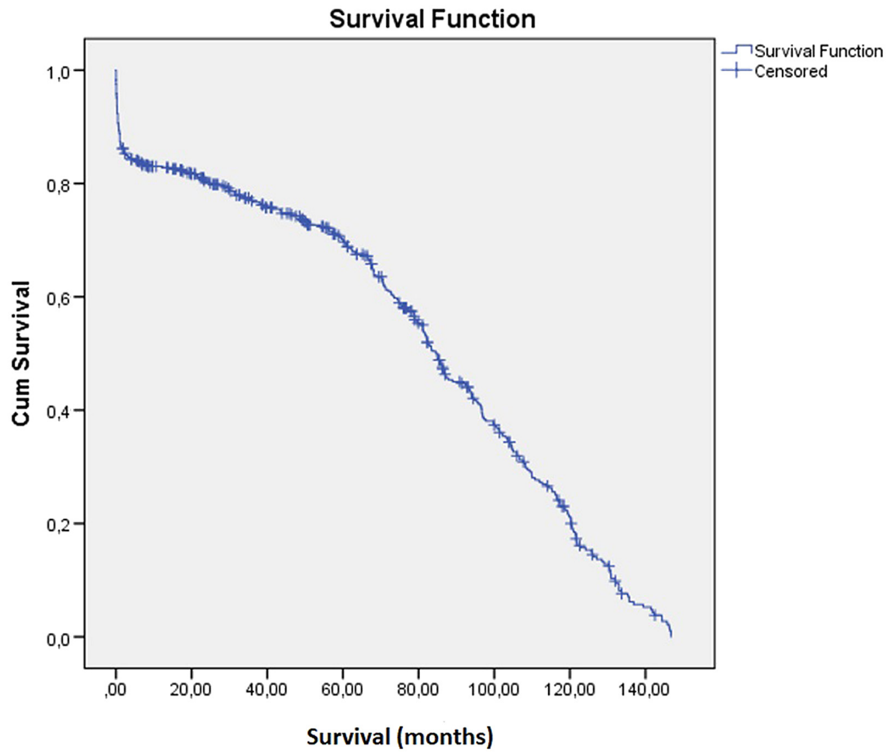


**Figure 1.** Kaplan–Meier survival curve of the study population.

($P < .001$) and low albumin ($P < .001$) levels for the preoperative period and low Hb ($P < .001$), low ESR ($P < .001$), high Na ($P < .001$), high K ($P = .009$), low platelet ($P < .001$), low albumin ($P < .001$), high CRP ($P < .001$), and high N/L ratio ($P < .001$) levels for the discharge period (Table 2).

In the Chi-squared test, in which the effect of the 4-variable amputation levels (below knee, above knee, bilaterally below knee, and hip disarticulation) on 1, 3, 6, and 12 months of mortality was analyzed, it was found that the mortality rates of the patients who underwent amputation above the knee were statistically significantly higher,

**Table 1.** Analysis of the factors that are effective on mortality at first and third months

| | First month | | | Three months | | |
|---|---|---|---|---|---|---|
| | Dead | Alive | *P* | Dead | Alive | *P* |
| Age | 69.1 ± 16.4 (47-89) | 56.7 ± 12 (41-83) | **<.001** | 71.8 ± 15.5 (47-89) | 54.8 ± 10.1 (41-75) | **<.001** |
| Charlson comorbidity score | 6.15 ± 1.75 (1-10) | 4.53 ± 2.13 (0-10) | **<.001** | 6.14 ± 1.8 (1-10) | 4.3 ± 2.1 (0-10) | **<.001** |
| Etiology (ischemic/diabetic) (n) | 31/62 | 126/265 | .464 | 48/93 | 109/234 | .352 |
| Transfusion (present/absent) (n) | 65/28 | 231/160 | **.034** | 100/41 | 196/147 | **.003** |
| Gender (female/male) (n) | 39/54 | 100/291 | **.002** | 60/81 | 79/264 | **<.001** |
| Amputation level (BKA/BBKA/AKA/HD) (n) | 48/5/37/3 | 285/9/94/3 | **<.001** | 79/6/51/5 | 254/8/80/1 | **<.001** |
| Preoperative | | | | | | |
| Hemoglobin | 10.10 ± 0.9 (8.6-11.3) | 9.9 ± 2.3 (6.1-14.3) | .472 | 9.6 ± 1.2 (7.6-11.3) | 10.0 ± 2.3 (6.1-14.3) | .387 |
| Platelet | 299 ± 212.2 (90.2-773) | 407.8 ± 170.4 (89-903) | **<.001** | 312.4 ± 193.4 (90.2-773) | 410.8 ± 174.9 (89-903) | **<.001** |
| Albumin | 2.5 ± 0.4 (2.2-3.25) | 2.8 ± 0.6 (2-4.3) | **<.001** | 2.45 ± 0.35 (2.2-3.25) | 2.82 ± 0.56 (2-4.3) | **<.001** |
| CRP | 74.3 ± 159.5 (6-468) | 70.7 ± 88.4 (1-330) | **.04** | 62.8 ± 142.7 (6-468) | 74.7 ± 90.5 (1-330) | **.035** |
| Sedimentation | 79.9 ± 29.1 (41-123) | 101.1 ± 32.2 (15-140) | .053 | 86.6 ± 29.6 (41-123) | 100.1 ± 33.1 (15-140) | .106 |
| Na | 137.6 ± 4.3 (133-144) | 133.4 ± 6.5 (114-145) | .774 | 136.6 ± 4.8 (128-144) | 133.4 ± 6.6 (114-145) | .448 |
| K | 4.3 ± 0.8 (3.36-6.1) | 4.6 ± 0.6 (3.4-6.28) | .958 | 4.31 ± 0.79 (3.36-6.10) | 4.6 ± 0.64 (3.4-6.28) | .606 |
| Neutrophil/lymphocyte | 8.08 ± 6.62 (0.81-33.33) | 11.44 ± 9.97 (0.45-50) | **.001** | 9.75 ± 7.9 (0.81-50) | 12.3 ± 10.07 (0.45-50) | .306 |
| Discharge | | | | | | |
| Hemoglobin | 9.2 ± 1.5 (6.4-11.7) | 10.5 ± 1.4 (8.6-13.3) | **<.001** | 9.36 ± 1.4 (6.4-11.7) | 10.54 ± 1.46 (8.6-13.3) | **<.001** |
| Platelet | 299.4 ± 235.3 (102-849) | 397.5 ± 178.3 (93-872) | **<.001** | 306.6 ± 210.9 (102-849) | 402.1 ± 183.1 (93-872) | **<.001** |
| Albumin | 2.4 ± 0.5 (2-3) | 3.0 ± 0.6 (2-4) | **<.001** | 2.4 ± 0.5 (2-3) | 3.1 ± 0.6 (2-4) | **<.001** |
| CRP | 61.1 ± 45.1 (3-125) | 38.6 ± 50.7 (0-167) | **<.001** | 60.5 ± 41.2 (3-125) | 37.2 ± 51.9 (0-167) | **<.001** |
| Sedimentation | 71.5 ± 57.3 (8-152) | 62.9 ± 36.3 (1-123) | **<.001** | 58.7 ± 57.4 (1-152) | 67 ± 34.1 (13-123) | **<.001** |
| Na | 138.9 ± 5.6 (130-146) | 136.7 ± 4.1 (130-146) | **<.001** | 138.1 ± 5.5 (130-146) | 136.8 ± 4.1 (130-146) | **<.001** |
| K | 4.55 ± 1.64 (2.96-7.6) | 4.19 ± 0.63 (3.17-5.21) | .883 | 4.29 ± 1.55 (2.96-7.60) | 4.26 ± 0.59 (3.17-5.21) | .051 |
| Neutrophil/lymphocyte | 16.62 ± 19.72 (1.1-100) | 6.12 ± 5.02 (0.79-50) | **<.001** | 13.97 ± 17.01 (0.97-100) | 5.73 ± 4.37 (0.79-50) | **<.001** |

AKA, above-knee amputation; BBKA, bilaterally below-knee amputation; BKA, below-knee amputation; CRP, C-reactive protein; HD, hip disarticulation; K, potassium; Na, sodium.

**Table 2.** Analysis of the factors that are effective on mortality at sixth and twelfth months

| | Six months | | | Twelve months | | |
|---|---|---|---|---|---|---|
| | Dead | Alive | *P* | Dead | Alive | *P* |
| Age | 71.8 ± 15.5 (47-89) | 54.8 ± 10.1 (41-75) | **<.001** | 71.8 ± 15.5 (47-89) | 54.8 ± 10.1 (41-75) | **<.001** |
| Charlson comorbidity score | 5.9 ± 1.1 (5-8) | 4.3 ± 1.9 (2-10) | **<.001** | 5.9 ± 1.1 (5-8) | 4.3 ± 1.9 (2-10) | **<.001** |
| Etiology (ischemic/diabetic) | 56/101 | 101/226 | .171 | 66/118 | 91/209 | .123 |
| Transfusion (present/absent) | 111/46 | 185/142 | **.002** | 124/60 | 172/128 | **.017** |
| Gender (female/male) (n) | 64/93 | 75/252 | **<.001** | 72/112 | 67/233 | **<.001** |
| Amputation level (BKA/BBKA/AKA/HD) | 87/6/59/5 | 246/8/72/1 | **<.001** | 109/6/65/5 | 224/8/66/1 | **.003** |
| Preoperative | | | | | | |
| Hemoglobin | 9.6 ± 1.2 (7.6-11.3) | 10.0 ± 2.3 (6.1-14.3) | .311 | 9.6 ± 1.2 (7.6-11.3) | 10 ± 2.3 (6.1-11.3) | .596 |
| Platelet | 312.4 ± 193.4 (90.2-773) | 410.8 ± 174.9 (89-903) | **<.001** | 312.4 ± 193.4 (90.2-773) | 410.8 ± 174.9 (89-903) | **<.001** |
| Albumin | 2.45 ± 0.35 (2.2-3.25) | 2.82 ± 0.56 (2-4.3) | **<.001** | 2.4 ± 0.3 (2.2-3.25) | 2.8 ± 0.6 (2-4.3) | **<.001** |
| CRP | 62.8 ± 142.7 (6-468) | 74.7 ± 90.5 (1-330) | **.037** | 62.8 ± 142.7 (6-468) | 74.7 ± 90.5 (1-330) | .095 |
| Sedimentation | 86.6 ± 29.6 (41-123) | 100.1 ± 33.1 (15-140) | .098 | 86.6 ± 29.6 (41-123) | 100.1 ± 33.1 (15-140) | .074 |
| Na | 136.6 ± 4.8 (128-144) | 133.4 ± 6.6 (114-145) | .426 | 136.6 ± 4.8 (128-144) | 133.4 ± 6.6 (114-145) | .438 |
| K | 4.31 ± 0.79 (3.36-6.1) | 4.6 ± 0.64 (3.4-6.28) | .777 | 4.31 ± 0.79 (3.36-6.1) | 4.6 ± 0.64 (3.4-6.28) | .179 |
| Neutrophil/lymphocyte | 10.01 ± 7.85 (0.81-50) | 11.16 ± 10.2 (0.45-50) | .646 | 10.59 ± 8.81 (0.81-50) | 10.9 ± 9.91 (0.45-50) | .852 |
| Discharge | | | | | | |
| Hemoglobin | 9.36 ± 1.4 (6.4-11.7) | 10.54 ± 1.4 (8.6-13.3) | **<.001** | 9.4 ± 1.4 (6.4-11.7) | 10.5 ± 1.4 (8.6-13.3) | **<.001** |
| Platelet | 306.6 ± 210.9 (102-849) | 402.1 ± 183.1 (93-872) | **<.001** | 306.6 ± 210.9 (102-849) | 402.1 ± 183.1 (93-872) | **<.001** |
| Albumin | 2.4 ± 0.5 (2-3) | 3.1 ± 0.6 (2-4) | **<.001** | 2.4 ± 0.5 (2-3) | 3.1 ± 0.6 (2-4) | **<.001** |
| CRP | 60.5 ± 41.2 (3-125) | 37.2 ± 51.9 (0-167) | **<.001** | 60.5 ± 41.2 (3-125) | 37.2 ± 51.9 (0-167) | **<.001** |
| Sedimentation | 58.7 ± 57.4 (1-152) | 67.1 ± 34.1 (13-123) | **<.001** | 58.7 ± 57.4 (1-152) | 67 ± 34.1 (13-123) | **<.001** |
| Na | 138.1 ± 5.5 (130-146) | 136.8 ± 4.1 (130-146) | **<.001** | 138.1 ± 5.5 (130-146) | 136.8 ± 4.1 (130-146) | **<.001** |
| K | 4.29 ± 1.55 (2.96-7.6) | 4.26 ± 0.59 (3.17-5.21) | **.006** | 4.29 ± 1.55 (2.96-7.60) | 4.26 ± 0.59 (3.17-5.21) | **.009** |
| Neutrophil/lymphocyte | 13.31 ± 16.29 (0.97-100) | 5.65 ± 4.36 (0.79-50) | **<.001** | 12.35 ± 15.58 (0.79-100) | 5.56 ± 3.81 (0.79-33.33) | **<.001** |

AKA, above-knee amputation; BBKA, bilaterally below-knee amputation; BKA, below-knee amputation; CRP, C-reactive protein; HD, hip disarticulation; K, potassium; Na, sodium.

according to the Bonferroni-corrected 2-proportion *z*-test results performed for the subgroup analysis.

When ROC curve analysis of N/L ratios was performed before the operation and at the time of discharge of the patients, a significant ROC curve could not be obtained for the preoperative values. However, ROC curves at discharge were more significant (Figures 2a-b, 3a-b, 4a-b, 5a-b, 6a-b). The threshold values for the N/L ratio at discharge were >10, >10, >9.09, >9.09, and >7.69 for 1, 3, 6, and 12 months and overall mortality, respectively.

According to the binary logistic regression analysis results, advanced age, female gender, high amputation level, high CCI, low preoperative N/L ratio, and high N/L ratio at discharge were found to be highly effective on mortality in the first month (Table 3). Unlike the first 1-month mortality, it was determined that the high N/L ratio at

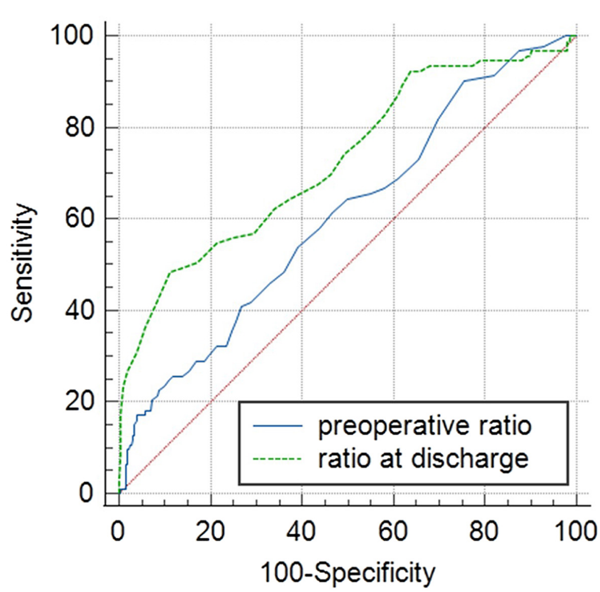


**Figure 2.** First month of mortality—preoperative neutrophil to lymphocyte ratio ROC curve analysis cutoff: ≤14.29, sensitivity: 90.3%, specificity: 24.6%, and the area under the curve: 0.606; neutrophil to lymphocyte ratio at discharge ROC curve analysis cutoff: >10, sensitivity: 48.39%, specificity: 88.8%, and the area under the curve: 0.728.

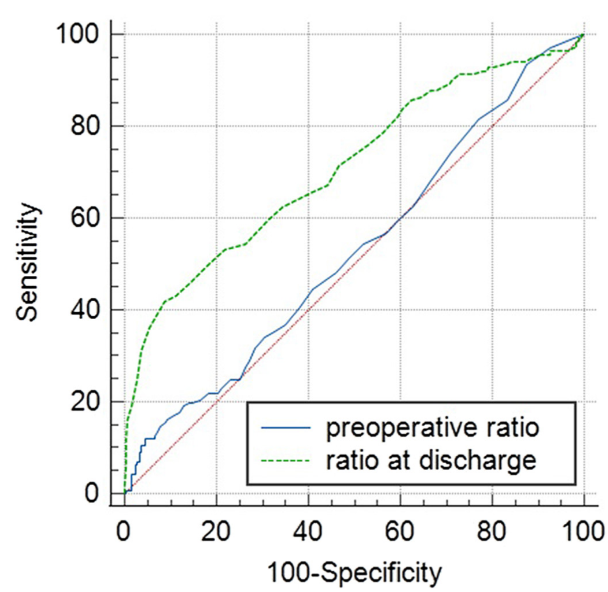


**Figure 3.** Three months of mortality—preoperative neutrophil to lymphocyte ratio ROC curve analysis cutoff: ≤2.13, sensitivity: 12.06%, specificity: 95.61%, and the area under the curve: 0.530; neutrophil to lymphocyte ratio at discharge ROC curve analysis cutoff: >10, sensitivity: 41.84%, specificity: 91.37%, and the area under the curve: 0.712.

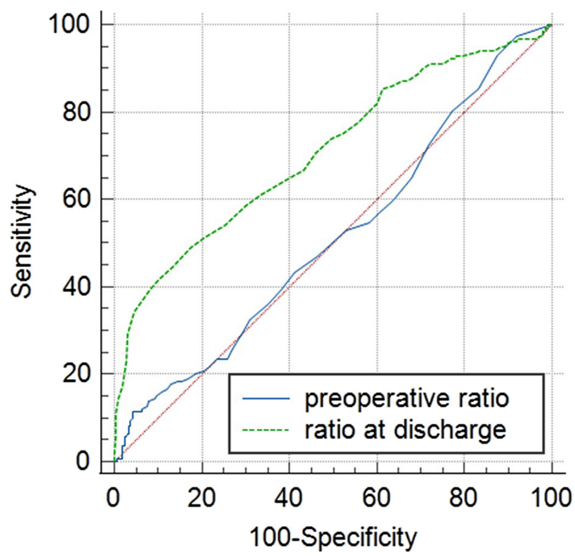


**Figure 4.** Six months of mortality—preoperative neutrophil to lymphocyte ratio ROC curve analysis cutoff: ≤2.13, sensitivity: 11.46%, specificity: 95.71%, and the area under the curve: 0.513; neutrophil to lymphocyte ratio at discharge ROC curve analysis cutoff: >9.09, sensitivity: 42.04%, specificity: 89.69%, and the area under the curve: 0.710.

discharge rather than the preoperative N/L ratio was effective in the 3-, 6-, and 12-month mortality (Table 3).

## Discussion

Early and late mortality rates and the factors affecting mortality have always been widely covered in the orthopedic literature after conditions that seriously affect the human organism, such as hip fracture or major lower extremity amputation. Undoubtedly, the main purpose of these studies is to identify the factors that cause these serious conditions to occur and to try to improve these factors, if they can be corrected, and to positively affect people's health. There are modifiable and non-modifiable factors that affect mortality. The main aim of this study was to investigate the modifiable causes of

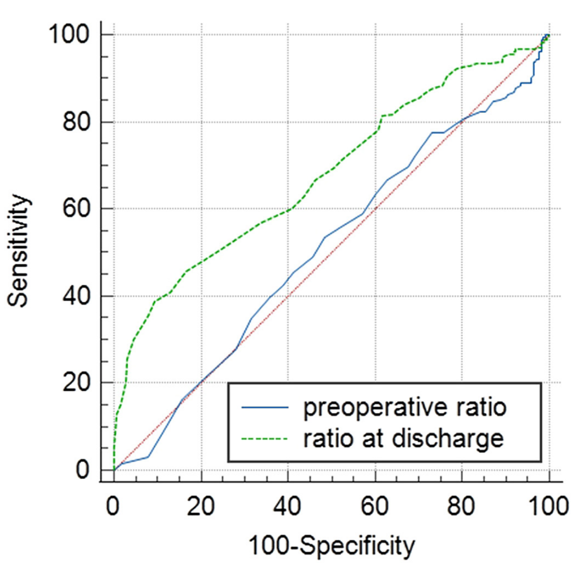


**Figure 5.** Twelve months of mortality—preoperative neutrophil to lymphocyte ratio ROC curve analysis cutoff: ≤2.13, sensitivity: 89.1%, specificity: 4%, and the area under the curve: 0.505; neutrophil to lymphocyte ratio at discharge ROC curve analysis cutoff: >9.09, sensitivity: 38.8%, specificity: 90.48%, and the area under the curve: 0.681.

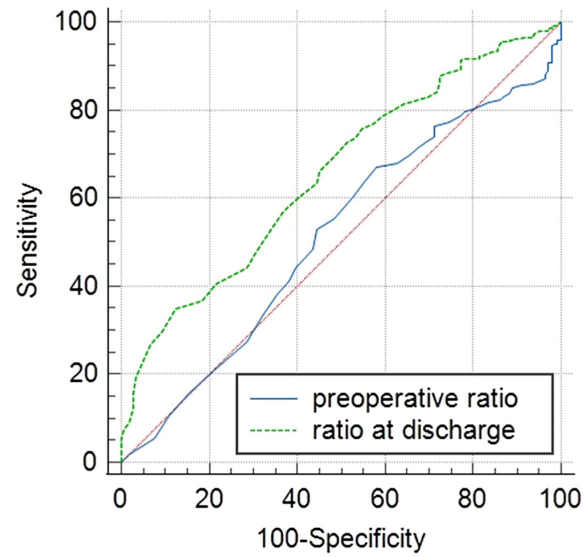


**Figure 6.** Overall mortality—preoperative neutrophil to lymphocyte ratio ROC curve analysis cutoff: >2.7, sensitivity: 87.46%, specificity: 3.38%, and the area under the curve: 0.510; neutrophil to lymphocyte ratio at discharge ROC curve analysis cutoff: >7.69, sensitivity: 34.74%, specificity: 87.67%, and the area under the curve: 0.652.

**Table 3.** Binary logistic regression analysis of the factors that are effective on 1-, 3-, 6-, and 12-month mortality

| | Variable | *P* | Odds ratio | 95% CI |
|---|---|---|---|---|
| 1-month mortality | Older age | .616 | 1.006 | 0.981-1.032 |
| | Female gender | .036 | 1.873 | 1.041-3.369 |
| | Higher amputation level | .004 | 2.397 | 1.324-4.341 |
| | Higher Charlson comorbidity index | .001 | 1.322 | 1.120-1.560 |
| | Low preoperative platelet | .441 | 0.999 | 0.997-1.001 |
| | Low Hb at discharge | .001 | 0.710 | 0.576-0.876 |
| | Low platelet at discharge | .014 | 0.997 | 0.995-0.999 |
| | Low preoperative N/L ratio | .005 | 2.945 | 1.379-6.290 |
| | High N/L ratio at discharge | <.001 | 0.284 | 0.162-0.499 |
| Three months of mortality | Older age | .087 | 1.020 | 0.997-1.044 |
| | Female gender | .001 | 2.535 | 1.459-4.402 |
| | Higher amputation level | .002 | 2.374 | 1.356-4.157 |
| | Higher Charlson comorbidity index | <.001 | 1.330 | 1.137-1.556 |
| | Low preoperative platelet | .782 | 1.000 | 0.998-1.002 |
| | Low Hb at discharge | <.001 | 0.706 | 0.581-0.858 |
| | Low platelet at discharge | <.001 | 0.996 | 0.994-0.998 |
| | High N/L ratio at discharge | <.001 | 5.360 | 2.899-9.910 |
| Six months of mortality | Older age | .062 | 1.022 | 0.999-1.045 |
| | Female gender | .002 | 2.324 | 1.355-3.985 |
| | Higher amputation level | <.001 | 2.743 | 1.585-4.747 |
| | Higher Charlson comorbidity index | .001 | 1.292 | 1.111-1.503 |
| | Low preoperative platelet | .762 | 1.000 | 0.998-1.002 |
| | Low Hb at discharge | <.001 | 0.709 | 0.586-0.857 |
| | Low platelet at discharge | <.001 | 0.996 | 0.994-0.998 |
| | High N/L ratio at discharge | <.001 | 5.162 | 2.771-9.616 |
| Twelve months of mortality | Older age | .001 | 1.039 | 1.016-1.062 |
| | Female gender | .011 | 1.936 | 1.165-3.215 |
| | Higher amputation level | .004 | 2.140 | 1.277-3.585 |
| | Higher Charlson comorbidity index | .005 | 1.222 | 1.062-1.407 |
| | Low preoperative platelet | .988 | 1.000 | 0.998-1.002 |
| | Low Hb at discharge | .029 | 0.831 | 0.703-0.981 |
| | Low platelet at discharge | .002 | 0.997 | 0.995-0.999 |
| | High N/L ratio at discharge | <.001 | 4.113 | 2.329-7.262 |

Hb, hemoglobin; N/L, neutrophil to lymphocyte.

mortality in a relatively large number of nontraumatic major lower extremity amputated patients. The most important results found in contrast to the literature were that mortality was more common in women among these patients and that the high N/L ratio at the time of discharge rather than before the operation was more associated with mortality. Although gender and N/L ratio are not modifiable factors, it is one of the important results of this study that normalizing laboratory findings such as Hb, Na, K, platelet, and albumin before discharge can reduce mortality rates.

In a systematic review, mortality rates after major lower extremity amputation were reported to be 7%-22% for the first month.[15] Gurney et al[16] reported a mortality rate of 11.1% for the first 30 days and 17.6% for the first 3 months in their study, in which only diabetic patients were examined. Kristensen et al[4] reported a mortality rate of 30% for the first 30 days, 44% for the first 3 months, and 54% at the end of the first year after minor and major amputation in the study group with a higher rate of PVD. Fortington et al[3] reported mortality rates of 22%, 44%, and 77%, respectively, for the first 30 days, 1 year, and 5 years after major lower extremity amputation in DM and PVD patients. In our study group, mortality rates at the end of the first month, third month, sixth month, and first year were 19.2%, 29.1%, 32.4%, and 38%, respectively. At the end of the follow-up period, 69.4% of the patients included in the study died. In the given literature, the most similar study group was Fortington et al.[3] The mortality rates we found were slightly lower when compared with the aforementioned study. The reason for this may be that more than half of the patients in the mentioned study population were over 75 years old, whereas the mean age of our study population was 64.2 years old.

Advanced age, female gender, high CCI, blood transfusion requirement, and proximal amputation level were determined as important factors in mortality in the present study. There are a lot of literature data on the effect of advanced age, proximal amputation level, and increased number of preoperative comorbidities such as cardiovascular disease and chronic renal failure, namely high CCI score on mortality after major lower extremity amputation.[3,4,6,16] Although lower extremity amputation is generally required in men with DM, it has been reported that mortality is more common in women.[17] Some studies which examine amputations in patients with DM or PVD indicate that gender does not affect mortality.[3,16] Regarding the effect of gender on mortality in each period, the results of the present study have shown that the female gender is effective. We think that the significantly higher age of the female patients compared to the males in our study group is important in this result. The high mortality rate in patients requiring blood transfusion is a contribution of our study to the literature. Considering that the Hb level in the preoperative period is not effective on mortality, we believe that the increase in the amount of bleeding in the surgery and the effect of blood transfusion on the patient may have increased mortality.

Although there are no data in the literature regarding the effect of low platelet, low albumin, and high CRP levels on mortality in the preoperative and postoperative periods, it is expected to assume that possible bleeding tendency, malnutrition, and increased inflammation may cause an increase in mortality.

The N/L ratio is an indicator that reflects the balance between acute and chronic inflammation.[18] It is an easily measurable marker that shows the effect of inflammation on health.[19] Probably one of the most interesting results of our study is that the low N/L ratio of patients who underwent lower extremity amputation in the preoperative period was effective only in the first 30-day mortality but not in other periods, and on the contrary, its high level in the postoperative period was very evident in all periods ($P < .001$). Contrary to the results of this present study, Wang et al[8], Coelho et al[10], and Pasqui et al[11] found that the N/L ratio of ≥8.08, ≥5.4, and ≥5.57 in the preoperative period affected mortality. Pierre-Louis et al[9] found that the high postoperative N/L ratio was effective in the first 30-day mortality, similar to the finding in our study (19.4 and 7.5 in deceased and surviving patients, respectively). Similarly, Chen et al[12] stated that a postoperative N/L ratio of ≥2.76 is important in determining the risk of mortality.

In this present study, more detailed analyses were made compared to the existing literature. One of the best examples of these is to investigate the relationship of age with mortality according to gender and to determine that female patients need amputation at a later age. The analysis of the correlation between the laboratory values of the patients both at the preoperative period and at the discharge with mortality has also added additional information to the existing literature. In the light of this information, especially the correction of laboratory values that can be modified at the time of discharge of patients may have a positive effect on mortality rates.

There are several limitations of this study. Its retrospective design is perhaps the most important limitation. The fact that the causes of death of the patients are not known exactly prevents making definite conclusions. The lack of information about the patients' possible admissions to other hospitals, and the reasons for these admissions, is another important limitation.

In conclusion, in this study, it was determined that approximately 7 out of 10 patients who underwent major lower extremity amputation for the first time in a 12-year follow-up period died. It was determined that advanced age, female gender, proximal amputation level, need for blood transfusion, low platelet levels, low albumin levels, high CRP levels, and high N/L ratio at discharge period were effective on mortality. Normalization of laboratory findings such as Hb, Na, K, platelet, and albumin before discharge can reduce mortality rates in these patients. A high N/L ratio at discharge is a very important prognostic indicator for mortality. Although it is not a modifiable factor, patients with a high N/L ratio at discharge should be called for follow-up examination more frequently. Taking precautionary measures about comorbidities can be effective in reducing mortality rates in these patients.

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