Aim: This study aims to determine the characteristics of patients undergoing major lower extremity amputation (LEA) surgery due to diabetic foot ulcers.

Material and Methods: The study was conducted by scanning files between January 2016 and December 2018. Patients were divided into two groups as survivors and non-survivors over the course of a 30-day follow-up period.

Results: The files of 43 patients (25 men, 18 women; mean age: 67±11 years) were examined. Thirty-seven of those patients underwent below-the-knee amputation and 5 of the surgeries were urgent. It was observed that 56% of the patients were in the ASA 3 and 40% were in the ASA 4 risk group. There was no significant difference between the groups in terms of age, gender, amputation level, surgical procedure, number of comorbidities, ASA risk group, postoperative laboratory values, or follow-up location (p>0.05). However, preoperative albumin levels were found to be lower in patients who died (p=0.02). General anesthesia was applied for 3 of the patients who died (p=0.08). It was determined that 23 patients were hospitalized postoperatively in intensive care for close hemodynamic follow-up and none of them needed a ventilator. During the postoperative 30-day follow-up period, the mortality rate was 9.3% and mean time to death was determined as 15.4±20 days. Three of 4 patients died due to cardiac reasons while 1 patient died because of respiratory failure.

Discussion: Since there were no significant differences in our study except low albumin levels among non-survivors, we think that supporting diabetic patients with nutritional programs in the preoperative period with a multidisciplinary approach will affect the treatment process positively.

Keywords
Diabetic Foot Ulcers, Amputation, Mortality
**Introduction**

Diabetes, which is steadily increasing in both frequency and morbidity, is a serious health problem with its complications. Untreated foot ulcers and resulting lower extremity amputations (LEAs) in diabetic patients are among the common complications of diabetes [1, 2]. It was reported that 10-25% of all diabetic patients have a risk of developing diabetic foot ulcers and 50-70% of amputation surgeries are caused by diabetic foot ulcers [3, 4]. Patients who have amputation surgeries due to diabetes are generally elderly patients with a high number of comorbidities and high risk for surgical intervention [5]. Although the mortality rates reported after diabetic foot amputation differ, the mortality rate in the first year is between 30% and 50%. Among the causes of death, heart diseases, stroke, chronic kidney failure, and sepsis are frequently noted [6].

In our study, we aimed to retrospectively evaluate patients who had undergone major LEA surgery for diabetic foot ulcers.

**Material and Methods**

After obtaining the approval of the local ethics committee, the study was completed by scanning the files of patients who underwent major LEA surgery between January 2016 and December 2018 in a tertiary university hospital. Study data were obtained by retrospective examination of the hospital automation system and anesthesia records. Records of 72 patients who underwent major LEA surgery were identified and 43 patients who underwent major LEA surgery for diabetic foot ulcers were included. The diagnosis of type 2 diabetes mellitus in all patients was confirmed by an endocrinologist according to fasting plasma glucose, preoperative HbA1c values, and previous drug reports obtained from hospital records. Transtibial, knee disarticulation, transfemoral, and hip disarticulation amputations were defined as major LEAs. Minor amputations (tarsal, metatarsal, and digital joints; n: 7 people), traumatic amputations (n: 4 people), and amputations due to peripheral circulatory disorders (n: 17 people) and malignancy (n: 1 person) were not included in the study. Failure of wound healing following appropriate infection control and wound debridement or the presence of serious systemic comorbidities that hinder treatment were identified as major LEA indications.

The following data were examined: demographic characteristics of the patients; amputation level (below the knee, above the knee); surgical procedure (emergency, elective); number of existing diseases (<4 diseases, ≥4 diseases); American Society of Anesthesiologists (ASA) risk score; anesthesia method [general, regional, combined (general + regional/peripheral nerve block), peripheral nerve block] and time; preoperative HbA1c and albumin values; preoperative and postoperative hemoglobin (Hb), leukocyte, urea, creatinine, and glucose values; amount of crystalloid administered intraoperatively; preoperative hospitalization duration; postoperative follow-up location [service, intensive care unit (ICU)]; reason for admission to the ICU (respiratory support, inability to awaken, close hemodynamic follow-up, cardiopulmonary resuscitation, multiple organ failure); presence of mechanical ventilator need; length of postoperative ICU stay and total length of stay in the hospital; fate of the patient (survivor, non-survivor); and cause of mortality (respiratory, cardiac reasons) and time to death. Thirty-day mortality and survival data were taken from hospital database records. Patients (n=43) were divided into two groups as survivors (n=39) and non-survivors (n=4) during the postoperative 30-day follow-up.

**Statistical analysis**

SPSS 24.00 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical evaluation. Results were expressed as mean ± standard deviation (mean±SD) for continuous values and as frequency (n) and percentage (%) for frequency data. The categorical data were analyzed by chi-square test. For statistical evaluations, p<0.05 was considered significant.

**Results**

Of the patients who underwent major LEA surgery due to diabetic foot ulcers, 25 (58.1%) were male, 18 (41.9%) were female, and the mean age was 67.7±11.1 years. While 37 (86%) of the patients underwent below-the-knee amputation, 6 (14%) had above-the-knee amputation; 5 (11.6%) of the surgeries were performed under emergency conditions and 38 (88.4%) under elective conditions. Half of the non-surviving patients had ≥4 additional diseases. It was observed that 4.7% of the patients were in the ASA 2 risk group, 55.8% were in ASA 3, and 39.5% were in ASA 4; half of the patients who died were ASA 5 and the other half were ASA 4. There was no statistically significant difference between the groups in terms of age, gender, amputation level, surgical procedure, number of comorbidities, or ASA risk group (p>0.05) (Table 1). While general anesthesia was applied for 3 (75%) of the patients who died, regional anesthesia (spinal anesthesia) was applied for 1 (25%) non-surviving patient. There was no statistically significant difference between the groups in terms of anesthesia management (p=0.08) (Table 1). It was observed that the duration of anesthesia of the non-surviving patients was longer, but there was no statistically significant difference between the groups (p=0.58) (Table 1).

The preoperative mean HbA1c value of our patients was calculated as 8.2±2.1%, while mean albumin was 2.7±0.5 g/dL. Hb was 10±1.5 g/dL, leukocyte level was 12.2±5.1 mm3, urea was 52.8±34 mg/dL, creatinine was 1.4±1.4 mg/dL, and glucose was 195±95 mg/dL. Similarly, postoperative mean Hb was calculated as 9.8±1.1 g/dL, leukocyte level as 12.4±4.4 mm3, urea as 47.6±38.4 mg/dL, creatinine as 1.3±1.6 mg/dL, and glucose as 200±89.4 mg/dL. There was no statistically significant difference between the two groups in terms of these preoperative and postoperative laboratory values, except for the albumin value measured preoperatively (p<0.05). Albumin levels were found to be lower in non-surviving patients (p=0.02) (Table 2).

It was observed that the mean amount of crystalloid administered intraoperatively to all our patients was 1532.14±642.95 mL and there was no difference between the groups (p=0.12). It was determined that 23 patients were admitted to the ICU for close hemodynamic follow-up in the postoperative period and no patient needed mechanical ventilation support. There was no significant difference between the groups in terms of postoperative patient follow-up location (p=0.11). No significant difference was found between the groups in
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Discussion

Our study, in which we examined patients who underwent major LEA for foot ulcers, one of the most common complications of diabetes, sought to identify these patients in terms of some specific characteristics. In this study, no statistical difference was found in the patients who died compared to surviving patients except for lower albumin levels among non-survivors. During the 30-day follow-up, the mortality rate was determined as 9.3%.

Kalpakçı et al. [7] stated in their study that the rate of surgeries performed for diabetic foot problems was 2.47 times higher in the age group of 60-69 compared to the age group of 43-59 and 9.4 times higher in the age group of 70 and over. Thus, advanced age was an important risk factor in cases of diabetic foot amputation. In the same study, the risk of diabetic foot amputation increased with age, and additional pathologies such as diabetes duration and atherosclerosis were added in the process as an expected result. In our study, the mean age of patients who underwent major LEA surgery for foot ulcers was 67.7±11.1 years. The fact that the mean age of our patients who died from amputation due to diabetic foot ulcers (72.5±14.45 years) was higher than the mean age of the surviving patients (67.28±10.88 years) suggests that the incidence of diabetes-related complications increased with increasing age, similar to the findings seen in the literature.

It was reported in many studies that male gender is an important risk factor for diabetic foot amputations [8]. The higher frequency of amputation due to diabetic foot ulcers in men in our study is consistent with the literature. Ankan et al. [9] reported that the most common surgical procedures in patients with diabetic foot ulcers were below-the-knee amputation (59.5%) and above-the-knee amputation (23.8%). Gutman et al. [10] also reported that 44% of 118 diabetic patients underwent small joint, 40.6% below-the-knee, and 15.2% above-the-knee amputation. Subramaniam et al. [11] found the mean survival to be 52 and 20 months among patients with below-the-knee and above-the-knee amputations, respectively. The same study revealed that diabetes was not a determinant in 30-day mortality or 3-year survival, but it was a determinant in 1-year survival. Amputation level and renal diseases were reported as important determinants of 30-day mortality. Based on this information, the authors suggested that below-the-knee amputations should be considered as medium-risk and above-the-knee amputations as high-risk surgeries. In our study, it was observed that 86% of the patients had below-the-knee amputations and 14% had above-the-knee amputations, and 3 patients died.

It was reported in the literature that age, gender, and amputation level are well-known risk factors for mortality in patients undergoing diabetic amputation [6]. The limited number of patients included in our study suggests that more comprehensive studies should be conducted to determine whether parameters such as age, gender, and amputation level are risk factors for mortality.

Scott et al. [12] reported trends of increasing perioperative mortality in patients with renal impairment who undergo surgery for LEA for diabetes and peripheral vascular disease outside of standard working hours. They also found that the average survival after amputations performed during working hours was longer than survival in the case of amputations performed outside of working hours (39 months and 11 months, respectively). They reported that increased urgency of the surgery may affect the possible outcomes with the coexistence of more comorbidities and emergency amputations with the participation of less experienced surgeons and anesthesiologists. In our study, it was observed that all of the patients who were operated on under emergency conditions (11.6%) were operated on during standard working hours, and 4 of them survived while 1 died.

The ASA risk score is a classification system used by anesthesiologists to predict surgical mortality and morbidity in the postoperative period by considering the patient's risk factors. In our study, the ASA risk score was calculated for all patients, and the mortality rate was found to be higher in patients with higher ASA risk scores. Therefore, it is important to consider the ASA risk score when planning surgery and predicting outcomes.

Table 1. Clinical and demographic data of the patients (n, mean±SD)

|                          | Survivors (n=39) | Non-survivors (n=4) | p     |
|--------------------------|------------------|---------------------|-------|
| Male/Female              | 22/17            | 3/1                 | 0.62  |
| Age (years)              | 67.28±10.88      | 72.5±14.45          | 0.37  |
| Amputation level (below-the-knee/above-the-knee) | 35/4          | 2/2                 | 0.08  |
| Surgical procedure (emergency/elective) | 4/35                      | 1/3                 | 0.40  |
| Number of existing diseases (<4/≥4) | 24/15                      | 2/2                 | 0.52  |
| ASA risk score (2/3/4)   | 2/22/15          | 0/2/2               | 0.76  |
| Anesthesia method (general/regional/combined/peripheral nerve block) | 29/0/2/8                      | 3/1/0/0             | 0.08  |
| Anesthesia time (min)    | 111.5±35.37      | 127.5±20.61         | 0.38  |

Table 2. Comparison of preoperative and postoperative laboratory values (mean±SD)

| Laboratory values                  | Survivors (n=39) | Non-survivors (n=4) | p     |
|------------------------------------|------------------|---------------------|-------|
| Preoperative HbA1c (%)             | 8.37±2.16        | 6.60±1.07           | 0.11  |
| Preoperative albumin (g/dL)        | 2.81±0.49        | 2.0±0.29            | 0.02  |
| Preoperative Hb (g/dL)             | 10.04±1.5        | 10.02±1.97          | 0.97  |
| Preoperative leukocytes (mm3)      | 12.07±4.98       | 13.65±7.35          | 0.56  |
| Preoperative urea (mg/dL)          | 50.07±28.48      | 80.25±68.76         | 0.44  |
| Preoperative creatinine (mg/dL)    | 1.42±1.46        | 1.35±1.5            | 0.92  |
| Preoperative glucose (mg/dL)       | 202.23±96.47     | 124.75±31.67        | 0.12  |
| Postoperative Hb (g/dL)            | 9.84±1.13        | 10.2±0.9            | 0.54  |
| Postoperative leukocytes (mm3)     | 12.35±4.65       | 12.92±2.47          | 0.81  |

Table 3. Comparison of the patients' lengths of stay (mean±SD)

| Duration of stay (days)            | Survivors (n=39) | Non-survivors (n=4) | p     |
|------------------------------------|------------------|---------------------|-------|
| Preoperative period                | 6.74±6.21        | 10.75±11.44         | 0.53  |
| Postoperative ICU stay             | 5.84±7.78        | 3.5±3.0             | 0.56  |
| Total                              | 16.51±11.31      | 21.9±4.5            | 0.44  |
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preoperative status [13]. Scott et al. [12] reported more than a fourfold increase in 30-day mortality and a twofold increase in long-term mortality in patients with an ASA risk score of ≥4 who underwent LEA surgery. Some authors have stated that an increased ASA score is a risk factor for increased perioperative and long-term morbidity and mortality after amputation [14]. Considering the patients’ comorbid diseases and general conditions, we thought that this scoring method determined early hospital mortality well, but we could not determine whether the ASA score was a risk factor for mortality in patients with amputation due to diabetic foot ulcers. However, the patients followed in the postoperative ICU had ASA scores of 5 and 4, ≥4 comorbidities, and ages of ≥70 years. Moreover, we found that 50% of our patients who died had ASA scores of 3 and 50% had ASA scores of 4.

Blood glucose level and HbA1c level, reflecting the last 3–4 months of glycemic status, are indicators that evaluate long-term glycemic control before surgery [15]. In their study, Aragón-Sánchez and Lázaro-Martínez [16] stated that pre-admission glycemic control based on HbA1c in the prospective follow-up of 81 patients with diabetic foot ulcers who underwent surgery for osteomyelitis had no effect on clinical outcomes. Stratton et al. [17] reported in their study that when HbA1c decreased by 1%, the risk of death from amputation decreased by 43%. It is known that hyperglycemia increases the length of hospital stay and rate of admission to intensive care, and it is an important factor affecting morbidity and mortality [18]. The mean HbA1c value of our patients was 8.2±2.1%. It was observed that both HbA1c and preoperative and postoperative glucose values were lower among non-surviving patients. We believe that the longer preoperative hospitalization periods of these patients were effective in the preoperative blood glucose regulation and that providing for preoperative glycemic control in all patients will increase the survival rate.

Scott et al. [12] showed that the type of anesthesia was not associated with survival in patients undergoing major LEA surgery, but the probability of 30-day mortality associated with neuraxial anesthesia increased. This contrasts with studies showing better survival with regional anesthesia [19]. In our study, anesthesiologists had a tendency to choose general anesthesia for patients with ASA scores of ≤3, and 32 patients receiving general anesthesia had ASA scores of 2. Patients with high mortality risk were more likely to receive neuraxial anesthesia (including 1 patient who died, ASA 3 risk group, spinal anesthesia). Four patients who underwent peripheral nerve block were ASA 3 and 4 patients were ASA 4.

It is reported that the nutritional status of patients before amputation can be measured by total lymphocyte count (TLC) and serum albumin level. Specifically, TLC should be >1500 and albumin level should be at least 3.0 g/dL. In patients with low immune resistance or malnutrition, surgery should be postponed until these conditions improve slightly, and poor glycemic control is a factor that increases the amputation rate [20, 21]. It was also reported in the literature that low serum albumin level and white blood cell count of >12.0 cells/µL are associated with an increased risk of amputation in cases of diabetic foot ulcers, whereas leukocytosis was reported to be associated with poor clinical outcomes in cases of diabetic foot ulcers [22, 23]. Scott et al. [12] reported that in-hospital mortality was associated with lower serum albumin, Hb, and sodium concentrations and higher concentrations of urea, creatinine, and potassium in patients undergoing LEA. We did not collect data for all these variables and could not compare these findings in terms of mortality due to limited data. However, the preoperative albumin levels in our study were 2.7±0.5 g/dL, albumin levels were found to be quite low in the patients who died (≤2.3 g/dL), and the mean preoperative and postoperative leukocyte counts were found to be >12.0 cells/µL, signifying that our findings are consistent with the literature.

Beyaz et al. [24] reported a first 30-day mortality rate of 16% in patients who underwent large bone amputation due to diabetes complications. In the same study, it could not be clearly concluded whether early mortality was due to the reasons for surgery or to surgical complications. In a study involving 19,727 patients in which factors affecting early hospital mortality were evaluated in patients who underwent orthopedic surgery, 237 (1.23%) patients were reported to have died in the early period after surgery. In the same study, it was stated that the surgical procedure with the highest mortality rate was amputation surgery (6.35%) [25]. In other studies, the mortality rate among cases of major diabetic amputation was reported as 31–41% in 1 year of follow-up and 68–77% in 5 years of follow-up [6]. In our study, postoperative 30-day mortality was found to be 9.3%, while mean time to death was found to be 15.37±20.01 days. Furthermore, 17 (39.5%) of our patients had ≥4 diseases. All of the patients who died had coronary artery disease and half of them had ≥4 diseases. We think that the relatively low number of patients with additional internal pathologies increased the survival rate in the present study.

It was observed that our patients who died were taken to the ICU postoperatively for hemodynamic follow-up purposes, and 30% of those patients died due to cardiac causes while 1 died due to respiratory causes during the first 30 days of follow-up. The shorter follow-up period in this study compared to the literature made the survival rate of our patients seem higher and also explains the difference between studies.

This study has some limitations. Our biggest handicap was that we could not determine the factors affecting mortality in cases of amputations due to diabetic foot ulcers as a result of the study’s retrospective nature and limited number of patients. In order to determine the causes of mortality in patient samples, we think that including the habits of the patients (smoking, alcohol, etc.), their education status, and the duration of dialysis in patients receiving dialysis treatment will allow for more valuable studies. Studies involving larger patient series are also needed.

In conclusion, since there were no significant differences in our study other than the low albumin levels among non-survivors, we think that supporting diabetic patients with nutritional programs in the preoperative period with a multidisciplinary approach will affect the treatment process positively.

Scientific Responsibility Statement

The authors declare that they are responsible for the article’s scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.
Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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