



## Analysis of Important Factors in Revision Surgery for Patients Undergoing Diabetic Major Lower Extremity Amputation Diyabetik Majör Alt Ekstremitte Ampütasyonu Uygulanan Hastalarda Revizyon Cerrahisinde Önemli Olan Faktörlerin Analizi

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### ABSTRACT

**Aim:** Diabetic foot is a disease associated with severe morbidity, mortality, and significant socioeconomic problems. Numerous risk factors influence revision amputations in diabetic feet; however, the literature does not reach a consensus on this matter. This study aims to analyze the significant factors affecting revision surgery in patients who have undergone major lower extremity amputations due to diabetes. **Materials and Methods:** This retrospective study was conducted at a university hospital in İzmir between April 10, 2023, and October 12, 2023. A total of 276 patients who underwent surgical operation due to diabetic foot between 2010 and 2022 were included in the study. The study evaluated the impact of demographic characteristics and various parameters, including a history of peripheral angiography or peripheral bypass, the surgical specialty performing the operation, hemoglobin, platelet count, hemoglobin A1c, albumin, sedimentation rate, C-reactive protein, sodium and potassium levels, lymphocyte-to-neutrophil ratio, blood transfusion requirements, and the Charlson Comorbidity Index, recorded at admission and discharge, on the need for revision surgery. **Results:** The patients were divided into two groups: those who underwent revision amputation (96) and those who did not (180). The revision amputation rate among all patients was determined to be 35%. The risk of revision amputation can be predicted by the admission and discharge albumin levels, as well as the admission and discharge potassium levels. In addition to high admission albumin levels and low discharge potassium levels, high admission potassium levels may also contribute to the adverse outcomes of revision surgery. **Conclusions:** In this study, it was found that albumin levels, which are considered important for wound healing in many sources, were not a determining factor for revision amputation as previously thought. Additionally, the regulation of potassium levels, which can be affected by various metabolic diseases, may have a significant impact on the revision surgery that becomes necessary after amputation.

**Keywords:** Diabetic foot, Clinical parameters, Laboratory parameters, Major lower extremity amputation

### ÖZ

**Amaç:** Diyabetik ayak; ciddi morbidite, mortalite ve yüksek sosyoekonomik sorunlarla bağlantılı bir hastalıktır. Diyabetik ayaklarda yapılan revizyon ampütasyonlarına birçok risk faktörü etki etmektedir; ancak bu konuda literatürde görüş birliği bulunmamaktadır. Bu araştırmanın amacı, diyabetik majör alt ekstremitte ampütasyonu uygulanan hastalarda revizyon cerrahisini etkileyen önemli faktörlerin analizini yapmaktır. **Gereç ve Yöntem:** Retrospektif türdeki bu araştırma, İzmir ilinde bir üniversite hastanesinde 10.04.2023-12.10.2023 tarihleri arasında yürütülmüştür. Araştırmaya, 2010-2022 yılları arasında diyabetik ayak nedeniyle cerrahi operasyon geçiren toplam 276 hasta dahil edilmiştir. Hastaların demografik özellikleri ile revizyon cerrahisi üzerindeki etkisi araştırılan periferik anjiyografi veya periferik bypass öyküsü, operasyonu gerçekleştiren cerrahi branş, başvuru ve taburcu sırasında kaydedilen hemoglobin, trombosit, Hemoglobin A1c, albümin, sedimentasyon, C-Reaktif Protein, sodyum, potasyum düzeyleri, lenfosit/nötrofil oranı, kan transfüzyon ihtiyacı ve Charlson Komorbidite İndeksi gibi parametreler değerlendirilerek veriler kaydedilmiştir. **Bulgular:** Hastalar revizyon ampütasyon yapılan (96), revizyon ampütasyon yapılmayan (180) grup olmak üzere iki gruba ayrılmıştır. Tüm hastalar arasında revizyon ampütasyon oranı %35 olarak belirlenmiştir. Revizyon ampütasyon riskini başvuru ve taburcu albümin düzeyi ile başvuru ve taburcu potasyum düzeyleri öngörebilmektedir. Yüksek başvuru albümin düzeyi ve düşük taburcu potasyum düzeyinin yanı sıra, yüksek başvuru potasyum düzeyi de revizyon cerrahisinin olumsuz sonuçlanmasına yol açabilmektedir. **Sonuç:** Yapılan bu çalışmada, birçok kaynaktan yara iyileşmesi açısından önemli olduğu belirtilen albümin düzeyinin, sanılanın aksine, revizyon ampütasyon açısından belirleyici bir faktör olmadığı görülmüştür. Buna ek olarak, çeşitli metabolik hastalıklardan etkilenebilecek olan potasyum düzeyinin regülasyonu, ampütasyon sonrası zorunlu hale gelen revizyon cerrahisi üzerinde önemli bir etkiye sahip olabilir.

**Anahtar Kelimeler:** Diyabetik ayak, Majör alt ekstremitte ampütasyonu, Klinik parametreler, Laboratuvar parametreleri

## INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder characterized by hyperglycemia, which can develop due to partial or absolute insulin deficiency or as a result of "insulin resistance" in peripheral tissues. It causes adverse effects on multiple organs and leads to multisystemic involvement (1). Advancements in diabetes treatment have extended patients' lifespans, leading to an increased prevalence of diabetes-related complications. Diabetic foot ulceration is recognized worldwide as a significant complication of diabetes and is reported to be one of the most common causes of hospital admissions (2).

The term diabetic foot syndrome is used to describe all pathological changes occurring in the feet of individuals with diabetes. Calluses are lesions that develop prior to ulceration, while ulcers and necrosis typically occur due to repetitive trauma associated with reduced pain and pressure sensation as a result of diabetic polyneuropathy. A study conducted in Germany revealed that peripheral arterial disease was present in over 50% of cases, with symptoms often obscured by polyneuropathy (3). The prevalence of diabetic foot syndrome ranges between 4% and 15%, with a 25% risk of foot ulcer development among individuals with diabetes. Moreover, the need for amputation arises within the first four years following diagnosis in a significant proportion of these patients. Five-year mortality rates following amputation are estimated to range between 39% and 68% (2).

Diabetic foot ulcers should be evaluated through a multidisciplinary approach. Patients should be evaluated by a multidisciplinary team consisting of specialists in endocrinology, infectious diseases, orthopedics and traumatology, plastic surgery, vascular surgery, hyperbaric medicine (if available), physical therapy and rehabilitation, along with a dietitian, diabetes nurse, and stoma and wound care nurse. Treatment plans should be developed within this collaborative framework. A multidisciplinary approach significantly reduces hospitalization duration, amputation rates, and treatment costs (1). In addition, the most critical aspect of treating diabetic foot wounds is prevention, with the primary focus in this context being on diabetes education (4).

This study aims to assess the predictive value of hematological and biochemical laboratory variables, a history of lower extremity peripheral angiography or peripheral bypass, and the surgical specialty performing the procedure in determining the likelihood of revision surgery in patients undergoing amputation for diabetic foot.

## MATERIAL and METHOD

### Type, Place and Time of the Study

This single-center, retrospective descriptive study was conducted at a public hospital in İzmir, Türkiye, between April 10, 2023, and October 12, 2023.

### Population Sample of the Study

The study population included patients diagnosed with diabetic foot, while the sample comprised 276 patients (n=276) who underwent amputation surgery for diabetic foot at Health Sciences University İzmir Tepecik Training and Research Hospital between 2010 and 2022.

### Evaluation of Study Data

Statistical analysis was performed using the SPSS 20.0 software for Windows. The results were evaluated at a 95% confidence interval, with a p value of <0.05 considered statistically significant. Descriptive statistics for categorical variables were reported as frequencies (n) and percentages (%), while numerical variables were presented as mean, standard deviation, and minimum (min) and maximum (max) values. Fisher's Exact Test, independent t-test, and Mann-Whitney U test were used to determine whether these variables were statistically independent risk factors for revision surgery.

### Ethical Aspects of the Study

Approval was given by the Health Sciences University İzmir Tepecik Training and Research Hospital Non-Interventional Research Ethics Committee (09.12.2022; Number: 2022/11-32).

## RESULTS

In the study, laboratory parameters and demographic data of patients who underwent amputation due to diabetic foot were examined, and the impact of the obtained data on amputation revision was investigated.

**Table 1.** Descriptive parameters of the patients

Variables	With revision		Without revision		p value
<b>Gender</b>	Female	23	Female	55	0.27
	Male	73	Male	125	
<b>Blood Transfusion</b>	Yes	62	Yes	106	0.19
	No	21	No	55	
<b>Peripheral Vascular Intervention</b>	Performed	11	Performed	9	0.05
	Not performed	85	Not performed	171	
<b>Surgical Specialty Performing the Surgical Operation</b>	Orthopedics and Traumatology	84	Orthopedics and Traumatology	168	0.12
	General Surgery	12	General Surgery	12	

Revision amputation was performed in 96 out of 276 patients (34.7%) who underwent diabetic foot amputation. Of the patients who underwent revision amputation, 73 (76%) were male, and 23 (24%) were female. Of the 180 patients who did not undergo revision amputation, 125 (69.4%) were male, and 55 (30.6%) were female. No significant difference was found in revision amputation rates between genders ( $p=0.27$ ).

Blood transfusion was administered to 168 out of 244 patients (69%) who underwent diabetic foot amputation. Revision amputation was performed on 62 (37%) of the patients who received a blood transfusion. No significant relationship was found between revision amputation and blood transfusion ( $p=0.19$ ).

Revision amputation was performed in 96 out of 276 patients (34.7%) who underwent diabetic foot amputation. Of these patients, 20 (7%) had undergone peripheral vascular intervention, while 256 (93%) had not. Revision amputation was performed in 11 out of 20 patients (55%) who had undergone peripheral vascular intervention. However, the relationship between peripheral vascular intervention and revision amputation was not statistically significant ( $p=0.05$ ).

**Table 2.** Admission parameters of the patients

Variables	With revision (n:96) Mean and standard deviation (minimum-maximum)	Without revision (n:180) Mean and standard deviation (minimum-maximum)	p value
<b>Hemoglobin</b>	9 ± 0.5 (6-14)	10.5 ± 0.45 (7-14)	0.65
<b>Platelet</b>	471 ± 50 (200-903)	373 ± 45 (79-785)	0.31
<b>Albumin</b>	2.96 ± 0.15 (2.2-4.3)	2.6 ± 0.12 (2-4)	0.001
<b>Sedimentation</b>	100 ± 9 (15-139)	96.7 ± 7.1 (25-142)	0.62
<b>CRP</b>	81 ± 119.5 (1-330)	81.6 ± 26.7 (1-468)	0.83
<b>Sodium (Na)</b>	135 ± 6.9 (126-145)	134 ± 1.5 (114-144)	0.32
<b>Potassium (K)</b>	4.8 ± 0.6 (3.6-6.3)	4.5 ± 0.13 (3.4-5.7)	0.03

CRP: C-reaktif Protein  
koyulacak  $p<0.05$

The mean age of patients who underwent revision surgery was  $56 \pm 3.03$  years (min: 41, max: 75), while the mean age of those who did not undergo revision surgery was  $58.55 \pm 0.73$  years (min: 42, max: 89). No significant difference was found between age and the frequency of revision amputation ( $p=0.32$ ).

The mean admission albumin level was  $2.96 \pm 0.15$  (min: 2.2, max: 4.3) for patients who underwent revision surgery, compared to  $2.6 \pm 0.12$  (min: 2, max: 4) for those who did not. It was found that revision amputation surgery was more frequent in patients with higher albumin levels ( $p=0.001$ ). The mean admission potassium level was  $4.8 \pm 0.6$  (range: 3.6–6.3) for patients who underwent revision surgery, compared to  $4.5 \pm 0.13$  (range: 3.4–5.7) for those who did not. It was determined that revision amputation surgery was more frequent in patients with higher discharge potassium levels ( $p=0.03$ ).

**Tablo 3.** Discharge parameters of the patients

Variables	With revision (n:96) Mean and standard deviation (minimum-maximum)	Not revised (n:180) Mean and standard deviation (minimum-maximum)	p value
Hemoglobin	$9.9 \pm 1.4$ (8.6-13.3)	$10.3 \pm 0.32$ (8.5-13.3)	0.1
Platelet	$467 \pm 215$ (235-872)	$346 \pm 48$ (93-849)	0.13
HbA1c	$7.7 \pm 0.42$ (6-11)	$9.4 \pm 0.65$ (5-15)	0.19
Albumin	$3.1 \pm 0.14$ (2-4)	$2.8 \pm 0.14$ (2-4)	0.002
CRP	$39.2 \pm 14.5$ (0-167)	$46.7 \pm 11.3$ (1-142)	0.59
Sedimentation	$68.1 \pm 10.1$ (1-123)	$70.2 \pm 9.5$ (8-152)	0.73
Sodium (Na)	$137.5 \pm 1.1$ (131-145)	$137.3 \pm 1.2$ (130-147)	0.35
Potassium (K)	$4.2 \pm 0.21$ (2.96-5.5)	$4.4 \pm 0.23$ (3.2-7.6)	0.02

HbA1c: Hemoglobin A1c  
koyulacak  
CRP: C reaktif protein  
koyulacak  $p<0.05$

The discharge sodium level was determined to be  $137.5 \pm 1.1$  (min: 131, max: 145) in patients who underwent revision surgery, and  $137.3 \pm 1.2$  (min: 130, max: 147) in those who did not. The discharge potassium level was calculated as  $4.2 \pm 0.21$  (min: 2.96, max: 5.5) in patients who underwent revision surgery and  $4.4 \pm 0.23$  (min: 3.2, max: 7.6) in those who did not. It was determined that revision amputation surgery was more frequent in patients with lower potassium levels ( $p=0.02$ ).

**Tablo 4.** Polikliniklerden İstenen Konsültasyonların Gereçeklerinin Dağılımı

Variables	With revision (n:96) Mean and standard deviation (minimum-maximum)	Without revision (n:180) Mean and standard deviation (minimum-maximum)	p value
Charlson Comorbidity İndex	$4.3 \pm 0.51$ (2-8)	$4.7 \pm 0.4$ (2-10)	0.77
Preoperative Neutrophil To Lymphocyte Ratio	$0.25 \pm 0.05$ (0.03-0.7)	$0.17 \pm 0.29$ (0.02-0.45)	0.75
Postoperative Neutrophil To Lymphocyte Ratio	$0.27 \pm 0.2$ (0.03-0.72)	$0.26 \pm 0.2$ (0.02-0.8)	0.67

The Charlson Comorbidity Index was found to be  $4.3 \pm 0.51$  (min: 2, max: 8) in patients who underwent revision surgery and  $4.7 \pm 0.4$  (min: 2, max: 10) in those who did not. The preoperative lymphocyte to neutrophil ratio was found to be  $0.25 \pm 0.05$  (min: 0.03, max: 0.7) in patients who underwent revision surgery and  $0.17 \pm 0.29$  (min: 0.02, max: 0.45) in those who did not. The

postoperative lymphocyte to neutrophil ratio was determined to be  $0.27 \pm 0.2$  (min: 0.03, max: 0.72) in patients who underwent revision surgery and  $0.26 \pm 0.2$  (min: 0.02, max: 0.8) in those who did not. No relationship was identified between these parameters and revision amputation surgery.

## DISCUSSION

In this study, no significant difference was found between genders in terms of revision amputation surgery. The impact of gender on lower extremity major revision amputation in diabetic foot was investigated. While some studies in the literature suggest an increased risk of revision amputation in male patients, many other studies report no such increase in risk. In the studies conducted by Font-Jiménez et al. (2016) and Acar and Kacira (2017), it was found that the revision surgery rate was higher in male patients. The results of this study are consistent with the findings of the relevant studies (5,6). In contrast, the study by Younger et al. (2009) found no significant difference between gender and revision amputation (7). Similarly, the study by Armstrong et al. (1997) also found no difference between gender and revision amputation (8). The results of this study are similar to the findings of the studies conducted by Younger et al. and Armstrong et al.

There are studies in the literature indicating a relationship between age and diabetic foot lower extremity major revision amputation, as well as studies where no such relationship was found. In a study conducted by Ohsawa et al. (2001), it was found that patients who required re-amputation were significantly older compared to those who did not require revision (9).

Age has been defined as an independent risk factor for re-amputation in diabetes (10). As age increases, the frequency of comorbidities also increases. In older individuals, complications related to diabetes and other diseases are more commonly observed. Additionally, as age progresses, a decline in self-care abilities increases the risk of developing diabetic foot ulcers. The care of an evolving ulcer will be both more inadequate and the healing process will become more difficult due to complications from existing diseases. In the study, no significant difference was found between age and revision amputation surgery ( $p=0.32$ ). However, in the study conducted by Kono and Muder (2012), no relationship was found between age and revision amputation surgery (10). The results of both studies support each other.

There are studies in the literature indicating a relationship between diabetic foot lower extremity major revision amputation and a history of peripheral vascular intervention, as well as studies where no such relationship was found. Font-Jiménez et al. (2016) found that revascularization was a risk factor independently associated with the need for reamputation, which is consistent with the results of the multivariate analysis of this study (6).

According to the study, no difference was found between patients who underwent peripheral vascular intervention and those who did not in terms of revision amputation surgery. Peripheral arterial disease emerges as an influential factor in the formation, progression, and delayed healing of diabetic foot ulcers. Due to vascular insufficiency, the progression of the wound and delayed healing lead to the process advancing towards amputation a significant predictor of re-amputation in multivariate analysis. This suggests that vascular disease is not significantly associated with re-amputation (11).

In this study, no difference was found between patients who underwent peripheral vascular intervention and those who did not in terms of revision amputation surgery. In a study by Nerone et al. (2013), a relationship was found between diabetic foot lower extremity major revision amputation and the surgical specialty performing the amputation, a difference was found in the frequency of revision surgery between amputations performed by vascular surgery and those performed by orthopedic and trauma surgery (12).

A literature review revealed that there are no studies specifying the separate values of hemoglobin at admission and discharge. In this study, no relationship was found between admission hemoglobin levels, discharge hemoglobin levels, and revision amputation surgery. In a study by Younger et al. (2009), it was noted that hemoglobin levels were not associated with the level of revision amputation (7). The results of the study are consistent with previous findings.

No studies were found that separately address platelet values at admission and discharge. In the study, no significant relationship was found between admission platelet levels, discharge platelet levels, and revision amputation surgery. However, in a study conducted by Mineoka et al. (2019) in patients with type 2 diabetes, a positive relationship was found between an increased lymphocyte to neutrophil ratio and the frequency of diabetic foot ulcers (13). However, the results of the two studies differ.

In a study by Nather et al. (2008), it was shown that HbA1c levels are an independent risk factor in determining the level of amputation (below-the-knee or above-the-knee) (14). Younger et al. (2009) highlighted HbA1c levels as one of the most important factors affecting success, attributing this to the fact that they indicate whether blood sugar (glucose regulation) is well-controlled (7). On the other hand, Nerone et al. (2013) found that major amputations were not affected by high HbA1c levels. In this study, no statistically significant relationship was found between admission HbA1c levels, discharge HbA1c levels, and revision amputation surgery (12).

In this study, revision surgery was more frequently observed in patients with higher admission and discharge albumin levels. The literature review revealed that there are no studies specifying the separate values of albumin at admission and discharge. In a study by Lipsky et al. (2007), it was noted that low serum albumin levels were associated with treatment failure (15). Flores Rivera et al. (1998) claimed that low serum albumin levels are associated with poor prognosis and an increased risk of amputation (16). In a study by Czerniecki et al. (2019), no relationship was found between albumin levels and revision amputation surgery (17).

The literature review revealed that there are no studies specifying the separate values of sedimentation at admission and discharge. In this study, no relationship was found between admission sedimentation levels, discharge sedimentation levels, and revision amputation surgery. In a study by Lipsky et al. (2007), it was stated that an increased sedimentation rate is one of the determinants of treatment failure in diabetic foot (15). However, in a study by Baumfeld et al. (2018), it was found that the sedimentation rate has no effect on wound healing (18).

In the literature review, no studies were found in which CRP admission and discharge values were reported separately. There are many studies evaluating the relationship between RP and revision lower limb amputation. In a study by Gulcu et al. (2020), it was found that increased CRP levels are associated with revision amputation surgeries (19). In a study by Volaco et al. (2004), a relationship was found between high CRP levels and revision surgery, while in the study by Baumfeld et al. (2018), no relationship was found between CRP levels and treatment failure (18,20). In our study, no relationship was found between admission CRP levels, discharge CRP levels, and revision amputation surgery.

## CONCLUSION AND RECOMMENDATIONS

The study found that revision amputation was more frequent in patients with higher initial albumin levels. Revision amputation was also more frequent in patients with higher albumin levels at discharge. The frequency of revision amputation increased in patients with higher potassium levels at admission. Revision amputation was more frequently observed in patients with lower potassium levels at discharge.

Contrary to common knowledge, the high levels of albumin at admission and discharge, which are generally considered important, may not be a factor influencing revision amputation. In fact, high albumin levels may emerge as a factor contributing to the need for revision in patients who undergo amputation. Maintaining balanced potassium levels is another notable point in the study. Uncontrolled high or low potassium levels can lead to the need for revision amputation. Patients should receive diabetes education, and a multidisciplinary approach should be adopted.

### Limitations

The study was conducted at a single center and represents the outcomes only for the patients included in the study.

### Conflict of interest

The authors declare no conflict of interest.

### Declaration

The article I have submitted to your journal has not been previously submitted to any other journal and has not been published.

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### Data availability statement

The original contributions presented in the article; further inquiries can be directed to the corresponding author.

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