Original Article / Özgün Araştırma

The Effect of Atherosclerotic Load on Transmetatarsal Amputation Failure in Patients with Diabetic Foot

Diyabetik Ayak Hastalarında Aterosklerotik Yükün Transmetatarsal Amputasyon Yetmezliğine Etkisi

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Abstract

Objective: The aim of this retrospective study was to investigate predictabilty of transmetatarsal amputation (TMA) failure in patients with diabetic foot with peripheral arterial disease.
Materials and Methods: Between January 2015 and November 2018, patients with diabetic foot, who had been followed up for 12 months after having TMA were evaluated. Atherosclerotic load was calculated from conventional angiographic images by using the modified Bollinger angiogram scoring method. Patients were classified as reamputation and non-reamputation groups after TMA at 12 months. Statistical difference analysis of atherosclerotic load was made between two groups.
Results: Twenty-seven diabetic foot patients whom have had TMA and angiographies before TMA were included in the study cohort. In the 12 month study period, 6 (22.2%) patients have had reamputation after TMA. The mean angiogram scores of reamputation group and non-reamputation group were 47.3 (±11.4) and 15.5 (±9.2), respectively. There was a statistically significant difference between the mean angiogram scoring of the two groups ($p<0.001$). Correlation was found between atherosclerotic load and TMA failure (r:-0,694, $p<0.001$). Receiver-operating characteristic curve analysis suggested that the optimum angiographic score cut-off value for reamputation at 12 month period was 29.5, with 100% sensitivity and 90.5% specificity.
Conclusion: Atherosclerotic load of lower limb arteries is associated with TMA failure. Atherosclerotic load that was calculated by using modified Bollinger angiographic score system can be used to predict TMA failure.

Keywords
Transmetatarsal amputation, atherosclerotic load, diabetic foot

Anahtar Kelimeler
Transmetatarsal ampütasyon, ateroskleroz, diyabetik ayak

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Öz

Amaç: Bu retrospektif çalışmanın amacı, periferik arter hastalığı olan diyabetik ayaklı hastalarda kısa dönemde oluşabilecek transmetatarsal ampütasyon (TMA) yetersizliğinin öngörülebilirliğini araştırmaktır.
Gereç ve Yöntemler: Ocak 2015-Kasım 2018 tarihleri arasında TMA yapılmış diyabetik ayak hastalarının 12 aylık takipleri değerlendirildi. Ameliyat öncesi aterosklerotik yük, modifiye Bollinger anjiyogram skorlama yöntemi kullanılarak hesaplandı. Hastalar, TMA sonrası 12 ay içinde yeniden ampütasyon olan ve olmayan gruplar olarak sınıflandırıldı. Aterosklerotik yükün yeniden ampütasyona etkisi istatistiksel analiz yapılarak hesaplandı.

Bulgular: Çalışma grubuna TMA öncesi anjiyografi yapılmış 27 diyabetik ayak hastası dahil edildi. On iki aylık çalışma döneminde 6 (%22,2) hastaya TMA sonrası yeniden ampütasyon uygulandı. Yeniden ampütasyon yapılan grubun ve yeniden ampütasyon yapılmayan grubun ortalama anjiyogram skorları sırasıyla 47,3 (±11,4) ve 15,5 (±9,2) idi. İki grubun ortalama anjiyografi skorları arasında istatistiksel olarak anlamlı fark vardı (p<0,001). Aterosklerotik yük ile TMA yetmezliği arasında korelasyon olduğu bulundu (r:-0,694, p<0,001). On iki aylık dönemde yeniden ampütasyon için optimum anjiyografik skor kesme değeri 29,5 olarak hesaplandı (%100 duyarlılık ve %90,5 özgüllük).
Sonuç: Alt ekstremite arterlerinin aterosklerotik yükü TMA yetmezliği ile ilişkili olabilir. Modifiye Bollinger anjiyografik skor sistemi kullanılarak hesaplanan aterosklerotik yük, kısa dönemde TMA yetersizliği olabileceğini tahmin etmek için kullanılabilir.

Introduction

Diabetic patients have high risk of complications. One of the most important complication is peripheral vascular disease, which may lead to diabetic foot ulcers (1). Diabetic foot ulcers may cause osteomyelitis or gangrene and cause lower extremity amputation. About 15% of all diabetic patients will develop a foot ulcer during their lifetimes (2). Diabetic patients with nonhealing ulcers of the midfoot, hindfoot, forefoot or ankle can be treated by transtibial amputations (TTA). However, TTA has high postoperative morbidity and mortality (3). Diabetic patients with nonhealing foot ulcers have operative alternatives that allow amputation at a more distal level. Transmetatarsal amputation (TMA) is an another effective surgical alternative method. However, TMAs are associated with significant failure or reamputation rates of between 26% and 63% (4,5). Peripheral arterial disease (PAD) was a risk factor for TMA failure (6). Although noninvasive ankle-brachial index measurements are often used for determining PAD, angiography is the gold standard method for PAD at lower extremity. Bollinger angiographic score system (7) is one of the way to analyze atherosclerotic load, and the bypass vs. Angioplasty in Severe Ischemia of the Leg trial showed its usability in patients with limb ischemia (8,9). In this retrospective study, we aimed to investigate the predictability of TMA failure in diabetic foot patients using the modified angiogram scoring method that detects atherosclerotic burden.

Materials and Methods

This retrospective study conducted between January 2015 and November 2018 on diabetic foot patients, who have had TMA and angiography before TMA procedure. The study was approved by the Adnan Menderes University Ethics Committee (protocol number: 2019/198, date: 19.12.2019). Informed written consent was received from all patiets. Inclusion criterias were patients who were undergone TMA for diabetic foot in study period and who were undergone conventional angiography and/or percutaneous balloon angioplasty (PBA) before TMA and patients who had monitoring 12 months. Exclusion criterias were initial amputation, patient who had not undergone conventional angiography and/or PBA before TMA. Each patient's assessment for decision of TMA and/or angiographic intervention were done in multi-disciplinary diabetic foot council.

Vascular interventions were performed via antegrade approach from the superficial femoral artery. PBA was performed when hemodynamically significant stenosis or occlusion was observed. All procedures were performed by an interventional radiologist. All angiography procedures were performed in operating room equipped with a C-arm brillance (Artis zee; Siemens, Erlangen, Germany).

TMA attempt was begun with removal of infected tissues and preserve plantar skin and soft tissue flaps for dorsal foot tissues. The metatarsals' sharp edges are smoothed. The first two metatarsals were amputated at the same level. The third to fifth metatarsals were amputated in as a cascade to the lateral border of the foot (Figure 1). All procedures were performed by an orthopedic surgeon.

Modified Bollinger scoring system (7) was used to assess the angiographies. Bollinger angiographic scoring system is based on the number and presence of stenoses and occlusions of each arterial segment. It consist of 13 infrainguinal arterial segments. Each of these arterial segment was scored with the severity of the disease. Four severities of disease are recognized in this method: occlusion, stenosis ≥50%, stenosis between 25% and 50%, and plaques affecting ≤25% of the luminal diameter. Each type of lesion was characterized by either a single lesion, multiple lesions affecting less than half of the artery

or multiple lesions affecting greater than half of the artery. For each severity of disease, only one extent of disease category is scored (Table 1). In this study, we made some modifications to Bollinger angiographic scoring system because of the antegrade approach of angiographies in our study. Five target infrainguinal arteries were assessed: superficial femoral artery, popliteal artery, anterior tibial artery (ATA), posterior tibial artery (PTA) and peroneal artery (Figure 2). Plantar arch was not evaluated because of unsatisfactory quality images in some angiographies. Also, in our modified Bollinger scoring system arteries were not divided as proximal and distal segments. Total angiographic scores were cumulative scores from each artery scores (maximum: 75; minimum: 0). Scoring was performed from post PBA images, in patients who had PBA.

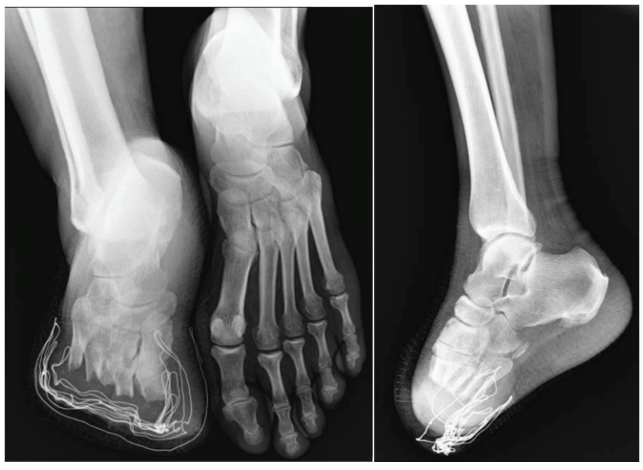

Figure 1. Sixty two year old male who had transmetetarsal amputation of right foot. Antero-posterior and lateral radiography show amputation level. This patient has no re-amputation at 12 mounths

Table 1. Bollinger scoring matrix*

Occlusion	Stenosis >50%	Stenosis <50%	Plaques	Location
	4	2	1	Single
13	5	3	2	Multipl <h
15	6	4	3	Multipl >h

*The vertical columns represent the different severities of atherosclerotic lesions observed, the horizontal ones the location of the lesions detected in each of the arterial segments. The numbers appering in the single field correspond to the score number. The additive score for each artery is obteined by adding the scores (see text for details).

h: Half the segment length

Patients were clinically evaluated after the procedure every 2 months by diabetic foot care team and were followed up for 12 months.

The patients were classified as reamputation and non-reamputation group after TMA at 12 months. We investigated whether there was any statistically significant difference of angiographic scoring system between the two groups. The predictive value of angiographic scoring system in TMA failure was analyzed by receiver-operating characteristic (ROC) curve. Optimal cut-off value for angiographic score was determined; sensitivity and specificity were calculated.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 17.0 statistical software for Windows (SPSS Inc, Chicago, IL, USA) was used for statistical analyses. Descriptive statistics for continuous parameters were expressed as arithmetic means ± standard deviation or median (interquartile range). Spearman's rank test was used to determine correlation. Mann-Whitney U test was used to determine statistical difference between groups. The effect of angiographic score was studied by constructing a ROC curve with TMA failure as the primary variable. Also area under the curve (AUC) value for ROC curve was determined. Optimal cut-off value for angiographic score was determined; sensitivity and specificity were calculated. P-values <0.05 were considered statistically significant.

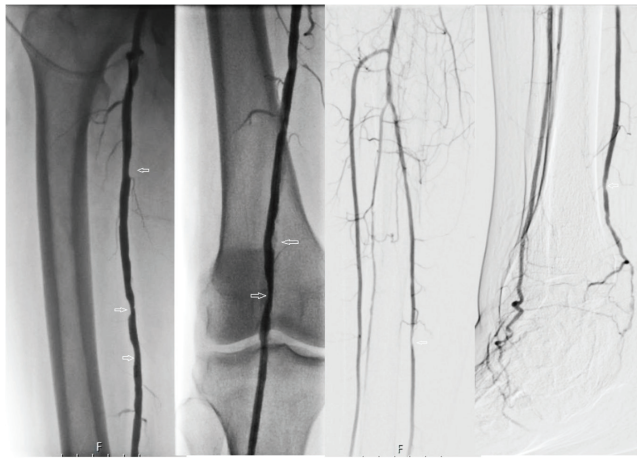

Figure 2. Conventional angiogram of the patient in Figure 1. Superficial femoral, popliteal and tibialis posterior artery have plaques and stenoses (arrows indicate the plaques and stenotic areas) Patients' angiogram score was 15

Results

Twenty-seven patients with diabetic foot matching the study criteria were found between January 2015 and November 2018. Of these patients, 20 (74.1%) were men and 7 (25.9%) were women. Mean age of patients were 65.4 years (range: 52-86). The mean duration of diabetes mellitus (DM) was 19.2 years (range: 9-28). Five (18.5%) severe stenosis, 7 (25.9%) mild stenosis and 15 (55.6%) total occlusions were detected on 27 angiograms. The mean total angiogram score was 22.5 (±16.5) in all patients. Based on affected arteries, ATA was the most affected artery and it affected in 11 (40.7%) patients. ATA and PTA were the most affected binary arteries 6 (22.2%). Infrapopliteal arteries were more affected than suprapopliteal arteries 24 (88.8%), 3 (11.1%), respectively. PBA was conducted in 17 (63%) patients (reamputation group 6 (100%), non-reamputation group 11 (52.4%). At post-PBA, 4 patients in reamputation group and 7 patients in non-reamputation group had an in-line flow to the foot, with at least a single-vessel below knee run-off. Remaining 10 (37%) patients either did not have severe stenosis-occlusion or did not accept PBA. In the 12 month study period, 6 (22.2%) patients have had reamputation due to TMA failure. In all of these patients, TMA failure had occured in the first 6 months. The mean angiogram score in reamputation group and non-reamputation group were 47.3 (±11.4) and 15.5 (±9.2), respectively (Table 2). Statistically significant difference was found between the mean angiogram scoring of the groups ($p<0.001$) (Figure 3). There was correlation between atherosclerotic load that was calculated by angiographic scoring system and TMA failure (r:-0,694, $p<0.001$). ROC curve analysis showed that the optimum angiographic score cut-off value for reamputation at 12 month was 29.5, with 100% sensitivity and 90.5% specificity. The AUC value was 0.98 (95% confidence interval: 0.95-1.00).

Discussion

TMA is an effective surgical approach in diabetic patients with forefoot gangrene and infection. In 1949, McKittrick first reported TMA as a method with 67% satisfactory outcomes in patients with DM (10). However, several studies have shown showed a high rate of TMA failure (4,5,11-13). In this situation, patients require more proximal amputation. In a meta analysis that include 24 studies with 1453 TMAs, Thorud et al. (14) found 33.2% rate of major amputation after TMA. Despite the high rates of failure, TMA is the preferred method because it maintains the ambulatory state of the foot.

Some studies have suggested risk factors associated with failure of amputations, such as sepsis, emergency surgery, renal disease, high body mass index, and longer operating duration (5,15,16). Also, abnormalities in leukocyte count, lymphocyte count, hemoglobin and albumin levels were found risk factors

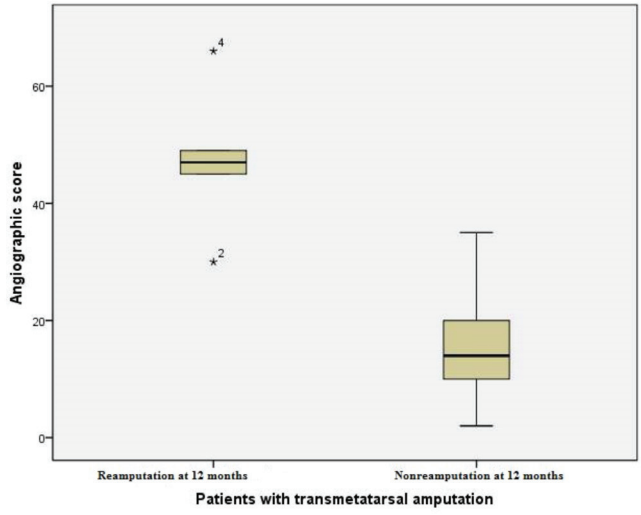

Figure 3. Graph showing a significant difference for angiographic score between patients with re-amputation and non re-amputation at 12 mounths

Table 2. Demographic characteristics, occlusive artery numbers and mean angiogram score of patients with reamputation and non-reamputation at 12 mounths after transmetatarsal amputation

	Patients with reamputation (n=6)	Patients without reamputation (n=21)
Gender (%male)	4 (66.7%)	16 (76.2%)
Mean age (years)	70.8 (±11.0*)	63.3 (±8.88*)
Steotic or occlusive artery number		
One artery	0	12
Two artery	3	7
Three artery	2	2
Four ≤ artery	1	0
Mean angiogram score	47.3 (±11.4*)	15.5 (±9.2*)

*Standard deviation, n: Number

for TMA failure (17). Another predictive risk factor for TMA failure is PAD of the lower extremity. Pollard et al. (16) suggest that TMA is associated with high complication rates in patients with vascular disease and they showed that palpable pedal pulse was a good predictor of healing (16). Some studies reported that forefoot amputations in patients with diabetus mellitus who had vascular disease were followed by subsequent proximal amputations (6,18,19). Humphrey et al. (6) showed 11% reoperation and 8% major amputation rate in their small cohort study with 41 patients, and found all patients who required reoperation, had peripheral vascular disease. Another study by Mandolfino et al. (19) analyzed 218 TMAs and reported presence of severe PAD is a significant risk factor for TMA failure. Shi et al. (20) showed that patients who underwent open bypass surgery have a better outcome than patients who underwent endovascular treatment. They found 44% rate of limb loss after TMA in a 3-year follow-up. Tan et al. (21) performed revascularization via open surgery or PBA and they showed complete healing of TMA in 63% of patients. In our study, endovascular treatment was performed in 17 (63%) patients (100% of reamputation group and 52.4% of non-reamputation group), and also 6 patients (22.2%) had reamputation after TMA procedure and all those TMA failures occured in the first 6 months.

In diabetic patients, PAD involves more distal arteries with diffuse calcification than non-diabetic patients (22). Although the importance of atherosclerotic burden in the treatment of patients with pulmonary arterial hypertension has been demonstrated, there is insufficient data on the effect of atherosclerotic burden in patients with TMA failure. The angiogram scoring method is feasible for showing the atherosclerotic load in infrapopliteal arteries (8,9). Matsukura et al. (23), used modified Bollinger scoring system of paramalleolar region arteries for investigate its usefulness at operative outcome of critical limb ischemia. Like Matsukura et al. (23), we made a new modified Bollinger scoring system on infrainguinal arteries in this retrospective study.

In our study, contrast to previous studies, we focused not only presence of vascular disease but also on the effects of atherosclerotic load in lower limb with TMA failure in 12 months period. We calculated atherosclerotic load by using modified Bollinger angiogram scoring system and we showed that patients with TMA failure have significantly higher atherosclerotic load than patients without TMA failure in the 12 month period. Patient with angiographic score of more than 29.5 is more likely to have TMA failure with 100% sensitivity and 90.5% specificity rates.

In contrast to our study, a study conducted by Toursarkissian et al. (24) reviewed 41 patients with TMA and 35 patients who had revascularization before TMA procedure, and foot vessels were assigned run off scores and this study showed that angiographic findings were insufficient to predict TMA failure.

Retrospective design of study, small number of cohort and limited arterial segmental evaluation (superficial femoral, popliteal, ATA, PTA and peroneal arteries) due to antegrade approach were limitations of this study. Also, in some patients, having PBA may lead to errors in scoring, because that angiographic scoring was done after PBA in these patients. The retrospective design and long term of study restricted our investigation into other possible predictive risk factors for TMA failure in our cohort.

Conclusion

This study showed that atherosclerotic load of lower limb arteries may be associated with TMA failure. Atherosclerotic load that was detected by using Bollinger angiographic score system may have a good prediction with high sensitivity and specificity values for TMA failure in diabetic foot patients. Additional angiographic studies with a large cohort group are needed to identify the effect of atherosclerotic load on the TMA failure in diabetic patients.

Ethics

Ethics Committee Approval: The study was approved by the Adnan Menderes University Ethics Committee (protocol number: 2019/198, date: 19.12.2019).

Informed Consent: Informed written consent was received from all patiets.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.C., Ş.Ö.Ş., Concept: M.B.Ç., T.Ş., E.C., Ş.Ö.Ş., Design: M.B.Ç., T.Ş., E.C., Ş.Ö.Ş., Data Collection or Processing: M.B.Ç.,

Analysis or Interpretation: M.B.Ç., Literature Search: M.B.Ç., Writing: M.B.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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