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Assessment of the efficacy of endovascular treatment in chronic limb-threatening ischemia in diabetic and non-diabetic patients

Diyabetik ve non-diyabetik hasta gruplarında kronik ekstremite tehdit eden iskemide endovasküler tedavi etkinliğinin değerlendirilmesi

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Abstract

Aim: Peripheral artery diseases are a very common manifestation of atherosclerosis. We assessed the clinical outcomes of diabetic versus non-diabetic patients with chronic limb-threatening leg ischemia who underwent Peripheral Transluminal Angioplasty (PTA).

Methods: The patients (84 diabetic/66 non-diabetic) who underwent percutaneous transluminal angioplasty (PTA) in the lower extremity arterial lesions (stenosis/occlusion) because of chronic limb-threatening leg ischemia (Rutherford class 4 and above) between June 2013 and March 2020 were included in the study.

Results: Six-month primary patency rates were 86.5% and 93.3% in the diabetic and non-diabetic group, respectively. The 12-month primary patency rates were 73.0% and 73.3%; and 12-month secondary patency rates were 66.7% and 77.8%. No differences were detected between the groups in terms of patency rates. Major amputation and total amputation rates were higher at statistically significant levels in the diabetic patient group (%16.7% vs. 6.1%; *P*=0.003) (34.6% vs. 22.8%); *P*=0.004)

Conclusion: When patency and amputation rates are evaluated in diabetic and non-diabetic patient groups with limb-threatening chronic leg ischemia after endovascular treatment, good clinical results were reported in these two groups. Current results suggest that endovascular treatment can be used safely and effectively in both patient groups.

Keywords: Limb-threatening ischemia, Endovascular intervention, Diabetes mellitus

Öz

Amaç: Periferik arter hastalıkları, aterosklerozun neden olduğu günümüzde giderek yaygınlaşan hastalıklardır. Çalışmamızda Periferik Transluminal Anjiyoplasti (PTA) uygulanan kronik ekstremite tehdit eden bacak iskemisi olan, diyabetik ve non-diyabetik hasta gruplarının, klinik sonuçlarını değerlendirmeyi amaçladık.

Yöntemler: Haziran 2013 - Mart 2020 tarihleri arasında kronik ekstremite tehdit eden bacak iskemisi (Rutherford sınıf 4 ve üzeri) nedeniyle alt ekstremite arteriyel lezyonlarına (darlık / tıkanıklık) perkütan transluminal anjiyoplasti (PTA) işlemi uygulanan 150 hasta (84 diyabetik / 66 non-diyabetik) çalışmaya dahil edilmiştir.

Bulgular: Altı aylık primer açıklık oranları diyabetik ve diyabetik olmayan grupta sırasıyla %86,5 ve %93,3 idi. 12 aylık primer açıklık oranları %73,0 ve %73,3 iken; 12 aylık sekonder açıklık oranları ise %66,7 ve %77,8 idi. Açıklık oranları açısından gruplar arasında farklılık tespit edilmedi. Diyabetik hasta grubunda majör ampütasyon (%16,7-%6,1; *P*=0,003) ve toplam amputasyon oranları (%34,6-%22,8; *P*=0,004) istatistiksel olarak anlamlı düzeylerde daha yüksekti.

Sonuç: Endovasküler tedavi sonrası ekstremite tehdit eden kronik bacak iskemisi olan diyabetik ve diyabetik olmayan hasta gruplarında açıklık ve amputasyon oranları değerlendirildiğinde, her iki grupta da başarılı klinik sonuçlar bildirilmiştir. Güncel sonuçlarımız, endovasküler tedavinin ekstremite tehdit eden iskemide her iki hasta grubunda da etkili bir şekilde kullanılabileceğini göstermektedir.

Anahtar kelimeler: Ekstremite tehdit eden iskemi, Endovasküler girişim, Diabetes mellitus

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Introduction

Peripheral artery diseases are a very common manifestation of atherosclerosis. Its incidence increases in the presence of advanced age and cardiovascular risk factors [1,2]. Peripheral artery diseases are more common in diabetic patients, and their prevalence ranges from 9.5% to 13.6% in this group [3,4], while it is approximately 4% in the general population [1].

The atherosclerotic plaques in the lower extremity cause stiffness in wrist arteries, reduce vascular resistance, and decrease blood flow, creating ischemic symptoms, which, eventually, leads to clinical conditions that range from claudication to limb-threatening leg ischemia and can result in tissue loss. This critical leg ischemia can be defined with ischemic rest pain and nocturnal recumbent pain as well as ischemic skin lesions, ulcers, and frank gangrene [5]. In these patients, medical treatment results do not provide the expected clinical recovery [6]. In recent times, the encouraging and successful results of the endovascular treatment option [7] have made the endovascular treatment the first-line treatment option in peripheral vascular diseases in our clinic.

We assessed the clinical outcomes of diabetic versus non-diabetic patients with chronic limb-threatening leg ischemia who underwent Peripheral Transluminal Angioplasty (PTA).

Materials and methods

A total of 150 patients (84 diabetic/66 non-diabetic) were included in the study. The patients underwent percutaneous transluminal angioplasty (PTA) in the lower extremity arterial lesions (stenosis/occlusion) because of chronic limb-threatening leg ischemia (Rutherford class 4 and above) between June 2013 and March 2020. The study was commenced after approval was obtained from Adıyaman University Ethics Committee (Approval number: 2020/5-29). The exclusion criteria included having aortoiliac endovascular reconstruction and advanced endovascular procedures like atherectomy and mechanical thrombectomy, acute critical ischemia and functionally unsalvageable limb. The demographic, clinical and procedural data of the patients were obtained from patient files and clinical records. Patients who were Class 4 and above according to Rutherford Qualification were included in the study [8].

The measurement of Ankle Brachial Index (ABI) was performed after 5 min resting in supine position to all patients routinely in our clinic after the diagnosis of peripheral artery disease. Again, all patients who are scheduled for intervention undergo 3D Computed Tomography Angiography (3D-CTA) from abdominal aorta to tiptoe. All interventions are performed by the same cardiovascular surgery team in the cardiac catheterization laboratory.

All interventions are carried out under local anesthesia. Vascular access is often provided with Retrograde 6 F or 7 F sheath from the counter-lateral femoral artery. However, access can also be provided by placing antegrade sheath (4 F) in cases with isolated popliteal or tibial artery lesions through the ipsilateral femoral artery. The location and degree of the lesion are determined after the angiography process. Anticoagulation is administered to all patients with intravenous heparin (5.000 units) with an activated clotting time value of 200-250 sec. All lesions are passed by using hydrophilic guidewires (0.014-, 0.018-, 0.035-inch) through endoluminal or subintimal routes, and it is checked whether they are in the endoluminal location after a subsequent angiography. The healthy distal part of the vessel that will undergo the intervention is taken as the reference for the balloon measure. A balloon (2.5-8.0 mm) in appropriate size is selected and inflated in a time interval of 120-180 sec with 6-12 atmospheric pressure; an angiogram is performed again after the process, and technical results are evaluated. The stent is applied to all patients with current-restricting dissection, residual stenosis above 30%, intimal flap and acute occlusion; and the detection of residual stenosis under 30% is considered a technical success after PTA and stent application.

Following the procedure, 100-mg aspirin a day is started in patients without contraindications, and is continued for life. For the patient group with stents, 75 mg clopidogrel is administered once a day after an additional 300 mg clopidogrel loading dose following the intervention to be continued for 1 year.

After discharge, patients are called for clinical follow-ups, first in the 4th week, with 3-month intervals. The follow-ups are carried out with non-invasive techniques like pulse examination and hand doppler ultrasonography. In case a lack of pulse, claudication or resting pain are detected, 3D Computed Tomography Angiography (3D-CTA) from abdominal aorta to tiptoe is performed. If necessary, angiography is performed again, and a new endovascular intervention is planned if ≥50% angiographic stenosis is detected in the vascular segment that was treated.

In our study, primary patency was defined as a permanent opening in the vascular segment treated, for which no new endovascular or surgical intervention was required. Secondary patency, on the other hand, was defined as permanent opening after a reintervention for the lesion. Partial amputations of the heel and foot were defined as minor amputations, and all amputations above the ankle were defined as major amputations.

Statistical analysis

The SPSS 11.5 Program was used in the analysis of the data. Mean (standard deviation) and median (minimum-maximum) were used descriptively for quantitative variables; and number of patients (percent) was used for qualitative variables. In quantitative variables, the qualitative variable with two categories was tested with the Mann-Whitney U-test since there were no differences between the categories, and normal distribution assumptions were not met. The Chi-Square test was used to examine the relationship between two qualitative variables. The statistical significance limit was 0.05.

Results

A total of 150 patients who underwent endovascular intervention because of chronic limb-threatening leg ischemia were included in the study. A total of 56% (n:84) of the patients included in the study were in the Diabetic Group, and 44% (n:66) were in the Non-Diabetic Group. The mean age was 65.02 (11.59) in the diabetic patient group, and 68.58 (7.43) in the non-diabetic group (Table 1). The mean follow-up duration of the diabetic patient group was 14.76 (2.72) months, and that of the non-diabetic group was 13.94 (2.54) months (Table 1). When compared with non-diabetic patients, diabetic patients had a higher percentage of coronary artery disease (92.9% vs. 78.8%; P=0.012) (Table 2). Other demographic data and additional diseases of the patients are given in Tables 1 and 2. Although pure SFA (superficial femoral artery) lesion was not detected in the diabetic patients, pure popliteal diseases were observed in 16.7% (n:14) of the patients, pure tibial, in 16.7% (n:14), SFA+distal, in 23.7% (n:20), popliteal+distal, in 28.6% (n:24), and tibial+distal artery diseases, in 14.3% (n:12). In the non-diabetic group, on the other hand, pure SFA lesion was detected in 6.1% (n:4) of the patients, pure popliteal disease, in 24.2% (n:16), pure tibial disease, in 18.2% (n:12), femoral+distal, in 24.2% (n:16), popliteal+ distal, in 21.2% (n:14), and tibial+distal artery diseases, in 6.1% (n:4). Distal disease was detected relatively more frequently in the diabetic patient group; however, this did not cause a statistically significant difference (P<0.05) (Table 2). Among the patients who underwent intervention in the diabetic patient group, 40.5% (n:34) were classified as Category 4 according to the Rutherford Qualification, 38.1% (n:32) were Category 5, and 21.4% (n:18) were Category 6. Among the patients who underwent intervention in the non-diabetic patient group, 42.4% (n:28) were classified as Category 4, 42.4% (n:28), as Category 5, 15.2% (n:10) as Category 6 according to the Rutherford Qualification. Although patients with Rutherford Classification Category 6 were relatively higher in the diabetic patient group, this did not cause a statistically significant difference (P<0.05) (Table 2).

Table 1: Preoperative data 1

Variables	Group				
	Diabetic		Non-Diabetic		
	Mean(SD)	Med (Min-Max)	Mean(SD)	Med (Min-Max)	P-value
Age	65.02(11.59)	65.00 (27.00-87.00)	68.58(7.43)	67.00 (55.00-87.00)	0.067
Hba1c	10.15(1.37)	10.00 (7.90-13.50)	4.17(0.97)	4 (3.90-5.50)	<0.001
ABI	0.37(0.09)	0.38 (0.11-0.54)	0.36(0.08)	0.37 (0.19-0.48)	0.306
Follow-Up Time (months)	14.76(2.72)	14.00 (10.00-24.00)	13.94(2.54)	14.00 (9.00-14.00)	0.121

ABI: Ankle Brachial Index

Table 2: Preoperative data 2

Variables		Group				
		Diabetic		Non-Diabetic		
		n	%	N	%	P-value
Gender	Male	66	78.6	50	75.8	0.683
	Female	18	21.4	16	24.2	
Smoking		60	71.4	52	78.8	0.304
HT		44	52.4	40	60.6	0.314
HL		62	73.8	50	75.8	0.785
CKD		14	16.7	8	12.1	0.435
ASA		76	90.5	60	90.9	0.928
CAD		78	92.9	52	78.8	0.012
	Sfa	0	0.0	4	6.1	0.096
Lesion location	Popliteal artery	14	16.7	16	24.2	
	Tibial+distally arteries	14	16.7	12	18.2	
	Sfa+distally arteries	20	23.7	16	24.2	
	Popliteal+distally arteries	24	28.6	14	21.2	
	Tibial+distally arteries	12	14.3	4	6.1	
Rutherford classification	4	34	40.5	28	42.4	0.610
	5	32	38.1	28	42.4	
	6	18	21.4	10	15.2	

HT: Hypertension, HL: Hyperlipidemia, CCD: Chronic Kidney Disease, ASA: Acetylsalicylic Acid, CAD: Coronary Artery Diease, Sfa: Superior Femoral Artery

Our technical success rate was 85.7% in the diabetic group and 90.9% in non-diabetic group (P=0.331). No significant differences were detected in technical complications in terms of dissection (11.9% vs 9.1%) and acute embolization (9.5% vs. 6.1%) (P>0.05). The reintervention rates among groups were similar (26.2% vs. 15.2%; P=0.101) (Table 3).

The clinical results of the patients are given in Tables 4 and 5. Six-month primary patency rates were 86.5% and 93.3% in the diabetic and non-diabetic groups, respectively. The 12-month primary patency rates were 73.0% and 73.3%; and 12-month secondary patency rates were 66.7% and 77.8%. No differences were detected between the groups in terms of patency rates (Table 4).

There were no differences between the groups in terms of minor amputation rates (17.9% vs. 16.7%; P=0.761). Major amputation and total amputation rates, on the other hand, were significantly higher in the diabetic patient group (%16.7% vs. 6.1%; P=0.003) (34.6% vs. 22.8%); P=0.004) Wound healing rates were lower in the diabetic patient group (64.0% vs. 86.8%); P=0.005). No differences were detected between the groups in terms of mortality rates during the follow-ups (21.4% vs. 21.2%); P=0.974) (Table 5).

Table 3: Angiographic results

Variables	Group				
	Diabetic		Non-Diabetic		
	n	%	N	%	P-value
Technical Failure	12	14.3	6	9.1	0.331
Dissection	10	11.9	6	9.1	0.579
Embolization	8	9.5	4	6.1	0.438
Reintervention	22	26.2	10	15.2	0.101

Table 4: Primer patency and secondary patency rates

Variables		Group				
		Diabetic		Non-Diabetic		
		n	%	n	%	P-value
SP	Yok	10	33.3	4	22.2	0.412
	Var	20	66.7	14	77.8	
6 months PP	Yok	10	13.5	4	6.7	0.198
	Var	64	86.5	56	93.3	
12 months PP	Yok	20	27.0	16	26.7	0.963
	Var	54	73.0	44	73.3	

SP: Secondary Patency, PP: Primer Patency

Table 5: Clinical results

Variables	Group				
	Diabetic		Non-Diabetic		
	n	%	n	%	P-value
Minor Amputation	15	17.9	11	16.7	0.761
Major Amputation	14	16.7	4	6.1	0.003
Minor+Major Amputation	29	34.6	15	22.8	0.004
Wound Healing	32	64.0	33	86.8	0.005
Mortality	18	21.4	14	21.2	0.974

Discussion

Amputation and mortality risks are high in patients with limb-threatening leg ischemia. Major amputation and mortality are observed in 30% of these cases within 1 year after the diagnosis [9]. Successful revascularization is required to reduce amputation rates, accelerate wound healing and reduce mortality rates. As a less invasive method, percutaneous intervention is preferred with the improvements in percutaneous treatment methods in many healthcare centers as a priority for these patients, since bypass surgery is a risky surgical intervention because of advanced age and cardiac comorbidities [10]. In our study, the purpose was to determine the effect of percutaneous interventions on wound healing, minor and major amputation rates in the diabetic and non-diabetic patient group with limb-threatening chronic ischemia in lower extremities and compare the re-intervention rates with primary and secondary patency rates.

Among other objective and non-invasive tests, Ankle-Brachial Index (ABI) can be used in the diagnosis of peripheral artery disease in lower extremities. ABI values are also among the independent variables of mortality and morbidity [11,12]. ABI values being at or below 0.9 confirms the peripheral artery disease diagnosis, and values below 0.4 show limb-threatening leg ischemia [5]. In diabetic patient group, ABI values may not always yield accurate values because of the inability of the arteries to compress due to medial arterial sclerosis [13]. For this reason, there are no significant correlations between the stenosis degree and ABI values in these patients [14]. In diabetic and non-diabetic patient groups with chronic limb-threatening leg ischemia included in our study, the ABI values were 0.37(0.09) and 0.36(0.08), respectively, and the differences were not significant. In their study, Santos et al. [15] also showed that the falsely elevated ABI was in high prevalence in diabetic patients with limb-threatening leg ischemia, and they did not find any differences in terms of ABI values in the diabetic and non-diabetic group when the false-positive ABI values were excluded from the study.

In the present study, after the intervention, 30% or more residual stenosis patients were considered a technical failure, which was observed as 14.3% and 9.1% in the diabetic and non-diabetic group, respectively, and there were no differences between the groups in this regard. The fact that there were excessive calcified lesions in diabetic patients caused relatively high results compared to the non-diabetic group without significance. In their study, Kahraman et al. [16] evaluated the results of endovascular intervention in limb-threatening leg ischemia, and reported the technical failure rate as 27%, and complication rates as 17% during the procedure. In their study, the TASC Group reported the technical success rate as 90% and 1-year primary patency rate as 61% in patients with femoropopliteal lesions that were admitted with claudication complaints [17]. In our study, no differences were detected between the groups in terms of complications like dissection and embolization during the procedure. The process complication rate in the diabetic group was 21.4%, and 15.1% in the non-diabetic group. Likewise, Hanna et al. [18] reported the procedural complication rate as 21% in diabetic patients with limb-threatening leg ischemia who underwent balloon angioplasty [18].

Chronic limb-threatening leg ischemia is more common in diabetic patient group than in non-diabetic patient group, and is associated with higher restenosis and amputation rates [19]. No differences were observed between the groups in our study in terms of 6-month and 1-year primary patency, secondary patency, and minor amputation rates. However, it was found that the major amputation and total amputation rates were statistically and significantly higher in the diabetic group.

Atherosclerosis is diagnosed more frequently in diabetic patients, and progresses in diffuse form. It is already known that chronic high blood glucose values cause abnormalities in vascular endothelium and prepare the ground for hypercoagulability and atherogenesis [20]. In our study, the mean Hba1c value in the diabetic group was 10.15(1.37), which suggested that the patient population had a poor long-term blood glucose control. This may explain why the major and total amputation rates are high with the damage done by diabetes mellitus at microvascular level compared to the non-diabetic group in our study. Also, because of peripheral neuropathy, diabetic patients being asymptomatic for longer durations and applying to the hospital at later stages might be another cause of poor clinical outcomes. In the study conducted by Levigne et al. [21], it was found that there were higher amputation rates after endovascular interventions in the diabetic patient group, which was associated with hyperglycemia, reducing the tolerance of tissue ischemia. Xiao et al. [22] conducted a study and evaluated the effectiveness of endovascular treatment in limb-threatening leg ischemia, and reported that there were no differences between the diabetic and non-diabetic patient groups in terms of 12-month primary and secondary patency and limb recovery rates. In the literature, up to 70% amputation rates were reported in limb-threatening leg ischemia patients, which were 5 times more common in diabetic patients [23, 24]. In our study, the total amputation rates being 34.5% in the diabetic group, and 22.7% in the non-diabetic group shows that endovascular treatment is an effective method reducing amputation rates in both patient groups.

The risk of developing feet wounds in patients with diabetes is up to 25%, and feet lesion is one of the most important risk factors for limb amputation [25]. Diabetes Mellitus and the infection of the wound in the feet are considered predictors of delayed wound healing after endovascular interventions [26]. The 1-year wound healing rate ranges from 54% to 86% after endovascular interventions [27, 28]. In our study, the wound healing rate was 64.0% in the diabetic group and 86.8% in the non-diabetic group. In our study, the delay in wound healing was significantly higher in the diabetic group, which may be a reason of higher amputation rates in the diabetic group despite similar patency rates due to increased metabolic demand in the feet.

Limitations

The retrospective, single-center design of this study, and low patient count can be listed as the disadvantages of this study. The significantly higher rate of preoperative coronary artery disease in the diabetic group might have affected the mortality rates between the two groups. The short mean follow-up duration in the study can also be mentioned as one of the limitations of the study.

Conclusion

When patency and amputation rates are evaluated in diabetic and non-diabetic patient groups with limb-threatening chronic leg ischemia after endovascular treatment, good clinical results were reported in these two groups. Current results suggest that endovascular treatment can be used safely and effectively in both patient groups. However, further prospective studies are required to be conducted with a higher patient population to determine optimal treatment options in especially diabetic patient populations with limb-threatening leg ischemia.

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