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ORIGINAL ARTICLE

Percutaneous angioplasty in the treatment of thrombosed hemodialysis fistulas: A single-center experience with 1 year of follow-up

Tromboze hemodiyaliz fistüllerinin tedavisinde perkütan anjiyoplasti: Bir yıllık takip ile tek bir merkez deneyimi

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ABSTRACT

Objective: Thrombosis of a hemodialysis arteriovenous fistula (AVF) is a serious complication that needs urgent treatment. Most cases are treated surgically, but recently, endovascular strategies have become a viable alternative. This study is an evaluation of the success and patency rate of percutaneous balloon angioplasty of thrombosed hemodialysis fistulas using a drug-coated balloon (DCB) contrasted with a standard balloon (SB).

Methods: The data of 33 patients with a thrombosed native hemodialysis AVF treated percutaneously in a tertiary care center were analyzed retrospectively. Success of the procedure was defined as restoration of flow with less than 30% residual stenosis and resumption of dialysis through the hemodialysis AVF. The success rate of the procedure and the patency rate at 1, 6, and 12 months were evaluated. The effect on patency of a DCB was compared to that of a SB.

Results: Twenty-five radiocephalic and 8 brachiocephalic thrombosed hemodialysis AVFs were treated during the study period. Flow was restored in 23 thrombosed fistulas, a success rate of 69.7%. The patency rate of successfully treated fistulas was 95.6% at 1 month, 76.1% at 6 months, and 57.9% at 12 months. Ten of the 23 re-established AVFs were treated with a DCB and the remainder were treated with a SB. The patency of the fistulas treated with a DCB was similar to that of a SB at 1 month (100% vs 92.3%, respectively; p=0.393). The patency rate of a DCB was greater than that of a SB at 6 months (88.9% vs 66.7%, respectively; p=0.258) and 12 months (75% vs 45.4%, respectively; p=0.219).

Conclusion: Percutaneous intervention for thrombosed hemodialysis AVFs is a safe, minimally invasive, and effective procedure. There was a positive trend in the patency rate of patients treated with a DCB at 6 and 12 months compared with a SB.

ÖZET

Amaç: Hemodiyaliz arteriyovenöz fistüllerinin (AVF) trombozu ciddi bir komplikasyondur ve ivedi bir şekilde tedavi gerektirir. Çoğu olgular cerrahi olarak tedavi edilmekle birlikte son zamanlarda endovasküler tedavi yöntemleri uygulanabilir bir alternatif haline gelmiştir. Bu çalışmada, ilaç kaplı ve standart balonlarla perkütan olarak tedavi edilen tromboze hemodiyaliz fistül işlemlerinin başarı oranlarını ve açıklık oranlarını değerlendirdik.

Yöntemler: Kliniğimizde perkütan olarak tedavi edilmiş tromboze nativ hemodiyaliz AVF'si olan 33 hasta geriye dönük olarak analiz edildi. İşlem başarısı, %30'dan daha az rezidü darlık ile akışın yeniden sağlanması ve hemodiyaliz AVF yoluyla diyalizin tekrar başlaması olarak tanımlandı. İşlemlerin başarı oranları; bir, altı ve 12 aylık açıklık oranları değerlendirildi. Bununla birlikte ilaç kaplı balonların standart balonlara göre açıklık oranlarına etkisi değerlendirildi.

Bulgular: Yirmi beş radiyosefalik ve sekiz brakisefalik hemodiyaliz AVF'si tedavi edildi. Hastaların 23'ünde akım tekrar sağlandı (başarı oranı %69.7). Açıklık oranları ilk ayda %95.6, altıncı ayda %76.1 ve 12. ayda %57.9 idi. Bu 23 hastanın 10'u ilaç kaplı balonla, diğerleri standart balonlarla tedavi edildi. Fistüllerin ilk aydaki açıklık oranları ilaç kaplı balon ve standart balonlarla tedavi edilenlerde benzerdi (sırasıyla, %100 ve %92.3; p=0.393). İlaç kaplı balon tedavisiyle altı (sırasıyla, %88.9 ve %66.7; p=0.258) ve onikinci ay (sırasıyla, %75 ve %45.4 p=0.219) açıklık oranları standart balonlara göre oransal olarak daha yüksekti.

Sonuç: Tromboze hemodiyaliz AVF'lerinin tedavisinde perkütan girişim az invaziv, güvenli ve etkili bir işlemdir. Bununla birlikte 6. ve 12. aydaki açıklık oranlarında ilaç kaplı balonlarda standart balonlara göre iyi sonuçlar izlenmiştir.

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Thrombosis of a hemodialysis arteriovenous fistula (AVF) is a serious complication. Most cases are treated surgically, but endovascular strategies are also now used to treat these patients. Endovascular treatment has become the preferred option because it is safe, less invasive, and associated with lower morbidity. However, the primary patency rate of percutaneously treated patients seems to be low compared with a surgical approach.[1,2] This report is an examination of the success rate, complications, and patency rate of percutaneously treated hemodialysis AVFs. The patency of fistulas treated with drug-coated balloon (DCB) and standard balloon (SB) angioplasty were compared.

Abbreviations:

AVF	*Arteriovenous fistula*
DCB	*Drug-coated balloon*
SB	*Standard balloon*

METHODS

Patients

This was a retrospective, observational, single-center study conducted in the interventional Cardiology Department of Sakarya University between March 2015 and December 2018. The study was performed in accordance with the Declaration of Helsinki, and the study protocol was approved by the Medical Research Ethics Committee of Sakarya University, Faculty of Medicine. All of the patients provided written, informed consent before enrollment in the study.

A total of 33 dialysis-dependent patients with an acute thrombosed hemodialysis AVF who underwent percutaneous intervention to treat the fistula were included. All of the patients were evaluated using color duplex ultrasound to confirm the thrombosed segment. Patients with chronic wall-adherent thrombi or an infected fistula, those unable to give informed consent, and those with a non-native hemodialysis AVF were excluded.

Technique

In all cases, arterial access was used as the entry site for the interventional procedure. Brachial artery access was used in 18 patients, femoral artery access in 10, distal radial artery access in 1, and multisite access (femoral, radial or brachial) was used in the remaining 4 patients. The selected artery was punctured with an angiographic needle using local anesthesia (2% prilocaine). After inserting a guidewire into the artery, the needle was removed and a 5-F or 6-F sheath (Terumo Corp., Tokyo, Japan) was inserted using the Seldinger technique. An antegrade approach was used for brachial artery access. Diagnostic angiography was performed to image the arterial side and

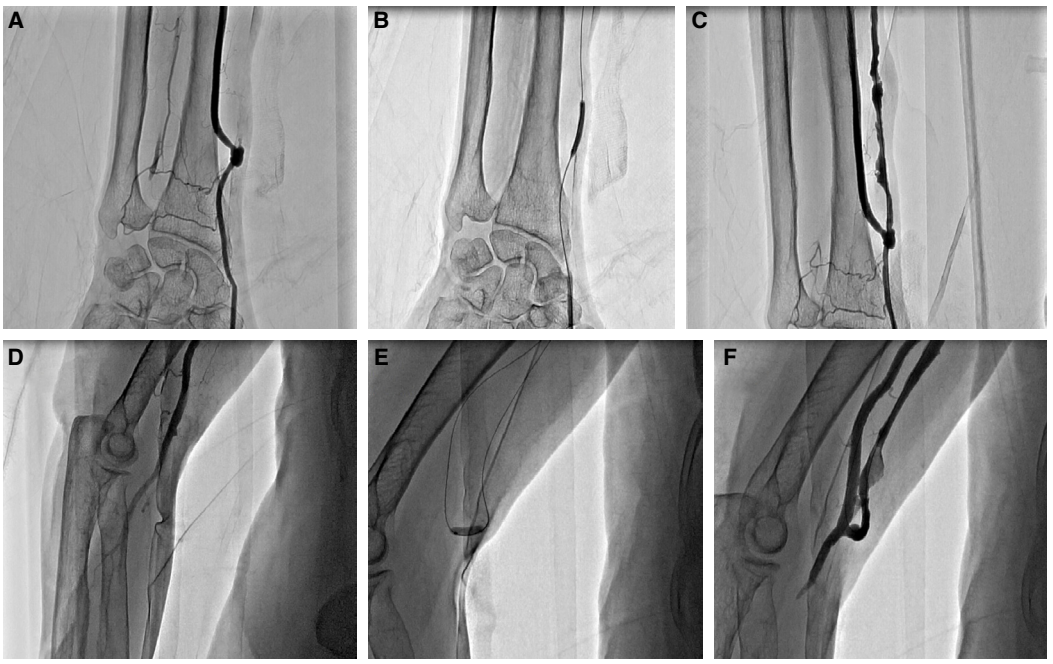

Figure 1. (A) Upper panels show a thrombosed radiocephalic hemodialysis arteriovenous fistula (AVF) and **(B, C)** successful treatment with balloon angioplasty. **(D-F)** Lower panels demonstrate successful treatment of thrombosed brachiocephalic hemodialysis AVF.

the anastomosis of the AVF (Fig. 1). After administering intra-arterial heparin (5000 IU), a 0.014-inch hydrophilic guidewire with an angled guiding catheter (6-F Judkins right or 6-F internal mammary artery guiding catheter; Cordis Corp., Hialeah, FL, USA) was used to pass the thrombosed segment. SB (Chocolate PTA balloon catheter; Medtronic, Inc., Minneapolis, MN, USA or Invader PTCA balloon catheter; Alvimedica, Istanbul, Turkey) sized 3-mm to 6-mm and DCB (Freeway 035 paclitaxel-releasing balloon; Eurocor Tech GmbH, Bonn, Germany) were used. SB angioplasty was performed with an inflation time of 2 minutes at nominal pressure (6 or 9 atm). In the DCB group, predilation with a SB was followed by angioplasty with a DCB with an inflation time of 2 minutes at 6 atm. The procedure was completed after achieving adequate flow to the venous side (Fig. 1). Success was defined as restoration of flow with less than 30% residual stenosis and resumption of dialysis through the hemodialysis AVF. All of the interventions were performed by an interventionalist cardiologist. The patients were discharged with a recommendation for dual antiplatelet therapy for 1 month and single antiplatelet therapy thereafter. Patency was evaluated at 1, 6, and 12 months after the procedure with Doppler ultrasonography. A hemodialysis AVF with a flow rate >500 mL/min was accepted as patent.

Statistical analysis

The data were analyzed using IBM SPSS Statistics for Windows, Version 20.0 software (IBM Corp., Armonk, NY, USA). The parameters were expressed as mean±SD when normal distribution was present, and variables with abnormal distribution were expressed as the median and 25^{th}-75^{th} percentile. The categorical variables were presented as a percentage. Comparisons between the SB and DCB groups of various continuous variables were performed with Student's t-test or the Mann-Whitney U test, according to the distribution. A chi-squared test was used to examine differences in categorical variables. Statistical significance was set at $p<0.05$.

RESULTS

A total of 33 patients (20 males, 60.6%; 13 females, 39.4%) with a thrombosed native hemodialysis AVF were enrolled the study. The mean age of the patients was 64±14 years (range: 23–91 years). The baseline characteristics of the patients are shown in Table 1. Twenty-five of the hemodialysis AVFs were radiocephalic and the remainder were brachiocephalic. The median time between the detection of the loss of thrill in the hemodialysis AVF and intervention was 36 hours (range: 20–72 hours). In all, 23 thrombosed fistulas were treated successfully (69.7%). The age of the thrombus was an important factor in the success of the procedure. The median age of the thrombus in the successfully treated hemodialysis AVFs was 30 hours (range: 18–48 hours), the median age was 66 hours (range: 42.5–78 hours) in the failed procedures ($p<0.05$). The hemodialysis AVFs that could not be recanalized were referred for surgical revision. Ten of the 23 successfully treated thrombosed fistulas were treated with a DCB and the others were treated with a SB. The characteristics and biochemical parameters of the DCB and SB angioplasty patients are shown in Table 2. In 4 patients, thromboaspiration was performed using a guiding catheter in addition to balloon angioplasty. We performed selective thrombolytic therapy in 2 patients. Thrombolytic therapy was preferred only in patients with a high thrombus burden and unresolved flow despite recurrent balloon dilatation. The hemodialysis flow of 1 patient with a reduced thrombus burden following the initial proce-

Table 1. Baseline characteristics of the patients

Number of patients (n)	33
Male/female (n)	20/13
Age (years)	64.03±13.8
Diabetes, n (%)	11 (33.3)
Hypertension, n (%)	12 (36.4)
Coronary artery disease, n (%)	11 (33.3)
Peripheral artery disease, n (%)	8 (24.2)
Dyslipidemia, n (%)	7 (21.2)
Thrombus age (hours)	36 (20–72)
Type of AVF, n (%)	
Radiocephalic	25 (75.8)
Brachiocephalic	8 (24.2)
Access site, n (%)	
Femoral	10 (30.3)
Brachial	18 (54.5)
Distal radial	1 (3)
Multisite	4 (12.1)

Data are illustrated as mean±SD or median (Q1-Q3). AVF: Arteriovenous fistula.

Table 2. Baseline characteristics and biochemical parameters of the DCB and SB angioplasty groups

	DCB Group (n=10)	SB Group (n=13)	Total (n=23)	*p*
Age (years)	63.7±8.9	62.6±14.9	63.1±12.4	0.841
Male sex, n (%)	8 (80)	8 (61.5)	16 (69.5)	0.340
Diabetes mellitus, n (%)	6 (60)	3 (23.1)	9 (39.1)	0.072
Hypertension, n (%)	4 (40)	5 (38.5)	9 (39.1)	0.940
Dyslipidemia, n (%)	4 (40)	2 (15.4)	6 (26.1)	0.183
Coronary artery disease, n (%)	5 (50)	3 (23.1)	8 (34.8)	0.179
Peripheral artery disease, n (%)	2 (20)	4 (30.8)	6 (26.1)	0.560
Thrombus age (hours)	33 (18–72)	30 (16–48)	30 (18–48)	0.474
Hemoglobin (g/dL)	11.5±1.6	10.4±1.4	10.9±1.6	0.086
Hematocrit (%)	35±5	32.3±4.5	33.5±4.8	0.182
Platelet (x10^3)	212.2±78.4	201.3±71.9	206±73.3	0.733
Total cholesterol (mg/dL)	187.9±58.7	158.6±41	171.3±50.5	0.173
LDL-cholesterol (mg/dL)	125.9±40.6	102.8±27.4	112.9±34.9	0.119
HDL-cholesterol (mg/dL)	41.9±9.3	38.7±6.3	40.1±7.7	0.337
Triglyceride (mg/dL)	184.8±111	145.4±59.8	162.6±86	0.287
Left ventricular ejection fraction (%)	57±5.3	56.1±7.1	56.5±6.3	0.757

Data are presented as mean±SD or median (Q1-Q3).
DCB: Drug-coated balloon; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SB: Standard balloon.

dure was restored, but the other patient's hemodialysis AVF flow was not resolved despite thrombolytic therapy. In 3 patients, an access site hematoma was treated conservatively. In 1 patient, an intra-arterial angioplasty balloon fracture and embolization was observed, and the embolized portion of the balloon was retrieved with a snare catheter. There was no procedural complication requiring urgent surgery. Two patients in each group died due to cardiovascular causes during the follow-up period. The patency rate of successfully treated fistulas was 95.6%, 76.1%, and 57.9% at the 1st, 6th, and 12th month after the procedure, respectively.

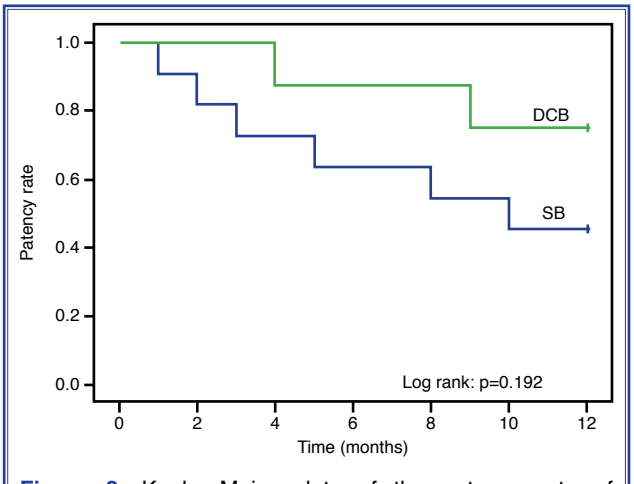

Figure 2. Kaplan-Meier plots of the patency rate of drug-coated and standard balloons. DCB: Drug-coated balloon; SB: Standard balloon.

The patency of the hemodialysis fistulas treated with a DCB was similar at 1 month compared with a SB (DCB: 10/10 AVFs, 100% vs SB: 12/13 AVFs, 92.3%; p=0.393). At the sixth month, 8/9 AVFs (88.9%) in the DCB group and 8/12 AVFs (66.7%) in the SB group were patent (1 patient in each group died within 6 months post procedure). At the 12th month, 6/8 AVFs (75%) in the DCB group and 5/11 AVFs (45.4%) in the SB group were patent (1 additional patient in each group died). There was no statistically significant benefit from a DCB compared with a SB at 6 or 12 months, but a trend in favor of a DCB was observed (p=0.258 at 6 months; p=0.219 at 12 months). Figure 2 illustrates Kaplan-Meier plots for patency of the DCB and the SB (Log rank: p=0.192).

DISCUSSION

An upper extremity AVF is the most common access site for hemodialysis. Thrombosis of this fistula is a

serious complication that requires urgent treatment. Most cases are treated surgically, but surgical revision can have poor outcomes, with a low success rate ranging from 28% to 73%.[3,4] Recently, endovascular strategies, such as percutaneous angioplasty and thromboaspiration, have been used to treat these patients. Conventional balloon angioplasty is performed in most cases, but recently DCBs have been developed for peripheral interventions. Paclitaxel-coated balloons are effective and commonly used for a peripheral intervention. Inflation of the DCB in the stenosis delivers an antiproliferative drug to the vessel wall and inhibits intimal hyperplasia, which can cause restenosis. However, there are few trials addressing the efficacy and safety of DCBs in the treatment of thrombosed hemodialysis AVFs.[5–8]

In our study, an arterial approach was used in all cases to access the entry site and treat the thrombosed segment. A femoral or brachial artery was used for the entry site in most cases. In the literature, venous access was most often selected as the primary entry to treat thrombosed hemodialysis AVFs. There are few studies reporting the use of a primary arterial approach to treat occluded hemodialysis AVFs.[9] In the present study, we used an arterial approach for the wire crossing and the angioplasty. We observed no major complication requiring urgent surgery or additional equipment. A minor access site hematoma developed in 3 patients: 1 in a femoral access site and 2 in a brachial access site. The patients were treated conservatively without any need for blood transfusion or surgical treatment. In 1 patient, angioplasty balloon fracture and embolization occurred during the procedure, however, the embolized part of the balloon was retrieved using a snare catheter without the need for surgery. There was no procedural complication requiring urgent surgery. Acute pulmonary thromboembolism, a rare but serious complication, has been reported in fewer than 1% of patients treated with angioplasty due to a thrombosed hemodialysis AVF.[10] In this study, we did not observe any clinically significant pulmonary embolism during the procedure or during the hospital stay. The success rate of the procedures in the study patients was 69.7%, which is consistent with literature reports.[11,12] The age of the thrombus has been reported as an important factor in the success of the procedure.[11] We found that early treatment of a hemodialysis AVF yielded a greater success rate, as seen in previous reports.

There are conflicting results in the literature regarding the treatment of thrombosed or stenotic hemodialysis AVFs with DCBs. Massara et al.[12] performed paclitaxel-coated balloon angioplasty in 16 patients with thrombosed hemodialysis AVFs and the primary patency rate was 89% at 6 months, 82% at 12 months, and 68% at 24 months. Katsanos et al.[5] reported the results of 40 patients with stenosed venous outflow lesion randomized for a DCB (paclitaxel-coated balloon) or SB. At 6 months, the cumulative target lesion primary patency was significantly higher in patients treated with a DCB (DCB: 70% vs SB: 25%; $p<0.001$). In contrast, Björkman et al.[13] observed in a recently published randomized trial that the target lesion revascularization-free survival after DCB treatment of stenotic hemodialysis AVFs was clearly worse and they discouraged DCB use in cases of hemodialysis AVF stenosis, especially in recent and/or immature hemodialysis AVFs based on the result of this trial.

Fistulas treated with a SB are more vulnerable to restenosis because neointimal hyperplasia may occur in response to arterial injury.[14] Paclitaxel inhibits its smooth muscle cell proliferation and migration, which may prevent neointimal hyperplasia.[15] Since neointimal hyperplasia may occur post intervention, the mechanism of action is important. This may be the primary explanation for the high success rate of a DCB in thrombosed hemodialysis AVF at 6 and 12 months compared with a SB in our study.

Thrombosis of a hemodialysis AVF is the leading cause of vascular access complications. Thrombosis is almost always associated with the underlying stenotic lesion. Percutaneous transluminal angioplasty is an accepted and effective treatment for stenotic lesions. A recent thrombus responds better to endovascular treatment than an established and organized thrombus. This may be the reason for the higher success rate of hemodialysis AVFs in our study that were treated early.

The limitations of this study include the relatively small size. In addition, the retrospective design is inherently subject to selection bias. Thirdly, an arterial route was the only entry site studied in our research, whereas a venous route has generally been used in other studies. To best compare the efficacy of a DCB in the treatment of thrombosed hemodialysis AVFs, an adequately sized randomized, prospective trial

with extended follow-up should be performed. We observed a trend in favor of a DCB for patency, but additional studies are needed.

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Ethical statement: This study was approved by the Sakarya University Faculty of Medicine Ethics Committee (no. 3, date: 24.05.2019).

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Keywords: Arteriovenous fistula; percutaneous treatment; thrombosis.

Anahtar sözcükler: Arteriyovenöz fistül; perkütan tedavi; tromboz.