Role of drug coated balloon angioplasty in treatment of recurrent dysfunctional arteriovenous fistulae for hemodialysis

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Received: 24 August 2023
Revised: 6 September 2023
Accepted: 9 September 2023
Published: 7 December 2023

The Egyptian Journal of Surgery 2023, 42:1081–1092

Objective
This study aimed to evaluate the safety, clinical benefits, and patency outcomes of using paclitaxel drug-coated balloons (DCBs) for the treatment of recurrent dysfunctional arteriovenous fistulae (AVF) in hemodialysis patients.

Study design
A nonrandomized clinical trial was conducted involving 20 patients who had previously undergone percutaneous transluminal angioplasty (PTA) for failing or failed AVF. Patients were assessed based on clinical criteria, and interventions were performed using paclitaxel-coated balloons. Clinical outcomes, including thrill, bruit, and hemodialysis function, were evaluated, and duplex assessments were conducted after 3 and 6 months to determine recurrent stenosis. Statistical analysis was carried out using SPSS.

Results
The study included 20 end-stage renal disease (ESRD) patients with a mean age of 49.4±17 years. After 2 weeks' postintervention, all patients had adequate bruit, 16 (80%) patients had adequate thrill, and 19 (95%) patients had adequate hemodialysis. After 6 months, 70% of patients exhibited adequate thrill, while adequate bruit, and hemodialysis were observed in 75% of patients. Duplex assessments showed minimal recurrent stenosis after 3 and 6 months, with only a few cases of new stenotic lesions. Postoperative complications were infrequent, including one unrelated death, and a small number of central venous occlusions and infections. The study indicated a significantly improved efficacy of drug-coated balloon angioplasty over traditional angioplasty in maintaining AVF patency.

Conclusion
Paclitaxel drug-coated balloons offer a promising approach for treating recurrent dysfunctional arteriovenous fistulae in hemodialysis patients. The study demonstrated favorable clinical outcomes, reduced restenosis rates, and improved patency compared with traditional angioplasty.

Keywords:
arteriovenous fistula, hemodialysis, drug-coated balloons, patency, percutaneous transluminal angioplasty

Egyptian J Surgery 42:1081–1092

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Introduction

The mature 'native' arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis given its improved performance and lower complications rates compared with prosthetic grafts or central venous catheters, while complications are less frequent in AVFs than in other vascular accesses, early and late AVF failure still remain major morbidities for dialysis patients, and important contributors to hemodialysis cost [1,2]. Maintaining vascular access patency represents a tremendous challenge in hemodialysis patients. Neointimal hyperplasia stenoses frequently develop, Stenosis prevents fistula maturation, impedes function and can precipitate thrombosis and vascular access loss [3]. For years, first-line treatment of AVFs stenoses has been percutaneous transluminal angioplasty (PTA), generally with high-pressure or cutting uncoated balloons. However, restenosis and reintervention rates remain incredibly high and occur, according to recent studies, in up to 60% and 70% of patients at 6 and 12 months, respectively. Surgical revision is more invasive and also has a high recurrence rate [3,4]. PTA restores the luminal diameter of venous fistula by stretching and dissection of the vessel wall. This induces vascular damage and may cause subsequent restenosis [5]. Recurrent stenosis is caused by intimal thickening after vessel wall injury from angioplasty and other factors (e.g., clinical, anatomical and technical

factors), leading to hyperplasia of intimal cells, increased extracellular matrix with migration, and proliferation of vascular smooth muscle cells stimulated by platelet-derived growth factor [6]. Repeated interventions by conventional angioplasty for recurrent stenoses (which itself may be a risk factor for recurrence) have been an issue needing multiple procedures over time increasing healthcare costs as well as morbidity and mortality [7]. Whether the mechanism of venous restenosis is similar to arterial restenosis or not, however venous restenosis seems to recur more frequently than that of its arterial counterpart [8]. Cutting balloon angioplasty reduces the amount of arterial wall damage by inducing a controlled fracture of atherosclerotic plaque. A recent study by Kariya *et al.* showed no significant differences between conventional and cutting balloon angioplasty regarding reducing the recurrence rate of venous stenosis. Paclitaxel, which is an antiproliferative and antineoplastic agent, has been shown to decrease cell proliferation and neointimal hyperplasia, hence being used in drug-coated balloons (DCBs) [9]. The effects of DCB on hemodialysis vascular access were recently explored in various randomized studies. Nonetheless, the sample sizes of these studies were usually not enough and conflicting findings were reported in some of these studies [10].

Patients and methods

A nonrandomized clinical trial including 20 patients, recruited from treatment registers, receiving at least one previous PTA for treatment of failing or failed AV fistula. Every patient was willing to provide informed consent, and was willing to comply with the protocol-required follow-up visits.

Inclusion criteria

(1) Male or female Patient greater than 18 years of age
(2) Native or synthetic arteriovenous fistula located in the upper limb, presenting with any clinical (e.g., Abnormal thrill or bruit), pathophysiological or hemodynamic abnormalities (e.g., Inability to achieve the target dialysis blood flow) warranting angiographic imaging and treatment as defined in the Kidney Disease Outcomes Quality Initiative guidelines. Angiographic evidence of at least one significant (>50%) venous outflow stenosis at their dialysis access circuit. Clinical signs of imminent vascular access failure included mostly detection of elevated venous pressure during dialysis, loss of thrill or bruit, increased bleeding with prolonged hemostasis after dialysis, and/or decreased blood flow along the dialysis circuit.
(3) Each trial entry is a stenosis or occlusion in an AVF that had received one or more prior endovascular interventions (angioplasty ± stent) to save failed or failing fistula.

Exclusion criteria

(1) Pregnancy or planned pregnancy or breast feeding.
(2) Severe allergy to contrast.
(3) Intolerance of platelet blockade.
(4) Hypercoagulable states.
(5) Active bleeding, or recent (< 3 months) intracranial hemorrhage.
(6) Infected AVF.
(7) Arterial element as a cause of fistula failure.
(8) Known hyper sensitivity to the drug (paclitaxel).
(9) Patients with compliance difficulties.

Patient assessment

(1) Full history taking: mainly presence of comorbidities, age of fistula, its type and time of previous intervention.
(2) Clinical examination:
    (a) limb examination for assessment of arterial blood supply and exclusion of manifestations of ischemia.
    (b) Assessment of limb edema.
    (c) Presence or absence of thrill, bruit, signs of infection or aneurysmal dilatation.
(3) Investigations:
    (a) laboratory: complete blood count (CBC), coagulation profile, Na, K and liver functions
    (b) Radiological: Duplex on fistula for assessment of:
        (1) Arterial inflow and venous outflow.
        (2) Volume flow rate.
        (3) Presence of stenosis or occlusion.
        (4) Length and site of lesion.
        (5) In addition to central neck veins.

Technique

(1) Access: radial or femoral access or outflow vein of fistula.
(2) Using 6 F sheath under local anesthesia then introduction of a hydrophilic guide wire and supporting catheter.
(3) After crossing the lesion, plain old balloon angioplasty (POBA) is done as a predilatation (vessel preparation) using diameter 5 and 6 mm or more and its length according to the length of

lesion using semi-complaint or noncomplaint balloons.
   (a) Vessel preparation with a plain balloon, defined as less than 30% residual stenosis, before drug-coated balloon inflation.
(4) Inflation of DCB of same diameter or 1 mm larger than that of the plain balloon and inflation time is 3 min.
   (a) The DCB was the Impact luminor (ivascular), a paclitaxel-coated balloon. Paclitaxel dose is 3 μg/mm^2 of balloon surface in a urea vehicle.
(5) Completion angiography is done to confirm technical success and then the patient is assessed for clinical success:
   (a) Technical success is confirmed by successful dilatation angiographically with no residual stenosis or residual stenosis less than 30% and absence of retrograde filling of the inflow artery.
   (b) Clinical success is confirmed by adequate thrill, bruit and adequate hemodialysis.
      (1) Adequate thrill: A normal adequate thrill has two components: a gentle, continuous (systolic and diastolic) vibration over the length of the AV access and a soft pulsation. The thrill is best felt with the palm of the hand. Stenotic lesions intensify the thrill over the area of stenosis and lead to loss of the diastolic component. An extremely strong ('water-hammer') pulse over an AV access is concerning for venous outflow stenosis. Weak pulsation suggests a problem with the inflow. In an AV graft, it is normal to feel a strong thrill at the arterial anastomosis that diminishes slightly as you move closer to the venous outflow.
      (2) A normal bruit should sound like a continuous (systolic and diastolic) hum. The normally low-pitched bruit will become squeaky and high-pitched if hemodynamically significant stenosis is present. As with the thrill, a stenotic lesion will cause the bruit to lose its diastolic component.
      (3) Adequate hemodialysis: A fistula was considered adequate if it supported a blood flow of >/=350 ml/min on at least six dialysis sessions in 1 month, each session lasts for about 4 h continuously without interruption of dialysis [11].
      (4) In this study, significant stenoses are those that have only a hemodynamic effect (50% decrease in lumen area or more) and are associated with decreased flow, elevated venous pressures, or an abnormal physical examination (reduced thrill or pulsatile flow) were included. While near total occlusion lesions were those having more than 90% decrease in lumen area.
   (c) N.B, the patient is discharged on the same day of intervention after confirming that there are no complications, on antiplatelet (Acetylsalicylic acid 100 once daily).

Follow-up

Patients were followed-up clinically after 1 week, 2 weeks, 1, 3, and 6 months and by duplex after 3 and 6 months to exclude any recurrent lesion and confirm adequate flow rate and well-functioning fistula.

Statistical analysis

Statistical Package for Social Sciences (SPSS) (version 20 windows) was used for data analysis. Continuous data was expressed as mean (±standard deviation) or median (range) while the categorical data was expressed as number (%). To test normality of data distribution, the Kolmogorov-Smirnov test, was used to measure the distribution of data.

Results

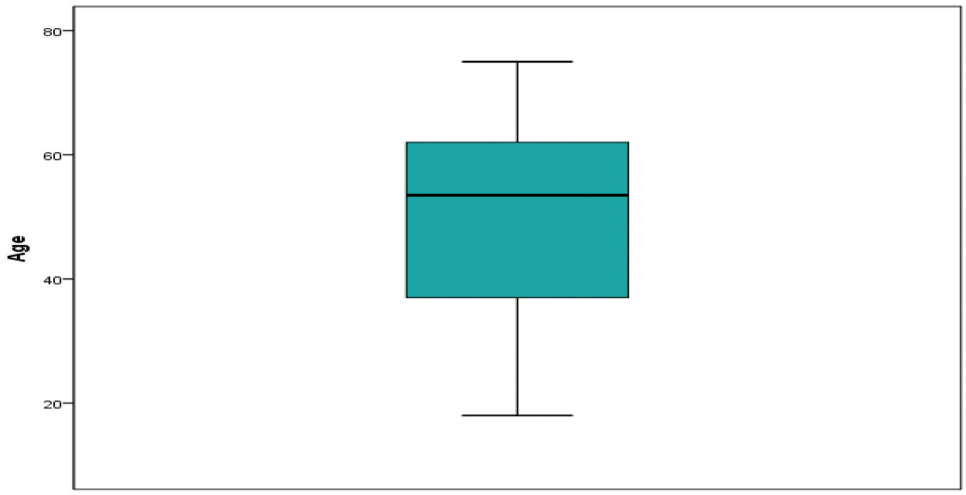
General characteristics of the included participants

In this study, we included 20 end-stage renal disease (ESRD) patients. The participants' mean age was 49.4 ±17 years old, and most were males (70%). The most common medical comorbidity among them was hypertension (50%), followed by coronary artery disease (CAD) (30%). Brachio-cephalic fistula represents the most common type of fistula (60%) with 55% of them were failed fistulae. Most patients had more than one lesion (40%). The most common type of lesion was near total occlusion representing (50%). While the most common site was the outflow vein (100%); Figs 1–7; Table 1. Drug coated balloons used are 5 mm diameter in 11 cases, 6 mm diameter in 8 cases, 7 mm diameter in 1 case and their length were ranging from 80, 150, and 200 mm; Table 2.

Postoperative clinical assessment at different time intervals

After 1 week postoperatively, all patients (n=20) (100%) had adequate bruit. Adequate thrill and adequate hemodialysis (HD) were reported in 15 (75%) patients each. After 2 weeks, all patients (20) had adequate bruit also, 16 (80%) patients had adequate thrill and 19 (95%) patients had adequate hemodialysis. After 6 months, 14 (70%) patients

Figure 1



Shows Age distribution of the included participants.

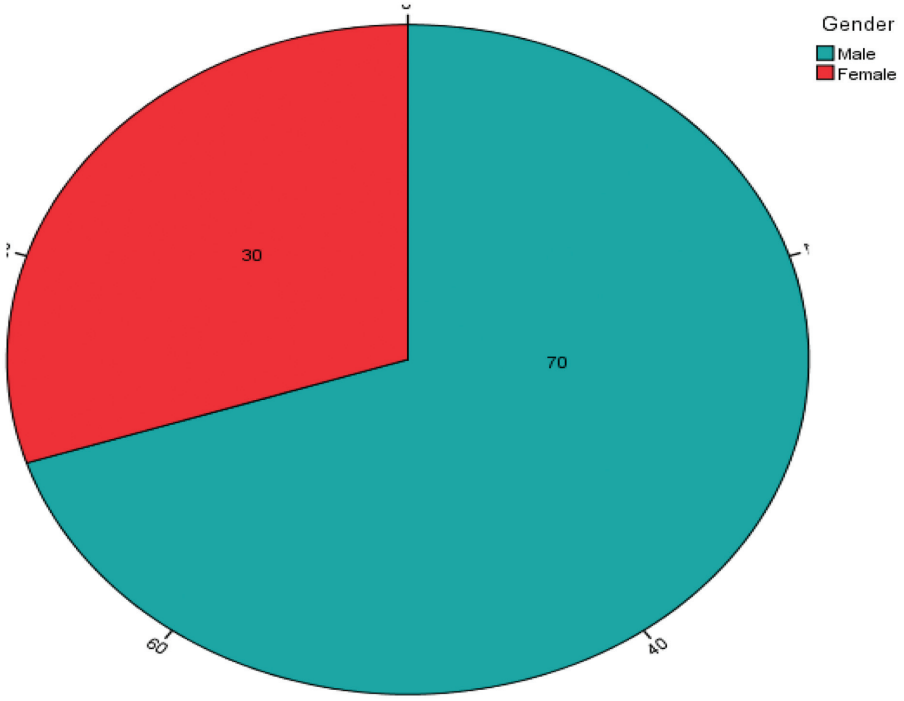
showed adequate thrill, while 'adequate bruit' and 'adequate HD' were detected in 15 (75%) patients each; Table 3, Fig. 8. A total of 14 patients revealed at least two signs of improved clinical outcomes detected at a time (adequate thrill, bruit, and adequate HD) till the end of 6-month follow-up.

A total of 14, and 16 patients revealed more than one sign of improved clinical outcomes at the same time (adequate thrill, bruit, and adequate HD) after 1 and 2 weeks, respectively. A total of 15, 14, and 13 patients revealed more than one sign of improved clinical outcomes at the same time (adequate thrill, bruit, and adequate HD) after 1, 3, and 6 months, respectively; Table 4.

Postoperative duplex assessment at different time intervals

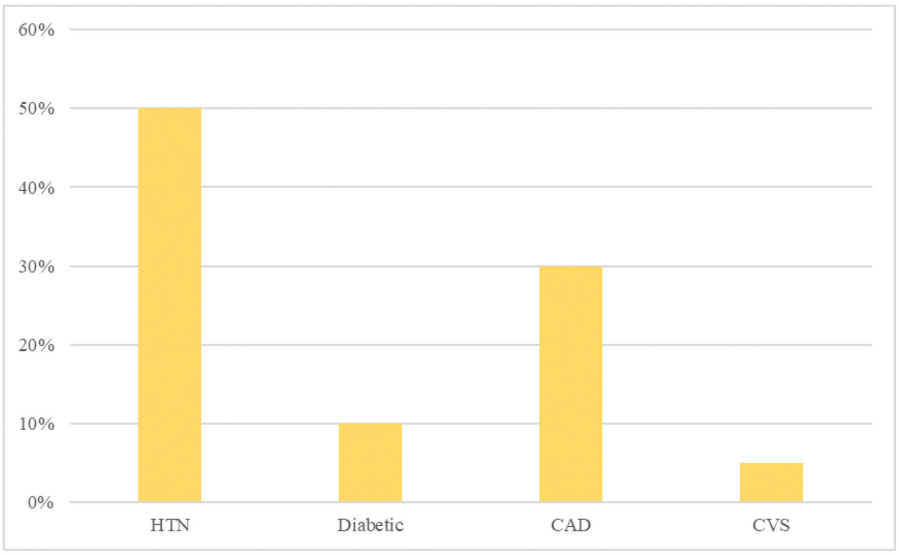
A total of 16 and 13 patients showed no recurrent stenosis after 3 and 6 months, respectively. While only two patients showed recurrent stenotic lesions after 3 months and one patient after 6 months. Notably only

Figure 2



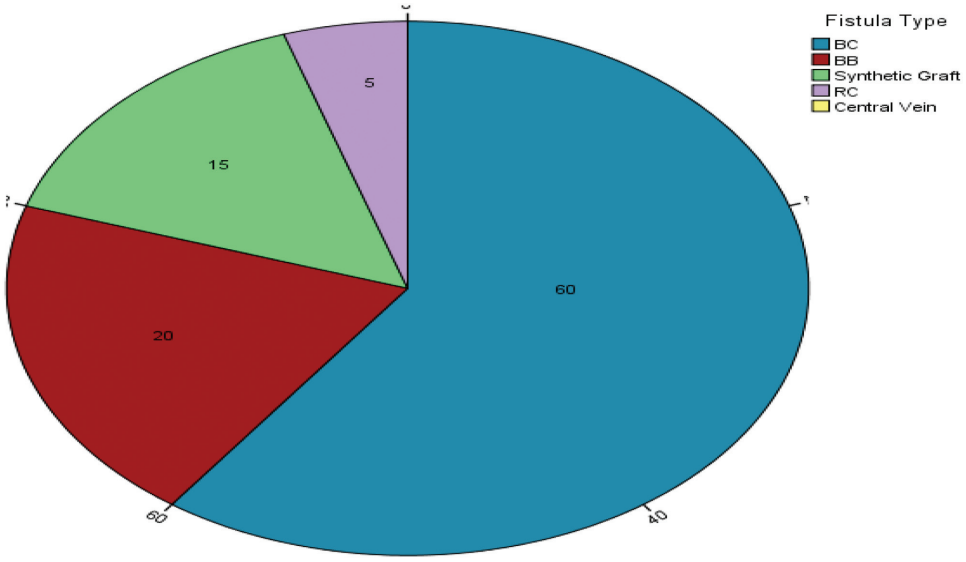
Shows sex distribution of the included participants.

Figure 3



Shows the frequency of different medical comorbidities.

Figure 4



Shows the different types of fistulas.

one patient developed new stenotic lesion after 3 months and 6 months each, also one patient only showed recurrence with another new stenotic lesion after 6 months; Table 5, Fig. 9. It was noted that number of nonfunctioning accesses after 3 months was 4 (20%) (2 failed and 2 failing) and after 6 months was 7 (35%) (6 failed and 1 failing).

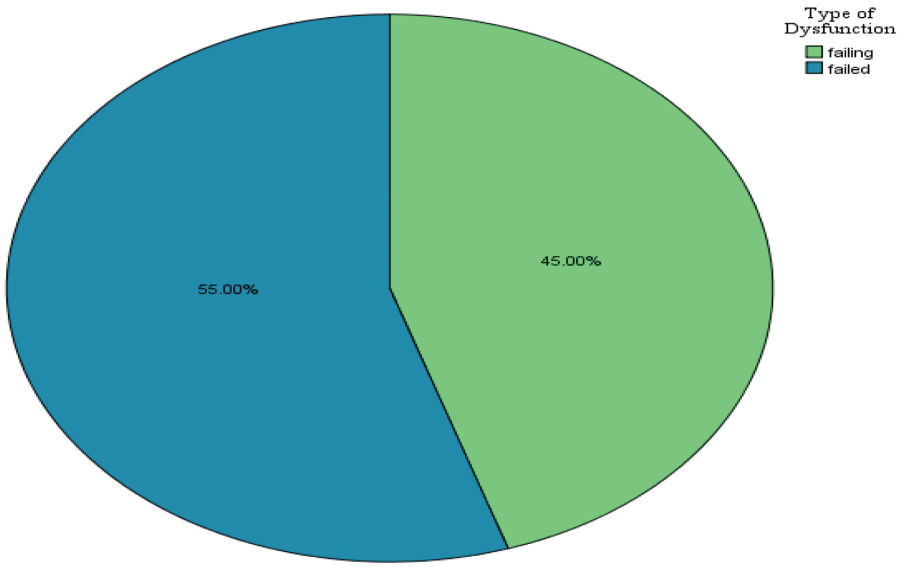
Postoperative complications

As for the postoperative complications, one patient died but due to cardiac arrest at 3 month follow-up, central venous occlusion occurs in 2 cases only after 6 month follow-up and infection occurs in one AVG case after 3 months then it had to be removed.

Patency of the previous angioplasty

Notably, after 6 months from the previous angioplasty, 30% (6) of the fistulae were functioning, while 70% (14) were failing or failed at the same period. Only 5% (1 fistula) was still functioning after 12 months; Table 6. This points to the lower efficacy rate of the traditional angioplasty compared with drug coated balloon angioplasty; rendering it as a promising alternative for the traditional angioplasty.

Figure 5

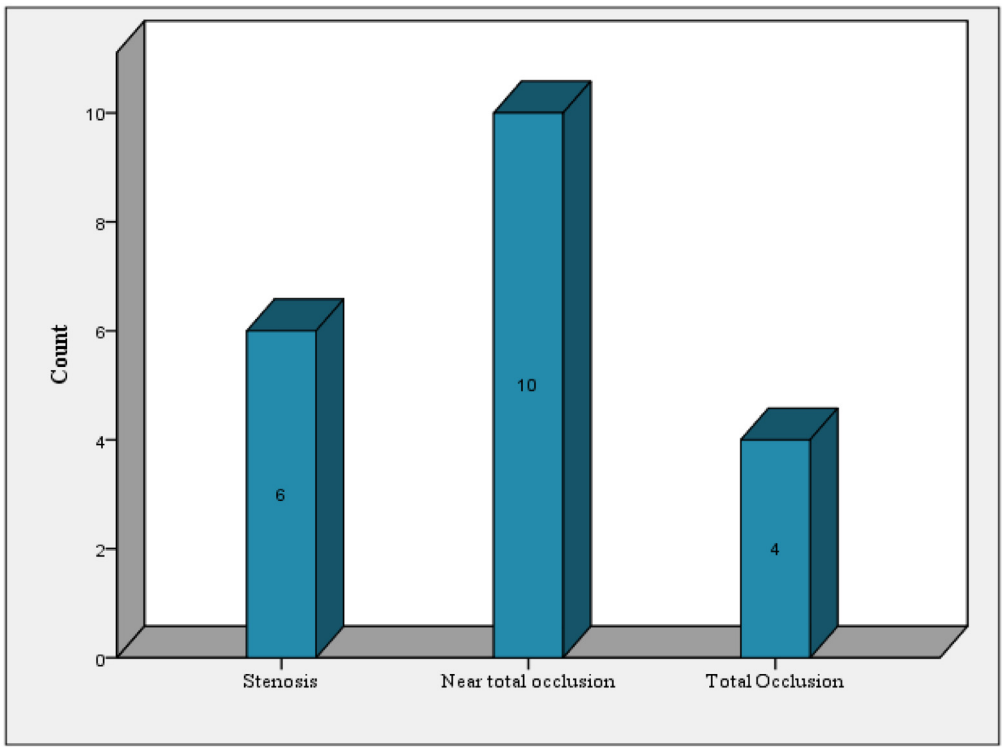


Shows the types of fistula dysfunction.

Discussion

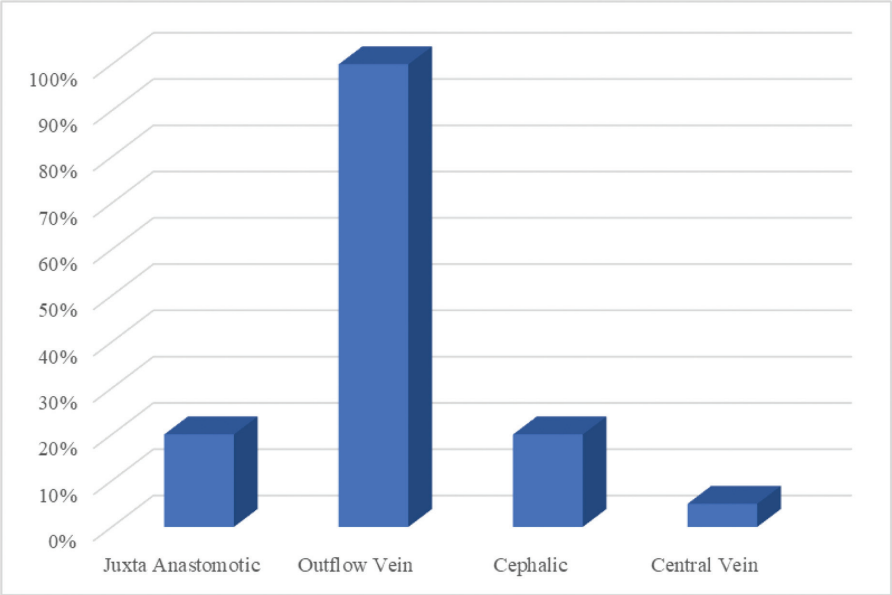
Native AVF or AVG is universally recommended as a permanent access for patients receiving HD, but maintenance of AVF patency remains a challenge for current medicine. According to a recent systematic review, 1-year patency rates are 62% to 68% and 2-year patency rates are 38% to 56% [12]. Maintaining patency and function of dialysis access circuits often becomes a dire need for dialysis patients. In an attempt to rescue the failing or thrombosed vascular access, a variety of surgical or catheter-based interventions can be used. The interventional vascular approach has become the treatment of choice, securing access in greater than 80% of cases and allowing patients to undergo immediate hemodialysis without the need of temporary dialysis catheters or surgical consumption of additional venous conduits [13].

Figure 6



Shows the different types of lesions.

Figure 7



Shows the locations of the target lesions.

Table 1 Shows the general characteristics of the included participants

Parameters	Value, *n*=20
Age, years, mean (SD)	49.4±17
Sex	
Male	14 (70%)
Female	6 (30%)
Comorbidities	
HTN	10 (50%)
Diabetic	2 (10%)
CAD	6 (30%)
CVS	1 (5%)
Type of fistula	
RC	1 (5%)
BC	12 (60%)
BB	4 (20%)
Synthetic Graft	3 (15%)
Type of Fistula Dysfunction	
Failing	9 (45%)
Failed	11 (55%)
Type of Lesion	
Stenosis	6 (30%)
Near total occlusion	10 (50%)
Total Occlusion	4 (20%)
Location of the target lesion	
Juxta Anastomotic	4 (20%)
Outflow Vein (cephalic or basilic or synthetic graft)	20 (100%)
Cephalic arch	4 (20%)
Central Vein	1 (5%)
Hemodialysis Duration (years), median (range)	4 (24)
Age of the target fistula (years), median (range)	1.5 (13)
Number of Stenotic lesions, median (range)	2 (2)

Data are presented as n (%), median (range) or mean (±SD). BB, brachio-basilic; BC, brachio-cephalic; CAD, coronary artery disease; CVS, cerebrovascular stroke; HTN, hypertension; RC, radio-cephalic.

However, angioplasty itself can cause intima and media rupture, followed by neointimal hyperplasia (normal vessel response to the injury), and subsequent development of restenosis with recurrent vascular access failure. Therefore, Balloon angioplasty of the vascular access is characterized by poor midterm patency, with an increasing rate of repeated procedures [14]. Our study addresses restenosis in the fistula circuit. This restenosis is, in part or in whole, the result of neointimal hyperplasia (NIH). It is important to emphasize that the role of drug elution in the treatment of vascular stenoses is *not* to obtain a good result; the role of drug elution is to preserve a good result, obtained on the day of intervention, maintaining possible longer patency so DCB was projected as a more cost-effective option to prolong primary patency of access circuits, leading to decreased overall angioplasty procedures [15]. The safety and effectiveness of drug-coated balloons have been confirmed in percutaneous coronary interventions [16] and in peripheral interventions. There is increasing evidence on the benefit of using DCBs

Table 2 Shows different types of drug-coated balloons used in this study

Parameter	Values (patent)
Types of drug-coated balloons used in this study	
5*150	6 (30%)
5*200	5 (25%)
6*150	6 (30%)
6*200	2 (10%)
7*80	1 (5%)

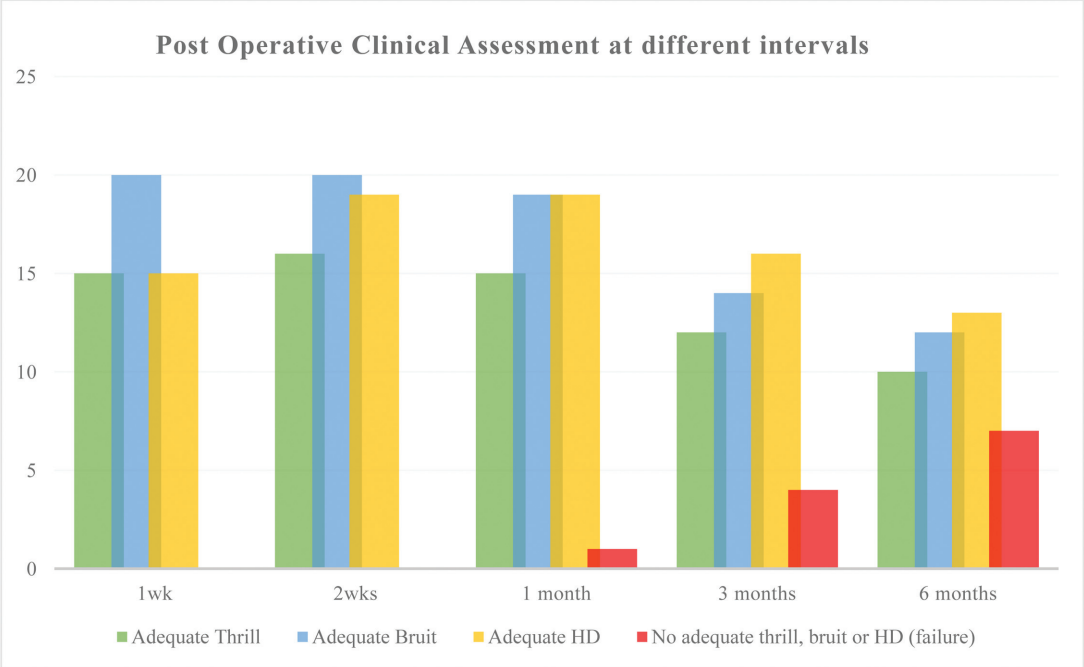
Data are presented as n (%).

Table 3 Shows the results of postoperative clinical assessment at different time intervals

Results of clinical assessment at different time intervals	
Parameters	Value (*n*=20)
Clinical assessment after one week	
Adequate Thrill	15 (75%)
Adequate Bruit	20 (100%)
Adequate HD	15 (75%)
Clinical assessment after two weeks	
Adequate Thrill	16 (80%)
Adequate Bruit	20 (100%)
Adequate HD	19 (95%)
Clinical assessment after 1 Month	
Adequate Thrill	15 (75%)
Adequate Bruit	19 (95%)
Adequate HD	19 (95%)
No adequate thrill, bruit or HD (failure)	1 (5%)
Clinical assessment after 3 Months	
Adequate Thrill	12 (60%)
Adequate Bruit	14 (70%)
Adequate HD	16 (80%)
No adequate thrill, bruit or HD (failure)	4 (20%)
Clinical assessment after 6 Months	
Adequate Thrill	10 (50%)
Adequate Bruit	12 (60%)
Adequate HD	13 (65%)
No adequate thrill, bruit or HD (failure)	7 (35%)

Data are presented as n (%). HD, Hemodialysis.

Figure 8



Shows the results of postoperative clinical assessment at different time intervals.

for the treatment of dysfunctional vascular access, whereas there are, at the same time, studies with conflicting results [10,17–20]. Relatively few observational and randomized control studies (Fig. 10) have evaluated the use of DCBs for prolonging access patency, thereby avoiding the need for recurrent preemptive interventions which by itself is associated with significant harms from higher complications attributed to increasing number of procedures [7]. In addition, studies done were clinically heterogeneous with smaller number of participants. Inclusion and exclusion criteria of patients in this study were similar to most of studies mentioned before but the main difference is that the patients in this study were chosen mainly by their history of previous angioplasty then failed shortly after it. Thus, necessitating the need for another treatment achieving longer patency for these dysfunctional fistulae other than conventional angioplasty. This is similar to patients' criteria in a comparative study between conventional and DCB angioplasty. It must be emphasized that the patients in our study represent the most difficult patients, with the most aggressive restenosis in different types of AVFs and AVGs. A degree of pervious scarring from repeated angioplasty and repeated needling were clinically evident in such cases. Regarding

Table 4 Shows the results of clinical assessment combined

Parameters	Value (*n*=20)
Clinical assessment after one week	
Patients with Adequate Thrill, Bruit and HD	14 (70%)
Adequate thrill and bruit only	1 (5%)
Adequate bruit and HD only	1 (5%)
Adequate bruit only	4 (20%)
Clinical assessment after two weeks	
Patients with Adequate Thrill, Bruit and HD	16 (80%)
Adequate bruit and HD only	3 (15%)
Adequate bruit only	1 (5%)
Clinical assessment after 1 Month	
Patients with Adequate Thrill, Bruit and HD	15 (75%)
Adequate bruit and HD only	4 (20%)
No adequate thrill, bruit or HD (failure)	1 (5%)
Clinical assessment after 3 months	
Patients with Adequate Thrill, Bruit and HD	12 (60%)
Adequate bruit and HD only	2 (10%)
Adequate HD only	2 (10%)
No adequate thrill, bruit or HD (failure)	4 (20%)
Clinical assessment after 6 Months	
Patients with Adequate Thrill, Bruit and HD	10 (50%)
Adequate bruit and HD only	2 (10%)
Adequate HD only	1 (5%)
No adequate thrill, bruit or HD (failure)	7 (35%)

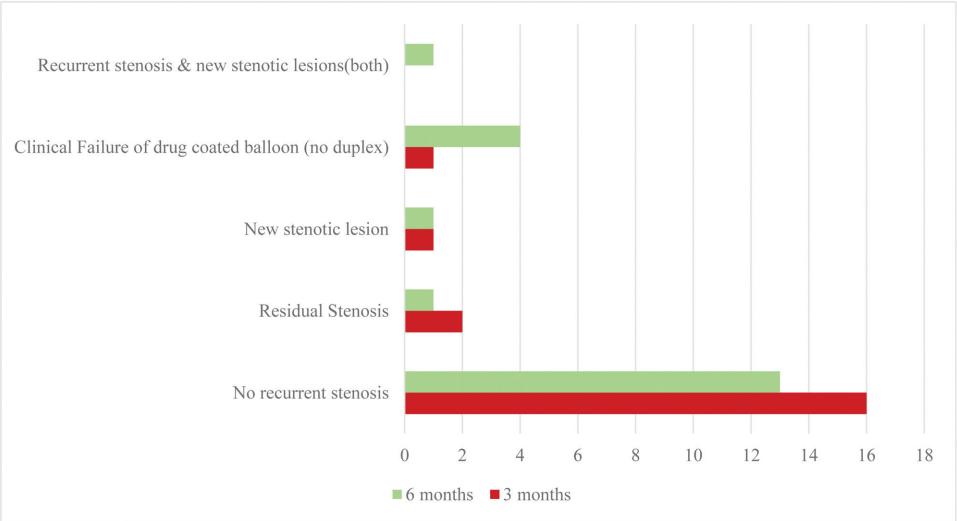
Data are presented as n (%). HD, Hemodialysis.

Table 5 Shows the results of postoperative clinical assessment at different time intervals

Results of duplex assessment at different time intervals	
Parameters	Value
Duplex assessment after 3 Months	
No recurrent stenosis	16 (80%)
Recurrent Stenosis	2 (10%)
New stenotic lesion	1 (5%)
Clinical Failure of drug coated balloon (no duplex)	1 (5%)
Duplex assessment after 6 months	
No residual stenosis	13 (65%)
Recurrent Stenosis	1 (5%)
New stenotic lesion	1 (5%)
Recurrent stenosis and new stenotic lesions(both)	1 (5%)
Clinical Failure of drug coated balloon (no duplex)	4 (20%)

Data are presented as n (%).

Figure 9



Shows the results of duplex assessment at 3 and 6 months postoperatively.

Table 6 Shows the duration of the previous angioplasty in our participants

Parameter	Values (patent)	Nonfunctioning
Patency of previous angioplasty (patients' groups)		
After 3 months	14 (70%)	6
After 6 months	6 (30%)	14
After 9 months	4 (20%)	16
After 12 months	1 (5%)	19

Data are presented as n (%) or median (minimum-maximum).

methodology, they had all received endovascular intervention to their lesions using the same angioplasty techniques (plain angioplasty then DCB balloons were used) which are capable of treating them successfully (technical success 100%) rendering them 20 cases only after initial number of 26 cases as in the remaining 6 patients, our trials of salvage failed. The drug used in balloons was paclitaxel which is used by almost all studies done on DCBs except few studies as a study done by Tan C W *et al*. using sirolimus DCB in the management of thrombosed arteriovenous graft (AVGs) on 20 patients with thrombosed upper limb AVGs by 7-and 8-mm diameter balloons after successful pharmaco-mechanical thrombectomy of AVGs then followed up for 6 months. In contrast, in the studies of Katsanos *et al*. and Kitrou *et al*., DCB angioplasty was performed first. If the angiographic result was insufficient, which occurred in nearly half of the cases, these investigators performed an additional angioplasty with a PTA balloon catheter, accepting high pressure to completely reopen the stenosis [19]. Technical success was almost the same in all DCB AVF hemodialysis angioplasty studies defined as residual stenosis less than 30%. In relation to clinical success evaluation, the main prognostic factors used in our study were adequate thrill, bruit and the most important and reliable was an adequate hemodialysis. Studies on DCB angioplasty on AVFs vary widely between those three previously mentioned parameters for clinical follow-up. For example,

Figure 10

Year	Author	N	Access	Results
2012	Katsanos et al. [21]	40	AVF, AVG	TLPP at 6 mo, 70% DCB vs. 25% POBA ($p < 0.001$)
2015	Kitrou et al. [22]	40	AVF	TLR-free survival: 308 days DCB vs. 161 days POBA ($p = 0.03$)
2015	Kitrou et al. [23]	40	AVF, AVG	TLPP at 12 mo: 35% DCB vs. 5% POBA ($p < 0.001$)
2017	Kitrou et al. [24]	40	AVF, AVG	Median intervention free period (central vein) 179 days DCB vs. 124.5 days POBA ($p = 0.026$)
2018	Irani et al. [25]	119	AVF, AVG	TLPP at 6 mo: 81% DCB vs. 61% POBA ($p = 0.03$) TLPP at 12 mo: 51% DCB vs. 34% POBA ($p = 0.04$) ACPP at 6 mo: 76% DCB vs. 56% POBA ($p = 0.048$) ACPP at 12 mo: 45% DCB vs. 32% POBA ($p = 0.16$)
2018	Trerotola et al. [26]	285	AVF	TLPP at 6 mo: 71% DCB vs. 63% PTA ($p = 0.06$) PP at 3 mo: 88% DCB vs. 80% PTA ($p = 0.43$)
2018	Maleux et al. [27]	64	AVF	PP at 6 mo: 67% DCB vs. 65% PTA ($p = 0.76$) PP at 12 mo: 42% DCB vs. 39% PTA ($p = 0.95$)
2019	Bjorkman, et al. [28]	39	AVF	Mean intervention free period 110 days DCB vs. 193 days POBA ($p = 0.06$)
2020	Lookstein et al. [20] IN.PACT	330	AVF	TLPP at 180 days: 82.2% DCB vs. 59.5% POBA ($p < 0.001$) Adverse event: 4.2% DCB vs. 4.4% POBA ($p = 0.002$)
2020	Trerotola et al. [19] LUTONIX	285	AVF	TLPP at 9 mo: 58% DCB vs. 46% POBA ($p = 0.02$) TLPP at 12 mo: 44% DCB vs. 36% POBA ($p = 0.04$) TLPP at 18 mo: 34% DCB vs. 28% POBA ($p = 0.06$) TLPP at 24 mo: 27% DCB vs. 24% POBA ($p = 0.09$)
2020	Moreno-Sanchez, et al. [29]	136	AVF, AVG	TLPP at 6 mo: 153.0 days DCB vs. 141.7 days POBA ($p = 0.068$) TLPP at 12 mo: 265.8 days DCB vs. 237.8 days POBA ($p = 0.369$) Mortality: 5.7% DCB vs. 9% POBA ($p > 0.05$)
2021	Karuanithy et al. [14] PAVE	212	AVF	TLPP at 6 mo, 71.7% DCB 84.5% POBA TLPP at 12 mo, 52.5% DCB and 58.8% POBA Time to loss of TLPP: DCB compared with the POBA-HR, 1.18; 95% CI, 0.78 to 1.79; $p = 0.440$)

Randomized controlled trials on the effect of drug-coated balloons on vascular access stenosis in hemodialysis patients. AVF, arteriovenous fistula; AVG, arteriovenous graft; TLPP, target lesion primary patency; DCB, drug-coated balloon; POBA, plain old balloon angioplasty; ACPP, access circuit primary patency; HR, hazard ratio; CI, confidence interval; mo, months; PAVE, paclitaxel-coated balloons and angioplasty of AV fistulas trial.

clinical success was defined as three adequate dialysis sessions after angioplasty with normal dialysis parameters in Moreno-Sánchez T *et al.*' study [21]. The follow-up in our study was distinguished from other studies by duplex assessment at 3 and 6-month interval for confirmation of clinical assessment and early detection of any recurrence or failure. In contrast to the majority of other studies done on use of DCB angioplasty for de novo AVF dysfunction, our study focused only on a recurring AVF lesions. This was done to compare previous angioplasty results with DCB angioplasty to assess efficacy of both methods on same fistulas. In a study done by Haave and colleagues on Treatment of restenosis in radio cephalic arteriovenous hemodialysis fistulas comprising 26 patients receiving at least one previous PTA and a re-intervention (13 PTAs and 13 DCBs) at the same anatomic location, were observed for 24 months. After 12 and 24 months, the estimated proportions of stenosis-free patients were 61 and 31%, respectively, in the DCB group, compared with 40 and 15% in the PTA group [22]. There is also a study by Troisi and colleagues done on 27 hemodialysis patients with recurrent stenosis of arteriovenous fistula undergoing endovascular treatment with a DCB balloon. About inclusion criteria, all patients were previously treated at the target lesion with a standard balloon angioplasty (BA) and results came as follows: estimated 2-year rates of primary patency, primary assisted patency, secondary patency, and freedom from TLR (target lesion restenosis) were 31.8, 76.4, 90.5, and 30.2%, respectively [23]. In our study, target lesions primary patency in AVFs and AVGs at 3 months was (80%) and at 6 months was (65%). These patency rates are higher than those of the same AVFs and AVGs since previous plain angioplasty (70% patency after 3 months and 30% after 6 months). It was found that the all 3 AVGs included in this study were reoccluded and failed (2 of them after 3-month follow-up and the remaining one after 6 month follow-up). This result goes along with a study done by Micheal Allon finding that there is a high frequency of early AVG restenosis after angioplasty caused by aggressive neointimal hyperplasia resulting from vascular injury occurring mainly at venous anastomosis [24]. Regarding safety and complications following DCB angioplasty, no adverse events in our study directly related to DCB use. One patient died but due to cardiac arrest at 3 month follow-up, central venous occlusion occurs in 2 cases only and infection occurs in one AVG case then it had to be removed. The DCBs achieved a high safety endpoint (freedom from local or systemic adverse event) in 95% of patients at 30 days, which was changed to 80% at 6 months due to causes not related to DCBs. The increased risk of mortality that was observed with DCBs in peripheral arterial disease has raised concerns for the population on dialysis. To date, there has been no similar signal observed in the population on hemodialysis. A meta-analysis that included eight studies revealed that the cause of mortality also did not show any difference between DCBs and conventional balloons (11.2%; RR, 1.26; 95% CI, 0.85 to 1.89; P=0.25; I2=0%) [25]. Despite that, DCB is seldom used in ambulatory surgical centers or outpatient vascular access centers due to decreasing reimbursements for access angioplasties over the years and higher costs associated with DCB, which are 10 times more expensive compared with conventional balloons. Considering that vascular access stenosis frequently occurs in patients on dialysis, the relatively high costs of DCBs should be offset by their apparent superiority in patency and safety. The main limitations in our study were that the number of patients eligible for inclusion criteria was low in addition to absence of randomization of cases with difficult providence of DCBs with variable sizes. Follow-up was limited to 6 months which should be longer to 1 year at least.

Conclusion

DCB angioplasty showed superiority in primary patency according to clinical and duplex assessment at 3 and 6 months follow-up and better intervention-free survival of the target lesion, without evidence of greater adverse events. DCB angioplasty carries better extended patency when compared with conventional percutaneous angioplasty especially in recurrent AVF stenoses and occlusions. An extended follow-up period and larger or different populations should be investigated to confirm the efficacy and safety of DCB treatment for failing and failed fistula.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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