Prospective, Randomized Controlled Study of Paclitaxel-Coated versus Plain Balloon Angioplasty for the Treatment of Failing Dialysis Access

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Purpose: To compare primary patency rates and target lesion revascularization of paclitaxel-coated balloon (PCB) versus plain balloon angioplasty (PBA) to preserve the patency of the vascular access circuit in patients undergoing hemodialysis after one year of follow-up.

Patients and methods: Within 24-month period, during 2015 and 2016, 96 patients (54 men=56%; mean age 60.3±13.8) with hemodialysis-dependent end-stage renal disease were enrolled in the study. In total, 48 patients were randomly assigned to group PCB (29 AVGs & 19 AVFs) & 48 patients to group PBA (29 AVGs & 19 AVFs). Baseline & procedural variables were comparably distributed in PCB & PBA groups.

Results: There were no significant differences in age of the treated vascular access circuit (2.31±1.62 years in PCB group vs. 2.63±1.94 years in PBA group, p=0.483), nor in the overall length of the treated target vein lesion (5.2±1.4 cm in PCB group vs. 5.4±1.6 cm in PBA group, p=0.641). All patients enrolled in the study completed the 1-year follow-up period. Device success rates were 100% in the PBA group and 39.6% in the PCB group, as further dilation with PBA was needed in 29 of 48 cases (60.4%) in the PCB group to achieve acceptable immediate postprocedural residual stenosis less than 30% (p=< 0.001). Anatomic and clinical success rates were 100% in both groups. No minor or major procedure-related complications occurred in either group. TLR free survival was significantly superior in the PCB group according to the Kaplan–Meier survival analysis curve (PCB, 316 days; PBA, 172 days; p=0.041), access circuit primary patency results were also significantly in favor of PCB angioplasty (PCB, 287 days; PBA, 156 days; p = 0.04). There were three cases in the PBA group (15%) and four cases in the PCB group (20%) in which lesions had been treated in a previous session with a PBA. There was no statistically significant difference in this subgroup analysis (p>0.1).

Conclusion: In this three-center study, paclitaxel-coated balloon angioplasty results in improved vessel patency and is superior to plain balloon dilation in the treatment of venous stenoses of failing native or prosthetic arteriovenous shunts used for dialysis access. In the PCBs group, additional HPB postdilatation was required in the majority of cases. These results combined with the "do not leave any metal behind" principle, characteristic in balloon angioplasty, marks paclitaxelballoon as a really promising technology and merits larger-scale trails for PCBs to have a future place in the armamentarium for the treatment of venous stenosis in failing dialysis access.

Key words: Paclitaxel, arteriovenous fistula, fistuloplasty, hemodialysis, neointimal hyperplasia.

Abbreviations: AVF = arteriovenous fistula, AVG = arteriovenous graft PCB = paclitaxel-coated balloons, PBA = plain balloon angioplasty, DSA = digital subtraction angiography, TLR = target lesion revascularization.

Introduction

As the incidence of ESRD has been escalating over the last years, the creation of hemodialysis access (the so called "lifeline" for dialysis patients) has become a common vascular procedure in the form of either an autologous arteriovenous fistula (AVF) or prosthetic arteriovenous graft (AVG).[1]

The autogenous arteriovenous fistula is considered as the optimum access for patients with end-stage renal disease (ESRD) on hemodialysis as, when the access has matured, it results in higher patency rates and lower complication rates than the other dialysis options as the prosthetic grafts and cuffed, tunneled dialysis catheters.[2] However,

juxtaanastomotic venous stenosis is a major concern associated with AVFs, which is mainly as a result of neointimal hyperplasia.[3] The presence of this occlusive neointimal hyperplasia at the anastomosis and/or the outflow veins, which may be accelerated by chronic kidney disease, has been considered to be the leading cause of AVF failure.[4]

An established method of preserving failing dialysis access is plain balloon angioplasty (BA) of significantly stenotic lesions occurring in the dialysis circuit of failing arteriovenous shunts. Although BA remains the cornerstone treatment for vascular access stenosis because of its minimally invasive percutaneous nature and widespread availability, the combination of venous anatomy and physiology, with the pre-existing endothelial dysfunction of uremic patients, generally leads to poor mid-and long-term results, necessitating multiple repeat angioplasty sessions in the same circuit.[1,2,5,6]

In an attempt to improve immediate technical success and long-term vascular patency, several methods have been applied in the past, with bare metal stents having been most widely tested, albeit with controversial outcomes.[7-9]

Theoretically, vascular access patency may be optimized by a technology that would both block negative vessel wall remodeling and inhibit fibromuscular hyperplasia formation after standard balloon angioplasty. One such approach could be the use of angioplasty with paclitaxel-coated balloons (PCBs), which are already known to effectively inhibit neointimal hyperplasia and reduce vascular restenosis after angioplasty of the superficial femoral artery for leg ischemia.[10]

PCB provides rapid delivery of the antiproliferative drug to the local vessel wall and inhibition of neointimal hyperplasia compared with PB.[11]

Thus, the purpose of our study was to compare primary patency rates and target lesion revascularization of paclitaxel-coated balloon (PCB) versus plain balloon angioplasty (PBA) to preserve the patency of the vascular access circuit in patients undergoing hemodialysis after one year of follow-up.

Patients and methods

Study Design

From 1st January 2015 to 31th December 2016, 96 patients with different types of hemodialysis access stenosis in whom PTA was indicated were prospectively, randomized (using an internet randomization service6) to have either paclitaxel-coated balloon angioplasty (PCB) or plain balloon angioplasty (PBA).

The study was performed at Ain Shams University Hospitals and 2 tertiary referral centers in Saudi Arabia (Security Forces Hospital Program & Al-Noor Specialist Hospital – Makkah).

This prospective, multicenter, randomized study was designed to compare the immediate and long-term angiographic and clinical outcomes of the application of paclitaxel-coated balloon angioplasty (PCB) versus plain balloon angioplasty (PBA) in the treatment of failing dialysis accesses with angiographic documentation of a significant venous stenotic lesion in patients with AVF or AVG circuits. The study protocol was approved by the local hospital's Ethical and Scientific Review Board in the enrolled hospitals and registered on the Hospital's Intranet database as a copyrighted access.

Table 1: Inclusion & exclusion criteria for study enrollment

Inclusion criteria	Exclusion criteria
Age 18 – 90 years	Patient unable to provide informed consent
Autogenous arteriovenous fistula or prosthetic arteriovenous graft in the arm	Patient unable to abide with study follow-up protocol
Vascular access actively used for hemodialysis (at least 1 successful session)	Patient participating in other relevant or conflicting studies
Clinical signs of failing access due to presence of significant anatomic stenosis as detection of elevated venous pressure during dialysis &/or decreased blood flow	Vascular access circuit placed in the lower extremities
Angiographically proven venous outflow stenosis >50% as compared to proximal segment of the reference vein diameter. Aneurysmal venous segments were avoided	Bare metal stent or stent-graft placed previously
Reference diameter of proximal outflow vein <7mm*	Metastatic cancer or other terminal medical condition
	Hemodynamically significant stenosis of the central venous system
	Limited life expectancy (<6 months)
	Blood coagulation disorders
	Sepsis or active infection
	Recent arm superficial thrombophlebitis (<6 months)
	Allergy or other known contraindication to iodinated contrast material, heparin, or paclitaxel
	Pregnancy

*The rest of the lesion morphological parameters were chosen according to largest IN.PACT PCB device available at the time of the study.

Study devices:

The IN.PACT over-the-wire balloon paclitaxel-eluting, dilatation catheters (Invatec-Medtronic, Brescia, Italy) were used in patients randomized in the experimental comparator group (PCB group). The balloon's surface was coated with a paclitaxel-eluting formulation using urea as a spacer. This highly hydrophilic combination enables a better contact of the lipophilic paclitaxel with the vascular wall. The specific balloon catheters were available at a maximum diameter of 7 mm and a maximum length of 80 mm, while the dose of paclitaxel on the balloon's surface was 3 μg/mm.[2] The balloon was coated with FreePac, a paclitaxel-eluting formulation that contains hydrophilic urea to optimize transfer of lipophilic paclitaxel to the endothelial cells upon contact with the vessel wall. Paclitaxel is a cytotoxic agent that

promotes tubulin polymerization, unlike other anti-microtubule drugs targeting the disassembly of microtubules. Limiting the microtubules' ability to turn back to their prior state interrupts a number of cell processes, including cell division and protein transport, hence, the cell cycle is arrested in the mitosis phase, inhibiting smooth muscle cell (SMC) proliferation and fibromuscular hyperplasia. Patients randomized to the control group (PBA group) underwent angioplasty with a variety of high-pressure balloon catheters brands [Dorado PTA balloon dilatator catheter (Bard Peripheral Vascular, Tempe, AZ, USA), Blue Max PTA (Boston Scientific, Natick, MA, USA), conquest PTA Dilatation Catheter (Bard Peripheral Vascular, Tempe, AZ, USA)].

Index Intervention:

Detailed full medical history of the patient was taken and a physical examination of the dialysis access circuit was performed in accord with the KDOQI (Kidney Disease Outcome Quality Initiative) recommendations.[7] A single, intravenous 750-mg dose of cephalosporin was given as a prophylactic antibiotic against potential infection of the vascular access. Percutaneous access was gained in an appropriately chosen non-aneurysmal site of the dialysis access circuit with a micropuncture set (Venastick Set; Angiotech, PBN Medicals, Stenlose, Denmark) after the application of local anesthetic (2–3 mL of 1% lidocaine). Vascular access was then secured with the introduction of a 0.035-inch stiff hydrophilic guidewire (Terumo, Tokyo, Japan) and placement of a 6-F vascular sheath. Five thousand units of unfractionated heparin were administered intravenously to avoid thrombotic events, and selective digital subtraction angiography (DSA) of the access circuit was performed to outline the anatomy and delineate the location and morphology of the stenosis. The lesion was crossed with routinely used catheters and guidewires, while the size of the PCB or plain high-pressure balloon was selected according to the reference diameter of the most proximal non-aneurysmal vein segment.

High-pressure (>18 atmospheres) balloon catheters, considered the instrument of choice for dilation of highly resistant venous stenoses that develop in AVFs or AVGs, were most frequently used in the control arm of the study. In the active comparator group, PCB dilation was performed without predilatation because IN. PACT is considered to be a combination of balloon angioplasty catheter and drug-elution device. Post-dilatation with another high-pressure balloon was performed only for residual stenosis >30%. According to protocol, duration of balloon inflation was at least 1 minute at the recommended nominal inflation pressure in all cases. A final angiogram of the entire dialysis vascular access, including the arterial inflow and the vein outflow circuit, was performed to exclude any immediate complications. After completion of the procedure, hemostasis was achieved with the use of a purse-string suture. Patients were prescribed daily antiplatelet therapy with clopidogrel (75 mg). Clinical surveillance was performed during regular dialysis sessions, and DSA follow-up was scheduled every 2 months or earlier if deemed necessary.

Study Endpoints and Outcome Measures

Device success was defined as a <30% residual stenosis after PCB application or BA in comparison to the reference diameter of the most proximal non-aneurysmal vein segment. The need for further postdilatation because of suboptimal angioplasty was recorded as device failure. In a similar way, procedural success was defined as a final angiogram with <30% residual stenosis after PCB application or PBA (regardless of additional postdilatation) and at least one successful dialysis session using the treated AVF or AVG circuit. The primary endpoint was primary patency of the treated lesion and of the treated circuit at 6 months. Secondary endpoints included (1) overall dialysis circuit survival, defined as a patent and functional vascular access regardless of the number of repeat surgical and/or percutaneous procedures in the interim, and (2) major and minor complications, classified according to published international reporting standards.[7] Primary patency was defined as the angiographic visualization of a patent lesion or circuit with <50% angiographic restenosis and no need for any repeat procedures during the entire follow-up period. Loss of primary patency was recorded in the event of significant binary restenosis, clinically-driven surgical or percutaneous reintervention, or thrombosis of the target lesion or treated circuit. Angiographic restenosis was set at a binary 50% threshold. Both residual stenosis and restenosis were assessed on DSAs using vessel analysis software tools (Allura Xper FD20; Xcelera Release 7.2; Phillips Medical Systems, Amsterdam, The Netherlands), clinically driven reintervention was defined as the percutaneous or surgical treatment of a ≥50% target lesion restenosis associated with clinical and/or hemodynamic abnormality of the dialysis circuit, while thrombosis was clinically evaluated as the presentation of an impalpable dialysis circuit, resulting in an inability to perform hemodialysis. Thrombosis of vascular access had to be further confirmed by duplex ultrasonography.

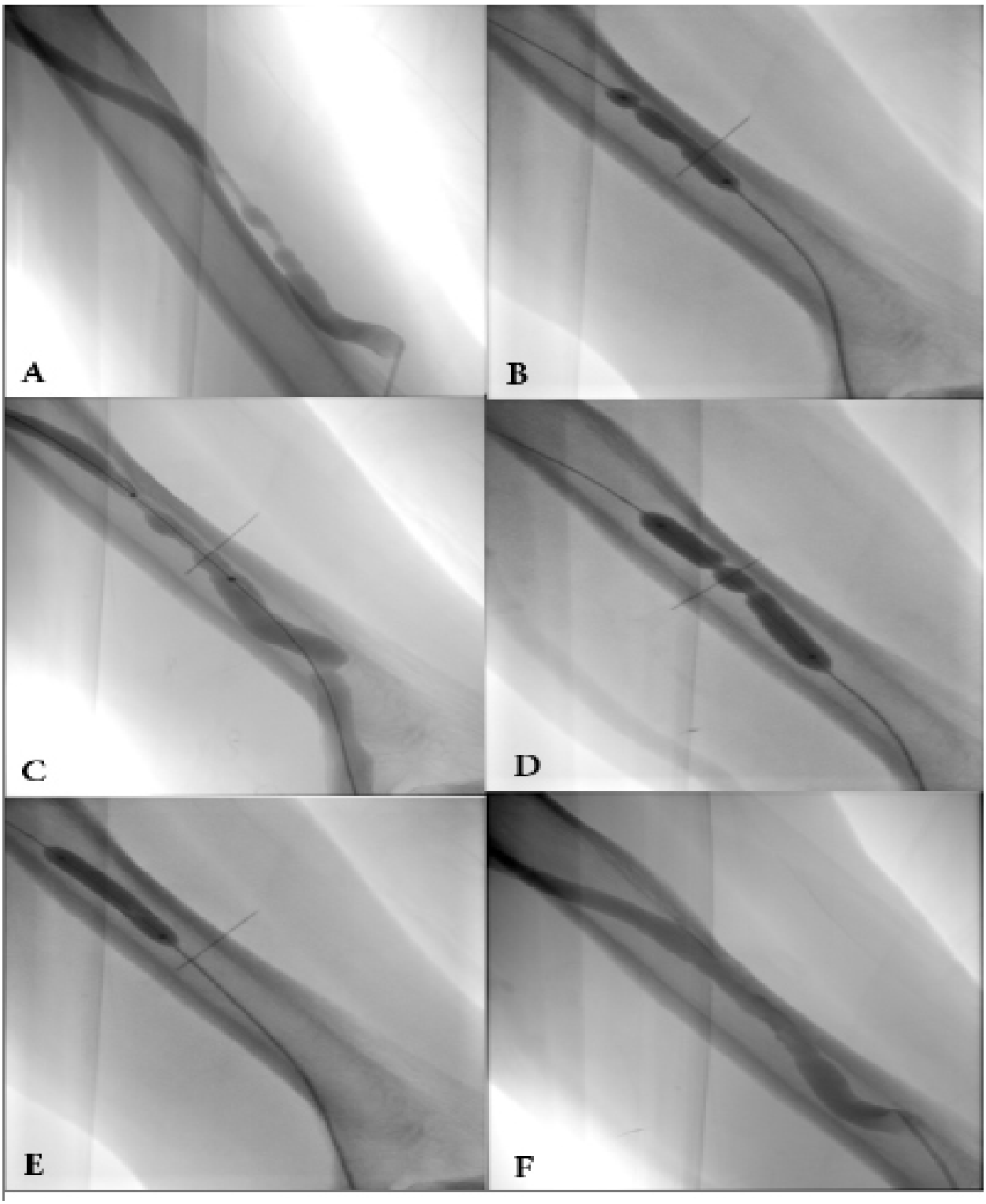

Fig 1: Serial fistulograms depict the study procedures in (A) two stenotic lesions of the main cephalic vein stem which have been selected for dilatation by PCB. (B) The two lesions have been simultaneously treated with IN.PACT balloon size 5mm diameter X 70mm length) with apparent two waists. (C) Residual stenoses post dilatation in the venography. (D&E) Repeat dilatation by using Dorado conventional balloon at 18 atmospheres with gradual disappearance of the 2 waists. (F) Final postdilatation venogram showing full dilatation of the mid-vein stenotic lesions and rapid flow of the injected dye.

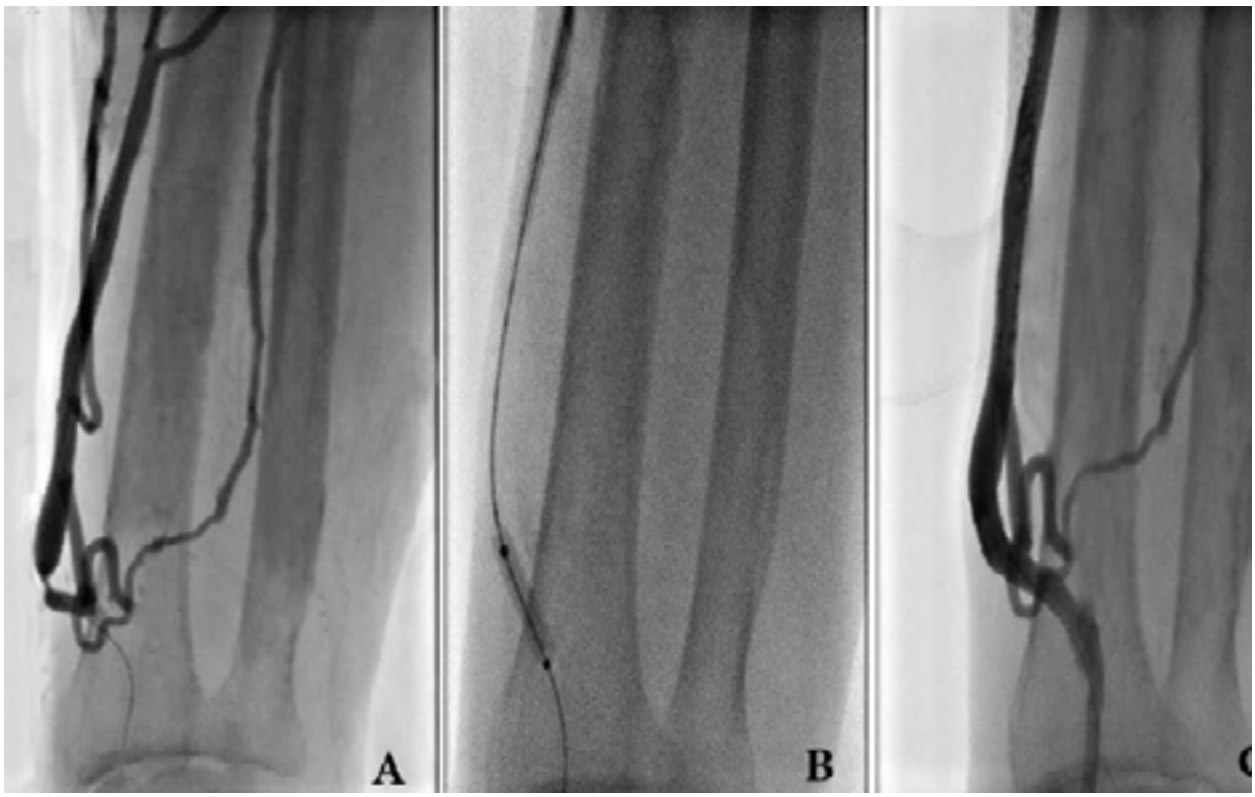

Fig 2: Tight stenosis of radiosefalic fistula vein (A) was dilated with 4/20mm PCB (B) with successful result as shown in the postdilatation venography (C).

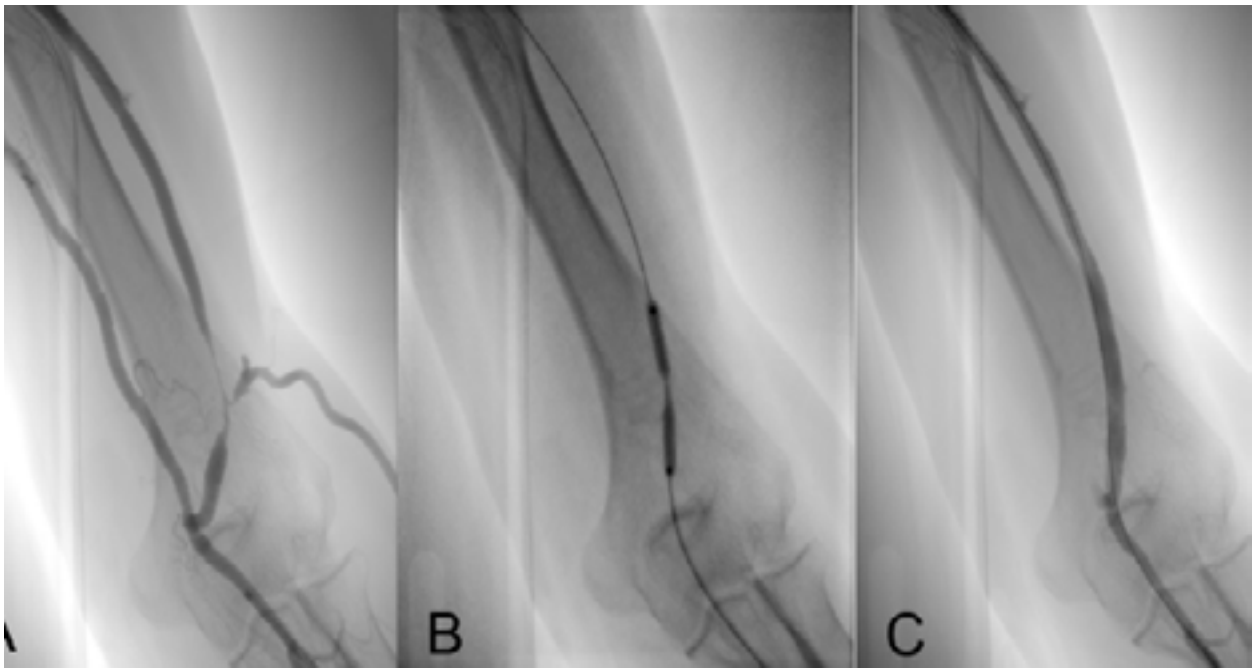

Fig 3: Dilatation of the juxtaanastomotic cephalic vein segment stenosis (A) using paclitaxelcoated balloon 4mm*70mm (B) with successful postdilatation venography (C).

Statistical Analysis

Discrete variables were expressed as counts (percentages), and continuous variables were given as medians with interquar-tile ranges (i.e., between the 25th and 75th percentiles) in parentheses or as means±standard deviation if they passed the Kol-Mogorov-Smirnov goodness-of-fit normality test. The unpaired Student t test was used to test normally distributed continuous variables. the Mann-Whitney test was used for qualitative variables and for non-parametric continuous variables, comparison of proportions was done by testing the null hypothesis that the proportions were equal, with an appropriate quantity as a standardized normal deviate test. Results were stratified according to the type of treatment (PCB vs. BA). Life-table analysis using the Kaplan-Meier method was employed for graphical illustration of proportional outcomes up to the 6-month follow-up. Kaplan-Meier curves were compared with the log-rank (Mantel Cox) test; the associated hazard ratio (HR) and corresponding 95% confidence intervals (CI) were provided. The threshold of statistical significance was set at $p<0.05$. Statistical analysis was performed with the SPSS Statistics (Version 22, IBM Corporation, New York, USA) and plots were produced with the Graph-Pad Prism statistical software package (Version 6.01; GraphPad Software, La Jolla, CA, USA).

Results

Within 24-month period, during 2015 and 2016, 96 patients (54 men=56%; mean age 60.3±13.8) with hemodialysis-dependent end-stage renal disease were enrolled in the study. In total, 48 patients were randomly assigned to group PCB (29 AVGs & 19 AVFs) & 48 patients to group PBA (29 AVGs & 19 AVFs). Baseline & procedural variables were comparably distributed in PCB & PBA groups **(Table 2)**. There were no significant differences in age of the treated vascular access circuit (2.31±1.62) years in PCB group vs. 2.63±1.94 years in PBA group, p=0.483), nor in the overall length of the treated target vein lesion (5.2±1.4 cm in PCB group vs. 5.4±1.6 cm in PBA group, p=0.641). All patients enrolled in the study completed the 1-year follow-up period. Device success rates were 100% in the PBA group and 39.6% in the PCB group, as further dilation with PBA was needed in 29 of 48 cases (60.4%) in the PCB group to achieve acceptable immediate postprocedural residual stenosis less than 30% (p=<0.001) **(Table 3)**. Anatomic and clinical success rates were 100% in both groups. No minor or major procedure-related complications occurred in either group, access circuit primary patency results were also significantly in favor of PCB angioplasty (PCB, 287 days; PBA, 156 days; p=0.04; **(Figure 4)**. TLR-free survival was significantly superior in the PCB group according to the Kaplan–Meier survival analysis curve (PCB, 316 days; PBA, 172 days; p = 0.041; **(Figure 5)**. There were seven cases in the PBA group (15%) and 10 cases in the PCB group (21%) in which lesions had been previously treated with angioplasty using a PBA, there was no statistically significant difference in this subgroup analysis (p > 0.1).

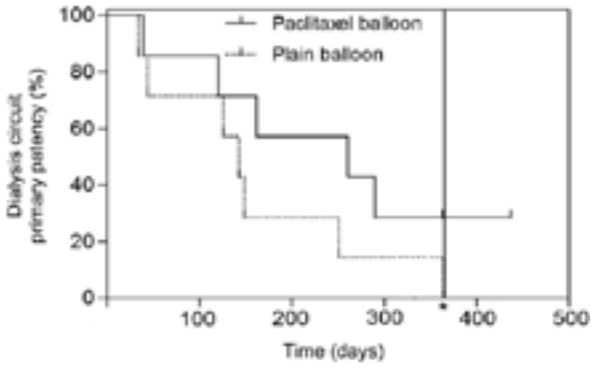

Fig 4: Kaplan-Meier survival plots of dialysis circuit primary patency. Vertical line with asterisk (*) represents 1-year time point. Subjects at risk are presented for intervals of 100, 200, 300, & 400 days.

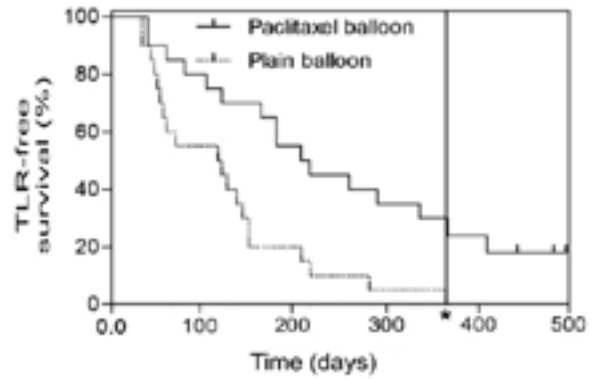

Fig 5: Kaplan-Meier survival plots of TLC-free survival. Vertical line with asterisk (*) represents 1-year time point. Subjects at risk are also presented.

Table 2: Demographic characteristics of the two patient groups

Characteristic	PCB (n=48)	PBA (n=48)	P Value
Age (years)	61.4 ± 13.6	59.2 ± 14.1	.143
Gender (males)	26 (54%)	28 (58%)	.461
Age of dialysis access (years) (from the date of access creation to date of the angioplasty)	2.4 ± 1.62	2.4 ± 1.94	1.000
Type of vascular access:			
Autogenous arteriovenous fistula (AVF)	19 (40%)	19 (40%)	1.000
Prosthetic arteriovenous graft (AVG)	29 (60%)	29 (60%)	1.000
Etiology of dialysis-dependent ESRD:			
DM	24 (50%)	24 (50%)	1.000
HTN	12 (25%)	12 (25%)	1.000
Polycystic kidney disease	4 (8%)	2 (4%)	0.473
Lupus nephropathy	1 (2%)	2 (4%)	0.274
Other	4 (8%)	4 (8%)	1.000
Unknown	3 (6%)	4 (8%)	0.362
Anastomosed vein:			
Axillary vein	16 (33.4%)	18 (37.5%)	0.348
Cephalic vein	26 (54.1%)	24 (50%)	0.416
Basilic (superficialized)	6 (12.5%)	6 (12.5%)	1.000
Anastomosed artery:			
Brachial artery	38 (79%)	34 (71%)	0.752
Radial artery	10 (21%)	14 (29%)	0.621
Site of stenosis:			
Juxtaanastomotic (± 3cm from AV anastomosis)	24 (50%)	24 (50%)	1.000
Main vein segment used for puncture sites	24 (50%)	24 (50%)	1.000
Degree of stenosis (%) ± SD (by visual estimation)	72 ± 9.21	75 ± 8.47	0.514
Overall length of the treated target vein lesion (cm)	5.2 ± 1.4	5.4 ± 1.6	0.641

Table 3: Procedural primary & secondary outcome measures at 12-months for PCB vs. PBA groups

Outcome	PCB (n=48)	PBA (n=48)	P Value
Completed 12-months follow-up	48	48	-
Device success (residual target lesion stenosis <30% without any further PBA postdilatation)	19	48	<0.001
Postdilatation	29	0	<0.001
Technical success (<30% remaining stenosis after postdilatation)	48	48	-
Procedural success	48	48	-
Major complication	0	0	-
Minor complications	0	0	-
TLR-free survival (days)	316	172	0.041
Primary patency of dialysis circuit (days)	287	156	0.040
Circuit thrombosis during follow-up period	4	2	1

Discussion

ESRD is typically characterized by a state of massive endothelial dysfunction, which in turn is associated with vascular inflammation, oxidative stress, and reduced flow-mediated vasodilatation.[12-14] In addition, diabetes mellitus, which is the most common cause of ESRD, is a group of chronic metabolic diseases that is characterized by dysfunction of endothelial cells and SMCs, as well as by deceased vessel wall dilation.[15]

In a newly formed hemodialysis access, neointimal hyperplasia may develop at the anastomotic site and leads to outflow stenosis, which prevents flow-mediated vasodilation, enlargement, and maturation in the case of AVFs; in venous juxta-anastomotic AVG stenoses, it may cause poor graft flow and early thrombosis.[1,16] Mild neointimal hyperplasia may also lead to a tight AVF stenosis if dilatation fails, while significant neointimal hyperplasia may not result in venous stenosis if it is compensated by outward positive vascular remodeling or vein dilatation.[17] Other factors inculpated as primary irritators leading to neointimal hyperplasia formation include vascular trauma during access creation, vessel and injury from needle punctures.[18]

Events that may contribute to early AVF failure include small vessel diameter, surgical injury during AVF creation, previous venopunctures, newly developed accessory veins after surgery, fluid shear stress at the anastomosis, genetic predisposition to vasoconstriction and neointimal hyperplasia, and preexisting venous neointimal hyperplasia.[18] In late AVF failure, the increased shear stress in the thin-walled outflow vein causes fibromuscular hyperplasia (fibrotic lesion formation) and consequent blood flow reduction (and stasis) that finally leads to thrombus formation.[1,17]

The initial events of neointimal hyperplasia include trauma at the time of vascular access creation, elevated hemodynamic shear stress across the dialysis circuit, vessel injury from dialysis needle punctures, uremia resulting in endothelial dysfunction, and repeated angioplasties that may exacerbate endothelial injury.[18,19] The vessel injury leads to downstream events (oxidative stress, inflammation, endothelial dysfunction, alternative origins for neointimal cells) that trigger the migration of vascular SMCs from the media to the intima, precipitating neointimal hyperplasia.[6,16,20] The same causes generally account for venous AVF stenoses and for venous juxta-anastomotic AVG stenoses, as well as for hemodynamically significant venous stenoses that may develop at any point along the venous outflow circuit.[1] In uremic patients, the endothelial dysfunction may exaggerate any preexisting venous neointimal hyperplasia, medial hypertrophy, and vessel wall intima-media thickening that may be present even before vascular access formation.[21,22,23]

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. Minimally invasive endovascular methods are established treatment options for dialysis access maintenance & the interventional vascular approach has become the treatment of choice, securing access in >80% of cases and allowing patients to undergo immediate hemodialysis without the need of temporary dialysis catheters or surgical consumption of additional venous conduits.[1,2] The majority of critical venous stenoses develop either along the venous outflow tract of the AVF or at the venous juxta-anastomotic site of the AVG. However, angioplasty itself can cause intima-media rupture, followed by neointimal hyperplasia (normal vessel response to the injury), and subsequent development of restenosis with recurrent vascular access failure. Therefore, BA of the vascular access is characterized by poor midterm patency, with an increasing rate of repeat procedures.[24]

Several devices and techniques such as cutting balloons and cryoplasty have been used in the past in an attempt to improve patency outcomes of conventional percutaneous transluminal angioplasty in failing dialysis vascular access.[25-27] Recent outcomes from a multicenter randomized controlled trial[28] demonstrated that stent-grafts perform better than percutaneous transluminal angioplasty in the management of arteriovenous graft juxtaanastomotic stenosis. To our knowledge, no equivalent data are available for AVFs. Although etiology of stenosis in the latter case is considered a multifactorial trait, extending from circuit age and lesion length to vascular wall level changes, it is mainly attributed to aggressive neointimal hyperplasia.[29,30] With neointimal hyperplasia being the main contributing factor to restenosis, the use of a local drug-delivery device that has been proven to inhibit this process in other vascular beds would be of interest.[31-33]

According to the 2000 National Kidney Foundation's KDOQI Vascular Access Clinical Practice Guidelines, placement of bare metal stents should be reserved as a bailout solution in cases of suboptimal or complicated BA.[34]

Excitement has been fueled recently by a multicenter, controlled trial focusing on treatment of the venous anastomotic stenoses of AVGs, the trial compared the effectiveness of traditional BA

with that of BA followed by the insertion of a self-expanding stent-graft at the stenosed venous anastomotic site of the AVG. Of interest, 6-month primary patency rates of both the treatment area and the entire treated access circuit were significantly superior, i.e., approximately double in the stent-graft group [51% vs. 23% (p = 0.001) and 38% vs. 23% (p=0.008), respectively].[28]

Drug-coated balloon technology has emerged during the recent years as a potential solution to the limitations presented by the use of drug-eluting stents (DES) in the management of atheromatous cardiovascular disease, DES technology was revolutionary since it both eliminated early elastic recoil with vessel scaffolding and significantly inhibited neointimal hyperplasia with elution of antirestenotic agents. However, the need for long-term antiplatelet therapy and the risk of abrupt late stent thrombosis remain fundamental limitations of DES technologies.[10,11]

Theoretically, the absence of any source of chronic inflammation, such as the metal stent or polymeric coating material, avoids an exaggerated vessel reparative process responsible for the phenomenon of restenosis and acute late thrombosis. To date, positive results have been obtained with the application of PCB angioplasty for the treatment of leg ischemia due to peripheral artery disease and recurrent coronary obstructions due to in-stent stenosis. A strong and significant reduction in angiographic late lumen loss, which is a surrogate quantitative endpoint of late vascular restenosis, was achieved in both disease conditions with the use of PCB technologies.[35,36]

In the review of literature, few other randomized controlled studies have compared traditional PBA with PCB angioplasty for the treatment of venous outflow stenoses of failing dialysis vascular access circuits. In the randomized trial of Katsanos et al,[34] the 6-month lesion primary patency rate was 70% in the group of dialysis recipients in whom PCBs were used, whereas it was 25% in the group treated with HPBs (P<.001). The difference was significantly in favor of PCBs in the recent pilot study by Lai et al,[35] which included only patients with an AVF (70% vs 0% at 6 months; P<.01). However there was not a statistically significant difference at 1 year in that study (20% vs 0%; P>.05). Unlike the present study, in that pilot study,[35] lesions treated either way were present in the same access circuit, although 6-month results of these two prospective trials were equivalent, only a small number of cases were investigated. As a result, more evidence is needed regarding the use of PCB in AVFs.

In our study, the treated stenotic segments within the failing dialysis access circuit required fewer interventions when treated with angioplasty using a PCB than with BPA. The fact that PCBs significantly improved dialysis access circuit primary patency outcomes is an important clinical outcome, as this extended event-free period for the AVF circuit increasingly strengthens the treatment success.

In the PCB group, 29 of 48 cases (60.4%), a further dilation was performed for gaining an acceptable procedural result to be achieved in this study group. In this 3-center prospective randomized controlled study, the use of PCBs resulted in less clinically driven TLR and superior dialysis access circuit primary patency of dysfunctional AVFs at 1 year. In the PCB group, additional HPB postdilatation was required in the majority of cases. Larger-scale trials are awaited to verify these results.

Among the limiting factors of our study were the limited diameter availability of PCBs (maximum of 7 mm) and low-pressure (12 atm) inflation force which influenced device success outcomes and the fact that different balloons with different maximum pressures were used in the PBA group constitutes an another additional limitation of the study.

Conclusion

In this three-center study, paclitaxel-coated balloon angioplasty results in improved vessel patency and is superior to plain balloon dilation in the treatment of venous stenoses of failing native or prosthetic arteriovenous shunts used for dialysis access. In the PCBs group, additional HPB postdilatation was required in the majority of cases. These results combined with the "do not leave any metal behind" principle characteristic in balloon angioplasty, marks paclitaxelballoon as a really promising technology and merits larger-scale trails for PCBs to have a future place in the armamentarium for the treatment of venous stenosis in failing dialysis access.

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