◆ CLINICAL INVESTIGATION ◆

Paclitaxel-Coated Balloon Angioplasty vs. Plain Balloon Dilation for the Treatment of Failing Dialysis Access: 6-Month Interim Results From a Prospective Randomized Controlled Trial

Konstantinos Katsanos, MSc, MD, PhD, EBIR; Dimitris Karnabatidis, MD, PhD; Panagiotis Kitrou, MD; Stavros Spiliopoulos, MD, PhD; Nikolaos Christeas, MD; and Dimitris Siablis, MD, PhD

Department of Diagnostic and Interventional Radiology, Patras University Hospital, School of Medicine, Rion, Greece.

Purpose: To report the 6-month results of a prospective randomized trial investigating angioplasty with paclitaxel-coated balloons (PCB) vs. plain balloon angioplasty (BA) for the treatment of failing native arteriovenous fistulae (AVF) or prosthetic arteriovenous grafts (AVG).

Methods: The enrollment criteria for this non-inferiority hypothesis trial included clinical signs of failing dialysis access with angiographic documentation of a significant venous stenotic lesion in patients with AVF or AVG circuits. From March to December 2010, 40 patients (29 men; mean age 64.1±14.3 years) were randomized to undergo either PCB dilation (n=20) or standard BA (n=20) of a stenosed venous outflow lesion. Regular angiographic follow-up was scheduled bimonthly. Study outcome measures included device success (<30% residual stenosis without postdilation), procedural success (<30% residual stenosis), and primary patency of the treated lesion (<50% angiographic restenosis and no need for any interim repeat procedures).

Results: Baseline and procedural variables were comparably distributed between both groups. Device success was 9/20 (45%) for the PCB device vs. 20/20 (100%) for standard control BA ($p<0.001$). Procedural success was 100% in both groups after further high-pressure post-dilation as necessary. There were no major or minor complications in either group. At 6 months, cumulative target lesion primary patency was significantly higher after PCB application (70% in PCB group vs. 25% in BA group, $p<0.001$; HR 0.30, 95% CI 0.12 to 0.71, $p<0.006$).

Conclusion: PCB angioplasty improves patency after angioplasty of venous stenoses of failing vascular access used for dialysis.

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Key words: paclitaxel-coated balloon, angioplasty, failing access, arteriovenous fistula, native fistula, prosthetic graft, dialysis access, restenosis, primary patency

In the United States, more than 350,000 patients with end-stage renal disease (ESRD) are currently undergoing hemodialysis, and this number is estimated to double by 2020.[1] 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

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Corresponding author: Konstantinos Katsanos, Lecturer of Radiology, Department of Interventional Radiology, Patras University Hospital, School of Medicine, Rion, 26504, Greece. E-mail: *katsanos@med.upatras.gr*

procedure in the form of either an autologous arteriovenous fistula (AVF) or prosthetic arteriovenous graft (AVG).[2] However, these conduits are characterized by a high rate of late failure, mainly because of stenosis developing in the venous component.[3,4] Dysfunction of the dialysis circuit is a significant cause of morbidity and mortality in patients undergoing hemodialysis and can eventually lead to loss of vascular access.[5,6] In spite of their increased risk of non-maturation, AVFs are preferred over AVGs due to their better long-term functionality.[2] Nonetheless, durability of both types of vascular access is limited, with an almost 50% failure rate after a median lifetime of 3 to 7 years for AVF and 12 to 18 months for AVG.[7–9] Unfortunately, in the United States, <50% of all hemodialysis accesses will remain patent after 3 years, and the economic burden of maintaining vascular access patency is calculated to exceed $1 billion, with a >6% annual increase trend.[10–12]

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.[2,5,7,13] 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.[14–16] Only recently, a large multicenter randomized trial investigated placement of covered stents or stent-grafts for the treatment of stenotic venous anastomotic sites of AVGs and concluded that this method may outweigh traditional BA.[17] Nevertheless, the benefit for any therapy other than BA for the treatment of AVF venous stenosis remains to be proven.

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.[18] We sought to compare the performance of PCBs vs. standard plain BA for the treatment of venous stenoses of the vascular access circuit in patients undergoing hemodialysis.

METHODS

Study Design

This prospective, single-center, non-blinded, randomized study was designed to compare the immediate and long-term angiographic and clinical outcomes of the application of PCBs vs. conventional high-pressure BA in the treatment of venous outflow stenoses of failing dialysis accesses. The study protocol was approved by the local hospital's Ethical and Scientific Review Board and was registered in an open access database available on the Internet (*www.clinicaltrials.gov*: NCT01174472).

The study's inclusion and exclusion criteria are outlined in Table 1. Eligible patients were at least 18 years old and presented with clinical signs of a dysfunctional dialysis access and 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. Patients eligible for recruitment were given the potential benefits and risks of PCB technology and provided written informed consent.

For the non-inferiority study design, a 15% margin of difference between the 2 treatments was used (α=0.05 and statistical power set at 0.80). The expected primary patency rate at 1 year was estimated as 50% in the active treatment group and as 25% in the reference treatment control group. The

TABLE 1
Study Enrollment Criteria

Inclusion criteria
Age 18 to 90 years
Native arteriovenous fistula or prosthetic arteriovenous graft in the arm
Vascular access actively used for hemodialysis (at least 1 successful session)
Clinical signs of failing access due to presence of significant anatomic stenosis*
Angiographically proven venous outflow stenosis >50%†
Reference diameter of proximal outflow vein <7 mm†
Exclusion criteria
Patient unable to provide informed consent
Patient unable to abide with study follow-up protocol
Patient participating in other relevant or conflicting studies
Vascular access circuit placed in the lower extremities
Mare metal stent or stent-graft placed previously
Hemodynamically significant stenosis of the central venous system
Metastatic cancer or other terminal medical condition
Limited life expectancy (<6 months)
Blood coagulation disorders
Sepsis or active infection
Recent arm thrombophlebitis (<6 months)
Allergy or other known contraindication to iodinated contrast media, heparin, or paclitaxel
Pregnancy

* Detection of elevated venous pressure during dialysis and/or decreased blood flow.
† Compared to proximal reference vein diameter. Aneurysmal segments were avoided.
The remainder of the lesion morphological parameters were chosen according to largest IN.PACT PCB device available at the time of the study.

number of patients required in each treatment arm was calculated to be 20. From March to December 2010, 40 patients (29 men; mean age 64.1±14.3 years) on active hemodialysis via an AVF or AVG vascular access were enrolled and randomly assigned to a treatment group using a sealed envelope system. Patient baseline demographics and characteristics of the dialysis accesses are outlined in Table 2.

Study Devices

The PCBs used in the present study were the over-the-wire IN.PACT balloon dilation catheters (Invatec-Medtronic, Brescia, Italy), which are available in diameters up to 7 mm and lengths up to 8 cm. The balloon is coated with FreePac, a paclitaxel-eluting formulation that contains hydrophilic urea to optimize transfer of the lipophilic paclitaxel to the endothelial cells upon contact with the vessel wall. The paclitaxel dose is 3.0 $\mu g/mm^2$ of balloon surface. 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. The cell cycle is thereby arrested in the phase of mitosis, inhibiting smooth muscle cell (SMC) proliferation and fibromuscular hyperplasia.

In the BA control group, various brands of mostly high-pressure balloons available in our department were applied [Ultra-Thin Diamond and Blue Max PTA (Boston Scientific, Natick, MA, USA), Profiler (Angiodynamics, Latham, NY, USA), or Dorado PTA balloon dilatator catheter (Bard Peripheral Vascular, Tempe, AZ, USA)].

Index Intervention

The 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 Outcomes Quality Initiative) recommendations.[7]

TABLE 2
Baseline Patient Demographics and Details of the Dialysis Access Circuits for Patients Randomized to Paclitaxel-Coated Balloons (PCB) vs. Plain Balloon Angioplasty (BA)

	PCB (n=20)	BA (n=20)	p
Age, y	65.7±13.2	62.5±15.4	0.485
Men	15 (75%)	14 (70%)	0.361
Dialysis access age, y	2.5±2.0	2.5±3.2	1.000
Type of vascular access			
Native arteriovenous fistula	7 (35%)	7 (35%)	1.000
Prosthetic arteriovenous graft	13 (65%)	13 (65%)	1.000
Dominant arm side	8 (40%)	7 (35%)	0.372
Cause of renal failure			
Diabetes	4 (20%)	4 (20%)	1.000
Hypertension	3 (15%)	2 (10%)	0.316
Polycystic kidney disease	1 (5%)	2 (10%)	0.274
Systemic lupus nephropathy	1 (5%)	0 (0%)	0.156
Unknown	4 (20%)	9 (45%)	0.046
Other	7 (35%)	3 (15%)	0.072
Venous anastomosis site			
Axillary vein	12	13	0.372
Cephalic vein	7	6	0.368
Basilic vein (transposed)	1	1	1.000
Arterial anastomosis site			
Brachial artery	20	18	0.073
Radial artery	0	2	0.073

Continuous data presented as mean ± standard deviation; categorical data are given as the count and percentage in parentheses.

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 predilation because IN.PACT is considered to be a combination of balloon angioplasty catheter and drug-elution device. Postdilation 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 as described elsewhere.[19] 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 postdilation 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 BA (regardless of additional postdilation) 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.

Statistical Analysis

Discrete variables were expressed as counts (percentages), and continuous variables were given as medians with interquartile ranges (i.e., between the 25th and 75th percentiles) in parentheses or as means ± standard deviation if they passed the Kolmogorov-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 GraphPad Prism statistical software package (version 5; GraphPad Software, La Jolla, CA, USA).

RESULTS

Baseline and procedural variables were comparably distributed between both groups (Table 2). Both treatment arms included the same number of AVFs (n=7) and AVGs (n=13). There were no significant differences in the age of the treated vascular access (2.5±2.0 years in PCB group vs. 2.5±3.2 years in BA group, p=1.000), nor in the overall treated lesion length (5.7±1.6 cm in PCB group vs. 5.9±1.2 cm in BA group, p=0.657).

TABLE 3
Primary and Secondary Outcome Measures at 6 Months for Patients Randomized to Paclitaxel-Coated Balloons (PCB) vs. Plain Balloon Angioplasty (BA)

	PCB (n=20)	BA (n=20)	p
Target lesion length, cm	5.7±1.6	5.9±1.2	0.657
Balloon diameter, mm	6.2±0.8	6.0±0.5	0.349
Device success	9 (45%)	20 (100%)	<0.001
Balloon postdilation (high-pressure)	11 (55%)	0 (0%)	<0.001
Procedure success	20 (100%)	20 (100%)	—
Major procedure-related complications	0 (0%)	0 (0%)	—
Other procedure-related adverse events	0 (0%)	0 (0%)	—
Target lesion primary patency	14 (70%)	5 (25%)	<0.001
Dialysis circuit primary patency	13 (65%)	4 (20%)	0.002
Dialysis circuit survival	19 (95%)	18 (90%)	0.274
Repeat procedures	4 (20%)	13 (65%)	0.002
Thrombosis	1 (5%)	2 (10%)	0.274

Continuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).

Device success was 9 (45%) for the PCB device vs. 20 (100%) for standard control balloons ($p<0.001$). In the PCB group, 11 lesions had to be further post-dilated with a high-pressure balloon because of an initially unacceptable angiographic result. Procedural success was 100% in both groups. There were no major, minor, or other procedure-related complications recorded in either treatment group.

Six-month angiographic follow-up was completed for all patients; at that time point, cumulative target lesion primary patency (Table 3, Fig. 1A) was significantly higher after PCB application (70% vs. 25% in BA group, $p<0.001$; HR 0.30, 95% CI 0.12 to 0.71, $p<0.006$). Likewise, cumulative primary patency of the treated dialysis circuit (Fig. 1B) was significantly improved with PCB treatment (65% vs. 20% in BA group, $p=0.002$; HR 0.32, 95% CI 0.14 to 0.75, $p<0.008$). One and 2 cases of AVG thrombosis occurred in the PCB and BA groups, respectively, during the 6-month follow-up period. A significantly higher number of repeat procedures were required in the BA control group (13, 65%) compared to the PCB group (4, 20%, $p=0.002$). No significant difference was noted in overall dialysis circuit survival (Fig. 1C) at 6 months (95% in PCB group vs. 90% in BA group, $p=0.274$; HR 0.33, 95% CI 0.03 to 3.36, $p=0.349$).

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 vasodilation.[20–23] 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 decreased vessel wall dilation.

In a newly formed hemodialysis access, neointimal hyperplasia may develop at the anastomotic site and lead 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.[2,24,25] 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.[24]

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 pre-existing venous

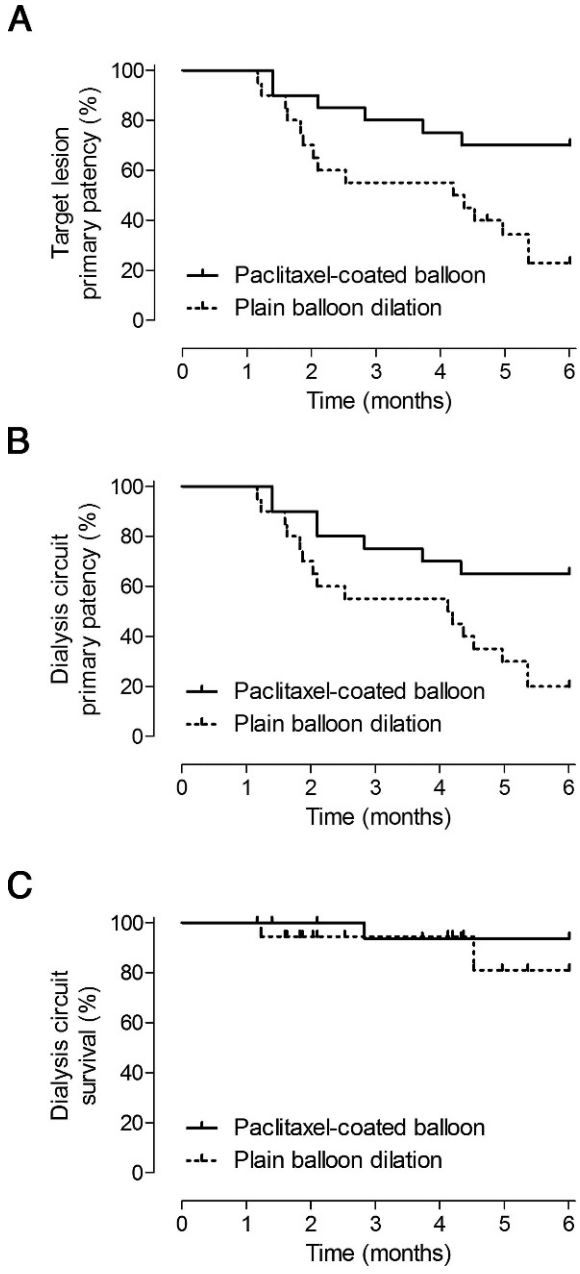

Figure 1 ◆ Kaplan-Meier graphs of (**A**) target lesion primary patency, (**B**) dialysis circuit primary patency, and (**C**) overall dialysis circuit survival up to 6 months in the PCB-treated lesions compared to the BA-treated controls.

neointimal hyperplasia.[26] 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.[2,25]

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.[26,27] 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.[12,13,24] 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.[2] 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.[20,21,23]

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. 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.[2,7] 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.[10] 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.[7]

Excitement has been fuelled 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].[17]

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 anti-restenotic agents. However, the need for long-term antiplatelet therapy and the risk of abrupt late stent thrombosis remain fundamental limitations of DES technologies.

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.[18,28–30]

To our knowledge, no other randomized controlled study has compared traditional BA with PCB angioplasty for the treatment of venous outflow stenoses of failing dialysis vascular access circuits. Our results have shown a highly significant, superior short-term primary patency in the PCB group compared to that of BA (Fig. 2). At 6 months, the 70% primary patency of the PCB-treated group was nearly 3 times that of the BA group, and the rate of repeat procedures was consequently significantly lower in the PCB-treated lesions compared to the controls (20% vs. 65%, $p=0.002$). Notably, although the trial was initially designed as a non-inferiority study on the basis of similar trials in the literature, the observed treatment effect (primary patency was improved by 45% at 6 months) exceeded by far the 15% margin of difference between the 2 treatments for the non-inferiority hypothesis.

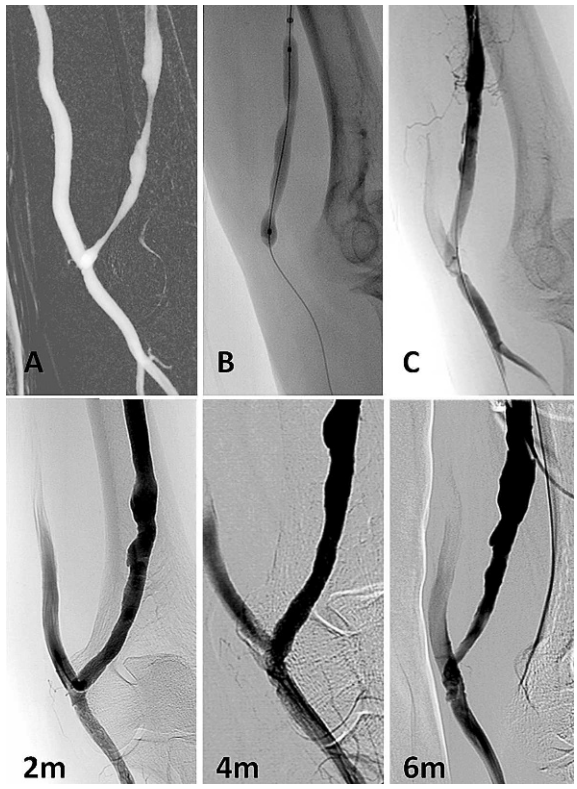

Figure 2 ◆ (**A**) Baseline fistulogram showing 2 tandem stenoses along the venous outflow of a failing brachiocephalic fistula. (**B**) Baseline treatment of the lesion with a 7×80-mm IN.PACT paclitaxel-coated balloon catheter. Note the resistant features of the stenoses when the balloon was inflated at 14 atmospheres. (**C**) Final fistulogram showing a successful immediate outcome after additional post-dilation with a 7×80-mm DORADO balloon catheter. (**Lower panel**) In the serial follow-up angiograms every 2 months (2m, 4m, and 6m), note the excellent outcome at 2 and 4 months, and the gradual reappearance of mild hyperplasia at the juxta-anastomotic venous level with an almost 50% restenosis at 6 months. There was no need for any repeat angioplasty according to functional evaluation of the vascular access by the referring nephrologist.

It is therefore acceptable to reject the null hypothesis and further interpret the data on the basis of a superiority study design, i.e., paclitaxel-coated balloons are superior to plain balloon dilation for the treatment of failing arteriovenous shunts.

Nonetheless, high-pressure postdilation was required in more than half of the PCB-treated lesions because of the resistant fibrotic nature of the stenoses, significantly reducing device success. However, overall procedure success was 100% in both groups after further high-pressure postdilation. This observation reflects the need for engineering of paclitaxel-coated high-pressure balloons with appropriate diameters dedicated for dialysis access treatment.

Although the use of stent-grafts has raised hope for the treatment of venous graft anastomotic stenosis in the case of AVGs, one might claim that this is actually an elongation of the synthetic bridge between the artery and the vein inasmuch as the material used for both the synthetic graft and stent-grafts is the same (i.e., polytetrafluoroethylene). PCB treatment leaves no foreign object behind, which gives the method a profound advantage compared with the metal scaffolds of bare or covered stents,[29] not to mention the fact that the arterialized venous wall behavior is inherently different from the native artery in terms of anatomy, physiology, and induced hemodynamics. On the basis of the present data, the authors believe that PCB technologies may be particularly suited to the treatment of aggressive recurrent hyperplasia developing at sites of critical venous stenosis of dialysis vascular accesses.

Study Limitations

Arguably, the present study is limited by its non-blinded single-center design and by the absence of independent event adjudication and angiographic core lab analysis. Another limitation is that most of the native fistulas were located in the upper arm and very few in the forearm. In addition, lesion predilation was not performed since the PCB device under investigation was applied as a combination of vessel angioplasty and drug-transfer instrument. The results might have proved different if high-pressure balloon dilation of the dialysis venous stenoses was performed first followed then by PCB drug delivery. It is plausible that adequate predilation, as proposed during femoral artery angioplasty, might have augmented paclitaxel delivery in the deeper layers of the vessel wall and further improved the anti-restenotic performance of PCBs.[31] Finally, the lack of paclitaxel-coated balloons with a diameter $>$7 mm prevented including more central venous lesions that are commonly detected in failing arteriovenous shunts.

Conclusion

Paclitaxel-coated balloon angioplasty improves 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. Final long-term data from our study are awaited, and further large-scale multicenter trials are necessary to establish whether PCBs have a future place in our armamentarium for the treatment of venous stenosis in failing dialysis access.

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