

# Endovascular Treatment of Haemodialysis Arteriovenous Fistula with Drug-Coated Balloon Angioplasty: A Single-Centre Study

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Received: 20 November 2017 / Accepted: 18 March 2018 / Published online: 26 March 2018

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## Abstract

**Purpose** To evaluate the effect of percutaneous transluminal angioplasty (PTA) on haemodialysis fistulas utilising drug-coated balloons with plain balloon vessel preparation (DCB).

**Materials and Methods** In the study group, 31 patients (16 men; mean age  $62.8 \pm 17.2$  years) with failing arteriovenous fistulas were treated, with DCB, and compared with a control group (31 patients; 15 men; mean age  $67.0 \pm 8.44$  years), in which only plain balloon PTA was performed. All stenoses were dilated with regular PTA balloons. After achieving haemodynamic success ( $< 30\%$  residual stenosis), drug-coated balloons were used for drug administration in the study group. The follow-up intervals were 6, 12 and 24 months. Target lesion primary patency, primary assisted patency and secondary patency were compared. The statistical significance was set at 0.05.

**Results** Target lesion primary patency was compared in both groups and was significantly higher in the study group (DCB) at 6 months (90.3 vs. 61.3%;  $p = 0.016$ ), 12 months (77.4 vs. 29%;  $p = 0.0004$ ) as well as 24 months (45.2 vs. 16.1%;  $p = 0.026$ ). Kaplan–Meier survival curves also showed a significant difference for target lesion primary

patency (534.2 vs. 315.7 days;  $p = 0.0004$ ). There were no significant differences in target lesion primary assisted patency and in secondary patency. However, only 38.7% of patients in the study group were treated twice or more versus 80.6% in the control group ( $p = 0.002$ ).

**Conclusion** DCB increases target lesion primary patency during the first 24 months and decreases the rate of reinterventions.

**Keywords** Haemodialysis fistula · Percutaneous transluminal angioplasty · Drug-coated balloon · Vessel preparation · Paclitaxel

## Introduction

The end-stage renal disease is a major healthcare problem [1–3]. In our country, 65% of the patients undergoing renal replacement therapy are treated with haemodialysis, 2.5% by peritoneal dialysis and 32.5% have a functioning kidney graft [4]. A major cause of hospitalisation in the haemodialysis population is vascular access dysfunction, due to stenosis at the anastomotic site of the arteriovenous fistula (AVF), with an almost 50% failure rate after 3–7 years [5–11]. Punctures during haemodialysis and other vascular manipulations damage endothelial and smooth muscle cells and lead to progenitor cell activation, resulting in neointimal hyperplasia [12]. Additional factors that promote neointimal hyperplasia are a combination of venous anatomy and physiology and pre-existing endothelial dysfunction in uraemic patients [13–15]. Plain

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balloon percutaneous transluminal angioplasty (PB) has become an established method of treating AVF dysfunction [2]. However, a major drawback of PB is poor midterm to long-term results, and secondary patency is prolonged only with multiple reinterventions [2, 3, 10, 16]. Neointimal hyperplasia can be influenced by paclitaxel application [16–19]. Recent studies have shown beneficial effects of drug-coated balloon percutaneous transluminal angioplasty (PTA) on neointimal hyperplasia inhibition in haemodialysis AVFs [3, 16, 18]. We used vessel preparation in the study group, as in our opinion, good vessel preparation with a plain balloon, defined as less than 30% residual stenosis, before drug-coated balloon inflation (i.e. drug-coated balloon PTA with plain balloon vessel preparation—DCB), could further improve target lesion primary patency, leading to decreased rates of reinterventions. Therefore, our study aimed to compare the effect of DCB with PB of AVF in haemodialysis patients. Our aim was also to assess the effect of vessel preparation by comparing our results with published data.

## Materials and Methods

### Study Design

The National Medical Ethics Committee approved this single-centre study. Thirty-one consecutive patients (16 men; mean age  $62.8 \pm 17.2$  years) on chronic haemodialysis therapy were included in the study group and were treated with DCB. Owing to a limited number of patients, the control group represented patients treated at our institution between 2006 and 2011 with PB. In the control group, the last 31 consecutive patients treated in this period were included (15 men; mean age  $67.03 \pm 8.44$  years). Inclusion criteria were signed informed consent, aged over 18 years and angiographically or ultrasonographically documented haemodynamically significant stenosis of the AVF, defined as at least 50% reduction in the diameter of the AVF in comparison with the most proximal non-aneurismatic venous part of the AVF [20]. Exclusion criteria were the presence of an active malignancy, pregnancy, known hypersensitivity to iodine contrast agent or lidocaine and abnormal coagulation parameters ( $\text{INR} > 1.5$ ).

The follow-up intervals were 6 months, 1 year and 2 years. Main objectives were to evaluate target lesion primary patency, target lesion primary assisted patency and target lesion secondary patency in both groups. Primary patency is defined as an absence of restenosis during follow-up [21]. Primary assisted patency is defined as patency after endovascular reintervention in case of symptomatic restenosis [21]. Secondary patency is patency between

initial intervention and the moment when AVF is surgically retreated or abandoned or the time of patency measurement [21, 22].

### Procedure

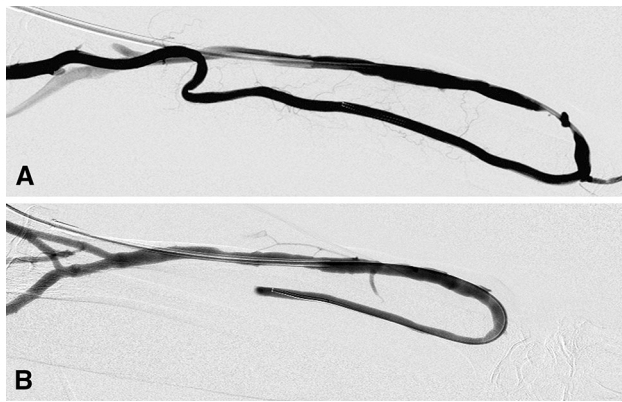
All procedures were performed on mature fistulas [6, 23]. Current guidelines recommend at least 1 month of maturation of AVF, more preferably 2–3 months [23–28]. A longer maturation period is associated with a lower rate of failure of the newly created fistula [29].

A Seldinger technique with a retrograde venous puncture and local subcutaneous anaesthesia (2–3 ml of 1% lidocaine) was used. Vascular access was secured with a 0.035-in. stiff hydrophilic guidewire (Terumo, Tokyo, Japan) and a 6 French (Fr) sheath, and a digital subtraction angiography was performed. Three-thousand i.u. of heparin were administered through the sheath, and the lesion was crossed with routinely used guidewires and catheters.

In the control group, standard PTA balloon catheters [Admiral Xtreme balloon catheters (Medtronic, Minneapolis, USA) and Reef HP balloon catheters (Medtronic, Minneapolis, USA)] with nominal pressures between 6 and 22 Bar were used. The diameter of the plain balloon was equal to the diameter of the most proximal non-aneurismatic venous part of the AVF, whereas the length of the balloon was equal to the length of the stenosis. In the control group, after achieving haemodynamic success (less than 30% residual stenosis), the procedure was finished [30].

In the study group, standard PTA balloon catheters were used first for vessel preparation in the same manner as plain balloons in the control group. After achieving a haemodynamic success, drug-coated balloons [IN.PACT Admiral balloon catheters (Medtronic, Minneapolis, USA)] were used according to the manufacturer protocol, for drug administration. According to the protocol, the length of the DCB should be 1 cm longer than the stenosis to avoid a geographic miss, and the duration of the inflation should be 3 min at recommended nominal pressures [31, 32]. The diameter of the DCB was 1 mm larger than a previously used plain balloon, to ensure proper contact with the vessel wall [33].

After the procedure, control fistulography was performed in two orthogonal planes, to evaluate the results and to exclude any other concurrent stenosis (Fig. 1). Daily anti-platelet therapy with clopidogrel (75 mg/day, 3 months) and acetylsalicylic acid (100 mg/day, lifelong) was prescribed in both groups.



**Fig. 1** **A** Angiographic image of juxta-anastomotic stenosis before the procedure. **B** Control angiography after drug-coated balloon percutaneous transluminal angioplasty with plain balloon vessel preparation

### Follow-Up

A day after the procedure, a duplex ultrasound was performed. Afterwards, clinical control was performed during regular haemodialysis with dynamic venous pressure and flow rate measurements followed by a control duplex ultrasound examination, in case of pathological findings. Angiography and reintervention were performed in case of haemodynamically significant restenosis. The definition of restenosis was identical to the definition of stenosis described in the inclusion criteria.

In cases where no reinterventions were needed, target lesion primary patency was monitored. If the reintervention was endovascular, we monitored target lesion primary assisted patency. In case of thrombosis of the AVF, a surgical reintervention was performed, and the new AVF was considered a final endpoint. Other possible endpoints were a functioning AVF throughout the observation period, transplantation and death of the patient. The period between the initial PTA and the endpoint was secondary patency.

### Statistical Analysis

Basic patient demographics and details of the dialysis access circuits are presented in a tabular manner. We use frequencies and percentages for descriptive nominal variables. For numerical variables, in the case of normal data distribution, the central tendency and variability, arithmetic mean, standard deviation and minimum and maximum are shown. In case of asymmetric data distribution, median, interquartile range (between 25 and 75 percentiles) and minimum and maximum are displayed. For numerical variables that are normally distributed, *t* test of independent samples was used. For variables that are not normally

distributed, we used Mann–Whitney *U* test. For nominally distributed variables, Chi-square test or Fisher's exact test was employed. Target lesion primary and secondary patency was compared using the zero hypothesis, which states the patency times in both groups are the same. Analysis of the patency time of the haemodialysis fistula was made according to the Kaplan–Meier survival curve. The Kaplan–Meier survival curves were compared using the log-rank (Mantel–Cox) test, with a hazard ratio and a 95% confidence interval (CI) reported. The statistical significance was determined at  $p < 0.05$ . Statistical analysis was performed using IBM SPSS Statistics Software.

### Results

There were no statistically significant differences in baseline patient demographics (Table 1). We observed a statistically significant difference in median age of the AVF in the study group (DCB) 255 (178–465) days versus 609 (294–991) days in the control group (PB) ( $p = 0.01$ ) (Table 1). Treated lesion median length [40 (40–80) mm in the DCB group vs. 40 (40–60) mm in the PB group,  $p = 0.37$ ] and other details of the dialysis access circuit did not show any statistically significant differences (Table 1). Technical success was 100% in both groups.

All patients have completed the 6-month follow-up assessment. At 12 months, one patient in the DCB group died because of a cardiac arrest. At 24 months, three more patients died (two patients had cardiac arrest and one died because of lymphoma) in the DCB group, one patient had kidney transplantation, and one patient ended up in surgery (for new fistula creation), because of AVF thrombosis. In the PB group, two patients were dead at 24-month follow-up. Both died because of a cardiac arrest. Two more patients had AVF thrombosis and underwent surgery. We believe that none of these events were related to DCB.

The target lesion primary patency at 6 months was significantly higher in the DCB group 90.3 versus 61.3% in the PB group ( $p = 0.016$ ), 12 months (77.4% in the DCB group vs. 29% in the PB group,  $p = 0.0004$ ) and 24 months (45.2% in the DCB group vs. 16.1% in the PB group,  $p = 0.026$ ) (Table 2). Kaplan–Meier survival curves also showed the statistically significant difference between the DCB and PB groups (log-rank test  $p = 0.0004$ ). Mean primary patency in the DCB group was 534.2 days (SE 36.4; 95% CI 462.8–605.6) and in the PB group was 315.7 days (SE 38.3; 95% CI 240.65–390.8) (Fig. 2).

In target lesion secondary patency, no statistically significant differences were observed between the DCB and PB groups at 6 months (100% in the DCB group vs. 100% in the PB group,  $p = 1$ ), 12 months (96.8% in the DCB group vs. 100% in the PB group,  $p = 1$ ) and 24 months

**Table 1** Baseline patient demographics and details of the dialysis access circuits

	DCB (n = 31)	PB (n = 31)	p
Mean age (years)	62.81 ± 17.2	67.03 ± 8.44	0.22
Male gender	16 (51.6%)	15 (48.4%)	1
Hypertension	18 (58.1%)	26 (83.9%)	0.5
Hyperlipidaemia	5 (16.1%)	7 (22.6%)	0.75
Diabetes mellitus	13 (41.9%)	12 (38.7%)	1
Smoking	8 (25.8%)	5 (16.1%)	0.53
AVF median age (days)	255 (178–465)	609 (294–991)	0.013
Radiocephalic fistula	17 (54.8%)	20 (62.5%)	0.6
Brachiocephalic fistula	12 (38.7%)	8 (25.8%)	0.4
Brachiobasilic fistula	2 (6.6%)	3 (9.7%)	1
Juxta-anastomotic stenosis	30 (96.8%)	29 (93.5%)	1
Arterial stenosis	0 (0%)	1 (3.2%)	1
Anastomotic stenosis	1 (3.2%)	1 (3.2%)	1
Stenosis median length (mm)	40 (40–80)	40 (40–60)	0.37
Technical success	31 (100%)	31 (100%)	1
Previous EVT of the ipsilateral AVF	0 (0%)	0 (0%)	1

Continuous data are presented as mean ± standard deviation; categorical data are given as counts and percentages in parentheses. For AVF age and stenosis length, asymmetric data distribution was observed, median and interquartile range (between 25 and 75 percentile) are presented

DCB drug-coated balloons with plain balloon vessel preparation percutaneous transluminal angioplasty, PB plain balloon percutaneous transluminal angioplasty, EVT endovascular therapy, AVF arteriovenous fistula

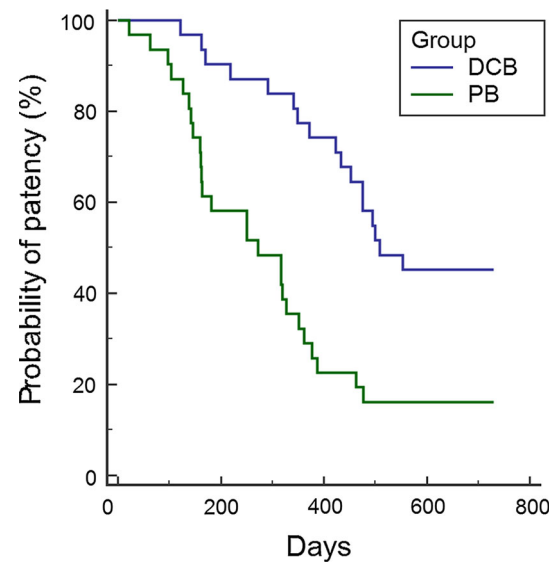
**Table 2** Target lesion primary patency and target lesion secondary patency in DCB and PB group at 6 months, 1 year and 2 years and target lesion primary assisted patency in DCB and PB group at 6 months and 1 year

	DCB (n = 31)	PB (n = 31)	p
Target lesion primary patency			
6 months	28 (90.3%)	19 (61.3%)	0.016
1 year	24 (77.4%)	9 (29%)	0.000
2 years	14 (45.2%)	5 (16.1%)	0.026
Target lesion secondary patency			
6 months	31 (100%)	31 (100%)	1
1 year	30 (96.8%)	31 (100%)	1
2 years	25 (80.6%)	27 (87.1%)	0.731
<hr/>			
	DCB (n = 18)	PB (n = 40)	
Target lesion primary assisted patency			
6 months	11 (61%)	26 (65%)	0.771
1 year	6 (33%)	14 (35%)	0.883

Data are given as counts and percentages in parentheses

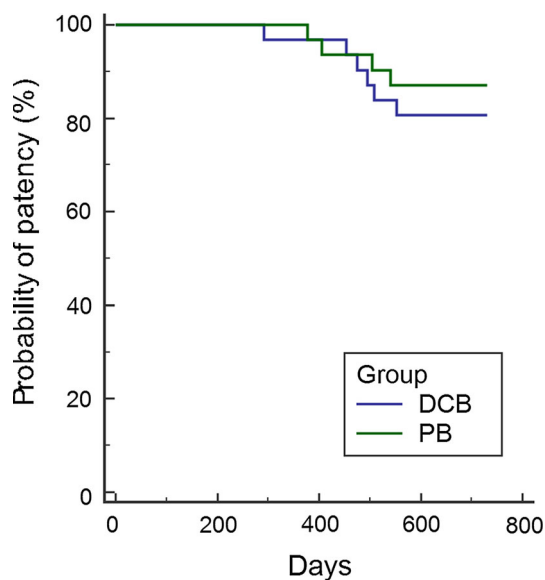
DCB drug-coated balloons with plain balloon vessel preparation percutaneous transluminal angioplasty, PB plain balloon percutaneous transluminal angioplasty

(80.6% in the DCB group vs. 87.1% in the PB group, p = 0.731) (Table 2). Also, the Kaplan–Meier survival curves did not show any significant difference between



**Fig. 2** Kaplan–Meier survival curves for target lesion primary patency showed statistically significant difference between both groups; mean primary patency in the DCB group was 534.2 days (SE 36.4; 95% CI 462.8–605.6) and in the PB group was 315.7 days (SE 38.3; 95% CI 240.65–390.8); log-rank test p = 0.0004

both groups (log-rank test p = 0.501). Mean secondary patency in the DCB group was 678.19 days (SE 20.08; 95% CI 638.83–717.55) and in the PB group was 694.71 days (SE 17.03; 95% CI 661.32–728.09) (Fig. 3).

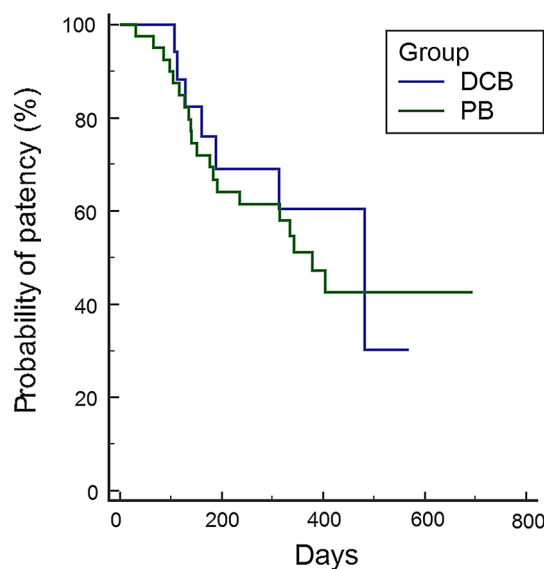


**Fig. 3** Kaplan–Meier survival curves for target lesion secondary patency did not show any significant difference between both groups; mean secondary patency in DCB group was 678.19 days (SE 20.08; 95% CI 638.83–717.55) and in PB group 694.71 days (SE 17.03; 95% CI 661.32–728.09); log-rank test  $p = 0.501$

No statistically significant differences were observed in target lesion primary assisted patency between the DCB and PB groups at 6 months (61% in the DCB group vs. 65% in the PB group,  $p = 0.771$ ) and 12 months (33% in the DCB group vs. 35% in the PB group,  $p = 0.883$ ) (Table 2). In the DCB group, 18 procedures were performed. In comparison, 40 procedures were performed in the PB group. The Kaplan–Meier survival curves also did not show any significant difference between both groups (log-rank test  $p = 0.63$ ). Mean primary assisted patency in the DCB group was 387.919 days (SE 48.36; 95% CI 293.11–482.27) and in the PB group was 414.237 days (SE 43.30; 95% CI 329.36–499.11) (Fig. 4). However, only 12 (38.7%) patients in the DCB group were treated twice or more during the follow-up. In the PB group, 25 (80.6%) patients were treated twice or more. The difference was statistically significant ( $p = 0.002$ ).

## Discussion

The results of our study indicate that DCB could be a promising approach to the clinical problem of AVF dysfunction, especially in decreasing the rate of reinterventions. The results of the DCB group in our study are in accordance with Patane et al. [3] where vessel preparation was also used. Vessel preparation is a new concept in the endovascular treatment of stenosis with DCB [34]. It seems to be one of the major factors in drug-coated balloon PTA.



**Fig. 4** Kaplan–Meier survival curves for target lesion primary assisted patency did not show any significant difference between both groups; mean primary assisted patency in DCB group was 387.919 days (SE 48.36; 95% CI 293.11–482.27) and in PB group 414.237 days (SE 43.30; 95% CI 329.36–499.11); log-rank test  $p = 0.63$

It causes fractures and fissures in the vessel wall as well as the formation of a homogeneous surface, which allows the DCB better contact with the vessel wall [35, 36]. Vessel preparation also reduces the loss of drug when passing the stenosis and, probably even more importantly, improves paclitaxel transfer to the vessel wall, and finally, the absorption of the drug [11, 31, 37, 38].

Because of the lack of the drug-coated balloon PTA control group without vessel preparation, we compared our results with published data. The first studies of the effect of paclitaxel on neointimal hyperplasia inhibition in AVF were performed by Katsanos et al. [2] and Kitrou et al. [18]. Plain balloon post-dilatation was performed if angiographic success was not achieved during drug-coated balloon PTA. Target lesion primary patency at 1 year was 35% in the drug-coated balloon PTA group versus 5% in the plain balloon group ( $p = 0.001$ ). Median primary patency according to Kaplan–Meier survival curves was 233.6 days in the drug-coated balloon PTA group versus 131.4 days in the plain balloon group ( $p = 0.0004$ ) [18]. Lai et al. [5] presented comparable results using a similar method. The DCB used in our study was similar (Lai et al.) or the same as in the studies of Katsanos and Kitrou et al. They are coated with FreePac compound, which contains hydrophilic urea [2]. This compound optimises the transfer of lipophilic paclitaxel to endothelial cells when the balloon is in contact with the vessel wall [2]. The paclitaxel dose is 3.0 mg/mm<sup>2</sup> at the surface of the balloon [2].

Our results, consistent with published data, indicate that DCB significantly increases target lesion primary patency during the first 24 months. Interestingly, with regard to target lesion secondary patency, no statistically significant differences were observed between the DCB and PB groups, which could be attributed to relatively short follow-up period.

Also, there were no statistically significant differences in target lesion primary assisted patency between the DCB and PB groups. However, in the DCB group, fewer reinterventions were needed to prolong target lesion secondary patency, which could possibly be explained by some genetic polymorphisms. Tubulin polymorphisms were shown to be capable of conferring resistance to paclitaxel in humans, suggesting that these differences could contribute to variability in patient response to anti-mitotic drugs [39].

### Study Limitations

One of the main limitations of our study is a retrospective data collection for the PB group. Another important limitation is the lack of a drug-coated balloon PTA without vessel preparation control group. At the time we started using the drug-coated balloons, we almost immediately started performing the vessel preparation. Therefore, we could compare the results only with the PB method (performed at our institution in previous years). However, we could compare our results with published drug-coated balloon PTA data. We are aware that a more systemic review of published data would be appropriate; however, in our opinion, it exceeds the scope of the manuscript.

Another limitation was the statistically significant difference in median age of the AVF between the groups, which could be explained by a different surgical technique leading to differences in haemodynamic stress in the AVF anastomosis area. However, in both groups, AVFs were mature according to current guidelines [6, 23]. Furthermore, as published data suggest, the age of the AVF is not a confounding factor for primary and secondary patency of AVF [40].

A potential study limitation could be that in the study group a twofold dilatation was used. In some studies, twofold, prolonged dilatation was used, to achieve the haemodynamic success, and the data presented do not show any statistically significant differences in the prolongation of the patency [41]. Also, the larger size and diameter of the DCB and longer inflation time in the study group could be argued. As already described, the inflation protocol for the DCB group was in accordance with the manufacturer protocol. This protocol was also used in the IN.PACT SFA randomised trial [33]. Studies have shown that with prolonged inflation time there are no differences in the amount

of intimal hyperplasia, medial wall thickening or lumen diameter compared with standard inflation times and that prolonged dilation does not result in superior long-term patency rates [41, 42]. The diameter of the DCB in our study was 1 mm larger than a previously used plain balloon, to ensure proper contact with the vessel wall [33]. Studies have shown that over-inflation of the vessel wall promotes neointimal hyperplasia, resulting in early stenosis [43]. So, the larger diameter of the DCB would promote neointimal hyperplasia, if the effect of paclitaxel would be negligible. Studies on porcine model support this statement by showing that paclitaxel prevents constrictive remodelling due to inhibition of intimal and media fibrosis [44].

### Conclusion

DCB is a promising approach to the clinical problem of AVF dysfunction, especially in prolonging primary patency and in decreasing the rate of re-procedures, indicating less invasiveness as well as the possible economic advantage of the method.

**Acknowledgements** This work was previously presented as an electronic poster (P-114) during CIRSE 2017 meeting in Copenhagen, September 16–20 and as oral scientific presentation (B-0864) during the European Congress of Radiology (ECR) 2018 in Vienna, February 28–March 4.

### Compliance with Ethical Standards

**Conflict of interest** The authors declare that there are no conflicts of interests.

**Ethical Approval** The authors declare that all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** The authors declare that informed consent was obtained from all individual participants included in the study.

### References

1. Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv.* 2010;3(1):1–11.
2. Katsanos K, Karnabatidis D, Kitrou P, Spiliopoulos S, Christeas N, Siablis D. 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. *J Endovasc Ther.* 2012;19(2):263–72.
3. Patane D, Giuffrida S, Morale W, L'Anfusa G, Puliatti D, Bisceglie P, et al. Drug-eluting balloon for the treatment of failing hemodialytic radiocephalic arteriovenous fistulas: our experience in the treatment of juxta-anastomotic stenoses. *J Vasc Access.* 2014;15(5):338–43.

4. Buturovic-Ponikvar J, Gubensek J, Arnol M, Adamlje T, Cegljar Z, Damevska G, et al. Renal replacement therapy in Slovenia: excerpts from 2013 data. *Ther Apher Dial.* 2016;20(3):223–8.
5. Asif A, Gadalean FN, Merrill D, Cherla G, Cipleu CD, Epstein DL, et al. Inflow stenosis in arteriovenous fistulas and grafts: a multicenter, prospective study. *Kidney Int.* 2005;67(5):1986–92.
6. Daugirdas JT, Depner TA, Inrig J, Mehrotra R, Rocco MV, Suri RS, et al. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis.* 2015;66(5):884–930.
7. Feldman HI, Kobrin S, Wasserstein A. Hemodialysis vascular access morbidity. *J Am Soc Nephrol JASN.* 1996;7(4):523–35.
8. Huber TS, Carter JW, Carter RL, Seeger JM. Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous hemodialysis accesses a systematic review. *J Vasc Surg.* 2003;38(5):1005–11.
9. Long B, Brichart N, Lermusiaux P, Turmel-Rodrigues L, Artru B, Boutin JM, et al. Management of perianastomotic stenosis of direct wrist autogenous radial-cephalic arteriovenous accesses for dialysis. *J Vasc Surg.* 2011;53(1):108–14.
10. Malka KT, Flahive J, Cszinszky A, Aiello F, Simons JP, Schanzer A, et al. Results of repeated percutaneous interventions on failing arteriovenous fistulas and grafts and factors affecting outcomes. *J Vasc Surg.* 2016;63(3):772–7.
11. Roy-Chaudhury P, Sukhatme VP, Cheung AK. Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint. *J Am Soc Nephrol JASN.* 2006;17(4):1112–27.
12. Caplice NM, Wang S, Tracz M, Croatt AJ, Grande JP, Katusic ZS, et al. Neoangiogenesis and the presence of progenitor cells in the venous limb of an arteriovenous fistula in the rat. *Am J Physiol Renal Physiol.* 2007;293(2):F470–5.
13. Asif A, Lenz O, Merrill D, Cherla G, Cipleu CD, Ellis R, et al. Percutaneous management of perianastomotic stenosis in arteriovenous fistulae: results of a prospective study. *Kidney Int.* 2006;69(10):1904–9.
14. Croatt AJ, Grande JP, Hernandez MC, Ackerman AW, Katusic ZS, Nath KA. Characterization of a model of an arteriovenous fistula in the rat: the effect of L-NAME. *Am J Pathol.* 2010;176(5):2530–41.
15. Mezzano D, Pais EO, Aranda E, Panes O, Downey P, Ortiz M, et al. Inflammation, not hyperhomocysteinemia, is related to oxidative stress and hemostatic and endothelial dysfunction in uremia. *Kidney Int.* 2001;60(5):1844–50.
16. Lai CC, Fang HC, Tseng CJ, Liu CP, Mar GY. Percutaneous angioplasty using a paclitaxel-coated balloon improves target lesion restenosis on inflow lesions of autogenous radiocephalic fistulas: a pilot study. *J Vasc Interv Radiol JVIR.* 2014;25(4):535–41.
17. Baek I, Hwang J, Park J, Kim H, Park JS, Kim DJ. Paclitaxel coating on the terminal portion of hemodialysis grafts effectively suppresses neointimal hyperplasia in a porcine model. *J Vasc Surg.* 2015;61(6):1575–82.e1.
18. Kitrou PM, Katsanos K, Spiliopoulos S, Karnabatidis D, Siablis D. Drug-eluting versus plain balloon angioplasty for the treatment of failing dialysis access: final results and cost-effectiveness analysis from a prospective randomized controlled trial (NCT01174472). *Eur J Radiol.* 2015;84(3):418–23.
19. Portugaller RH, Kalmar PI, Deutschmann H. The eternal tale of dialysis access vessels and restenosis: are drug-eluting balloons the solution? *J Vasc Access.* 2014;15(6):439–47.
20. Mortamais J, Papillard M, Girouin N, Boutier R, Cougnaud L, Martin X, et al. Endovascular treatment of juxta-anastomotic venous stenoses of forearm radiocephalic fistulas: long-term results and prognostic factors. *J Vasc Interv Radiol JVIR.* 2013;24(4):558–64 (**quiz 65**).
21. Zeller T. Current state of endovascular treatment of femoropopliteal artery disease. *Vasc Med (London, England).* 2007;12(3):223–34.
22. Sidawy AN, Gray R, Besarab A, Henry M, Ascher E, Silva M Jr, et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses. *J Vasc Surg.* 2002;35(3):603–10.
23. Owens CD, Wake N, Kim JM, Hentschel D, Conte MS, Schanzer A. Endothelial function predicts positive arterial-venous fistula remodeling in subjects with stage IV and V chronic kidney disease. *J Vasc Access.* 2010;11(4):329–34.
24. III. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: update 2000. *Am J Kidney Dis.* 2001;37(1 Suppl 1):S137–81.
25. Baker LD Jr, Johnson JM, Goldfarb D. Expanded polytetrafluoroethylene (PTFE) subcutaneous arteriovenous conduit: an improved vascular access for chronic hemodialysis. *Trans Am Soc Artif Intern Organs.* 1976;22:382–7.
26. Ravani P, Brunori G, Mandolfo S, Cancarini G, Imbasciati E, Marcelli D, et al. Cardiovascular comorbidity and late referral impact arteriovenous fistula survival: a prospective multicenter study. *J Am Soc Nephrol JASN.* 2004;15(1):204–9.
27. Rayner HC, Pisoni RL, Gillespie BW, Goodkin DA, Akiba T, Akizawa T, et al. Creation, cannulation and survival of arteriovenous fistulae: data from the Dialysis Outcomes and Practice Patterns Study. *Kidney Int.* 2003;63(1):323–30.
28. Saran R, Dykstra DM, Pisoni RL, Akiba T, Akizawa T, Canaud B, et al. Timing of first cannulation and vascular access failure in haemodialysis: an analysis of practice patterns at dialysis facilities in the DOPPS. *Nephrol Dial Transpl.* 2004;19:2334–40.
29. Brunori G, Ravani P, Mandolfo S, Imbasciati E, Malberti F, Cancarini G. Fistula maturation: doesn't time matter at all? *Nephrol Dial Transpl.* 2005;20(4):684–7.
30. Wang N, Fulcher J, Abeyuriya N, Adams M, Lal S. Predictors of successful chronic total occlusion percutaneous coronary interventions: a systematic review and meta-analysis. *Heart.* 2018;104(6):517–24.
31. Kleber FX, Mathey DG, Rittger H, Scheller B. How to use the drug-eluting balloon: recommendations by the German consensus group. *EuroIntervention.* 2011;7(Suppl K):K125–8.
32. Posa A, Hemetsberger R, Petnehazy O, Petrasi Z, Testor M, Glogar D, et al. Attainment of local drug delivery with paclitaxel-eluting balloon in porcine coronary arteries. *Coron Artery Dis.* 2008;19(4):243–7.
33. Tepe G, Laird J, Schneider P, Brodmann M, Krishnan P, Micari A, et al. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. *Circulation.* 2015;131(5):495–502.
34. Herten M, Torsello GB, Schönefeld E, Stahlhoff S. Critical appraisal of paclitaxel balloon angioplasty for femoral–popliteal arterial disease. *Vasc Health Risk Manag.* 2016;12:341–56.
35. Marzullo RAA, Biondi-Zoccai G, et al. Drug-eluting balloon technology. *Card Interv Today.* 2011;2011:40–9.
36. Bountouris I, Kristmundsson T, Dias N, Zdanowski Z, Malina M. Is repeat PTA of a failing hemodialysis fistula durable? *Int J Vasc Med.* 2014;2014:6.
37. Speck U, Scheller B, Hamm B. Drug-coated balloons for restenosis prophylaxis. *RoFo : Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin.* 2014;186(4):348–58.
38. Scheller B, Speck U, Abramjuk C, Bernhardt U, Bohm M, Nickenig G. Paclitaxel balloon coating, a novel method for prevention and therapy of restenosis. *Circulation.* 2004;110(7):810–4.
39. Yin S, Bhattacharya R, Cabral F. Human mutations that confer paclitaxel resistance. *Mol Cancer Ther.* 2010;9(2):327.

40. Sugimoto K, Higashino T, Kuwata Y, Imanaka K, Hirota S, Sugimura K. Percutaneous transluminal angioplasty of malfunctioning Brescia-Cimino arteriovenous fistula: analysis of factors adversely affecting long-term patency. *Eur Radiol.* 2003;13(7):1615–9.
41. Soder HK, Manninen HI, Rasanen HT, Kaukanen E, Jaakkola P, Matsi PJ. Failure of prolonged dilation to improve long-term patency of femoropopliteal artery angioplasty: results of a prospective trial. *J Vasc Interv Radiol JVIR.* 2002;13(4):361–9.
42. Lantis JC II, Boone D. Standard versus prolonged inflation time in balloon angioplasty of atherosclerotic rat aortas. *J Vasc Surg.* 2011;54(3):925.
43. Humphrey WR, Simmons CA, Toombs CF, Shebuski RJ. Induction of neointimal hyperplasia by coronary angioplasty balloon overinflation: comparison of feeder pigs to Yucatan minipigs. *Am Heart J.* 1994;127(1):20–31.
44. Pavo N, Samaha E, Sabyusheva I, von Strandmann RP, Stahnke S, Plass CA, et al. Coating of intravascular balloon with paclitaxel prevents constrictive remodeling of the dilated porcine femoral artery due to inhibition of intimal and media fibrosis. *J Mater Sci Mater Med.* 2016;27:131.