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# Paclitaxel coated-balloon (PCB) versus standard plain old balloon (POB) fistuloplasty for failing dialysis access

**AG Karmota**

Faculty of Medicine, Kasr Alainy – Cairo University Hospitals, Cairo, Egypt

**ABSTRACT**

INTRODUCTION This study aimed to evaluate the safety and efficacy of paclitaxel-coated balloon compared with conventional plain balloon for the treatment of failing native dialysis access.

MATERIALS AND METHODS This prospective study included 60 patients presenting to the Kasr Alainy Hospitals and Aseer Central Hospital in the period from September 2015 to December 2017 with failing native vascular access. Dilatation with a plain balloon was done in 30 patients (group I) and with a paclitaxel-coated balloon in 30 patients (group II) with either stenosis or occlusion. The majority were outflow lesions, with 20 (66.7 %) patients in group I and 21 (70%) patients in group II. Mean balloon diameter was 7.1mm (± 1.5mm) compared with 6.5mm (± 1.2mm) and length 66mm (± 19.1mm) compared with 54.6mm (± 15.7mm), respectively. Safety endpoint was reported as 30 day's freedom from procedure-related major complications and mortality. Procedural technical success was defined as a residual diameter 30% or less for treated lesions. Target lesion primary patency, circuit primary patency and secondary patency were reported at 3, 6 and 12 months.

RESULTS There were no 30-day procedure-related major complications or mortality in either group. Procedural technical success of 100% was achieved in both groups. Target lesion primary patency, circuit primary patency and secondary patency in group II were better than in group I, especially at 12 months (90% vs 66.7%, 83.3% vs 60% and 96.7% vs 93.3%, respectively). There was a statistically significant difference in target lesion primary patency ($p = 0.029$) in patients who were treated with paclitaxel-coated balloon angioplasties.

CONCLUSION The paclitaxel-coated balloon proved to be safe and effective, and improved the patency of failing vascular access. Results are comparable with previous studies.

**KEYWORDS**

Paclitaxel – Balloon fistuloplasty – Failing – Vascular access

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**CORRESPONDENCE TO**

**Ahmed Karmota**, E: ahmedgamil_25@hotmail.com

## Introduction

The most common problem following the creation of arteriovenous fistula is access stenosis with the sequelae of progression to total occlusion and dysfunction of function of dialysis access.[1] Dysfunction of the dialysis circuit is an important cause of mortality and morbidity in patients with renal failure and can eventually end with loss of access for dialysis.[2] One of the documented techniques for saving failing dialysis access is plain balloon angioplasty of significantly stenotic lesions.[3] Although balloon angioplasty is the cornerstone management for vascular access lesions as it is a less invasive percutaneous procedure and because of its widespread availability. The venous physiology and anatomy with the endothelial dysfunction of patients with end-stage renal disease generally leads to poor mid- and long-term results that need repeated balloon dilatation in the same circuit.[3] Theoretically, patency of the dialysis access may be maintained by a technology that prevents negative vessel wall remodelling and inhibits fibromuscular hyperplasia formation following standard balloon angioplasty. One of these methods is the use of angioplasty with paclitaxel-coated balloons, which are known to effectively inhibit neointimal hyperplasia and decrease vascular re-stenosis following balloon dilatation.[4] Immediate alternative management for treating elastic recoil is bare-metal stenting.[5] Stent grafts are considered as a good option for the treatment of venous juxta-anastomotic stenosis in recent years, with significantly improved results compared with balloon dilatation and patency rates as high as 26.9% at two years.[6] they are preserved for lesions at arteriovenous graft venous anastomotic stenosis only, or outflow veins and as a bailout choice within the circuit due to scaffolding and metallic mesh left behind.[7] Various paclitaxel-coated balloons have been tested for their safety and efficacy.

Results suggest that paclitaxel-coated balloons might have a role against re-stenosis in dialysis access. The results from two randomised controlled trials using paclitaxel-coated balloons in the treatment of venous stenosis in failing arteriovenous fistula were significant with paclitaxel-coated balloons at six months and one year,[8] while Lai *et al* had significantly improved results in favour of paclitaxel-coated balloons in their study at six months but not at one year.[17]

## Patients and methods

This prospective study included 60 patients with end-stage renal diseases who presented to the Kasr Alainy Hospitals Cairo University and Aseer Central Hospital with failing arteriovenous access to assess the immediate and long-term outcomes of drug-coated balloons compared with conventional plain balloons in failing access for dialysis treatment in a prospective study with blinded randomisation of one to one in each group. The original procedure was radiocephalic, brachiocephalic or brachiobasilic, and was performed in our hospitals and other centres. All operative data were documented. Dilatation with a standard plain balloon was done in 30 patients (group I) while percutaneous transluminal angioplasty and post-dilation with a paclitaxel-coated balloon were done in 30 patients (group II).

## Selection criteria

Inclusion criteria:

- Arteriovenous fistula in the upper limb.
- Clinical signs of failing access for dialysis due to presence of a high-grade stenosis (high venous pressure during dialysis, loss of thrill or bruit, increased bleeding with prolonged haemostasis after dialysis, decreased blood flow along the dialysis circuit, pulsatility, upper limb swelling, difficult puncture, blood clot and/or recirculation).
- Angiographically significant stenosis greater than 50% either inflow perianastomotic (at or within 2–3cm from anastomosis) or in the venous outflow (cannulation site, cephalic arch, proximal swing point or axillary vein).

Exclusion criteria:

- Haemodynamically significant central venous lesions (subclavian, innominate or superior vena cava lesions).
- Arteriovenous synthetic graft.
- Synchronous venous lesions in the same access circuit.
- Recent access thrombosis.
- Allergy or contraindication to heparin, iodinated contrast or paclitaxel.

## Preprocedural evaluation

Each patient was evaluated for epidemiological features: age, sex, smoking and comorbidity (diabetes, hyperlipidaemia, hypertension, asthma, cardiac, cerebrovascular and peripheral vascular diseases); clinical presentation: radial pulse, vein palpation as regards pulsation, thrill, bruit, upper limb swelling with venous hypertension, presence of blood clot or bleeding with prolonged haemostasis after dialysis, decreased flow of the blood along the dialysis circuit, difficult puncture and/or recirculation.

## Imaging

Patients were evaluated with duplex ultrasound to diagnose the presence of significant lesions and fistulogram was taken during the procedure to confirm the diagnosis. Significant stenosis was diagnosed if peak systolic velocity more than 375cm/second or stenosis more than 50% with B-mode ultrasound or during the fistulogram.

All interventions were done following the ethical standards of the institutional research. The procedure, possible complications, benefits and other alternative interventions were all explained to the patients and an informed consent was signed before the procedure.

## Procedure

All procedures were performed in the angiosuite under local anaesthesia. Antegrade or retrograde transvenous access was used according to the site of stenosis according to preprocedural ultrasound. A 5F or 6F introducer sheath was inserted. Intravenous heparin (5000iu) was given and a fistulogram imaged the conduit. In group I, 10 (33.3%) patients had perianastomotic inflow lesions and 20 (66.7%) patients had venous outflow lesions. In group II, 9 (30%) patients had perianastomotic inflow lesions and 21 (70%) patients had lesions at the venous outflow. Crossing of the lesion was done using 0.35 TERUMO GLIDEWIRE® guidewire and an angled vertebral or Bern catheter.

In group II, the lesion was predilated with an undersized balloon prior to inserting the standard balloon. Inflation time was 1–2 minutes and balloon diameters ranged from of 5mm to 9mm; balloon length ranged from 40mm to 100mm. In group II patients, the lesion was predilated with a traditional balloon to full effacement or stenosis less than 30% prior to paclitaxel-coated balloon angioplasty.

All cases were treated with a paclitaxel-coated balloon (Lutonix® 035, Bard Peripheral Vascular) with an inflation time of three minutes and balloon diameters ranging from 5mm to 9mm and balloon length ranging from 40mm to 100mm in both groups. We defined procedural technical success as residual stenosis less than 30% after the final fistulogram.

## Follow-up

Patients were discharged on antiplatelet therapy. Patients were followed monthly for signs of failing access and by ultrasound if needed. The safety endpoint was reported as 30 days' freedom from procedure-related major complications or mortality. Primary endpoints were target lesion primary patency rates, which were reported at 3, 6 and 12 months. Secondary endpoints included circuit primary patency rate and secondary patency rate, which were reported at 3, 6 and 12 months.

We defined target lesion primary patency as a patent lesion with no requirement for repeat intervention during the follow-up period. Loss of primary patency was reported with significant binary re-stenosis greater than 50%

needing further intervention at the target lesion or within 5mm distal or proximal to target lesion.

We defined access circuit primary patency as a patent access circuit (from arterial anastomosis to atriocaval junction) with no need for repeat interventions anywhere in the access circuit during the follow-up period.

Secondary patency was defined as a patent lesion and circuit with the need for repeat procedures to maintain patency after failure and thrombosis in the follow-up period.

## Results

### Demographics

The age of the patients in group I ranged from 31 to 81 years, with a mean age of 49.2 ± 11.5 years with 16 (53.3%) men and 14 (46.7%) women; in group II the ages ranged from 33 to 80 years, with a mean age of 54.7 ± 13.2 years with 13 (43.3%) men and 17 (56.7%) women (Table 1).

### Lesions

The present study found no statistically significant difference between two groups regarding the characteristics of the lesions (Table 2).

### Procedural technique

Antegrade or retrograde transvenous access was planned according to the site of the lesion from preprocedural ultrasound with balloon length covering the lesion with at least 5mm distal and proximal to it (Table 3).

### Follow-up

The safety endpoint was defined as 30 days free from procedure- or device-related mortality or major complications. These endpoints were achieved in both groups with no major complications or mortalities.

Procedural technical success was defined as a residual diameter of 30% or less for treated patients, which occurred in 100% of both groups. Target lesion primary patency, circuit primary patency and secondary patency were reported at 3, 6 and 12 months of follow-up (Table 4).

The 12-month outcomes in group II show that the incidence of re-stenosis was significantly lower than in group I ($p = 0.029$). At 12 months, the target lesion primary patency, circuit primary patency and secondary patency in group II were better than in group I (90% vs 66.7%; 83.3% vs 60%; and 96.7.% vs 93.3% respectively) showing the effect of paclitaxel in decreasing the occurrence of neointimal hyperplasia and re-stenosis in failing dialysis access.

### Statistical analysis

Statistical analysis was done using SPSS software, the results were analysis of paired T-test to compare quantitative values between the two groups. Results were given as mean plus or minus standard deviation. Cross tables (chi-square) were used to compare qualitative data between the two groups. In all tests, a $p$-value less than 0.05 was considered to indicate significance.

**Table 1** Demographics of the patients

| Characteristic | Group I | | Group II | | *p*-value |
|---|---|---|---|---|---|
| | (*n*) | (%) | (*n*) | (%) | |
| Age, years (mean ± SD) | 49.2 (± 11.5) | | 54.7 (± 13.2) | | 0.35 |
| Sex: | | | | | |
| Female | 14 | 46.7 | 17 | 56.7 | 0.30 |
| Male | 16 | 53.3 | 13 | 43.3 | |
| Comorbidities: | | | | | |
| Smoking | 8 | 26.7 | 9 | 30 | 0.50 |
| Diabetes | 15 | 50 | 19 | 63.3 | 0.21 |
| Hypertension | 17 | 56.7 | 15 | 50 | 0.38 |
| Hyperlipidaemia | 7 | 23.3 | 9 | 30 | 0.38 |
| IHD | 5 | 16.7 | 4 | 13.3 | 0.5 |
| RHD | 3 | 10 | 2 | 6.7 | 0.5 |
| Cardiovascular disease | 2 | 6.7 | 2 | 6.7 | 0.69 |
| PVD | 3 | 10 | 3 | 10 | 0.66 |
| Asthma | 3 | 10 | 2 | 6.7 | 0.5 |

**Table 2** Lesion characteristics

| Characteristic | Group I | | Group II | | *p*-value |
|---|---|---|---|---|---|
| | (*n*) | (%) | (*n*) | (%) | |
| Fistula type: | | | | | |
| Radiocephalic | 9 | 30 | 8 | 26.7 | 0.71 |
| Brachiocephalic | 14 | 46.7 | 17 | 56.6 | 0.71 |
| Bachiobasilic | 7 | 23.3 | 5 | 16.7 | 0.85 |
| Fistula side: | | | | | |
| Right | 12 | 40 | 9 | 30 | 0.30 |
| Left | 18 | 60 | 21 | 70 | |
| Lesion site: | | | | | |
| Inflow | 10 | 33.3 | 9 | 30 | 0.21 |
| Outflow | 20 | 66.7 | 21 | 70 | |
| Fistula age, years (mean ± SD) | 4.1 (± 2.3) | | 4.6 (± 2.2) | | 0.94 |
| Lesion type: | | | | | |
| Stenosis | 22 | 73.3 | 22 | 73.3 | 0.61 |
| Occlusion | 8 | 26.7 | 8 | 26.7 | |
| Lesion length, cm (mean ± SD) | 5.3 (± 1.9) | | 4.1 (± 1.8) | | 0.64 |
| Other lesions during follow-up | 4 | 13.3 | 3 | 10 | 0.50 |

## Discussion

The arteriovenous shunt is considered as the access of choice for patients with end-stage renal disease due to its higher patency and low complication rate. Complications of vascular access are one of the main causes of the increase in mortality and morbidity in patients with end-stage renal disease.[9] Stenosis is one of the major causes of fistula dysfunction. The pathophysiology of stenosis consists of microvessel formation, cellular proliferation and cytokine excretion by smooth muscle cells, macrophages and endothelial cells.[10] Cytokines result in more activation and proliferation of these cell types, resulting in neointimal hyperplasia.[10] Maintaining patency and function of dialysis access circuits often becomes a dire need for dialysis patients.

Aa variety of surgical or catheter-based interventions can be employed to rescue the failing or thrombosed dialysis access. The endovascular approach has become the treatment of choice, securing access in 80% of dialysis patients and allowing them immediate dialysis without the insertion of temporary catheters or construction of another venous access.[11] The majority of critical venous stenoses develop either along the venous outflow tract of the arteriovenous fistula or at the venous juxta-anastomotic site. However, angioplasty itself can cause intima-mediate rupture, followed by neointimal hyperplasia (normal vessel response to the injury) and subsequent re-stenosis with recurrent access failure. Therefore, balloon access of the vascular access is characterised by poor midterm patency, with an increasing rate of recurrent stenosis.[12]

High technical success was achieved using plain balloon angioplasty (> 90%) but re-stenosis is common within six months.[13] Inflation of the drug-coated balloon in the area of stenosis allows rapid release of paclitaxel to the regional vessel wall and inhibition of neointimal hyperplasia compared with a plain balloon.[14] The drug-coated balloon was used in saving the failing arteriovenous shunt and has shown positive results from different centres.[15]

The mean age of the patients in our study was 49.2 years (± 11.5 years) with 29 (48.3%) men and 31 (51.7%) women, which is comparable to Katsanos *et al*, who studied 40 patients (29 men and 11 women with a mean age of 64.1 years).[14]

Procedural technical success and 30-day safety endpoints occurred in 100% of our patients, which is comparable to Patanè *et al*, who had immediate technical and clinical success in 100% of patients.[16] Katsanos *et al* used paclitaxel-coated balloon dilation in 20 patients and standard balloon access for another 20 cases with stenosed venous access lesions. Cumulative target lesion primary patency was significantly higher after paclitaxel-coated balloon at six months (70% in the paclitaxel-coated balloon group vs 25% in plain balloon group, $p < 0.001$). Secondary patency (95% in the paclitaxel-coated balloon group vs 90% in the standard balloon dilatation group). Circuit cumulative primary patency was 65% in the paclitaxel-coated balloon group compared with 20% in the plain balloon group).[14] Lai *et al* studied 10 patients with synchronised lesions; those treated with the standard balloon and with paclitaxel-coated balloon had significantly higher results compared with percutaneous transluminal angioplasty at six months (70% for the paclitaxel-coated balloon and 0% for the standard balloon) but not at one year (20% vs 0%).[17]

The Patanè *et al* included 26 patients with juxta-anastomotic stenosis in radiocephalic fistulas that were treated with angioplasty with a drug-coated balloon.[16] Primary patency was 96%, 82% and 58% at 6, 12 and 24 months, respectively.[16]

In our study, at six months the target lesion patency rate, circuit primary patency and secondary patency in group II were better than in group I (96.7% vs 90%, 96.7% vs 90% and 100% vs 100%). At 12 months, the target lesion patency rate, circuit cumulative primary patency and secondary patency in group II showed a statistically

**Table 3** Procedural technique

| Characteristic | Group I | | Group II | | *p*-value |
|---|---|---|---|---|---|
| | (*n*) | (%) | (*n*) | (%) | |
| Access: | | | | | |
| Antegrade | 20 | 66.7 | 21 | 70 | 0.500 |
| Retrograde | 10 | 33.3 | 9 | 30 | |
| Balloon: | | | | | |
| Diameter, mm (mean ± SD) | 7.1 (± 1.5) | | 6.5 (± 1.2) | | 0.040 |
| Lenth, mm (mean ± SD) | 66 (± 19.1) | | 54.6 (± 15.7) | | 0.410 |

**Table 4** Patient follow-up

| Characteristic | After 3 months | | After 6 months | | | After 6 months | | |
|---|---|---|---|---|---|---|---|---|
| | Group I *n* (%) | Group II | Group I | Group II | *p*-value | Group I | Group II | *p*-value |
| Target lesion primary patency | 30 (100) | 30 (100) | 27 (90) | 29 (96.7) | 0.30 | 20 (66.7) | 27 (90) | 0.029 |
| Circuit primary patency | 30 (100) | 30 (100) | 27 (90) | 29 (96.7) | 30 | 18 (60) | 25 (83.3) | 0.070 |
| Secondary patency | 30 (100) | 30 (100) | 30 (100) | 30 (100) | 1 | 28 (93.3) | 29 (96.7) | 0.500 |

significant improvement over group I (90% vs 66.7%, 83.3% vs 60% and 96.7% vs 93.3%, respectively). Our results are comparable to other studies and show the superiority of the paclitaxel-coated balloon over the standard plain balloon in short- and long-term patency, especially in the long term, where results are statistically significant.

## Conclusion

The paclitaxel-coated balloon is considered to be safe and effective; it also improves the patency of failing access. The results of this study are comparable to those in the available literature. Further studies are needed to confirm our results, including a larger number of patients, subgroup analysis including native and synthetic access and the effect of drugs other than paclitaxel.

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