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RESEARCH LETTER

Utility of Sirolimus Coated Balloons for Salvaging Dysfunctional Arteriovenous Fistulae: One Year Results From the MATILDA trial

The current endovascular standard of care for the treatment of conduit stenosis in dialysis access is conventional balloon angioplasty (CBA),[1,2] achieving approximately 31% primary patency at 12 months.[3] Paclitaxel coated balloons (PCBs) have been used to offset the neointimal hyperplasia (NIH) process and increase the target lesion revascularisation (TLR) free duration, but results of PCB use in AV access are mixed to date.[3,4] Furthermore, their use has been questioned in the meta-analysis by Katsanos *et al.*, suggesting an increased mortality risk when used in the lower limb arena,[5] although this has not been corroborated in any subsequent analysis, using patient level data.

Sirolimus, like paclitaxel, is a potent antiproliferative agent that prevents activation of smooth muscle cells after vascular injury. However, unlike paclitaxel, sirolimus has beneficial potent anti-inflammatory effects and a broader therapeutic range. Until recently it has been difficult to package sirolimus onto a stentless balloon platform, which can deliver it directly to the vessel wall in an adequate quantity to inhibit NIH. MagicTouch is a novel sirolimus coated balloon (SCB) catheter (Concept Medical Inc., Tampa, FL, USA), which uses proprietary nanolute technology designed to improve the lipophilicity and bioavailability of sirolimus. Sirolimus is converted into submicron sized particles and encapsulated into phospholipid drug nanocarriers. Submicron carriers mimic the body lipids and liberate sirolimus to achieve antirestenotic activity. The dose of sirolimus corresponds to 1.25 $\mu g/mm^2$.

The MAgicTouch Intervention Leap for Dialysis Access (MATILDA; NCT04698512) single arm prospective pilot trial enrolled 33 Asian patients with end stage renal failure (18 males, mean age 64.7 $\pm$ 11.6 years; 64% with diabetic nephropathy), with failing AVF with *de novo* and recurrent stenoses. The primary efficacy endpoint was target lesion primary patency (TLPP) at six months. There were 47 target lesions (34/47, 72% recurrent lesions) and mean percentage stenosis and lesion length were 84 $\pm$ 10% and 35 $\pm$ 19 mm, respectively. Further patient demographics and procedural details have been published previously.[6] Based on a performance goal of 70% for TLPP, the sample size of 33 had at least 80% power to demonstrate non-inferiority using a margin of 10% compared with the known six month TLPP of approximately 40% with CBA.[3] Trial approval was obtained from the local Human Research Ethics Committee (CIRB ref: 2018/2557).

All lesions were pre-dilated with a high pressure non-compliant balloon (Mustang, Boston Scientific, Marlborough, MA, USA) and lesion effacement and recoil $<$ 30% were mandatory for subsequent drug elution. There was 100% technical and procedural success. There were no peri-procedural complications related to the SCB. The TLPP and circuit access patency rates at six months were previously reported at 29/35 (83%) and 17/25 (68%), respectively.[6] At 12 months, TLPP and circuit access patency dropped to 22/38 (58%) and 12/27 (44%), respectively. Secondary patency rates were 31/32 (97%) and 27/29 (93%) at six and 12 months, respectively (Fig. 1). Mean time to TLR was 6.8 $\pm$ 2.1 months with a mean TLR free duration of 10.6 $\pm$ 4.3 months. The juxta-anastomosis (portion of the AVF that is immediately adjacent to, and within 5 cm of, the arterial anastomosis) was the main target lesion location for re-intervention (16/38; 42%).

There were 4/33 (12%) deaths attributable to the patient's underlying comorbidities (three cases of ischaemic heart disease and one cerebral vascular accident) at 2.3, 6.5, 7.5, and 8.7 months, respectively. There were 3/29 (10%) access thromboses at 12 months; two were abandoned. Seven of 10 AVFs re-intervened upon between the six and 12 month timepoints were those with recurrent lesions with an average of 2.1 $\pm$ 1.0 re-interventions already performed prior to enrolment.

This is the first study, albeit a small series and with no direct comparator arm, to publish safety and one year efficacy data on the use of SCB in the AVF circuit. Despite initial encouraging six month performance results, the drop in TLPP and circuit access patency rates at one year are disappointing but are comparable with the current paclitaxel data reported to date at the same points (PCB pooled TLPP was 75% and 53% at six and 12 months, respectively).[3] The Kaplan–Meier curve morphology comparing the difference in TLPP between CBA and PCB use in the AVF circuit is similar between studies. The effect size in TLPP between the two groups becomes less the longer the follow up period is observed, where the curves tend to converge. The paclitaxel dose that is delivered, penetrates, and remains within the vessel, probably differs between PCBs with different types of excipient carriers and is likely to explain the difference in effect. The decay of paclitaxel over time may explain the decline in TLPP between the six and 12 month periods, and suggests the need to perform repeated drug elution fistuloplasty to obtain longer TLPP. MagicTouch using nanocarriers may allow a more efficient load to be delivered into the vessel wall with longer drug retention, which may reflect the improved TLPP at 12 months but ultimately a top up of drug may well be required as time passes. However, more research is required in this area and RCTs comparing SCB and PCB use in the AVF setting against CBA as the standard of care are required urgently. In conclusion, SCB angioplasty for dysfunctional AVF circuits appears to be a safe modality in Asian haemodialysis patients, with no reported device related adverse events at 12 months.

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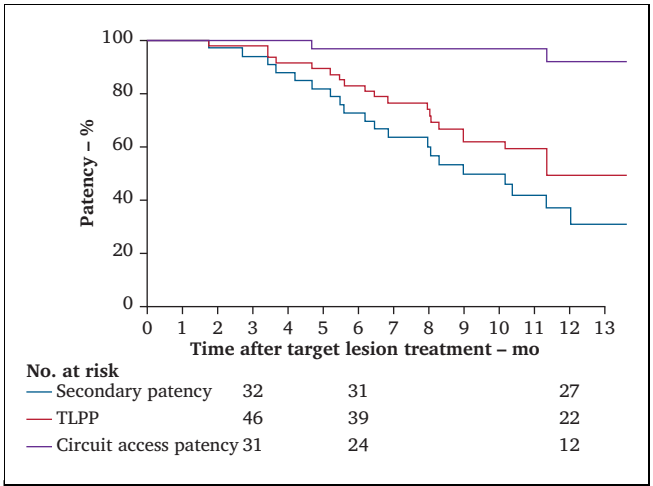

Figure 1. Cumulative Kaplan-Meier estimate for secondary patency, target lesion primary patency (TLPP), and circuit access patency of failing arteriorvenous fistulas in 33 patients with end-stage renal failure.

CONFLICT OF INTEREST

TYT has received honoraria from Concept Medical to travel and to give presentations.

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