Drug-Coated Balloon Angioplasty for Hemodialysis Fistula Maintenance

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Vascular access is the lifeline for patients with ESKD on hemodialysis. Mature arteriovenous fistulas (AVFs) are the best type of vascular access, because they have a lower infection rate, have longer durability, and need fewer maintenance procedures compared with arteriovenous grafts and tunneled central venous dialysis catheters. Stenosis is a major pathologic lesion afflicting hemodialysis AVFs. Early stenosis that occurs shortly after AVF creation results in nonmaturation, whereas stenosis that develops after maturation and use causes dysfunction, inadequate dialysis, and a shortened lifespan (1). Although the pathologic lesions causing stenosis have been well studied, their management remains elusive (1).

Patients on hemodialysis are referred regularly to vascular centers for angioplasty of AVF stenosis, increasing the burden of morbidity and cost. Angioplasty successfully dilates the stenosis and restores AVF function, but unfortunately, the trauma of the procedure results in recurrence, propagating a vicious cycle. Primary patency of AVFs after angioplasty (time from angioplasty to recurrence) has been abysmal, with <25% of lesions remaining patent at 1 year (2). The rate of recurrent stenosis is slower in surgically manipulated segments (juxta-anastomosis) compared with surgically naïve ones (cephalic arch) (3). Application of an antiproliferative agent with drug-coated balloons (DCBs) to the site of successful angioplasty is a rational approach to delay recurrence. Peripheral arterial and coronary disease has been successfully treated with DCBs, suggesting that similar results could be achieved in the venous segments of an AVF (4).

In this issue of the *Clinical Journal of American Society of Nephrology*, Trerotola *et al.* (5) report the preliminary results of the first prospective, global, multicenter (n=23), randomized, controlled trial (RCT) that compared the efficacy and safety of paclitaxel-coated, balloon-assisted angioplasty (n=141) with conventional angioplasty (n=144) in patients with dysfunctional mature AVFs. All AVFs had to have a target stenosis ≥50% that matched a clinical indicator to be included in the trial. For example, an AVF that had a ≥50% stenosis in the outflow vein (target lesion) on angiogram and was pulsatile on physical examination (matched clinical indicator) met the inclusion criteria. Because some dysfunctional AVFs have multiple stenoses, fistulas with two stenoses on an angiogram (one target and one incidental) were also included in the study as long as both stenoses were successfully treated before randomization. The access circuit was defined as the portion of the AVF from the anastomosis to the axillary vein. Patients with central vein stenosis were, therefore, excluded from the study. The DCB was inflated only at the target lesion. The primary efficacy end point was defined as continued AVF patency with no need for a clinically driven (referral on the basis of any clinical indication during follow-up or a mandatory physical examination at 6 months) reintervention on the target lesion (target lesion primary patency [TLPP]) or risk of access thrombosis at 6 months. Access circuit primary patency (ACPP) ended when either the target lesion recurred or any other stenosis was detected, whereas the TLPP ended when the target lesion recurred.

The prespecified 6-month primary efficacy end point was not met with the TLPP of 71%±4% for the DCB and 63%±4% for control (P=0.06), representing a difference of 8%±6% (95% confidence interval [95% CI], 3% to 20%). There were three possible reasons for this. First, the conventional angioplasty group (control) outcomes were better than historical outcomes. Second, controls had the angioplasty balloon inflated a second time instead of an identical sham balloon, resulting in a difference in inflation pressure (9.7±2.1 atm in the DCB arm versus 12.1±5 atm in the control arm). Using an identical sham non-DCB angioplasty in the control arm would have removed variability in treatment parameters, and more importantly, it would have kept the operators and study coordinators blinded. Third, the mandatory physical examination window extended from 5 to 7 months, and therefore, the 6-month analysis missed physical examinations done in the seventh month. When the primary efficacy end point was extended to 7 months, thereby capturing all patients who had missed their 6-month mandatory examination, the primary efficacy end point showed significance for DCB (64%±4%; 95% CI, 55% to 72%) versus control (53%±4%; 95% CI, 44% to 61%; P=0.02), representing a difference of 12%±6% (95% CI, 0% to 23%). Thrombosis of the AVFs was rare in both arms (2.4% DCB and 4.3% control). Despite the improvement of the TLPP, the ACPP was not different at 6 and 7 months after enrollment. If the DCB was applied to both the target and incidental stenosis (20% of AVFs), an improvement in ACPP could have occurred. Long-term results are awaited to show whether ACPP will improve with better outcomes of the TLPP at 1 and 2 years

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of follow-up. Interventions to maintain target lesion patency were fewer for the DCB at 6 months (0.31 versus 0.44 per patient; P=0.03), a 30% reduction in procedure rate. The DCB was not associated with an increased risk of complications.

Treatment options to delay the recurrence of stenosis in mature AVFs are limited. Cutting balloons and bare metal stents have not shown a clear benefit over conventional angioplasty (1,6,7). In RCTs, stent grafts have shown superiority over conventional balloon angioplasty to delay recurrence of stenosis in arteriovenous grafts (8,9), but similar RCTs have not been conducted in AVFs. Deployment of stent grafts in AVFs is challenging, with concerns of local and distant migration, pain, and infection when located in the sticking zone and recurrent in-stent and end stent stenosis (6). The prospect of delaying recurrence of stenosis in AVFs by simply inflating a DCB at the site of angioplasty seems a very simple and straightforward approach. On the basis of the results of this trial, the Food and Drug Administration has approved the use of paclitaxel drug-eluting balloon angioplasty for treatment of recurrent stenosis in dysfunctional mature AVFs (10). Because stenosis in AVFs has varying rates of recurrence, it may respond inconsistently to DCB application, hence the need to further study response in varied locations of stenosis. The preliminary findings of this study are encouraging and hopefully, will be borne out over the 12 and 24 months of observation. It is our hope that DCB angioplasty will delay recurrent stenosis in AVFs and thereby, decrease morbidity and cost for patients on hemodialysis.

Disclosures

None.

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