

# The Potential Role for DEBs to Treat Hemodialysis Access Stenoses

A look at the mechanics of this interventional therapy and why it warrants further study.

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After initial percutaneous balloon angioplasty (PTA), restenosis represents a common threat to the function of arteriovenous fistulas (AVFs) and polytetrafluoroethylene (PTFE) grafts in patients on hemodialysis. The 6-month restenosis rate tends to be as high as 62% to 77% after angioplasty.<sup>1,2</sup> To overcome this drawback, different techniques, such as cutting-balloon angioplasty, cryoplasty, stent or stent graft implantation, and local irradiation after PTA, have been applied, with varying success.

Recently, the 6-month primary patency rate of PTFE grafts was enhanced to 51% after stent graft implantation in venous outflow stenoses.<sup>2</sup> However, it would be beneficial to find a way to dramatically reduce the restenosis rate while leaving nothing behind. Drug-eluting balloons (DEBs) could offer such an opportunity, as they were found to decrease the 6-month restenosis rate from approximately 45.5% (plain balloon angioplasty) to about 18.7% in the femoropopliteal arteries.<sup>3</sup>

## THE MECHANICS OF DEB USE IN HEMODIALYSIS ACCESS STENOSES

DEBs are usually coated with paclitaxel, an antineoplastic substance that deranges cell replication by stabilizing polymerized microtubules and enhancing microtubule assembly. It has been shown that paclitaxel inhibits smooth muscle cell proliferation and migration and thus

has the potential to prevent neointimal hyperplasia.<sup>4</sup>

However, hemodialysis access fistulas and PTFE grafts maintain certain hemodynamic properties due to the nonphysiological direct conduction of high-pressure fluid into a low-pressure system. After creating an AVF or PTFE graft, the veins involved (usually the cephalic vein in AVFs and the downstream vein central to the venous anastomosis in grafts) react to the high blood flow and pressure with dilatation and wall thickening.<sup>5</sup> If the vessel wall thickens focally, a stenosis may develop. This may appear at critical sites where elevated shear stress and eddy flow are present. Needle punctures in the course of the dialysis sessions and compliance mismatch at the graft-vein or artery-graft anastomoses represent additional stimulations of neointimal formation. Moreover, uremia aggravates endothelial dysfunction and excites venous intimal hyperplasia.<sup>6</sup>

Balloon angioplasty induces excessive mechanical stress with consecutive disruption of the vessel intima and media, as well as tension of the adventitia. This triggers the migration and proliferation of fibroblasts, myofibroblasts, smooth muscle cells, and consecutive neointimal hyperplasia.<sup>7</sup> These biological reactions to angioplasty are regarded to be equally present in arteriosclerotic arteries and shunt veins, respectively. In the femoropopliteal arteries, the mechanical stress is a single event and terminates

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with the deflation of the angioplasty balloon. Hence, the wall injury may heal without disturbance when the systemic blood pressure is under control and other risk factors of arteriosclerosis are omitted. In hemodialysis access vessels, a certain mechanical burden is likely to continue at the site of a dilated lesion, as the nonphysiological hemodynamic state remains the same. Thus, neointimal formation may be constantly stimulated.

## RESULTS TO DATE

These factors may hamper the performance of DEBs in hemodialysis access vessels when compared to the lower extremity or coronary arteries. However, the first encouraging results of a recently published study seem to belie an overly pessimistic attitude. In a prospective randomized study, 40 patients with AVF or PTFE-graft venous outflow lesions were assigned to either paclitaxel-coated or standard balloon PTA. Treatment success was significantly higher after DEB angioplasty than after standard balloon angioplasty, with 6-month primary patency rates of 70% versus 25%, respectively ( $P < .001$ ).<sup>8</sup> Although the nonblinded, single-center study design may limit its evidence, the overwhelming performance of DEB PTA justifies the initiation of further prospective randomized trials with larger patient populations, preferably in a blinded, multicenter fashion.

A substantial reduction of hemodialysis shunt restenoses implies prolonged dialysis access survival, which is essential to reducing patient discomfort, as well as morbidity. It is in this context that the performance of DEBs in the course of high-evidence trials will be eagerly expected. ■

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