Towards the Application of Endovascular Treatment for Superficial Femoral Artery

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In the 21st century, peripheral artery disease (PAD) has become a global problem. Lower extremity PAD (LE-PAD) is currently the 3rd leading cause of atherosclerotic cardiovascular death, following coronary artery disease and stroke worldwide. Even governments need to assess the best strategies for optimum treatment and prevention of this disease.1

Recently, the strategy of revascularization for LE-PAD has shifted from surgical treatment toward endovascular therapy (EVT).2 EVT with self-expanding nitinol bare-metal stent (BMS) produces better clinical outcomes compared with balloon angioplasty, but the restenosis rate after self-expandable BMS implantation in superficial femoral artery (SFA) lesions is approximately 45% at 2 years.3 However, the 2-year vessel patency in femoropopliteal (FP) lesions may be improved through the use of nitinol stents in combination with pharmacotherapy. Soga et al4 showed favorable clinical efficacy of nitinol BMS implantation for FP disease, up to 5 years. They also concluded that TASC II C/D status, hemodialysis, stent fracture, and cilostazol administration were independent predictors of primary patency after FP lesions.

Against this background, drug-eluting stents (DES) have shown superior outcomes for PAD compared with self-expanding nitinol BMS. The primary patency rate after DES implantation for SFA is reported to be 83% at 2 years.5 But the phenomenon of in-stent restenosis (ISR) caused by neointimal hyperplasia remains even after DES and includes BMS implantation.6 So there is increased interest in the etiology of ISR.

Neointimal proliferation is the arterial healing response to the vessel wall injury that occurs as a result of mechanical dilatation.7 Previous data suggest that chronic, continuous expansive force to the vessel wall from self-expanding BMS may play a key role in neointimal proliferation.
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which induces restenosis.\textsuperscript{8,9} According to reports, a high ratio (\(>1.4\)) of nominal BMS diameter to vessel size in the target artery results in exuberant neointimal proliferation and restenosis.\textsuperscript{10,11}

The optimal sizing of self-expanding paclitaxel-eluting stents (PES) in the treatment for SFA lesions is also unclear. Miki et al\textsuperscript{12} investigated the influence of PES diameter on stent patency in SFA lesions using optical frequency domain imaging. Their results suggested that neointimal proliferation was attenuated by paclitaxel and that in the 8-mm stent group the lumen area at follow-up may be compensated by greater stent enlargement regardless of the accelerated vessel injury. They concluded that stent diameter might be important for stent patency when using self-expanding PES for SFA lesions.

In this issue of the Journal, Kurata et al\textsuperscript{13} show that the stent-to-vessel (S/V) diameter ratio at the lesion site but not at the distal healthy site was an independent determinant of restenosis after treatment with a self-expanding nitinol BMS in de novo SFA lesions. It is interesting to note that this study found an association between restenosis and the S/V diameter ratio at the lesion site rather than at the distal healthy site. They assessed the mechanism of restenosis from the point of artery stretch, and vascular injury. However, the mechanism responsible for the association between restenosis and stent size is still largely unknown. But at the very least, this study suggests that appropriate selection of stent size in reference to the vessel diameter plays an important role in achieving better patency in de novo SFA interventions.

In the development of atherosclerosis, endothelial cells proliferate and form vessels under hypoxic stimuli. Vascular smooth muscle cells (VSMC) proliferating and migrating in response to vascular injury contribute to vessel narrowing and play an important role in the atherosclerotic process. It is recognized that hypoxia is a stimulus for VSMC proliferation and migration, a process known as vascular remodeling. Hypoxia and hypoxia-induced vascular endothelial growth factor expression are involved in the pathogenesis of progressive atherosclerosis.\textsuperscript{14} Atherosclerosis is also caused by a number of mechanisms, including endothelial dysfunction, upregulation of cell adhesion molecules, proliferation of VSMC, apoptosis of endothelial cells, lipid oxidation, activation of matrix metalloproteinases and platelet activation.

A prospective study is needed to prove the precise mechanism of ISR, which will assist in decision making for optimal stent size. Thus, further studies are necessary to overcome the limitations of the present study and to precisely understand the vascular response to stent implantation.

Recently, stent grafting was used for SFA lesions. Ohki et al reported that endovascular stent grafting appears to be a safe and less invasive alternative to above-knee bypass surgery,\textsuperscript{15} providing 88–92% primary patency at 12 months in long, complex lesions.

Conclusion
Because of the recent advancements in technology and improvement in outcomes, EVTs are now widely used as the first-line treatment for treating complex PAD (Figure). In the future, we will be selecting the most suitable strategy from among alternatives including drug-coated balloon, atherectomy devices and combinations of these.

Disclosures
Conflict of Interest: None.

References