Vascular Response to Bare Metal Stents in the Superficial Femoral Artery as Assessed on Optical Coherence Tomography

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**Figure.** Representative optical coherence tomography of stents in the superficial femoral artery. (**A,B**) At the relatively early phase (≤15 months), (**A**) peri-strut low-intensity areas surrounding the self-expanding stent (arrowheads) and (**B**) intra-intima microvessels (white arrow) were observed. (**C–F**) At the very late phase (>10 years), in addition to (**C,D**) microvessels, (**E,F**) the lipid-rich intima (asterisks) and (**F**) calcium deposits (yellow arrows) were also found in the in-stent tissue.
Numerous clinical studies have investigated the vessel response to coronary stents using optical coherence tomography (OCT), but it remains unknown whether the vessel response to stents in the peripheral arteries is similar to that in the coronary arteries. Hence, we here assessed the peripheral vascular response to bare metal stents (BMS) in the superficial femoral artery (SFA) on OCT.

The subjects consisted of 7 patients with peripheral artery disease (6 claudicant patients and 1 patient with critical limb ischemia) who had previously received BMS (7 self-expandable and 2 balloon-expandable stents) in the SFA. OCT (C7 OCT system; St. Jude Medical, St. Paul, MN, USA) of the stents performed at the time of angioplasty showed in-stent restenosis in 5 patients (6 stents) and de novo stenotic lesions in 2 patients (3 stents). A sheath introducer (4 or 6 Fr) was inserted into the common femoral artery via the antegrade ipsilateral approach or via the retrograde contralateral approach. OCT was acquired before balloon dilatation of the stents in all patients with in-stent restenosis. To remove the blood from the vessel lumen, contrast medium was injected into the SFA through a sheath introducer, which was positioned proximally to the stent, with or without obstructive manual compression of the common femoral artery. Injection of contrast was adjusted either using automatic injection (volume 15–32 ml, injection rate 5–10 ml/s) or by manual injection. Cross-sectional images of the stented segments were analyzed at 1-mm intervals. Signal attenuation regions with diffuse borders were determined as lipid-rich intima if the penetration depth was sufficient for the evaluation of in-stent tissue (based on tissue at the same distance around the OCT catheter). Peri-strut low-intensity areas (PLIA), calcification, and microvessels were defined according to previous studies of coronary arteries, but insufficient OCT penetration depth may result in inappropriate evaluation of peri-stent microvessels, and therefore, only intra-intima microvessels were evaluated in the present study. The study protocol was approved by the institutional review board (M26-45).

Patients 2 and 5 underwent OCT observation of 2 stents each (Table S1). Stent type consisted of 2 different self-expandable nitinol stents (SMART Control; Cordis, Miami Lakes, FL, USA; and Misago; Terumo, Tokyo, Japan) and 1 balloon-expandable stainless steel stent (Palmaz stent; Cordis). The time from stent implantation to OCT was relatively early (≤15 months) in all patients with self-expandable stents, whereas it was very late (>10 years) in patients with balloon-expandable stents. PLIA was observed in all of the 7 stents in the relatively early phase (Figure), while it was not observed in the 2 stents in the very late phase (PLIA could not be evaluated in stent 9 due to insufficient penetration depth). Lipid-rich intima and calcification were observed in both balloon-expandable stents in the very late phase. Intra-intima microvessels were observed in 4 out of 7 stents in the relatively early phase and in both stents in the very late phase.

Several previous studies have shown that PLIA can be identified following coronary stent implantation on OCT. Pathology using a porcine model showed that PLIA reflects fibrin deposition with inflammatory cell infiltration around the stent struts, and PLIA has been more frequently observed in the very late phase. The frequency of PLIA in BMS in the current study (100%) was substantially higher than that reported in a previous study evaluating drug-eluting stents in coronary arteries at 6 months following implantation (58% in sirolimus-eluting stents and 86% in paclitaxel-eluting stents). Considering that all stents evaluated in the present study were BMS, this finding may not be solely attributable to fibrin deposition resulting from the lack of drug effects in these stents. Instead, this finding could be at least partly explained by the fact that self-expandable stents have a mechanical property of exerting an outward force against the vessel wall. This chronic stimulus on the vessel wall from the stent might consequently cause prolonged vessel injury and an inflammatory response, resulting in the manifestation of PLIA on OCT. Another possible explanation for the greater frequency of PLIA in peripheral as compared with coronary arteries is the different underlying plaque morphology between the two vascular beds. Although the literature describing the characteristics of femoral atherosclerosis is limited, it has been reported that foam cell lesions and lipid core plaques are more frequently observed in coronary as compared with femoral arteries, whereas femoral arteries are associated with age-dependent advanced atherosclerosis with calcification dominated by fibrous and fibrocalcific plaques.

Greater underlying calcification in peripheral as compared with coronary arteries may lead to more frequent incomplete stent apposition and thrombus formation around stent struts, which in turn may result in the greater prevalence of PLIA in the peripheral arteries.

To our knowledge, this is the first report on the development of in-stent neoatherosclerosis within BMS implanted in the arteries of the lower extremities as seen on OCT. In the coronary arteries, this phenomenon has been previously demonstrated in both pathological and OCT studies at the late phase (>5 years) after stent implantation. Thus, the present results imply that newly formed atherosclerotic lesions within neointimal tissues can moreover occur systemically during a prolonged period after BMS implantation. It has been hypothesized that the mechanisms responsible for this phenomenon in the coronary arteries include incompetent and dysfunctional re-endothelialization following stent placement, characterized by poorly formed cell-cell junctions that allow a greater amount of lipoproteins to enter the subendothelial space. Nevertheless, it remains unknown whether the mechanisms and the timing of the development of in-stent neoatherosclerosis are similar between the peripheral and coronary arteries.

References
OCT Assessment of BMS in the SFA


Supplementary Files

Supplementary File 1

Table S1. Stent characteristics and OCT findings

Please find supplementary file(s); http://dx.doi.org/10.1253/circj.CJ-14-1069