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EDITORIAL COMMENT

Stenting Chronic Coronary Artery Occlusions

One Step Closer?*

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Traditionally, catheter-based intervention to treat chronically occluded coronary arteries has been associated with poorer acute and long-term success compared with intervention on patent arteries (1,2). From the earliest days of balloon angioplasty, the main challenge in revascularization of a coronary occlusion has been the ability to pass a guidewire through the area of occlusion into the "true lumen" of the distal vessel. Despite quantum gains made in the ability to treat other difficult lesion subsets, such as aorto-ostial stenoses and saphenous vein graft disease, the technology needed to safely and predictably revascularize the chronically occluded coronary artery has been elusive.

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The development of stiffer and lubricious guidewires coated with hydrophilic polymers has led to modest improvement in the ability of the interventionalist to cross these occlusions. Yet none of these wires has met with predictable success. Beyond simple guidewire technology, there are several innovative devices that extend the armamentarium of the interventionalist in his/her quest to conquer this formidable adversary. The Frontrunner CTO Catheter (Lumend Inc., Redwood City, California) is a blunt dissection device that creates controlled dissection planes in the plaque, allowing the operator to then pass a conventional wire. The Safe-Steer wire (IntraLuminal Therapeutics Inc., Carlsbad, California) utilizes optical coherence reflectometry technology to guide transit of the wire through plaque and away from the arterial wall.

However, successful passage of the guidewire through the occlusion is only the first hurdle that must be overcome to achieve long-term arterial patency. Early generation balloons had difficulty crossing these lesions and were intolerant of high pressures often required to dilate these lesions. Newer, low-profile balloons, which can be expanded with high pressure, and atheroablative devices facilitate acute luminal enlargement. Nevertheless, the high plaque burden and diffuse disease commonly associated with chronic occlusion predispose to a high incidence of restenosis (3). Even when the occlusion is crossed and the lesion dilated, the rates of restenosis may be as high as 70% with balloon angioplasty alone (2). Given the unequivocal successes of endovascular stenting for treating other lesions subsets associated with high rates of restenosis, it was natural to hypothesize that this breakthrough technology would yield favorable effects when treating chronic coronary occlusions (4–6).

Initially, many operators were reluctant to stent chronic occlusions out of fear of subacute stent thrombosis resulting from flow reduction due to retrograde collateral filling. However, several randomized clinical trials have documented that stenting is associated with better acute angiographic outcome and freedom from restenosis and need for repeat revascularization of chronic coronary artery occlusion (7–9). In one such study, the Gruppo Italiano di Studio sullo Stent nelle Occlusioni Coronariche (GISSOC) trial (8), postprocedure minimum lumen diameter was significantly larger (2.46 vs. 1.91 mm) in patients randomized to stent placement. By nine months, follow-up angiography demonstrated a 53% reduction in angiographic restenosis in stented lesions. Furthermore, the worst-case scenario of restenosis (i.e., complete reocclusion) was also significantly reduced by stenting (8% vs. 34%). More importantly, this translated into a more favorable clinical outcome, with a marked reduction in the need for repeat revascularization of the target lesion from 22% to 5.3%. Although these findings are impressive and certainly validate the concept of stenting for treatment of chronic occlusions, it is merely one "snapshot" in the temporal continuum of a chronic disease.

Naively, many in the interventional community have traditionally assumed that freedom from angiographic restenosis at six to nine months guaranteed long-term patency and freedom from clinical events. We now have a more realistic appreciation that additional revascularization events driven by target lesion restenosis occur beyond this time interval (10). As newer treatment modalities that alter the biologic response to arterial injury (e.g., vascular brachytherapy and drug-eluting stents) become incorporated into everyday practice, it is imperative that we collect extended follow-up data to ensure that the salutary outcomes reported within the first year are maintained.

In this context, Rubartelli et al. (11), in this issue of the *Journal*, are to be commended for extending the follow-up of the GISSOC trial to six years. The major criticism of the original GISSOC study relates to the characteristics of the treated lesions. Approximately one-third of the lesions had a Thrombolysis In Myocardial Infarction (TIMI) flow grade >0, and small vessels (<3.0 mm) and long lesions (>13 mm) were excluded. Furthermore, the relative duration of the occlusion was relatively brief. Thus, the findings of the GISSOC study may not be generalizable to all patients with chronic total occlusions. Nevertheless, clinical follow-up at six years supports the superiority of stenting

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compared with balloon angioplasty alone. Percutaneous coronary intervention with stenting afforded greater freedom from target lesion revascularization (14.9% vs. 34.5%, $p = 0.0165$) compared with angioplasty alone. Although the incidence of other clinical end points, such as death or nonfatal myocardial infarction, did not differ, the small GISSOC study is clearly underpowered to detect a significant difference in these outcomes. Also, approximately two-thirds of the patients enrolled had single-vessel coronary artery disease with a low incidence of diabetes mellitus and reduced ejection fraction, portending an excellent long-term prognosis for the entire cohort.

The favorable outcome reported for lesions treated with stenting in the GISSOC study is even more impressive when one considers that the stent deployed in these patients, the Palmaz-Schatz coronary stent (Cordis Corp., Miami Lakes, Florida), was a "first generation" device with significant structural limitations, such as the presence of an articulation site and rigid segments. In addition, the operators hand-crimped these stents and deployed them at relatively low pressures. It is generally accepted that suboptimal stenting techniques (low pressure deployment and incomplete expansion) are associated with poorer acute and long-term outcome. In the GISSOC study, the post-treatment residual stenosis was 18%, suggesting that later generation stents deployed using optimal stenting techniques may have led to even better outcomes in the stent cohort. The use of the archaic warfarin-based pharmacologic regimen rather than the more contemporary dual antiplatelet therapy probably explains the 4.7% incidence of hemorrhagic complication observed in the patients treated with stents.

Despite these impressive findings in the GISSOC study, the decision to attempt catheter-based intervention on any given patient with a chronic total occlusion must be made on a lesion-by-lesion basis. If the patient is asymptomatic and there is no evidence of provokable ischemia in the myocardium subtended by the occluded vessel, it is difficult to justify subjecting the patient to the risk, albeit low, of attempted revascularization. If there is clinical evidence of ischemia, consideration should be given to attempted percutaneous revascularization. Although it is sometimes said that restoring patency to a chronically occluded coronary occlusion does not change long-term prognosis, Suero et al. (12) recently reported that successful revascularization of a chronically occluded coronary artery was *independently* associated with improved 10-year survival.

Nevertheless, interventional cardiologists must carefully weigh factors predictive of success in crossing coronary total occlusions, such as operator experience, larger vessel size, younger age of occlusion, shorter lesion length, absence of proximal vessel tortuosity, minimal bridging collaterals, and presence of a tapering funnel at the end of the occlusion (13). If the occluded segment of the artery can be traversed with a conventional guidewire or one of the newer total occlusion devices, documenting the presence of the wire in the true lumen of the vessel is mandatory before balloon dilation. Following balloon dilation, in light of the GISSOC study results, stand-alone balloon angioplasty can no longer be justified unless endoluminal stenting cannot be performed safely. Every effort should be made to optimize the acute angiographic outcome because every large prospective analysis supports the link between greater post-treatment lumen diameter and freedom from angiographic and clinical restenosis (10). "Bigger is still better," at least in the bare stent era. Ultimately, drug-eluting stents may provide additional benefit to the impressive results documented with bare stents in the GISSOC trial. Preliminary data from the randomized Sirolimus-Eluting Stent in De Novo Native Coronary Lesions (SIRIUS) trial showed a 75% reduction in angiographic restenosis and target lesion revascularization in patients treated with the sirolimus-eluting stents compared with bare stents. Although the use of drug-eluting stents has not been prospectively evaluated for the treatment of chronic total occlusion, there is hope that the extraordinary results reported for nonoccluded vessels may also be realized in this high-risk subset. The combination of improved technology to safely cross the occlusion and future generation stents may affirm that we are indeed "one step closer" to the necessary "one-two punch" needed to achieve long-term patency for endovascular treatment of total coronary occlusion.

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