First-Generation Drug-Eluting Stents for Chronic Total Occlusion

In Danger of Extinction?*

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An attempt to recanalize a chronic total occlusion (CTO) is only made in one-half of the patients presenting with an occluded vessel during angiography (1). Possible reasons for hesitating to perform a percutaneous coronary intervention (PCI) for a CTO may be the length and complexity of the procedure and the accordingly lower procedural success rate (2). Hence, patients with CTO are, in case of single-vessel disease, often managed medically or, in case of multivessel disease, are likely scheduled for bypass graft surgery even if the remaining lesions are suitable for PCI. In 2 randomized trials comparing coronary artery bypass surgery with PCI, CTO remains the strongest predictor of referral to bypass surgery rather than randomization (3,4).

The presumably most important development, which stimulated the interest in CTO-PCI, was the advent of drug-eluting stents (DES). With bare-metal stents, any effort by the interventionalist and burden for the patient associated with a recanalization procedure was curssed with a restenosis rate of 30% to 50% and a reocclusion rate of up to 20% (5). In contrast, the introduction of DES directly correlated with dramatically improved restenosis and reocclusion rates (6,7).

With this newfound potential to keep a recanalized coronary artery open, enormous efforts have been made recently to improve the success rate of the procedure, which remained stable at 50% to 70% for over 25 years (8). Technological advances and procedural developments include retrograde wiring through collateral channels, both antegrade and retrograde subintimal dissection, and re-entry techniques. Data from trials conducted in the United States (9), Europe (10), and Japan (11) show that in specialized centers with high operator volume, procedure success rates of 80% to 90% are now achievable.

In this issue of the Journal, Valenti et al. (12) assessed the incidence of reocclusion and predictors of angiographic failure after successful DES-supported recanalization of CTO from a single-center registry comprising 1,035 patients. Sixty-six percent of the successfully recanalized patients received a paclitaxel- or sirolimus-eluting stent (first-generation DES), 34% an everolimus-eluting stent (EES; second-generation DES). Follow-up angiography was performed 6 to 9 months after successful intervention in 82% of eligible patients. The main findings of the study are a significantly lower reocclusion rate of 3% for the EES compared with 10.1% for the other DES and a reocclusion rate of 57% after successful subintimal tracking and re-entry technique. In a multivariate analysis, the subintimal tracking and re-entry technique was highly associated with reocclusion (odds ratio [OR]: 29.5). Although performed in only a small subset of patients (4%), this confirms the very high reocclusion rate found by others (13). As the investigators suggested, its application should be limited to a small subset of patients with no other therapeutic options.

What characterizes this study is the difference in the performance of second- versus first-generation DES in CTO. Multivariate analysis revealed the use of EES (OR: 0.22) as an independent predictor of risk of reocclusion. These findings were substantiated by a propensity score-matched analysis.

Newer DES have a stent platform of a cobalt-chromium alloy and are thinner than the first-generation DES and are less likely to cause vessel trauma. Later-generation stents also have improved biocompatibility, resulting in less of an inflammatory response and more rapid vessel endothelialization or healing. For nonocclusive lesions, it has been shown that second-generation DES perform better than first-generation DES do (14,15). By contrast, for CTO, data on this issue are scarce (16,17). The investigators are to be commended for providing us with new information on the performance of EES in CTO in a fairly high number of patients with angiographic follow-up.

Does the present study put the whammy on the first-generation DES in CTO? This may be too early to conclude for several reasons. First, although this is the largest series of angiographic follow-ups after CTO-PCI to date, the data are derived from a single-center nonrandomized registry. Among CTO patients comorbidities and lesion morphologies are very variable and for the complex procedures different techniques are applied. These confounding factors cannot be excluded other than by performing an additional, randomized trial. Second, the EES findings cannot necessarily be applied to other second-generation DES. Third, the differences were only seen in the reocclusion rate and not in the binary restenosis rate. Unfortunately, the investigators...
did not provide us with the data necessary to comprehend the reasons for reocclusion. Was this a result of diffuse intima proliferation or rather a late thrombotic event? In many patients with reocclusion of a CTO, these events are not accompanied by symptoms. If thrombosis is the main mechanism, antiplatelet agents more potent than clopidogrel could potentially diminish the differences seen in the reocclusion rate between both groups of stents (18, 19), which might still keep first-generation DES on the shelf.

In conclusion, first-generation DES for CTO will stay alive until randomized trials have clearly demonstrated their inferiority in terms of safety and efficacy compared with that of newer generation DES, but they are in danger of extinction.

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