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Editorial

The Clinical Significance and Management Implications of Chronic Total Occlusion Associated With Surgical Coronary Artery Revascularization

Lorenzo Azzalini, MD, PhD, MSc

San Raffaele Scientific Institute, Milan, Italy

See article by Pereg et al., pages 1326–1331 of this issue.

Chronic total occlusions (CTOs) are observed in approximately one fifth of patients undergoing coronary angiography,[1] and if not revascularized they are associated with increased mortality.[2] Therefore, CTOs represent an epidemiologically relevant problem in routine clinical practice. CTO percutaneous coronary intervention (PCI) has traditionally been associated with lower success rates, higher technical complexity, and increased rates of complications compared with non-CTO PCI.[1] Additionally, patients with CTO often have multivessel coronary artery disease (CAD) and other comorbidities (eg, diabetes, left ventricular dysfunction), for which guidelines usually recommend revascularization with coronary artery bypass grafting (CABG).[3] As a matter of fact, in all-comer patients undergoing multivessel CAD, CABG provides a more complete and durable revascularization than does PCI because it is not influenced by upstream lesion complexity, and long-term patency rates for arterial grafts compare favourably with those of stents.[4,5] Therefore, one might expect that patients with CTO will have good clinical outcomes when treated with CABG.

Unfortunately, CTOs represent a difficult lesion subset to treat, even with CABG. In the **Syn**ergy Between PCI with **Tax**us and Cardiac Surgery (SYNTAX) trial, up to 32% of CTOs eventually did not undergo bypass because of multiple reasons, including vessel size that was too small or CTO vessel disease that was too extensive, thus leading to incomplete revascularization.[6] Despite the relevance of this clinical problem, very limited published data are available on the outcomes of patients with CTO undergoing CABG. Fefer et al.[7] studied 405 patients undergoing CABG and found that ≥ 1 CTO was present in 43% of them. Despite the fact that 16% of patients with CTO experienced incomplete revascularization, the presence of a CTO was not independently associated with 5-year mortality. Banerjee et al.[8] conducted a similar analysis in 605 patients undergoing CABG. Rates of complete revascularization were very high in patients with CTO (100% for left anterior descending [LAD] artery CTOs and > 92% for circumflex artery and right coronary artery [RCA] CTOs). Propensity-matched analysis comparing patients with CTO and patients without CTO showed higher 1-year cardiac mortality in the patients with CTO. Therefore, the available evidence on the topic so far is limited and is based on small single-centre registry and conflicting results.

In the current issue of the *Canadian Journal of Cardiology*, Pereg et al.[9] have provided a relevant contribution to the topic. They conducted a subanalysis of the **R**adial **A**rtery **P**atency **S**tudy (RAPS),[10] which randomized patients with 3-vessel disease to 2 strategies of CABG. The left internal mammary artery (LIMA) was used to bypass the LAD, and patients were randomized to either a radial artery graft to the RCA and a saphenous vein graft (SVG) to the circumflex artery, or vice versa. In a previous report on the same patient population, Pereg et al.[11] showed that ≥ 1 new native coronary artery CTO developed in 43.6% of patients at 1 year after CABG. Patients in whom a new CTO developed more frequently had Canadian Cardiovascular Society class 4 angina preoperatively. A new CTO was almost 5 times more likely to occur in vessels with pre-CABG stenoses > 90%, compared with vessels with stenoses < 90%. The development of a new CTO was more common in vessels bypassed with either an SVG or a radial artery graft (29.2% and 27.4%, respectively) compared with use of the LAD (18.4%), which was grafted with the LIMA. In 7.5% of patients, a complete occlusion of both the bypassed native vessel and its graft was demonstrated at 1 year.

In their current study, Pereg et al.[9] analyzed the long-term outcomes in 388 patients of the RAPS population according to the presence of ≥ 1 CTO at baseline and the development of ≥ 1 new native coronary artery CTO at 1-year angiographic follow-up. At baseline, 240 (61.9%) patients presented with a CTO for a total of 305 occluded vessels (1.27 CTOs per patient). At 1 year, ≥ 1 new native coronary artery CTO occurred in 169 (43.6%) patients (50.0% of patients in

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Corresponding author: Dr Lorenzo Azzalini, Interventional Cardiology Division, San Raffaele Hospital, San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milan, Italy. Tel.: +390226437331; fax: +390226437339.
E-mail: azzalini.lorenzo@hsr.it

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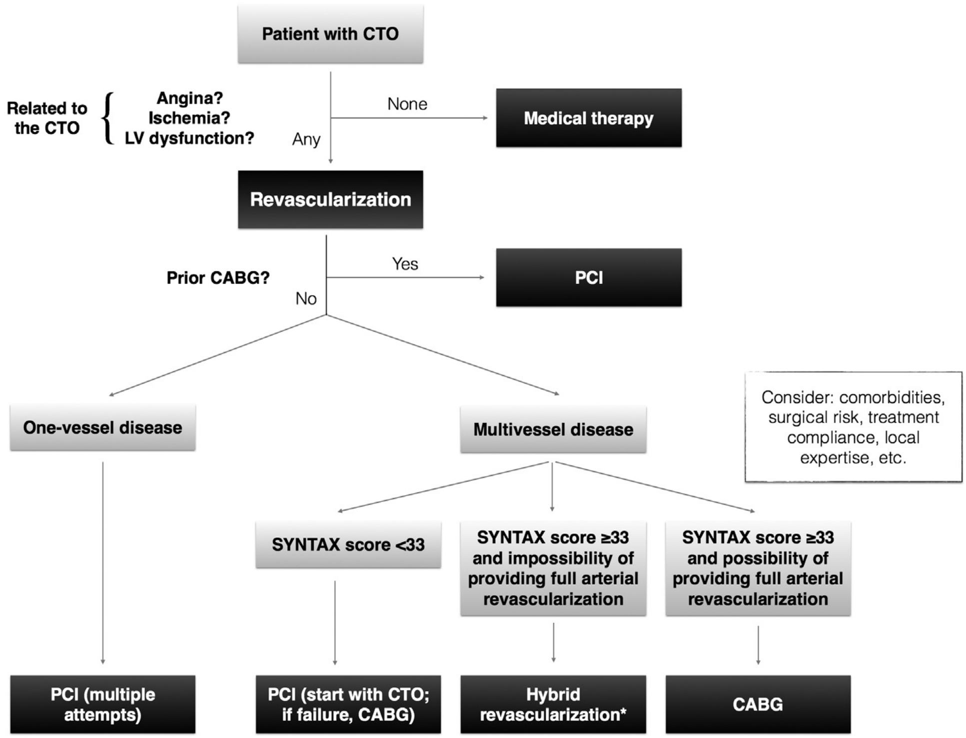

Figure 1. Suggested algorithm to manage patients with chronic total occlusion (CTO). Percutaneous coronary intervention (PCI) should be performed with second-generation drug-eluting stents. *If hybrid revascularization cannot be performed (eg, lack of local expertise), consider conventional coronary artery bypass grafting (CABG). LV, left ventricular; SYNTAX, Synergy Between PCI with Taxus and Cardiac Surgery.

the group without and 39.6% of patients in the group with ≥ 1 preoperative CTO); there were 212 new occluded coronary arteries (1.25 CTOs per patient). Overall, 86.3% of patients had ≥ 1 (either new or pre-existing) CTO at 1-year follow-up. In other words, patients with 3-vessel disease undergoing CABG have a very large burden of CAD at baseline, which progresses even further and more rapidly after surgery, thus leaving only approximately 14% of patients free of CTOs at 1 year after CABG.

After a mean follow-up of 7.3 ± 2.9 years, the composite primary end point of all-cause death, nonfatal myocardial infarction, and repeated revascularization occurred more frequently in patients with ≥ 1 CTO at baseline compared with patients without a preoperative CTO (20% vs 11%; $P =$ 0.048). Preoperative CTO remained an independent predictor of the primary outcome after multivariate analysis (odds ratio, 1.95; $P = 0.028$). Similarly, the primary end point occurred significantly more often in patients in whom a new CTO developed at 1 year after CABG compared with those in whom a new CTO did not develop (21% vs 13%; $P =$ 0.028). Multivariate analysis confirmed development of a new CTO after CABG as an independent predictor of the primary end point (odds ratio, 1.84; $P = 0.025$).

The strengths of the study by Pereg et al.[9] include the quality of trial data, the homogeneous CABG protocol, the multicentre nature of their study, and the availability of 1-year angiographic follow-up data. Limitations include the fact that the RAPS trial was conducted between 1996 and 2001, when modern surgical techniques such as bilateral internal mammary arteries (BIMAs) were not used. Another important limitation is the unavailability of data on the overall preoperative and follow-up CAD burden, such as the SYNTAX score and the CABG-SYNTAX score,[12] which assesses residual CAD burden after CABG, similar to the residual SYNTAX score developed for patients undergoing PCI. Although the SYNTAX score and the residual SYNTAX score have been shown to predict long-term outcomes in patients undergoing PCI,[13,14] there are no such data on CABG cohorts; therefore, Pereg et al. have missed the opportunity of being the first to report such relevant information. Finally, and most importantly, a substudy of a trial still represents observational data (albeit of high quality). Even if a trial on the particular topic dealt with by Pereg et al. in this issue of the *Canadian Journal of Cardiology* is impossible to perform (patients undergoing CABG cannot possibly be randomized to develop a CTO), residual confounders unaccounted for in their analyses can still be present; in other words, the presence of a CTO preoperatively or the development of a new one after CABG might not be the cause for adverse outcomes on follow-up but rather a marker for high-risk patients.

The findings by Pereg et al. have several potentially important implications. Although causality might not be claimed ("CABG caused the development of CTOs"), because patients might have experienced CTOs independent of their post-CABG status, it might be worthwhile to undertake a thorough reflection on whether CABG represents the optimal revascularization modality in certain clinical settings (eg, a SYNTAX score < 33, inability to provide complete arterial revascularization). In fact, the long-term superior patency rates

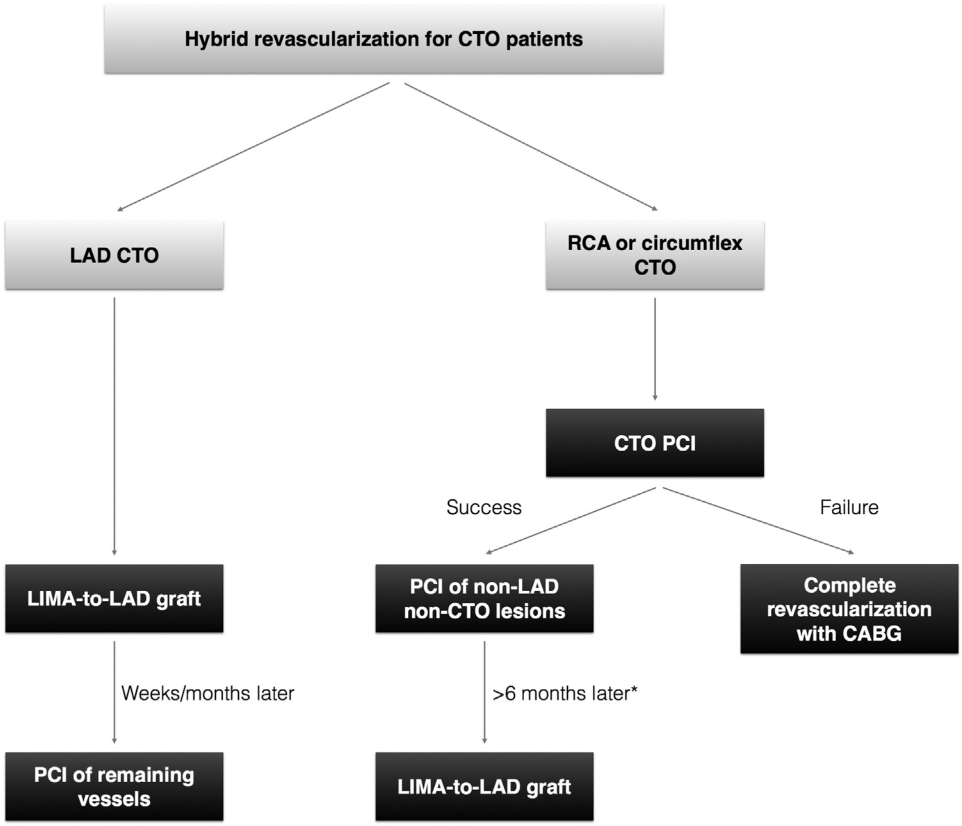

Figure 2. Suggested approach to hybrid revascularization for patients with chronic total occlusion (CTO). In hybrid revascularization, minimally invasive direct coronary artery bypass (MIDCAB) with a left internal mammary artery—to—left anterior descending artery (LIMA-to-LAD) graft is performed, and percutaneous coronary intervention (PCI) is used to treat the circumflex artery or right coronary artery (RCA), or both. An extensive dissertation on hybrid revascularization can be found elsewhere.[16] *Dual antiplatelet therapy should be given for at least 6 months after successful PCI (unless clinically contraindicated; eg, high bleeding risk), and MIDCAB should be performed thereafter.

for CABG conduits, compared with PCI, are ensured only by arterial grafts, because SVGs suffer a higher incidence of failure than do second-generation drug-eluting stents ($\sim$ 30% vs $\sim$ 10% at 5 years).[4,5,15] Additionally, CABG enhances the progression of atherosclerosis and increases the risk for the development of new CTOs in native coronary arteries (incidence of 43.6% at 1 year).[9] As a consequence of these 2 observations, a frequent scenario in clinical practice is a patient with occlusion of both the native vessel and the SVG supplying it (7.5% at 1 year),[11] which undoubtedly complicates a percutaneous attempt at revascularization. Therefore, if full arterial revascularization cannot be guaranteed with CABG (eg, a patient at high risk for on-pump CABG, lack of surgical expertise using BIMAs or radial arteries, or both), PCI or hybrid revascularization might represent reasonable strategies in certain clinical scenarios (Figs. 1 and 2). "Hybrid revascularization aspires to bring together the 'best of both worlds': the excellent patency rates and survival benefits associated with the durable LIMA graft to the LAD,[15] alongside the good patency rates of drug-eluting stents, which outlive SVG to non-LAD vessels."[4,5,16] A recent well-designed (albeit observational) study suggested the benefit of hybrid revascularization over both CABG and PCI in the highest EuroSCORE tertile (> 6) and recommended it over PCI in the highest SYNTAX score tertile (≥ 33).[17]

Since redo CABG surgery is often considered to be high risk in the setting of CABG patients with unrevascularized CTO territories who remain very symptomatic, the only remaining options are intensive medical therapy and CTO PCI. Observational data indicate that medical therapy is inferior to PCI in decreasing the ischemic burden in patients with CTO.[18] Even patients with CTO who have well-developed collateral circulation benefit from revascularization compared with medical therapy, because patients who undergo revascularization have better survival rates on long-term follow-up.[19] Therefore, the only truly effective strategy to manage this important patient population is PCI. The outstanding advances in procedural techniques and devices for CTO PCI that the interventional arena has witnessed in the past decade currently allow success rates > 90%, with very low rates of complications and acceptable procedural efficiency metrics, even when compared with non-CTO PCI.[1] Because primary prevention and revascularization in the setting of acute coronary syndrome are constantly improving, the incidence of native coronary artery CTOs will likely decrease in the future. However, given the high prevalence of patients undergoing CABG and the continuing occurrence of new CABG procedures, surgical revascularization of CAD will create an opportunity (and often the need) for skilled PCI operators to be able to successfully and efficiently open chronically occluded coronary arteries in complex CABG patients. With this perspective, further research on both procedural aspects and outcome data of CTO PCI is eagerly awaited.

Disclosures

The author has no conflicts of interest to disclose.

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