Should Chronic Total Occlusion Be Treated With Coronary Artery Bypass Grafting?

**Chronic Total Occlusion Should Be Treated With Coronary Artery Bypass Grafting**

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Coronary artery chronic total occlusions (CTOs) are an exacerbation of stable coronary artery disease (CAD) with advanced calcification. CTOs are defined as 100% coronary occlusions with Thrombolysis in Myocardial Infarction grade 0 flow persisting for >3 months. National database registries and large single-center series suggest that in patients with CAD the overall incidence of CTOs may vary from 16% to 19% in Japan2 and 29% to 33% in North America,3 making this a common problem globally. Treatment of CTOs should be considered if associated with symptoms or viable/ischemic myocardial territories. Historically, treatments have been via coronary artery bypass grafting (CABG) or medical therapy.3–9

Response by Weintraub and Garratt on p 1817

The use of percutaneous coronary intervention (PCI) to treat CTOs (CTO-PCI) against established practice is controversial.10 This controversy is facilitated by the poor evidence available and by lack of clarity in the European and American guidelines for revascularization, including those for patients with stable CAD.11–15 The lack of robust evidence and the unclear guidelines can lead to ill-defined clinical indications determining serious geographical discrepancies in CTO-PCI medical practice. In a recent report from Japan, >61% of patients diagnosed with CTOs (19% of all CAD patients) were treated with CTO-PCI.2 This is a significant increase compared with a previous report from North America in which only 6% to 9% of all CTOs (29%–33% of all CAD cases) were treated with CTO-PCI (range, 1%–16% by geographical area/center).1 The report by Yamamoto and coworkers2 suggests widespread use of CTO-PCI in patients with multivessel CAD. This is likely to be at the expense of more established treatments such as CABG. The difference in CTO-PCI practice observed between Japan and North America is not easily explained. Contributing factors may be differences in study period, unclear guidelines, misrepresentation of safety/efficacy evidence supporting the use of CTO-PCI, neglect of the evidence supporting more established treatments, gatekeeper effect, and lack of policies by health authorities.

In this article, we provide evidence to support the view that CABG surgery remains the gold standard for the treatment of CTOs in patients with isolated left main stem (LMS) CTOs, left anterior descending (LAD) CTOs, or CTOs in the context of multivessel CAD. In addition, we explore safety and efficacy concerns behind the widespread use of CTO-PCI.

Baseline Determinants of Health Outcome and Decision Making in Patients With CTOs

For patients with CTO, the decision-making process should be based on a meticulous evaluation of the coronary anatomy, the complexity of each patient risk profile, the support of the heart team, the reference to evidence-based medicine, and a fully informed patient.

Clinical and Cardiac-Specific Variability of Patients With CTOs

Patients with CTOs may have a complex risk profile with a higher incidence of diabetes mellitus, multivessel disease

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Coronary Anatomic Variability of CTOs

The anatomic assessment of CAD is based on coronary angiography. However, with CTOs, the affected coronary artery often is poorly seen via retrograde filling from collaterals. This may trigger a degree of uncertainty of its quality and size. Contrast computed tomography, however, may provide information on the severity and distribution of coronary calcification and length of CTOs. Intravascular ultrasound and optical coherence tomography have no diagnostic benefits, although they may be helpful during CTO-PCI. The Canadian Multicentre CTO Registry showed that in only <10% of cases is an isolated CTO lesion outside the LMS, LAD, or MVD CAD context. In particular, the registry showed that 47% of solitary CTOs occur in the right coronary artery, 20% in the LAD, and 16% in the left circumflex; that CTOs in >1 coronary artery were noted in 17% of the cases; and that MVD was present in 76% of patients with CTOs, of whom 7% were afflicted by LMS disease. Similar distributions of CTOs have been reported by other investigators.

The anatomic location of CTOs within each coronary artery can be either the proximal/mid segment or at the mid/distal segment. This may have treatment implications because PCI procedures are in the majority of cases not suitable for distal coronary segments (hence are not able to treat distal CTOs), whereas CABG procedures are generally performed in distal coronary segments and hence are able to treat both proximal and distal CTOs (Figure 1). This is supported by the inclusion criteria of both the Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion (DECISION-CTO) and the European Study on the Utilization of Revascularisation Versus Optimal Medical Treatment for the Treatment of Chronic Total Coronary Occlusion (EuroCTO) trials (clinicaltrials.gov identifiers NCT01078051 and NCT01760083, respectively), which include in their angiographic inclusion criteria a target coronary segment of 2.5 to 3.0 mm, thus clearly excluding patients with distal CTOs. Similarly, the Evaluation of the XIENCE PRIME™ Everolimus Eluting Coronary Stent (Abbott Vascular, Abbott Park, Illinois) pilot trial (clinicaltrials.gov identifier NCT01435031) included in its angiographic inclusion criteria “segment not located in an excessively distal location.” The inclusion/exclusion criteria of these studies suggest that CTO-PCI procedures target CTOs in proximal-mid coronary segments while generally excluding those with distal coronary CTOs.

In addition, the length of CTOs may vary from a few millimeters to >40 mm, with long CTOs often associated with scarred/infarcted myocardium and worse health outcome. Long CTOs may at times affect coronary bifurcations of sizable branches, and this may have implications on which treatment to select to ensure a complete and effective revascularization of both branches.

Pathophysiology of Stable CAD and CTOs

Severe atherosclerotic CAD is associated with endothelial dysfunction affecting the ability to increase blood flow in response to changing metabolic demands, thus leading to myocardial ischemia. Spontaneous rupture of severely stenotic plaques and thrombotic complications often lead to myocardial infarction (MI) and sudden death, although they may also go clinically undetected because of healing of the ruptured plaque. However, MI and acute coronary syndromes more often occur by rupture/thrombosis of mild/moderate plaques, suggesting that “in-plaque” events play a role in sudden death and fatal MI. Hence, methods of coronary revascularization should minimize the chances of additional iatrogenic in-plaque or distal events. Given that CTO-PCIs are in-plaque procedures determining iatrogenic plaque ruptures during prolonged wiring/balloon/stenting, they can lead to acute thrombosis or distal coronary microembolization. Thus, these procedures pose potential safety concerns that need proper investigation.

Evidence Supporting the Use of CABG for the Treatment of CTOs in Patients With LMS Disease, LAD Disease, and MVD

Impact of CABG on Revascularization Rates, Health Outcome, and Graft Patency Rates

Historically, the treatment of CTOs has been assigned to CABG or medical therapy. The superiority of CABG...
surgery over PCI stenting in patients with MVD, LMS disease, or impaired LV function is confirmed by the SYNTAX trial.\textsuperscript{16,17} This evidence-based medicine trial illustrates that treating CTOs with CABG is associated with excellent early and long-term health outcome. Hence, alternative methods of CTO revascularization targeting this type of patients should be compared with CABG surgery as the established standard. Data from the UK National Data Registry\textsuperscript{32} show that for all patients with stable and elective CAD, the use of a left internal mammary artery (LIMA)–LAD graft is at 95%. This is associated with a 30-day mortality of only 1.0% and a postoperative incidence of stroke and reopening for bleeding of 0.9% and 2.9%, respectively. Only 0.2% of patients are reoperated on for revision of grafts problems. Of note, the observed mortality has decreased markedly over time and is consistently lower than the mortality predicted by the logistic EuroSCORE.\textsuperscript{32} In keeping with the outcome of the UK Registry, a study of 21,640 patients from a US registry undergoing CABG with on- or off-pump techniques reported a 2.3% in-hospital mortality rate, 2.1% rate of reoperation for bleeding, 1.5% rate of stroke, and 0.5% rate of perioperative MI.\textsuperscript{33} This outcome was obvious at 12 months for the primary outcome of major adverse cardiac or cerebrovascular events (MACCEs).\textsuperscript{16} The difference became striking at the final 5-year evaluation (MACCEs, 26.9% versus 37.9%; cardiac death, 5.3% versus 9.0%; MI, 3.8% versus 9.7%; and need for repeat revascularization, 13.7% versus 25.9%).\textsuperscript{17} This trial showed that patients with intermediate or high SYNTAX score (many with CTOs) disproportionately benefited from CABG.\textsuperscript{16,17} The 5-year rate of MACCEs of the CABG arm of the SYNTAX trial was low and comparable to the rate of MACCEs observed in the parallel SYNTAX CABG registry (26.9% versus 23.2%, respectively). This is a remarkable finding in that the CABG registry cohort (n=644) included as many as 56.4% of patients with CTOs compared with 22.2% of the CABG arm of the trial. However, the rate of completeness of revascularization was 74.7% versus 63.2%, respectively. This finding also suggests that a rate of CTOs as high as 56.4% in CABG surgery practice does not affect long-term health outcome. This important finding derived from an evidence-based medicine trial establishes a comparative standard for CTO-PCI practice to match. The SYNTAX PCI registry cohort (n=192) included fewer patients with CTOs compared with the CABG registry (36.5% versus 56.4%, respectively) as reflected in a lower SYNTAX score (31.6±12.3 versus 37.8±13.3). However, the completeness of revascularization in this group was much lower at 36.5% compared with 74.7% of the CABG registry cohort. Hence, CABG surgery can achieve a very high rate of completeness of revascularization, regardless of the incidence of CTO lesions and the level of SYNTAX score. This is not the case for PCI. The rate of MACCEs at 5 years between the CABG and PCI registries, both with higher incidence of CTOs compared with the trial cohorts, favored CABG disproportionately (23.2% versus 49.2%, respectively).\textsuperscript{35}

Other studies focusing on patients with CTOs also demonstrate excellent outcomes associated with the use of CABG. Data are available comparing the 2 subsets of CTO patients entered in the SYNTAX trial.\textsuperscript{35} The trial included a total of 543 patients with CTOs (CABG, n=266; PCI, n=277) with similar coronary distributions and SYNTAX scores between these 2 cohorts. The overall success rate for the treatment of CTOs (including cases not attempted) was 68.1% versus 49.4% for CABG versus PCI, respectively. In the CABG subset, 97.8% of CTOs were treated with at least 1 arterial graft. In the PCI subset, the procedure was staged in 20.3% of patients, with the use of an average of 5.0±2.2 stents per patient (range, 8- to 80-mm stents). In these subgroups, health outcome at 12 months showed a significant difference in MACCEs at 12.2% versus 18.9% for CABG versus PCI, respectively.\textsuperscript{16}

Banerjee et al\textsuperscript{35} reported a series of 605 consecutive patients undergoing CABG, of whom 256 patients (42%) had CTOs. All LAD CTOs (27.2% of all CTOs) were bypassed successfully (with LIMA grafts) compared with 92% of the left circumflex and right coronary arteries. Among patients with multiple CTOs (26.2%), 85.2% had all CTO territory bypassed. At 1 year, there was no difference in the incidence of major adverse cardiac events (8.0% versus 7.8%, CTO versus non-CTO group). However, longer CTO length (>40 mm) was associated with higher mortality at 1 year. The need for repeat revascularization (including PCI) was higher in the non-CTO group, although no difference was observed in need for repeat CABG (5.0% versus 5.1%, CTO versus non-CTO group, respectively). Freedom from cardiac death at 1 year was significantly lower in the CTO group (P<0.048). These findings are in keeping with the report by Fefer et al\textsuperscript{16} in a series of 405 consecutive CABG patients, including 174 with a total of 221 CTOs, of which 86% were successfully bypassed (100% LAD CTO bypassed successfully).

**Effectiveness of LIMA-LAD Graft and Long-Term Patency Rates of CABG**

There is evidence in the literature that CTO-PCI is being used extensively in patients with CTO lesions of the LAD alone or in the context of MVD.\textsuperscript{3} This is surprising considering that the patient benefits associated with the LIMA-LAD graft have been transformational, with limited in-hospital risks, improved life expectancy benefits, and very high patency rates (92%–95%) at 15 to 20 years.\textsuperscript{37,38} The benefits of the LIMA-LAD grafts bring into question the reasons for undertaking CTO-PCI of the LAD in symptomatic patients. Confirmatory studies demonstrate improved 10-year actuarial survival rates associated with the use the LIMA conduit as opposed to saphenous vein grafts (SVGs) only, making the pedicled LIMA-LAD graft the dogma of modern coronary surgery. In keeping with these findings, other confirmatory studies suggest that not using an LIMA-LAD graft is associated with an
increased risk of late MI, recurrence of angina, and need for repeat revascularization.37,38 The excellent long-term patency rate of the LIMA-LAD graft is confirmed also for patients with CTO-LAD (Figure 2A and 2C). Holzhey et al39 reported a series of 1800 patients undergoing single LIMA-LAD grafts via a left mini-thoracotomy on the beating heart, of whom 420 had LAD CTOs. In this series, 99.8% of LAD CTOs were grafted successfully. Five-year survival rates were excellent at 90.5% and 90.4% for the CTO and non-CTO group, respectively (P=0.91). In addition, 5-year freedom from MACCEs was 83.2% versus 85.5% for the CTO versus non-CTO group, respectively (P=0.64), whereas CTOs were not found to be predictors of late MACCEs. Accordingly, Di Giammarco and colleagues40 reported 143 patients with isolated LAD CTO treated with LIMA-LAD grafts on the beating heart via a small left anterior thoracotomy. Thirty-day mortality was 0.7%, with no occurrence of MI, cerebrovascular accident, or need for repeat revascularization. One-year survival was 98.6%, with 99.3% freedom from cardiac death, 100% freedom from MI, 99.3% freedom from any form of repeat revascularization, and 97.9% freedom from major adverse cardiac events. In addition, 8-year survival was 94.9%, with freedom from cardiac death of 96.3%, freedom from MI of 99.2%, freedom from any repeat revascularization of 94.4%, and freedom from major adverse cardiac events of 92.8%. At 6 months after surgery, 56% of patients had undergone control angiography with patency rates of 98.2%. Finally, the PRAGUE-4 trial in 400 patients undergoing off-pump coronary surgery showed a patency rate of CTO-LAD grafts of 100% at 1 year.41

CABG Revascularization of CTOs With SVGs One of the arguments against surgical intervention for single-vessel CAD other than LAD disease is the long-term patency rates of SVGs. Historical data on the long-term patency rate of SVGs suggest that ≈50% of these grafts become occluded within 10 years.37,38 This also means that the remaining 50% of SVGs remain patent beyond the 10-year cutoff (Figure 2B). However, more recent reports suggest SVG patency rates as high as >80% at long-term follow-up in some centers, possibly as a result of improved management of postoperative antiplatelet function, refinement of surgical approaches with the use of less invasive SVG harvesting techniques,42 and a better understanding of the mechanisms involved in the development of inflammation and intimal hyperplasia of vein grafts.43-45 For example, the 7-year patency rates of the Beating Heart Against Cardioplegic Arrest Studies (BHACAS) assessed with multislice computed tomography scans showed an overall 89% patency rate in both the on-pump and off-pump groups despite the use of SVGs for ≈75% of grafts.46

Efficacy of CABG for CTOs Affecting Coronary Vessels Other Than the LAD For the rare condition of LMS CTO (0.04%-0.4% of all CTOs), small surgical series have been reported with excellent revascularization rates and late outcome with successful use of LIMA-LAD grafts.47-49 Successful revascularization rates are reported at 80% to 90% for CTOs of the left circumflex artery, with >80% of patients having all multiple CTOs treated successfully and concomitantly.23,36 Fefer et al40 showed that the presence of CTOs was not associated with increased mortality by multivariate analysis. The study also suggested that failure to revascularize a non-LAD CTO was not associated with adverse long-term outcome.

CTOs Requiring Endarterectomy During CABG Occasionally, surgeons have had to deal with complex, distal, and long CTO lesions by performing more invasive procedures such as endarterectomy. Gill et al50 reported a small series of 74 patients undergoing LIMA-LAD in whom 25 patients received endarterectomy to remove the CTO lesion before positioning of the LIMA graft. This approach was associated with a high inotropic requirement in 25% of the patients and a 6.7% incidence of postoperative MI. Unfortunately, this study is too small for any meaningful considerations. However, it is worth noting that the rates of these postoperative complications were unusually high by routine CABG standards while supporting the concept that increased coronary invasiveness is associated with worse cardiac-specific outcome.

Evidence Supporting the Use of PCI Stenting for the Treatment of CTOs in Patients With LMS Disease, LAD Disease, and MVD The use of CTO-PCI is spreading as a result of advances in PCI technologies, including parallel and seesaw wire techniques, balloon anchoring, subintimal tracking and reentry, retrograde approach, contralateral injection, and intravascular ultrasound guidance.51 Claims of PCI efficacy for CTO-PCIs

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Figure 2. A case of multiple chronic total occlusions (CTOs) treated with coronary artery bypass graft surgery in 2002 at our institution. Images are from a coronary angiogram taken in 2015. A, A native left coronary system showing long CTOs involving the left anterior descending artery and diagonal/intermediate branches. B, Patent saphenous vein diagonal/intermediate graft. C, Patent left internal mammary artery–left anterior descending artery graft. Unpublished data.
are based mostly on observational studies comparing successful and failed CTO-PCI recanalizations, with misrepresentation of the iatrogenic effects determined by CTO-PCI in the cohorts suffering failed procedures.

**Comparing Successful and Failed CTO-PCIs: A Fair Tradeoff?**

Comparing successful and failed PCI stent for CTOs does not provide evidence of the efficacy of CTO-PCI compared with other forms of revascularization. Rather, this approach may allow potential safety concerns to be ascertained on the basis of the severity and rates of serious complications observed in the failed CTO-PCI groups. We simply do not know what would have happened to the patients suffering a failed CTO-PCI if they had instead been offered more established treatments such as medical therapy or CABG. Surprisingly, despite the lack of comparisons with real control interventions, the outcome of the successful CTO-PCI procedures is being wrongly marketed as evidence of efficacy. Jones et al reported retrospectively the outcome of 6996 patients treated with PCI stent, of whom 836 (11.9%) had CTOs. The CTO-PCI success rate was suboptimal at 69.6%, with failed CTO-PCIs in 64 of 232 LAD CTOs (28%), 35 of 112 left circumflex CTOs (31%), and 106 of 298 right coronary artery CTOs (35%). These failures triggered a wide range of complications, including coronary dissection, which was much higher in the failed cases (20.5% versus 4.9%: *P* < 0.0001), with 3.1% requiring urgent CABG. Multivariate analysis demonstrated that procedural failure was independently predictive of mortality (hazard ratio, 0.32; 95% confidence interval, 0.18–0.58). In a retrospective study in 621 CTO-PCI patients, Fang et al compared the outcome of PCI stent in 551 LAD CTOs versus 70 ostial LAD CTOs. Ostial LAD CTO-PCIs were more complex and associated with prolonged operative and fluoroscopic time, as well as increased use of contrast volumes. The European outcome of retrograde CTO-PCI procedures was reported by Galassi et al in 1395 patients with 1582 CTOs from 44 European centers. Despite the fact that the procedures were undertaken by skilled and experienced operators, on-table success rates were suboptimal at 70% to 75%. Distribution of CTO-PCI procedures included 70.4% in right coronary arteries, 7.8% in left circumflex arteries, 20.3% in LADs, and 1.5% for combined LMS and bypass grafts. The rate of technical failure was almost 20% for LAD CTOs, accounting for ≈4.5% of all failures. Procedural failures were independent predictors of MACCEs at the long-term follow-up (hazard ratio, 2.48; 95% confidence interval, 1.72–3.57; *P* < 0.001). In addition, there were serious vascular complications in 16 patients, 30 cases of vessel thrombus or dissection, 4 emergency reinterventions, and 2 deaths in the failed CTO-PCI group. The clinical follow-up of about one third of the patients was missing. For the remaining two thirds of patients who were followed up, there were major discrepancies in type and completeness of variables collected, thus providing meaningless information on the late impact of CTO-PCI. Patel et al performed a meta-analysis of 18,061 pooled CTO patients with 18,941 target CTOs. On-table angiographic success was 77%. Early complication rates included MI at 2.5%, coronary perforation at 2.9%, tamponade at 0.3%, and contrast nephropathy at 3.8%. The use of CTO-PCI in the failed group was associated with higher rates of death (0.42% versus 1.54%; *P* < 0.001). Moreover, very few data were presented on late functional evaluations and angiographic patency rates. Galassi et al analyzed data of 905 patients treated for 922 CTOs, including 244 bifurcation CTOs (26.5%). The undertaking of bifurcation CTO-PCI was associated with larger use of contrast load, a higher number of stents, and a higher rate of coronary perforations compared with nonbifurcation procedures (4.9% versus 1.7%; *P* < 0.001), resulting in more tamponades (2.4% versus 0.2%; *P* < 0.001). The EXPERT-CTO study has recently reported 250 CTO-PCI patients from 20 centers treated with a new generation of drug-eluting stent. Although the authors claims that the use of this stent may improve health outcome compared with the results of previous studies, it is fair to maintain that this was only a feasibility/pilot study with no control group and that the potential efficacy of the new stent will need to be ascertained in a proper head-to-head comparison in future trials.

**Late Functional or Angiographic Evidence Supporting the Use of CTO-PCI**

Lack of functional or angiographic data is a consistent issue with CTO-PCI reports in the literature. However, anecdotal cases of early recurrences after CTO-PCI requiring surgical intervention are increasingly being discussed among surgeons (Figure 3A–3D). Valenti and colleagues reported 2 series of CTO-PCI procedures undertaken in 258 and 1005 consecutive patients. On-table recanalization success rates were 81% and 77%, respectively. Six- to 9-month angiographic follow-up was available for 80% of all successful CTO-PCI procedures in both series. This showed an overall incidence of reocclusion or restenosis of >50% in 23.3% and 21% of patients, respectively. This indicates an overall 6- to 9-month procedural failure (on-table failed recanalization plus late reocclusion/restenosis) of 42.3% and 44%, respectively. These angiographic data seem to raise a word of caution on the effectiveness of CTO-PCI. We hope that more robust evidence will soon be available in this area.56,57

One recurrent claim in CTO-PCI retrospective reports is that the procedure leads to improvement in angina symptoms, LV function, and survival.20,21 This is based on the assumption that CTO-PCI increases the blood supply to the ischemic CTO territory (often already supplied by collaterals). However, this assumption remains unsubstantiated. In the Occluded Artery Trial (OAT), 2166 patients with stable CAD with total occlusion of the infarct-related artery 3 to 28 days after MI were randomized to PCI stenting plus optimal medical therapy versus optimal medical therapy alone. This trial did not show any benefit associated with the use of PCI stenting for the composite of death, myocardial infarction, or New York Heart Association class IV heart failure at 4 years (17.2% in
the occluded artery group and 15.6% in the medical therapy group; hazard ratio, 1.16; 95% confidence interval, 0.92–1.45; \( P=0.20 \), and death rates were also similar (9.1% versus 9.4%). Although the total occlusions of OAT were not >3 months after MI and hence probably easier to reopen, it is worth noting that the use of PCI stenting was not superior to medical therapy alone. In the FlowCardia’s Approach to Chronic Total Occlusion Recanalization (FACTOR) Trial,60 125 patients with ischemic myocardium were treated with CTO-PCI. They completed the Seattle Angina Questionnaire at baseline and 1 month after the procedure. At 1 month, in asymptomatic patients, no benefit was associated with the use of CTO-PCI. This finding highlights the limitation of this approach in patients with ischemic myocardium but without angina, for whom a measure of prognostic outcome would be of greater value. In the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, the impact on ischemic myocardium measured by nuclear imaging did not improve the midterm prognosis in the PCI stent group.6 Accordingly, in a meta-analysis of trials in stable CAD patients with ischemic myocardium, Stergiopoulos et al61 highlighted that the use of PCI stent did not improve the observed rates of death, MI, angina, and need for revascularization compared with medical therapy. Similarly, others have suggested that CTO-PCI to LV hibernated/dysfunctional territories leads to only marginal, if any, effect even when a sensitive imaging tool such as magnetic resonance imaging is used.6 However, the evidence of LV impairment triggered by failed CTO-PCIs is of greater concern, given the excessive rate of coronary dissection, perforations, and distal microembolizations reported.62,63

Another argument is that successful CTO-PCIs improve prognosis compared with failed CTO-PCIs. This claim is surprising, given that CTO-PCI is the direct determinant of serious complications in the failed cohorts. One could simply argue the reverse: that CTO-PCIs in fact worsen the prognosis of patients undergoing failed procedures. The argument used by CTO-PCI promoters is based on pooled observations64 and is questionable because retrospective pooled comparisons often cannot take into account key differences in baseline characteristics between pooled groups owing to a lack of or nonhomogeneous data being available. This is supported by the analysis of patients from the Coronary Revascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) Registry (1192 successful CTO-PCIs versus 332 failed CTO-PCIs), which in the presence of homogeneous baseline data available for the entire cohort suggests that at 3 years there is no difference in all-cause mortality between groups.2

Invasiveness of CTO-PCI

CTO-PCIs are very invasive procedures affecting patients at both the systemic and coronary/cardiac-specific levels. They are associated with very long procedural and fluoroscopic times, as well as increased use of contrast volumes and related incidence of renal failure.52–54 Poor tolerance by sedated patients, complex risk profile, and prolonged procedural time are regarded as factors triggering the adoption of general anesthesia instead of sedation.65 The need for significant and
prolonged platelet inhibition after CTO-PCI is not a trivial factor. Evidence suggests that patients with extensive coronary stents undergoing noncardiac surgery early after stenting are at increased risk of major adverse cardiac events, with perioperative mortality rates as high as 85% being reported for different reasons, including stent thrombosis as a result of stopping or changing the antiplatelet regimen.66,67

One of the most concerning aspects of CTO-PCI is its excessive coronary invasiveness, which is unprecedented. This causes serious complications, including coronary perforation, dissections, tamponade, acute thrombotic events, LV impairments, and peripheral vascular injuries. The occurrence of these complications is not surprising and probably should be expected considering the level of coronary invasiveness applied during CTO-PCI, the off-label use of stents designed for non-CTO lesions, the CTO-PCI–related activation of pathophysiological mechanisms triggering acute thrombosis, chronic inflammation, and repeated intracoronary microembolization in the relevant viable myocardial territory, which may impair LV function, in line with the principles of established models of chronic heart failure.68 In a meta-analysis of 18061 pooled CTO patients with 18941 target CTOs, Patel et al55 reported a rate of coronary perforation of 3.65% versus 10.70% in successful versus failed CTO-PCIs (P<0.001), with a related incidence of tamponade of 0% versus 1.65% (P<0.001). These numbers are equal to hundreds of patients suffering poor health outcome caused by CTO-PCI procedures. This is not an isolated observation. Mehran et al62 reported an analysis from the Multi-National CTO Registry in 1791 CTO patients. The rate of serious complications including coronary dissection and perforation were 4.3% and 1.7% in successful and 9.4% and 7.4% in failed CTO-PCI. Of note, the mortality rate of the failed CTO-PCI cohort was not reported. High rates of MI and need for emergency CABG were reported, but deaths after emergency CABG were omitted (to be allocated by intention to treat to the failed CTO-PCI cohort). Excessive rates of serious complications have been reported by Japanese centers. In a series of 1014 CTOs in 943 patients, Kimura69 compared the antegrade (n=733) and retrograde (n=277) approaches. Kimura reported extremely high rates of coronary dissection (14.7% versus 10.1%), perforation (8.2% versus 13%), and distal myocardial embolization (3.7% versus 1.4%) in the antegrade versus retrograde cohorts, respectively.

The goal of CTO-PCI is to position the anastomosis in a health coronary segment distal to the blockage (Figure 4A). Conversely, the goal of CTO-PCI stenting is to perform a variety of “in-blockage procedures,” including complex antegrade/retrograde wiring, high-pressure balloononing, and multiple stenting (ie, leaving behind foreign bodies, continuously triggering in-plaque chronic thrombosis and inflammation) to achieve recanalization (Figure 4B). These technical differences between CABG and CTO-PCI are not trivial and might explain the rates of serious complications reported during CTO-PCI stenting, as well as the higher rates of early recurrence, cardiac-specific complications, and worse late health outcome. Of note, when referred for emergency CABG, patients with failed CTO-PCIs present with rather dramatic findings (Figure 4C) often associated with death or major complications that are unlikely to be retained in the CTO-PCI cohorts of the observational studies available in the literature.62,63,69

**Conclusions**

Available evidence-based medicine findings derived from COURAGE and OAT suggest that in patients with stable CAD or in those with occluded coronary arteries <3 months after MI, the use of PCI stenting is not superior to medical therapy alone. The ongoing DECISION-CTO and the EuroCTO trials will help clarify the impact of CTO-PCI versus medical therapy alone in these patients once completed.

The use of CTO-PCI is spreading quickly worldwide across CABG anatomic categories such as LMS disease, LAD disease, and MVD disease despite the establishment of heart teams and despite strong evidence from large subanalyses of CABG versus PCI stent trials and large database registries supporting the superiority of CABG. The recent evidence-based medicine SYNTAX trial confirms the superiority of
CABG at 1 and 5 years in MACCEs across all the patient categories, including large subsets of CTO patients.

The global promotion of CTO-PCI as an effective procedure across all CAD anatomic categories is of concern because it is based on questionable evidence derived only from comfortable comparisons between successful and failed CTO-PCI procedures with no controls. In fact, these comfortable comparisons suggest that CTO-PCI might be causing significant injury to patients suffering procedural failures. This key safety concern seems to be grossly misrepresented in the available CTO-PCI literature, whereas a disproportionate emphasis on efficacy seems to be based on soft findings such as on-table successful recanalization, which is neither synonymous with improved myocardial perfusion/function nor evidence of late patency. In this context, the undertaking of randomized trials comparing CABG and CTO-PCI in patients with LMS disease, LAD disease, and MVD does not seem to be justified on pure clinical grounds at this stage.

On the basis of the available evidence, we strongly suggest that all patients with CTO be carefully discussed at multidisciplinary heart team meetings that include a balanced professional representation of surgeons and interventional cardiologists, bearing in mind that at this stage for CTO patients with LMS disease, LAD disease, and MVD, CTO-PCI may have a role only for a certain sick populations deemed not to be suitable for CABG.

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Disclosures

None.

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