Revascularization of Chronic Total Occlusions
Time to Reconsider?

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ABSTRACT

Up to 20% of all coronary angiograms reveal coronary chronic total occlusions (CTOs). The lack of robust type A evidence with hard clinical outcomes on the benefits of CTO revascularization has hampered attempts to develop recommendations regarding the optimal management of CTOs. This review presents issues surrounding CTO revascularization within the framework of the appropriate use criteria ratings. Appropriate use criteria ratings downgrade CTO percutaneous coronary intervention revascularization relative to non-CTOs and to surgical revascularization. Specific aspects of CTO revascularization include ischemic burden, impact of revascularization on quality of life, risks in CTO revascularization, and the importance of complete revascularization. Contemporary data suggest CTO revascularization may have substantial impact on patient outcomes; thus, revascularization should likely be held to similar criteria as nonocclusive lesions. However, additional large clinical trial data are required to more definitively determine CTO revascularization guidelines. (J Am Coll Cardiol 2014;64:1281–9) © 2014 by the American College of Cardiology Foundation.

Coronary chronic total occlusions (CTOs), a distinct subset of coronary artery disease (CAD), are defined on invasive angiography as coronary arteries with either absent or minimal antegrade blood flow for >12 weeks duration. In recent years, coronary CTO management has become increasingly important in routine practice and a focus for pre-clinical and clinical research (1–3). This interest is stimulated by the prevalence of CTOs (nearly 20% of all coronary angiograms) (4); yet, there is a paucity of data on how best to manage the need for revascularization and the preferred modality (coronary artery bypass grafting surgery [CABG] or percutaneous coronary intervention [PCI]).

Critics of CTO revascularization generally perceive that symptoms are rare and are easily controlled by medications and that revascularization frequently supplies infarcted left ventricular (LV) myocardium that would not benefit. Empirically, physicians treat CTOs and nonocclusive coronary stenosis differently, evident from relatively low rates of overall revascularization compared with medical therapy and substantially less PCI than CABG. Only approximately 35% of CTOs are currently treated by revascularization (either CABG or PCI) (4). In CTO patients, only about one-third of PCI attempts are directed toward the CTO artery; non-CTO arteries are preferentially targeted (4). In these multivessel CTO patients, surgical revascularization of the CTO artery is variable, with published reports ranging from 69% to 89% (4,5). For CTO patients who had a revascularization strategy recommended, CABG is the mainstay by a nearly 3:1 ratio (4). In contrast, observational studies suggest that approximately 60% of patients with nonocclusive chronic stable ischemic disease undergo revascularization, with PCI as the modality almost twice as often. This review examines the rationale for this distinct treatment of CTO lesions, concentrating...
on 2 key clinical decision points: first, whether to revascularize; and second, which modality. We hope to provide a framework to facilitate discussion between physicians and patients and to improve decision-making for these complex patients.

**REVASCULARIZATION DECISION MAKING IN CAD WITH CTO**

To facilitate clinical decision-making, an expert panel representing the views of major American cardiovascular organizations developed appropriate use criteria (AUC). A formal document outlining 180 clinical scenarios graded by whether revascularization was appropriate, uncertain, or inappropriate was initially published in 2009 (6), and most recently updated in 2012 (7). According to the AUC’s conceptual framework, a revascularization procedure would be considered appropriate if its expected benefits in terms of survival or health outcomes (symptoms, functional status, and/or quality of life [QOL]) exceed its expected risks by a sufficiently wide margin (7). The AUC classifies patients on the basis of symptom severity, findings on pre-procedural stress testing, and anatomic location and extent of coronary stenosis. The only modifier of coronary anatomy included in the current AUC is the lesion being a CTO; other forms of anatomic complexity are not considered. The implicit assumption is that for the same lesion location, symptom severity, and ischemic burden, a CTO differs from a non-CTO, either due to the perceived benefit of revascularization or the harm of the procedure. We will examine this rationale in detail.

There are 2 broad clinical revascularization scenarios involving CTOs: isolated CTOs or multivessel disease.

**ISOLATED (“LONE”) CTO**

Clinical indications 23 to 27 specifically approach single-vessel CTOs, making different recommendations for CTO and nonocclusive lesions (Central Illustration) for the same symptom severity, lesion location, extent of ischemia, and intensity of medications (7). In several scenarios, CTO revascularization is downgraded compared with non-CTO vessels (“uncertain” in CTO from “appropriate” in non-CTO, and “inappropriate” in CTO from “uncertain” in non-CTO), supporting a more conservative approach to revascularization of CTOs relative to non-CTOs. The document does not clearly state why CTO revascularization was discouraged. However, the conceptual framework presented earlier suggests that the rationale is the elevated risk due to the procedure’s complexity, balanced against their uncertain benefits. Several points should inform this decision as to whether CTOs should be considered separately from non-CTOs in revascularization decisions:

**DO PATIENTS WITH CTO HAVE ISCHEMIA?** The AUC heavily emphasize ischemic burden and suggest that revascularization is appropriate in cases with large territories of ischemia, even without symptoms. It is important to dismiss the common misconception that CTOs overwhelmingly supply infarcted myocardial territories not prone to ischemia. In the Canadian CTO registry, LV function was normal (grade 1) in 50% of patients, and only 17% had significantly reduced LV function (grade 3 to 4), with electrocardiographic evidence of infarction in only one-third of patients (4).

The evaluation of myocardial ischemia can be challenging (8); indeed, invasive assessment of ischemia through fractional flow reserve (FFR) is increasingly preferred, given studies showing clinical benefit with revascularization decisions on the basis of FFR results (9). Using FFR, Sachdeva et al. (10) showed that every CTO evaluated in their series was
hemodynamically significant, even in the presence of extensive collateralization and/or with regional LV dysfunction. Furthermore, resting ischemia was present in 78% of CTO patients, evidenced by a resting Pd/Pa < 0.80 (Pd = pressure distal to the lesion, Pa = pressure proximal to the lesion) (10). This finding suggests that, irrespective of location, collaterals, or noninvasive imaging, most CTOs are ischemic.

Percutaneous revascularization of CTOs significantly decreased the ischemic burden (assessed by quantitative noninvasive imaging) from 13.1% to 6.9% (11). The majority of patients had moderate to severe ischemic burden (≥10% ischemic myocardium) at baseline. The risk of future adverse cardiac events, as related to baseline ischemic burden, and clinical benefits of reduced ischemic burden post-revascularization, remains under investigation. A nuclear imaging study in coronary artery patients suggested that there was improved survival following revascularization (PCI or CABG) only in the presence of moderate to severe baseline ischemic burden (≥10% ischemic myocardium) (12). A COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) nuclear substudy also reported significant angina class improvements following percutaneous revascularization in patients with baseline moderate to severe ischemic burden (≥10% ischemic myocardium), with subsequent improvements of >5% (13). Additional studies are required in the specific CTO subgroup.

DO PATIENTS WITH CTO HAVE SYMPTOMS? Clinicians should be aware of several unique features of CTOs. Anecdotal experience suggests that typical anginal chest pain symptoms may be less prominent than shortness of breath; thus, physicians may underestimate symptom severity. Additional evidence pertaining to a CTO’s impact on patient symptoms is provided by studies on patient-reported QOL.

In the past 3 years, several studies reported broad patient improvements in QOL indexes (an important criterion in developing the AUC guideline) following successful CTO revascularization. Three studies compared PCI treatment in CTO, and 1 compared successful CTO revascularization (by either surgery or PCI) to medical therapy (14–17). Beneficial effects of CTO recanalization on QOL included less physical activity limitation (p = 0.01), rarer angina episodes (p < 0.001), and greater treatment satisfaction (p = 0.03) compared with patients with failed procedures (15). Symptoms, function, QOL, and dyspnea improved to the same degree following CTO PCI as following non-CTO PCI (14).

A recent multicenter, prospective cohort study evaluated QOL at 1 year in CTO patients who underwent 1 of the following 4 treatment options: medical therapy, PCI to non-CTO, PCI to CTO, and CABG (17). Medically-treated patients did not improve. Patients with CTO territory revascularization with either PCI or CABG had significant improvements in physical limitation (PCI to CTO: 60.5 to 76.4; CABG: 61.6 to 80.1; p < 0.001), angina frequency (PCI to CTO: 79.0 to 92.7; CABG: 82.1 to 97.9; p < 0.001), and disease perception (PCI to CTO: 50.5 to 75.0; CABG: 50.2 to 80.0; p < 0.001) domains. These studies suggest that CTO patients are often limited by their symptoms and, importantly, experience improvement with revascularization.

CAN CTOs BE RELIABLY OPENED BY PCI? Historically, PCI procedural success for CTOs ranged from 70% to 75% (18). Advanced CTO techniques and equipment, along with increasing operator experience, significantly enhanced success rates of percutaneous CTO revascularization. The Euro CTO club reported an overall procedural success rate of almost 83% in the ERCTO (European Registry of Chronic Total Occlusion) (19). Recent publications suggest that very experienced and expert operators have even higher success rates. Successful percutaneous revascularization at the Toyohashi Heart Center recently increased to 90% from around 80% in 2002. Overall procedural success was achieved in 780 (86.2%) lesions (20). Thompson et al. (21) reported that the success rate of dedicated CTO operators increased to 90% over time (94.4% for retrograde and 85.7% for antegrade approaches). The Multicenter CTO Registry of Japan also reported higher success rates with additional experience: 68.4% to 88.1% in difficult cases, and 42.0% to 78.9% in very difficult cases (22). Similarly, the FAST-CTOs (Facilitated Antegrade

| TABLE 1 CTO Revascularization in Canadian CTO Registry According to Number of Diseased Vessels |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| 1 VD (n = 225)                                | 2 VD (n = 297)                                | 3 VD (n = 1,019)                              | LM (n = 127)                                  |
| Medical                                       | 72                                            | 46                                            | 46                                            | 20                                            |
| PCI                                           | 21                                            | 41                                            | 26                                            | 6                                             |
| CABG                                          | 5                                             | 11                                            | 27                                            | 72                                            |
| PCI + CABG                                    | 2                                             | 2                                             | 1                                             | 2                                             |
| CTO intervention                              |                                               |                                               |                                               |                                               |
| PCI to CTO                                    | 21                                            | 12                                            | 7                                             | 2                                             |
| CABG to CTO                                   | 5                                             | 10                                            | 22                                            | 54                                            |

Values are %.
CABG = coronary artery bypass graft; CTO = chronic total occlusion; LM = left main; PCI = percutaneous coronary intervention; VD = vessel disease.
Steering Technique in Chronic Total Occlusions) trial using the Crossboss catheter and stingray balloon re-entry system (Boston Scientific, Marlborough, Massachusetts) had a 67% success rate in the first 75 CTOs, increasing to 87% in the last 75 (23). It is difficult to know whether these expanded skill sets significantly impact the overall number of CTOs attempted. It is also unclear if the frequency of CTO PCI procedures can substantially increase while remaining the CTO expert’s domain.

**IS A CTO PROCEDURE MORE RISKY?** Lone CTOs are typically addressed by PCI (Table 1). Complication rates are decreasing, although they are higher than non-CTO revascularization. A meta-analysis of 65 CTO PCI studies performed between 2000 and 2011 reported 77% angiographic success, with low periprocedural complication rates: 0.2% death, 2.5% myocardial infarction (MI), 0.1% emergent CABG, <0.01% stroke, and 2.9% coronary perforation, with 0.3% cardiac tamponade (24). Although coronary perforation is a serious PCI complication, occurring more frequently in CTO than in non-CTO PCI procedures, it is relatively rare and generally requires no specific intervention or need for bypass surgery (25).

However, the true complication rates of CTO PCI in routine practice may not be reflected in published reports (predominantly from experienced operators and sites), and may not be representative of lower-volume operators. More complex techniques (e.g., the retrograde approach or subintimal tracking devices) enable successful revascularization in the most complex group of CTOs, but carry an increased risk of complications compared with more conventional anterograde guidewire strategies.

The highly experienced, dedicated European CTO PCI operators who contributed to the ERCTO registry reported a higher complication rate with the retrograde approach. Coronary perforation occurred in 4.7% of procedures, compared with 2.1% in the anterograde approach (p = 0.04). Retrograde approach procedures were longer, with higher fluoroscopy times and larger contrast load administration, and were associated with increased rates of non-Q-wave MI at 30 days, (2.1% vs. 1%; p = 0.08) (19). A meta-analysis of 3,482 patients from 26 studies who underwent a retrograde approach reported an overall success rate of 83.3%, lower than non-CTO PCI. Major adverse cardiac event (MACE) rates (0.7% death, 0.7% urgent CABG, 3.1% MI, and 0.5% stroke) with the retrograde approach were low, although collateral vessel perforations were still common (6.9%), with 4.3% coronary perforation and 1.4% cardiac tamponade (26). Other negative consequences of CTO PCI include increased radiation exposure and high contrast loads related to prolonged procedures.

**SUMMARY OF LONE CTO.** Patients with lone CTO often have atypical, yet functionally limiting, symptoms with substantial ischemia. Recent history suggests that complex PCI procedures have improved success and relatively low risks, albeit still below the levels of non-CTO PCI. The critical caveat to expanding PCI therapy for “appropriate” CTOs is that the primary basis of published statistics is the experience of interventionists with specific CTO training and procedure volumes.

**CTOs IN MULTIVESSEL DISEASE**

CTO is more common in the presence of other significantly-narrowed coronary arteries. In the Canadian CTO Registry (4), multivessel CAD (>50% diameter stenosis) was present in three-fourths of patients with CTOs, and revascularization frequency and modality differed according to the disease’s extent (Table 1). In single-vessel disease, PCI was performed 4-fold more frequently than CABG, although overall CTO revascularization was only 21%. In 2-vessel disease, both CTO revascularization procedures were performed equally (approximately 10% each). For 3-vessel disease (the largest group, accounting for >60% of the registry), CABG was the overwhelming CTO vessel revascularization modality, performed 3-fold more often than PCI (22% vs. 7%). In patients with 2- and 3-vessel disease undergoing percutaneous revascularization, the CTO artery was attempted in only 22% of cases (Table 1). Thus, current clinical practice for percutaneous treatment of multivessel disease (including CTO) is to perform PCI in nonoccluded vessels, leaving the CTO unrevascularized (incomplete revascularization [IR]). We will examine the rationale for CTO revascularization as part of a complete revascularization (CR) strategy.

**CR VERSUS IR.** CR may be defined on the basis of anatomy, extent of ischemia, and other criteria (27). The most accepted definition is simply successful treatment of all major epicardial coronary vessels by a revascularization modality, either bypass surgery or percutaneous revascularization (27). A summary of studies and registries comparing CR and IR can be found in Table 2.

**Surgical versus medical studies.** Many published studies on surgical coronary bypass show the importance of CR for long-term outcome, including survival benefits (28,29). As early as the 1970s, CR was evaluated in the registry of nonrandomized patients treated surgically from CASS (Coronary Artery
Surgery Study), a randomized trial of coronary artery bypass surgery versus medical therapy. Patients with severe angina who underwent CR had improved survival and cardiac events (death, MI, reoperation, and definite angina). The patient subgroup with ejection fraction <35% also showed this survival benefit, even without severe angina (28).

**Surgery versus PCI studies.** The CR rate was consistently and significantly lower in the PCI arms of multivessel trials published in the 1990s. MASS-II (Medicine, Angioplasty, or Surgery Study) was a randomized, controlled clinical trial of medical therapy, PCI, or CABG for multivessel CAD. In the PCI arm, immediate angiographic success was achieved in 92% of patients; however, CR was achieved in only 41% (30). The reason(s) for low CR rates in the PCI arm were not revealed, including CTO prevalence and revascularization. Over the 10-year follow-up, CR was associated with reduced cardiovascular mortality compared with IR, especially due to a greater increase in cardiovascular-specific mortality in PCI-treated patients (31).

Few CTO lesions were included in these comparative studies. In the BARI (Bypass Angioplasty Revascularization Investigation), CTOs were present in 68% of 8,000 patients and were the main angiographic reason patients were deemed unsuitable for PCI (32). Other studies almost completely excluding CTO patients include ARTS (Arterial Revascularization Therapies Study) I and II, in which only 3% of lesions were American Heart Association type C (including CTOs) (33). In the ERACI II (Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients With Multiple Vessel Disease; IR = incomplete revascularization; MACE = major adverse cardiac events; MASS = Medicine, Angioplasty, or Surgery Study; SoS = Stent or Surgery; SYNTAX = Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; other abbreviations as in Table 1).

In the SoS (Stent or Surgery) trial only recruited patients suitable for both PCI and CABG, excluding many CTO cases (35).

CR’s critical importance was reinforced by meta-analysis of CR versus IR in patients with multivessel CAD (36). CR was more often achieved with CABG than with PCI, and was associated with 30% reduction in long-term mortality, 22% reduction in MI, and 26% reduction in repeat coronary revascularization procedures. In these major clinical trials, percutaneous interventions were frequently incomplete due to several factors, but particularly failed CTO revascularization (other factors included a decision to treat only the culprit artery or patient factors such as poor LV function, elevated creatinine, or frailty).

### Table 2: Completeness of Revascularization and CTOs in Multivessel Revascularization Trials and Registries

<table>
<thead>
<tr>
<th>Trial, Years (Ref. #)</th>
<th>Patients, n</th>
<th>Design</th>
<th>CTO in Trial</th>
<th>Impact of CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASS, 1974-1979 (28)</td>
<td>3,372</td>
<td>Registry of nonrandomized surgical cohort</td>
<td>NA</td>
<td>Mortality in patients with either severe angina or ejection fraction &lt;35%</td>
</tr>
<tr>
<td>MASS-II, 1995-2000 (30,31)</td>
<td>611</td>
<td>Randomization to CABG, PCI, or medical therapy</td>
<td>NA</td>
<td>PCI arm: CR in 41%, Cardiovascular mortality in CR. Survival 90.6% in CR vs. 84.4% IR (p = 0.04)</td>
</tr>
<tr>
<td>BARI, 1988-1991 (32)</td>
<td>1,829</td>
<td>Randomization to PCI or CABG</td>
<td>60% excluded due to PCI unsuitability of 8,000 screened</td>
<td>No differences</td>
</tr>
<tr>
<td>ERACI II, 1996-1998 (34)</td>
<td>450</td>
<td>Randomization to PCI or CABG</td>
<td>PCI not attempted in CTOs (23.4%)</td>
<td>No data on CR. CR in high and intermediate syntax scores. CR with CABG. Cardiac mortality with high syntax score at 1 yr and intermediate at 3 yrs</td>
</tr>
<tr>
<td>SoS, 1996-1999 (35)</td>
<td>988</td>
<td>Randomization to PCI or CABG</td>
<td>CTOs excluded from trial</td>
<td>No data on CR. Mortality in CABG compared with PCI (6.8% vs.10.9%)</td>
</tr>
<tr>
<td>SYNTAX, 2005-2007 (37,39,40)</td>
<td>1,800</td>
<td>3-vessel disease or left main disease; randomization to PCI or CABG</td>
<td>23%</td>
<td>CR in high and intermediate syntax scores. CR with CABG. Cardiac mortality with high syntax score at 1 yr and intermediate at 3 yrs</td>
</tr>
<tr>
<td>New York State PCI Reporting System, 1997-2000 (43)</td>
<td>21,945</td>
<td>PCI registry</td>
<td>NA</td>
<td>Mortality (adjusted hazard ratio: 1.35) in IR patients compared with CR in the presence of either a single IR CTO or ≥2 IR vessels</td>
</tr>
</tbody>
</table>
The SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial randomized 1,800 patients with either 3-vessel or left main disease to bypass surgery or PCI. CTOs were common, with an overall 23% prevalence in SYNTAX study patients (37). In the SYNTAX trial, coronary anatomy complexity on diagnostic angiograms was graded by a Syntax score algorithm (38), with patients divided into high-, intermediate-, or low-score groups. The Syntax score highly depended on the presence and specific features of CTO, with a single CTO contributing a substantial 10 to 15 points. Although relatively low in both treatment groups, successful CTO revascularization was much higher in bypass surgery (69%) than PCI (49%), possibly contributing to differences in MACE including mortality between the 2 revascularization strategies (5).

The most common reason for not achieving CR with PCI was the presence of a CTO (odds ratio: 2.46, 95% confidence interval: 1.66 to 3.64; p < 0.001) (39). Generally, the Syntax score, a surrogate marker for disease complexity, was higher in IR than in CR patients (31.4 ± 11 vs. 26.2 ± 10; p < 0.01) (39). Thus, CTO lesions were over-represented in the high Syntax score group, with vastly inferior revascularization success rates in the PCI group. Indeed, procedural success of CTO revascularization with PCI in the SYNTAX study was <50%, highlighting insufficient CTO operator expertise for these complex lesions. In contrast, PCI or CABG procedural success rates in patients with lower SYNTAX scores were very similar, with minor outcome differences between the 2 modalities. MACE (death, cerebrovascular accident, MI, repeat revascularization) and even cardiac mortality were significantly worse in PCI patients with a high Syntax score (>32 points). These differences were evident at the 1-year data analysis and were even more pronounced at 3 years (including the intermediate Syntax score of 23 to 32 points) (40).

Residual Syntax score is derived from the extent and complexity of residual coronary disease after PCI, and represents an assessment of completeness of revascularization. In the SYNTAX trial, a residual Syntax score >8 significantly increased mortality (35.3%) at 5 years (41). More recently, Syntax scoring for predicting IR rates and clinical outcomes was used in a reanalysis of 2,686 angiograms from ACUITY (Acute Catheterization and Urgent Intervention Triage strategy) trial PCI patients (42). CR’s importance was again supported by higher 1-year ischemic event rates in the IR group compared with the CR group, particularly with a high residual Syntax score. These data reinforce the potential importance of CR, with CTO as the major barrier.

**PCI registries.** The New York State Percutaneous Coronary Intervention Reporting System provided additional evidence supporting CTO revascularization as key to achieving CR (43). Hannan et al. (43) subdivided 22,000 patients with multivessel disease undergoing revascularization by PCI into CR (31%) and IR (69%). Mortality was significantly increased (adjusted hazard ratio: 1.35) in IR patients compared with CR in the presence of either a single IR CTO or ≥2 IR vessels (43). A PCI registry study using the large APPROACH (Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease) database similarly showed the association of CTOs with IR and a reduction in death and need for future bypass surgery in patients with CR compared with IR (44).

**VIABILITY IN MULTIVESSEL DISEASE.** Patients with multivessel disease often have LV dysfunction, in some cases remaining viable, and thus potentially reversible (45). The term hibernating myocardium describes “a state of myocardial hypocontractility during chronic hypoperfusion, in the presence of completely viable myocardium which recovers functionally upon revascularization” (46). Hibernating myocardium is associated with LV dimension and shape alterations that significantly revert after revascularization (47). Accordingly, viability testing utilizing a variety of imaging techniques, including dobutamine stress echocardiography, single-photon emission computed tomography nuclear scintigraphy, contrast-enhanced cardiac magnetic resonance (CMR), and positron emission tomography, is crucial for evaluating the potential revascularization treatment benefit (48,49). Several studies showed beneficial effects of CTO revascularization on abnormal LV geometry and function if the CTO artery supplies viable myocardium (50,51). CTO revascularization benefits were related to the transmural extent of infarction; PCI only improved segmental contractility in areas where transmural extent of infarction was <75%, with no effect with higher extent of infarction (52). These beneficial effects were observed up to 3 years after recanalization (53,54). No data specifically address the relationship between viability and clinical outcomes in CTO patients; however, several small observational studies and 2 randomized trials addressed this question (55-58). In a study of 144 patients with CAD and LV dysfunction by CMR, survival was improved in patients with viable myocardium that was subsequently revascularized, compared with nonrevascularized patients. There was no significant difference in survival in patients with nonviable myocardium, irrespective of revascularization (59).
Interestingly, 2 randomized controlled surgical trials—PARR-2 (PET and Recovery Following Revascularization Phase 2) using positron emission tomography imaging and the STICH (Surgical Treatment for Ischemic Heart Failure) Viability Substudy using thallium scintigraphy—showed no significant effects of viability assessment on clinical outcomes following revascularization (57,58). However, their interpretation is challenged by significant methodological flaws, including low adherence to image-guided recommendations, baseline patient differences, post-hoc subgroup analyses, revascularization not guided by the presence of viable myocardium, and small size of the nonviable myocardium group (60). Further studies are essential to provide reliable data for assessing the requirement for viability testing in patients with LV dysfunction to guide revascularization strategies, particularly in CTOs.

**AUC AND CTO IN MULTIVESSEL DISEASE.** The AUC for coronary revascularization 2012 update highlights CTOs as important contributors to “intermediate to high” CAD burden in patients with 3-vessel disease. The AUC differentiates the revascularization modality for CTOs in the setting of multivessel disease, with an AUC rating of “appropriate” for surgical revascularization and “uncertain” for PCI (and, in LM + 3-vessel disease, “appropriate” for CABG and “inappropriate” for PCI) (7). This reflects the fact that successful PCI performance in CTO is difficult for most PCI physicians. However, procedural success and safety highly depend upon the operator’s experience; thus, this rating should be interpreted in the context of whether a CTO expert performed the procedure.

**THE FUTURE OF CTO REvascularization**

Many studies and several meta-analyses compared patient outcomes with successful and failed PCI CTO, consistently finding improved outcomes with successful procedures. Khan et al. (61) evaluated 23 observational studies comparing clinical outcomes between patients with successful CTO recanalization and those managed conservatively as a result of failed PCI. Successful CTO PCI was significantly associated with improved all-cause mortality (relative risk: 0.54), and lower MACE rates (relative risk: 0.70) (61). Similarly, a meta-analysis of 13 observational studies found that, compared with unsuccessful PCI, successful PCI is associated with improved mortality and reduced need for CABG (62). These studies (and the majority of studies cited in this review) are observational and are thus prone to confounding. There is a lack of robust type A evidence with hard clinical outcomes on the benefits of CTO revascularization. Several trials expected to advance these discussions are currently underway or in advanced planning stages. The EXPLORE (Evaluating Xience V and LV function in Percutaneous coronary intervention on occlLusiOns afteR ST-Elevation myocardial infarction) trial, a randomized study in the final enrollment stages, addresses whether revascularization of a CTO nonculprit artery in patients presenting with ST-segment elevation MI will be beneficial for LV function at 4 months. DECISION-CTO (Drug-Eluting Stent Implantation versus Optimal Medical Treatment in Patients with Chronic Total Occlusion) is a randomized trial to compare the long-term (3-year) outcome of drug-eluting stent implantation with optimal medical treatment. EURO-CTO (European Study on the Utilization of Revascularization vs. Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions) is a multicenter trial to evaluate 1- and 3-year outcomes and assess QOL in patients randomized to revascularization or optimal medical therapy.

**CONCLUSIONS**

The therapeutic nihilism often associated with revascularization in CTO has been plagued by misconceptions as to the degree of symptoms and ischemia caused, and the potential benefit of revascularization. Over the last few years, evidence is increasing that CTO lesions have substantial impact and should be held to similar criteria as nonocclusive lesions. We are optimistic that new studies with compelling data will assist clinicians and the AUC guidelines writing groups to more judiciously determine CTO revascularization indications.

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