

## Management of Coronary Chronic Total Occlusion

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A 67-year-old man with chronic stable angina presented with worsening angina to class III despite maximal medical therapy. He was referred for myocardial perfusion imaging, which showed a large area of inferior ischemia. Subsequent coronary angiography revealed a chronic total occlusion (CTO) of the right coronary artery with brisk collateral flow from the left anterior descending artery (Figure 1). There was minimal obstructive disease in the remainder of the coronary tree. An attempt at percutaneous coronary intervention (PCI) was unsuccessful. He was treated with continuation of his medical therapy, although he remained with lifestyle-limiting class II to III angina.

### Chronic Total Occlusion: Definition, Incidence, and Presentation

Coronary CTO is characterized by heavy atherosclerotic plaque burden within the artery, resulting in complete (or nearly complete) occlusion of the vessel. Although the duration of the occlusion is difficult to determine on clinical grounds, a total occlusion must be present for at least 3 months to be considered a true CTO.<sup>1</sup> Patients with

CTO typically have collateralization of the distal vessel on coronary angiography, but these collaterals may not provide sufficient blood flow to the myocardial bed, resulting in ischemia and anginal symptoms. CTO is clinically distinct from acute coronary occlusion, which occurs in the setting of ST-segment–elevation myocardial infarction, or subacute coronary occlusion, discovered with delayed presentation after ST-segment–elevation myocardial infarction. Clinical features and treatment considerations of these entities differ considerably from CTO.

Among patients who have a clinical indication for coronary angiography, the incidence of CTO has been reported to be as high as 15% to 30%.<sup>2,3</sup> Patients with CTO are referred for angiography because of anginal symptoms or significant ischemia on noninvasive ischemia testing. Patients who are symptomatic will have stable exertional angina resulting from a limitation of collateral vessel flow to meet myocardial oxygen demand with stress. Of patients referred for PCI in clinical trials of CTO PCI, only 10% to 15% of patients are asymptomatic. It is likewise uncommon for patients with CTO to present with an acute coronary syndrome caused by the CTO itself.<sup>4–6</sup>

### Treatment Options for Patients With Chronic Total Occlusion

The mode of treatment selected for a patient with CTO is individualized on the basis of the severity of symptoms and ischemia and on the severity of concomitant coronary artery disease (CAD). As with any patient with stable CAD, treatment should include anti-anginal therapy and therapies to promote vascular health. Patients who remain symptomatic or have a large burden of ischemia despite maximal medical therapy can be considered for revascularization.

Choosing the better revascularization mode, PCI or coronary artery bypass grafting surgery (CABG), is not always simple. For patients with CTO and significant concomitant left main and/or multivessel CAD, CABG is often chosen, given the complexities involved with PCI in this setting and the greater likelihood of achieving complete revascularization compared with PCI. The Synergy between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial showed that in patients with multivessel CAD, there were no major differences in death and myocardial

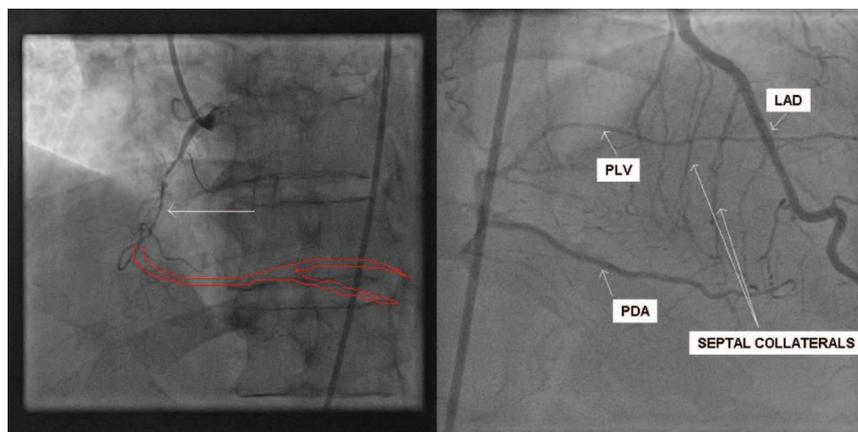
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**Figure 1.** Left, The totally occluded right coronary artery with the expected course of the distal vessel outlined in red and the total occlusion shown by the arrow. Right, Collateralization of the right coronary artery from the left anterior descending (LAD) artery with arrows pointing to the posterior descending artery (PDA) and posterolateral ventricular (PLV) branches of the right coronary artery. The septal collaterals from the LAD to RCA are highlighted.

infarction between patients treated with PCI and those treated with CABG; however, PCI patients were more likely to require repeat revascularization procedures in follow-up, particularly those patients with more complex CAD manifested by a high SYNTAX score.<sup>7</sup> Chronic total occlusion is a major contributor to a high SYNTAX score.

Although the revascularization decision is more straightforward in patients with CTO and left main/multivessel CAD, patients with symptomatic isolated CTO represent a challenging patient subset in which to make revascularization decisions. Medical treatment may not be sufficient to relieve symptoms or to improve long-term outcomes, and CABG may be deemed too invasive for single-vessel disease. Therefore, most patients will be referred for PCI.

### Reasons to Consider Chronic Total Occlusion Percutaneous Coronary Intervention

Three possible benefits of CTO PCI are improvement in symptoms, improvement in left ventricular (LV) function, and improvement in survival. If collateral insufficiency is the cause of angina in patients with collateralized CTO, it stands to reason that restoration of antegrade flow in the

occluded vessel will relieve angina. In a recent meta-analysis of 6 observational studies comparing recurrent angina events in patients undergoing successful CTO PCI and those undergoing unsuccessful CTO PCI, Joyal et al<sup>8</sup> showed that patients undergoing successful PCI had a significant reduction in recurrent angina during a 6-year follow-up compared with patients undergoing unsuccessful PCI (odds ratio, 0.45; 95% confidence interval, 0.30 to 0.67).

In patients with LV dysfunction in a viable territory subtended by a CTO, successful CTO PCI may improve overall LV function. Two recent studies using cardiac magnetic resonance imaging have shown significant improvements in LV end-systolic volume, LV end-diastolic volume, and fractional shortening at 5 months and later after successful CTO PCI.<sup>9,10</sup> The benefits were greater in patients with viable myocardium subtended by the CTO.

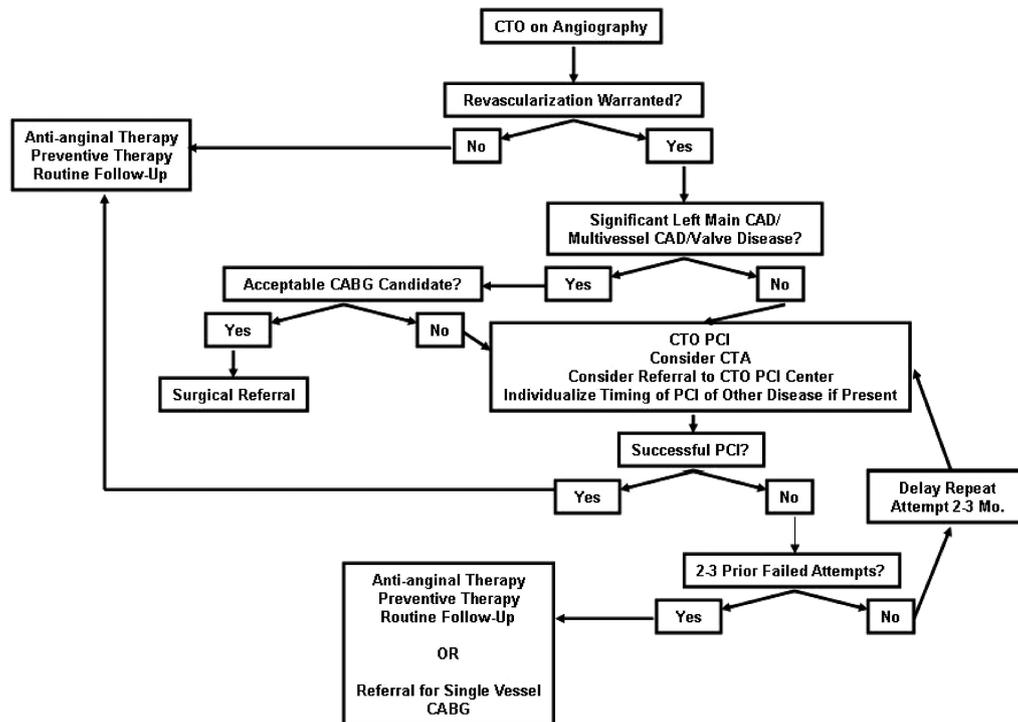
Several observational studies suggest that these improvements in LV function may result in improved long-term survival. In the Joyal et al<sup>8</sup> meta-analysis of 13 observational studies comparing mortality in patients undergoing successful CTO PCI and patients undergoing unsuccessful CTO PCI, mortality was significantly reduced in the successful PCI group during an

average follow-up of 6 years (14.3% versus 17.5%; odds ratio, 0.56; 95% confidence interval, 0.43 to 0.72).<sup>8</sup> It is important to note that there is no randomized trial comparing CTO PCI with medical therapy. The influence of confounding on these observational data must be considered.

### Limitations of Percutaneous Coronary Intervention for Chronic Total Occlusion

Despite these potential benefits, the attempt rates for CTO PCI are significantly lower than attempt rates for PCI for other lesion subsets. A review of the National Heart, Lung, and Blood Institute's Dynamic Registry has shown a decrease in the attempt rate of PCI for CTO from 1997 to 1998 to 2004 (9.6% versus 5.7%;  $P < 0.0001$  for trend).<sup>11</sup> Before SYNTAX, one of the major angiographic exclusions for consideration in clinical trials of PCI versus CABG for multivessel CAD was the presence of a CTO, which usually led to referral for CABG.

Historically low PCI success rates, increased complexity of CTO procedures, and the potential for important complications are major limitations of CTO PCI that account for low PCI attempt rates. In a single-center multi-decade review from the Mayo Clinic, the procedural success rate for CTO PCI between 1979 and 1989 was 51%.<sup>12</sup> With the introduction of coronary stents, success rates increased to  $\approx 70\%$ , and this rate has been consistent across several studies.<sup>11-13</sup> However, this rate is still far below the expected 97% angiographic success rate for PCI in non-CTO lesions.<sup>11</sup> The lower-than-normal success rate for CTO PCI indicates that CTO PCI is the most challenging lesion subset to treat in coronary interventional practice. Because of heavy atherosclerotic plaque burden, inability to see the course of the vessel at the site of occlusion, and often longer length of lesions, reliably crossing a CTO with a coronary guidewire is difficult and is the most common reason for failure of CTO PCI.<sup>14</sup> Even with successful wire



**Figure 2.** Suggested management algorithm for a patient with coronary chronic total occlusion (CTO). CAD indicates coronary artery disease; PCI, percutaneous coronary intervention; CTA, computed tomographic angiography; and CABG, coronary artery bypass graft surgery.

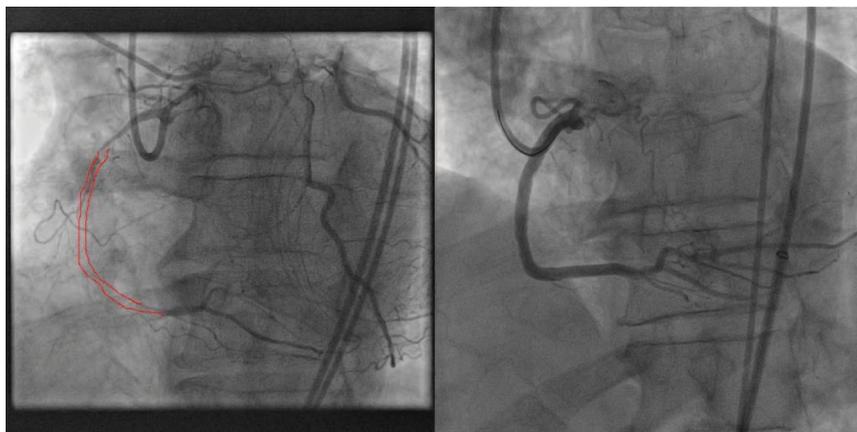
crossing, delivery of coronary balloons and stents into these fibrotic, calcific lesions can be difficult.

Percutaneous coronary intervention for CTO is also associated with a significant use of catheterization laboratory resources, with procedure times and fluoroscopic times being twice as long as those for PCI for non-CTO lesions.<sup>15</sup> Chronic total occlusion PCI can lead to inefficient use of catheterization laboratory personnel and physician time, which can reduce patient flow through the laboratory. Additionally, the amount of equipment necessary for successful completion of the procedure can be greater than for standard PCI, because physicians will often require multiple guiding catheters, coronary guidewires, lesion crossing devices, and stents to complete the procedures. For many physicians and laboratories, this increase in resource use may be difficult to justify for a procedure that has reduced success rates, perhaps influencing the decision to treat these patients with medical therapy or to refer for CABG.

Several significant complications are associated with CTO PCI that are not seen as frequently with PCI for other lesion subsets, which further limits the enthusiasm for CTO PCI for many operators. Because procedures are longer, the potential for radiation dermal injury and contrast-induced renal dysfunction must be considered. Chronic total occlusion PCI also carries a significant risk for vessel dissection because aggressive coronary guidewires are advanced into vascular spaces that cannot be visualized on fluoroscopy. Severe dissections can result in vessel perforation and tamponade. If the vessel distal to the occlusion is reliant on antegrade collaterals, disruption of these collaterals can result in significant ischemia and periprocedural infarction. An experienced CTO PCI center in Japan recently reported in-hospital complication rates of 0.5% for death, 3% for myocardial infarction, 0.2% for emergency CABG, and 0.6% for tamponade.<sup>16</sup> Although these rates are excellent, they may not reflect the rates at less experienced centers.

### Improving Outcomes for Chronic Total Occlusion Percutaneous Coronary Intervention

Advances in the use of coronary imaging, interventional devices, and novel interventional techniques hold promise for improving the success rates of CTO PCI. Patients referred for CTO PCI are now often referred for preprocedural computed tomographic angiography. Unlike cine angiography, computed tomographic angiography can image the course of the vessel and length of the occlusion. Newer-generation catheterization laboratory imaging equipment allows the simultaneous use of computed tomographic angiographic data and cine angiographic data. This facilitates the use of guidewire to traverse the occlusion. Additionally, intracoronary imaging with intravascular ultrasound is routinely being used to identify entry channels into CTO lesions and to improve the ability to redirect coronary guidewires from dissection planes into the true vessel lumen.



**Figure 3.** Left, A simultaneous angiogram of the left and right coronary systems. The entire length of the chronic total occlusion can be visualized and is outlined in red. Right, The final result after treatment with drug-eluting stents.

Advances in coronary guidewire technology allow more facile crossing of CTO lesions. Coronary guidewires are now available with hydrophilic coatings and lower-profile tips. This permits wires to find microchannels within the CTO that may allow access to the distal vessel. Wires have also been developed that have more support at the wire tip, improving torque control of the tip for the operator and providing a greater ability to push the wire tip through coronary occlusions with minimal alteration or deflection of the tip.

Experienced operators are now using novel interventional techniques for CTO PCI to improve crossing success. It is now routine for operators to engage both the left main coronary artery and the right coronary artery with 2 catheters to perform simultaneous injections and angiography of the entire coronary tree. In doing so, the occluded vessel and the collaterals to the distal vessel can be imaged together. This approach facilitates the direction of guidewires into the distal vessel. Additionally, operators have now gained expertise at using collaterals as a means of accessing the total occlusion in a retrograde fashion. A coronary guidewire can be passed from the collateralizing vessel into the collateral and directed to the distal portion of the CTO. The distal portion of the CTO is often easier to cross than the proximal

portion and may be an easier entry point to cross the lesion. Once the retrograde wire is advanced into the proximal occluded vessel, a variety of techniques can be used to dilate the lesion in either a retrograde or an antero-gradate fashion.

### The Importance of Operator and Center Experience

Consideration should be given to referral of patients for CTO PCI (particularly after a failed prior PCI attempt) to centers that have operators with specific expertise in CTO PCI. Operator volumes in CTO PCI significantly affect success rates. In a recent analysis by Thompson et al,<sup>17</sup> high-volume CTO operators had a significantly higher PCI success rate than low-volume CTO operators (75.2% versus 58.9%;  $P < 0.001$ ) when using retrograde access techniques.

In addition to skilled operators, it is imperative that such centers have the catheterization laboratory resources to perform these complex cases. Specifically, a dedicated support staff is necessary to ensure familiarity with infrequently used devices and to assist in the recognition and management of the unique complications that occur with these cases. Additionally, the laboratory should have the capacity to perform potentially lengthy cases in the time period necessary to obtain a successful

outcome without impeding routine patient flow within the laboratory.

### Suggested Approach to the Management of Chronic Total Occlusion

Figure 2 shows a suggested algorithm for management of patients with CTO. Patients with limited ischemia and minimal symptoms can be managed medically. However, those with significant ischemia or symptoms despite maximal medical therapy warrant consideration for revascularization. The initial decision regarding mode of revascularization should be based on the severity of concomitant CAD. If there is enough coronary disease to consider surgery and if the patient is a reasonable candidate for surgery, CABG is a reasonable option. If the concomitant coronary disease does not warrant CABG, consideration should be given to PCI. Failure of an initial attempt at PCI should not prevent consideration for future repeat attempts, because alternative techniques may be used on subsequent attempts that may lead to a successful result.

### Case

Because of continued limiting symptoms, the patient was referred for repeat attempt at PCI of the CTO of the right coronary artery in 2009. Bilateral femoral access was used to perform simultaneous angiography of the left and right coronary artery systems, which provided visualization of the entire length of occlusion (Figure 3). The lesion was ultimately crossed with specialized CTO coronary guidewires. A low-profile coronary balloon was delivered through the lesion to dilate the lesion. Three overlapping 3.5-mm drug-eluting stents were placed, resulting in an excellent final angiographic result (Figure 3). The patient remains free of angina 10 months after the procedure.

### Disclosures

None.

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