

# Management of coronary chronic total occlusion

## ABSTRACT

Percutaneous coronary intervention (PCI) for coronary artery chronic total occlusion (CTO) is an important treatment to be used in conjunction with non-CTO PCI, coronary artery bypass grafting, and optimal medical therapy to achieve complete revascularization in patients with coronary artery disease.

## KEY POINTS

Coronary CTO is not benign and is associated with ischemic burden.

There is a threshold of ischemic burden at which revascularization is superior to optimal medical therapy.

Revascularization based on physiology rather than angiography can produce superior clinical results.

CTO PCI procedures are technically demanding and heavily operator-dependent in order to achieve high success rates at an acceptably low complication rate.

In patients with stable coronary artery disease (CAD), the cornerstone of treatment is medical management to control symptoms such as angina and dyspnea on exertion. But in a select group of patients, percutaneous coronary intervention (PCI) is indicated in addition to medical management. Invasive and noninvasive hemodynamic assessments of coronary artery stenosis in conjunction with anatomic considerations play a role in decision-making and in advising patients on revascularization vs medical management. However, in the case of coronary artery chronic total occlusion (CTO), the decision-making process remains challenging due to limited evidence supporting clinical efficacy of CTO PCI, as well as practical considerations including lower success rates and higher complication rates in comparison with patent-vessel PCI.

## CLINICAL VIGNETTE

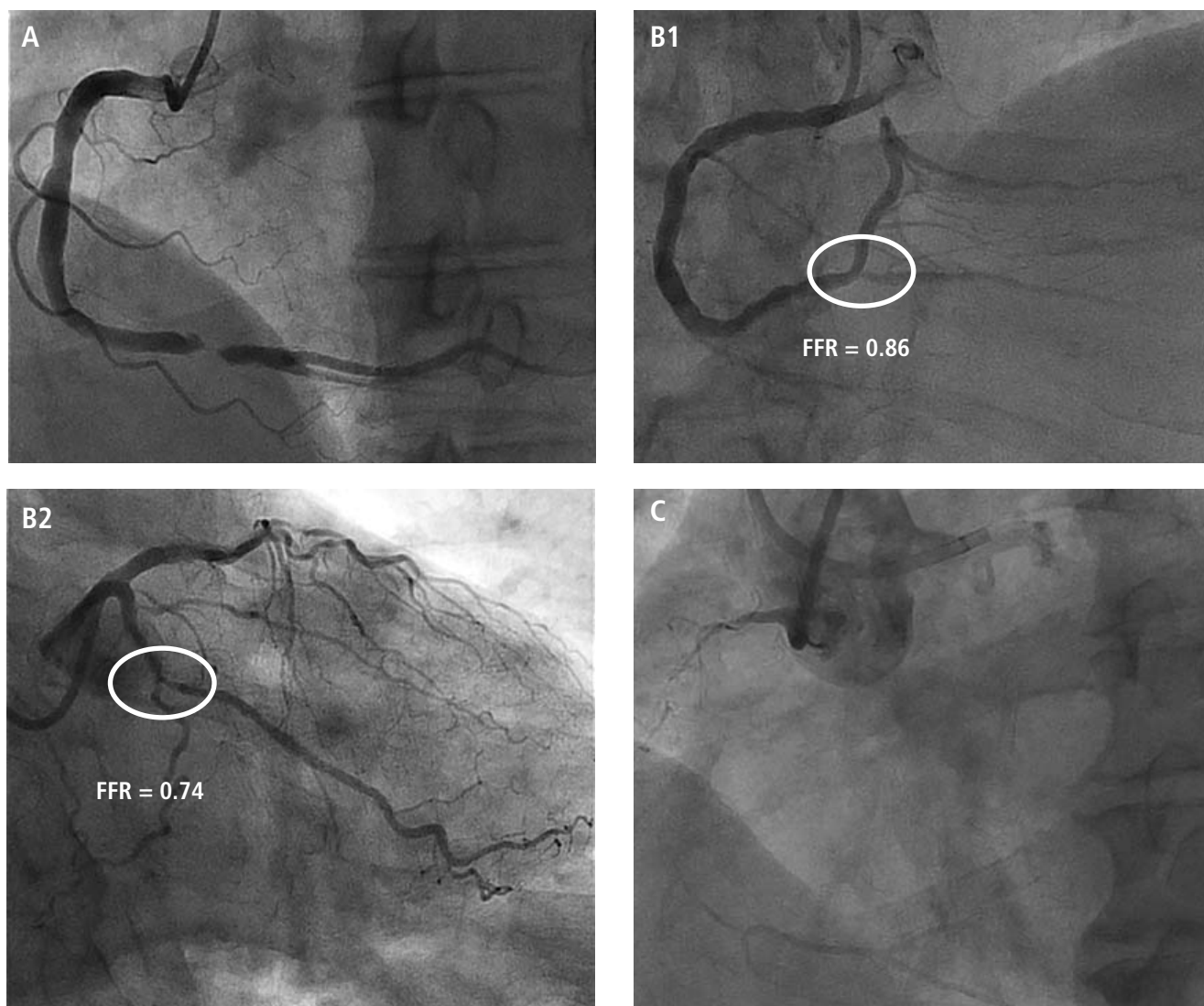
A 42-year-old man, an avid runner with hyperlipidemia and a strong family history of premature CAD, presents with several months of declining exercise tolerance. His physical examination and electrocardiogram are unremarkable. Myocardial perfusion imaging shows stress-induced ischemia affecting about 20% of the inferolateral myocardium. He is then referred for coronary angiography.

Confidence in the appropriate treatment strategy is highly dependent on potential angiographic findings. All 3 of the following coronary angiograms could explain our patient's clinical presentation (Figure 1):

- Panel A: Discrete, high-grade stenosis of the mid-right coronary artery
- Panel B: Diffuse, multivessel disease involving the distal right coronary artery (B1) and the proximal left circumflex coronary artery (B2)
- Panel C: Total occlusion of the proximal right coronary artery with extensive left-to-right collaterals.

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**Figure 1.** Results of angiography. (A) Discrete, high-grade mid-right coronary artery stenosis corresponds to abnormal stress test results and is appropriate for coronary intervention to treat the patient's symptoms. (B) Diffuse multivessel disease involves the distal right coronary artery (B1) as well as the proximal left circumflex coronary artery (B2). Based on fractional flow reserve (FFR), the left circumflex coronary artery lesion is hemodynamically significant and is thus an appropriate target for coronary intervention. Conversely, the right coronary artery lesion is not hemodynamically significant and can be managed medically. (C) Angiography shows total occlusion of the proximal right coronary artery with extensive left-to-right collaterals provided by the left coronary artery.

## Treatment based on angiographic findings

In panel A, there is little to debate. The patient is likely to benefit from percutaneous revascularization of the right coronary artery to treat symptoms.

In panels B1 and B2, there is abundant evidence that the hemodynamic assessment of stenosis is superior to a visual estimate in directing PCI.<sup>1,2</sup> Hemodynamic assessments including fractional flow reserve (FFR) inform the risk-benefit analysis of percutaneous vs medical treatment of coronary stenosis. In the case of FFR, 0.8 represents an inflection point. The lower FFR

values are below 0.8, the greater the benefit of PCI as opposed to medical therapy. Conversely, the greater FFR values are above 0.8, the greater the benefit of medical therapy as opposed to PCI.

However, in panel C, there is significant variability in the data supporting the best treatment strategy for symptomatic patients with CTO.

## CORONARY CTO

Coronary CTO is defined as TIMI 0 flow for more than 3 months in an epicardial coronary artery. CTO

is not uncommon, seen on 30% of routine coronary angiograms. In the United States, attempt rates of PCI for CTO remain low and have been static at around 12.4%, representing less than 5% of total PCI volume.<sup>3</sup> In addition, success rates of CTO PCI are disappointingly low at 59% compared with success rates of patent-vessel PCI at 96%.<sup>3</sup> The most frequently cited barriers to CTO PCI are incomplete evidence for efficacy and concerns about safety. Because of the ongoing controversy about the risks and benefits of CTO PCI, it remains a class IIa indication in current American and European practice guidelines.<sup>4,5</sup> In addition, these procedures remain technically challenging, and thus variability in local expertise can influence the decision to manage patients medically or refer for CTO PCI.

Patients are often advised that CTO is benign. However, the myocardium affected by a CTO is ischemic. Collateral vessels do not provide adequate flow reserve. FFR data collected from CTOs that were successfully crossed and subsequently interrogated with a pressure wire prior to stenting show that the myocardium supplied by the reconstituted distal bed remains ischemic. This ischemic burden appears to be independent of the size and quality of collaterals.<sup>6,7</sup> In addition, a moderate stenosis in a donor coronary artery supplying collateral vessels to a CTO may result in an ischemic FFR as a consequence of coronary “steal” from the donor artery to the collateral vessels. The ischemic FFR in the donor artery can be corrected by treating the recipient CTO vessel.<sup>8</sup>

Similar to FFR, noninvasive assessment using myocardial perfusion imaging can define ischemic burden and a threshold for benefit of percutaneous vs medical management of CAD. Ischemia greater than 10% on myocardial perfusion imaging is associated with a high risk of major adverse cardiac events (MACE).<sup>9</sup> Similar findings were noted in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy, which showed superior reduction in angina and MACE in patients with greater than 10% ischemia on myocardial perfusion imaging treated with PCI vs medical therapy.<sup>10</sup> In the case of coronary CTO, ischemia greater than 12.5% is predictive of significant improvement in symptoms after intervention.<sup>11</sup>

## ■ PROGNOSIS AND DISEASE BURDEN

CTO is associated with adverse prognosis, implying the importance of incomplete revascularization. The Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial used a scoring system to direct surgical vs percutaneous

revascularization strategies in patients with complex or multivessel CAD. A post hoc analysis of the SYNTAX trial showed that incomplete revascularization was associated with significantly higher rates of 4-year mortality and MACE.<sup>12</sup> This was likely from the ischemic burden remaining from incomplete revascularization. The presence of CTO was the strongest independent predictor of incomplete revascularization in the SYNTAX PCI arm. Similarly, the negative prognostic impact of having a CTO has been observed in a large population of patients followed prospectively after undergoing coronary angiography.<sup>13</sup> Furthermore, the presence of CTO in a non-infarct-related artery at the time of ST-elevation myocardial infarction appears to be an independent predictor of death at 30 days, with a persistent negative prognostic impact lasting for up to 36 months of follow-up.<sup>14</sup>

## ■ CLINICAL BENEFITS OF CTO PCI

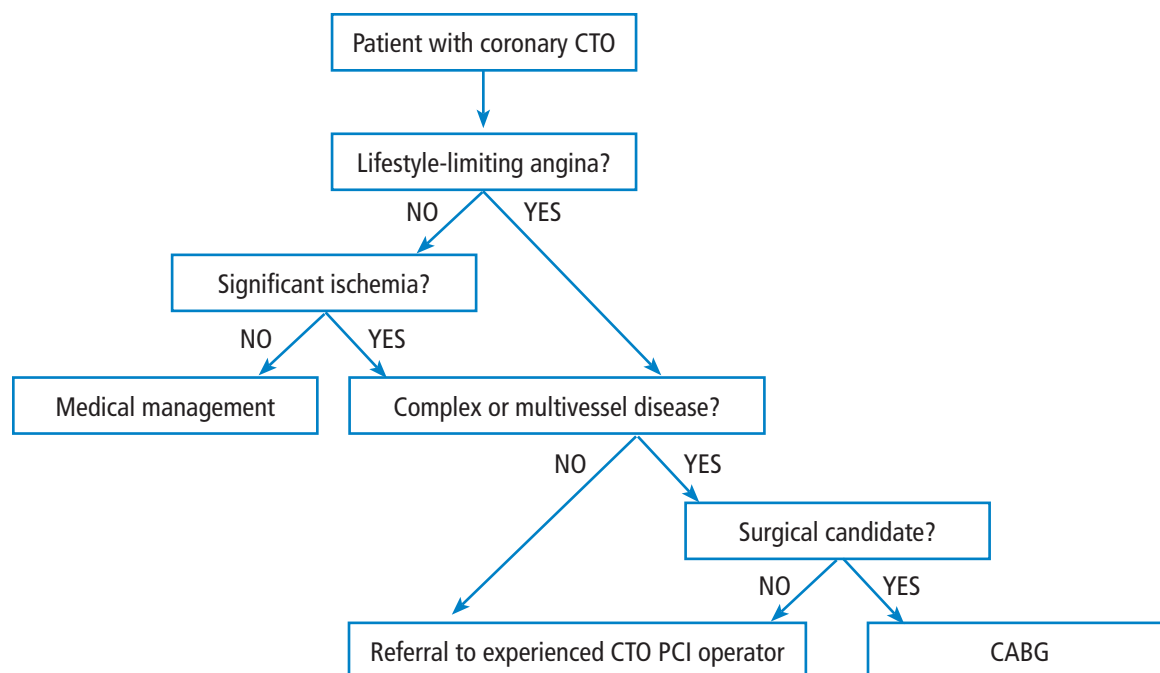
In patients with significant ischemic burden, CTO PCI has multiple clinical benefits. Symptomatic relief based on the Seattle Angina Questionnaire appears to be similar to that obtained with coronary artery bypass grafting (CABG) at 1-month follow up.<sup>15</sup> Successful CTO PCI can have a positive impact on the risk of mortality in prospective<sup>13</sup> and retrospective observational studies.<sup>16</sup>

CTO intervention may also have beneficial effects on left ventricular systolic function in patients with viable myocardium in the corresponding coronary territory.<sup>17</sup> This improvement in systolic function appears to be sustained at 3 years of follow-up.<sup>18</sup> Meta-analysis of observational data in symptomatic and ischemic patients who underwent successful CTO PCI shows reduced rates of all-cause mortality and MACE and a reduced need for subsequent CABG.<sup>19</sup> This is in contrast to the frequently cited Occluded Artery Trial (OAT) trial, which showed no clinical benefit of PCI for a subacutely occluded infarct-related artery.<sup>20</sup>

An algorithmic approach to assessing the need for and the method of coronary revascularization is provided in **Figure 2**.

## ■ EVIDENCE-BASED BENEFITS

Evidence of the merits of CTO PCI from randomized clinical trials is mixed. The only published study to date, the Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Segment Elevation (EXPLORE) trial, showed no difference in left ventricular systolic function 4 months after ST-elevation myocardial infarction in patients undergoing staged CTO PCI of a non-infarct-related artery vs optimal medical ther-



**Figure 2.** An algorithmic approach to determining the need for and the method of coronary revascularization in patients with coronary chronic total occlusion (CTO). Coronary artery bypass grafting (CABG) is preferable to percutaneous coronary intervention (PCI) in patients with complex or multivessel disease, whereas PCI is a reasonable option in patients with anatomically simple or single-vessel disease. Deciding on the appropriate treatment requires consultation with a surgeon and an interventionalist experienced in CTO PCI. Dual-injection angiography may be required to determine the technical feasibility of CTO PCI.

apy.<sup>21</sup> Two larger trials presented at scientific meetings in 2017 remain unpublished. One trial showed noninferiority of optimal medical therapy vs successful CTO PCI in reducing the composite end point of all-cause mortality, myocardial infarction, stroke, and repeat revascularization; the other trial showed significant improvement in quality of life measures using the Seattle Angina Questionnaire score and Canadian Cardiovascular Society angina classification in patients who underwent successful CTO PCI compared with medical management.

High-volume CTO PCI centers now report procedural success rates as high as 92.9%<sup>22</sup> and a correlation between the CTO PCI volume and CTO PCI success rates.<sup>3</sup> The dramatic improvement in success rates achieved by high-volume operators globally can be attributed to a combination of operator experience, improved technology, and widespread adoption of the hybrid algorithm, which has helped to improve efficiency and standardize treatment in CTO PCI based on angiographic criteria.<sup>23</sup> CTO PCI remains a highly specialized procedure, unique from patent-vessel PCI and with little correlation between total PCI volume and CTO PCI success rate. Despite

recent advances, CTO PCI success remains heavily dependent on operator expertise, with a steep and long learning curve. In addition, the unique technical aspects of CTO PCI such as a retrograde and subintimal guidewire tracking that have accelerated procedural success are associated with higher rates of MACE compared with traditional antegrade and intraluminal guidewire tracking.<sup>24,25</sup> Therefore, CTO PCI requires unique considerations beyond standard PCI in terms of potential complications. Uncommon but potentially life-threatening complications such as donor artery thrombosis, collateral vessel trauma, gear entrapment, and radiation skin injury demand a specialized informed consent process for the patient.<sup>26</sup>

In light of incomplete evidence based on extensive observational data and limited randomized clinical trials, the decision to refer patients for CTO PCI requires a comprehensive clinical evaluation. We know from data derived from patients with patent but stenotic coronary arteries that physiologically rather than angiographically driven decisions to revascularize can produce superior clinical results. There is an ischemic burden threshold beyond which revascular-

*Continued on page 38*



Continued from page 30

ization is superior to optimal medical therapy. In this context, we know that CTO is not benign and is associated with ischemic burden. Consequently, patients with symptoms related to CTO represent a subset of patients with incomplete revascularization.

## CONCLUSION

Despite recent advances, CTO PCI procedures remain technically demanding, and success with a low complication rate is heavily dependent on operator expertise. Therefore, CTO PCI should be used judiciously in patients with angina refractory to optimal medical therapy. It is an important tool to be used in conjunction with non-CTO PCI, CABG, and optimal medical therapy to produce favorable outcomes in patients with CAD.

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## Altered mental status and an acid-base disturbance

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TABLE 2

**'Rules of 5' for acid-base problem-solving****1 Determine the arterial pH status**

pH < 7.40 is acidemic, pH > 7.44 is alkalemic  
But a normal pH does not rule out an acid-base disorder

**2 If the arterial pH is abnormal, determine whether the primary process is respiratory, metabolic, or both**

	pH	Pco <sub>2</sub>	Bicarbonate
Respiratory acidosis	Low	High	—
Metabolic acidosis	Low	—	Low
Mixed respiratory and metabolic acidosis	Low	High	Low
Respiratory alkalosis	High	Low	—
Metabolic alkalosis	High	—	High
Mixed respiratory and metabolic alkalosis	High	Low	High

**3 Calculate the anion gap**

**Anion gap = sodium – (chloride + bicarbonate)**

If serum albumin is low, add 2.5 mmol/L to the anion gap  
for every 1 g the serum albumin is below normal

An anion gap > 10 mmol/L is elevated

**4 Check the degree of compensation (respiratory or metabolic)**

Pco<sub>2</sub> and bicarbonate should move in the same direction

Nominal normal levels: bicarbonate 25 mmol/L and Pco<sub>2</sub> 40 mm Hg

**In respiratory acidosis**, for every 10-mm Hg increase in Pco<sub>2</sub>,  
bicarbonate should increase by 1 mmol/L in the first 48 hours  
and 4 mmol/L afterward

**In metabolic acidosis**, for every 1-mmol/L decrease in bicarbonate,  
Pco<sub>2</sub> should decrease by 1.3 mm Hg

**In respiratory alkalosis**, for every 10-mm Hg decrease in Pco<sub>2</sub>,  
bicarbonate should decrease by 2 mmol/L in the first 48 hours  
and by 5 mmol/L afterward

**In metabolic alkalosis**, for every 1-mmol/L increase in bicarbonate,  
Pco<sub>2</sub> may increase by 0.6 mm Hg

**5 If the patient has metabolic acidosis with an elevated anion gap, check whether the bicarbonate level has decreased as much as the anion gap has increased**

In metabolic acidosis, the anion gap should increase by the same amount that bicarbonate decreases; a difference in these two changes is called a delta gap

Pco<sub>2</sub> = partial pressure of carbon dioxide

Based on information in reference 1

In the article "A patient with altered mental status and an acid-base disturbance" (Mani S, Rutecki GW, *Cleve Clin J Med* 2017; 84:27–34), 2 errors occurred in Table 2. The corrected table appears at left, with corrections shown in red:

In addition, two sentences in the text regarding the osmol gap should be revised as follows:

On page 31, the last 3 lines should read as follows: "When the anion gap metabolic acidosis is multifactorial, as it was suspected to be in a case reported by Tan et al,<sup>23</sup> the osmol gap may be elevated as a consequence of additional toxic ingestions, as it was in the reported patient."

And on page 33, the last sentence should read as follows: "As reflected in the revisions to MUD PILES and in the newer GOLD MARK acronym, the osmol gap has become more valuable in differential diagnosis of metabolic acidosis with an elevated anion gap consequent to an expanding array of toxic ingestions (methanol, propylene glycol, ethylene glycol, and diethylene glycol), which may accompany pyroglutamic acid-oxoproline."

**Cardiopulmonary exercise testing**

FEBRUARY 2017

In the article, "Cardiopulmonary exercise testing: A contemporary and versatile clinical tool" (Leclerc K, *Cleve Clin J Med* 2017; 84:161–168), an error occurred in Table 1. Heart rate reserve was defined as maximum heart rate minus resting heart rate. It should be defined as (maximum heart rate minus resting heart rate) divided by (predicted maximum heart rate minus resting heart rate).