

The impact of percutaneous coronary intervention of chronic total occlusions on left ventricular function and clinical outcomes

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Abstract: A meta-analysis by Hoebers *et al.* reported that successful chronic total occlusion (CTO) recanalization resulted in an increase in left ventricular (LV) ejection fraction by 4.44% ($P<0.01$) and a reduction in LV end-diastolic volume by 6.14 mL/m² during follow-up as compared with baseline, suggesting beneficial LV remodeling. These findings are important as the myocardium supplied by a CTO frequently has sustained irreversible injury and further support the clinical benefits of CTO interventions.

Keywords: Percutaneous coronary intervention (PCI); chronic total occlusion (CTO); left ventricle; outcomes

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Percutaneous coronary interventions (PCIs) of chronic total occlusions (CTOs) can provide significant clinical benefits (1). Although no randomized controlled trial has been performed to date, several observational studies and meta-analyses have shown significant reduction in mortality, angina severity, need for coronary bypass surgery (CABG), major adverse cardiac events (MACE) and stroke after successful *vs.* failed CTO PCI (2-7).

Another important potential benefit of CTO PCI is left ventricular (LV) function improvement. Several studies have shown LV function improvement following successful CTO PCI, but the power of each individual study to detect a difference was low due to small sample size. To overcome this limitation Hoebers *et al.* performed an elegant systematic review and meta-analysis on the impact of CTO PCI on LV function [left ventricular ejection fraction (LVEF) and left ventricular end-diastolic volume (LV-EDV)] and on long-term mortality (8). They found that successful CTO recanalization resulted in an increase in LVEF by 4.44% ($P<0.01$) and a reduction in LV-EDV by 6.14 mL/m² during follow-up as compared with baseline, suggesting beneficial LV remodeling. However, the LVEF improvement disappeared upon re-occlusion of a previously successfully treated CTO vessel. Similar to prior meta-analyses long-term mortality was lower after successful *vs.*

failed CTO PCI (OR: 0.52, $P<0.01$) (2-7).

The finding of improved LVEF after successful CTO PCI is of particular importance since myocardium perfused by a CTO vessel is likely to have sustained irreversible injury. Choi *et al.* performed magnetic resonance imaging in 170 consecutive patients with coronary CTOs showing evidence of prior myocardial infarction by late gadolinium enhancement in 86% of patients, a much higher proportion that previously recognized, even though only 25% of patients had Q waves on their electrocardiogram (9). The percent hyper-enhancement in another study by Cheng *et al.* was 47% for CTO lesions *vs.* 29% for non-CTO lesions, suggesting larger area of irreversible injury in myocardium perfused by a CTO (10). The significant improvement in LVEF and decrease in LV-EDV shown in the Hoebers meta-analysis suggests that CTO PCI can improve LV function among patients undergoing clinically-indicated CTO PCI, in spite of pre-existing myocardial injury. The actual magnitude of improvement may be larger among patients with decreased baseline LVEF, although the granularity of published reports was not detailed enough to answer this question in the present meta-analysis.

Will LVEF improve in all patients undergoing CTO PCI? The answer is likely no, as the extent of potential recovery likely depends on baseline myocardial viability. In

the study by Choi *et al.*, increased angiographic collateral flow was associated with lower degree of late gadolinium enhancement transmural, providing an indirect means of predicting the likelihood of LV function improvement after CTO recanalization: poorly collateralized myocardial segments would be less likely to recover function as compared with well collateralized segments. Similar findings were reported by Ripley *et al.*: viable myocardium was present in 83% of patients with good collaterals *vs.* 38% of those with poor collaterals (11).

Should all patients undergoing CTO PCI undergo myocardial viability testing? The answer to this question is also likely no. The clinical indication for CTO PCI in most cases is improvement of symptoms, rather than a desire to improve LVEF (12,13). CTO PCI is indicated in patients with classic angina uncontrolled by medical therapy (14), but ischemia and viability testing may be of particular importance in patients with no symptoms or atypical symptoms, such as dyspnea.

How can one optimize the likelihood of LV function improvement? By completely revascularizing the patient (15) and by preserving the patency of all major side branches, as occlusion of side branches during CTO PCI has been associated with higher risk for periprocedural myocardial infarction (16,17), as well as coronary perforation and tamponade (18). It may be preferable to use antegrade crossing techniques for CTO recanalization, as retrograde crossing techniques have been associated with higher risk for periprocedural myocardial infarction and procedural complications (17,19). However, retrograde techniques may often be needed for recanalizing complex CTOs and preserving bifurcations (20,21). Although the success of CTO PCI has been steadily increasing over time (22,23), it remains heavily dependent on operator experience (24,25), hence complex cases may be best performed at high-volume expert CTO centers (21,26).

As outlined by the authors, their meta-analysis has important limitations. First, several imaging modalities were used to assess LVEF, each with different accuracy and reproducibility. Second, and most important, all studies included in the meta-analysis were observational, limiting the ability to derive definitive conclusions, as conclusive proof of a beneficial effect of a treatment can only be provided by adequately powered, prospective, randomized-controlled clinical trials (1). The first randomized controlled CTO PCI trial with LVEF as the primary endpoint is the Evaluating Xience V and LV function in PCI on occlusions after ST-Elevation myocardial infarction (EXPLORE) trial

(<http://www.explorettrial.com/>). EXPLORE randomized 300 patients presenting with ST-segment elevation acute myocardial infarction and a CTO in a non-infarct vessel to either CTO PCI within 7 days of presentation or standard medical therapy. The study's primary endpoint is LV ejection fraction and end-diastolic volume at 4 months, measured using cardiac magnetic resonance imaging. Enrollment in the study was recently completed and results are anticipated to be presented at the 2015 Transcatheter Cardiovascular Therapeutics meeting. The EXPLORE trial results are eagerly anticipated as they will provide novel insights on the impact of CTO PCI on LV function and structure.

In conclusion, the carefully designed and executed meta-analysis by Hoebers *et al.* adds to our understanding of the benefits and underlying mechanisms of successful CTO PCI (8), providing further (albeit indirect) support of its clinical utility and need for continued development.

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Footnote

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