ORBITA-CTO: CTO PCI Offers No Angina Relief Over Placebo

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> Percutaneous coronary intervention for chronic total occlusion (CTO PCI) is frequently offered to patients with stable angina, primarily for symptom and quality of life improvement. However, the efficacy of this intervention has lacked blinded, randomized evidence. The ORBITA-CTO trial, presented at ACC.26, directly addresses this gap, demonstrating that CTO PCI did not improve angina symptoms or quality of life compared to a placebo procedure.1

KEY TAKEAWAYS

- The Pivot: CTO PCI, previously offered for symptom relief, now lacks blinded randomized evidence for this indication.
- The Data: There was no significant difference in the change in angina frequency score between CTO PCI and placebo (mean difference: -0.1, 95% CI: -1.2 to 1.0, p=0.85).
- The Action: Clinicians should reconsider the routine recommendation of CTO PCI for symptom improvement in stable angina, given the absence of demonstrated benefit over placebo.

Chronic total occlusion (CTO) of a coronary artery is defined as complete obstruction with TIMI 0 flow for an estimated duration of at least three months. Percutaneous coronary intervention (PCI) for CTOs is a complex procedure, often undertaken with the primary goal of alleviating angina symptoms and improving patient quality of life in those with stable angina. Despite its widespread use, the evidence base for CTO PCI, particularly regarding its symptomatic benefits, has been limited by the absence of blinded, randomized controlled trials. This gap has meant that clinical decisions were often made without robust data comparing the intervention to a sham procedure, leaving uncertainty about the true efficacy of CTO PCI beyond the effects of medical therapy.1

CTOs are prevalent in patients with coronary artery disease, affecting approximately 18-50% of those undergoing coronary angiography. The presence of a CTO is associated with a higher burden of angina, reduced exercise capacity, and impaired quality of life. Historically, the rationale for CTO PCI has been extrapolated from studies on non-CTO PCI, which demonstrated symptomatic relief and improved exercise tolerance. However, CTOs present unique challenges, including extensive plaque burden, calcification, and tortuosity, making the procedure technically demanding and potentially associated with higher risks. The presumed mechanism of benefit from CTO PCI involves restoring blood flow to ischemic myocardial territories, thereby reducing angina and improving myocardial function. However, the extent to which this translates into symptomatic improvement beyond the placebo effect and optimal medical therapy has remained a subject of debate. Prior observational studies and non-blinded randomized trials have reported conflicting results, highlighting the need for a rigorously designed, placebo-controlled investigation.1

The ORBITA-CTO Trial

The ORBITA-CTO trial was a randomized, placebo-controlled study designed to evaluate the efficacy of CTO PCI in improving angina symptoms and quality of life in patients with stable angina. The trial enrolled 200 patients with stable angina and at least one CTO, randomized in a 1:1 ratio to either CTO PCI or a placebo procedure. Patients were blinded to their treatment assignment. The primary endpoint was the change in angina frequency score from baseline to 6 weeks, measured using the Seattle Angina Questionnaire (SAQ). Secondary endpoints included changes in SAQ physical limitation score, quality of life scores, and exercise capacity.1

Patient eligibility criteria included stable angina despite optimal medical therapy, evidence of myocardial ischemia in the territory supplied by the CTO, and a CTO amenable to PCI as determined by an experienced operator. Exclusion criteria included recent myocardial infarction, severe valvular heart disease, or other conditions that could confound angina assessment. The blinding protocol involved a comprehensive strategy, where patients, referring physicians, and outcome assessors remained unaware of the treatment allocation. The placebo procedure was meticulously designed to mimic the active intervention's diagnostic phase, including local anesthesia, femoral artery access, and coronary angiography, ensuring that patients experienced similar procedural sensations without the revascularization itself. This rigorous blinding aimed to minimize bias associated with patient expectations and the Hawthorne effect, which can significantly influence subjective symptom reporting.1

Patients in both arms received optimal medical therapy throughout the study. The placebo procedure involved a coronary angiogram without intervention, mimicking the diagnostic phase of the PCI procedure to maintain blinding. Technical success of CTO PCI was achieved in 85% of patients randomized to the active treatment arm.1

At 6 weeks, the trial found no significant difference in the primary endpoint. The mean change in angina frequency score from baseline was -0.1 (95% CI: -1.2 to 1.0, P=0.85) for CTO PCI compared to the placebo group. This indicates that CTO

PCI did not provide a statistically significant improvement in angina frequency over the placebo procedure. Similarly, there were no significant differences observed in secondary endpoints, including changes in SAQ physical limitation score, other quality of life metrics, or exercise capacity between the two groups. The safety profile was comparable between the two arms, with no significant differences in major adverse cardiac events.1

The ORBITA-CTO trial provides critical blinded, randomized evidence regarding the symptomatic efficacy of CTO PCI in stable angina. The absence of a significant difference in angina relief or quality of life improvement between the active intervention and placebo procedure challenges the current practice of offering CTO PCI primarily for symptom management. The study's design, including blinding and a placebo control, strengthens the validity of its findings, addressing a long-standing evidence gap in interventional cardiology.1

The trial's findings suggest that the symptomatic benefits attributed to CTO PCI in previous unblinded studies may have been influenced by a strong placebo effect or other biases. While CTO PCI successfully revascularized the occluded artery in a high percentage of cases, this anatomical success did not translate into a measurable symptomatic advantage over a sham procedure. Limitations of the study include its relatively short follow-up period of 6 weeks, which may not capture longer-term benefits or risks. Additionally, the study population consisted of patients with stable angina, and the results may not be generalizable to patients with acute coronary syndromes or those with more severe ischemia. The trial's findings prompt a re-evaluation of the indications for CTO PCI, particularly when the primary goal is symptom relief, and emphasize the importance of robust, blinded evidence in guiding clinical practice.1

CLINICAL IMPLICATIONS

The ORBITA-CTO trial delivers a clear message: the symptomatic benefit of CTO PCI in stable angina, when compared to a placebo procedure, is negligible. This finding should prompt a re-evaluation of current guidelines and clinical practice, particularly for patients whose primary indication for CTO PCI is angina relief. For too long, the absence of blinded evidence allowed for an assumption of benefit that this trial now directly refutes. Clinicians must now consider whether the risks and costs associated with a complex procedure like CTO PCI are justified when the primary outcome, symptom improvement, is not demonstrably better than a sham intervention.

The implications extend beyond individual patient discussions. Interventional cardiology societies and guideline bodies, such as the American College of Cardiology and the European Society of Cardiology, will need to integrate these data into their recommendations. The industry, particularly manufacturers of PCI devices and guidewires, may face scrutiny regarding the marketing and utilization of their products for this indication. The trial underscores the importance of rigorous, placebo-controlled studies, even for established procedures, to ensure that interventions truly deliver the intended patient benefit.

Patients with stable angina and CTOs, who are often seeking relief from debilitating symptoms, deserve interventions proven to be effective. This trial suggests that for many, the perceived benefit of CTO PCI may have been a placebo effect. Moving forward, the focus for these patients should remain on optimizing medical therapy and exploring other evidence-based approaches for symptom management, reserving CTO PCI for specific circumstances where a clear, non-symptomatic benefit can be demonstrated, or within the context of further research.

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REFERENCES

1. 1. Khan S, Sajjad U, Fawaz S. Randomized, Placebo-Controlled Trial of Chronic Total Occlusion Percutaneous Coronary Intervention in Stable Angina: The ORBITA-CTO Trial. J Am Coll Cardiol 2026;87(20):2000-2009.

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