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EDITORIAL COMMENT

Chronic Total Occlusion Revascularization and Quality-of-Life Improvement Across All Levels of Left Ventricular Function

Many Questions Still Unanswered*

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Because of the wide adoption of earlier reperfusion therapies, aggressive cardiovascular risk profile modification, and improvement in percutaneous and surgical revascularization techniques, outcomes continue to improve in patients with coronary artery disease (CAD) (1,2). Approximately 16% to 31% of angiograms in patients with stable CAD are noted to show coronary chronic total occlusions (CTOs) (3–5). Over the past 15 years, advances in technologies and techniques have made it possible for these lesions to be treated percutaneously with success rates exceeding 90% at experienced centers (4). Multiple retrospective and prospective cohort studies have shown significantly worse outcomes for those patients with unsuccessful revascularization of CTO lesions compared with those with successful intervention (6). Still, percutaneous coronary intervention (PCI) of these lesions is performed infrequently. This may be due to the complexity and relatively increased risk for periprocedural complications compared with nonocclusive CAD PCI but is probably more importantly due to the lack of substantial evidence supporting the benefits of CTO PCI (4,7). Even though it would be more stimulating to confirm an improvement in major clinical outcomes like decreased mortality, decreased incidence of myocardial infarction or improvement in left ventricular (LV) function, alleviation of symptoms and improvement in quality of life (QOL) appear to be a more realistic first step in evaluating the clinical benefits in patients with CTO interventions. Recently, Werner et al. (8) showed for the first time in a randomized fashion a significant reduction of angina symptoms, improvement in QOL, and reduction of physical limitations in patients undergoing CTO intervention compared with those receiving optimal medical treatment.

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In this issue of *JACC: Cardiovascular Interventions*, Khariton et al. (9) provide additional reassuring information to the field of CTO PCI, evaluating its impact on QOL according to LV function. OPEN-CTO (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion) is a single-arm, prospective registry that enrolled consecutive patients who underwent attempted CTO PCI (either single-vessel CTO or CTO as part of multivessel revascularization) using the hybrid approach at 12 high-volume centers in the United States (10). The present work included a prospectively collected questionnaire on QOL and angina symptoms prior to the attempted intervention, which was repeated at 12-month follow-up. Disease-specific health status was assessed using the Seattle Angina Questionnaire, a 19-item questionnaire that measures 5 domains related to CAD: angina frequency, physical limitations, QOL, angina stability, and treatment satisfaction. The study focused on the summary score and the angina frequency score. To measure dyspnea, the investigators used the Rose Dyspnea Scale. The study included 762 patients with successful interventions and complete data. Among them,

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56% had normal LV function, 25% had mild to moderate dysfunction, and 8.3% had severe dysfunction. The 137 patients with unsuccessful intervention were excluded from the analysis. The study demonstrates significant improvements in QOL, angina measurement, and dyspnea scale across all different levels of LV function at 12-month follow-up. Despite smaller improvements, patients with very low ejection fractions also had significant benefit, providing for the first time supporting data in this growing population of patients. Importantly, when the analysis was performed in the subgroup of patients with single vessel CTO intervention alone (n = 658), similar to the results of the entire cohort, significant benefits were also demonstrated.

There is a clear need for good-quality data in this field. In this regard, the present study provides very encouraging and reassuring information. However, there are several important limitations, as outlined by the investigators. These include the fact that this was a retrospective registry (although QOL and angina data were collected prospectively), the lack of a control group, the exclusion of unsuccessful interventions, the lack of data on pre-procedural viability and/or ischemia studies to correlate with long-term QOL outcomes, the lack of data on change in LV function at follow-up and its association with clinical improvement, and the inclusion of patients from high-volume and very highly selected groups of operators. Although all are important, some deserve additional comment.

First, the study did not have a control group. Although it is generally acknowledged that randomized controlled studies are the optimal design to determine the potential benefit of any new therapy, the need for a control group is even more important when subjective variables are the main goal of the study. The potential for the placebo effect to influence subjective outcomes is well described in the context of symptomatic CAD (11). To that end, only 2 randomized trials have been performed to date, demonstrating conflicting and opposite information regarding QOL improvement and angina symptom alleviation. The European study mentioned earlier showed a significant improvement in QOL; in contrast, the study from South Korea showed no improvement (8,12).

Second, clinical events were not included, and particularly unsuccessful procedures were excluded from the present study. It is well known that the incidence of major clinical events is higher with CTO interventions, with the highest in those with unsuccessful intervention. When a new treatment alternative is offered to a patient, the balance between potential benefits and potential risks must be considered to determine the overall likely benefit. For instance, in the EuroCTO randomized study, despite the significant improvement in the primary endpoint of QOL, there were 2 deaths and 5 acute myocardial infarctions in the PCI group versus none in the optimal medical treatment group (8). The EXPLORE study, which randomized patients to CTO intervention versus medical treatment in patients with recent myocardial infarction, showed a statistically nonsignificant but doubled incidence of major adverse cardiac events (5.6% vs. 2.6%, p = 0.20) in the CTO PCI group (13). The increased complication rate is probably more critical in patients with low ejection fractions. Complications such as perforation, transient loss of collateral flow with poorly tolerated ischemia, the potential vascular and bleeding complications when operators use temporary LV assist devices to perform the procedure safely, the more prolonged ischemia associated with vessel dissection and the permanent loss of collateral flow noted in unsuccessful procedures, and the large amount of contrast use with the risk for contrast-induced nephropathy (which is even higher in patients with low ejection fractions) are some of the potential clinical detrimental events in this patient population that need to be taken in consideration.

Last, these registry data were obtained from centers with the highest experience in dealing with these complex interventions. Operator experience has been associated with significant differences in success and complications in PCI, and these differences are no less common in the context of CTO PCI. Including patients with impaired LV function adds yet another layer of complexity. The generalizability of the present study's findings to low-volume operators and to centers without developed CTO programs will require additional research.

In summary, the present study provides important additional information to the field of CTO PCI, demonstrating QOL improvement in patients with successful procedures irrespective of baseline LV function. Dedicated prospective registries with detailed definitions such as the OPEN-CTO registry provide a better understanding of the role of this rapidly evolving therapy. Nevertheless, randomized trials remain critical if we are to fully understand the potential clinical benefit and likely risk of CTO PCI, especially as we advance into higher risk patient populations, such as those with impaired LV function.

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