

LETTERS TO THE EDITOR

Very High Perforation Rate in Patients Undergoing Unsuccessful Percutaneous Coronary Interventions of Chronic Total Occlusions Could Explain Worse Outcome in These Patients and Not Chronically Occluded Artery

In the paper by Mehran et al. (1), the authors concluded that failure to open chronic total occlusion (CTO) lesions leads to a higher rate of cardiac death, total death, and coronary artery bypass surgery (CABG). The authors explain their findings on the basis of the possible deleterious effects of a persistently closed artery leading to more adverse events. However, the authors did not comment on the procedural complications, such as perforations, that could have occurred during a long, complicated CTO procedure, such as renal failure, bleeding, or peripheral vascular injury. In this registry, patients with unsuccessful CTO percutaneous coronary intervention had a high rate of procedural-related coronary perforation (7.4% vs. 1.7% in the successfully treated arm). The authors did not mention the rate of death or urgent CABG occurring among those with coronary perforation and whether this might explain the higher frequency of CABG, mortality, and myocardial infarction occurring in the unsuccessful CTO intervention cohort.

Let us compare this study to a hypothetical randomized clinical trial where any complication (including death or perforation) would be assigned to the treatment group independent of successful delivery of the treatment (i.e., an intention-to-treat analysis). Applying this rule to the current study and transferring the perforation rate of 7.5% in the unsuccessful CTO intervention arm (higher than the 5.8% cardiac mortality in the failed CTO arm after 5 years) to the arm with successful CTO intervention would clearly show that overall CTO intervention led to a relatively poor outcome. Therefore, their conclusion should have been that intervention of CTO lesions would have been harmful due to the very high procedural complication rate, offsetting any potential benefit. Multivariate analysis adjusting for perforation would be invalid, because perforation was related to intervention and not due to a permanently occluded artery that was blamed for the poor long-term outcome. Other important percutaneous coronary intervention-related complications, such as contrast-induced nephropathy and bleeding, were not mentioned. Lee et al. (2) published their experience with regard to unsuccessful CTO intervention in the same month that this current report was published. In the Lee et al. (2) paper, they showed no difference in any outcomes between successful or unsuccessful CTO intervention, despite worse baseline characteristics of patients undergoing unsuccessful CTO attempt, thereby somewhat contradicting the current paper.

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doi:10.1016/j.jcin.2011.10.007

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Chronic Total Occlusion Recanalization

A Call for a Randomized Trial

Mehran et al. (1) recently reported the results of a multicenter observational study examining long-term outcomes of 1,791 patients after percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) lesions, comparing the patients who succeeded in the procedure with those who failed. The authors report an overall procedural success rate of 68% and detected in their model that a successful CTO procedure was an independent predictor of reduced cardiac mortality with a strong trend toward lower all-cause mortality. Although the authors should be congratulated for reporting on such a large cohort of patients undergoing PCI to CTO lesions, we found the analysis biased against the patients who failed PCI. Furthermore, there are several methodological deficiencies in the study that significantly impair the power of this study and put into question the accuracy of their conclusion.

To address the question of whether treating CTO by PCI impacts on late clinical events, the control group should have appropriately included patients assigned to medical therapy and not those who failed PCI. Comparing the treatment effect of a device between a group that succeeded in a procedure and another that failed might directly lead to a major bias and does not offer any meaningful conclusion other than the intuitive fact that when the procedure fails it is bad for the patient.

Second, the authors also reported that the rate of coronary artery bypass graft procedures for the failed PCI group was higher in patients whose occlusions could not be opened (13.3% vs. 3.2%, $p < 0.01$), leading to an impression that such an event is more frequent when the attempt to open a difficult CTO has failed;

however, it might be related to vascular injuries that were more frequent in patients with failed PCI, such as coronary perforation (7.4% vs. 1.7%, $p < 0.01$) and residual dissection (9.4% vs. 4.3%, $p < 0.01$), thereby exaggerating the relative benefits of a successful opening of the occluded artery. Consistent with that, our group previously reported analysis of a cohort of patients with failed but uncomplicated CTO PCI procedures, showing similar rates of death and myocardial infarction at a mean follow-up of 2 years (2). It would be appropriate to repeat the analysis of the authors and compare the successful PCI group with the noncomplicated failed group and examine whether their conclusion still holds.

Finally, with regard to the use of drug-eluting stents (DES) versus bare-metal stents (BMS), the authors reported that treatment with DES in comparison with BMS resulted in similar definite/probable stent thrombosis rates (1.7% vs. 2.3%, $p = 0.58$); however, only 4.2% of patients in the DES group versus 42% of the patients in the BMS group reached 5-year follow-up. This major difference in follow-up time could lead to a bias as well.

We agree that performing a randomized clinical trial comparing PCI for CTO and conservative therapy with medications only, such as in the upcoming DECISION-CTO (Drug-Eluting Stent Implantation vs. Optimal Medical Treatment in Patients with Chronic Total Occlusion) trial, might reveal whether treating these complex lesions has an effect on clinical result.

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doi:10.1016/j.jcin.2011.11.001

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Reply

We thank Dr. Movahed and Dr. Badr and colleagues for their expressed interest in our study. Dr. Movahed refers to the potential implications of the relatively high perforation rate observed in our study (1). In our study, the definition we employed for coronary perforation included any one of the 3 types proposed by Ellis et al. (2). However, the specific type of perforation was not recorded. A recent Bayesian meta-analysis by Shimony et al. (3) showed that

morbidity and mortality after coronary perforation vary directly with the Ellis classification. Mortality was 0.3%, 0.4%, and 21.2% after type I, II, and III perforations, respectively, clearly indicating that not every type of perforation is associated with catastrophic outcomes.

In our study, 30-day mortality in patients with a coronary perforation was 0%, and 1-year mortality was 5.2%. Therefore, it is highly unlikely that a significant number of type III perforations occurred. Finally, the performance of coronary artery bypass surgery was not within an urgent time frame, but within months of the failed percutaneous coronary intervention (PCI) procedure, therefore reflecting the decision to proceed with complete revascularization at a later point. Because of the low mortality rate after coronary perforation, we do not agree with the suggestion that chronic total occlusion (CTO) PCI overall is associated with a poor outcome.

Nonetheless, we do acknowledge the fact that despite favorable outcomes, the rate of this complication was high. Operators performing CTO intervention should make every effort to minimize this potentially hazardous complication and should inform the patient of the risk of a coronary perforation during the informed consent process. Moreover, future randomized clinical trials investigating the potential benefit of CTO PCI should carefully record the incidence, types, and outcomes of coronary artery perforation.

Regarding the comments by Dr. Badr and colleagues, we agree that our study is limited by its observational nature and by the fact that the control group does not include patients assigned to medical therapy. Nonetheless, as our control group consisted of patients with CTO lesions that were deemed suitable for PCI, the applicability of the study results extends beyond the mere intuitive fact that when a procedure fails, it is bad for the patient. In the absence of randomized controlled trials investigating the effect of PCI of CTOs compared with medical therapy, we cannot exclude that part of the observed worse outcome in the failed PCI group in our study may be attributed to harmful effects of a failed procedure. The other part may be attributed to a beneficial effect of a successful procedure.

Finally, we agree wholeheartedly that the results of well-designed randomized controlled trials investigating a potential benefit of CTO PCI, such as EXPLORE (Evaluating Xience V and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions after ST-Elevation Myocardial Infarction) (4), DECISION-CTO (Drug-Eluting Stent Implantation vs. Optimal Medical Treatment in Patients with Chronic Total Occlusion), and the EURO-CTO (European Study on the Utilization of Revascularization vs. Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions) are eagerly awaited. Long-term follow-up of these studies will also provide further insight into the safety and efficacy of (newer-generation) drug-eluting stents in CTO lesions.

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