occlusion length was 37 ± 25 mm, mean J-CTO score among successful versus failed CTO PCIs was 2.5 ± 1.2 versus 3.3 ± 1.0, and final successful crossing strategy was the retrograde approach in 28% of cases. Therefore, Lee et al. (1) might have selected a low-risk CTO population, which might explain why they found no association between successful revascularization and survival.

Another explanation might stem from the fact that "almost complete" revascularization (all lesions excluding the CTO) was achieved in 71% of unsuccessful CTO PCI patients. Additionally, coronary artery bypass graft was performed in 17% of these patients during follow-up. This can further confound the analyses, since the failed CTO PCI group actually included a relevant number of successfully (and completely) revascularized patients. Complete and "reasonably incomplete" revascularization has been associated with improved survival (3). Further speculations are hampered by the lack of assessment of the SYNTAX(Synergy Between PCI With Taxus and Cardiac Surgery) and residual SYNTAX score in the study by Lee et al. (1), as well as the fact that they did not provide a definition of complete revascularization.

Finally, their results contrast with those of much larger multicenter registries, which observed improved survival when successful CTO revascularization is achieved. George et al. (4) studied 13,443 patients who underwent CTO PCI and found that successful PCI was associated with improved survival after a median follow-up of 2.65 years.

The final answer to the neverending debate about the possible survival benefit of CTO PCI will not likely come from observational studies. Well-designed and adequately powered randomized trials are eagerly awaited.

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REPLY: Does Chronic Total Occlusion Percutaneous Coronary Intervention Improve Survival

A Never-Ending Debate

We thank Dr. Azzalini and colleagues for their comments concerning our article (1).

Perhaps, among various registries intended for percutaneous coronary intervention (PCI) studies, chronic total occlusion (CTO) registries may have the most extreme form of biased sampling. CTO is more common in the presence of other significantly narrowed coronary artery and a substantial portion of these patients may be excluded due to referral for bypass surgery. Accordingly, registries from experienced centers may include patients with more complex clinical and angiographic characteristics that may affect outcomes. However, the issue pointed out by Azzalini and colleagues should be interpreted from a different viewpoint. The independent variables of Japanese-CTO (J-CTO) score represent the "lesion" complexity, and thus the scoring system predicts procedural efficiency (i.e., guidewire crossing time of <30 min) as well as the probability of overall success. The overall retrograde attempt rate was low, correctly because of the long enrollment period of the study (the first retrograde case was performed in 2008 at our institution). But similarly, retrograde technique and systematic algorithmic strategy both represents the contemporary CTO-PCI, which puts emphasis on procedural efficiency and success. Therefore, several numbers shown in our report, which implies relatively less complex anatomic substrate for CTO lesion itself, might explain why the overall success rate was high, but does not explain why we could not find the association between CTO recanalization and improved survival.

To ultimately answer the title question proposed by Dr. Azzalini and colleagues, several methodological

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aspects should be considered when enrolling patients for a clinical study. First, myocardium originally perfused by an occluded artery should be identified to possess viability. Second, concomitant coronary stenosis in a territory other than CTO artery should be controlled. Third, CTO lesion of the control group should be treated medically from the beginning and throughout the follow-up period. To date, no study has yet succeeded to confine patients that satisfy all these criteria. The relatively high rate of subsequent coronary artery bypass grafting after unsuccessful PCI in our study correctly confounds the overall analyses as we briefly drew attention in the second paragraph of the discussion. However, the positive results of other studies, including the recent report by George et al. (2), were also not adequately drawn by including patients who were medically treated after undergoing failed PCI. The majority of studies that reported survival advantage of successful CTO-PCI do not provide information on how they treated non-CTO lesions and, more importantly, how the CTOs were subsequently managed after failed PCI. The absence of this information also puts previous studies into question the accuracy of their conclusion. The additional subgroup analysis of our data at least provides some evidence for the hypothesis that medical therapy for CTO may not increase long-term mortality as long as the donor artery for collateral circulation is patent. Because future studies are extremely unlikely to enroll proper patients in an observational approach, this hypothesis should be confirmed through well-designed randomized controlled trials.

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