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REPLY: Immediate Versus Delayed Invasive Intervention for Non-ST-Segment Elevation Myocardial Infarction Patients (RIDDLE-NSTEMI Study)



A Game Changer for Interventional Cardiologists?

We thank Drs. Bertrand and Tanguay for their in-depth analysis and constructive comments on our study (1), which demonstrated improved clinical outcomes in patients with non-ST-segment elevation myocardial infarction (MI) treated with an immediate versus a delayed invasive strategy, and we agree with the conclusion that such results, if confirmed by a larger, multicenter study, may have a significant impact on health care infrastructure. Because of inherent problems of determining periprocedural MI in the setting of early percutaneous coronary intervention (PCI) in patients with non-ST-segment elevation MI, we adopted a time-specific definition of MI similar to the hitherto largest study on this subject, the TIMACS (Timing of Intervention in Acute Coronary Syndromes) trial (2). This definition allowed differential assessment of new MI between the treatment groups, with a possibility of biomarker-based adjudication preferentially in the delayed-intervention group. However, the definition also required new-onset ischemic symptoms >20 min, and our records show that in all cases of new MI after PCI in the delayed-intervention group, there was a supporting electrocardiographic correlate of ischemia as well. Importantly, the main difference in the primary outcome resulted from the higher rate of pre-catheterization MI in delayed-intervention patients (10 vs. 0 new MIs in the delayed- vs. immediate-intervention group, respectively). An additional 6 patients in the delayed-intervention group had new MI after PCI and up to 30-day follow-up. Of these, 4 patients had biomarker elevations within 24 to 48 h post-PCI, accompanied by new-onset chest pain lasting >20 min and corresponding new ischemic electrocardiographic changes. In the remaining 2 patients,

new MI occurred after hospital discharge. Hence, we believe that the definition of new MI had no significant impact on the overall study results.

In our study, baseline risk profile, as expressed by GRACE (Global Registry of Acute Coronary Events) and TIMI (Thrombolysis In Myocardial Infarction) risk scores, was similar in the immediate- and delayed-intervention groups (1). The higher rate of surgical revascularization in patients assigned to undergo delayed invasive intervention is listed as a potential limitation of our study. More specifically, 38 and 20 patients were treated with coronary artery bypass grafting in the delayed- and immediate-intervention groups, respectively. The final decision on revascularization strategy for these patients was made by the institutional heart team, blinded to randomization code. However, even after excluding patients referred for coronary artery bypass grafting from the analysis, immediate intervention was still associated with reduced rates of death or MI at both 30 days (2.1% vs. 13.9%, $p < 0.001$) and 1 year (3.5% vs. 17.2%, $p < 0.001$). Therefore, the observed difference in the rate of coronary artery bypass grafting seems not to have significantly influenced the overall study results, and nor has the time-specific definition of new MI. However, we agree that further studies are needed to corroborate our findings, as they may have substantial implications for health care systems in terms of increased resource allocation to expedite early invasive treatment in patients with ischemic electrocardiographic changes and biomarker elevation on admission.

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