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REPLY: Lights and Shadows of Antiplatelet Therapy in Primary Percutaneous Coronary Intervention



We thank Lozano et al. for their thoughtful comments on our ETAMI (Early Thienopyridine Treatment to Improve Primary PCI in Patients With Acute Myocardial Infarction) trial (1) and fully agree with their statement that in antithrombotic therapy, there should always be a balance between efficacy and safety. Our study has investigated the very acute phase of primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) in which a faster onset of action of a platelet inhibition effect is desirable to reduce ischemic complications of the procedure. In the recently published ATLANTIC (A 30 Day Study to Evaluate Efficacy and Safety of Pre-hospital vs. In-hospital Initiation of Ticagrelor Therapy in STEMI Patients Planned for Percutaneous Coronary Intervention) trial, a very early initiation of ticagrelor in the pre-hospital phase leading to clinical relevant difference in platelet inhibition 1 h after PCI was associated with a reduction in stent thrombosis compared with the same loading dose started on average 31 min later in the hospital (2). In addition, there are several reports linking inadequate platelet inhibition at the time of PCI to ischemic complications, underscoring the importance of an effective platelet periprocedural inhibition during primary PCI (3). In the TRITON (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel) trial, patients with STEMI have especially benefited from prasugrel compared with clopidogrel without an increase in bleeding complications (4). These results were confirmed by recent reports from real-life experience of registries. Bleeding complications in TRITON accumulated over time but were not statistically different between clopidogrel and prasugrel in the primary PCI group at 30 days as well as at 15 months (4). The net clinical benefit was clearly in favor of prasugrel. The statement about a differential effect of prasugrel between secondary and primary PCI in STEMI is not correct, and this reference indicated no statistical heterogeneity between the 2 groups (4). This has been now well evaluated, and there is no significant interaction for the primary and secondary endpoints and a consistent effect of prasugrel across

all types of PCI performed in STEMI patients (5). The numerical differences are related to the difficulties in measuring periprocedural MI in primary PCI versus secondary PCI and not related to the efficacy of prasugrel (5). The statement about contraindications against prasugrel majorly relates to patients with prior stroke, which is present in up to 3% of STEMI patients. Elderly or patients with low body weight <60 kg might be treated with the same loading dose of 60 mg and a lower maintenance dose of 5 mg to reduce bleeding complications.

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Triple Antithrombotic Therapy Following Anterior ST-Segment Elevation Myocardial Infarction



We would like to commend LeMay et al. (1) for their work addressing the important clinical conundrum of whether to provide triple antithrombotic therapy (TATT) for patients presenting apical akinesis/

dyskinesia following anterior ST-segment elevation myocardial infarction. This study takes advantage of a patient population with consistent follow-up within the same regional health system, managed at a high-volume academic center, and participating in a detailed prospective clinical database. In reviewing the report, however, we were left with a few questions; the answers to which might be of interest to other readers.

First, it is not clear to us from our reading of the paper how the propensity score was derived, for what clinical parameter propensity was determined (i.e., propensity for TATT vs. propensity for net adverse clinical events) (2), or how the propensity score was used to determine the net adverse clinical events odds ratio reported for warfarin therapy. Was this also part of the inverse-probability weighting multi-variable regression analysis?

Second, and somewhat related, it would seem, from the data presented, that anticoagulation with warfarin for apical dysfunction is the exception rather than the rule at this particular institution, with fewer patients treated and with TATT patients having more apical dysfunction, worse ejection fractions, and a 3-fold higher rate of cardiogenic shock. As such, we are left to wonder whether this retrospective analysis suffers from intractable confounding, which would explain the apparent paradoxical increase in non-hemorrhagic events in this group.

Finally, we would ask the authors to comment on both the timing of adverse bleeding events prior to hospital discharge (post-procedure vs. post-initiation of warfarin) and the decision to include these in the primary analysis. It would stand to reason that most patients in this group did not have a therapeutic International Normalized Ratio until the last day or 2 of hospitalization. A “back of the envelope” calculation suggests that the exclusion of in-hospital events would make the difference in outcomes between the 2 groups considerably less dramatic. Would a landmark analysis from the time of discharge have also achieved statistical significance?

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The Imperfections and Perils of Procedure-Based Risk Scores



Sherwood et al. (1) report that groups that perform more high-risk percutaneous coronary interventions have similar risk-adjusted mortality to those who perform fewer. The data are interesting, but a number of limitations preclude the final conclusion that adopting a more aggressive practice pattern will not increase risk-adjusted mortality.

Subgroups do not have uniform risk. Patients in cardiogenic shock have mortality rates that range from 22% to 88% (2). Physicians preferentially treat patients at the lower spectrum of risk and thus will have lower observed mortality than predicted by risk scores. At the same time, motivated practitioners have an incentive to “up-code,” which artificially inflates the estimated risk. The fact that in Sherwood et al. (1), “high-risk” cases tended to have lower-than-expected mortality is consistent with these limitations.

The conclusion also assumes that risk-averse operators are as adept as those who regularly perform high-risk cases. One of the benefits touted for public reporting is that it directs higher-risk cases towards superior operators (3).

A final limitation is the exclusion of patients who receive angioplasty at one site, but are then transferred to a different site. This excludes high-risk patients and procedural complications that might significantly alter the final results.

These limitations were not present at a Canadian regional care center, free of the medico-legal and public reporting concerns of the United States. In this setting, regional efforts to more aggressively treat high-risk myocardial infarction patients led to an increase in risk-adjusted mortality despite evidence for preserved procedural quality (4).

This debate also distracts from the more important issue. The real question is whether risk aversion related to public reporting results in public harm. This