Response to Letter Regarding Article
“Clinical Outcomes Using a Platelet Function-Guided Approach for Secondary Prevention in Patients With Ischemic Stroke or Transient Ischemic Attack”

Response:

We thank Drs Meves and Neubauer for their interest in our recent article, “Clinical Outcomes Using a Platelet Function-Guided Approach for Secondary Prevention in Patients With Ischemic Stroke or Transient Ischemic Attack.”

Regarding the definition for aspirin nonresponse in our study, we had used the available clinical test at our institution during the time period of the study. Aspirin resistance was defined as meeting 2 criteria for mean platelet aggregation based on testing with arachidonic acid and adenosine diphosphate; patients who met only one of the 2 criteria were defined as incomplete responders. The modifications in antiplatelet management did not differ between patients labeled as aspirin-resistant or incomplete responders; thus, we chose to combine both to comprise our aspirin nonresponse cohort.

Nonadherence to antiplatelet therapy is indeed a major issue in interpreting platelet function studies. In fact, nonadherence is likely of greater clinical importance than resistance. Given that our study was retrospective, adherence could not be assessed and may have been a confounder.

Before testing, the mean aspirin dosage was lower in the antiplatelet therapy modification group compared with the no modification group, whereas the mean clopidogrel dosage was higher in the modification group. After testing, the mean dosages of aspirin and clopidogrel were significantly higher for patients with antiplatelet therapy modification compared with patients without any modification. In the modified group, the posttesting mean dosages were significantly higher compared with the pretesting mean dosages. Thus, higher mean dosages of aspirin and clopidogrel in the modification group did not improve clinical outcomes and were associated with increased adverse events.

The specific reasons for increased use of dual antiplatelet therapy in our patient population were not known. The heterogeneous antiplatelet regimens that patients were on before platelet function testing coupled with diverse modifications in antiplatelet regimens after testing made subgroup analyses of the data unreliable given the study’s overall sample size.

Despite using a time-to-event analysis for each clinical outcome, temporal changes in platelet function after an acute event may also contribute to variability in antiplatelet therapy response. The low rate of retesting in our study population did not allow for an assessment of the temporal variability in antiplatelet response or to determine if modifying antiplatelet therapy improved antiplatelet response and subsequent clinical outcomes.

We agree that the diagnosis of transient ischemic attack can be difficult. In our study population, every patient was evaluated by a stroke neurologist. Thus, we felt confident including the transient ischemic attack subset.

In summary, the results of our retrospective study should be interpreted with caution given the potential confounders that we already acknowledged in our article. Our results certainly do not prove that there is no value in platelet function testing; in fact, our hypothesis was that there would be benefit. However, our study did not find any reduction in ischemic events and instead found increased bleeding. Therefore, before routine clinical use, a randomized trial is necessary to determine if a platelet function-guided approach is beneficial and safe in patients with ischemic stroke or transient ischemic attack.

Disclosures

Dr Bhatt is on the Advisory Board of Medscape Cardiology; the Board of Directors of Boston VA Research Institute, Society of Chest Pain Centers; Chair of the American Heart Association Get With The Guidelines Science Subcommittee; received honoraria from the American College of Cardiology (Editor, Clinical Trials, Cardiosource), Duke Clinical Research Institute (clinical trial steering committees), Slack Publications (Chief Medical Editor, Cardiology Today Intervention), and WebMD (CME steering committees); received research grants from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Sanofi Aventis, and The Medicines Company; performed unfunded research with PLx Pharma and Takeda.

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