Defining the Optimal Activated Clotting Times During Percutaneous Coronary Intervention: Aggregate Results From 6 Randomized, Controlled Trials

To the Editor:

A recent article in *Circulation* by Chew et al.1 stated that the optimal range of activated clotting time (ACT) for unfractionated heparin therapy in percutaneous coronary interventions (PCI) is between 350 and 375 seconds. These data have been obtained by a post hoc analysis from 6 randomized trials. As reported by the authors, this range of ACT is substantially higher than those previously reported and recommended.2

We would like to comment on the analysis by quartiles of ACT (Figure 2) provided by the authors. As stated in the article, the lowest probability of 7-day combined end point (death, myocardial infarction, revascularization) is obtained with an ACT greater than 350 seconds (7.7%). However, the 7-day combined end point probability is only slightly higher (9.0%) for an ACT lower than 170 seconds; this is not commented on by the authors. They do not say whether the difference between these probabilities is significant. Moreover, the 9.0% probability of the 7-day combined end point for an ACT <170 seconds is lower than the 11.6% probability of the next quartile (ACTs between 171 and 295 seconds). This is not expected in a model that links low ACT and high risk of ischemic events. We would be interested to know the authors’ interpretation of these data.

We do believe that this interesting result in the lowest ACT quartile is in accordance with recent reports3,4 showing that lower doses of unfractionated heparin are associated with equivalent clinical outcomes. Therefore, the optimal range of ACT in PCI needs further prospective study and is still unknown.


Response

In our recent retrospective analysis of 6 randomized trials examining the relationship between activated clotting times (ACTs) at the time of device activation and outcome, we observed a reduction in 7-day ischemic events associated with increasing ACT levels.1 As noted by Dr. Helft et al, within the quartile analysis, the event rate in the first quartile is lower than the event rate observed in the next higher quartile (9.0% versus 11.6%, *P* = 0.032). While, by univariate analysis, the lower event rate in the first quartile is statistically significant, this relationship does not persist after adjusting for other important clinical and procedural factors by multivariate testing. Within the context of retrospective data, the precise explanation for the lower event rate among patients with low ACT levels in the absence of glycoprotein IIb/IIIa inhibition remains speculative. However, given this relationship is no longer statistically significant by multivariate analysis, factors such as lower clinical risk and shorter procedural duration likely account for much of this observation. For example, an operator may be less vigilant with the ACT if a quick intervention in an ACC/AHA type A lesion in a stable patient was anticipated. Thus, in such a scenario, the low ACT did not account for the beneficial outcome, but rather the lower underlying risk did (for which multivariate analysis adjusts). Hence, this observation should not be construed as support for targeting low ACT levels, as advocated by other investigators.2,3,4 We agree that prospective evaluation of this question would be valuable.

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