10 min post-contrast (6) and may have led to a higher incidence of MVO in the latter.

In conclusion, IMR at the time of PPCI can identify those patients with MVO, allowing the implementation of treatment to minimize this complication. We provide weighted mean IMR values in patients with MVO (49 ± 33 U) and without MVO (27 ± 22 U), information that may be used to estimate sample sizes when planning future studies to assess the efficacy of novel therapies for reducing its burden.

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APPENDIX For an expanded Methods section, please see the online version of this article.

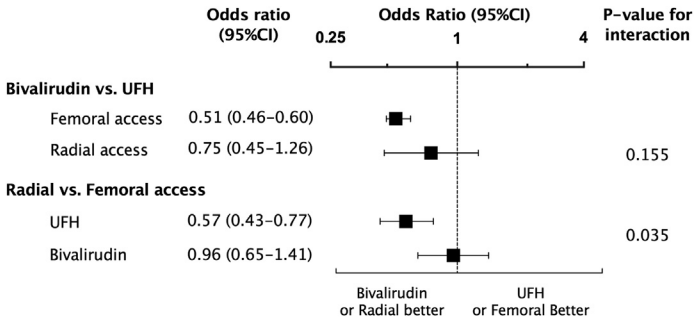
Antithrombotic Therapy and Vascular Access Site

Comparing Effect Sizes, Not Only p Values

In a recent paper, Mina et al. (1) presented an interesting meta-analysis of 8 randomized trials evaluating the safety and the efficacy of antithrombotic therapy according to the type of vascular access and vice versa. The investigators concluded that bivalirudin reduced the risk for major bleeding in patients who underwent femoral access but was ineffective in case of radial access. Analogously, radial access reduced the risk for bleeding among patients who received unfractionated heparin, but not bivalirudin.

However, the investigators did not formally assess the presence of treatment heterogeneity through interaction testing. As shown in **Figure 1**, although bivalirudin versus heparin significantly reduced the risk for major bleeding in patients with femoral access (odds ratio [OR]: 0.51; 95% confidence interval [CI]: 0.46 to 0.60) compared with radial access (OR: 0.75; 95% CI: 0.45 to 1.26), the test for interaction was not significant (p for interaction = 0.155). However, radial versus femoral access significantly reduced the risk for major bleeding in patients who received unfractionated heparin (OR: 0.57; 95% CI: 0.43 to 0.77), but not in those who received bivalirudin (OR: 0.96; 95% CI: 0.65 to 1.41), and, importantly, the test for interaction was significant (p interaction = 0.035). Therefore, a more nuanced interpretation would be that bivalirudin reduces the risk of major bleeding irrespective of the type of access, whilst radial access reduces the risk for major bleeding predominantly among patients receiving unfractionated heparin. Although apparently puzzling, this result is easily explained by the fact that bivalirudin decreases the risk for both access- and non-access-site bleeding, and therefore, its safety profile is not determined exclusively by the type of vascular access (2). Of course, radial access is only able to reduce access-site bleeding.

FIGURE 1 Results of Interaction Testing



CI = confidence interval; UFH = unfractionated heparin.

In addition, other considerations should guide the choice of vascular access and antithrombotic therapy. Radial compared with femoral access reduces the risk for mortality among patients with acute coronary syndrome (3), whereas the use of bivalirudin is associated with a higher risk for stent thrombosis, which is particularly increased among patients with acute myocardial infarctions and tends to be less pronounced among those pretreated with unfractionated heparin (4). Therefore, in clinical practice, it seems reasonable to prefer radial access over bivalirudin and to consider bivalirudin particularly in patients with failed or contraindicated radial access undergoing femoral procedures.

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REPLY: Antithrombotic Therapy and Vascular Access Site

Comparing Effect Sizes, Not Only p Values

We thank Dr. Danzi for his interest in our article regarding the effect of access site and anticoagulation regimens on outcomes of patients with acute coronary syndrome (1). Although we agree with Dr. Danzi, that the p value for interaction was not statistically significant when bleeding outcome of bivalirudin versus heparin was stratified by access site. Additional published and unpublished findings validates our unmoderated interpretation. First, the HEAT PPCI (How Effective Are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention) trial (2), which included 81% radial access patients, showed absence of any benefit with bivalirudin, implying that radial access use masked the bleeding-lowering benefit with bivalirudin. We excluded HEAT PPCI due to our stringent inclusion criteria, and we could not obtain access specific bleeding outcomes data from the authors. Although patients with femoral access patients were included in the trial, when we include the bleeding outcomes from HEAT PPCI in the meta-analysis, the bleeding-lowering effect of bivalirudin remains comparable with heparin in radial access patients (odds ratio, 0.84; 95% confidence interval, 061 to 1.15; p = 0.28), and the p value for interaction (access site and bleeding) becomes statistically significant (p = 0.005), suggesting that bleeding outcomes do differ between access site subgroups. Another meta-analysis by Mahmoud and Elgendy (3) included HEAT PPCI in their analysis and suggested absence of significant bleeding lowering effect of bivalirudin when radial access is used.