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REPLY: Efficacy of Radial Versus Femoral Access in the Acute Coronary Syndrome

Is It the Operator or the Operation That Matters?

Our viewpoint was a critical assessment of a trial and not intended to diminish the outstanding work done by physicians who have developed and promoted transradial access (TRA) for coronary intervention. That said, Dr. Rao and colleagues should not confuse 2 different factors that can independently influence an outcome in such a trial: 1) a center's annual percutaneous coronary intervention (PCI) volume; and 2) a center's proportion of radial PCI. In the MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) trial (1), comparing TRA with transfemoral (TFA), the center's annual PCI volume had the following impact on net adverse clinical events (NACE): low volume 10.8% versus 14.0% ($p = 0.011$), intermediate 9.4% versus 9.1% ($p = 0.76$), and high 9.0% versus 11.8% ($p = 0.025$); the p value for interaction was 0.89, indicating that the center's volume did not differentially impact on the results. However, the p value for interaction of 0.0048 for a center's proportion of radial PCI was so strong that to compare TRA and TFA without taking the center's experience into consideration may not be appropriate. The benefit of TRA was entirely confined to the subset of patients randomized in centers where the proportion of radial PCI was very high (i.e., 80% to 98%). Moreover, the rates for NACE in the TFA group were quite excessive in the "high" TRA centers. In keeping with this, a high-volume academic radial PCI center recently reported that total vascular complications were higher in a contemporary cohort where both TRA and TFA were used as compared with a historical cohort where only TFA was used; the benefit associated with TRA was offset by a paradoxical increase in vascular complications among TFA patients (2). The report suggests that a center may become deskilled at performing TFA and that education and training are needed to ensure proficiency at TFA.

Dr. Rao and colleagues indicated that there was no difference in the use of glycoprotein IIb/IIIa inhibitors (GPIs) between groups in MATRIX. However, these drugs are known to increase bleeding and mortality, and fewer events would likely have occurred had GPIs not been used.

The reference to the ISAR-CLOSRE (Instrumental Sealing of ARterial puncture site–CLOSURE device vs manual compression) trial is not appropriate as this study evaluated vascular closing devices (VCDs) in stable patients undergoing diagnostic coronary angiography; yet VCDs significantly reduced the rates of large hematomas. Dr. Rao and colleagues' claim that "the costs are not justified" is unfounded as a cost-effective analysis showed that the use of a VCD lowers direct hospital costs by $44/patient after PCI (3).

In the large seminal trials quoted by Dr. Rao and colleagues, the major adverse cardiovascular events (MACE) ratio for non-ST-segment elevation myocardial infarction (NSTEMI)/ST-segment elevation myocardial infarction (STEMI) was 1:1 while it was 2:1 in the MATRIX trial (11.7% [TRA] and 13.8% [TFA] for NSTEMI vs. 6.1% [TRA] and 6.3% [TFA] for STEMI), suggesting selection bias. In the MATRIX trial, both STEMI and NSTEMI appeared to benefit from TRA as the interaction p value for MACE and NACE was not significant. In the RIVAL (RadIal Vs femorAL access for coronary intervention) trial (4), it was quite the opposite: MACE and NACE were significantly lower with TRA in the STEMI population but not in the NSTEMI population; the interaction p values were significant (i.e., the benefit was entirely confined to the STEMI population). Finally, in MATRIX, the p value for mortality ($p = 0.045$) was not adjusted for the multiple testing of the components of the composite outcome. Regardless, these trials were not powered for mortality. Many questions remain unanswered and a dedicated STEMI trial is needed. As

recommended by Lee et al. (5), the SAFARI-STEMI (SAfety and efficacy of Femoral Access versus RadIal access in ST-Elevation Myocardial Infarction) trial is designed to support liberal use of VCDs and contemporary oral antiplatelet medication without GPIs; in response to researchers and granting agencies, the sample size for the SAFARI-STEMI trial has been substantially increased in order to evaluate the seminal outcome of mortality.

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Digital Gangrene Following Transradial Coronary Angiogram

We enjoyed reading the case report by Singh et al. (1) reporting on a vascular complication following transradial access (TRA) in a middle-age woman requiring percutaneous coronary intervention after thrombolysis.

Notably, the transradial procedure was successfully completed and no site-access crossover was needed, thus minimizing the well-known access-site bleeding liability shortly after fibrinolytic administration, as previously shown in the context of the ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention) trial (2). This case emphasizes once more that evaluating ulnar patency prior to percutaneous coronary intervention with Allen's test (AT) neither prevents nor reduces the risk of ischemic hand events, which, while extremely rare, can occur irrespective of whether ulnar collateral circulation is patent before the procedure.

In the RADAR (Should Intervention Through Radial Approach be Denied to Patients With Negative Allen's Test Results) study we evaluated the safety and feasibility of TRA in patients with abnormal or intermediate AT results compared with those with normal AT results, measuring lactate levels, plethysmographic readings, and angiographic frame count to assess ulnar flow (3). No hand ischemic complication occurred in the 2 groups; likewise, lactate level, handgrip strength, and discomfort level reported by the patients were similar, with a decrease in post-test ulnar frame count among those with abnormal AT, indicating an enhanced ulnar flow.

We therefore believe that the assessment of ulnar circulation patency should not be evaluated prior to TRA as this may lead to avoid TRA in patients who could safely receive it. The MATRIX (Minimizing Adverse haemorrhagic events by TRansradial access site and systemic Implementation of AngioX) trial was the only randomized controlled study so far performed not mandating the performance of AT prior to TRA: importantly, no ischemic complication has been observed due to TRA catheterization in 8,404 patients (4).

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