

Letters

TO THE EDITOR

Efficacy of Radial Versus Femoral Access in the Acute Coronary Syndrome



Is It the Operator or the Operation That Matters?

We read with great interest and concern the paper by Le May et al. (1) regarding the role of radial approach in patients with acute coronary syndrome (ACS). Our concerns are due to their inappropriate interpretation of clinical trial data and spurious arguments against radial access that runs of the risk of slowing the adoption of transradial procedures and thus potentially lead to increased adverse outcomes among high-risk patients undergoing percutaneous coronary intervention.

The concerns of Le May et al. (1) over multiple comparisons in the MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) trial are unfounded. While there are several techniques to account for multiple comparisons, the Bonferroni-Holm correction, which was pre-specified in the MATRIX trial (2), is by far the most conservative one. In the MATRIX trial, radial approach significantly reduced the incidence of 30-day net adverse clinical events (NACE) ($p = 0.009$). These results are robust even when accounting for 4 comparisons. In addition, many of the large seminal trials of acute coronary syndromes have included both non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) patients (3). The correct interpretation of subgroups is to use interaction p value to determine consistency of benefit in subgroups and the benefit was consistent in both NSTEMI and STEMI in MATRIX. In addition, randomization in the MATRIX trial was stratified according to NSTEMI or STEMI presentation. Taken together, the available trials strongly demonstrate that transradial intervention (TRI) is superior to femoral approach in ACS patients regardless of presentation. Regarding the effect of center volume, the beneficial effect of radial approach was more

pronounced at centers with high radial volume in the RIVAL (Radial Vs femoral access for coronary intervention) and MATRIX trials. The positive interaction term by center volume demonstrates that the primary effect may be affected to some degree by the subgroup—in other words, the results of the MATRIX trial stand alone and the finding in the subgroups of center radial volume demonstrate that centers that perform a high proportion of TRI realize its greater benefits—a finding that is completely consistent with the volume-outcome relationship for cardiovascular procedures. There was no significant difference in the use of glycoprotein IIb/IIIa inhibitors between the radial and femoral groups in the MATRIX trial, and the benefit of radial access was irrespective of glycoprotein IIb/IIIa inhibitor use. Finally, a commonly held belief among interventional cardiologists is that vascular closure devices (VCDs) reduce bleeding, and Le May et al. (1) repeat this misconception in their review. The ISAR-CLOSURE (Instrumental Sealing of ARterial puncture site—CLOSURE device vs manual compression) trial showed that VCDs were noninferior, not superior, to manual compression with respect to 30-day vascular complications (4). The added cost of VCDs is not justified when their outcomes are either no better or worse than manual compression.

The randomized trial data clearly support the use of radial access in patients with ACS undergoing angiography or intervention. Given the robustness of the data, performing more randomized trials, such as the SAFARI STEMI (Femoral vs. Radial Access For Primary PCI) trial, which is one-third the size of the MATRIX trial and is most likely underpowered for the primary outcome, is unlikely to be informative. Instead, effort should be directed at increasing the adoption of radial approach and ensuring proficiency with the procedure using “best practices” as the foundation (5).

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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-CLOSURE (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