

## EDITORIAL COMMENT

# Radial Access for ST-Segment Elevation Myocardial Infarction Interventions

## Does It Really Lower Mortality?\*

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Although the radial access option has existed for over 20 years, only recently has it been adopted for coronary angiography and percutaneous coronary intervention (PCI) in the United States. Despite the recent enthusiasm for this approach, only 16.1% of PCI procedures in the United States are performed radially (1), and it has been suggested that with experienced operators, the radial or femoral approach leads to comparable clinical outcomes (2). Furthermore, at least in the United States, limited radial access training has resulted in the majority of interventional cardiologists being unfamiliar with radial access and, therefore, they have failed to embrace this technique (2). In contrast, outside of the United States, most interventionalists have adopted the radial approach as the predominant access for PCI (3).

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In acute ST-segment elevation myocardial infarction (STEMI) patients, timely reperfusion is the primary goal, and the femoral approach would appear to provide the advantages of rapid arterial access, more predictable vascular anatomy, and the ability to provide supplemental hemodynamic support as necessary. However, in STEMI patients there is also greater use of potent adjunctive anticoagulation and antiplatelet therapy, potentially leading to higher bleeding rates, which in turn are associated with adverse long-term ischemic consequences after PCI (4–6). Though

there have been limited studies evaluating the optimal access site for PCI patients, a recently published randomized controlled trial (RCT) of radial versus femoral approach for primary PCI in STEMI patients showed significant reductions in major adverse cardiac events (MACE) including cardiac mortality in favor of the radial approach (7).

Karrowni et al. expand on the results of this single study in the meta-analysis published in the current issue of *JACC: Cardiovascular Interventions* (8). Analyzing the published and presented RCT (n = 12) of STEMI patients (n = 5,055) randomized to the radial versus femoral approach, they show that radial access leads to superior outcomes with reductions in both mortality and major bleeding. Statistically, the dataset was homogeneous with consistent and pertinent endpoints, and matched anti-coagulation and antiplatelet therapies. Their analysis revealed significant reductions in mortality (2.7% vs. 4.7%; odds ratio [OR]: 0.55, 95% confidence interval [CI]: 0.40 to 0.76; p < 0.001), major bleeding (1.4% vs. 2.9%; OR: 0.51, 95% CI: 0.31 to 0.85; p = 0.01), access site bleeding (2.1% vs. 5.6%; OR: 0.35, 95% CI: 0.25 to 0.50; p < 0.001), and overall MACE (4.6% vs. 6.8%; OR: 0.64, 95% CI: 0.49 to 0.83; p < 0.001) with the radial approach. No differences were observed in the incidence of stroke, myocardial infarction, or target lesion or target vessel revascularization. Procedure time was minimally prolonged in the radial arm by 1.5 min (p = 0.01), whereas crossover rates were 4.6% with the radial and 1.1% with the femoral approach.

The reduction in ischemic time and mortality for STEMI patients treated with primary PCI (using the femoral approach in the majority of studies) is well documented and has resulted in this being the preferred reperfusion strategy (9,10). The current study suggests that an additional incremental lowering of mortality using the radial approach in STEMI patients, beyond that previously achieved with early mechanical reperfusion using the femoral approach, is possible without a delay in the procedure time. However, these mortality data need to be interpreted with caution. A meta-analysis to define an optimal treatment strategy is often performed when prior data are incongruent, or in the absence of an adequately powered multicenter RCT. In the current meta-analysis, mortality data are heavily weighted from 3 studies: the STEMI cohort from RIVAL (Radial Versus Femoral Access for Coronary Intervention Trial) (n = 1,958) (11); RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) (n = 1,001) (7); and the STEMI-RADIAL (A Prospective Randomized Trial of Radial vs. Femoral Access in Patients With ST-Segment Elevation Myocardial Infarction) trial (n = 707) (12). The STEMI cohort in RIVAL was a subgroup analysis of a larger trial that failed to demonstrate a difference in major bleeding or ischemic events between the radial and femoral approach in 7,021 patients with an acute coronary syndrome. The majority of

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deaths were in patients who did not have a major bleed or an access site complication (11), and the results from a subgroup analysis should always be interpreted with caution. In RIFLE-STEACS, a 4-center clinical trial performed in Italy at high-volume radial access centers, patients presenting up to 24 h after their index event or in cardiogenic shock were included, and the majority of patient deaths were from pump failure and not related to access site complications or bleeding (7). Both RIVAL and RIFLE-STEACS also included patients who underwent rescue PCI after failed thrombolysis. In contrast, the STEMI-RADIAL trial had the strictest inclusion criteria, with patients undergoing primary PCI within 12 h of symptom onset, and despite significant reduction in bleeding and access site complications with radial access, this study did not demonstrate a mortality difference between the 2 approaches (12). Therefore, individually evaluating the 3 major studies included in this meta-analysis shows significant heterogeneity in inclusion criteria and the lack of a mechanistic link between individual patient access site complications, bleeding, and mortality. At best, these data are hypothesis-generating and are awaiting confirmation from a large, adequately powered, multicenter RCT.

Anticoagulation strategies with low use of the direct thrombin inhibitor bivalirudin (<10% in the included studies) and higher than contemporary use of glycoprotein IIb/IIIa inhibitors (30% to 70% in the included studies) also favored the radially treated patients when considering access site bleeding as an endpoint and might have contributed to the mortality difference in the 2 groups (7,8,11,12). A contemporary strategy of thienopyridine pre-treatment, judicious use of glycoprotein IIb/IIIa inhibitors, and routine bivalirudin use for STEMI patients as part of a bleeding avoidance strategy might lead to a less significant difference in bleeding rates with the femoral approach. However, until such an approach is tested, the radial approach is clearly associated with lower access site complications and major bleeding, and the data are consistent in all of the trials included. The association between bleeding and long-term adverse events after PCI is well established, though secondary transfusion and premature discontinuation of adjunctive pharmacotherapy for hemodynamically unstable patients after a bleeding event are likely among the contributing factors (4-6).

The definition of MACE and length of follow-up for clinical events was highly variable in the studies included and the lower MACE rate seen with the radial approach was primarily a result of the mortality benefit observed in the RIVAL (STEMI cohort) and RIFLE-STEACS studies. Individual MACE rates were comparable with both access strategies. Notably, data regarding the reduction in bleeding and mortality with radial access in the current analysis are also consistent with a recent large ACC-NCDR (American College of Cardiology-National Cardiovascular

Data Registry) database analysis showing lower bleeding and in-hospital mortality with radial access PCI during STEMI (13). However, in order to replicate these findings in clinical practice, primary PCI for STEMI using radial access requires experienced operators at high-volume radial catheterization laboratories. This was common in all of the studies included, and though exact definition of an experienced radial operator is unclear, a steep radial access learning curve is well recognized.

To achieve uniform proficiency in this technique, we have to: 1) ensure that radial access is a formal part of all training programs in interventional cardiology; 2) provide high-quality radial access training programs throughout the country for practicing interventional cardiologists; 3) promote a change of culture in catheterization labs so that staff are also engaged and trained; and 4) engage regional proctors/experts who can rapidly disseminate the technique to enable the majority of interventional cardiologists managing STEMI patients in becoming facile with radial access. This should lower access site bleeding and has the potential to further lower mortality rates in STEMI patients.

Based on the current data, the radial approach to PCI in STEMI patients appears to be the preferred approach for experienced radial operators. However, in the absence of adequate training in radial access, primary PCI operators and centers should perfect the radial access approach in elective PCI patients prior to routinely using it in STEMI patients. Additional benefits of using the radial approach, including improved patient comfort, efficient catheterization lab throughput, and easier same day discharge, particularly applies to elective PCI patients in whom a mortality benefit likely does not exist or would be impossible to demonstrate. An adequately powered, multicenter RCT for STEMI patients testing radial versus femoral access with contemporary antiplatelet and anticoagulation strategy, and routine vascular closure device for the femoral access, is imperative to determine if a mortality benefit truly exists with the radial approach and to further explore the relation between access site, bleeding, MACE, and mortality.

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