

# Radial Access in Non-ST-Segment Elevation Acute Coronary Syndrome



We read the study by Bavishi et al<sup>1</sup> recently published in the *American Journal of Cardiology*. The investigators systematically reviewed the current body of evidence about efficacy and safety of radial access, compared with femoral, in patients with acute coronary syndrome without persistent ST-segment elevation (NSTEMI-ACS) who are invasively managed. By pooling outcomes of 9 studies, they found a consistent reduction in access site-related major bleeding in the short-term period, which also translated into a statistically significant reduction in 1-year mortality. There was only a trend toward a reduction of in-hospital and 30-day mortality despite the large study population.

This study adds further to the notion that radial access is the most valuable mechanical strategy aimed at reducing the impact of bleeding on patient outcomes in the setting of ACS.<sup>2</sup> Randomized studies<sup>3</sup> and real-world experiences<sup>4</sup> have proved that radial access is associated with a consistent mortality benefit in patients with ST-segment elevation myocardial infarction.<sup>5</sup> The mechanistic relation behind this association is intuitive if one considers the high risk of access site complications and bleeding in patients with ST-segment elevation myocardial infarction, who undergo an emergency invasive procedure while receiving a cocktail of potent antithrombotic drugs, often for the first time in their life. Given the more variegated ischemic and bleeding risk profile of patients with NSTEMI-ACS and the lack of adequately powered trials, it is no surprise that no overwhelming evidences about a clear benefit of radial access in this specific subset of patients have emerged to date, and this is also consistent with subgroup analyses of RIVAL (A Trial of Transradial Versus Trans-femoral Percutaneous Coronary Intervention Access Site Approach in Patients With Unstable Angina or Myocardial Infarction Managed With an Invasive Strategy)<sup>6</sup> and MATRIX (Minimizing Adverse Hemorrhagic Events by Transradial

Access Site and Systemic Implementation of Angiox)<sup>7</sup> randomized trials.

Nonetheless, several points of the study by Bavishi et al<sup>1</sup> deserve comment. The investigators summarized 9 studies with, in turn, have extremely different designs: 2 are prespecified subgroups of landmark randomized trials, 2 are observational registries, 3 are post-hoc non-randomized comparisons of vascular access in randomized trials exploring different antithrombotic regimens, and 2 are retrospective databases from the United Kingdom. Specifically, it is likely that the London data by Iqbal et al<sup>8</sup> (London Heart Attack Centre) had been already included in the larger study by Ratib et al,<sup>9</sup> who analyzed the comprehensive national database of the British Cardiovascular Intervention Society. The heterogeneity of the populations examined across the 9 studies, with an imbalanced distribution of patients receiving radial versus femoral access (on average, 30,000 patients less received radial access compared with femoral in the present meta-analysis, and this is especially due to the post hoc studies), makes the results of the study by Bavishi et al<sup>1</sup> hard to be put in the context of current evidence from randomized studies conducted across the whole spectrum of patients with ACS.<sup>5</sup> Indeed, it is unexpected that such a striking 48% reduction in major bleeding did not confer a short-term mortality benefit. This observed reduction was flawed by substantial heterogeneity ( $I^2 = 71\%$ ) and 2 of the 3 largest (in magnitude) reductions in major bleeding come from UK databases,<sup>8,9</sup> in which bleeding rates were definitely lower than randomized studies. One may argue that a major bleeding rate below 1% in patients receiving femoral access may be biased by an underreporting of complications in an observational database (such as the one maintained by the British Cardiovascular Intervention Society) in which no systematic monitoring is prespecified. Unfortunately, Bavishi et al<sup>1</sup> could not explore possible other sources of statistical heterogeneity nor performed tests for interaction between registries and randomized studies.

In conclusion, Bavishi et al<sup>1</sup> should be congratulated for their efforts in

summarizing the elusive data about the potential benefit of radial access in patients with NSTEMI-ACS. It is expected that statistical pooling of heterogeneous studies will ultimately end in statistically heterogeneous results; however, this meta-analysis provides the plausible information that the dramatic reduction in bleeding complications obtained with radial access in patients with NSTEMI-ACS offers a survival benefit which can be appreciated only later on. The mechanisms supporting this benefit are only partially understood and are likely to be searched in the indirect consequences of bleeding, which may for instance involve a later deterioration in renal function.<sup>10</sup> Whether radial access represents a sort of "life insurance" we may offer to patients with ACS remains to be fully elucidated, but we are convinced that, more generally speaking, any bleeding avoidance strategy will also have a profound impact on mid long-term mortality.

Giuseppe Andò, MD  
Messina, Italy

Italo Porto, MD  
Rome, Italy  
12 November 2015

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<http://dx.doi.org/10.1016/j.amjcard.2015.11.018>

## Different Approaches for Coronary Computed Tomography Angiography–Derived Versus Invasive Fractional Flow Reserve Assessment



We read the meta-analysis by Gonzalez et al, published in the November issue of the *American Journal of Cardiology*. This meta-analysis compared the diagnostic

performances of coronary computed tomography angiography (CCTA), computed tomography perfusion, and computed tomography–based fractional flow reserve (CT-FFR).<sup>1</sup>

CT-FFR has been shown to significantly improve diagnostic assessment compared with CCTA alone. However, owing to time consuming offsite calculations, the clinical impact of this innovative approach remains unclear. Thus, a solution for physician-driven CT-FFR derivation using regular onsite workstations was developed, as noted by the first results produced by our research group<sup>2</sup> and Coenen et al.<sup>3</sup> This new CT-FFR algorithm applies reduced order models for more expedient calculations.

We note that the study by Coenen et al<sup>3</sup> was not included in the current meta-analysis by Gonzalez et al.<sup>1</sup> Inclusion of this study might have strengthened the study, as it would have added 106 patients and 189 vessels, reporting a pooled sensitivity of 81.3% and 87.5%, a pooled specificity of 37.6% and 65.1%, a pooled positive predictive value of 48.9% and 64.8%, and a pooled negative predictive value of 73.2% and 87.7% for CCTA and CT-FFR on a per-vessel level, respectively.<sup>3</sup> Furthermore, a discussion of the various CT-FFR approaches currently in exploration would have enriched the study.

Nevertheless, the investigators of the meta-analysis are to be congratulated for their work, as it constitutes a well-written study and covers a highly topical and recurrent subject of discussion that will likely be very interesting for readers.

**Stefan Baumann, MD**

Charleston, South Carolina  
Mannheim, Germany

**Ibrahim Akin, MD**

**Martin Borggrefe, MD**  
Mannheim, Germany

**B. Devon Ball Jr, BA**

**U. Joseph Schoepf, MD**  
Charleston, South Carolina

**Matthias Renker, MD**

Charleston, South Carolina  
Bad Nauheim, Germany  
11 November 2015

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<http://dx.doi.org/10.1016/j.amjcard.2015.11.019>

## Asymptomatic Severe Aortic Stenosis and Noncardiac Surgery



Severe aortic stenosis (AS) is considered a condition at high risk for cardiac complications during noncardiac surgery. This conclusion is mostly based on reports published more than a decade ago, which included mixed cohorts of patients with AS who were symptomatic, had left ventricular dysfunction and concomitant other valvular disease (e.g., mitral regurgitation). Granted, although symptomatic patients with severe AS are at higher perioperative risk for noncardiac surgery, more controversial is the asymptomatic patient. To this regard, the current European Society of Cardiology guidelines on valvular heart disease state that low-intermediate risk elective noncardiac surgery should be considered in asymptomatic patients with severe AS (level of evidence C).<sup>1</sup> Notwithstanding, many of these patients still undergo aortic valve replacement (AVR) or transcatheter aortic valve implantation (TAVI), with an inherent AVR/TAVI perioperative risk that is twofold to fourfold higher than that reported for noncardiac intervention in the presence of AS.<sup>2–4</sup>

Accordingly, we aimed to evaluate this issue by pooling into a meta-analysis the data of asymptomatic patients with severe AS undergoing noncardiac surgery compared to age- and gender-matched controls without AS. We searched studies conducted in the last decade through MEDLINE and Embase databases, using the keywords AS, noncardiac surgery, and perioperative risk. AS was defined severe when aortic

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