

EDITORIAL COMMENT

Radial Primary Angioplasty

The Gold Standard Treatment for STEMI Patients*

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We are flooded with studies on new drugs or devices because they attract commercial sponsorship. If their results show small incremental benefits compared with existing tools, immediate changes in guidelines and practice are requested by self-appointed opinion leaders, irrespective of the cost and compatibility for a sustainable health system. Mamas et al. (1) show a highly significant 29% reduction in 30-day mortality in 46,128 ST-segment elevation myocardial infarction (STEMI) patients using the radial access site, a huge benefit that comes with no additional cost. Radial angioplasty was introduced 20 years ago by Kiemeneij et al. (2), and immediately showed advantages in terms of reduction in bleeding, patient discomfort, and hospital stay. Small-scale studies also suggest improvements in hard endpoints, especially in acute coronary syndromes

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(ACS). Yet, we had to wait 15 years before a trial with more than 7,000 patients, a sufficient number to detect outcome changes, showed a significant 61% reduction in mortality at 30 days in the STEMI radial subgroup (3). Because this reduction was not consistent in all ACS patients and the primary endpoint was not met, results could not be considered conclusive (4). The smaller Italian RIFLE-STEACS (Radial Versus Femoral Randomization Investigation in ST-Elevation Acute Coronary Syndrome) trial (5), with 1,001 patients, found a significant reduction in mortality in the radial group, but mortality in the femoral group was abnormally high (5.2% vs. 9.2%; $p = 0.020$). Despite the strong message from a meta-analysis with 2,977 patients (6), new confirmatory trials were requested. We would probably have had to wait another 20 years if the initiation of large national registries in Sweden, the United

States, and now the United Kingdom had not offered the opportunity of providing new data. Combined, this now includes almost 160,000 STEMI patients with consistent results, revealing a 22% reduction in the adjusted one-year cumulative risk of death in 21,339 STEMI patients in the SCAAR (Swedish Coronary and Angioplasty Registry) (7), and a 24% reduction in in-hospital mortality in the 90,879 NCDR (National Cardiovascular Data Registry) U.S. patients (8). Nevertheless, this paper does not solve the radial paradox: What is the mechanism of the mortality improvement? How can radial angioplasty induce a reduction in mortality over and above the reduction in major bleeding and vascular complications? The investigators blame underestimation and lack of data auditing on bleeding. But these considerations also apply to the radial substudies of the RIVAL (Radial Versus Femoral Access for Coronary Intervention) (3) and HORIZONS (Harmonizing Outcomes With Revascularization and Stents) trials (9), which were fully monitored and highly focused on bleeding events. Without a clear mechanistic explanation and rationale, it is difficult to convince the skeptics that changes observed are not caused by differences in the radial and femoral patient groups. A major confounder can be the natural urge for experienced radial operators to turn to the femoral in a hemodynamically unstable patient, for whom you expect there is a chance to insert a balloon pump during or after angioplasty. In the recent SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial (10), mortality is still 40%, unfortunately, it is not helped by the use of intra-aortic balloon pump. Clustering of high-risk patients in the femoral group is not easy to correct with statistical adjustments. The U.K. radial operators in this registry had differences in concomitant treatment, which not everybody would agree might result in a mortality benefit. They used glycoprotein IIb/IIIa inhibitors and manual thrombectomy more frequently. Whereas glycoprotein IIb/IIIa inhibitors might be "out-of-fashion," in a clinical scenario where almost all patients were anticoagulated with heparin and very few received novel antiplatelet agents, especially in the early years of data collection, it is hard to argue with countless publications and meta-analysis in favor of these drugs (11). Reluctance to add the strongest and most rapid platelet inhibitors at our disposal even when there is high thrombus burden or slow flow during angioplasty, because fear of bleeding at the access site, may be deleterious. We are awaiting the results of large trials on manual thrombectomy, but the general view is that you do not need to treat everybody with thrombectomy. Still, radial operators perform thrombectomy more liberally than femoral operators do, reflecting an attitude of avoiding shortcuts. Whereas a rapid time to reperfusion is important, when flow is re-established, patience, a common virtue of radialists, and liberal use of

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adjuvant vasodilators, often already used by radialists to prevent spasm, may facilitate spontaneous thrombolysis and limit reperfusion injury through minimal technical differences. No Cox regression or propensity analysis can catch these subtle differences in practice.

The BCIS-NICOR (British Cardiovascular Intervention Society–National Institute for Clinical Outcomes Research) registry has an advantage over previous publications. Like SCAAR (7), it collects nationwide data and is not limited to selected centers. This study was conducted in a phase of rapid change in “access” policy, with radial angioplasty increasing from 12.5% in 2006 to 49.5% in 2010. Mamas et al. (1) do not correlate outcome with individual operator or center utilization using the radial approach. Still the message is clear, switching to a wide-scale radial policy, which necessarily means inclusion of operators and centers in a relatively early learning phase, still offers an advantage in mortality. This relatively high presence of initial adopters may explain the reason why outcome changes are not as large as in other registries and trials. However, it overrides the common belief that the radial approach is only helpful if you are a fully committed radial operator and center and eliminates the last excuse for operators and centers unwilling to change, despite overwhelming clinical evidence. Training is obviously still essential, and it is inconceivable to use a radial approach in an acute STEMI patient alone, in the middle of the night, without adequate experience of more predictable “simple” diagnostic and angioplasty cases. Young trainees must be trained in radial angioplasty and STEMI treatment using radial angioplasty, and these numbers should be separately collected. Mature operators should feel a moral obligation in learning new basic skills that will increase their performance (12). In the end, the 2012 European Society of Cardiology STEMI guidelines give a strong Class IIa Level B recommendation for radial angioplasty (13). Training and proctorship are universally accepted prerequisites for performing transcatheter aortic valve replacement implantation. So why not develop skills that, in absolute terms, will probably save more lives?

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