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EDITORIAL COMMENT

Radial Access in Women for Percutaneous Coronary Intervention

Toward the End of the Sex Paradox?*

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A growing body of evidence now supports the concept of "radial-first" access in acute coronary syndrome (ACS) for diagnostic angiography and intervention, and has led to the adoption of a Class Ia recommendation by the European Society of Cardiology for radial over femoral access in non-ST-segment elevated ACS (1). Updates from North American societies are pending.

To sum up its many benefits, radial access has been shown to reduce mortality, limit hospital stay, promote earlier ambulation and patient comfort, and most consistently, to reduce access-site bleeding and vascular complications (2). This latter finding is of particular interest in women, who are known for higher bleeding risk compared with men, especially in the context of ACS and its mandatory very potent antithrombotic regimens for percutaneous coronary interventions (PCIs) (3).

However, even though women would potentially benefit from radial access due to their higher baseline risk, observational retrospective data on large registries suggest that they are much less likely to undergo radial access than men, mostly because of feared technical challenges related to the small caliber of the radial artery and its propensity to spasm (4). Additionally, the majority of landmarks trials comparing radial and femoral access included mainly men, so that the impact of radial access on bleeding and vascular complications in women still remains unclear. Much alike the "radial paradox" previously described for obese patients, there seems to be a "sex paradox" depriving women of a potentially beneficial vascular access.

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In this issue of *JACC: Cardiovascular Interventions*, Gargiulo et al. (5) report a post hoc analysis drawn from the large MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) research program in which investigators specifically aimed at determining the impact of radial access on bleeding, vascular complications, and major adverse cardiovascular and cerebral events (MACCE) according to sex in ACS patients. The trial was initially designed and powered to detect differences between the 2 access sites regarding MACCE (composite of death, myocardial infarction, or stroke) and net adverse clinical events (NACE) (a composite of MACCE or major bleeding). The authors randomized 8,404 patients to radial or femoral access, of which 27% (n = 2,232) were women. Because the trial was not randomized on the basis of sex, there were significant differences between men and women in baseline characteristics: women were older, had a lower body mass index, and presented more frequently with non-ST-segment elevated ACS at an advanced Killip stage. After adjustment, the authors did not find significant differences in MACCE or NACE between men and women. They found, however, that women were at higher risk of access site bleeding (rate ratio [RR]: 1.36), severe bleeding (RR: 1.83), and transfusion (RR: 1.44) than men. Moreover, and perhaps most importantly, they found a significant reduction of both co-primary endpoints for women with radial access without any statistical interaction between access sites and sex. Hence, the feared technical challenges to gain vascular access did not seem to preclude favorable outcomes in women. Ultimately, the authors concluded that radial

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access should now be preferred to femoral access regardless of sex, and that it might even be more beneficial in women than in men.

This post hoc study drawn from the largest research program to date (and probably latest) comparing radial to femoral access provides convincing evidence to support a wider adoption of radial access as first intent in ACS. Although the trial was not initially designed or powered to detect differences according to sex, authors found a relative risk reduction of about 40% in BARC (Bleeding Academic Research Consortium) 3 or 5 bleeding in women undergoing radial access. These results are of the same magnitude as those reported in the RIVAL (Radial Vs femorAL access for coronary intervention) post hoc analysis previously published in *JACC: Cardiovascular Interventions* (6), in which authors found a 50% reduction in both bleeding (3.7% vs. 7.0%, hazard ratio 0.5; $p = 0.001$) and major vascular complications (3.1% vs. 6.1%, hazard ratio 0.5; $p = 0.002$) with radial access in women, equivalent to a number needed to treat of 33.

Therefore, conclusions drawn from the MATRIX and RIVAL research programs strongly support and confirm the early findings learned in the U.S.-based SAFE-PCI for Women (Study of Access Site for Enhancement of PCI for Women) trial that included 1,787 women randomized by access site within a national registry (7). Although the trial was stopped early due to a low event rate, the authors found a major 68% reduction in a composite outcome of bleeding and vascular complications (0.6% vs. 1.7%, odds ratio 0.32; $p = 0.03$) in the combined cohort of diagnostic catheterization and PCI.

Despite these encouraging results, it should be reminded that cross-over rates still remain higher in women compared with men (7.6% vs. 5.2% in the MATRIX cohort). Similar data were found in the RIVAL (11.1% vs. 6.3%) and SAFE-PCI for Women (6.1% for PCI and 6.7% for total cohort) trials. Considering the large benefits for women using radial artery access, every effort should now be made to reduce the risk of spasm and increase the likelihood of a "clean" radial access, for example by using ultrasound guidance or smaller sheaths and catheter sizes (4- to 5-F).

Adding the new evidence provided by Gargiulo et al. (5) to the RIVAL and the SAFE-PCI for Women trials, a few conclusions may now be drawn:

1. There are now clear benefits with radial access for women undergoing a diagnostic angiography or PCI for an ACS (including ST-segment elevation myocardial infarction).
2. These benefits are consistent with bleeding and vascular complications reduction observed in mixed-sex populations.
3. Data drawn from the MATRIX trial suggest that radial access might be associated with a significant reduction in MACCE and NACE in women.
4. Radial access for diagnostic angiography and PCI in women remains technically challenging.

There is now definite evidence supporting the adoption of radial access in first intent in both men and women, yet additional effort must still be made to complete coronary procedures initiated via the radial artery in women. With current imaging equipment and miniaturized techniques, operators should now offer radial access to all, especially to women, who might benefit most from it!

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