

EDITORIAL COMMENT

Large-Bore Radial Access for Complex PCI

A Flash of COLOR With Some Shades of Grey*

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Expansion means complexity, and complexity decay.

—C. Northcote Parkinson (1)

The adoption of radial artery access (RA) for cardiac catheterization steadily increased over time, given the proven benefit over femoral access (FA) in reducing the risk of major bleeding, vascular complications, and all-cause mortality (2-5), as well as improving patient comfort and health care costs (6). The large MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox) access trial demonstrated that RA reduces net adverse clinical events in patients with acute coronary syndromes undergoing invasive management, mainly driven by a reduction in major bleeding and cardiovascular mortality (4).

In line with this mounting evidence, a “radial-first” strategy has been strongly endorsed by American and European guidelines (7,8). As a result, the growing adoption of RA paved the way forward to its use even in complex interventional procedures, such as percutaneous coronary intervention (PCI) for chronic total occlusion (CTO), heavily calcified lesions, complex bifurcation, or left main stem. Nonetheless, the transition from femoral to radial approach may be

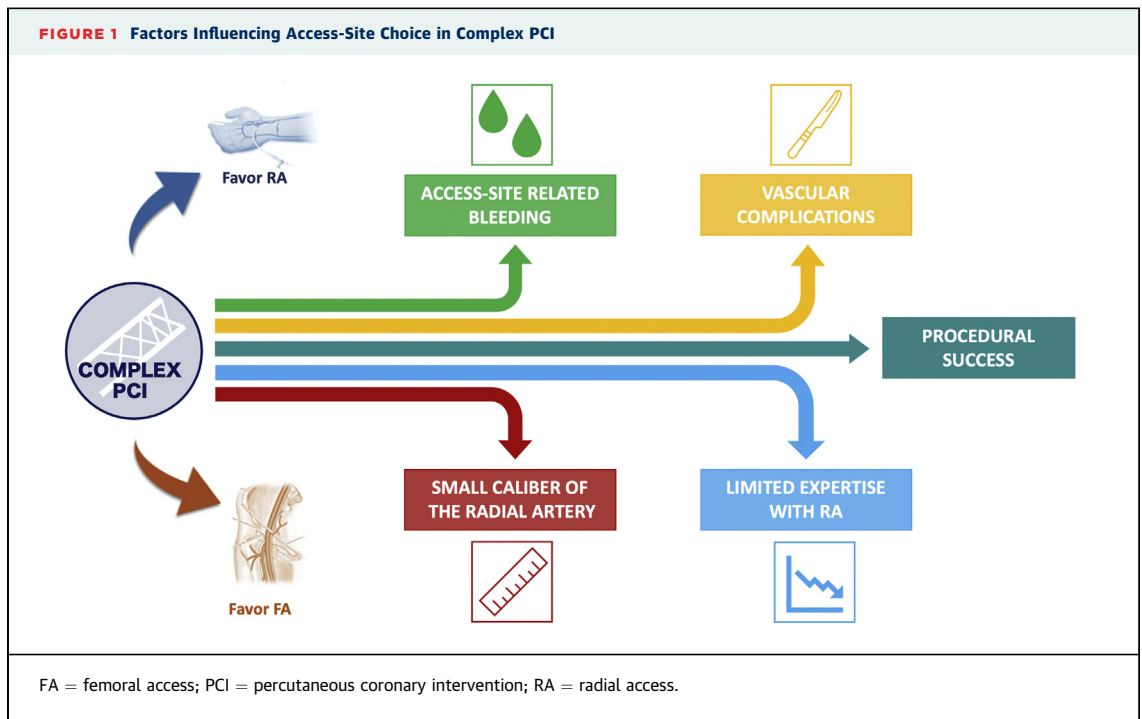
challenging in this setting and hampered by potential drawbacks, as the need for large-bore guiding catheters (≥ 7 Fr) and operator’s expertise with RA. Importantly, the use of large guide catheters through RA has been associated with increased risks of radial artery occlusion (9). The development of novel technologies as sheathless guide catheters or a thin-walled radial introducer sheath, allowing PCI with large-caliber guiding catheters, supported the preliminary use of RA also in these scenarios (10-12). A recent meta-analysis of observational studies on CTO PCI highlighted that RA is associated to fewer access-site complications and major bleeding with similar technical success compared with FA (13). However, RA was used in patients with lower baseline risk and less complex coronary lesions (13). From a theoretical standpoint, the expected benefit of RA could be even higher in patients undergoing complex PCI procedures, who usually exhibit high-risk clinical characteristics and complex coronary anatomy.

In this issue of *JACC: Cardiovascular Interventions*, Meijers et al. (14) report the results of the COLOR (Complex Large-Bore Radial PCI) trial, a randomized controlled clinical trial investigating the superiority of RA versus FA in 388 patients undergoing complex PCI with large-bore guiding catheters (7 Fr). In the overall cohort, CTO was present in 58%, heavy calcification in 19%, left main disease in 14% and complex bifurcation lesions in 9%. Secondary arterial access was used in 41% of patients. The primary endpoint was the composite of clinically relevant access-site-related bleeding (Bleeding Academic Research Consortium [BARC] 2, 3, or 5) or vascular complications requiring intervention of the randomized access site during hospitalization. The study met the superiority hypothesis concerning the composite primary endpoint (19.1% in the FA vs. 3.6% in the RA group;

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

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$p < 0.001$), mainly driven by a reduction in BARC 2 bleeding (16.5% in the FA vs. 3.6% in the RA group; $p < 0.001$) and fewer vascular complications requiring intervention (4.1% in the FA vs. 0.5% in the RA group; $p = 0.04$). Access-site crossover was comparable between the 2 groups, occurring in 3.6% of patients randomized to RA and 2.6% of those randomized to FA. There was no significant difference in terms of procedural success (86% in the FA group vs. 89.2% in the RA group; $p = 0.29$) or major adverse cardiovascular events (MACE) at 30 days (2.6% in the FA vs. 6.7% in the RA group; $p = 0.06$). Additionally, procedural time, fluoroscopy time, and contrast use did not significantly differ between the groups.

So, what does this multicenter randomized trial tell us in the “radial-first” era? First and foremost, it confirms that RA is safe even in complex PCI requiring large-bore guiding catheters, with fewer bleeding events (mainly BARC 2 bleeding) and vascular complications compared with FA. Second, procedural success and clinical outcomes are comparable between the 2 access sites in complex coronary lesions. Third, dual access is frequently used in complex PCI, mainly for CTO intervention, and secondary RA is associated with reduced BARC 1, but not BARC 2 bleeding compared with secondary FA, perhaps reflecting the smaller number of patients in this subgroup and/or the smaller caliber of the secondary access. An additional element to consider is

the low rate of radial crossover, which compares favorably with recent findings (15). This may reflect the elective nature of these procedures or alternatively, the patient selection process, for which no information is provided. Given the prognostic impact of radial crossover which has been shown to abolish the bleeding benefit offered by RA (15), the results of this study are further reassuring.

However, the design and findings of the COLOR trial raise important questions. In this study, Meijers et al. (14) included clinically relevant access site-related bleeding including BARC 2 into the primary composite endpoint. The investigators argue that BARC 2 access site bleeding has been shown to influence prognosis even beyond 1 year (16). However, standardization of BARC 2 bleeding events remains challenging especially considering that event adjudication was made by clinical events committee members not blinded to the randomization arm. Furthermore, only up to one-third of BARC 2 bleeding in the femoral group resulted in prolonged hospitalization. Therefore, it remains unclear whether these, most likely minor, events could influence prognosis. Importantly, one would expect that the mitigation of bleeding and vascular complications with RA would favorably (or at least neutrally) affect the 30-day MACE rate. Conversely, the MACE rate at 30 days was nearly doubled in the RA group (6.7%) compared with the femoral group (2.6%) with a borderline

statistical significance. In this regard, as properly acknowledged by the investigators, the trial is inconclusive, given the small sample size and the low number of events; therefore, this finding should not be overemphasized.

RA could entail clinical benefits that go beyond the reduction of major bleeding or vascular complications, such as prevention of acute kidney injury, which has been shown to act as 1 of the main players of the mortality benefit of RA over FA (17). Although contrast volume use did not differ between the 2 randomized groups in this study, the magnitude of acute kidney injury prevention with RA could be greater in complex PCI procedures. Unfortunately, the investigators did not collect renal outcomes data, and further studies are warranted to address this issue.

An additional element of concern in the present study is the lack of standardization for operators' expertise with RA. In the RIVAL (Radial vs Femoral Access for Coronary Intervention) (2) and MATRIX access (3) trials, RA expertise emerged as a potential effect modifier, indicating that RA is associated with improved outcomes compared with FA especially if performed in high-volume radial centers. This effect might be more relevant for complex PCI procedures, in which skilled operators manage a wide array of materials and techniques through RA or, frequently, dual vascular access. It is very likely that only operators with very high proficiency for RA participated in this study (14), and this needs to be taken into great account in interpreting the study results.

Overall, preliminary evidence for RA use in complex PCI are promising given the reduction of bleeding and vascular access-site complications with similar procedural success compared to FA. However, it is important to emphasize that high complexity of coronary lesions and operators' expertise with RA are

equally important to ensure optimal procedural and long-term clinical outcomes (Figure 1). Consequently, upfront selection of access site in complex interventions remains essential and should balance the benefit of bleeding avoidance with the operator's proficiency with RA to perform complex PCI.

In conclusion, the current study by Meijers et al. (14) demonstrated that RA is technically feasible and safer in complex PCI. Alongside this, interventional cardiologists should maintain high expertise in both radial and femoral access especially in complex interventions, basing access site selection on individual clinical and technical/procedural features (Figure 1). In this regard, the numerical imbalance in MACE events in favor of FA will most likely raise concern among many "femoral believers" that RA may not adequately support complex intervention. Therefore, further randomized adequately powered trials of RA versus FA in complex intervention are warranted. Only then, will RA be ready for prime time in complex PCI and become truly persuasive to the "femoral believer" community.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Prof. Valgimigli has received grants from Abbott, Terumo, Mediceur, and AstraZeneca; and personal fees from Abbott, Chiesi, Bayer, Daiichi Sankyo, Amgen, Terumo, Alvimedica, AstraZeneca, Biosensors, and Idorsia, outside the submitted work. Dr. Landi has reported that he has no relationships relevant to the contents of this paper to disclose.

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KEY WORDS complex percutaneous coronary intervention, femoral access, radial access