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EDITORIAL COMMENT

Should the Benefit of Transradial Access Still Be Questioned?*

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In the search for an alternative vascular access for coronary procedures that would be associated with lower bleeding risk, less vascular complications, and improved patient comfort, Campeau and Kiemeneij pioneered transradial access for coronary angiography and interventions (1). Subsequent adoption of this vascular access modality occurred at a relatively faster pace in Canada, Europe, and Japan where transradial access is currently used in the majority of cases.

Adoption of transradial access has been slower in the United States, mostly for lack of training opportunities, unavailability of specific equipment for radial artery puncture and access, and lack of interest among busy practicing physicians. However, this reality is rapidly changing and the use of transradial access has recently reached more than 30% in the United States (2).

Numerous observational studies have compared femoral versus transradial access for percutaneous coronary intervention (PCI). The results have consistently shown a reduction of approximately 80% in relative risk of bleeding and transfusions, coupled with a mortality benefit (3). In addition, transradial access has been associated with improved patient comfort, lower costs, shorter stay, and decreased workload for nursing staff. The trade-off is a steeper learning curve, higher crossover rates, inability to use large bore catheters, and longer procedural times associated with slightly higher radiation exposure (4).

In randomized clinical trials, the advantage of transradial over transfemoral access has been clear and consistent in patients with ST-segment elevation myocardial infarction (STEMI) (5–7), but less obvious in patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS), where patients are generally older (7). Possible explanations for this difference is that STEMI patients are exposed to higher intensity antithrombotic therapy at the time of angiography and PCI, and that the most frequent source of bleeding in this population is access site. In contrast, NSTE-ACS patients tend to experience lower bleeding rates and the source is less frequently associated with vascular access (1).

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In this issue of *JACC: Cardiovascular Interventions*, Porto et al. (8) analyzed the outcomes of the ACCOAST (A Comparison of prasugrel at the of percutaneous Coronary intervention Or as pre-treatment At the time of diagnosis in patients with non-ST-segment elevation myocardial infarction) trial according to access site (8). This was a multicenter, prospective, placebo-controlled trial that assessed the efficacy and safety of pretreatment with prasugrel in a randomized fashion among 4,033 patients undergoing early coronary angiography for NSTE-ACS. The main results of the study showed that the composite of cardiovascular death, myocardial infarction, stroke, urgent revascularization, and bail-out use of glycoprotein IIb/IIIa inhibitors was not reduced with pre-treatment. It was identical in the two-thirds of patients who underwent PCI, but major bleeding risk tripled with pretreatment (9). In the ACCOAST trial, 42% of patients underwent transradial angiography and therefore provided an opportunity to examine outcome differences according to access site in a moderate-high risk cohort of NSTE-ACS patients treated with more intense dual anti-platelet therapy. The analysis showed that only combined major and minor Thrombolysis In

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TABLE 1 Incidence of Stroke in Observational and Randomized Studies That Reported Outcomes According to Access Site

Study (Ref. #)	N	Radial	Femoral	p Value
PREVAIL (18)	1,052	0.0%	0.2%	0.50
BCIS (12)	370,238	0.1%	0.1%	0.91
RIVAL (7)	7,021	0.6%	0.4%	0.30
MATRIX (19)	8,404	0.3%	0.3%	1.00
ACCOAST (8)	3,987	0.7%	0.2%	0.02
EUROMAX (17)	2,152	0.3%	1.1%	0.02
RIFLE-STEACS (6)	1,001	0.8%	0.6%	0.73
STEMI RADIAL (5)	707	0.3%	0.3%	1.00

Myocardial Infarction bleeding was reduced with transradial access. Analysis of the efficacy endpoint using propensity score matching revealed that transradial access was associated with a slightly significant decrease in urgent revascularization but a significantly higher risk of stroke (0.7% vs. 0.2%; p = 0.02) compared with transfemoral access in all patient that underwent catheterization. Using propensity score matching to adjust for the differences in the radial versus femoral access populations, the difference became more pronounced (p = 0.005) The ACCOAST trial investigators highlighted this stroke difference as a "disturbing signal" (8).

The difference in stroke risk in the ACCOAST trial deserves careful attention and analysis. A clinically manifested stroke occurs rarely in the setting of PCI, with an incidence in the order of 0.2% to 0.4%, which has remained stable for the past 20 years (10). Stroke is a feared complication because of its strong association with mortality and its devastating effects on disability and quality of life. Pathophysiologic mechanisms leading to a stroke include embolization of aortic atheroma fragments, air embolus, severe hypotension, intracranial bleed secondary to antithrombotic therapy, and contrast-induced osmolar changes affecting the blood-brain barrier. Patient factors associated with stroke include older age, female gender, diabetes, hypertension, renal insufficiency, prior stroke, peripheral vascular disease, and cardiogenic shock. Procedural factors include longer and more complex procedures, larger contrast volumes, larger number of catheter exchanges, and catheters ≥7-F (11,12).

The overarching question is whether or not the transradial technique, highly regarded as a safer modality for cardiac catheterization, is truly associated with increased stroke risk. The presence of aortic atheroma is a well-recognized independent risk factor for stroke. Scraping of atheroma debris from the aorta occurs in more than 50% of cases during coronary engagement with transfemoral procedures (13). However, transesophageal echocardiography has shown that aortic atheromas are more complex and more frequently located in the descending aorta and the arch compared with the ascending aorta, where catheter manipulations occur during both transradial and transfemoral catheterization (14). A small randomized study showed a numerically higher incidence of silent cerebral infarcts on diffusion-weighted magnetic resonance imaging with transradial compared with transfemoral access (18% vs. 12%; p = 0.31) (15). It has also been shown that solid microemboli do occur when the catheters pass from the right innominate to the aorta (16). However, analyses of large registries, observations from clinical trials, and randomized studies have not been able to demonstrate an association between higher stroke risk and transradial access (5-7,12,17-19) (**Table 1**).

How should we then approach the risk of stroke when using radial access? First the investigators of all the randomized trials of radial versus femoral access should aggregate their data and define the stroke risk and the location of access. In particularly, they should try to establish the location of stroke in the right or left hemisphere in relationship to left or right radial access to better establish if the right radial access poses a greater risk as the catheters pass through the right innominate artery (and close to the right carotid). Furthermore, we should all pay more attention to the number of catheter exchanges we undertake, as higher number of catheters exchanges is associated with higher stroke risk. Randomized trials have suggested that angiography using radial access can many times be performed by a single catheter, which thereby can reduce the risk of stroke.

In conclusion, the ACCOAST trial investigators provided us with an important contribution to our current knowledge on choice of vascular access for patients with NSTE-ACS. They have identified a risk of periprocedural stroke with radial access, thereby raising awareness of this dreaded complication. Operators should identify patient factors associated with increased risk of stroke and continue to pay attention to procedural details utilizing best practices for vascular access (transradial or transfemoral) and minimize catheter manipulation. The vast majority of published data still supports the use of transradial access due to its superior safety, and it is expected that the use of this approach will continue to grow over time.

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REFERENCES

1. Rao SV, Cohen MG, Kandzari DE, Bertrand OF, Gilchrist IC. The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. J Am Coll Cardiol 2010;55:2187–95.

2. Feldman DN, Swaminathan RV, Kaltenbach LA, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the national cardiovascular data registry (2007–2012). Circulation 2013;127:2295–306.

3. Bertrand OF, Belisle P, Joyal D, et al. Comparison of transradial and femoral approaches for percutaneous coronary interventions: a systematic review and hierarchical Bayesian meta-analysis. Am Heart J 2012;163:632–48.

4. Plourde G, Pancholy SB, Nolan J, et al. Radiation exposure in relation to the arterial access site used for diagnostic coronary angiography and percutaneous coronary intervention: a systematic review and meta-analysis. Lancet 2015;386:2192–203.

5. Bernat I, Horak D, Stasek J, et al. ST-segment elevation myocardial infarction treated by radial or femoral approach in a multicenter randomized clinical trial: the STEMI-RADIAL trial. J Am Coll Cardiol 2014;63:964–72.

6. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, et al. Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. J Am Coll Cardiol 2012;60:2481–9.

7. Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011;377:1409–20.

8. Porto I, Bolognese L, Dudek D, et al. Impact of access site on bleeding and ischemic events in patients with non-ST-segment elevation myocardial infarction treated with prasugrel: the ACCOAST access substudy. J Am Coll Cardiol Intv 2016;9:897–907.

9. Montalescot G, Collet JP, Ecollan P, et al. Effect of prasugrel pre-treatment strategy in patients undergoing percutaneous coronary intervention for NSTEMI: the ACCOAST-PCI study. J Am Coll Cardiol 2014;64:2563–71.

10. Hamon M, Baron JC, Viader F, Hamon M. Periprocedural stroke and cardiac catheterization. Circulation 2008;118:678–83.

11. Hoffman SJ, Routledge HC, Lennon RJ, et al. Procedural factors associated with percutaneous coronary intervention-related ischemic stroke. J Am Coll Cardiol Intv 2012;5:200–6.

12. Ratib K, Mamas MA, Routledge HC, Ludman PF, Fraser D, Nolan J. Influence of access site choice on incidence of neurologic complications after percutaneous coronary intervention. Am Heart J 2013;165:317–24.

13. Keeley EC, Grines CL. Scraping of aortic debris by coronary guiding catheters: a prospective evaluation of 1,000 cases. J Am Coll Cardiol 1998;32:1861–5.

14. Khoury Z, Gottlieb S, Stern S, Keren A. Frequency and distribution of atherosclerotic plaques in the thoracic aorta as determined by transesophageal echocardiography in patients with coronary artery disease. Am J Cardiol 1997;79:23–7.

15. Hamon M, Lipiecki J, Carrie D, et al. Silent cerebral infarcts after cardiac catheterization: a randomized comparison of radial and femoral approaches. Am Heart J 2012;164:449–54.e1.

16. Lund C, Nes RB, Ugelstad TP, et al. Cerebral emboli during left heart catheterization may cause acute brain injury. Eur Heart J 2005;26:1269–75.

17. Hamon M, Coste P, Van't Hof A, et al. Impact of arterial access site on outcomes after primary percutaneous coronary intervention: prespecified subgroup analysis from the EUROMAX trial. Circ Cardiovasc Interv 2015;8:e002049.

18. Pristipino C, Trani C, Nazzaro MS, et al. Major improvement of percutaneous cardiovascular procedure outcomes with radial artery catheterisation: results from the PREVAIL study. Heart 2009;95:476–82.

19. Valgimigli M, Gagnor A, Calabro P, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015;385:2465–76.

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