

Bleeding Complications Associated With Transradial Versus Transfemoral Access

A review of the diminishing impact of bleeding with these two approaches and how the femoral route remains safe and viable in practice.

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Percutaneous coronary intervention (PCI) has assumed an indispensable role in the worldwide treatment of ischemic heart disease during the past 2 decades. In the United States alone, more than 1 million PCIs are performed annually. A rigorous commitment to randomized clinical trials and evidence-based practice has facilitated a rapid evolution of interventional techniques, equipment, and adjunctive pharmacology. These gains have afforded the ability to not only treat increasingly complex anatomy and improve long-term outcomes, but also to reduce procedural complications. Whereas the ischemic complications of PCI once predominated, they are now relatively rare and have been supplanted by bleeding complications in contemporary practice.^{1,2} As a result, increasing focus has been placed on reducing access site bleeding (ASB) complications through both pharmacologic and procedural improvements.

PCI has been traditionally performed via transfemoral (TF) arterial access. However, increasingly, there has been a renewed interest in transradial access (TRA). Initially described by Campeau in 1989, TRA confers certain advantages over the traditional TF approach, particularly insofar as ASB complications are concerned.³ Specifically, the radial artery is both superficial and easily compressible, resulting in low associated ASB complications. Additional benefits include enhanced patient comfort, essentially

immediate ambulation, and evidence of similar efficacy to TF with regard to procedural success by experienced operators.^{4,5} Although TRA has not been widely adopted in the United States, it has been more widely embraced in Europe, Canada, and Eastern Asia.^{6,7} Given these relative merits, there have been increasingly vocal calls for not only

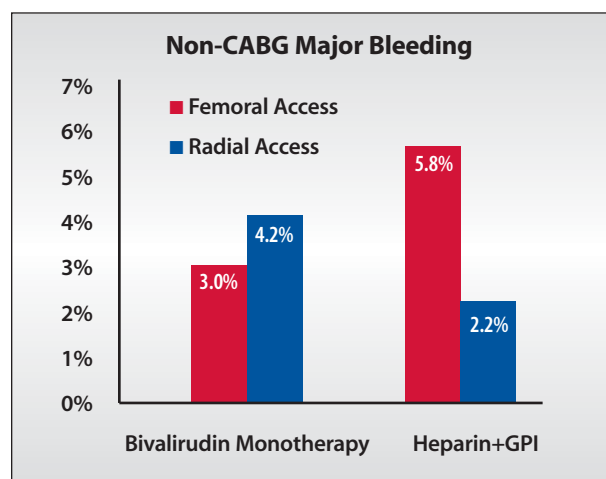


Figure 1. Adapted from Hamon M, et al. Choice of arterial access site and outcomes in patients with acute coronary syndromes managed with an early invasive strategy: the ACUTY trial. *EuroIntervention*. 2009;5:115–120.²⁶

a more widespread adoption of TRA access, but also a default “radial first” strategy.

Although TRA has many merits, the traditional TF approach retains important advantages. The femoral artery is able to accommodate larger sheath sizes and a wider array of equipment. TRA is associated with an initially steep learning curve, which is particularly problematic for low-volume operators. In addition, evidence suggests that preprocedural risk stratification for ASB complications and utilization of contemporary bleeding avoidance strategies has narrowed the gap of ASB complications between the two methods of arterial access. Specifically, the use of bivalirudin monotherapy for procedural anticoagulation clearly reduces TF ASB, and contrary to current dogma, the use of vascular closure devices (VCDs), particularly in conjunction with bivalirudin, may also significantly reduce TF ASB complications.

PREVALENCE, RISK FACTORS, AND IMPACT OF ASB

There are wide variations in the reported rates of bleeding complications via the TF approach, ranging from 1% to as high as 12%. In contemporary practice, the generally accepted incidence of bleeding complications ranges from 2% to 6%, with wide variability across institutions.⁸⁻¹² More than two-thirds of all hemorrhagic complications are directly attributable to bleeding at the arterial access site. Generally accepted risk factors for ASB complications include acute coronary syndrome, female gender, congestive heart failure, hypertension, peripheral vascular disease, renal insufficiency, diabetes, and advanced age.¹³ Both large randomized controlled trials (RCTs) and numerous registries have shown that post-PCI bleeding is associated with an adverse prognosis. Major ASB results in an increased incidence of nonfatal myocardial infarction, stroke, and both early and late mortality.^{8,14-17} Additionally, major bleeding events result in an average 4- to 6-day increased length of hospital stay and increased costs (\$6,000–\$8,000).^{14,18,19}

Available information regarding the incidence of ASB complications via the TRA approach is mostly composed of comparatively small RCTs and registry data. The reported incidence of major ASB via the TRA approach ranges from 0% to 3%. The first randomized comparison of elective PCI with TRA, brachial, or TF approaches found a significantly lower risk of ASB complications in the radial group (no complications in the TRA group compared with 2.3% and 2% in the brachial and TF groups, respectively; $P = .035$).²⁰ Subsequently, several comparatively small randomized trials have shown that TRA access significantly reduces ASB compared to the TF approach. Meta-analysis by both Agostoni et al and Jolly et al showed that

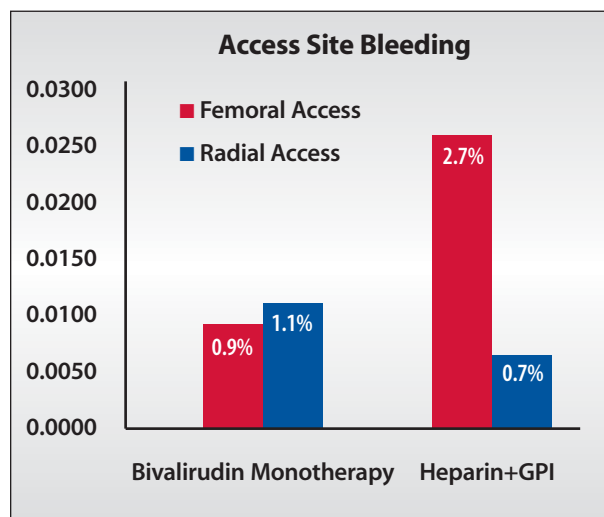


Figure 2. Adapted from Hamon M, et al. Choice of arterial access site and outcomes in patients with acute coronary syndromes managed with an early invasive strategy: the ACUTY trial. *EuroIntervention*. 2009;5:115–120.²⁶

TRA was superior to the TF approach with regard to major ASB complications (0.3% vs 2.8%; $P = .0001$; and 0.05% vs 2.3%; $P = .001$, respectively).^{4,21} However, it must be noted that none of these trials, or the aforementioned meta-analysis, included the use of contemporary anticoagulants such as bivalirudin, which have been unequivocally shown to significantly reduce femoral ASB complications. Additionally, TRA data primarily come from high-volume transradial operators or centers committed to TRA PCI.

NARROWING THE GAP: CONTEMPORARY BLEEDING REDUCTION STRATEGIES

Bivalirudin

The use of bivalirudin during PCI as compared to traditional unfractionated heparin or unfractionated heparin plus a glycoprotein IIb/IIIa inhibitor has been consistently shown to significantly reduce the incidence of femoral ASB complications. Reductions in major femoral ASB complications have been demonstrated across a wide spectrum of patient populations, ranging from high-risk acute coronary syndromes to elective PCI. This benefit has been shown in both large RCTs and real-world registry data.^{9,22-24} Bivalirudin use is consistently associated with 30% to 40% relative reduction in major femoral ASB complications. The 2007 American College of Cardiology/American Heart Association guidelines for unstable angina and ST-elevation myocardial infarction gave bivalirudin a class I recommendation and state that bivalirudin should be considered in all patients and is the preferred means of anticoagulation in patients with an increased risk of bleeding.²⁵

Previous randomized comparisons of major ASB complication rates between TF and TRA were conducted before the widespread adoption of bivalirudin. A retrospective analysis of the ACUITY trial evaluated the impact of arterial access strategy (TRA vs TF) on ischemic and bleeding outcomes. Overall, there was no significant difference in terms of ischemic endpoints between the two groups. Bivalirudin monotherapy significantly reduced major ASB complications with TF but not with TRA, although non-ASB was reduced by bivalirudin monotherapy in all patients regardless of access site. In the overall cohort, including those receiving heparin plus glycoprotein IIb/IIIa inhibitor, TRA was associated with fewer major ASB events (3% vs 4.8%; $P = .02$).²⁶ However, the benefit of TRA access was pharmacologically dependent. There was no statistically significant difference in non-coronary artery bypass grafting major bleeding complications between access strategies in patients receiving bivalirudin monotherapy alone (Figure 1). Similarly, there was no significant difference in the incidence of ASB in patients receiving bivalirudin monotherapy (Figure 2). Overall, the most significant predictor of major bleeding was not the choice of arterial access site, but rather the use of heparin plus glycoprotein IIb/IIIa inhibitor versus bivalirudin monotherapy.

Vascular Closure Devices

After the widespread commercial availability and adoption of VCDs, numerous case reports and some centers' negative experiences with VCDs led the US Food and Drug Administration to launch an investigation into their safety. Examination of data from the American College of Cardiology's National Cardiovascular Data Registry databases showed that VCDs were associated with significantly lower rates of vascular complications than manual compression.²⁷ Subsequently, three meta-analyses were published in 2004. Koreny et al examined 30 RCTs comprising 4,000 patients, and Nikolsky et al examined both RCTs and registry data comprising a total of 37,066 patients. Koreny found no reduction in the overall rates of vascular complications, and Nikolsky reported an overall higher rate of vascular complications with VCDs compared to manual compression.^{28,29} The third meta-analysis conducted by Vaitkus et al found a significant 11% reduction in vascular complications from 16 PCI studies comprising 5,048 patients.³⁰ The results of the meta-analyses by Koreny and Nikolsky are frequently cited as evidence that VCDs are no safer than manual compression and may in fact be harmful. However, if the VasoSeal device (Datascope Corp., Montvale, NJ, purchased by St. Jude), which was subsequently removed from the market secondary to safety concerns, is excluded from the meta-analyses by Koreny

and Nikolsky, the odds ratio for ASB complications for VCDs versus manual compression becomes 1.03 ($P = \text{NS}$) and 0.82, respectively.³¹

More recently, a growing body of persuasive evidence suggests that VCDs may in fact reduce major ASB complications, particularly when used in conjunction with bivalirudin monotherapy. An analysis of the ACUITY trial assessing the impact of femoral VCDs and antithrombotic therapy on ASB complications showed a statistically significant decrease in major ASB associated with VCD use ($P = .01$) and showed that patients who were treated with bivalirudin monotherapy and a VCD had the lowest rate of major ASB (0.7%).³² Logistic regression analysis revealed that both bivalirudin monotherapy and VCD use were independent determinants of freedom from major ASB.

In addition, two recently published papers relying on registry data have shown improved outcomes in terms of major ASB complications associated with both bivalirudin and VCD use. A review of the Northern New England PCI registry comprising more than 45,000 patients showed a statistically significant decrease in major ASB with both VCD use and bivalirudin monotherapy.³³ A paper by Marso et al drawing upon an analysis of the National Cardiovascular Data Registry database comprising more than 1.5 million patients showed similar results.²⁴ Once again, both VCD and bivalirudin use were shown to result in statistically significant reductions in ASB complications. The benefit of both strategies became more pronounced with increasing preprocedural bleeding risk. The rate of ASB complications in the highest-risk patients receiving both VCDs and bivalirudin was 2.3 % versus 6.1% for manual compression and standard means of anticoagulation ($P \leq .01$). This translates into a number needed to treat of 33 to prevent one major bleeding complication and compares favorably with reported rates of ASB via the TRA approach. Interestingly, it was found that bleeding reduction strategies using VCDs and bivalirudin were least often utilized in those at highest risk for complications.

CONCLUSION

ASB complications have a clear and incontrovertible association with significant morbidity and mortality. Historically, the incidence of major ASB complications has been higher when utilizing TF access as compared to TRA. The radial artery offers unique anatomic advantages as compared to the femoral artery in this regard. However, the incidence of ASB via the TF approach may be reduced by preprocedural risk stratification and by employing bleeding avoidance strategies. When these measures are employed, the incidence of ASB complications via the TF route may be significantly decreased and compare favorably with TRA. As such, calls for the widespread abandon-

ment of TF access are, at best, unfounded. Unfortunately, there is evidence of a “risk-treatment paradox” in the sense that the patients at the highest risk of TF ASB complications are the least likely to receive these preventative strategies.²⁴

Ultimately, both methods of arterial access offer unique advantages and disadvantages. To this end, perhaps one need not be a “radialist” at the expense of being a “femorolist” or vice versa. As a community, we should move beyond the paradigm of Maslow’s hammer (if all you have is a hammer, everything looks like a nail) and strive to become equally adept at both methods of arterial access. Such a strategy allows for sound clinical judgment based on specific patient factors rather than individual bias and/or ingrained habit. ■

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