Periprocedural bleeding complications after percutaneous coronary intervention (PCI) are associated with increased short- and long-term morbidity and mortality. Although clinical trials have primarily assessed pharmacological strategies for reducing bleeding risk, there is a mounting body of evidence suggesting that adoption of a transradial rather than a transfemoral approach to PCI may permit greater reductions in bleeding risk than have been achieved with pharmacological strategies alone. However, despite a long history of use, a lack of widespread uptake by physicians coupled with the technological limitations of available devices has in the past confined transradial PCI to the status of a niche procedure, and many operators lack experience in this technique. In this review, we examine the history of the transradial approach to PCI and discuss some of the circumstances that have hitherto limited its appeal. We then review the current state of the peer-reviewed literature supporting its use and summarize the unresolved issues affecting broader application of this technique, including lack of operator familiarity and an insufficient evidence base for guiding practice. Finally, we describe potential directions for future investigation in the transradial realm.

Transradial PCI: Historical Perspective

Although the transfemoral approach to cardiac catheterization has dominated the explosive growth of invasive cardiology in past decades, transradial access appeared early in the development of cardiac catheterization techniques. In 1948, Radner (8) published one of the first descriptions of transradial central arterial catheterization and attempts at coronary artery imaging using radial artery cut-down and 8- to 10-F catheters. Despite early enthusiasm for the transradial approach, limitations of
contemporary equipment resulted in a shift to larger vessels such as the brachial, carotid, and femoral systems for most catheter-based procedures, and the radial artery was relegated to use as a site for monitoring arterial pressure.

In the late 1970s, percutaneous coronary angioplasty was introduced using predominantly 9-F guiding catheters (9). Building on reports of successful transradial angiography from Canada in 1989 (10), Kiemeneij and Laarman (11) first reported on the transradial approach for coronary stenting in 1993. Given observed reductions in periprocedural bleeding and reported improvements in patient comfort with this approach, a few enthusiastic early adopters emerged, but the transradial approach generally remained a niche technique.

As experience with the transradial approach grew, the lack of severe access-site complications when compared with the transfemoral approach was repeatedly demonstrated in small observational studies. A “learning curve” for developing proficiency in transradial procedures was noted (12), cost-effectiveness was demonstrated (13,14), and small single-center or limited multicenter randomized comparisons to femoral (with or without vascular closure devices) and brachial approaches (15,16) showed the superiority of transradial procedures with respect to vascular access site complications, speed of post-procedural recovery, and patient preference. The safety of transradial PCI in patients therapeutically anticoagulated with warfarin (17) and the potential for same-day coronary revascularization were described (18). In addition, transradial techniques have been expanded to peripheral arterial interventions, including carotid (19), superficial femoral (20), mesenteric (21), and renal (21,22) arteries, as well as for pediatric percutaneous procedures (22).

As we summarize below, the future adoption of transradial PCI in the U.S. and other countries with low penetration of transradial techniques will depend on the generation of high levels of evidence that confirm advantages seen in smaller observational and randomized studies, the availability of training programs, commitment from operators and professional societies, and comparative effectiveness data that demonstrate not only better clinical outcomes compared with the transfemoral approach, but also better economic outcomes, such as cost savings or cost-effectiveness, and acceptable safety as it pertains to radiation dose and exposure.

**Procedural and Clinical Outcomes After Transradial PCI**

When comparing the transradial with the traditional transfemoral route for PCI, the discussion must include comparisons of procedural success, fluoroscopy times, and bleeding/vascular complications.

**Procedural success and procedure time.** In a systematic overview of 12 randomized trials \( n = 3,224 \) comparing radial and femoral approaches for diagnostic (7 studies) and interventional (5 studies) procedures, Agostoni et al. (23) reported significantly higher rates of procedural failure for transradial access (odds ratio [OR]: 3.30; 95% confidence interval [CI]: 1.63 to 6.71). When compared with earlier studies included in the analysis, more contemporary trials demonstrate no differences in procedural failures between treatment strategies, likely reflecting advances in both technique and technologies, including vasodilator pharmacology and hydrophilic catheters. However, the composite outcome of death, myocardial infarction, emergency repeat revascularization, or stroke did not statistically vary between groups. Mann et al. (15) reported a single-center observational study comparing the transradial with the transfemoral approach in which the Perclose (Abbott Vascular, Santa Clara, California) femoral closure device was used. Procedural success, complications, post-procedural length of stay (LOS), and percentage of patients discharged the same day were similar across groups; however, total procedure time was significantly longer in the femoral group \( 57 \pm 22 \text{ min} \) femoral vs. \( 44 \pm 22 \text{ min radial, p < 0.01} \) because of time needed to deploy the closure device.

The largest observational study to compare procedural success rates between radial and femoral approaches used data from the National Cardiovascular Data Registry \( 593,094 \text{ procedures; 606 institutions} \) (24). Although radial approaches represented a modest proportion \( (1.32\%) \) of case volume, risk-adjusted procedural success (defined as residual stenosis \( \leq 50\% \) and reduction in stenosis \( \geq 20\% \) with TIMI flow grade \( \geq 2 \) did not differ between access methods \( \text{OR: 1.02; 95\% CI: 0.92 to 1.12} \). In contrast, a more recent systematic overview (23 trials; \( >7,000 \text{ patients} \) by Jolly et al. (25) found that the radial approach was associated with a trend toward a higher rate of inability to cross the lesion with a wire, balloon, or stent, compared with the femoral approach (Fig. 1).

Although overall procedural time may be similar between methods, radial access has been associated with modest but statistically significant increases in fluoroscopic time. Among 420 patients undergoing diagnostic coronary angiography and percutaneous revascularization, procedural duration and fluoroscopic time were significantly longer for radial compared with femoral procedures, corresponding to significantly higher radiation exposure for operators and patients (26), although there was significant variability among operators. In the meta-analysis by Agostoni et al. (23), fluoroscopy time was significantly lower in the femoral cohort \( 7.8 \text{ min vs. 8.9 min, p < 0.001} \). Similarly, in the National Cardiovascular Data Registry, radial PCI had longer fluoroscopy time \( (13.5 \text{ min vs. 11.3 min, p < 0.01}) \), but there was no significant difference in total volume of contrast used (24). Many of these studies did not correct for potential improvements in procedure and
fluoroscopy times that may be realized with greater transradial experience.

In general, it seems that increasing experience with the transradial approach is associated with decreased rates of procedure failure. In one observational study, an annual procedural volume >80 transradial cases correlated with significant reductions in access failure, sheath insertion time, and overall procedural time (Fig. 2) (27). Similarly, other trials demonstrate an initial difference in procedural time between radial and femoral cases that resolved by trial completion as operator experience improved (12,16,23,28). Jolly et al. (25) demonstrated that among operators who preferred the radial route, there was no significant difference in successful lesion crossing (adjusted OR: 1.18; 95% CI: 0.77 to 1.81; p = 0.44); among less experienced operators, there was a strong trend toward higher failure rates (adjusted OR: 3.47; 95% CI: 0.91 to 13.21; p = 0.07) (25).

Bleeding and vascular outcomes. Bleeding complications after PCI are most commonly related to vascular access site (Figs. 3 and 4) and are associated with an increased risk of post-PCI morbidity and mortality (4,5,29,30). A consistent body of observational and small randomized studies supports an advantage of the transradial approach in reducing PCI-related hemorrhagic complications compared with the transfemoral approach (24,25). In the National Cardiovascular Data Registry, the radial approach was associated with a significant reduction in bleeding complications that was more pronounced in certain high-risk subgroups, such as women and patients with acute coronary syndromes (ACS) (24). These findings are consistent with those of other studies evaluating the safety of a radial approach regarding significantly reduced bleeding events, especially among ACS patients (31), those receiving more potent antithrombotic agents (32), and elderly patients (33). Jolly et al. (25) found that the transradial approach was associated with a 73% reduction in major bleeding compared with the transfemoral approach (Fig. 1). The radial approach may also afford advantages in patients with peripheral arterial disease and/or obesity, in whom the femoral artery may be difficult to access and compress manually due to body habitus. However, less experienced transradial operators should probably avoid these challenging patients until they gain more experience.
When vascular complications do occur after transradial PCI, they consist mainly of early and late radial artery occlusion (34). Rarely, instances of radial artery eversion or perforation (35), chronic regional pain syndrome (36), and forearm hematoma or compartment syndrome (37) have been described. There are no published reports of hand ischemia occurring after transradial PCI, which may be due to avoidance of the radial approach in patients with a positive Allen test result or reporting bias. Post-PCI radial artery occlusion may be reduced by using smaller diameter catheters and anticoagulation, and by avoiding prolonged high-pressure compression of the radial artery after arterial sheath removal. Two clinical trials have examined the role of “patent hemostasis,” or allowing antegrade flow in the radial artery during hemostatic compression at the occurrence of radial occlusion. In one study, compression was guided by mean arterial pressure (the pressure applied was equal to the mean arterial pressure) versus usual compression (38). The incidence of radial occlusion at 24 to 72 h was 1.1% in the mean arterial pressure–guided group and 12.0% in the usual care group (p = 0.0001). In the other trial, patients were randomized to either compression that allowed antegrade flow in the radial artery (Table 1) or usual care (39). Again, the incidence of radial occlusion at 24 h and 30 days was significantly reduced (24 h: 5.0% patent hemostasis group vs. 12.0% usual care, p < 0.05; 30 days: 1.8% vs. 7%, p < 0.05).

Studies have also found an association between the reduction in bleeding events with transradial PCI and an improvement in clinical outcomes such as death and myocardial infarction. In the PRESTO ACS (Comparison of Early Invasive and Conservative Treatment in Patients With Non–ST-Elevation Acute Coronary Syndromes) vascular substudy, for example, the radial approach was associated with a significant decrease in bleeding complications compared with the femoral approach during hospitalization (0.7% vs. 2.4%; p = 0.05), as well as a significant reduction in 1-year death or recurrent infarction (5.5% vs. 9.9%; p = 0.05) (31). Among procedural and clinical outcomes data collected for 38,872 PCI patients (radial approach, 20.5%) included in the British Columbia Cardiac Registry, radial access for PCI was associated with a significantly lower rate of post-procedural blood transfusion (1.4% vs. 2.8%, p < 0.01) and a significant decrease in 30-day (OR: 0.71; 95% CI: 0.61 to 0.82) and 1-year mortality compared with femoral access (40). In contrast, Jolly et al. (25) found no significant association between the radial approach and reduced 1-year mortality (Fig. 1). An important limitation of these data should be noted, however; most of these studies are either observational (and subject to confounding) or are from small randomized trials conducted at centers with operators proficient in the radial approach. The challenges of translating the potential advantages of the radial approach seen in these studies to the interventional community at large are discussed in the following.

Transradial Approach and Economic Outcomes

As noted previously, the most common complication in patients undergoing PCI via transfemoral access relates to
Sites of Bleeding in PCI Trials

the vascular access site. These complications are also associated with increased LOS and costs (24, 41, 42). Dedicated cost analyses comparing vascular access sites have consistently shown a significant reduction in hospital costs with transradial access. In a randomized study of patients undergoing diagnostic catheterization, Cooper et al. (14) showed that transradial access was associated with a median cost reduction of approximately $290/case driven by lower bed cost, including nursing utilization, and decreased pharmacy costs. A subsequent study comparing diagnostic catheterization via transradial versus transfemoral access with closure devices showed that, despite comparable recovery times, total costs were still significantly lower with transradial access (transradial $369.50 ± $74.60 vs. transfemoral $446.90 ± $60.20 vs. transfemoral with closure devices $553.40 ± $81.00) (43). In a small randomized study of 142 patients undergoing PCI for ACS, post-procedural LOS was reduced by approximately 1.5 days and total hospital charges were decreased from $23,389 to $20,476 with transradial access (44). A study comparing stenting via transradial and transfemoral access with a suture closure device showed a comparable LOS with both strategies at the expense of higher cost and complication rates in the transfemoral group (15).

There is also evidence that nursing workload can be significantly reduced when the transradial approach is systematically used. In one single-center study, the time spent to care for patients after PCI can be reduced from 174 min with transfemoral access to 86 min with transradial access. In addition, nursing time outside the catheterization laboratory on the medical ward was also reduced from 720 min with transfemoral access to 386 min with transradial access (45).

We note, however, that these studies are small and conducted in limited numbers of centers where practice patterns may have influenced both costs and cost savings. Whether these advantages are widely applicable needs further study in larger multicenter randomized trials.

Unresolved Issues and Future Directions

The data summarized here illustrate several advantages of the transradial versus the transfemoral approach to PCI. Although these data strongly support use of the transradial approach as the default method for coronary intervention, it is also important to review several limitations of this technique and the data supporting it (Table 2). These limitations relate broadly to practical issues (training and experience of operators and catheterization laboratory staff), patient issues (previous coronary artery bypass grafting, challenging forearm and chest arterial anatomy), technical issues (e.g., limitation in the size of the guide catheter that can be used, potentially increased procedure times and radiation exposure), and gaps in evidence (lack of large multicenter randomized data on efficacy and safety). Importantly, changing practice from the transfemoral to the transradial approach will, in most cases, result in increased contrast use and radiation exposure to operator and patient early in the learning curve. Table 3 lists selected transradial procedural challenges and outlines strategies for addressing them.

There is scant discussion of the transradial approach in current published training guidelines. Although there is a minimum number of diagnostic and interventional cases recommended for fellows undergoing interventional training, no minimum number of transradial cases is specified (notably, no minimum of femoral or brachial cases is specified either) (46). The obvious result is the continuous production of cardiovascular specialists without training or even exposure to transradial PCI during fellowship. Currently, there are no transradial training programs supported by the major cardiovascular professional societies; there are, however, a limited number of courses supported by industry. This lack of systematic training leads to the transradial PCI being viewed as a niche procedure, a fact underscored by data from large registries showing that the radial approach accounts only for 1.3% of all PCI procedures in the U.S. (24). This ultimately affects both the quality of care provided to the majority of PCI patients as well as the quality of studies examining the relative merits of transradial PCI (see the following text).

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Table 1

<table>
<thead>
<tr>
<th>Technique for Post-Procedural Hemostasis</th>
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<tbody>
<tr>
<td>1. Apply hemostasis device (e.g., HemoBand, RAD-Stat, TR-Band) to wrist</td>
</tr>
<tr>
<td>2. Place pulse oximeter on ipsilateral index finger or thumb</td>
</tr>
<tr>
<td>3. Tighten hemostasis device and remove sheath</td>
</tr>
<tr>
<td>4. Occlude ipsilateral ulnar artery</td>
</tr>
<tr>
<td>5. Loosen hemostasis device until plethysmographic signal returns or bleeding occurs</td>
</tr>
<tr>
<td>If bleeding occurs, use manual compression</td>
</tr>
<tr>
<td>If hemostasis is maintained in the presence of the plethysmographic signal, then leave hemostasis device in place for 2 h</td>
</tr>
<tr>
<td>6. Check for maintenance of plethysmographic signal every hour</td>
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</tbody>
</table>

Adapted from Pancholy et al. (39).

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Table 2

<table>
<thead>
<tr>
<th>Advantages and Disadvantages of Transradial Approach to PCI</th>
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</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Reduced bleeding risk</td>
</tr>
<tr>
<td>Reduced length of stay and costs</td>
</tr>
<tr>
<td>Early ambulation</td>
</tr>
<tr>
<td>Improved patient comfort</td>
</tr>
<tr>
<td>Obliviates discontinuation of oral anticoagulant therapy</td>
</tr>
<tr>
<td>Same-day discharge possible</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Learning curve</td>
</tr>
<tr>
<td>Not routinely taught in fellowship programs</td>
</tr>
<tr>
<td>Limits guide catheter size</td>
</tr>
<tr>
<td>Possible greater radiation exposure to operator*</td>
</tr>
<tr>
<td>Long-term consequences to radial artery (e.g., for re-access or for use as bypass graft) unknown</td>
</tr>
</tbody>
</table>

*May be a function of operator experience.*
A related issue is patient-specific factors that remain challenging in the transradial context. These include difficulties in accessing the radial artery, traversing the radial/brachial/subclavian arterial anatomy, achieving adequate guiding catheter support, and performing transradial catheterization and PCI using the left radial artery in patients who have undergone previous coronary artery bypass grafting (47). All of these challenges can increase procedure time and radiation exposure to both operator and patient, but can be addressed with adequate operator experience (12). These limitations are offset by the advantages offered to patients (Table 2). Operator experience can be positively influenced through formal training programs and a commitment to transradial PCI in daily practice. Other technical limitations are being addressed through the evolution of radial equipment, such as sheathless 7.5-F guiding catheters that allow greater support and accommodate dual-stent techniques and larger devices, but which create arteriotomies that are smaller than 6-F sheaths (48).

The compartmentalization of transradial PCI to a few centers or operators has also limited the quality of data supporting its use. Most of the studies reviewed in this article are retrospective and observational and therefore subject to significant selection bias. Even when randomized trials are performed, they are either single-center studies or include only a few centers with high concentrations of experienced radialists. The practice of PCI has evolved to include pharmacotherapy that reduces bleeding risk with the transfemoral approach (7) and very-low-profile coronary devices that substantially improve the odds of procedural success. In this context, unresolved issues related to transradial PCI in the modern era include the true incidence of radial artery occlusion and its clinical sequelae, re-access of the radial artery for repeat procedures, the durability of previously accessed radial arteries as conduits for coronary artery bypass grafting, the utility of the Allen test in preventing complications related to vascular compromise after transradial PCI, the true learning curve for transradial PCI including the rate of crossover to the transfemoral approach, the effect of the transradial approach on bleeding and “hard” clinical outcomes such as death or post-procedural stroke, the influence of transradial PCI on costs, the safety of same-day discharge after transradial PCI, and the advantages and disadvantages of the transradial approach for primary PCI for ST-segment elevation myocardial infarction.

Although many of these topics have been addressed in previous studies, none have been the focus of recent studies that take into account modern pharmacotherapy, patent hemostasis for post-procedural radial artery compression, or the current attention on door-to-balloon times for primary PCI. Upcoming investigations capable of illuminating some of these important issues are summarized in Table 4.

Another important contribution possible with wider application of transradial PCI is the study and potential application of higher doses of antithrombosis. Antithrombotic doses studied in phase 2 trials are often determined by examining complications that occur across a range of doses explored during phase 2 trials. The upper limit of dosing for anticoagulants and parenteral antiplatelet agents commonly used in PCI is determined by bleeding complications, many of which occur at the vascular access site. Figure 4 displays the overall bleeding rates and proportion of bleeding related to access site across a sampling of PCI, non–ST-segment elevation ACS, and ST-segment elevation myocardial infarction trials. The substantial reduction in access-site bleeding afforded by the transradial approach may allow higher doses to be carried forward into phase 3 trials and ultimately into clinical practice.

For example, current guidelines for dosing of unfractionated heparin during PCI are based on data demonstrating an association between higher activated clotting times and increased bleeding events (49). However, some studies have...
also demonstrated an association between higher heparin doses and reduced ischemic events (50). The transradial approach may allow a wider therapeutic index for anticoagulants such as unfractionated heparin—preserving ischemic reduction with higher doses while minimizing the penalty of increased bleeding.

Conclusions

The evolution of PCI practice has led to an emphasis on minimizing post-procedural vascular and bleeding complications while maintaining procedural success. A growing body of literature supports the use of the radial artery over the femoral artery to achieve these goals, and data demonstrate an association between the transradial approach and reduced costs and post-procedural LOS. Despite these advantages, there are some limitations to this approach, such as the potential impact on radial artery patency and greater radiation exposure during the learning curve—a factor that has limited adoption of this technique. Greater penetration of the transradial approach will depend on the availability of educational programs for interventionalists and fellows-in-training, commitment from professional societies to support transradial PCI, and the generation of high-quality evidence to determine its comparative effectiveness against the traditional femoral approach. Systematic use of the transradial approach may also affect drug development by allowing higher (and potentially more efficacious) doses of anticoagulants to be studied in phase 3 trials and implemented in clinical practice.

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REFERENCES


Table 4 Ongoing Trials Evaluating the Transradial Approach

<table>
<thead>
<tr>
<th>ClinicalTrials.gov Identifier</th>
<th>Comparisons</th>
<th>Planned Sample Size, n</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01014273</td>
<td>Radial vs. femoral approach to PCI in UA, NSTEMI, STEMI</td>
<td>7,000</td>
<td>30-day death, MI, stroke, or major bleeding</td>
</tr>
<tr>
<td>NCT00815997</td>
<td>4- vs. 6-F guide catheter for transradial PCI</td>
<td>160</td>
<td>Radial artery patency 2 days post-procedure</td>
</tr>
<tr>
<td>NCT00329979</td>
<td>Radial vs. femoral diagnostic catheterization in severe aortic stenosis</td>
<td>152</td>
<td>Acute brain injury assessed by diffusion-weighted brain MRI</td>
</tr>
<tr>
<td>NCT00697324</td>
<td>Transradial catheterization in patients with normal and abnormal Allen test results</td>
<td>180</td>
<td>30-day levels of capillary lactate in the thumb of instrumented hand</td>
</tr>
<tr>
<td>NCT00821106</td>
<td>Right radial vs. left radial approach for diagnostic and interventional procedures</td>
<td>1,500</td>
<td>Fluoroscopy time and patient radiation dose</td>
</tr>
<tr>
<td>NCT00638586</td>
<td>Radial vs. femoral access for PCI</td>
<td>160</td>
<td>Post-procedure anxiety, pain, satisfaction</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; MRI = magnetic resonance imaging; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina.


