Radial Artery Patency After Transradial Catheterization

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The transradial approach to cardiac catheterization has many advantages over the transfemoral approach and is increasingly being used for both diagnostic coronary angiography and percutaneous coronary intervention (PCI). The technique is associated with fewer vascular access complications1–3 and has been shown to reduce major bleeding when compared with the femoral approach.4 Patients prefer the radial approach and score higher on quality-of-life questionnaires after transradial catheterization.3,5 Radial access allows for earlier patient ambulation and same-day hospital discharge in PCI patients4–6 and is associated with decreased cost.5,7,8

Radial artery occlusion (RAO) is a complication of transradial catheterization that can lead to permanent occlusion of the radial artery. Estimated to occur in 1–10% of cases,9–14 it has been described as the “Achilles’ heel” of the transradial technique.15 RAO is usually clinically silent because of the dual blood supply to the hand, and for this reason it is often overlooked. In fact, more than 50% of transradial operators do not routinely assess radial artery patency before hospital discharge.16 However, the complication is not benign, as hand ischemia resulting from RAO has been reported.17–19 Furthermore, once the artery is occluded, it cannot be used as an access site for future catheterization or as an arterial conduit for bypass surgery. RAO renders the ipsilateral ulnar artery unusable as well, because instrumenting and cannulating the ulnar would put the patient’s hand at risk of ischemia. In this report, we review the pathophysiology, clinical presentation, and risk factors for RAO, discuss prevention and treatment options, and suggest directions for future research aimed at minimizing this complication.

Pathophysiology
Acute loss of radial artery patency after cardiac catheterization is thought to be due to a thrombotic process. Sheath insertion leads to local endothelial injury and cessation of blood flow in the radial artery, creating an environment conducive to thrombosis. Many observations about RAO provide indirect evidence to support this hypothesis. RAO tends to occur early after transradial catheterization, and roughly 50% of patients have spontaneous recanalization of the artery within 1–3 months.10,12 Furthermore, rates of RAO are higher with prolonged cannulation times,20–22 whereas RAO is reduced with anticoagulation23 and nonocclusive hemostasis.11,24,25 Direct support for the thrombotic hypothesis has come from recent studies that have confirmed the presence of radial artery thrombus on vascular ultrasound,26 angiography,27 and pathology.28 Transradial catheterization can also negatively affect radial artery structure and function. A study using optical coherence tomography found that 67% of radial arteries had intimal tears and 36% had medial dissections immediately after transradial PCI.29 Other studies have found that minimal lumen diameter and minimal lumen area are smaller in repeat transradial patients than in first-time transradial patients as the result of an increase in intimal hyperplasia and intima-media thickness in the repeat transradial patients.12,29–31 A study of radial artery function after radial sheath insertion found that flow-mediated dilatation was blunted and remained blunted 9 weeks later, when compared with a non-cannulated control.32 The radial artery response to nitroglycerin was also decreased, suggesting that the impairment in function was more than just temporary damage to the endothelium and involved long-term changes to the smooth muscle layer.

The arterial remodeling that occurs after transradial catheterization has important clinical implications. Sakai et al33 studied patients undergoing repeated transradial interventions in the same arm and found that the rate of radial access site failure increased with successive procedures. This appears to be due to progressive narrowing of the artery with each procedure, rendering it more difficult to cannulate. A study of patients undergoing bypass surgery with radial artery conduits found that radial artery grafts in patients with previous transradial catheterization had reduced graft patency and were more likely to have intimal hyperplasia when compared with radial grafts of patients whose radial arteries had not been used for catheterization,34 leading some authors to argue that a radial artery previously cannulated for angiography should not be used for bypass surgery.32

Clinical Presentation
In the majority of patients, the radial and ulnar arteries are connected at the wrist by the deep and superficial palmar arches. Interosseous collaterals often provide additional communications. If the radial artery becomes occluded, perfusion to the hand is usually maintained by increasing flow in the ulnar collateral circulation. RAO is thus usually a clinically
silent event, with most cases coming to attention during follow-up visits or repeat procedures. Only a few cases of severe hand ischemia after radial occlusion have been reported. In RIVAL, the largest randomized trial of radial versus femoral access, symptomatic radial occlusion requiring medical attention occurred in only 0.2% of patients.

On examination, patients with RAO may have a weak or absent radial pulse, reflecting the fact that some patients have development of acute thrombosis of the artery, whereas others have segmental stenosis with residual flow. Some patients with complete occlusion may have a palpable pulse caused by retrograde filling of the radial artery through collaterals. In one study, 2% of patients had an absent radial pulse early after transradial catheterization but 9% had undetectable radial flow by color Doppler. Of the 12 patients who had a radial pulse but no flow in the artery, flow was detectable through collaterals in 2, retrogradely through the ulnar artery in 2, and was undetectable in 8 patients. Thus, the diagnosis of RAO should not depend on the presence or absence of a radial pulse but should be confirmed using a more objective technique such as duplex ultrasonography or the reverse Barbeau test, described below.

**Natural History**

Data on the long-term course of patients with RAO are limited. Nagai et al assessed 162 consecutive patients with routine ultrasound at 2 days and an average of 3 months after transradial catheterization. Twenty-two percent of patients had segmental stenosis at the puncture site and 9% had no flow in the radial artery on the initial ultrasound. Segmental stenosis improved in 71% of patients, but 20% of patients who initially had no stenosis had diffuse stenosis in the artery at long-term follow-up. Of patients who had complete RAO, 60% were found to have complete or partial recanalization of the artery at 3 months. Out of the entire cohort, 1 patient with no occlusion and 1 who had segmental stenosis at early follow-up had complete RAO at long-term follow-up. In another series of 563 patients, the rate of RAO was 5.3% at the time of hospital discharge. At 1-month follow-up, 47% of these patients showed evidence of spontaneous recanalization. No cases of RAO occurred after hospital discharge.

**Assessing Dual Hand Circulation**

Given the importance of the ulnar artery and interosseous collaterals in maintaining hand perfusion in the event of RAO, a reliable method of assessing the collateral circulation before radial artery cannulation is essential. The modified Allen test is a simple qualitative test that is used for this purpose. The patient is instructed to clench the fist. The examiner then compresses the radial and ulnar arteries simultaneously, and the patient is asked to relax the hand. The ulnar artery is then released and the time needed for maximal palmar blush to return is recorded. Return of the palmar blush within 5–10 seconds is typically considered normal (ie, a positive modified Allen test) and indicates adequate collateral circulation. False-positive and false-negative results are common, and there is no consensus regarding the optimal cutoff time for a positive result.

Barbeau developed a test using plethysmography and pulse oximetry (known as the Barbeau test) to improve the sensitivity of the modified Allen test. A pulse oximeter is placed on the ipsilateral thumb and the morphology of the plethysmography tracing is noted. The examiner then occludes the radial artery, and any change in the tracing is noted. The examiner also notes whether the pulse oximeter still gives a constant reading (positive oximetry) or whether it cannot find a reading (negative oximetry). The response to this maneuver is categorized into 1 of 4 types (Figure 1). Patients with type A and type B responses have uninterrupted arterial filling during radial occlusion. The delayed appearance of a pulsatile tracing in patients with a type C response probably represents the recruitment of collaterals. These patients might have been excluded from radial catheterization, based on a traditional Allen test. Patients with a type D response (1.5% of patients) do not have pulsatile collateral flow and are excluded from transradial catheterization. Using this system, the authors report that they have not observed a single case of hand ischemia in more than 7000 patients undergoing transradial procedures at their institution.

The most accurate way of assessing dual hand circulation is with duplex ultrasonography. Ultrasound imaging allows for a detailed assessment of the patient’s anatomy, including the size of the radial and ulnar arteries. Doppler is used to characterize blood flow in the artery, in collaterals, and can also be used to guide compression of the artery at the end of...
the case and to assess for RAO. Despite these advantages, ultrasound imaging is not routinely used in practice. The majority of radial operators (58%) use the modified Allen test, 16% use the Barbeau test, and 23% do not routinely assess dual hand circulation before the procedure. A clinical diagnosis of RAO can be made by using modifications of these techniques. In the reverse Allen test, the patient is instructed to clench the fist, both arteries are compressed, and the radial artery is released after the fingers are extended. Failure of palmar blush to return indicates occlusion of the radial artery. A reverse Barbeau test can be performed in a similar fashion.

Predictors of RAO

Several studies examining the rates of RAO have used multivariable models to identify independent predictors of RAO. The following factors have been identified as independent predictors in the majority of studies: the diameter of the sheath and its relationship to the size of the radial artery,9,12,38 postprocedure compression time and the presence of antegrade flow in the artery during hemostasis,9,11,39 and the use of anticoagulation.9

Sheath Size

The radial artery tapers in size distally and is occasionally smaller than the outer diameter of the sheath. An oversized sheath can damage the artery, leading to vascular remodeling and possibly thrombosis. Saito et al40 used ultrasound to study radial artery size in 250 consecutive Japanese patients undergoing transradial PCI. All patients were pretreated with nitrates. The mean internal diameter of the radial artery (measured 10 mm proximal to the styloid process) was 3.10±0.60 mm in men and 2.80±0.60 mm in women (Figure 2). Given that a 6F sheath has an external diameter of 2.52 mm, only 86% of men and 73% of women in the study had a resting radial artery diameter that was larger than the external diameter of the sheath. Despite this size mismatch, vascular sheaths (6F and larger) were successfully inserted in all study patients, demonstrating that arteries do have elastic properties and can be stretched. Although none of the patients had complete RAO, the authors observed a relationship between the ratio of the sheath external diameter to the radial artery internal diameter and severe flow reduction. The incidence of severe flow reduction was 13% when the sheath-to-artery ratio (S-A ratio) was >1 and only 4% when the S-A ratio was ≤1 (P=0.01). Others have made similar observations.12,38 It is interesting to note that an S-A ratio >1 is associated with pain during sheath insertion and removal.41

In a prospective, randomized trial designed to test the hypothesis that sheath-artery mismatch contributes to RAO, Dahm et al42 assigned patients to receive transradial PCI by means of a 5F system or a 6F system. Procedural success was similar between the 2 groups, but there was less RAO in the 5F group (1.1% versus 5.9%, P=0.05). Four of the 5 patients who had RAO in the 6F group had S-A ratios >1. The NAUSICAl trial (clinicaltrials.gov identifier No. NCT00815997) is an ongoing trial in Japan in which patients are being randomly assigned to transradial PCI by means of a 4F system using the HeartRail II guide (Terumo) or a 6F system. RAO is the primary outcome measure.

Several authors have explored the question as to whether there might be a bedside clinical tool that could predict radial artery size without ultrasound imaging.38,40,41 Associations between radial artery diameter and body height, body weight, and body surface area are weak (r=0.23–0.33).38,40,41 Brachial artery diameter may correlate more closely with body size, whereas the relative size of the radial and ulnar arteries is less predictable. The radial artery is larger than the ulnar in 51% of patients.43 Greenwood et al19 found that a longer Allen test time is associated with larger radial and smaller ulnar artery size.

Several options should be considered to minimize the risk of RAO when the radial artery is known to be small. First, a 5F system can be used for diagnostic angiography in most patients and for many noncomplex coronary interventions. New sheathless hydrophilic guiding catheters have been developed that have the external diameter of a 5F sheath while providing a 6.5F internal diameter, enabling operators to proceed with most complex interventions (Figure 3).44,45 Larger guides with an external diameter of a 6F sheath that have an internal diameter equivalent to a 7F guide (2.49 mm) can be used for cases that require complex techniques such as atherectomy with burrs >1.75 mm in diameter or delivery of 2 stents for simultaneous kissing stent or crush techniques for treatment of complex bifurcation lesions.46 These guides are not yet available in the United States, but a sheathless technique using standard nonhydrophilic guiding catheters has been described.45 If the left radial artery is larger than the right, consideration may be given to using the left arm. Experience using the ulnar artery for PCI is limited, but there are some data to suggest that an ulnar approach is comparable to the radial, with similar procedural success and no difference in the rate of vascular access complications and arterial occlusion.43,47

Patent Hemostasis

Achieving hemostasis after transradial catheterization is relatively straightforward because the artery is superficial and easy to compress. If compression of the artery is too aggres-
sive, however, a no-flow state will develop, and this may lead to thrombosis. Using the reverse Barbeau test to assess radial artery flow in patients who received conventional compressive dressings, Sanmartin et al.\textsuperscript{11} found that 60\% of patients had absent radial flow during compression. The rate of RAO was 10\% at 7-day follow-up. The only independent predictor of RAO was absence of anterograde flow during hemostasis. These observations led to the concept of patent hemostasis, whereby just enough pressure is applied to the puncture site to stop bleeding while maintaining anterograde flow in the radial artery.

The Prevention of Radial Artery Occlusion-Patent Hemostasis Evaluation Trial (PROPHET) tested the concept of patent hemostasis using the HemoBand (HemoBand Corporation, Portland, OR).\textsuperscript{25} Patients were randomly assigned to conventional pressure application versus compression guided by pulse oximetry (the ulnar artery was occluded and the HemoBand was loosened until a pulsatile plethysmography signal was observed). The intervention group had significantly less RAO than the control group, both at 24 hours (5\% versus 12\%, $P<0.05$) and at 1 month (1.8\% versus 7.0\%, $P<0.05$). The importance of patent hemostasis was confirmed in the Radial Compression Guided by Mean Artery Pressure Versus Standard Compression with a Pneumatic Device Trial (RACOMAP),\textsuperscript{24} which tested the concept using the TR Band (Terumo Medical Corporation, Somerset, NJ), a device with an inflatable bladder that is used to apply differential amounts of pressure to the artery. Patients were randomly assigned to compression guided by mean arterial pressure (the TR Band bladder was inflated to mean arterial pressure) versus a control group that received a standard 15 cc pressure (the TR Band bladder was inflated to mean arterial pressure). This intervention led to a 10-fold reduction in the rate of RAO (1.2\% versus 12.0\%, $P=0.0001$). In a nonrandomized comparison of the HemoBand versus the TR Band, the group treated with the TR Band had a lower rate of RAO.\textsuperscript{39}

**Anticoagulation**

Given that RAO is a thrombotic process, anticoagulation is often used to minimize the risk of the complication. This practice is based on observational data because no randomized trials have tested the efficacy of heparin to reduce RAO. The initial evidence for heparin in diagnostic catheterization comes from a nonrandomized study in which asymptomatic RAO was noted in 71\% of patients receiving no heparin, 24\% of patients receiving 2000–3000 U of heparin, and 4.3\% of patients receiving 5000 U of heparin ($P<0.05$).\textsuperscript{23} In current practice, transradial operators administer between 2000–5000 U of heparin, although practice patterns vary and approximately 5\% of operators give no heparin at all.\textsuperscript{16} Whether the heparin is given intravenously or through the arterial sheath does not have an impact on RAO.\textsuperscript{48} More recently, Schiano et al.\textsuperscript{49} randomly assigned 162 patients to 5000 U of heparin versus 50 U/kg with an upper limit of 5000 U. All patients received hemostasis with the TR band. No RAO was observed in either group, but compression time was shorter in the weight-adjusted group (204.5 minutes versus 235.5 minutes, $P<0.00001$). Another study randomly assigned patients to 2000 U versus 5000 U of heparin and found that there was a trend toward increased RAO in the very-low-dose group, although it was not statistically significant (5.9\% versus 2.9\%, $P=0.17$).\textsuperscript{50} The difference became significant after patients with RAO were treated with 1 hour of ipsilateral ulnar artery compression (4.1\% versus 0.8\%, $P=0.03$).\textsuperscript{50}

In the case of elective and uncomplicated PCI, bivalirudin is the anticoagulant of choice in the United States, whereas 70–100 U/kg heparin is the most commonly used regimen outside the United States.\textsuperscript{16} It is unclear whether patients who are given bivalirudin for PCI should also be given heparin to prevent RAO. The addition of heparin to bivalirudin has been shown to reduce acute stent thrombosis in patients with ST-elevation myocardial infarction undergoing primary PCI,\textsuperscript{51} but it is unclear whether this can be extrapolated to radial artery thrombosis in an elective PCI setting. Two small studies have shown that giving bivalirudin in combination with low-dose heparin (1000–2500 U) is not associated with any adverse events,\textsuperscript{52,53} but larger trials are needed to assess the risks of bleeding and the impact on radial occlusion. Plante et al.\textsuperscript{54} performed a nonrandomized study of 400 consecutive patients presenting for cardiac catheterization. No anticoagulation was given until after the diagnostic part of the procedure was done. If the patient needed angioplasty, bivalirudin was given as a bolus (0.75 mg/kg), followed by infusion (1.75 mg/kg per hour). If angioplasty was not required, an intravenous heparin bolus was given (70 U/kg) and the sheath was removed. There was no difference in RAO.
at 4- to 8-week follow-up (3.5% bivalirudin versus 7.0% heparin, *P*=0.18).

Treatment
Patients with RAO are relatively asymptomatic and often do not come to medical attention. Even when they do, they are usually treated with observation alone. However, in some instances, recanalization of the artery may be desirable, either to relieve ischemic symptoms in the hand or to save the artery for future procedures. The radial artery has been successfully recanalized using percutaneous techniques, particularly in the initial days to weeks after occlusion. The occluded segment can be approached either from the distal radial artery (if it fills by collaterals) or from the brachial artery using an antegrade approach. It is important to aspirate after wiring the occlusion because embolization of thrombus down the ulnar artery has been described. The largest case series reported success in 12 of 14 patients.

If RAO is noted early after the procedure, 2 potential treatment options have been described. In an uncontrolled study of acute RAO documented by ultrasound 3–4 hours after TR Band removal, Bernat et al treated patients with ipsilateral ulnar artery compression for 1 hour, aiming to promote radial artery reopening by increasing peak velocity blood flow into the radial artery. This intervention reestablished radial flow in the majority of patients who had received 5000 U as the initial anticoagulant dose and a minority of those who had received 2000 U of heparin. An alternative approach involves anticoagulation. Zankl et al conducted a prospective, nonrandomized study in which patients with symptomatic RAO were treated with enoxaparin or fondaparinux for 4 weeks, whereas those with asymptomatic RAO were treated with observation alone. The recanalization rate after 1 month was higher in the anticoagulated group (87% versus 19%, *P*<0.01). Randomized studies are needed before either strategy can be recommended as standard of care.

Future Directions
Although the rate of acute thrombotic radial artery occlusion can be decreased with patent hemostasis, anticoagulation, and avoidance of sheath-to-artery mismatch (Table), the fact remains that radial access site failure increases with successive procedures due to progressive narrowing of the artery. Strategies aimed at minimizing this arterial remodeling are needed. One approach may be to develop a sheath that minimizes trauma to the artery. A new nitric oxide–coated sheath was recently shown to decrease intimal inflammation, intimal hyperplasia, and luminal thrombosis in a porcine model. A group in Korea is evaluating the effect of statins on radial intima-media thickness after transradial PCI (ClinicalTrials.gov identifier No. NCT00952770).

Another research direction is aimed at minimizing the duration of radial artery compression. Given that compression is done with systemic anticoagulation, the length of time required to achieve hemostasis with the radial approach is significantly longer than with the femoral. Strategies to reduce the length of time required to achieve hemostasis are desirable from a patient comfort perspective but cannot come at the cost of increased RAO. One possibility may be to replace heparin in diagnostic cases with bivalirudin. Bivalirudin has a much shorter half-life than heparin but has not yet been studied in this role. An alternative approach may be to use a hemostatic device with local procoagulant properties.

The QuikClot Interventional Bandage (Z-Medica Corporation, Wallingford, CT) is a new kaolin-filled pad, applied for 15 minutes with a compressive dressing, that in a small, randomized trial has been shown to reduce rates of RAO.6 More research is needed into the treatment of this condition. Early anticoagulation appears to decrease the risk of persistent occlusion; however, the optimal anticoagulant regimen remains to be determined.

Conclusions
Radial artery occlusion occurs in 1–10% of patients undergoing transradial catheterization. The primary mechanism appears to be arterial thrombosis, superimposed on a background of vascular injury from sheath insertion. Strategies for minimizing RAO include the use of smaller sheaths or sheathless guides, nonocclusive hemostasis, and appropriate anticoagulation. Further research is needed on additional preventive strategies and treatment of this condition.

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References


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