Circulation: Cardiovascular Interventions

EDITORIAL

Vasodilators and Radial Artery Occlusion

A Concept to Reduce Radial Artery Occlusion?

See Article by Chen et al

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Radial artery occlusion remains the Achilles heel of the transradial approach to arterial catheterization. Granted, radial artery occlusion is usually asymptomatic, not associated with hand ischemia, and resolves in a majority of cases by 30 days after the procedure, but in those patients, who persist with chronic radial occlusion, the future potential for radial artery reuse as a route for catheterization, dialysis shunt, or as an arterial graft for surgical bypass is forever lost. Early radial operators were pleased to have developed an approach that reduced bleeding and enhanced the experience for the patient. Radial artery occlusion was occasionally noted but remained asymptomatic and appeared to be an unavoidable tradeoff for this novel approach that otherwise was an advancement over the classical femoral approach.

With further experience with transradial procedures, it became apparent that radial occlusion was not an inevitable downside of transradial access but rather a potentially modifiable outcome. Adequate anticoagulation for every transradial procedure whether diagnostic or interventional was perhaps the first lesson in risk modification. Unlike the legacy femoral approach that appeared safe when done without anticoagulation at least for diagnostic procedures, radial artery occlusion could be reduced by a factor of 16 from 71% to 4.5% with the simple addition of 5000-U heparin.[1] Radial arteries, in general, have an average diameter on the same order as a 6F sheath. This results in a snug arterial fit for the vascular sheath, setting up an environment of reduced blood flow and endothelial damage from the physical trauma of catheter contact. This milieu of damaged endothelium, a localized puncture wound to the arterial wall, and sluggish blood flow from subsequent hemostatic compression is a perfect set up for thrombosis. The use of heparin attenuates this prothrombotic environment while hemostasis is obtained and reduces the risk of radial occlusion.[2] Hemostasis with techniques of patent hemostasis balance the external pressure exerted to prevent bleeding against the internal lumen blood pressure. The technique maintains antegrade radial artery flow through the region of arterial injury during hemostasis and can further reduce the incidence of radial artery occlusion to <1%.[3]

Despite successes in reducing radial artery occlusion, not all operators have been able to replicate the success of some hemostasis experts, and room for further innovations to minimize this complication remains. One attempt to reduced occlusion at hemostasis was recently demonstrated by our group[4] in a multicenter trial in which the simple addition of a bolus of 500 μg of intraarterial nitroglycerin before sheath removal resulted in a significant reduction in radial artery occlusion over placebo. Was it the NO donor property of nitroglycerin that improved the results with vasodilation enhancing flow through the region of hemostasis

Key Words: Editorials ■ catheterization ■ hemostasis ■ ischemia ■ radial artery ■ vasodilator agents

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and discouraging luminal thrombosis, or was it merely a fluke of science from statistical luck? In this issue of the Journal, Chen et al[5] have confirmed the adjunctive potential for nitroglycerin in techniques to reduce the incidence of radial artery occlusion. This single-centered, single-blinded trial tested a 500 μg subcutaneous injection of periradial nitroglycerin versus placebo that was administered before radial artery cannulation and sheath insertion. The therapy was applied on a uniform background of an initial intraradial injection of nitroglycerin 200 μg at the time of sheath insertion. The use of subcutaneous nitroglycerin significantly reduced radial artery occlusion at 24 hours post-procedure from 14.4% versus 5.4% (P=0.04). Although the intraarterial nitroglycerin cocktail administered at the initiation of the procedure pharmacologically has a half-life too short to effect hemostasis, subcutaneous nitroglycerin has a longer pharmacological effect. Historical work before the advent of transdermal nitroglycerin patches showed improvements in patient exercise tolerance on treadmills performed 20 minutes after subcutaneous nitroglycerin injection similar to that experienced in subjects 2 minutes after sublingual nitroglycerin.[6] The prolonged biological action of subcutaneous nitroglycerin is probably reflected in the increased diameter of the radial arteries noted in the nitroglycerin group in the present study.

The study of Chen et al does have some limitations. First, it is a relatively small study of 188 patients that was a single-centered, single-blind design with the inherent potential for unaccounted confounders interfering with the results. Second, radial artery occlusion was relatively common in the studied patient population and was higher than some recent studies that have reported radial occlusion rates of <1%. An adequate explanation may originate with the 6F sheath that was used for access. Although the exact model sheath is not specified, the typical 6F Terumo Glide Sheath has an external diameter of 2.62 mm (Terumo Interventional Systems, Somerset, NJ). This is significantly larger than the median subject's radial diameter (≈2.45 mm) that would result in the sheath to radial artery ratio >1 that is associated with radial trauma and occlusion.[7] Previous investigations have noted a higher rate of radial occlusion in Japanese patients versus western populations[8] in trials with mixed populations, and a similar propensity for radial occlusion may be operative in this Chinese population. Whether the susceptibility for radial occlusion is driven by differential sizes of radial arteries between populations or genetic differences in vascular biology independent of arterial size is unclear. Third, the study's protocol did not mandate continuous patent hemostasis, and this too may have been in part responsible for relatively high radial occlusion rates. Would the addition of nitroglycerin in the setting of patent hemostasis, or a lower sheath to radial artery ratio, produce better results? The relatively prolonged hemostatic times of 6.5±1.3 hours (nitroglycerin group) and 6.4±1.3 hours (placebo group) in the studied population may also contributed to the incidence of radial artery occlusion reported.[9] Finally, the direct mechanism of this nitroglycerin-associated benefit is not clear. Nitroglycerin not only vasodilates veins and arteries but also has other properties different from other vasodilators such as calcium channel blockers. Would a similar benefit be seen if a calcium channel blocker was used before sheath removal, or is this specific to nitroglycerin? Our catheterization laboratory (Penn State Hershey, Hershey, PA) has for years routinely used intraradial nicardipine 250 μg just before sheath removal followed by patent hemostasis. In the previously mentioned study of Aminian et al,[10] our site (Penn State Hershey, unpublished site data) had 0 out of 90 patients with radial occlusion documented by ultrasound. Good fortune or maybe this association with reduced radial artery occlusion is a class effect of vasodilators and not just nitroglycerin. Another recent publication[11] has suggested that the effects of verapamil (5 mg) may be similar to heparin (5000 U) in preventing radial occlusion but unfortunately did not use a 2×2 design to look for additive effects. In any case, it seems that pharmacological therapy beyond just adequate anticoagulation remains a fertile ground of investigation in the effort to reduce radial artery occlusion after transradial procedures.

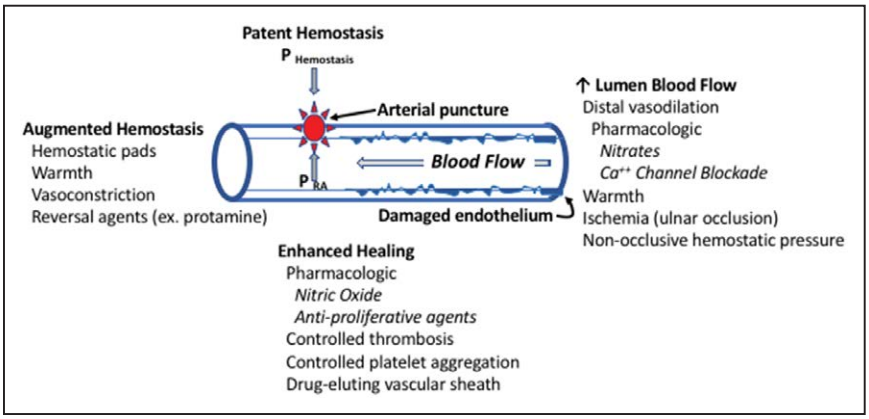

Figure. Concepts to enhance preservation of radial artery function after transradial catheterization.

Stepping back from nuances of subcutaneous or intraarterial nitroglycerin, a variety of proven techniques and also some unproven potential pathways remain to be explored in the field of radial artery preservation. This is graphically summarized in the Figure. Radial artery procedures are typically associated with at least 1 thru-and-thru puncture from an access-needle, in addition to the trauma of subsequent sheath placement. This results in an intense focus of platelet aggregation and stimulus for thrombus formation from the exposed deep layers of the arterial wall. This local injury is followed proximally with variable amounts of catheter-induced endothelial damage that further activates the thrombosis pathways. To prevent runaway clotting in such a prothrombotic environment, adequate antithrombin therapy, typically with heparin or its equivalent, is required. On top of these anticoagulants, medications such as aspirin are often used and may also be theoretically helpful in quelling uncontrolled thrombosis. After sheath removal, controlled pressure on the access site with just enough force to prevent bleeding but not enough to cause cessation of antegrade radial artery flow has proven itself to be best practice to reduce radial thrombosis.[12]

With intraluminal thrombosis controlled, the process of hemostasis at the injury site needs attention. Vascular sheaths with coatings that shed therapeutic agents on removal might be one answer.[13] Hemostatic pads placed on the skin at the entry site[14] may speed hemostatic times by diffusion of agents down the path of sheath entry through the arterial wall. Vasoconstriction is another technique that may reduce bleeding analogous to the ancient adage to ice an injury. Unfortunately, the radial artery has a relatively small diameter, and in the setting of arterial wall damage and its prothrombotic environment, cold-induced vasoconstriction might also result in radial artery occlusion. Localized warmth, on the contrary, could provide distal vasodilation that might accelerate radial artery flow and suppress arterial thrombosis while the sheath site heals. Thermovasodilation and increased blood flow may offer a mechanism common to the use of nitroglycerin and other vasodilating drugs. Likewise, ischemia can also be used to induce vasodilation and may in part explain the utility of ulnar occlusion at the same time as radial hemostasis. The net effect of vasodilation may be to enhance antegrade flow in the radial artery that then reduces stasis-induced thrombosis in the lumen while the artery wall undergoes hemostasis at the site of the entry wound.

The article of Chen et al supports the potential of pharmacological interventions that may modulate the risk of radial artery occlusion after radial procedures. Keys to reducing radial occlusion start with equipment choice that minimizing the size of vascular sheaths to just that needed for the procedure planned. Next, access that is efficient with as few as possible needle sticks, such as can be performed with ultrasound,[15] limits prothrombotic iatrogenic damage to the artery. After access, the use of proper anticoagulation in every patient and the prompt removal of the sheath with patent hemostasis at the end of the procedure go a long way to preserving a functional radial artery. Beyond this, pharmacology may further help by maintaining or enhancing radial artery flow and therefore patency during hemostasis. This is a relatively new area of investigation and may provide further mechanisms to safeguard the radial artery for future use.

ARTICLE INFORMATION

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Disclosures

None.

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Circ Cardiovasc Interv. 2018;11:
doi: 10.1161/CIRCINTERVENTIONS.118.007011
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-7640. Online ISSN: 1941-7632