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Optimization of Transradial-Band Removal Following Transradial Arterial Access for Interventional Radiology Diagnostic and Interventional Procedures (A Pilot Study)

PROTOCOL TITLE:

Optimization of Trans-Radial (TR)-Band Removal Following Transradial Arterial Access for Interventional Radiology Diagnostic and Interventional Procedures (a pilot study)

PRINCIPAL INVESTIGATOR:

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Objectives/Specific Aims

The specific aim of the study is to evaluate the safety and efficacy of initiating earlier TR-Band weaning following transradial access procedures, while minimizing access site complications including hematoma formation and radial artery occlusion (RAO).

The primary objective is to evaluate the rate and severity of complications (i.e. hematoma, ecchymosis and radial artery occlusion) from an expedited weaning protocol wherein the time to wean is reduced significantly.

The secondary objective is to identify potential risks factors for complications following early weaning of the TR-Band.

It is hypothesized that the time to wean of the TR-Band can be safely reduced while minimizing access site complications including hematoma formation and radial artery occlusion (RAO).

Background

The use of transradial (TR) access for the purpose of diagnosis and intervention in the arterial system is a well-established concept, particularly in coronary angiography, with many distinct advantages over conventional transfemoral (TF) access. The first series of 100 coronary angiographic procedures performed via TR access, published by Campeau in 1989[1], demonstrated 88% technical success rate and a 6% asymptomatic radial artery occlusion rate. Since then, TR access for coronary artery interventions in the United States has grown exponentially with the proportion of transradial percutaneous coronary interventions (PCI) procedures increasing from 1.2% in the first quarter of 2007 to 16.1% in the third quarter of 2012[2]. And yet, its usage is largely absent in the interventional radiology and vascular surgery communities. Reasons for this include a lack of appropriate training and equipment, but the potential advantages of TR over TF access are abundant in both coronary and non-coronary applications. Firstly, the radial artery is more superficial than the femoral artery without surrounding neurovascular structures susceptible to injury. In addition, any sustained arterial damage is significantly less detrimental because of the hand's dual arterial vascular supply. In addition, the radial artery is readily compressible regardless of the patient's body habitus. This compressibility has been shown to decrease the incidence of post-procedural bleeding complications as well as cardiac mortality during PCI[3,4,5]. In addition to patient safety, there are numerous benefits to overall patient comfort and convenience. For one, after TR access, patients may sit up in bed and ambulate immediately with faster discharge to home. In one randomized trial, Cooper et al demonstrated a strong patient preference, improved quality-of-life metrics, and decreased hospital costs for TR over TF access during cardiac catherization[6].

Ultimately, complications with TR approach have proven rare in both coronary and noncoronary applications. Most commonly, a local small hematoma may develop with

mild pain, usually treated with NSAIDS if necessary. Despite meticulous hemostatic technique, radial artery thrombosis may occur. Nevertheless, this thrombosis almost always remains asymptomatic[7], at least partially because a modified Allen's test or Barbeau test is performed before all procedures using TR access. Additional possible complications of TR access include radial artery pseudoaneurysm, spasm, dissection, digit ischemia, as well as cerebral infarction, but all of the following have proven to be extremely low incidence particularly with the usage of intraprocedural heparinization and vasodilators, which are included in our procedure protocol.

Finally, and increasingly more important in the modern era of health care reform, TR access offers many benefits to hospital costs and patient satisfaction. Many studies have demonstrated decreased costs associated with TR versus traditional TF access[5,8,9], primarily due to the non-utilization of arterial closure devices and decreased readmission for bleeding complications. International studies have long promoted TR access as a feasible, safe, and well tolerated method for performing hepatic transarterial chemoembolization[10,11]. In a recent series performed in the United States, technical success was obtained in all procedures. Furthermore, 100% of patients who underwent both TF and TR access preferred TR to TF access[12]. Our study seeks to further establish earlier TR Band deflation as a viable and preferable method following transarterial cases to further decrease unnecessary PACU recovery time and expenses.

Intervention to be Studied

TR-Band is an FDA approved device to assist achievement of hemostasis following redial access procedures**.** The TR-Band is not specifically FDA approved for the expedited protocol being studied here, but the standard of care FDA guidelines allow flexibility as need for the deflation protocol for each patient.

Per MUSC standard policy, after an angiographic procedure is performed via the transradial approach, hemostasis at the arterial puncture site is attained using a TR-Band (Terumo Medical Corporation, Tokyo, Japan). The TR-Band consists of a part-rigid, Velcro-secured wristband with an inflatable bladder that provides compression of the radial artery when air is injected into the cuff-valve system via the supplied syringe.

Per the Terumo guidelines[14], to place the TR-Band, the introducer sheath in the radial artery is first retracted 2-3 cm and the center of the compression balloon is positioned 1-2 mm proximal to the puncture site. The TR-Band is then affixed on the wrist with the adjustable Velcro fastener and 15 cc of air is injected into the cuff-valve system while simultaneously removing the introducer sheath. The amount of air in the compression balloon is subsequently titrated by removing 1 cc of air until bleeding occurs or 5 cc of air is removed. Once one of those two endpoints is met, 2 cc of air are injected into the cuff-valve system. To confirm patent hemostasis the ulnar artery at the level of the wrist is then compressed and the morphology of the plethysmographic waveform is observed – this is referred to as the reverse Barbeau's test. Absence of a plethysmographic waveform indicates interruption of antegrade radial artery flow. If this occurs, the volume

of air in the compression balloon is again titrated until the plethysmographic waveform returns.

The standard protocol is for the TR-Band to remain in place for 60 minutes. After 60 minutes, 1/4 of the total volume in the TR-Band is removed at 15-minute intervals until it is fully deflated.

The rationale for an expedited weaning protocol is based in part on the observation that after access of the femoral artery for an angiographic procedure the standard to attain hemostasis without the use of a percutaneous closure device is manual pressure at the puncture site for 15 minutes. Since the radial artery, in contradistinction to the femoral artery, is superficial and readily compressible due to the flat surface of the radius, it is counterintuitive that to attain hemostasis pressure at the radial puncture site, pressure would need to be maintained for 60 minutes. In addition, Pancholy et al concluded based on a retrospective study of 10 consecutive patients undergoing transradial coronary angiography that “shorter duration of hemostatic compression is associated with a lower incidence of early and chronic RAO, without increase in bleeding complications.”

The standard of care (control) group in the study will consist of the subset of patients wherein the time to weaning of the TR-Band is 60 minutes.

Study Endpoints

The study participants will be randomly assigned into one of two groups; these groups will be defined based on the time from inflation to initiation of deflation of the TR-Band, i.e. the time to wean.

Group A (Total time about 60 minutes)	**Group B (Total time about 120 minutes)**
TR-Band Placed following your procedure	TR-Band Placed following your procedure
After 15 minutes deflated by 1/4	After 60 minutes deflated by 1/4
After 25 minutes deflated by 1/2	After 75 minutes deflated by 1/2
After 35 minutes deflated by 3/4	After 90 minutes deflated by 3/4
After 45 minutes deflated completely	After 105 minutes deflated completely
Observe your wrist for 15 minutes	Observe your wrist for 15 minutes
Remove TR-Band after 60 minutes	Remove TR-Band after 120 minutes

The primary outcomes will be the incidence of significant hematomas (> 5 cm in size), bleeding (continued ooze requiring re-inflation of the TR-Band or subcutaneous ecchymosis without a discernable hematoma) and occlusion of the left radial artery (based on ultrasound) at the procedure visit and at one month follow up visit

Inclusion and Exclusion Criteria/Study Population

Each patient will be screened prior to the procedure to determine if he or she is a candidate for trans-radial access. The screening process will consist of a Barbeau's test wherein a plethysmographic sensor is placed on the thumb or index finger of the upper extremity to be used during the procedure and the radial and ulnar arteries are simultaneously compressed. Once the pc waveform is absent, the pressure on the ulnar artery is released and the plethysmographic waveform is observed. Based on the morphology of the plethysmographic waveform, the patients are subdivided into 4 types: types A through C are considered candidates for transradial access while type D is considered a contraindication. As part of the screening process the patient's radial artery will also be evaluate with ultrasound to ensure that the diameter of the vessel is greater than or equal to 1.6 mm. The coagulation parameter of the patients, in particular the platelet count, INR and prothrombin time. In addition, due to inherent risk of radiation exposure associated with the angiographic procedure all premenopausal female patients will be screened with a urine hCG test.

To be included in the study patients will need to be:

- Age 18 years and older
- Have an acceptable Barbeau test (i.e. type A through C)
- Have acceptable coagulation parameters (based on PT, INR, platelet count, and appropriate pre-procedural management of anticoagulants, See Table 1)
- The caliber of the radial artery based on a pre-procedure sonographic evaluation will need to be greater than or equal to 1.6 mm.
- The appropriate pre-procedural management of anticoagulants is based on the consensus guidelines established by Patel et al[16].

Lab	Acceptable Range
INR	Less than 1.5
Platelet count	Greater than 50,000 platelets/μL
Prothrombin Time	Less than 15 seconds

Table 1. Acceptable Ranges of PT, INR and platelet count.

Patients will be excluded from the study if:

- If there is an unacceptable risk of bleeding diathesis, or

- If he or she is not a suitable candidate for transradial access based on a Barbeau test type D or a diameter of the left radial artery less than 1.6 mm.

There will be no exclusions based on gender/sex or race/ethnicity of the study participant.

Number of Subjects

The study cohort will consist of up to 30 enrolled and randomized patients age 18 years and older who undergo an angiographic procedure via the radial artery. The proposed study does not include children.

Setting

The setting of the study will be the Vascular and Interventional Radiology (VIR) Department at the Medical University of South Carolina. The VIR Department performs procedures at both the University Hospital and the Ashley River Tower. In addition, Dr. Yamada has weekly outpatient clinics at the North Charleston Medical Pavilion (8992 University Boulevard, North Charleston, SC 29406) and East Cooper Medical Pavilion (1600 Midtown Avenue, Mount Pleasant, SC 29464).

Recruitment Methods

Subjects scheduled for angiographic procedures will be asked by the PI, Co-I or IRB approved study team members to participate in the trial. Eligibility will be determined by laboratory test and medication review.

Consent Process

Once a patient is referred to Vascular and Interventional Radiology for consultation of an angiographic procedure that could be performed via the left or right radial artery, the patient will be informed of the study design by the PI, Co-I or IRB approved study team members. Some consents may be obtained prior to this during the initial consultation, but due to COVID precautions, consultations are mostly being conducted via telemedicine. We are not seeking obtain consent via tele methods. The recovery bay is great place to conduct this discussion due to privacy and that family members are often present. Patients are in prep bay for up to and over an hour prior to the procedure. The relative risks, benefits, and alternatives of the different approaches to attain hemostasis will also be discussed in detail. Informed consent will be obtained and appropriately documented in the patient's medical records. During the informed consent, it will be emphasized that regardless of the approach to hemostasis, the technical success of the intended procedure should not be affected.

The consent will be obtained at the time of the initial consultation. As stated above, no patients less than 18 years of age will be included in the study. On the day of the procedure, the design of the study and the relative risks, benefits, and alternatives of the different approaches to attain hemostasis will again be discussed in detail with the patient or patient's next of kin/medical power of attorney.

Study Design/Methods

Following approval of the methodology by IRB we will conduct a randomized, single center study of up to 30 subjects who undergo an angiographic procedure via the radial artery. Those patients who meet the inclusion criteria will be randomly assigned to one of two groups (A or B) based upon a standard randomized process using pre-designated sealed envelopes.

Pre-procedure, all patients participating in the study will be evaluated with a Barbeau test and a sonogram of the radial artery to determine the caliber of the vessel (in mm) and the distance (in mm) from anterior wall of the vessel to the skin surface. In addition, updated INR, PT and platelet count (within 14 days) and if applicable pre-procedure management of anticoagulants will be reviewed. All these variables will be documented in the TR-Band Form.

Intra-procedure, all patients participating in the study will receive conscious sedation with midazolam and fentanyl - dosage at the discretion of the operator. Once the area around the puncture site is infiltrated with less than 1 mL of 1% lidocaine, the radial artery will be cannulated with a 21-gauge needle using a modified Seldinger technique (i.e. a single wall puncture). The needle will subsequently be exchanged over a 0.021-inch wire for a hydrophilic-coated 5 Fr x 10 cm Glidesheath Slender sheath. Patients will then receive 200 micrograms of intra-arterial nitroglycerin and an initial bolus of 3000-5000 units of intra-venous heparin. Of note, patients undergoing a transradial uterine artery embolization will also receive 2.5 mg of intra-arterial verapamil. During the procedure patients will receive additional boluses of 1000 units of intra-venous heparin at 30-minute intervals. Prior to removal of the sheath, a second dose of 200 micrograms of intra-arterial nitroglycerin will be administered and an ACT value will be measured. After the sheath is removed, hemostasis will be attained with a TR-Band. The TR-Band consists of a part-rigid, Velcro-secured wristband with an inflatable bladder that provides compression of the radial artery when air is injected into the cuff-valve system via the supplied syringe.

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If bleeding were to occur, the TR-Band will be re-inflated to the previous volume and the weaning protocol will be restarted after 15 minutes. Once the TR-Band is removed the patient will be re-evaluated for complications including hematoma, ecchymosis and occlusion.

Post-procedure, patients will return to the clinic 1 month following their procedure and be re-evaluated for radial access complications including hematoma, ecchymosis and occlusion; and for re-evaluation of the Barbeau test, and ultrasound.

Data Management

The data from living human subjects will include the physical examination, laboratory, and ultrasound data collected both immediately before and after the procedure; these include the pre-procedure History and Physical note, the procedure report, nursing notes and clinic Progress notes.

Only IRB approved team members will have access to the records of the patient's involved, which should be effective in controlling the confidentiality of the study. Individual, unique patient codes will be utilized in an Excel data spreadsheet for anonymization and subsequent analysis. These patient codes will be stored in a separate, secure location at the VIR Research Coordinator Office. The patient's safety will be ensured by the following methods. Prior to discharge from the PACU the patients will be given the contact information of the VIR Nurse Coordinator and clinic for any concerns. In addition, in the case of emergency, a VIR team of physicians and staff are on call at all times (24/7) to manage any acute or emergent patient issues.

The patients' characteristics (e.g. demographic information) will be compared using a t-test or chi-squared tests. The primary outcomes, i.e. rates of complications will be compared using a McNemar's test. An odds ratio will be estimated and its 95% confidence interval reported. Associations between preoperative factors and complications will be evaluated using logistic regression with random effects to account for multiple observations per patient.

Risks to Subjects

The potential risks to subjects for both groups include access site hematoma, pain, radial artery occlusion, and prolonged PACU recovery time. Potential transradial procedural related complications including pseudoaneurysm, digital ischemia, and arterial dissection are not inherently related to the timing of TR-Band deflation.

Per institutional protocol, the subjects will receive standard of care treatment as any similar patient in the same clinical scenario. Each planned procedure will involve a preprocedural evaluation including a sonogram of the radial artery that will be accessed during the procedure and Barbeau test conducted by the co-investigators under the supervision of the principal investigator. The Barbeau test will serve to rule out vascular compromise that may occur in the absence of sufficient vascular pressure. Not subject will be discharged until this is confirmed. Pre- and post-procedural laboratory values, including platelet count, activated clotting time and coagulation profile, will also be reviewed and analyzed. Following each procedure,

the subjects will be monitored for any immediate adverse events per the standard of care. As stated above, following discharge, the patient will be provided instructions as well as the contact information of the Nurse Coordinator for routine scheduling and care issues. In the case of an emergency, a Vascular and Interventional Radiology team of physicians and staff are on call 24 hours to manage any acute or emergent patient issues. All adverse events will be monitored, resolved, and recorded in the patient's medical record. Each case will be review by PI or Co-I and IRB approved study staff to evaluate unanticipated problems or adverse events. These will be reported to IRB within 10 business days. An experienced VIR nurse, Megan Shinner will serve and independent evaluator of each case to determine if unanticipated problem and adverse even might warrant the cessation of the study. The independent evaluator is not part of the IRB approved study team and will not be part of the publication of the findings. She will remain blinded to the unique study ID and will only have access to standard of care procedures and non-study data.

There is also a risk of loss of confidentiality. Being randomized to the expedited deflation group may be an additional risk.

Sharing of Results with Subjects

Individual test results, diagnostic tests and incidental findings will not be shared with subjects or others (e.g. the subject's primary care physicians).

Potential Benefits to Subjects or Others

The potential benefits to the patients include a shorter PACU recovery times, less postoperative discomfort related to the insufflated TR-Band, and lower cost. The preoperative physical, laboratory and ultrasound examination will also help to clarify patient criteria for indications and contraindications for Expedited TR Band deflation by identifying demographic and anatomic risk factors for complications.

Drugs or Devices

There no drug or devices that will be used for this study that are outside what is used for the standard of care.

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