Journal of the American Heart Association

ORIGINAL RESEARCH

A Randomized Comparison of Radial Artery Intimal Hyperplasia Following Distal Versus Proximal Transradial Access for Coronary Angiography: PRESERVE RADIAL

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BACKGROUND: Distal transradial access (dTRA) is an alternative to conventional forearm transradial access (fTRA) for coronary angiography (CAG). Differences in healing of the radial artery (RA) in the forearm have not been evaluated between these 2 access strategies. We sought to compare the mean difference in forearm RA intimal-medial thickening (IMT) in patients randomized to dTRA versus fTRA.

METHODS AND RESULTS: In this single-center randomized clinical trial, 64 patients undergoing nonemergent CAG were randomized (1:1) to dTRA versus fTRA. Ultra–high-resolution (55-MHz) vascular ultrasound of the forearm and distal RA was performed pre-CAG and at 90 days. The primary end point was the mean change in forearm RA IMT. Secondary end points included procedural characteristics, vascular injury, RA occlusion, and ipsilateral hand pain and function.

Baseline demographics and clinical characteristics, mean forearm RA IMT, and procedural specifics were similar between the dTRA and fTRA cohorts. There was no difference in mean change in forearm RA IMT between the 2 cohorts (0.07 versus 0.07 mm; P=0.37). No RA occlusions or signs of major vascular injury were observed at 90 days. Ipsilateral hand pain and function (Borg pain scale score: 12 versus 11; P=0.24; Disabilities of the Arm, Shoulders, and Hand scale score: 6 versus 8; P=0.46) were comparable.

CONCLUSIONS: Following CAG, dTRA was associated with no differences in mean change of forearm RA IMT, hand pain, and function versus fTRA for CAG. Further investigation is warranted to elucidate mechanisms and predictors of RA healing and identify effective strategies to preserving RA integrity for repeated procedures.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04801901.

Key Words: distal transradial access ■ intimal-medial thickening ■ transradial coronary angiography ■ vascular healing

Transradial access (TRA) reduces the risk of bleeding and vascular complications after percutaneous coronary intervention (PCI) compared with femoral access.[1] However, following TRA, the radial artery (RA) is subjected to acute injury, dissection, vasospasm, thrombosis, intimal-medial thickening (IMT), and RA

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Preprint posted on MedRxiv, July 6, 2023. doi: https://doi.org/10.1101/2023.07.05.23292274.

This article was sent to Hani Jneid, MD, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.123.031504

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JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Distal transradial access (TRA) has been proposed as an alternative to traditional forearm TRA in the wrist for coronary angiography and percutaneous coronary intervention because of ergonomic and postprocedural recovery benefits to the patient, as well as potential reductions in occlusion of the forearm radial artery.
- There are gaps in knowledge about the differences in remodeling of the forearm radial artery in patients undergoing distal TRA versus forearm TRA.
- In this randomized clinical trial, ultra–high-resolution (55-MHz) ultrasound revealed no differences in change in forearm radial artery intimal-medial thickening and other patterns of vascular injury and healing at 90 days between patients randomized to distal TRA versus forearm TRA for elective and nonemergent coronary angiography and percutaneous coronary intervention.

What Are the Clinical Implications?

- Our findings highlight the need for further investigation to better understand the predictors of radial artery intimal-medial thickening after TRA so that mitigation strategies can be developed, especially in patients requiring multiple cardiac catheterization procedures during their lifetime.

Nonstandard Abbreviations and Acronyms

CAG	coronary angiography
dTRA	distal transradial access
fTRA	forearm transradial access
IMT	intimal-medial thickening
RA	radial artery
RAO	radial artery occlusion
TRA	transradial access

occlusion (RAO), which may compromise its use as a conduit for future heart catheterizations, coronary artery bypass graft surgery, and hemodialysis.[2,3] Recently, distal TRA (dTRA) in the anatomic snuffbox has been proposed as an alternative RA cannulation site for coronary angiography (CAG) and PCI.[4] A recent meta-analysis suggested that dTRA was associated with a lower risk of forearm RAO.[5] Although it is plausible that puncturing the RA more distally might result in less forearm RA IMT, vascular healing following dTRA versus conventional forearm TRA (fTRA) has not been compared.

The purpose of the PRESERVE RADIAL (A Prospective Randomized Clinical Study Comparing Radial Artery Intimal Hyperplasia Following Distal Versus Forearm Transradial Arterial Access for Coronary Angiography) Study was to determine if dTRA is associated with less ipsilateral forearm RA IMT at 90 days compared with fTRA in patients undergoing CAG. Secondarily, we aimed to compare other end points that reflect procedural ease/success, vascular access site healing, and patient-reported ipsilateral upper extremity pain and motor strength.[6,7]

METHODS

The data that support the findings of this study are available from the corresponding author, Dr Behnam Tehrani, on reasonable request.

Subjects and Study Design

The PRESERVE RADIAL Study was a single-center, prospective, open-label randomized clinical trial designed to study differences in intimal-medial thickness, patterns of vessel injury, procedural success, and ipsilateral upper extremity pain and motor strength in patients randomized to undergo dTRA versus fTRA for coronary angiography, PCI, or both. The study was approved by the Inova Health System's institutional review board, registered at clinicaltrials.gov (registration number: NCT04801901) and supported by an investigator-initiated research grant from Boston Scientific Corporation (Maple Grove, MN). The study authors were solely responsible for the design and conduct of this study and drafting and editing of the manuscript. Statistical analysis was provided by the George Mason University Department of Biostatistics. The study sample was drawn from consecutive patients undergoing elective and nonemergent CAG, PCI, or both at Inova Fairfax Medical Campus. Informed consent was required for participation in the study and was obtained from each patient. Eligibility criteria included the following: age ≥18 years and nonemergent CAG, PCI, or both in the setting of symptomatic ischemic heart disease (stable angina, unstable angina, and non–ST-segment–elevation myocardial infarction). Study subjects had to agree to return for 90-day postprocedural RA ultrasound and completion of Borg and Disabilities of the Arm, Shoulders, and Hand questionnaires for hand pain and functional assessments.[6,7] Exclusion criteria included the following: confirmed pregnancy, uncorrected bleeding disorders, inability to take antiplatelet therapy, prior cannulation of both RAs, acute ST-segment–elevation myocardial infarction, cardiogenic shock, and known hypersensitivity to stainless steel, platinum, chromium, nickel, molybdenum, or everolimus. Patients with prior cannulation of both RAs were excluded, and in those in whom only 1 RA was previously accessed, then the contralateral vessel was cannulated for this study. Patients were randomized 1:1 to dTRA or fTRA. Given the historical association between female sex and RA patency following TRA, permuted randomization was performed in blocks of 3 sequentially numbered, opaque-sealed envelopes to stratify for patient sex and to ensure equal distribution of women in each group.[8] Patient study flow is shown in Figure 1.

Ultra–High-Resolution Ultrasound Imaging Technique

The decision to use right or left RA was at the discretion of the interventional cardiologist. Distal and forearm RA segments were evaluated at baseline and 90 days using FUJIFILM VisualSonics 55-MHz ultra–high-resolution duplex ultrasound. With spatial and lateral resolutions of <40 and <80 μm, respectively, this device distinguishes between the anatomic layers of the RA.[9] In patients without contraindications, nitroglycerine (0.4 mg) was administered 3 to 5 minutes before ultrasound to provide optimal arterial vasodilation.[10] Patients underwent ultrasound imaging of both the distal and forearm RA segments at baseline and 90 days. RA IMT was measured using a technique that has been previously reported.[10] For assessment of the forearm RA, the ultrasound probe was placed over the forearm RA with imaging beginning at the distal end of the radius bone and progressing proximally. To measure the average IMT over an appropriate length of the vessel, a 3-cm length of the forearm RA was assessed, starting from centering the probe over the distal radius and moving proximally. Three successive IMT measurements were recorded within each of three 1-cm long segments. The numerical mean of all measurements was recorded as the final IMT. For assessment of the dTRA segment, the ultrasound probe was positioned over the triangular depression on the dorsum of the hand bordered by the extensor pollicis brevis and the abductor pollicis longus tendons laterally and by the extensor pollicis longus tendon medially. In a similar manner, three 1-cm segments of vessel were also acquired, and the IMT was recorded as the numerical mean of all measurements. The IMT was measured as the distance between the intima and media-adventitia interfaces (Figure 2). Final measurements of IMT were

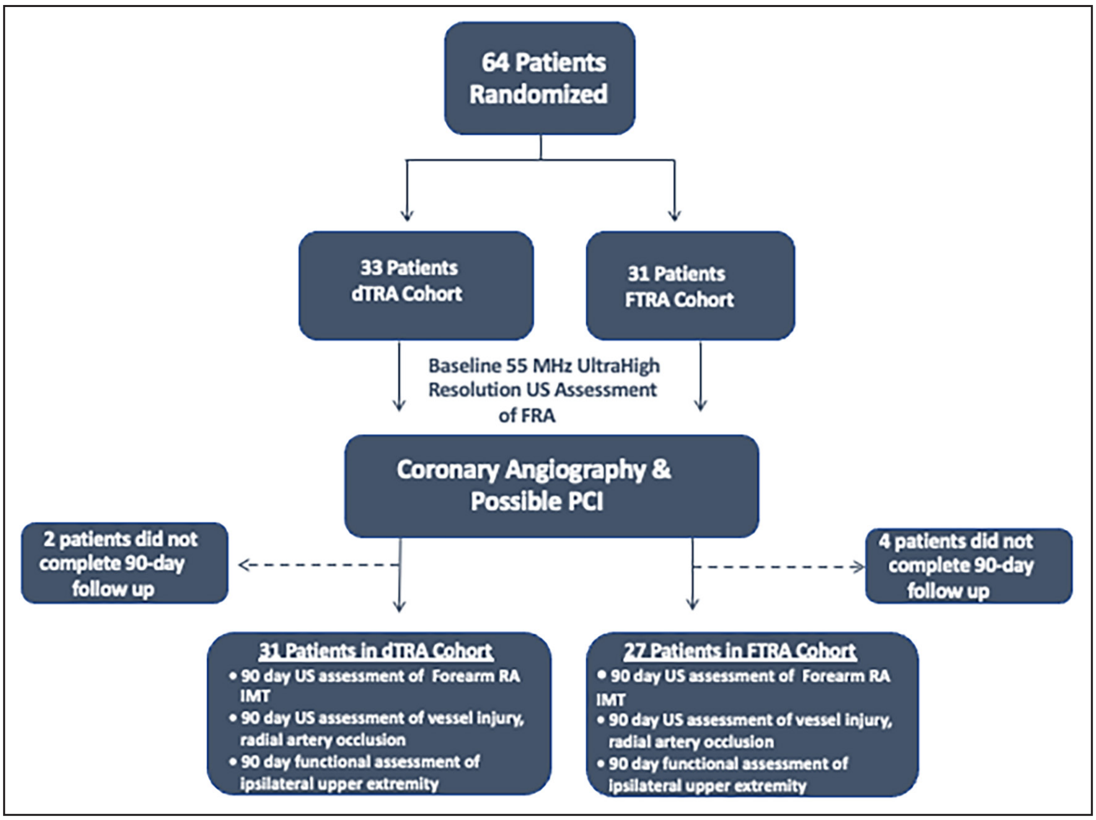

Figure 1. PRESERVE RADIAL (A Prospective Randomized Clinical Study Comparing Radial Artery Intimal Hyperplasia Following Distal Versus Forearm Transradial Arterial Access for Coronary Angiography) Consolidated Standards of Reporting Trials flow diagram and study design.
dTRA indicates distal transradial access; FRA, forearm radial artery; FTRA, forearm transradial access; IMT, intimal-medial thickness; PCI, percutaneous coronary intervention; RA, radial artery; and US, ultrasound.

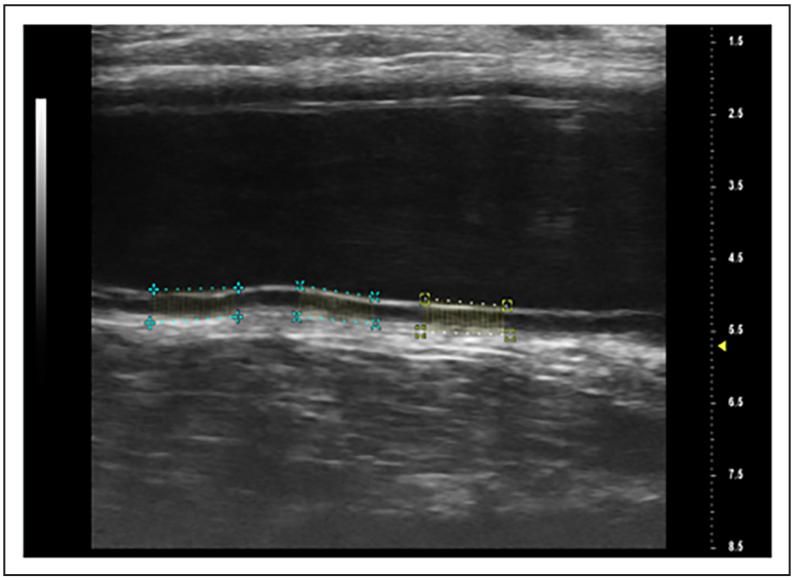

Figure 2. Two-dimensional ultra–high-resolution ultrasound of radial arterial intimal-medial thickness (IMT) using a 55-MHz probe.
IMT was measured as the distance from the intima to the outer edge of the media.

validated by an interventional cardiologist (W.B.B.) blinded to treatment allocation. The sonographer and interventional cardiologist validating the finalized IMT measurements had dedicated training in vascular ultrasound, and along with the analytics team, they were blinded to treatment allocation. Other measurements recorded included RA cross-sectional vessel and lumen diameters. Vessel diameter (ie, interadventitial diameter) was measured as the distance between the media-adventitia interfaces of the anterior and posterior walls of the RA. Lumen diameter was measured as the cross-sectional distance between the anterior and posterior intima. We also assessed for signs of vessel trauma, including limited access site intimal tears, medial dissections, and RA thrombosis, occlusion, and pseudoaneurysms.[10]

Coronary Angiography and PCI Technique

In patients undergoing dTRA, the right or left hand was positioned with the thumb flexed underneath the other 4 digits, and the hand positioned above the right groin. After sterile preparation and administration of 2% lidocaine subcutaneously, arterial puncture was performed under ultrasound guidance using a single anterior wall puncture technique with a 21-gauge needle. Once access was confirmed, a 0.014-inch×190-cm hydrophilic Hi-Torque Whisper MS guidewire (Abbott, Chicago, IL) was advanced under fluoroscopic guidance to the level of the elbow, at which time the access needle was removed, and the coronary wire served as a rail for sheath insertion. In patients undergoing fTRA, the hand was supinated and positioned on an arm board directly adjacent to the patient's ipsilateral hip. Arterial access was obtained with ultrasound guidance using a single-puncture technique with a 21-gauge needle or a double-wall puncture method with a 22-gauge needle. A 6/7F Glidesheath Slender (Terumo, Somerset, NJ) was used in both cohorts given its hydrophilic coating and large inner diameter, allowing for advancement of 6F or 7F guide catheters for PCI. All patients received an RA antispasmodic cocktail consisting of 5.0 mg verapamil, 200 μg nitroglycerine, and 5000 units of unfractionated heparin administered through the sheath.[11] If PCI was performed, additional intravenous heparin was administered to achieve an activated clotting time of 250 to 300 seconds, or 200 to 250 seconds if a glyoprotein IIb to IIIa inhibitor was given. Patients undergoing PCI were considered for a SYNERGY or Promus Elite (Boston Scientific, Maple Grove, MN) drug-eluting stent; however, final stent selection was according to physician discretion.

RA Hemostasis Protocol

Following CAG, PCI, or both, RA hemostasis was achieved using a standardized patent hemostasis protocol.[11] In the fTRA cohort, a trained cardiac catheterization laboratory cardiovascular technician or nurse applied a TR band radial compression device (Terumo) to the wrist over the access site with the green box on the band placed proximal to the arteriotomy. As the sheath was slowly withdrawn, 15 mL of air was injected into the 1-way valve on the TR band, a pulse oximeter was placed over the thumb, and the plethysmography waveform was observed. While performing manual occlusion of the ipsilateral ulnar artery, the hemoband was tightened until the plethysmography waveform was obliterated. The TR band was then loosened 1 mL at a time until the waveform first returned and was maintained, thus confirming patent hemostasis. In the dTRA cohort, a Safeguard Compression Device (Merit Medical, Jordan, UT), was applied proximal to the arteriotomy, and 3 mL of air was inflated into the pillow compartment while the sheath was withdrawn. In both patient cohorts, hemostasis was maintained for at least 2 hours following diagnostic CAG and at least 4 hours following PCI.

Study End Points

Clinical and procedural data were recorded. The primary study end point was the mean change in ipsilateral forearm IMT between the dTRA and fTRA cohorts. Secondary outcomes included the following: number of cannulation attempts to obtain access, TRA failure necessitating crossover to either an alternative RA or femoral arterial access, total procedure time, radiation exposure (cumulative air kerma and fluoroscopy time), contrast use, duration of hemostasis, and incidence of class III or greater hematomas, as defined by the EASY (Early Discharge After Transradial Stenting of Coronary Arteries Study) criteria.[12] In patients undergoing PCI, procedural outcomes and complications were also recorded, including successful PCI (defined as <30% residual stenosis with thrombolysis in myocardial infarction 3 flow), coronary perforation, in-hospital death, myocardial infarction, and urgent revascularization within 24 hours.[13] Other secondary end points included patient perceived pain and function of the ipsilateral hand at 90 days using the Borg and Disabilities of the Arm, Shoulders, and Hand scales, respectively.[6,7] The study Consolidated Standards of Reporting Trials flow diagram is shown in Figure 1.

Statistical Analysis

An intention-to-treat analysis was used to study the primary outcome in the dTRA and fTRA cohorts, according to the access site assignment following randomization. This method was used given the limit sample size and to avoid risk for bias. The null hypothesis assumed no between-group difference in forearm RA IMT at 90 days. From previous studies, we anticipated that 90-day forearm RA IMT would be ≈0.34±0.08 mm for the control group (fTRA).[10] Assuming similar SD and a 2-sided test with type 1 error of 0.05, we estimated that a sample size of 56 would provide 90% power to detect a 0.07-mm (20%) difference in 90-day IMT.[10] To account for 10% patient dropout or loss to follow-up, an additional 3 patients per group would be required. Summary statistics were presented as a mean±SD, or frequency and percentage, where deemed appropriate. Comparisons were made via Student t test for continuous variables and χ^2 or Fisher exact test for discrete variables. Statistical significance was defined as $P<0.05$ using 2-sided tests. Multivariable regression analysis was performed to examine for a relationship between baseline clinical demographics and 90-day forearm RA IMT. Variables included in the model were

Table 1. Baseline Clinical Characteristics

Characteristic	dTRA (n=33)	fTRA (n=31)	Total (N=64)
Age, y	66.4±11.4	68.7±13.6	67.5±12.4
Sex			
Men	23 (69.7)	22 (71.0)	45 (70.3)
Women	10 (30.3)	9 (29.0)	19 (29.7)
Race			
White	26 (78.8)	27 (87.1)	53 (82.8)
Black	4 (12.1)	2 (6.5)	6 (9.4)
Asian	0 (0.0)	1 (3.2)	1 (1.6)
Other	3 (9.1)	1 (3.2)	4 (6.2)
Ethnicity			
Hispanic	1 (3.0)	2 (6.5)	3 (4.7)
Other	32 (97.0)	29 (93.5)	61 (95.3)
BMI, kg/m^2	32.6 (6.8)	31.3 (7.2)	32.0 (7.0)
Hypertension	17 (51.5)	14 (45.2)	31 (48.4)
Diabetes	12 (36.4)	11 (35.5)	23 (35.9)
Chronic renal failure	3 (9.4)	1 (3.3)	4 (6.5)
Atrial fibrillation	8 (25.8)	3 (10.0)	11 (18.0)
Peripheral vascular disease	3 (9.1)	6 (19.4)	9 (14.1)
Prior PCI	9 (27.3)	7 (22.6)	16 (25.0)
LV ejection fraction, %	58.6 (10.6)	55.7 (11.9)	57.2 (11.2)
Clinical presentation			
Stable ischemic heart disease	28 (84.8)	22 (71.0)	50 (78.1)
NSTEMI	4 (12.1)	5 (16.1)	9 (14.1)
Unstable angina	1 (3.0)	2 (6.5)	3 (4.7)
Cardiomyopathy	0 (0.0)	2 (6.5)	2 (3.1)
Aspirin	22 (66.7)	19 (61.3)	41 (64.1)
Clopidogrel	10 (30.3)	7 (22.6)	17 (26.6)
Prasugrel	0 (0.0)	1 (3.2)	1 (1.6)
Ticagrelor	0 (0.0)	1 (3.2)	1 (1.6)
Oral anticoagulation	3 (9.1)	0 (0.0)	3 (4.7)
β-Blocker	21 (63.6)	23 (74.2)	44 (68.8)
ACE-I/ARB	18 (54.5)	12 (38.7)	30 (46.9)
ARNI	1 (3.0)	4 (12.9)	5 (7.8)
MRA	0 (0.0)	1 (3.2)	1 (1.6)
Statin	25 (75.8)	29 (93.5)	54 (84.4)
Nitrate	4 (12.1)	2 (6.5)	6 (9.4)

Data are given as mean±SD or number (percentage). ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BMI, body mass index; dTRA, distal transradial access; fTRA, forearm transradial access; LV, left ventricular; MRA, mineralocorticoid receptor antagonist; NSTEMI, non–ST-segment–elevation myocardial infarction; and PCI, percutaneous coronary intervention.

those historically associated with incidence of RAO: age, female sex, tobacco use, diabetes, chronic renal insufficiency, and PCI.[11,14] All analyses were performed using R (4.0.2) software for statistical computing.

RESULTS

Patient and Procedural Characteristics

From October 1, 2021 to March 31, 2022, 64 consecutive patients were randomized: 33 in the dTRA group and 31 in the fTRA cohort. Two patients in the dTRA cohort and 4 patients in the fTRA cohort were lost to follow up (Tables S1–S3). Five patients were not contactable for their 90-day follow-up assessments, and 1 patient died. Baseline clinical and procedural characteristics for all patients are shown in Tables 1 and 2, and patient study flow is shown in Figure 1. For the overall sample, mean age was 67.5 years, 70% were men, 83% were White race, 36% had diabetes, and 7% had chronic renal failure. There were no differences in baseline clinical characteristics between the dTRA and fTRA cohorts (Table 1). Mean baseline left ventricular ejection fraction was 57%, 80% of patients presented with stable ischemic heart disease, and 25% had undergone prior PCI. Of all patients, 72% (n=46) underwent right arm TRA. The dTRA and fTRA cohorts underwent a similar number of cannulation attempts for RA access (1.2 versus 1.0, respectively; P=0.11), and there was no difference in the incidence of RA spasm (0% versus 6.5%; P=0.23), access site crossover (3.0% versus 0%; P=1.0), radiation exposure (0.6 versus 0.5 Gy; P=0.48), contrast use (79 versus 93 mL; P=0.34), and postprocedural hemostasis time (157 versus 161 minutes; P=0.86) between the 2 groups. Of all patients, 34% (n=22) underwent PCI (33% of dTRA patients versus 36% of fTRA patients; P=1.0), and 19% had adjunctive atherectomy performed (26% of dTRA PCIs versus 11% of fTRA PCIs; P=0.41). All PCIs were successful, with no coronary dissections, perforations, or acute stent thromboses. There were no postprocedural RA access site hematomas (EASY class ≥3) in either group.

Table 2. Procedural Characteristics

Characteristic	dTRA (n=33)	fTRA (n=31)	Total (N=64)	*P* value
Arm accessed				1.00
Left	9 (27.3)	9 (29.0)	18 (28.1)	
Right	24 (72.7)	22 (71.0)	46 (71.9)	
No. of cannulation attempts	1.2 (0.4)	1.0 (0.2)	1.1 (0.3)	0.11
RA access time, s	55.5 (40.4)	42.4 (13.2)	49.1 (30.9)	0.09
Antispasmodic cocktail				
Heparin	33 (100.0)	31 (100.0)	64 (100.0)	1.00
Verapamil	33 (100.0)	31 (100.0)	64 (100.0)	1.00
Nitroglycerine	33 (100.0)	31 (100.0)	64 (100.0)	1.00
RA spasm	0 (0.0)	2 (6.5)	2 (3.1)	0.23
Access site crossover	1 (3.0)	0 (0.0)	1 (1.6)	1.00
Single wall puncture	33 (100.0)	24 (77.4)	57 (89.1)	0.00
Diagnostic angiogram only	19 (57.6)	18 (58.1)	37 (57.8)	1.00
Atherectomy	5 (26.3)	2 (11.1)	7 (18.9)	0.41
No. of diagnostic catheters	1.5 (0.8)	1.8 (0.7)	1.7 (0.8)	0.09
No. of PCI guide catheters	0.5 (0.6)	0.5 (0.6)	0.5 (0.6)	0.98
Cumulative air kerma, Gy	0.6 (0.6)	0.5 (0.5)	0.5 (0.5)	0.48
Total contrast use, mL	79.2 (48.0)	93.0 (64.1)	85.8 (56.2)	0.34
Total hemostasis time, min	157.4 (77.3)	160.9 (86.2)	159.1 (81.1)	0.86
Same-day discharge	25 (78.1)	20 (64.5)	45 (71.4)	0.27
Hospital duration, d	0.7 (1.1)	1.1 (1.5)	0.9 (1.3)	0.21
PCI performed	11 (33.3)	11 (35.5)	22 (34.4)	1.00
Successful PCI	11 (100.0)	11 (100.0)	22 (100.0)	1.00
Coronary dissection/perforation	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Acute stent thrombosis	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Hematoma (EASY class ≥III)	0 (0.0)	0 (0.0)	0 (0.0)	1.00

Data are given as mean (SD) or number (percentage). dTRA indicates distal transradial access; EASY, Early Discharge After Transradial Stenting of Coronary Arteries Study; fTRA, forearm transradial access; PCI, percutaneous coronary intervention; and RA, radial artery.

Table 3. Baseline Ultrasound RA Measurements

Variable	dTRA (n=33)	fTRA (n=31)	Total (N=64)	*P* value
Forearm RA vessel diameter, mm	3.31 (0.53)	3.35 (0.42)	3.33 (0.48)	0.73
Forearm RA luminal diameter, mm	2.56 (0.47)	2.64 (0.43)	2.60 (0.45)	0.47
Forearm RA IMT, mm	0.31 (0.05)	0.31 (0.05)	0.31 (0.05)	0.97
Distal RA vessel diameter, mm	2.80 (0.39)	2.92 (0.34)	2.86 (0.37)	0.18
Distal RA luminal diameter, mm	2.03 (0.39)	2.19 (0.32)	2.11 (0.36)	0.08
Distal RA IMT, mm	0.31 (0.06)	0.31 (0.05)	0.31 (0.05)	0.99

Data are given as mean (SD). dTRA indicates distal transradial access (snuffbox); fTRA, forearm transradial access; IMT, intimal-medial thickness; and RA, radial artery.

Baseline Ultra–High-Resolution Ultrasound Results

Baseline RA ultrasound measurements are shown in Table 3. There were no differences in baseline distal RA vessel diameter (2.80 versus 2.92 mm; *P*=0.18), distal RA luminal diameter (2.03 versus 2.19 mm; *P*=0.08), and distal RA IMT (0.31 versus 0.31 mm; *P*=0.99) between the dTRA and fTRA groups. Similarly, there were no differences in baseline forearm RA vessel diameter (3.31 versus 3.35 mm; *P*=0.73), forearm RA luminal diameter (2.56 versus 2.64 mm; *P*=0.47), and forearm RA IMT (0.31 versus 0.31 mm; *P*=0.97) between the dTRA and fTRA groups.

Ninety-Day Ultra–High-Resolution Ultrasound and Functional Assessments

The 90-day ultrasound findings and Borg and Disabilities of the Arm, Shoulders, and Hand scale assessments are shown in Table 4. Complete data were available for the 58 patients (31 in the dTRA cohort and 27 in the fTRA cohort) who completed 90-day ultrasound measurements. There were no differences in 90-day change in mean forearm RA IMT (0.07 versus 0.07 mm; *P*=0.61), and no differences in 90-day assessments of forearm RA IMT (0.37 versus 0.38 mm; *P*=0.73), vessel diameter (3.04 versus 2.95 mm; *P*=0.48), change in vessel diameter (−0.29 versus −0.39 mm; *P*=0.13),

Table 4. The 90-Day Ultrasound Findings and Functional Assessments

Variable	dTRA (n=31)	fTRA (n=27)	Total (N=58)	*P* value
90-d Forearm RA measurements				
Forearm RA IMT, mm	0.37 (0.05)	0.38 (0.06)	0.38 (0.05)	0.73
Forearm RA IMT change from baseline, mm	0.07 (0.05)	0.07 (0.04)	0.07 (0.04)	0.61
Forearm RA vessel diameter, mm	3.04 (0.54)	2.95 (0.40)	3.00 (0.48)	0.48
Forearm RA change in vessel diameter, mm	−0.29 (0.25)	−0.39 (0.27)	−0.34 (0.260)	0.13
Forearm RA luminal diameter, mm	2.32 (0.53)	2.34 (0.47)	2.33 (0.49)	0.85
Forearm RA change in luminal diameter, mm	−0.25 (0.25)	−0.32 (0.24)	−0.28 (0.25)	0.27
90-d Distal RA measurements				
Distal RA IMT, mm	0.38 (0.06)	0.31 (0.05)	0.35 (0.06)	<0.001
Distal RA IMT change from baseline, mm	0.07 (0.04)	0.00 (0.02)	0.04 (0.04)	<0.001
Distal RA vessel diameter, mm	2.47 (0.38)	2.87 (0.27)	2.66 (0.39)	<0.001
Distal RA change in vessel diameter, mm	−0.33 (0.25)	−0.03 (0.16)	−0.19 (0.26)	<0.001
Distal RA luminal diameter, mm	1.77 (0.37)	2.20 (0.31)	1.97 (0.40)	<0.001
Distal RA change in luminal diameter, mm	−0.26 (0.25)	0.00 (0.12)	−0.14 (0.24)	<0.001
Other 90-d outcomes				
Limited access site intimal tears	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Dissection	0 (0.0)	0 (0.0)	0 (0.0)	1.00
RA occlusion	0 (0.0)	0 (0.0)	0 (0.0)	1.00
RA pseudoaneurysm	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Borg scale pain	11.5 (3.4)	10.56 (2.6)	11.1 (3.1)	0.24
DASH scale score	5.7 (10.2)	8.0 (12.9)	6.8 (11.5)	0.46

Data are given as mean (SD) or number (percentage). DASH indicates Disabilities of Arm, Shoulder, and Hand; dTRA, distal transradial access; fTRA, forearm transradial access; IMT, intimal-medial thickness; and RA, radial artery.

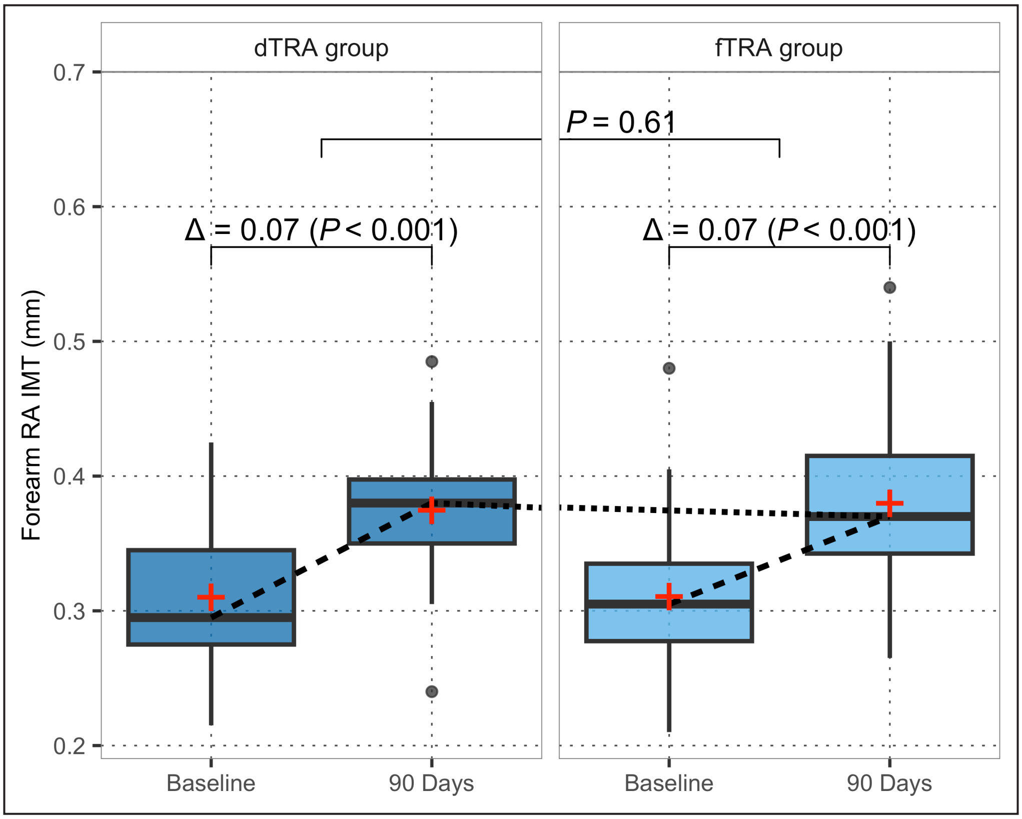

Figure 3. Box-and-whisker plots depicting the change in forearm radial artery (RA) intimal-medial thickness (IMT) from baseline to 90 days. dTRA indicates distal transradial access; and fTRA, forearm transradial access.

luminal diameter (2.32 versus 2.34 mm; P=0.85), or change in luminal diameter (–0.25 versus –0.32 mm; P=0.27) (Figure 3). No access site intimal tears, dissections, RA occlusions, or RA pseudoaneurysms were noted at 90 days, and there were no differences in 90-day Borg pain scale score (12 versus 11; P=0.24) or Disabilities of the Arm, Shoulders, and Hand scale score (6 versus 8; P=0.46).

Ultrasound of the distal RA showed significant differences between groups. At 90 days, patients in the dTRA group showed greater distal RA IMT (0.38 versus 0.31 mm; P<0.001), larger increase in dTRA IMT (0.07 versus 0.00; P<0.001), smaller distal RA vessel diameter (2.47 versus 2.87 mm; P<0.001), greater reduction in distal RA vessel diameter (–0.33 versus –0.03 mm; P<0.001), smaller distal RA luminal diameter (1.77 versus 2.20 mm; P<0.001), and greater reduction in distal RA luminal diameter (–0.26 versus 0.00 mm; P<0.001) compared with those undergoing fTRA.

Clinical Predictors of Forearm RA IMT at 90 Days

Multivariable regression analysis identified age and diabetes as the only independent predictors of 90-day forearm IMT (Figure 4). With every 1-year increase in age, there was a 1.4×10^{-3} mm increase in forearm RA IMT at 90 days (95% CI, 0.78×10^{-3} to 0.28×10^{-2}; P<0.01). Similarly, diabetes was associated with a 2.4×10^{-2} mm increase in forearm RA IMT at 90 days (95% CI, 0.13×10^{-2} to 0.55×10^{-1}; P=0.04).

DISCUSSION

The PRESERVE RADIAL Study is the first study to compare RA access site healing in patients undergoing dTRA versus fTRA for CAG and PCI. We found that, compared with conventional fTRA, dTRA was associated with the following: (1) no significant difference in 90-day change in forearm RA IMT; (2) no significant change in forearm RA vessel or luminal diameter at 90 days; (3) increased 90-day distal RA IMT; (4) favorable patterns of vascular healing; and (5) no significant difference in 90-day ipsilateral upper extremity pain and motor strength (Figure 5).

Although prior studies have demonstrated the feasibility of dTRA for CAG, little is known about differences in vessel healing compared with conventional fTRA.[4,11] In addition to potential ergonomic benefits

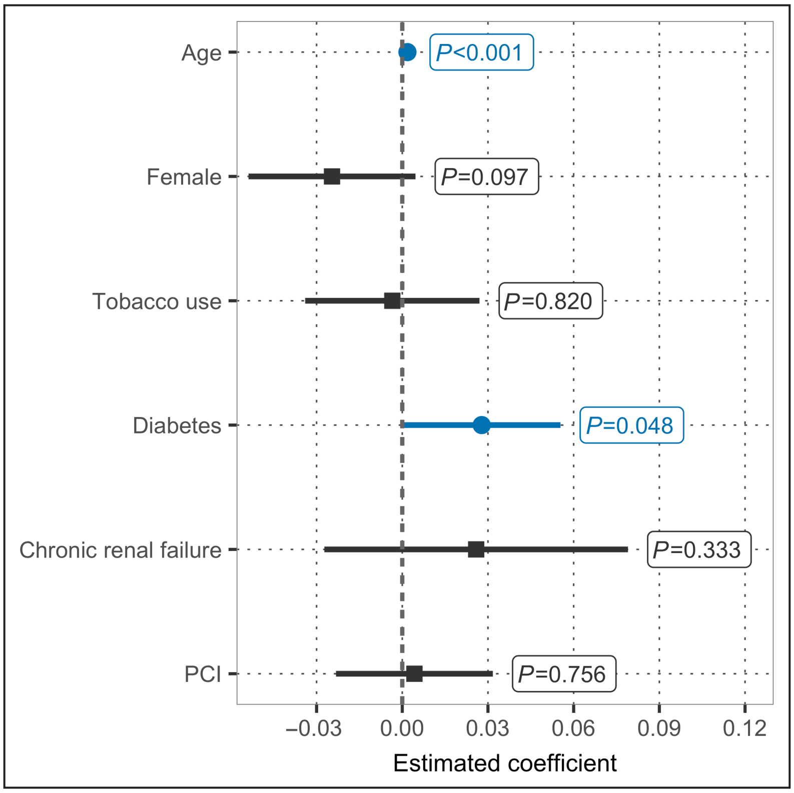

Figure 4. Clinical predictors of 90-day forearm radial artery intimal-medial thickness.
Assessment of independent clinical predictors of 90-day intimal-medial thickness of the ipsilateral forearm radial artery. PCI indicates percutaneous coronary intervention.

and postprocedural comfort for the patient, dTRA has been reported to be associated with less forearm RA occlusion, perhaps attributable to collateral networks between the distal radial and ulnar arteries by way of the superficial and deep palmar arches.[15] We hypothesized that more distal RA puncture would be associated with less forearm RA IMT. This was not the case, suggesting that RA remodeling may result not only from direct vessel puncture, but also advancement of the sheath into the more proximal segment.

Several studies have compared the risk of RAO between dTRA and fTRA. A recent contemporary meta-analysis of 14 randomized controlled trials (n=6208 patients) comparing dTRA versus fTRA for CAG noted a nearly two-thirds reduction in the risk of in-hospital and 60-day RAO with dTRA.[5] dTRA was also associated with fewer EASY class II or greater hematomas, but more time for RA cannulation, more puncture attempts, and higher access site crossover. This contrasts with our findings, which may be attributable to the increased operator experience and adoption of standardized vascular access and patent hemostasis protocols in our center. These are similar findings to these noted in the DISCO RADIAL (Distal Versus Conventional Radial Access) trial, in which the incidence of RAO with both dTRA and fTRA was <1%.[16]

RA remodeling, a process that occurs over weeks to months following TRA, is triggered by acute vessel wall trauma at the time of sheath insertion and subsequent inflammatory processes that signal medial smooth muscle cells to migrate into the intima and deposit extracellular matrix.[17] These events ultimately translate into a nearly 20% reduction in RA diameter.[10] Using a similar technique to our study, the PRAGMATIC (A Prospective Randomized Trial comparing Radial Artery Intimal Hyperplasia resulting from a 7F Transradial Sheathless Guide [Mach 1] versus a 6F Transradial Sheath/Guide Combination in Coronary Intervention) Trial also described changes in IMT and vascular trauma following TRA.[10] Although the degree of IMT (0.07 mm) noted in our study is comparable to that reported in the PRAGMATIC Trial, we observed less arterial shrinkage (10%–12% versus 20%).[10] We postulate that this may be attributable to our study's use of a frictionless hydrophilic RA sheath; however, this remains speculative. Using 40-MHz ultrasound, the Rotterdam Radial Artery Research Study showed frequent signs of vascular injury, with nearly 90% of

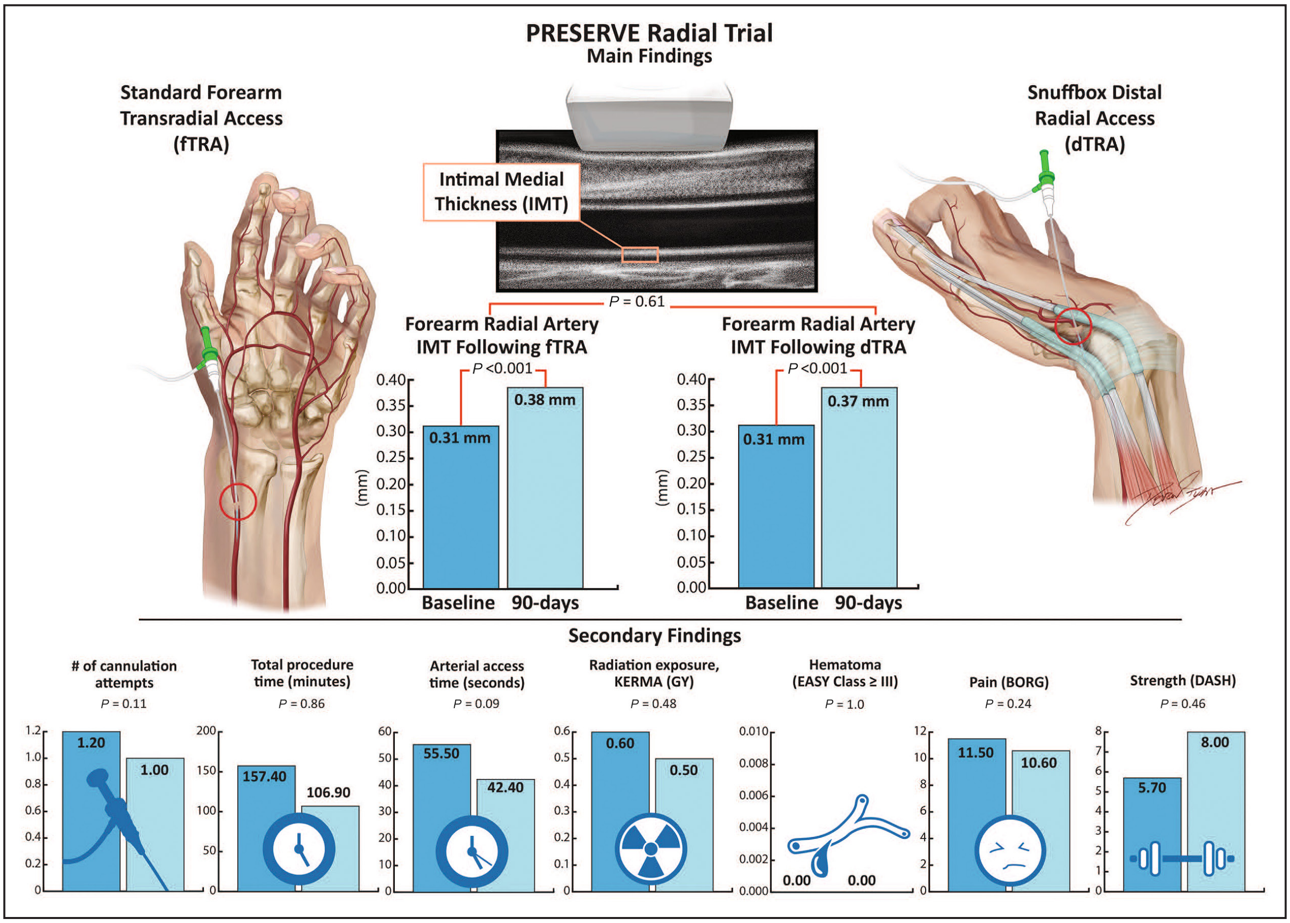

Figure 5. PRESERVE RADIAL (A Prospective Randomized Clinical Study Comparing Radial Artery Intimal Hyperplasia Following Distal Versus Forearm Transradial Arterial Access for Coronary Angiography) main findings.
Using ultra–high-resolution ultrasound, no differences were noted in mean change of forearm radial artery intimal-medial thickness (IMT) from baseline to 90 days in patients randomized to distal transradial access (dTRA) vs forearm transradial access (fTRA) for coronary angiography. Number of cannulation attempts, time to radial artery access, procedure time, radiation exposure, access site hematomas, and patient-reported hand pain and functional end points were similar between the groups. DASH indicates Disabilities of the Arm, Shoulder, and Hand; and EASY, Early Discharge After Transradial Stenting of Coronary Arteries Study.

cases showing evidence of RA dissection, and 74% showing intramural hematomas; and there was a 45% increase in RA IMT.[18] Other imaging techniques, including intravascular ultrasound and optical coherence tomography, have also shown neointimal thickening, vessel shrinkage, loss of vasomotor function, and reduced long-term RA patency.[2,3,19–21] It has been proposed that the factors associated with Virchow triad are implicated in RAO (namely, endothelial injury, stasis of blood, and hypercoagulability).[11] We also believe that RA trauma induced by vessel puncture and sheath advancement and the degree to which RA flow is maintained after sheath removal contribute to the risk of RAO, especially with using ulnar artery compression. Still, an improved understanding of RA remodeling, in particular intimal hyperplasia, is necessary to fully understand these dynamics and mitigate against the pathologic changes that may compromise the RA for future access.

A substantial number of patients require repeated TRA heart catheterization, attributable to complications following the index PCI or to facilitate staged revascularization.[22] Although the safety and feasibility of repeated ipsilateral TRA has been demonstrated, procedural failure attributable to RAO occurs in nearly 6% of patients undergoing a second procedure, and in 13% requiring a third procedure.[22,23] When the RA has been previously cannulated for CAG, patients undergoing coronary artery bypass graft surgery with the RA as a conduit show a higher rate of RA graft occlusion within 30 days.[19] Intimal hyperplasia, adventitial inflammation, and periarterial tissue necrosis have been thought to contribute to reduced RA graft patency in this setting.[19,24] Although we hypothesized that dTRA might provide an advantage to fTRA by reducing forearm RA intimal hyperplasia, our study results did not confirm this. RA intimal hyperplasia and adverse remodeling were not governed by the location of access site puncture, but instead by other factors, such as age and diabetes.

We also noted a greater degree of IMT in the ipsilateral distal RA segment with dTRA versus fTRA. Recently, there has been increased interest in dTRA access because of theorized potential advantages in forearm RAO rates, bleeding risks, vascular access site complications, and enhanced patient and operator comfort, particularly when approaching the left RA in patients with prior coronary artery bypass grafting or when right radial access is not feasible.[25] Our results suggest that dTRA may limit future repeated distal radial access in patients requiring multiple heart catheterizations, because it is associated with an increase in IMT in both the distal RA and the forearm RA, whereas forearm RA access is only associated with an increase in IMT in the forearm RA. PRESERVE RADIAL is the first study to report on distal RA injury and healing in patients undergoing dTRA. This is noteworthy as it would seem to implicate similar inflammatory and fibroproliferative processes in the distal RA at the time of sheath insertion and catheter exchanges as a potential mechanism for IMT in the anatomic snuffbox location.[17] Given the single-center nature of this study, these findings are hypothesis generating and merit further research to identify strategies during TRA aimed at preserving RA integrity across the entire length of the vessel, thereby allowing operators to choose the access site that may be most feasible based on body habitus, coronary anatomy, and ergonomic considerations.

Lastly, increased age and diabetes predicted IMT in our study. Both are known to increase inflammatory cytokines, decrease NO synthetase, and impair endothelial function.[26] Previous studies have shown that other patient characteristics (female sex, low body mass index, diabetes, and South Asian descent) and procedural factors (multiple puncture attempts, insufficient anticoagulation, sheath/artery ratio >1, and prolonged hemostasis) may also contribute to the risk of RA occlusion.[11,18,27–29] Further investigation is required to better understand the clinical and procedural factors that contribute to adverse RA remodeling.

Limitations

The sample size of our trial was relatively small. However, we had >90% power to detect a 20% change in IMT at 90 days. Still, the lack of differences in secondary end points may have been attributable to type 2 error. Our findings were also studied using an intention-to-treat analysis. This method may have limitations in cases of limited sample size and higher rates of patient dropout, such as our study, in which 6 patients were lost to follow up. Although we believe that our study was representative of real-world clinical practice, it was single center in design with intermediate complexity case mix. As such, these findings may not be fully generalizable to centers using different TRA and hemostasis protocols, and in potentially more complex procedures with longer procedure times, more catheter manipulation/catheter exchanges, and higher doses of anticoagulation. Finally, we excluded patients with ST-segment–elevation myocardial infarction, cardiogenic shock, or both who have greater degrees of inflammation, vasoconstriction, and risk of thrombosis.[30,31]

CONCLUSIONS

In this single-center study of patients undergoing elective TRA for CAG, we observed no difference in 90-day change in forearm RA IMT between dTRA and fTRA. These 2 vascular access strategies shared similar procedural outcomes, vascular forearm RA healing patterns, and pain/functional outcomes. Age and diabetes independently predicted IMT. Further investigation is warranted in the form of large multicenter pragmatic clinical trials with longer-term follow-up to better elucidate the dynamics of RA healing following TRA and to identify effective strategies to preserve RA integrity for future access.

ARTICLE INFORMATION

Received July 1, 2023; accepted October 24, 2023.

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Acknowledgments

The authors would like to thank Dwight and Martha Schar for their generous support of Inova Schar Heart and Vascular, and the Dudley Family for their continued contributions and support of the Inova Dudley Family Center for Cardiovascular Innovation.

Disclosures

Dr Tehrani serves on the advisory board for Abbott and has received research grants from Boston Scientific. He also served as a consultant for Boston Scientific. Dr Damluji receives research funding from the Pepper Scholars Program of the Johns Hopkins University Claude D. Pepper Older Americans Independence Center, funded by the National Institute on Aging (P30-AG021334), and a mentored patient-oriented research career development award from the National Heart, Lung, and Blood Institute (K23-HL153771-01). Dr Batchelor serves as a consultant for Boston Scientific, Abbott, Edwards, Medtronic, and V-Wave. The remaining authors have no disclosures to report.

Sources for Funding

This study was supported by an investigator-initiated research grant from Boston Scientific Corporation (Maple Grove, MN).

Supplemental Material

Tables S1–S3

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