JACC: CARDIOVASCULAR INTERVENTIONS VOL. 17, NO. 16, 2024

ORIGINAL RESEARCH

PERIPHERAL

Clinical Outcomes of Transradial vs Nontransradial Aortoiliac Endovascular Therapy

Osamu Iida, MD, PhD,[a] Mitsuyoshi Takahara, MD, PhD,[b] Masahiko Fujihara, MD,[c] Naoko Higashino, MD,[d] Naoki Hayakawa, MD,[e] Kazunori Horie, MD,[f] Yoshito Yamamoto, MD,[g] Amane Kozuki, MD, PhD,[h] Kenji Suzuki, MD,[i] Norihiko Shinozaki, MD,[j] Hiroyoshi Yokoi, MD,[k] Shinsuke Nanto, MD, PhD,[l] Yoshiharu Higuchi, MD, PhD,[a] Masato Nakamura, MD, PhD,[m] the COMFORT Investigators

ABSTRACT

BACKGROUND The introduction of radial-specific equipment has made transradial (TR) aortoiliac (AI) endovascular therapy (EVT) more convenient.

OBJECTIVES The authors aimed to investigate the perioperative outcomes of the TR approach in patients undergoing AI EVT for symptomatic peripheral artery disease.

METHODS The COMFORT (Contemporary Strategy for Aortoiliac Intervention) registry was a prospective, multicenter, observational study enrolling patients with symptomatic peripheral artery disease undergoing AI EVT between January 2021 and June 2023. The primary outcome was perioperative complications, whereas the secondary outcomes included core laboratory–evaluated residual stenosis >30%, time to hemostasis, time to ambulation, 30-day patency, and 30-day limb symptoms. These outcomes were compared between TR and non-TR AI EVT after propensity score matching.

RESULTS The TR approach was selected for 231 of the 947 patients (24.3%). The TR approach was chosen more in patients with a higher ankle-brachial index, chronic total occlusion, aortic lesion, bare nitinol stent implantation, and plain angioplasty, whereas it was chosen less in patients with dialysis, a history of AI EVT, chronic limb-threatening ischemia, bilateral calcification, and simultaneous infrainguinal EVT (all $P < 0.05$). After propensity score matching, the incidence of perioperative complications did not differ significantly between the groups (TR group: 6.0% vs non-TR group: 5.1%; $P = 0.69$). The proportions of residual stenosis, 30-day patency, and 30-day limb symptoms were not significantly different (all $P > 0.05$); however, the time to hemostasis and the time to ambulation were shorter in the TR group (both $P < 0.05$).

CONCLUSIONS Non-TR AI EVT and TR AI EVT using radial-specific equipment were associated with a similar risk of perioperative complications. The TR approach helps shorten the time required for hemostasis and ambulation. (JACC Cardiovasc Interv. 2024;17:1891–1901) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Cardiovascular Division, Osaka Police Hospital, Osaka, Japan; [b]Department of Diabetes Care Medicine, Osaka University Graduate School of Medicine, Suita, Japan; [c]Department of Cardiology, Kishiwada Tokushukai Hospital, Kishiwada, Japan; [d]Cardiovascular Center, Kansai Rosai Hospital, Amagasaki, Japan; [e]Department of Cardiology, Asahi General Hospital, Asahi, Japan; [f]Department of Cardiology, Sendai Kousei Hospital, Sendai, Japan; [g]Division of Cardiology, Iwaki City Medical Center, Iwaki, Japan; [h]Department of Cardiology, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan; [i]Department of Cardioligy, Tokyo Saiseikai Central Hospital, Tokyo, Japan; [j]Division of Cardiology, Asama General Hospital, Nagano, Japan; [k]Cardiovascular Center,

ISSN 1936-8798 https://doi.org/10.1016/j.jcin.2024.06.002

ABBREVIATIONS AND ACRONYMS

ABI = ankle-brachial index

AI = aortoiliac

CLTI = chronic limb-threatening ischemia

CTO = chronic total occlusion

EVT = endovascular therapy

PAD = peripheral artery disease

TB = transbrachial

TF = transfemoral

TR = transradial

In patients with symptomatic peripheral artery disease (PAD) presenting with lifestyle-limiting intermittent claudication resistant to guideline-directed medical therapy or those presenting with chronic limb-threatening ischemia (CLTI), revascularization is recommended to improve quality of life or prevent major amputation.[1-3] Endovascular therapy (EVT) is widely used as a first-line revascularization strategy, especially for aortoiliac (AI) lesions, because of its acceptable long-term durability.[4,5]

Although AI EVT is conventionally performed via the transfemoral (TF) approach, the transradial (TR) approach has gained increasing popularity for the treatment of AI disease because of its potential to reduce procedural complications and invasiveness.[6-8] In recent years, several radial-specific endovascular devices have become clinically available. In 2019, Terumo introduced the comprehensive radial to peripheral (R2P) approach with radial-specific longer-length devices such as wire, sheath, and stent specifically tailored for peripheral procedures. In 2022, Cordis launched the Radianz Radial Peripheral System, which includes wires, sheaths, and stents. With the advent of these devices, the popularity of the TR approach in AI EVT is expected to increase, but there is still scarcity of previously published data. This study aimed to clarify the current criteria for selecting the TR approach and perioperative outcomes of the TR approach in patients undergoing AI EVT for symptomatic atherosclerotic PAD.

METHODS

STUDY POPULATION. The COMFORT (Contemporary Strategy for Aortoiliac Intervention) registry was a multicenter prospective observational study that registered adult patients (20 years of age or older) undergoing AI EVT for symptomatic atherosclerotic PAD at 42 cardiovascular centers across Japan between January 2021 and June 2023, and 30-day follow-ups were scheduled. The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Boards of the participating centers. Informed consent was obtained from the participants or their families if not possible. The inclusion criteria for this study were patients who: 1) were 20 years of age or older; 2) had an ischemic symptom caused by atherosclerotic PAD; 3) were planned for AI EVT; and 4) could participate in a 30-day follow-up survey. The exclusion criteria were patients who: 1) had an ischemic symptom caused by acute lower limb ischemia; 2) were scheduled for major amputation or surgical therapy within 30 days after EVT; and 3) had a history of surgical reconstruction or major amputation on either the ipsilateral or contralateral leg. From a total of 1,119 patients registered in the study, 119 who did not satisfy the eligibility criteria (ie, the presence of relevant symptoms and AI lesions), 1 patient with missing data on the approach site, and 52 with missing data on outcomes (perioperative complications and core laboratory–evaluated residual stenosis) were excluded. Ultimately, 947 patients were included in the analysis (**Figure 1**). Patients who started EVT with and without radial artery (RA) were classified into the TR and non-TR groups, respectively, for comparison.

PREPROCEDURAL EVALUATION AND EVT PROCEDURE. Registration was performed before AI revascularization. Before revascularization, baseline characteristics, lower limb condition, and anatomical severity of the patients were evaluated. The anatomical location and severity of the arterial lesions were routinely assessed using duplex ultrasound as a noninvasive test. If arterial disease detected by duplex ultrasound was hemodynamically significant, the presence of a significant arterial lesion was diagnosed using computed tomography angiography or digital subtraction angiography before revascularization. The treatment strategy, such as the selection of access sites and device use, was determined at the discretion of vascular specialists, including vascular surgeons and interventional cardiologists in clinical practice. The 30-day clinical and hemodynamic follow-up was scheduled for all study participants.

ANGIOGRAPHIC CORE LABORATORY. An angiographic core laboratory (ENDO CORE) conducted a

Fukuoka Sanno Hospital, Fukuoka, Japan; [l]Department of Cardiology, Nishinomiya Municipal Central Hospital, Nishinomiya, Japan; and the [m]Division of Less Invasive Treatment in Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo, Japan.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received February 16, 2024; revised manuscript received May 31, 2024, accepted June 4, 2024.

quantitative vascular analysis to measure the reference vessel diameter and the percentage of diameter stenosis. In this study, a radiopaque ruler was placed on the patient, which covered the umbilical region to the outer crease of the groin. On the initial angiogram, the entire lesion was identified, and the treatment segment was determined. The most normal-looking proximal and distal reference vessel diameters were evaluated by calibrating the fluoroscope along with the ruler placed in the fluoroscopic field. The percentage of diameter stenosis at the most severely stenotic site was evaluated based on the initial and completion angiograms.

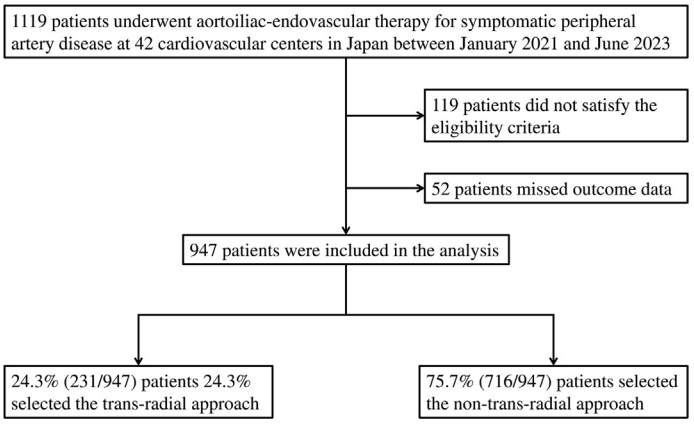
DEFINITION. The puncture time was defined as the duration from local anesthesia administration to successful sheath cannulation. Sheath placement time was defined as the duration from sheath cannulation to positioning the sheath either above or below the target lesion. The wire crossing time was calculated from the initiation of wire advancement toward the lesion to the successful crossing of the target lesion by the guidewire. The time to achieve hemostasis was defined as the period from sheath removal to the initial observation of hemostasis, characterized by the absence of arterial pulsatile bleeding or indications of hematoma expansion. The time to ambulation was defined as the duration from sheath removal to the point at which the patient's condition returned to the preoperative level of daily activity.

OUTCOME MEASURES. The primary outcome measure was the safety endpoint, including the incidence of perioperative complications such as a composite of bleeding at the puncture site, arterial occlusion at the approach site, perioperative death, cerebral hemorrhage, renal failure, major amputation, vessel rupture, lower extremity artery embolism, and other bleeding requiring transfusion. The secondary outcome measures were efficacy endpoints, including core laboratory-evaluated residual stenosis >30%, procedural time, time to hemostasis, time to ambulation, 30-day vessel patency, and 30-day limb symptoms. The outcomes were compared between the TR and non-TR groups.

STATISTICAL ANALYSIS. Data on baseline characteristics are presented as mean ± SD or median (IQR) for continuous variables and as frequency (percentage) for discrete variables if not otherwise mentioned. Statistical significance was set at $P < 0.05$.

The association between baseline characteristics and the TR approach was investigated using a logistic regression model. ORs are presented with 95% CIs.

FIGURE 1 Study Flowchart



When clinical outcomes were compared between the groups, propensity score matching was adopted to minimize intergroup differences in baseline characteristics. The propensity score was developed using a logistic regression model that included the following variables: age, sex, mobility, smoking, diabetes mellitus, renal failure on dialysis, ischemic stroke, coronary artery disease, CLTI, ankle-brachial index (ABI), history of AI EVT, lesion distribution, chronic total occlusion (CTO), arterial calcification, reference vessel diameter, lesion length, endovascular devices, and simultaneous infrainguinal EVT. A 1:1 matching was performed on the logit of the propensity score within the caliper of 0.2 SD of the logit of the propensity score. After matching, the intergroup differences were analyzed with stratification by the pairs and tested using the paired Student's *t*-test for continuous variables and the McNemar test and the Stuart-Maxwell test for 2 and more category discrete variables, respectively. During the paired Student's *t*-test, procedural time, time to hemostasis, and time to ambulation were log-transformed.

For sensitivity analysis, we conducted a propensity score matching analysis after excluding the transbrachial (TB) approach and compared the TR and TF approaches. We also performed a propensity score matching analysis after further excluding cases with both TR and TF approaches.

Missing data were addressed using multiple imputation by the chained equations method. In the procedure, we generated 10 imputed data sets and combined the analytic results according to Rubin's rule, except for the chi-square statistics, which were pooled as the D2 statistic. During the propensity score matching analysis, matching was performed within each imputed data set, and the intergroup differences

were estimated in each of the matched data sets to be pooled together (the so-called "within approach"). All statistical analyses were performed using R version 4.1.1 (R Development Core Team).

RESULTS

The baseline characteristics of the study population are summarized in Table 1. The mean age was 74 ± 9 years, and 74.6% (n = 706/947) were men. The prevalence of diabetes mellitus, renal failure on dialysis, and a history of aortoiliac EVT was 49.6% (n = 470/947), 20.0% (n = 189/947), and 22.9% (n = 217/947), respectively. The proportion of CLTI was 21.1% (n = 200/947), and the mean ABI before AI EVT was 0.58 ± 0.25. In terms of lesion characteristics, the frequency of CTO was 28.3% (n = 268/947), whereas the mean lesion length and reference vessel diameter were 6.4 ± 4.6 cm and 8.1 ± 1.7 mm, respectively. Covered stents and bare nitinol stents were implanted in 18.6% (n = 176/947) and 83.4% (n = 790/947), respectively. Simultaneous infrainguinal EVT was performed in 18.2% (n = 172/947). The TR approach was selected for 231 of the 947 patients (24.3%), 27% of whom also received an additional TF access. The frequency of multiple approaches did not differ between the groups.

As shown in Table 2, baseline characteristics that were independently associated with the TR approach were renal failure on dialysis (adjusted OR: 0.06; 95% CI: 0.02-0.19; $P < 0.001$), CLTI (adjusted OR: 0.53; 95% CI: 0.29-0.97; $P = 0.041$), ABI (adjusted OR: 2.68; 95% CI: 1.10-6.53; $P = 0.031$), a history of AI EVT (adjusted OR: 0.57; 95% CI: 0.35-0.93; $P = 0.023$), the presence of an aortic lesion (adjusted OR: 2.47; 95% CI: 1.17-5.25; $P = 0.018$), CTO (adjusted OR: 1.79; 95% CI: 1.17-2.73; $P = 0.007$), bilateral calcification (adjusted OR: 0.54; 95% CI: 0.38-0.77; $P = 0.001$), bare nitinol stent implantation (adjusted OR: 2.47; 95% CI: 1.03-5.93; $P = 0.042$), plain angioplasty (adjusted OR: 2.94; 95% CI: 1.10-7.89; $P = 0.032$), and simultaneous infrainguinal EVT (adjusted OR: 0.18; 95% CI: 0.09-0.35; $P < 0.001$). Of the 10 associated factors, renal failure on dialysis and simultaneous infrainguinal EVT had an OR with a lower limit of 95% CI <0.5. In patients with renal failure on dialysis, simultaneous infrainguinal EVT, or both (accounting for 33.6% [Q1-Q3: 30.6%-36.6%] of the overall population), the proportion of the TR approach was only 3.8% (Q1-Q3: 3.7%-3.8%). In contrast, in patients without renal failure on dialysis or simultaneous infrainguinal EVT (accounting for 66.4% [Q1-Q3: 63.4%-69.4%] of the overall population), the proportion reached 34.8% (Q1-Q3: 34.7%-34.9%).

TABLE 1 Baseline Characteristics of the Study Population (N = 947)

Age, y	74 ± 9
Male	706 (74.6)
Nonambulatory	80 (8.4)
Smoking history	742 (78.4)
Diabetes mellitus	470 (49.6)
Renal failure on dialysis	189 (20.0)
Ischemic stroke	179 (18.9)
Coronary artery disease	436 (46.0)
Chronic limb-threatening ischemia	200 (21.1)
Ankle brachial index	0.58 ± 0.25
Missing data	42 (4.4)
History of aortoiliac EVT	217 (22.9)
Diseased region	
Aorta	55 (5.8)
Left common iliac artery	412 (43.5)
Right common iliac artery	357 (37.7)
Left external iliac artery	402 (42.4)
Right external iliac artery	389 (41.1)
Number of diseased regions	
1 region	537 (56.7)
2 regions	245 (25.9)
3 regions	86 (9.1)
4 regions	65 (6.9)
5 regions	14 (1.5)
Angiographic findings (on site)	
Chronic total occlusion	268 (28.3)
Bilateral calcification	592 (62.5)
Reference vessel diameter, mm	8.1 ± 1.7
Missing data	170 (18.0)
Lesion length, cm	6.4 ± 4.6
Missing data	166 (17.5)
Angiographic findings (core laboratory)	
Chronic total occlusion	248 (27.3)
Missing data	39 (4.1)
Severe calcification	114 (12.1)
Missing data	7 (0.7)
Reference vessel diameter, mm	7.7 ± 2.2
Missing data	222 (23.4)
Lesion length, cm	8.0 ± 5.5
Missing data	222 (23.4)
Transradial approach	231 (24.3)
Endovascular device	
Covered stent implantation	176 (18.6)
Bare nitinol stent implantation	790 (83.4)
Plain angioplasty	46 (4.9)
Intravascular ultrasound use	633 (66.8)
Simultaneous infrainguinal EVT	172 (18.2)

Values are mean ± SD or n (%).
EVT = endovascular therapy.

Propensity score matching extracted 227 pairs on average (range: 223-230) in each of the imputed data sets. There were no significant intergroup differences in the baseline characteristics (Table 3). Table 4 shows

TABLE 2 Association Between Baseline Characteristics and Transradial Approach

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age, y	0.98 (0.97-1.00) ($P = 0.052$)	1.00 (0.98-1.02) ($P > 0.99$)
Male	1.67 (1.15-2.42) ($P = 0.006$)	1.38 (0.87-2.19) ($P = 0.17$)
Nonambulatory	0.37 (0.18-0.75) ($P = 0.006$)	0.83 (0.35-1.97) ($P = 0.68$)
Smoking history	1.54 (1.05-2.28) ($P = 0.028$)	1.09 (0.66-1.79) ($P = 0.74$)
Diabetes mellitus	0.73 (0.54-0.98) ($P = 0.039$)	0.80 (0.56-1.14) ($P = 0.21$)
Renal failure on dialysis	0.04 (0.01-0.12) ($P < 0.001$)	0.06 (0.02-0.19) ($P < 0.001$)
Ischemic stroke	0.62 (0.41-0.94) ($P = 0.025$)	0.67 (0.42-1.07) ($P = 0.097$)
Coronary artery disease	0.84 (0.63-1.14) ($P = 0.26$)	1.12 (0.79-1.59) ($P = 0.54$)
Chronic limb-threatening ischemia	0.30 (0.19-0.48) ($P < 0.001$)	0.53 (0.29-0.97) ($P = 0.041$)
Ankle-brachial index	3.44 (1.77-6.67) ($P < 0.001$)	2.68 (1.10-6.53) ($P = 0.031$)
History of aortoiliac EVT	0.55 (0.37-0.81) ($P = 0.003$)	0.57 (0.35-0.93) ($P = 0.023$)
Presence of aortic lesion	2.18 (1.24-3.82) ($P = 0.007$)	2.47 (1.17-5.25) ($P = 0.018$)
Number of diseased regions	1.07 (0.92-1.23) ($P = 0.40$)	0.98 (0.78-1.220 ($P = 0.84$)
Chronic total occlusion	1.88 (1.37-2.57) ($P < 0.001$)	1.79 (1.17-2.73) ($P = 0.007$)
Bilateral calcification	0.39 (0.29-0.53) ($P < 0.001$)	0.54 (0.38-0.77) ($P = 0.001$)
Reference vessel diameter, mm	0.99 (0.91-1.09) ($P = 0.91$)	0.95 (0.85-1.07) ($P = 0.40$)
Lesion length, cm	1.01 (0.98-1.05) ($P = 0.49$)	0.98 (0.94-1.03) ($P = 0.49$)
Covered stent implantation	0.38 (0.24-0.62) ($P < 0.001$)	0.63 (0.29-1.34) ($P = 0.23$)
Bare nitinol stent implantation	3.56 (2.05-6.20) ($P < 0.001$)	2.47 (1.03-5.93) ($P = 0.042$)
Plain angioplasty	0.97 (0.49-1.95) ($P = 0.94$)	2.94 (1.10-7.89) ($P = 0.032$)
Intravascular ultrasound use	1.22 (0.89-1.68) ($P = 0.22$)	1.06 (0.73-1.55) ($P = 0.75$)
Simultaneous infrainguinal EVT	0.15 (0.08-0.30) ($P < 0.001$)	0.18 (0.09-0.35) ($P < 0.001$)

Adjusted ORs were derived from multivariate logistic regression models in which all variables listed in the table were entered.
EVT = endovascular therapy.

the procedural characteristics and clinical outcomes of the matched population. The primary outcome measure of the incidence of perioperative complications was not significantly different between the TR and non-TR groups (6.0% [Q1-Q3: 2.5%-9.6%] vs 5.1% [Q1-Q3: 1.2%-9.1%]; $P = 0.69$) (**Central Illustration**). In the TR approach group, the median times for puncture and wire crossing were not significantly different; however, the median time for sheath placement was longer (5.2 minutes [Q1-Q3: 4.7-5.8 minutes] vs 3.2 minutes [Q1-Q3: 2.8-3.5 minutes]; $P < 0.001$). The median time to hemostasis and the time to ambulation were significantly shorter in the TR group (5.6 hours [Q1-Q3: 5.1-6.0 hours] vs 6.2 hours [Q1-Q3: 5.8-6.7 hours] and 2.6 hours [Q1-Q3: 2.2-3.0 hours] vs 8.7 hours [7.4-10.2 hours]; $P = 0.035$ and $P < 0.001$, respectively). The residual stenosis evaluated by the core laboratory and the 30-day outcomes did not significantly differ between the 2 groups ($P > 0.05$).

Supplemental Tables 1 and 2 show the comparison after cases using the TB approach were excluded, which yielded similar findings. Supplemental Tables 3 and 4 demonstrate the comparison after cases using both TR and TF approaches were further excluded, again providing similar findings, except for the frequency of multiple approach sites, which was higher in the TR group, and the time to hemostasis, which lost statistical significance ($P = 0.061$). **Figure 2** shows the cost comparison of ipsilateral iliac stenting treated by the TR approach vs the TF approach. The TR approach is 25,260 Japanese yen cheaper than the TF approach when the target lesion is focal and simply treated.

DISCUSSION

CLINICAL ISSUE OF NON-TR APPROACH IN THE CATHETER INTERVENTION. The non-TR approach, including TF and TB, is the standard method of choice for EVT, and approximately 70% of EVT for PAD in the United States and over 80% in Japan are performed using this approach.[9,10] However, the TF approach is occasionally challenging in cases of morbid obesity, the presence of complicated inguinal arterial lesions, a history of prior open femoral surgery, the absence of

TABLE 3 Baseline Characteristics After Propensity Score Matching

	Transradial (n = 227[a])	Nontransradial (n = 227[a])	*P* Value
Age, y	74 (72-75)	74 (72-75)	0.66
Male %	79.2 (72.5-86.0)	81.2 (75.6-86.7)	0.67
Nonambulatory, %	4.4 (0.6-8.3)	4.0 (1.0-6.9)	0.67
Smoking history, %	81.5 (75.1-87.9)	83.3 (78.0-88.6)	0.68
Diabetes mellitus, %	46.8 (39.0-54.6)	44.1 (37.2-51.0)	0.62
Renal failure on dialysis, %	1.2 (0.0-3.7)	1.3 (0.0-3.2)	0.54
Ischemic stroke, %	16.0 (10.4-21.7)	14.1 (9.1-19.0)	0.60
Coronary artery disease, %	44.0 (36.9-51.0)	43.0 (36.1-49.9)	0.87
Chronic limb-threatening ischemia, %	10.2 (5.1-15.2)	9.1 (4.9-13.3)	0.77
Ankle brachial index	0.62 (0.58-0.65)	0.63 (0.60-0.66)	0.48
History of aortoiliac EVT, %	19.0 (13.1-24.9)	15.8 (10.6-21.0)	0.39
Diseased region, %			
Aorta	7.9 (3.7-12.0)	8.8 (4.6-12.9)	0.75
Left common iliac artery	43.4 (35.4-51.3)	43.1 (36.2-50.0)	0.74
Right common iliac artery	37.4 (30.2-44.5)	36.7 (29.9-43.4)	0.81
Left external iliac artery	43.5 (36.0-50.9)	43.5 (36.5-50.4)	0.77
Right external iliac artery	41.9 (34.6-49.1)	42.8 (35.9-49.8)	0.83
Number of diseased regions, %			>0.99
1 region	57.8 (50.5-65.0)	57.4 (50.5-64.3)	
2 regions	22.9 (16.2-29.6)	23.1 (17.2-29.0)	
3 regions	9.1 (4.7-13.6)	9.3 (5.0-13.5)	
4 regions	8.1 (3.5-12.6)	7.8 (3.9-11.8)	
5 regions	2.2 (0.0-4.5)	2.4 (0.0-4.9)	
Angiographic findings (on site)			
Chronic total occlusion, %	36.9 (29.9-43.8)	37.8 (30.9-44.7)	0.82
Bilateral calcification, %	52.5 (44.5-60.4)	45.9 (39.0-52.9)	0.19
Reference vessel diameter, mm	8.0 (7.8-8.3)	8.0 (7.8-8.2)	0.80
Lesion length, cm	7.2 (6.4-8.1)	7.0 (6.2-7.9)	0.66
Angiographic findings (core laboratory)			
Chronic total occlusion, %	35.4 (28.3-42.5)	37.1 (30.3-44.0)	0.71
Severe calcification, %	14.2 (8.8-19.5)	12.5 (7.7-17.3)	0.66
Reference vessel diameter, mm	8.3 (7.7-8.8)	8.4 (7.8-8.9)	0.75
Lesion length, cm	8.7 (5.6-11.8)	8.6 (5.4-11.7)	0.86
Endovascular device, %			
Covered stent implantation	10.4 (5.7-15.0)	9.6 (5.4-13.9)	0.86
Bare nitinol stent implantation	92.3 (87.9-96.8)	93.4 (89.7-97.1)	0.60
Plain angioplasty	5.0 (1.4-8.6)	4.8 (1.5-8.0)	0.78
Intravascular ultrasound use	71.2 (64.8-77.7)	69.8 (63.4-76.2)	0.75
Simultaneous infrainguinal EVT	5.0 (0.5-9.5)	4.4 (1.3-7.5)	0.62

Values are estimates (95% CI). The estimates are percentages for discrete variables and (arithmetic) mean for continuous variables. [a]The matching extracted 227 pairs on average (range: 223-230) in each of the imputed data sets.

EVT = endovascular therapy.

palpable inguinal pulses, and difficulty in maintaining full hip extension. Although the TB approach has been proposed as an alternative, it is often accompanied by anatomical concerns about an increased risk of local vascular and neurologic complications. A previous study reported that the OR for the TB vs the TF approach for access site complications was 4.58, indicating that the TR approach is definitely a better alternative than a TB approach for an endovascular procedure.[11] In the field of percutaneous coronary intervention, the TR approach has been established as a safer approach to avoid local vascular bleeding complications compared with the TF and TB approaches. Percutaneous coronary intervention with TR has been shown to be superior to TF with respect to mortality and is recommended as Class 1.[12] However, EVT with the TR approach has disadvantages such as backup support and complexity of the procedure because of the long distance to the lesion. To overcome these issues, several radial-specific endovascular devices for peripheral interventions have become clinically available in recent years, making the TR approach more convenient and popular in the field of EVT. [13] Indeed, in the present study, conducted between January 2021 and June 2023, almost one-quarter of the patients underwent AI EVT using the TR approach.

ASSOCIATION OF BASELINE CHARACTERISTICS WITH TR APPROACH. The baseline characteristics were considerably different between the TR and non-TR approach groups, suggesting that the interventionists intentionally chose the TR approach over the non-TR approach in cases with specific characteristics. Renal failure on dialysis was negatively associated with TR. This trend likely reflects the use or strategic preservation of the radial artery as the access site for arteriovenous dialysis. Simultaneous infrainguinal EVT was negatively associated with the TR approach, likely because of the limited device shaft length, making it feasible only for proximal infrainguinal lesions, even if the patients are not tall. A history of revascularization and the presence of CLTI have been reported to be associated with poor long-term outcomes, such as vessel restenosis and major adverse limb events, possibly because of the anatomical complexity.[14,15] A history of revascularization and the presence of CLTI also signify prolonged exposure to arteriosclerotic changes with vascular tortuosity and calcification along the route of catheter advancement.[16,17] The anatomical severity of both the systemic and local arteries might be challenging for the currently available TR devices. CTO and the presence of an aortic lesion were positively associated with the TR approach, whereas bilateral calcified lesions were negatively associated because the latter requires more backup force for wire and device crossing, which may not be sufficiently provided by the TR approach. In contrast, CTOs, typically dominated by thrombotic lesion morphology,[18] are often amenable to antegrade completion of the procedure. Aortic lesions that can

TABLE 4 Procedural Characteristics and Clinical Outcomes After Propensity Score Matching

	Nontransradial (n = 227[a])	Transradial (n = 227[a])	*P* Value
Preoperative angiographic assessment at approach sites			0.88
Not performed, %	31.3 (24.2-38.3)	29.3 (22.9-35.7)	
By CT, %	48.0 (40.7-55.3)	49.5 (42.5-56.5)	
By angiography, %	20.7 (14.1-27.3)	21.2 (15.4-27.0)	
Femoral approach, %	96.7 (93.6-99.8)	27.0 (20.7-33.3)	<0.001
Brachial approach, %	8.4 (4.1-12.7)	0.0 (0.0-0.4)	<0.001
Multiple approach sites, %	30.4 (23.5-37.3)	27.9 (21.6-34.2)	0.60
Hemostatic device use, %	62.2 (54.9-69.5)	60.2 (53.4-67.1)	0.69
Procedural time, min			
Puncture	3.0 (2.7-3.4)	3.1 (2.8-3.4)	0.75
Sheath placement	3.2 (2.8-3.5)	5.2 (4.7-5.8)	<0.001
Wire crossing	5.1 (4.2-6.2)	5.6 (4.7-6.8)	0.50
Time to hemostasis, h	6.2 (5.8-6.7)	5.6 (5.1-6.0)	0.035
Time to ambulation, h	8.7 (7.4-10.2)	2.6 (2.2-3.0)	<0.001
Perioperative complication, %	5.1 (1.2-9.1)	6.0 (2.5-9.6)	0.69
Bleeding at puncture site, %	2.9 (0.0-5.8)	2.1 (0.0-4.4)	0.58
Requiring repat hemostasis, %	1.6 (0.0-3.8)	1.8 (0.0-3.9)	0.97
Requiring transfusion, %	0.4 (0.0-1.7)	0.0 (0.0-0.4)	0.48
Requiring percutaneous hemostasis, %	0.9 (0.0-2.6)	0.8 (0.0-2.4)	0.92
Requiring surgical hemostasis, %	0.1 (0.0-0.9)	0.0 (0.0-0.4)	>0.99
Arterial occlusion at approach site, %	0.6 (0.0-2.2)	0.9 (0.0-2.5)	0.68
Perioperative death, %	0.3 (0.0-1.5)	0.0 (0.0-0.4)	0.75
Myocardial infarction, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Heart failure, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Ischemic stroke, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Cerebral hemorrhage, %	0.2 (0.0-1.3)	0.0 (0.0-0.4)	0.76
Renal failure, %	0.1 (0.0-0.9)	0.8 (0.0-2.5)	0.27
Major amputation, %	0.0 (0.0-0.7)	0.4 (0.0-1.7)	0.41
Emergency surgery, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Reintervention, %	0.4 (0.0-1.8)	0.0 (0.0-0.4)	0.39
Vessel rupture	0.1 (0.0-1.0)	0.9 (0.0-2.5)	0.30
Lower extremity artery embolism, %	0.6 (0.0-2.2)	0.4 (0.0-1.7)	0.77
Mesenteric artery embolism, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Other arterial embolism, %	0.0 (0.0-0.4)	0.0 (0.0-0.4)	>0.99
Other bleeding requiring transfusion, %	0.4 (0.0-1.8)	0.9 (0.0-2.5)	0.63
Residual stenosis (core laboratory), %	21 (19-23)	22 (20-24)	0.46
>30%	22.2 (15.7-28.6)	28.1 (21.8-34.4)	0.17
30-day patency, %			0.50
Patency	92.2 (87.7-96.7)	92.2 (88.3-96.1)	
Nonocclusive restenosis	0.5 (0.0-2.1)	1.7 (0.0-3.9)	
Occlusive patency	0.4 (0.0-1.7)	0.4 (0.0-1.7)	
30-day ankle brachial index	0.89 (0.87-0.92)	0.93 (0.90-0.95)	0.12
30-day clinical symptoms, %			0.38
No symptoms	65.8 (58.5-73.1)	69.4 (63.0-75.9)	
Intermittent claudication	27.8 (20.9-34.6)	21.3 (15.5-27.1)	
Chronic limb-threatening ischemia	3.7 (0.0-7.4)	5.3 (1.9-8.6)	

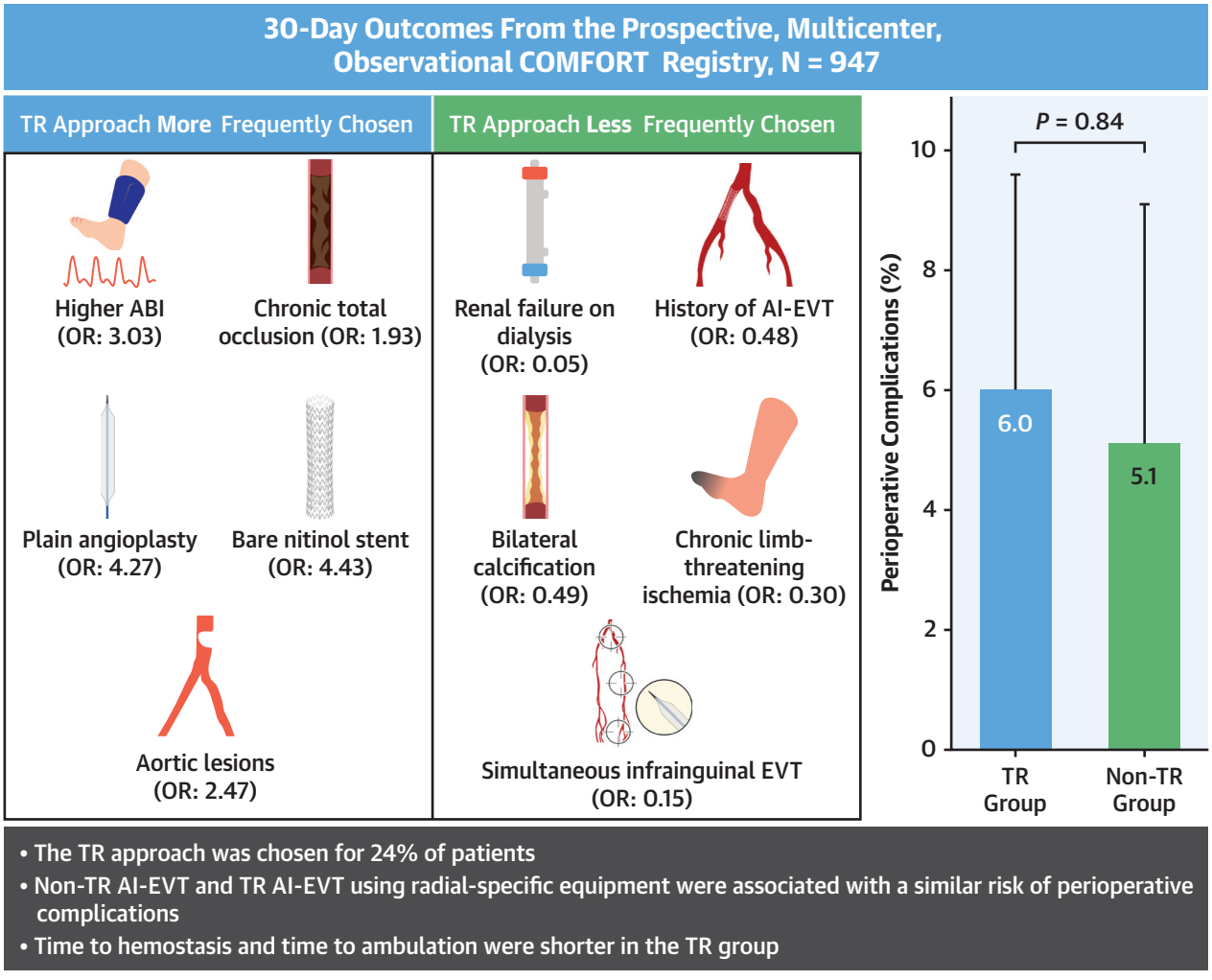
Values are estimates (95% CI). The estimates are percentages for discrete variables and (arithmetic) means for continuous variables, except for procedural time, time to hemostasis, and time to ambulation, for which the geometric means are presented. [a]The matching extracted 227 pairs on average (range: 223-230) in each of the imputed data sets.

CT = computed tomography.

be treatable endovascularly are typically less complex. The choice of TR approach may be favored for less complex lesions located more proximally, allowing easier access through the radial artery.

CLINICAL OUTCOMES OF CASES WITH THE TR VERSUS NON-TR APPROACHES. In this study, the incidence of perioperative complications as the primary outcome measure was not significantly different between the TR and non-TR groups, confirming the safety of the TR approach. Previous reports indicated that the non-TR approach had a higher incidence of bleeding complications at the puncture site than the TR approach during AI EVT.[6-9]

CENTRAL ILLUSTRATION **Outcomes With Transradial vs Nontransradial Approach for Aortoiliac Interventions**



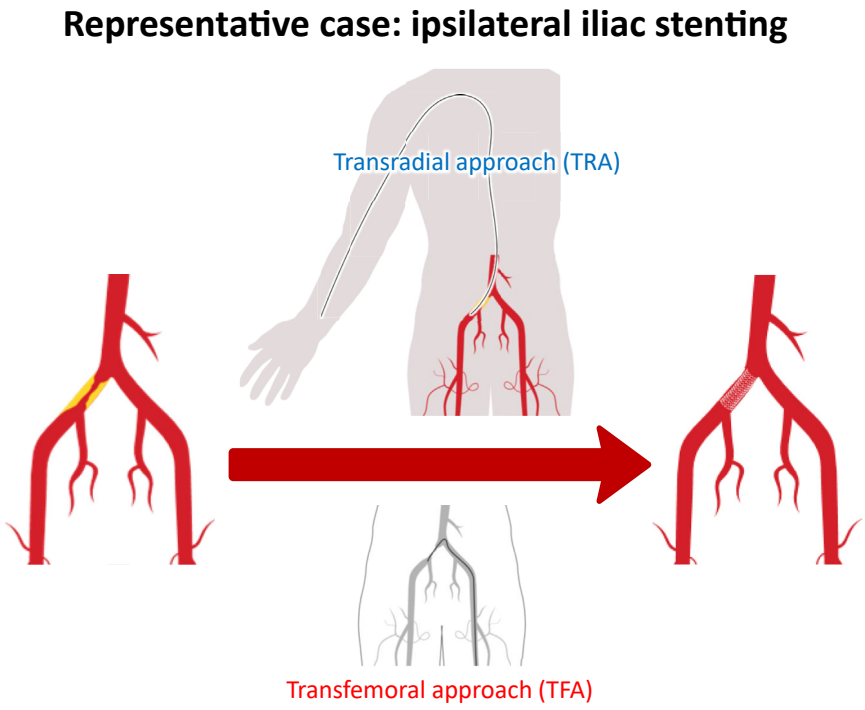
Iida O, et al. JACC Cardiovasc Interv. 2024;17(16):1891-1901.

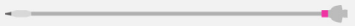
The association between the baseline characteristics and transradial (TR) approach selection are shown on the left, whereas the incidence of perioperative complications between the TR and non-TR approach is shown on the right. ABI = ankle brachial index; AI = aortoiliac; EVT = endovascular therapy.

The present findings contrast with those of previous studies. This could be attributed to the use of arteriotomy closure devices in the non-TR group and the downsizing of the TF approach, thereby lowering the incidence of bleeding complications. Nonetheless, a certain incidence of bleeding complications was noted, suggesting that there is room for improvement through the refinement of hemostatic devices. RA can reduce bleeding episodes but conversely increase vascular complications, such as cerebral thromboembolism and cholesterol embolism. Complications related to the TR approach were not observed in the TR approach group. In addition, radial artery occlusion, another complication related to this approach, was observed in only 0.9% of cases, which was numerically lower than that previously reported.[19] Concerns associated with the use of TR-specific devices might be less problematic in ideal case selection.

Although the TR approach was associated with a 2-minute increase in sheath placement time, it shortened the time to hemostasis by 1 hour and the

FIGURE 2 Cost Comparison of Ipsilateral Iliac Stenting Treated by the TR Approach vs the TF Approach



		Cost (yen)	
		TFA	TRA
	Sheath Introducer	2,160	2,160
	Guiding Sheath	18,700	18,700
	Angiographic Catheter	1,790	1,790
	Guidewire (0.035 inch)	2,180	2,180
	Balloon catheter	35,300	35,300
	Bare nitinol stent	160,000	160,000
	Vascular Closure Device	28,400	0
	Radial Compression Device	0	3,140
	Total cost	248,530	223,270
	Difference		-25,260

The total cost of the device used during ipsilateral iliac stenting treated by the transradial (TR) approach vs the transfemoral (TF) approach is shown in the lower table. The TR approach is 25,260 Japanese yen cheaper than the TF approach. FA = femoral approach; TRA = transradial approach.

time to ambulation by 4 hours. The TR approach can potentially reduce discomfort and increase the treatment satisfaction of the patients. The clinical significance of patient-reported outcomes in satisfaction has become increasingly important, which strongly suggests that patient comfort is an important determinant of EVT strategy.[20] In contrast, a supplemental analysis excluding cases with the TB approach in the

non-TR group revealed that the TR approach was associated with a higher proportion of significant residual stenosis than the TF approach. This may be because the TF approach is superior to the TR approach in more aggressive vessel dilatation facilitated by the immediate availability of bailout options with covered stent deployment. Future advancements in TR-specific devices may improve their technical performances and render the performances of TR EVT comparable to those of TF EVT.

CLINICAL IMPLICATION OF THE COMFORT STUDY. The TR approach did not lead to a significantly decreased incidence of perioperative complications in comparison to the TF approach, but it did shorten the time to hemostasis and the time to ambulation, suggesting the potential advantages of choosing the TR approach during AI EVT. This study identifies 8 determinants associated with the selection of the TR approach, some of which may be addressed by future advancements in TR-specific devices.

STUDY LIMITATIONS. First, the current study was not a randomized controlled trial. Although the propensity score analysis was alternatively adopted to minimize the differences in baseline characteristics, we cannot completely rule out potentially significant biases. Second, in the TR approach group, approximately 30% of the cases required adjunctive punctures for EVT, indicating that the evaluation did not exclusively reflect the pure procedures of the TR approach. However, in real-world clinical settings, it is common for treatment to be supplemented solely with small sheaths or microcatheters to facilitate guidewire crossing in addition to the TR approach. Consequently, this is the largest analysis of RA with EVT that reflects real-world clinical practice. Finally, data on the long-term outcomes were not collected. Future randomized studies are needed to establish the position of RA compared to that of the TF.

CONCLUSIONS

The COMFORT registry shows that TR AI EVT does not increase the risk of perioperative complications but cannot reduce it either. The TR approach can help to reduce the time to hemostasis and the time to acceptable technical, hemodynamic, and clinical success.

ACKNOWLEDGMENTS The authors thank the cardiac catheterization laboratory medical staff and the clinical research coordinators at the participating centers. The authors also thank Ms Sahoko Mitsui for managing this study.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This study was supported by the Japan Endovascular Treatment Conference. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Osamu Iida, Osaka Police Hospital, Cardiovascular Division, 10-31 Kitayamacho, Tennoji Ward, Osaka 543-0035, Japan. E-mail: iida.osa@gmail.com.

PERSPECTIVES

WHAT IS KNOWN? The TR approach is the first-line treatment of percutaneous coronary intervention.

WHAT IS NEW? During AI EVT, non-TR AI EVT and TR AI EVT using radial-specific equipment were associated with a similar risk of perioperative complications while shortening the time to hemostasis and the time to ambulation after the procedure.

WHAT IS NEXT? In the future, well-designed randomized controlled trials are warranted to establish robust evidence for TR EVT.

REFERENCES

1. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg*. 2007;45:S5–S67.

2. Society for Vascular Surgery Lower Extremity Guidelines Writing Group, Conte MS, Pomposelli FB, et al. Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: management of asymptomatic disease and claudication. *J Vasc Surg*. 2015;61:2S–41S.

3. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J*. 2018;39:763–816.

4. Soga Y, Iida O, Kawasaki D, et al. Contemporary outcomes after endovascular treatment for aortoiliac artery disease. *Circ J*. 2012;76:2697–2704.

5. Murphy TP, Cutlip DE, Regensteiner JG, et al. Supervised exercise, stent revascularization, or medical therapy for claudication due to aortoiliac peripheral artery disease: the CLEVER study. *J Am Coll Cardiol*. 2015;65:999–1009.

6. Meertens MM, Ng E, Loh SEK, et al. Transradial approach for aortoiliac and femoropopliteal interventions: a systematic review and meta-analysis. *J Endovasc Ther*. 2018;25:599–607.

7. Galyfos G, Sigala F, Filis K. Transradial versus transfemoral access in patients undergoing peripheral artery angioplasty/stenting: a meta-analysis. *Cardiovasc Revasc Med*. 2018;19:457–465.

8. Ruzsa Z, Bellavics R, Nemes B, et al. Combined transradial and transpedal approach for femoral artery interventions. *JACC Cardiovasc Interv*. 2018;11:1062–1071.

9. Horie K, Takahara M, Iida O, et al. Comparing the safety and feasibility of endovascular therapy via transradial and transfemoral approaches in patients with aortoiliac occlusive disease: a propensity score-matched analysis of the Nationwide Registry. *J Endovasc Ther*. Published online July 21, 2023. https://doi.org/10.1177/15266028231187625

10. Soden PA, Zettervall SL, Curran T, et al. Regional variation in patient selection and treatment for lower extremity vascular disease in the Vascular Quality Initiative. *J Vasc Surg*. 2017;65:108–118.

11. Ciprian Cacuci A, Krankenberg H, Ingwersen M, et al. Access site complications of peripheral endovascular procedures: a large, prospective registry on predictors and consequences. *J Endovasc Ther*. 2021;28:746–754.

12. Nakano S, Kohsaka S, Chikamori T, et al. JCS 2022 guideline focused update on diagnosis and treatment in patients with stable coronary artery disease. *Circ J*. 2022;86:882–915.

13. Maximus S, Kwong M, Harding J, et al. Radial arterial access is a safe alternative to brachial artery and femoral artery access for endovascular lower extremity peripheral arterial disease. *J Vasc Surg*. 2023;77:870–876.

14. Soga Y, Takahara M, Iida O, et al. Vessel patency and associated factors of drug-coated balloon for femoropopliteal lesion. *J Am Heart Assoc*. 2023;12:e025677.

15. Iida O, Takahara M, Soga Y, et al. Three-year outcomes of surgical versus endovascular revascularization for critical limb ischemia: the SPINACH Study (Surgical Reconstruction Versus Peripheral Intervention in Patients With Critical Limb Ischemia). *Circ Cardiovasc Interv*. 2017;10:e005531.

16. Ciurică S, Lopez-Sublet M, Loeys BL, et al. Arterial tortuosity. *Hypertension*. 2019;73:951–960.

17. Demer LL, Tintut Y. Vascular calcification: pathobiology of a multifaceted disease. *Circulation*. 2008;117:2938–2948.

18. Motarjeme A, Gordon GI, Bodenhagen K. Thrombolysis and angioplasty of chronic iliac artery occlusions. *J Vasc Interv Radiol*. 1995;6:66S–72S.

19. Posham R, Biederman DM, Patel RS, et al. Transradial approach for noncoronary interventions: a single-center review of safety and feasibility in the first 1,500 cases. *J Vasc Interv Radiol*. 2016;27:159–166.

20. Raja A, Spertus J, Yeh RW, et al. Assessing health-related quality of life among patients with peripheral artery disease: a review of the literature and focus on patient-reported outcome measures. *Vasc Med*. 2021;26:317–325.

KEY WORDS aortoiliac diseases, endovascular therapy, peripheral artery disease, transfemoral approach, transradial approach

APPENDIX For supplemental tables, please see the online version of this paper.