Transradial Versus Transfemoral Arterial Access in Liver Cancer Embolization: Randomized Trial to Assess Patient Satisfaction

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ABSTRACT

Purpose: To determine whether transradial access (TRA) or transfemoral access (TFA) provides better patient satisfaction during intra-arterial therapy (IAT) for liver cancer.

Materials and Methods: This randomized, prospective, intra- and interpatient controlled trial compared TRA vs TFA accesses in patients with primary or metastatic liver cancer undergoing IAT. After having one of each type of access (1 TRA and 1 TFA), all patients selected their preferred access regardless of whether a third intervention was indicated. The primary endpoint was patient access preference; secondary endpoints were access-related complications, procedure time, contrast agent volume, and radiation doses to the patient and operator. Patients were evaluated on postprocedure days 1 and 30.

Results: Fifty-five patients with liver cancer (31 hepatocellular carcinoma, 24 metastatic disease) were enrolled, and 124 IAT procedures were performed. A total of 36 patients underwent at least 1 intervention each with TRA and TFA. Of those, 29 patients (81%) preferred TRA and 7 (19%) preferred TFA (ratio, 4:1; \( P < .001 \)). Median radiation exposure to the operator was significantly lower for TRA (5.5 mrem) vs TFA (13 mrem; \( P = .01 \)). Incidences of complications, procedure time, contrast agent volume, and radiation exposure to patients were similar between groups.

Conclusions: TRA was the preferred access for the majority of patients and was associated with less radiation exposure to the operator. No differences were detected in incidence of adverse events, procedure time, contrast agent volume, or patient radiation exposure.

ABBREVIATIONS

HCC = hepatocellular carcinoma, IAT = intra-arterial therapy, TFA = transfemoral access, TRA = transradial access

Transradial access (TRA) has been used in cardiology interventions for the past three decades (1). Recent studies in cardiology (2–6) present strong evidence favoring TRA versus transfemoral access (TFA), such as lower morbidity and mortality rates, shorter hospital admission, and a superior cost/benefit profile. Patient preference and quality of life were addressed in a randomized trial (7) favoring TRA over TFA during cardiac catheterization (87% of patients preferred TRA).

Shiozawa et al (8) were the first to retrospectively compare TRA with TFA in hepatic intra-arterial therapy (IAT), and demonstrated comparable efficacy (98.3%...
technical success with TRA). Although patient preference regarding access site was not addressed in a randomized, prospective fashion, preference for TRA in patients who had both accesses was reported, and there was a lower incidence of complications with TRA (4.5%) than with TFA (12.7%) (8). Recently, a large prospective cohort of more than 1,500 cases of noncoronary interventions via TRA confirmed the feasibility and safety of this approach, with a 98.2% technical success rate and an overall complication rate of less than 3% (9). Among the cases analyzed, 485 were transarterial chemoembolization procedures, confirming increasing use of this approach to perform IAT for liver malignancies.

The purpose of the present study was to define patient preference regarding arterial access for hepatic IAT and other potential benefits of TRA over TFA, including complication rate, procedure time, contrast media volume, and radiation exposures to the patient and operator, in a randomized controlled trial.

**MATERIALS AND METHODS**

**Inclusion and Exclusion Criteria and Preoperative Assessment**

This study was a randomized prospective trial with intraand interpatient controls approved by the institutional review board (protocol ID code NCT 03163186). Inclusion criteria were age > 18 years; performance status 0/1; radial artery with anteroposterior diameter ≥ 2 mm; type A, B, or C waveforms on Barbeau test; and diagnosis of primary or metastatic liver neoplasm amenable to transarterial bland embolization or chemoembolization. Patients were diagnosed with hepatocellular carcinoma (HCC) or metastatic neuroendocrine cancer. Patients were enrolled with the expectation of undergoing at least two of the three planned IAT procedures to obtain local tumor control. The Barbeau test was performed by using a pulse oximeter on the left second digit (10). Anteroposterior, inner wall–to–inner wall diameter of the radial artery was measured within 2 cm proximally from the styloid process under ultrasound (US) visualization.

Exclusion criteria were type D waveform on Barbeau test, radial artery anteroposterior diameter < 2 mm, history of stroke, presence of a heavily calcified aortic arch, and requirement for additional procedures during hospitalization. A total of 55 patients with primary or metastatic hepatic tumors were enrolled. A total of 124 procedures were performed, and 36 patients underwent at least two procedures, one with TRA and one with TFA. Nineteen patients had only one procedure and were therefore not included in the access preference analysis (Fig 1). Demographic characteristics of the 36 patients who had at least two procedures are presented in Table 1.

**Randomization**

The randomization process is demonstrated in Figure 2. Patients were randomly assigned by the study coordinator to undergo the initial procedure via TRA or TFA. The second procedure was performed via the alternate access by default, ie, if the patient had a TRA first, it was mandatory that the second procedure be performed via TFA, or vice-versa. Randomization was constrained to ensure equal numbers of patients in each arm and that each physician treated the same number of patients in each arm. There were two primary operators. The study design was counterbalanced so that 50% of patients underwent TFA first and 50% underwent TRA first.

**Hepatic Arterial Embolization Techniques**

**Femoral access.** —Percutaneous access to the right common femoral artery was obtained under US guidance with a micropuncture kit (Cook, Bloomington, Indiana). A 5-F
sheath (Terumo, Somerset, New Jersey) was used to secure the access. Over a 0.035-inch polytetrafluoroethylene-coated J wire (Boston Scientific, Marlborough, Massachusetts), the celiac trunk was catheterized with a 5-F Mikaelson Catheter (Boston Scientific) and superselective catheterization was performed with a 2.4- or 2.8-F Progreat microcatheter (Terumo). A femoral arteriogram was obtained before arterial closure with AngioSeal (Terumo). Radiation protection was provided with a lead shield skirt underneath the angiographic table between the radiation source and operator. No vasodilator or anticoagulant agents were used via TFA.

Radial access. — The patient’s left arm was abducted to 75°–90°. The left radial artery was accessed with single-wall puncture under US guidance with the use of a Radiofocus Transradial kit (Terumo). The kit includes a 21-gauge short needle, a 0.021-inch nitinol wire, and a 5-F hydrophilic sheath. When access had been secured, 2,000–3,000 IU of heparin was administered systemically through a peripheral intravenous access and 200 μg of nitroglycerin was instilled through the sheath. An additional 1,000 IU of heparin was administered every 30 minutes. A forearm angiogram was obtained to delineate the arterial anatomy. Under direct fluoroscopic visualization, a 0.035-inch angled J-tip Glidewire (1.5-mm radius) and a 5-F, 110-cm Jacky catheter (Terumo) were advanced coaxially into the descending aorta, and selective catheterization of the celiac trunk was performed. For superselective catheterization of the hepatic artery, a 2.4 or 2.8-F Progreat microcatheter (130 or 150 cm in length; Terumo) was used. After embolization, the catheter was removed over the wire and an additional 200 μg of nitroglycerin was instilled intra-arterially through the sheath, and a completion forearm angiogram was again obtained. Patent hemostasis technique was applied by using an external compression pneumatic device (TR Band; Terumo), and the reversed Barbeau test was performed to rule out excessive radial artery occlusive compression (confirmed by the presence of oximetry pulse waveform during compression of the ulnar artery). The TR Band insufflation volume and time were communicated to nursing staff in the recovery area. Band deflation started 1 hour after initial placement, and one fourth of the total volume was removed every 15 minutes. According to the manufacturer’s instructions, the band was removed after 2 hours. A lead shield mounted on wheels, measuring 7 feet in height and 4 feet wide, was positioned on the left side of the angiographic table, immediately caudally from the patient’s left arm.

Embolization
Superselective treatment was performed whenever possible. If that was not achievable, segmental or lobar treatment was pursued. For transarterial bland embolization, a combination of 300–500-μm polyvinyl alcohol particles (Cook), 5 mL of Lipiodol (Guerbet, Villepinte, France), 10 mL of saline solution, and 10 mL of contrast medium (Omnipaque 350; GE Healthcare, Milwaukee, Wisconsin) was administered. For conventional transarterial chemoembolization, 20 mg of the chemotherapy agent mitomycin was added to the aforementioned solution. Patients were admitted for overnight observation. The following morning, all patients were assessed for complications, and blood samples were collected.

Endpoints
Primary endpoint. — The primary endpoint was patient preference regarding arterial access. This was addressed by a postprocedural questionnaire (Fig 3) that was administered to patients on day 1 after intervention and at the 30-day
undergoing TRA and TFA as their first procedure. Access site hematoma/bruising was determined by physical examination. At each 30-day follow-up visit, radial artery patency was evaluated by physical and US examinations.

Radiation dose analysis was performed by intrapatient comparison. Given differences in fluoroscopy equipment (ie, flat-panel vs image intensifiers), only 52 of 124 procedures were included in the analysis: 26 with TRA and 26 with TFA. The analysis was also counterbalanced so that 50% of patients had TRA first and 50% had TFA first. Radiation dose to the patient was measured by air kerma and obtained from the fluoroscopy unit. Radiation dose to the operator was obtained from a Landauer (Glenwood, Illinois) dosimeter badge placed on the operator’s waist (outside the lead apron). Procedure time was defined as the duration of moderate sedation.

Statistical Analysis
The primary endpoint analysis was based on a one-sample, two-sided exact binomial test. The null hypothesis was that 50% of patients would prefer TRA to TFA. The alternative hypothesis was that 75% of patients would prefer TRA to TFA. The expectation was that no more than 10 patients would report no preference or undergo only one of the two procedures. As a result, the goal was to enroll at least 50 patients, providing 90% power. The two-sided α-value was prespecified at 0.025. A binomial test was used to assess complication rates for the femoral versus the radial approach, and a two-sided exact P value was reported. A 2 × 2 repeated-measures analysis of variance ([procedure: femoral vs radial] × [time: before vs after the procedure]) was used to evaluate potential changes in hemoglobin levels. Post-hoc comparisons were conducted with the Sidak procedure to account for multiple comparisons. Repeated-measures t tests were used to assess differences between radial and femoral approaches with respect to procedure duration. Two-tailed P values were reported. The aforementioned analyses were conducted on the first two procedures. A χ² test (Fisher exact test) was used to evaluate differences in preference for TRA or TFA as a function of the attending physician, and a two-sided exact P value was reported. Statistical significance was considered at the α = .05 threshold for all analyses.

RESULTS
Efficacy and Survey Results
There was equal distribution in access, with 18 patients each undergoing TRA and TFA as their first access. After undergoing treatment via both accesses, 29 of 36 patients (81%) preferred TRA and only 7 (19%) preferred TFA (P < .001). There was no difference in patient preference as a function of primary operator, with 87.5% and 72.2% preferring the radial approach for operators 1 and 2, respectively (P = .41). There was no difference in the volume of contrast medium between TRA and TFA, with respective means of 114.9 mL ± 49.56 (standard deviation) and 119.9 mL ± 34.23 (P = .66). There was no difference in procedure duration between TRA and TFA, with respective means of 57.5 minutes ± 49.56 and 54.0 minutes ± 20.40 (P = .70). There was no access conversion in either group. Median radiation exposure (as air kerma) to the patient was also similar between accesses: 1,200.5 mGy (range, 107–3,479 mGy) for TFA and 811 mGy (range, 80–5,458 mGy) for TRA (P = .229). Median radiation exposure to the operator was lower for TRA (5.5 mrem; range, 1–43 mrem) than for TFA (13 mrem; range, 1–121 mrem; P = .01; Table 2).

Safety
There were 25 acute minor complications documented among 18 patients in 124 interventions. Most patients (n = 12; 66.7%) experienced complications after only one procedure, with five patients (27.8%) experiencing complications on two occasions and only one patient (5.6%) experiencing complications on three occasions. Acute minor complications were limited to access-site bruising/pain on postprocedure day 1 in 17 of 71 procedures with TRA (22%) and 8 of 53 procedures with TFA (15%), which showed no significant difference (P = .11). Two patients experienced the late minor complication of partial radial artery thrombosis (less than one third of radial artery diameter) identified on US at 30-day follow-up; these were clinically silent. Resolution was noted on the day of a subsequent procedure (4–6 wk later) or on later follow-up.

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<th>Table 2. Comparison between TRA and TFA</th>
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Note—Values in parentheses are percentages. NA = not applicable; SD = standard deviation; TFA = trans-femoral access; TRA = transradial access.
consultation (12 wk) as part of standard care. No major adverse events occurred with either access type.

Although there was a decrease in mean hemoglobin level after procedures performed via both accesses (TRA, from 12.42 g/dL ± 1.81 to 11.84 g/dL ± 2.11; 95% confidence interval, 0.0312–0.858; TFA, from 12.5 g/dL ± 1.79 to 11.87 g/dL ± 1.67; 95% confidence interval, 0.382–0.879; $P < .001$), this did not have any clinical significance. Overall, there was no difference in hemoglobin level between the femoral versus the radial approach ($P = .78$). There was no clinically evident stroke or hand ischemia at 30 days.

**DISCUSSION**

The present randomized and prospective trial with intra- and interpatient control compared TRA versus TFA for IAT for liver malignancies and demonstrated that the majority of patients preferred the radial approach (4:1 ratio). In addition, there was no increased incidence of complications with TRA, and procedure durations were similar for both methods. Radiation exposure to the patient was similar for both accesses, but the operator exposure was lower with TRA.

According to most patients, TRA was the preferred option because of less pain and discomfort. Also, limited bed restriction made a major impact on the postprocedural experience. Patients could ambulate earlier, allowing them to go to the restroom instead of using a urinal. Furthermore, in case of abdominal pain and nausea/vomiting, patients could position themselves according to their needs and not be worried about leg straightening. This result is consistent with the cardiology literature, which has shown improved quality of life after TRA compared with TFA for coronary interventions, with 87% of patients favoring TRA (7). The previous study (7) had no intrapatient comparison because patients had one of the two accesses, whereas the present study was a randomized trial specifically designed to address patient experience regarding access site. For visceral interventions, the authors of another study (11) had a similar observation in their patient population, although not as their primary endpoint.

There were no major complications in either group in the present study, including stroke or hand ischemia, two of the most worrisome complications of TRA. Similarly, large case series of visceral interventions performed via TRA (9,11) showed low incidences of major complications: 0.13% in the study of Posham et al (9) and 0.17% in the study of Bishay et al (11). In the cardiology literature, a prospective randomized trial (12) demonstrated no difference in the incidences of silent cerebral infarcts with TRA versus TFA (11.7% vs 17.5%). Ratib et al (13) followed more than 5,000 patients for 5 years and reported a minimal rate of stroke after TRA of 0.11%–0.20%. Left radial access to avoid crossing most of the supra-aortic vessels, J-shaped soft-tip guide wire and catheter advancement under direct fluoroscopic visualization (thereby avoiding inadvertent cannulation of the left vertebral artery or ascending aortic arch), and patient selection can minimize the risk of stroke. Thorough preprocedural screening with the Barbeau test and US measurement of the radial artery is mandatory to avoid ischemic complications of the hand.

Minor complications in the present study were limited to superficial bruising (22%) and partial thrombosis of the radial artery (4.2%). The incidence of superficial bruising was higher than previously described by Bishay et al (11), who reported an incidence of 2.3% during hepatic embolization via TRA. This could be associated with subjective clinical assessment. Nonetheless, none of the complications in the present study were clinically relevant, and no radial artery occlusion was encountered. Administration of systemic heparin and nitroglycerin through the sheath immediately after its placement and immediately before sheath removal, as well as achieving patent hemostasis while applying the pneumatic compression device, are key factors in the prevention of radial artery occlusion (14).

A previous meta-analysis of 24 randomized trials of patients undergoing coronary catheterization (15) demonstrated increased fluoroscopy time and radiation exposure to patients with TRA (fluoroscopy time, 38 min ± 12 for TRA and 35 min ± 13 for TFA). The weighted mean difference of kermarea product for coronary interventions was 0.55 Gy·cm² favoring TFA (95% confidence interval, 0.08–1.02 Gy·cm²; $P = .02$). In the present study, despite the longer distance between the radial artery and celiac trunk and the need to manipulate the wire and catheter into the descending aorta, the procedure durations were similar for both approaches. This was also observed in a recent cardiology prospective trial (16) in which fluoroscopy time was not statistically different with TRA versus TFA (12.2 min vs 9.8 min; $P = .507$). Operator experience and device choice can influence the procedure duration and the use of an angled hydrophilic J-tip wire (1.5 mm radius), and the angle of the 5-F diagnostic catheter tip allowed easy access to the descending aorta.

Radiation exposure as measured by air kerma to the patient did not differ between accesses, similar to what was observed in the previously mentioned cardiology study (16). Another study of coronary interventions (17) in which patients were randomized to TRA or TFA showed no differences in radiation exposure to patients in centers with high procedure volumes (air kerma, 652 mGy for TRA vs 621 mGy for TFA; $P = .403$), suggesting that, similar to fluoroscopy time, radiation exposure can be influenced by operator experience. Finally, in the present study, radiation exposure to the operator was lower with TRA as a result of the positioning of the radiation shield and the longer distance between the operator and radiation source. We found no published studies in the literature that assessed this outcome.

TRA demonstrated distinct advantages over TFA, which has made TRA the default access for most visceral interventions at the authors’ institution. TRA not only provides a safe alternative access, but it also offers a new patient-centric model aligned with the best practices concept in the ever-changing health care landscape. Recent European Society of Cardiology guidelines (18) recommended that TRA become the preferred approach in coronary
interventions. Studies have demonstrated decreased costs associated with TRA versus TFA, primarily because there is no need for arterial closure devices and there is a decreased incidence of readmission for bleeding complications (4,7,19). The use of TRA has facilitated shorter hospital stays, partly as a result of the “radial lounge” concept (20).

In this model, postprocedural monitoring after TRA generally requires a decreased nursing ratio, and patients may sit up in a chair and ambulate immediately. Moreover, it has been postulated that TRA may cause less hematoma in patients with coagulopathies, a common underlying condition in HCC (21).

The present study is limited by several factors. There were limitations inherent to subjectivity in the patient survey, as patients could have had inherent bias in favor of TRA over TFA before enrollment. Also, patient preference is a subjective assessment, involving justifications such as less discomfort and limited bed restriction. Time to ambulate, which would be an objective assessment, was not analyzed in this study. TRA in female patients can be technically more difficult as a result of anatomic and physiologic factors. As 78% of patients in the present study were male, it is possible that TRA in this patient population was more feasible; however, sex was not an exclusion criterion, and patients were enrolled according to hospital/referral demand.

Radiation dose reduction to the operator with TRA was achieved with only the specific patient positioning and shielding used in this study. Different techniques such as left arm adduction may not show similar benefit. As mentioned before, the sample size was powered to identify patient preference only and not the other secondary endpoints, including complications. Therefore, interpretation of the results regarding the secondary endpoints is limited, and a larger sample size would be required for accurate assessment.

Finally, transarterial (chemo-)embolization procedures can vary significantly, given differences in tumor burden, number of selective catheterizations, and time to deliver embolic material. Despite the randomization process including intra- and interpatient comparison, those variables might have not been completely counterbalanced, leading to biased results.

In conclusion, for the majority of patients with primary or metastatic liver tumors undergoing transarterial (chemo-) embolization, TRA was the access of choice. TRA was not associated with an increased incidence of adverse events or increased procedure time. In addition, radiation exposure to the operator was lower with TRA.

REFERENCES