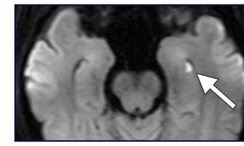

Prospective Multicenter Observational Study of Silent Brain Infarction following Transradial Hepatic Intervention (The MOSAIC Study)

Yuji Koretsune, MD, Miyuki Sone, MD, Shintaro Kimura, MD, Shunsuke Sugawara, MD, Yoshihisa Kodama, MD, Yasushi Kimura, MD, PhD, Kaishu Tanaka, MD, PhD, Yusuke Ono, MD, PhD, Hiroki Higashihara, MD, PhD, Yasuaki Arai, MD, Masahiko Kusumoto, MD, and Noriyuki Tomiyama, MD, PhD

ABSTRACT

Purpose: To investigate the incidence and risk factors of silent brain infarction following transradial hepatic interventional procedures.

Materials and Methods: In this multicenter prospective observational study, 57 patients scheduled for transradial hepatic intervention underwent preprocedural and postprocedural magnetic resonance (MR) imaging. The study was divided into 2 periods: August–December 2022 (former group) and June–December 2023 (latter group). In the latter period, selection criteria were modified to include only patients with a left subclavian artery (SCA) angle of $>50^\circ$, and the protocol was revised to incorporate strict heparinization and continuous catheter flushing. The primary end point was the incidence of silent brain infarction, and associated risk factors were analyzed.

Results: Among 57 registered patients, 55 underwent transradial access (TRA). Silent brain infarction was detected in 9 patients (16.4%), with no symptomatic cerebral infarction. The incidence reduced significantly in the latter compared with that in the former group (2.9% vs 40%; $P < 0.001$). Univariate analysis in the former group demonstrated prolonged catheterization time from the left SCA to descending thoracic aorta as a significant risk factor (575.0 seconds [SD ± 536.2] vs 57.9 seconds [SD ± 59.4]; $P = .008$), with a cutoff value of 58 seconds (sensitivity, 0.727; specificity, 0.875). Moreover, patients with a left SCA angle of $\leq 50^\circ$ demonstrated a significantly higher incidence of silent brain infarction ($P = .049$).

Conclusions: This study demonstrated that transradial hepatic intervention was associated with a 40% incidence of silent brain infarction, which may be reduced by protocols limiting TRA to patients with favorable anatomy and incorporating continuous heparinization and catheter perfusion.

ABBREVIATIONS

ACT = activated clotting time, CT = computed tomography, DWI = diffusion-weighted imaging, IRB = institutional review board, MR = magnetic resonance, SCA = subclavian artery, TAI = transarterial infusion, TFA = transfemoral access, TRA = transradial access, US = ultrasound

Transfemoral access (TFA) has long been the standard approach for a wide range of interventional procedures (1). TFA allows for the use of a broad array of catheters and devices, making it suitable for complex procedures without being affected by radial or subclavian anatomical variations (2).

In recent years, however, transradial access (TRA) has gained increasing popularity as an alternative vascular access route. Since Campeau (3) first reported it in 1989, TRA has been widely accepted worldwide. In coronary interventions, TRA has demonstrated reduced bleeding events and lower mortality rates compared with TFA,

Figure E1 can be found by accessing the online version of this article on www.jvir.org and selecting the Supplemental Material tab.

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RESEARCH HIGHLIGHTS

- This study found a 40% incidence of silent brain infarction following transradial hepatic intervention, which decreased to 2.9% by protocols excluding the patients with unfavorable arch anatomy, and incorporating continuous heparinization and catheter perfusion.
- Prolonged catheterization time from the left subclavian artery to the descending thoracic aorta was identified as the risk factor for silent brain infarction, with a cutoff value of 58 seconds (575.0 seconds [SD ± 536.2] vs 57.9 seconds [SD ± 59.4]; *P* = .008).
- Moreover, a left subclavian artery angle of $\leq 50^\circ$ relative to the horizontal plane was also identified as the risk factor for silent brain infarction (37.5% vs 0%; *P* = .049).

earning its Class I recommendation in the 2016 European Society of Cardiology guidelines and American guidelines in 2022 (4–7). Similarly, meta-analyses have shown that TRA reduces access-site adverse events in neurointerventions (8,9).

Despite these advantages, the adoption of TRA in abdominal interventions has not been as rapid as in other fields. Although previous reports have highlighted the advantages of TRA over TFA, such as improved patient satisfaction and shorter recovery times (10–12), it carries specific risks, including cerebral infarction (13). According to Posham et al (14), no symptomatic cerebral infarctions were observed in 946 patients evaluated for 1,512 consecutive noncoronary interventions via TRA. However, this study evaluated only clinically apparent cerebral infarctions. Asymptomatic cerebral infarctions—that is, silent brain infarctions—have not been taken into account. Silent brain infarctions, although clinically silent, are not neurologically benign and contribute to long-term cognitive impairment (15,16). For example, the Swiss-AF cohort, which followed up 1,227 patients with atrial fibrillation using serial brain magnetic resonance (MR) imaging, found that 5.5% of patients developed new infarctions after 2 years, with 85% being silent (17). Despite their smaller size, the cognitive impact of these silent infarcts was comparable with that of symptomatic strokes, emphasizing their clinical importance.

Previous studies have reported high rates of postprocedural high signal intensity on diffusion-weighted imaging ranging from 9.8% to 22% in coronary interventions (18–20), 10% to 34.8% in cerebral angiography (21–23), and 7.7% to 81% after cardiac surgery (24–26). Moreover, a previous systematic review identified the mean fluoroscopy duration and an elongated aortic arch as risk factors for silent brain infarction during diagnostic cerebral angiography and carotid artery stent placement (21,27).

However, its incidence following abdominal endovascular interventions remains unclear. Therefore, this study aimed to investigate the frequency of and risk factors for silent brain infarctions following abdominal endovascular procedures performed via TRA.

STUDY DETAILS

Study type: Prospective, observational, descriptive study

Level of evidence: 3 (SIR-C)

MATERIALS AND METHODS

Study Design and Patient Eligibility

The MOSAIC study was a multicenter prospective observational investigation focusing on silent brain infarctions following transradial hepatic intervention. The study protocol was approved by the National Cancer Center Hospital Certified Review Board (2022-001). This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients deemed eligible for participation.

The inclusion criteria were as follows: (*a*) patients with hepatocellular carcinoma scheduled to undergo transarterial chemoembolization, transarterial embolization, or transarterial infusion (TAI); (*b*) aged 18 years or older; and (*c*) provision of written informed consent. TAI was defined as a single-session treatment rather than continuous intrahepatic arterial infusion using a port.

The exclusion criteria were as follows: (*a*) inability to undergo MR imaging because of metallic implants or claustrophobia; (*b*) severe allergy to iodinated contrast material or other medications; (*c*) pregnancy, breastfeeding, or women of childbearing potential; (*d*) Barbeau test results of Type D or a radial artery diameter of <2 mm; and (*e*) ineligibility because of safety concerns, such as severe stenosis of the left subclavian artery (SCA), as determined by the investigators (Y.K., S.K., Y.K.). The degree of stenosis of the left SCA was assessed by the operators (Y.K., S.K., Y.K.) using preoperative contrast-enhanced computed tomography (CT).

End Points

After the registration of the eligible patients, MR imaging of the brain was performed within 48 hours before the procedure. Follow-up MR imaging was conducted within 12–120 hours postprocedurally to assess the presence of cerebral infarction. The imaging protocol included diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), and $T2^*$-weighted imaging. Although the MR imaging protocols were not standardized across institutions, all imaging was performed using scanners with at least 1.5 T, and the images were interpreted by board-certified radiologists (Y.K., S.K., Y.K.) at each participating institution.

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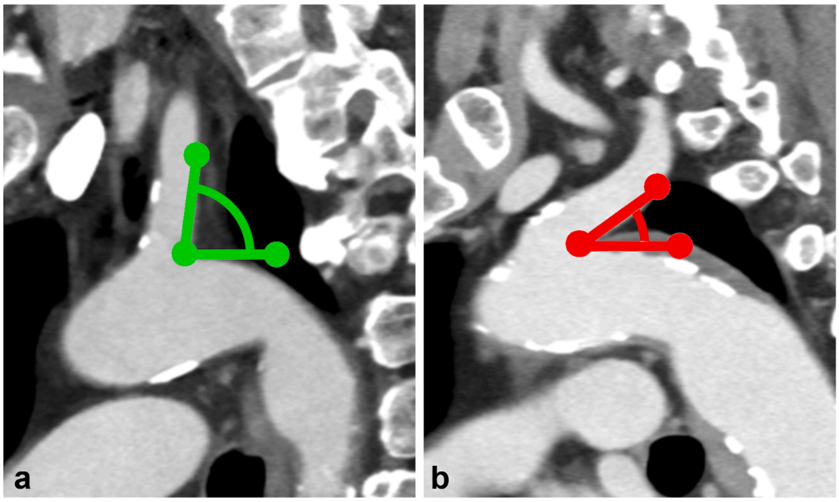

Figure 1. The left subclavian artery incident angle was measured using the sagittal plane of chest computed tomography (CT), defined as the angle between the line of the subclavian artery origin and the horizontal plane: **(a)** an angle of 85° (shown in green), **(b)** an angle of 27° (shown in red). Since angle in **(b)** was <50°, it was not eligible for inclusion in the latter period of this study.

The following data were collected: age, sex, underlying liver disease, medical history, anticoagulant medication, access site, preprocedural radial artery diameter, Barbeau test results, hematologic parameters, procedure time, intraprocedural and postprocedural adverse events, and the rate of radial artery occlusion. The anatomical morphologies of the left SCA and aortic arch were assessed using preprocedural CT. The catheterization times for the descending thoracic aorta via the left SCA and the celiac artery or superior mesenteric artery via the descending thoracic aorta were also measured using recorded fluoroscopic images. All intraoperative fluoroscopic images from the cases enrolled in this study were recorded and centrally archived at a single institution. Two board-certified radiologists jointly reviewed these images and conducted the time assessments together (Y.K., H.H.). The duration of catheter manipulation within the aortic arch was defined as the interval from the initial entry of the catheter into the aortic arch to its placement in the descending aorta. Periods without fluoroscopic observation were also included in the measurements.

The primary end point was the incidence of silent brain infarction, defined as high signal intensity on DWI on postprocedural MR imaging without accompanying neurological deficits. Neurological examinations were conducted and assessed by board-certified neurologists or neurosurgeons in each participating institution. Neurologic assessments were conducted at the discretion of each specialist, and no strict protocol was established for the evaluations. The secondary end points included the incidence of symptomatic brain infarction, rate of radial artery occlusion, and other adverse events. Other adverse events included access site hematoma and pseudoaneurysm.

Procedures

All procedures were performed by 1 or 2 interventional radiologists, at least one of whom was board-certified. The operators had between 3 and 28 years of experience in interventional radiology (mean, 11.3 years). When a trainee acted as the primary operator, the consultant was also scrubbed in and participated directly in the procedure alongside the trainee.

Procedures were performed under local anesthesia in an angiography suite equipped with conventional CT or cone-beam CT imaging. The left radial artery was punctured under ultrasound (US) guidance, and a 5-F introducer sheath (Glidesheath slender; Terumo, Tokyo, Japan) was inserted. The radial artery puncture site was selected based on the operator's preference (Y.K., S.K., Y.K.), using either traditional or distal TRA via the anatomical snuffbox. Intravenous heparinization (>50 U/kg) was performed. During the procedure, additional heparin was administered at a rate of 1,000 U/h.

A 5-F angiographic catheter (R.A.V.I. MG1; Terumo) and 0.035-inch hydrophilic angled guide wire (Radifocus Glidewire; Terumo; or Silverway; Asahi Intecc, Nagoya, Japan) were used to cannulate the celiac or superior mesenteric arteries via the descending aorta from the wrist. The Silverway guide wire features a distal 15-cm silicone coating, a hydrophilic coating extending from 15 to 80 cm, and a proximal silicone coating beyond 80 cm. In cases where navigation of the parent catheter from the left SCA to the descending aorta proved challenging, a pigtail catheter was used to navigate the guide wire into the descending aorta. Following successful cannulation of the celiac artery with the parent catheter, transarterial chemoembolization, transarterial embolization, or TAI was performed using the same

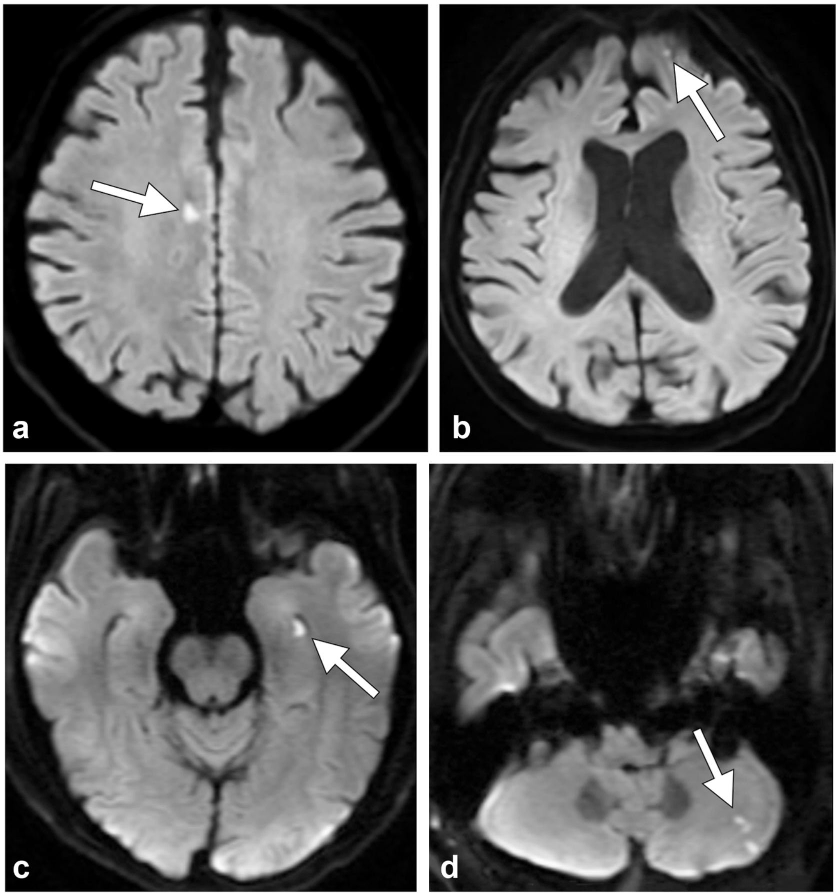

Figure 2. Diffusion-weighted imaging magnetic resonance (MR) images of patients with silent brain infarctions. Figure parts **(a)**, **(b)**, **(c)**, and **(d)** correspond to patients 7, 1, 4, and 6, respectively, in **Table 2**. Arrows in each image indicate punctate lesions of high signal intensity interpreted to represent microemboli.

methodology as used in the TFA (28). After the procedure, an external pneumatic radial compression band (TR Band; Terumo; or Prelude Sync Distal; Merit Medical Systems, South Jordan, Utah) was placed on the left wrist. Between 10 and 15 mL of air was injected into the band to ensure adequate pressure at the puncture site. Finally, a reverse Barbeau test was performed to confirm patent hemostasis (29). Radial artery patency was assessed upon achieving hemostasis and after removing the pneumatic radial compression band by the operator through palpation (Y.K., S.K., Y.K.).

Protocol Change

TRA was temporarily suspended in clinical practice in December 2022 owing to the higher-than-anticipated incidence of silent cerebral infarction. Consequently, patient enrollment in this study was also temporarily halted. Following consultation with external reviewers, procedural modifications were implemented for the TRA, which included precise intraoperative heparinization and continuous flushing through the parent catheter during the procedure. Regarding heparinization, the activated clotting time (ACT) was measured 5 minutes after heparin administration (>50 U/kg). The parent catheter was inserted only when the ACT exceeded 200 seconds. If the ACT was <200 seconds, an additional 1,000 U of heparin was administered, followed by a repeat ACT measurement 5 minutes later. Throughout the procedure, ACT was measured every hour, and if it was found to be <200 seconds, an additional 1,000 U of heparin was administered. Continuous saline flushing through the parent catheter using a pneumatic compression bag was sustained from insertion into the introducer until its removal. A Y-connector hemostatic valve was attached to the parent catheter to ensure prevention of air entry into the system.

Furthermore, considering that cases with steep angles of the left SCA relative to the horizontal plane might require prolonged catheter manipulation in the aortic arch, TRA was performed only when the angle exceeded 50°. The reason for setting 50° as the cutoff is that a review of past cases of abdominal intervention via TRA at authors' institution revealed that when the incident angle was ≤50°, guiding the parent catheter into the descending aorta required more time. The angle of the left SCA in the horizontal direction was measured using the sagittal planes of

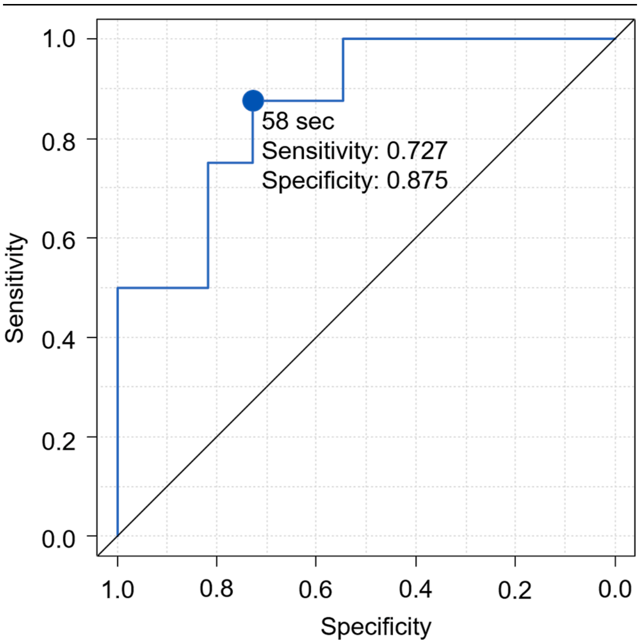

Figure 3. Receiver operating characteristic curve and a cutoff value of catheterization time for the descending thoracic aorta via the left subclavian artery. The cutoff value was 58 s, and the corresponding area under the curve was 0.864.

chest CT by a board-certified radiologist at the participating institution (Y.K., S.K., Y.K.) (**Fig 1a, b**).

TRA was reintroduced into clinical practice in June 2023, and study enrollment was resumed. Consequently, the study population was divided into the former and latter groups, delineated by the period of TRA suspension. In summary, compared with the former group, the latter group applied an additional inclusion criterion of an SCA angle of >50°, and, during the procedure, strict heparinization and continuous flushing through the parent catheter were also implemented.

Statistical Analysis

Previous reports have suggested that the rate of silent brain infarction following coronary angiography via TRA ranged from 9.8% to 22% (18–20). Before the initiation of this study, it was assumed that, compared with coronary angiography—which involves prolonged catheter manipulation in the ascending aorta—abdominal endovascular therapy via TRA would require only brief passage through the aortic arch during the procedure. In this study, the expected rate of silent cerebral infarction was estimated to be 2%, following discussions with the interventional radiology department and statistical experts in authors' institution. Therefore, using a 1-sided *t* test with H1 ($P = .02$), H0 ($P = .1$), and an 〈 error of 0.05, a sample size of 48 patients would provide a power >80% (https://stattools.crab.org/R/One_Arm_Binomial.html). Accounting for the possibility of patients ineligible for analysis, the planned enrollment was set at 55 patients.

The patients were categorized into the former group (August to December 2022) and latter group (June to December 2023). Factors potentially influencing the silent brain infarction were assessed using Fisher exact test or *t* test. *P* values of <0.05 were considered statistically significant. Owing to the protocol modifications, the former and latter groups represented entirely different populations; therefore, the analysis of risk factors was limited to the former group. Regarding catheterization time for the descending thoracic aorta via the left SCA, a receiver operating characteristic curve was drawn, and the cutoff value, sensitivity, and specificity were calculated when the area under the curve of the receiver operating characteristic curve was >0.7. The optimal cutoff value was calculated using the Youden J index method. All analyses were performed using EZR version 1.61 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (30), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Patient Characteristics

A total of 57 patients were enrolled in this study from 3 institutions between August 2022 and December 2023. Among these cases, 2 were treated via femoral access. One patient was incidentally found to have chronic subdural hematoma on preprocedural head MR imaging. Owing to the potential risk of hematoma enlargement with intraprocedural heparin administration for radial access, femoral access was chosen in this case. In another case, the catheter could not be navigated through a highly tortuous segment of the radial artery in the forearm, necessitating a switch to femoral access. Of the 55 patients who underwent TRA, 5 were taking antiplatelet drugs. Among them, 3 discontinued the medication before the procedure. Of the remaining 2, 1 underwent TRA while on aspirin, and the other while on prasugrel. The characteristics of the entire cohort of 55 patients are summarized in **Table 1**.

RESULTS

Procedural Outcomes

The incidence of high signal intensity on DWI on postprocedural MR imaging was 16.4% (n = 9/55). All patients were examined by board-certified neurologists or neurosurgeons, and no neurologic deficits were observed. Thus, all detected cerebral infarctions were asymptomatic, while the rate of symptomatic cerebral infarction was 0% (**Figs 2a–d**, **E1a–e**, available online on the article's Supplemental Material page at *www.jvir.org*). Among these 9 cases, 8 were from the former group, with only 1 case from the latter group (8/20 [40%] vs 1/35 [2.9%]; $P < .001$). A pigtail catheter was used in 4 cases to guide the parent catheter into the descending aorta, and all these cases were associated with silent brain infarction. The details of these 9 cases are presented in **Table 2**.

Table 1. Patient Characteristics

Patient characteristics (N = 55)	All (N = 55)	Former group (n = 20)	Latter group (n = 35)
Age (y)	72 (51–91)	76 (57–91)	72 (55–83)
Sex			
Male	49 (89.1)	18 (90.0)	31 (88.6)
Female	6 (10.9)	2 (10.0)	4 (11.4)
Etiology			
HBV	10 (18.2)	2 (10.0)	8 (22.9)
HCV	12 (21.8)	4 (20.0)	8 (22.9)
Alcohol	12 (21.8)	6 (30.0)	6 (17.1)
MASH	14 (25.5)	6 (30.0)	8 (22.9)
PBC	1 (1.8)	0 (0)	1 (4.5)
Unknown	6 (10.9)	2 (10.0)	4 (18.2)
Baseline RA diameter (mm)	2.5 (2–4)	2.7 (2.2–4)	2.4 (2–3.5)
Baseline Barbeau test			
A	23	10	13
B	29	9	20
C	3	1	2
D	0		0
Initial/repeat TRA			
Initial	35 (63.6)	14 (70.0)	21 (60.0)
Repeat	20 (36.4)	6 (30.0)	14 (40.0)
Preoperative CT findings			
Angle of incidence of the left SCA in the horizontal direction (◦)	72 (28–86)	72 (28–86)	72 (53–86)
Medical history			
Atrial fibrillation	3 (5.5)	1 (5.0)	2 (5.7)
Hypertension	29 (52.7)	11 (55.0)	18 (51.4)
Hyperuricemia	8 (14.5)	3 (15.0)	5 (14.3)
Diabetes	23 (41.8)	10 (50.0)	13 (37.1)
Smoking	11 (20.0)	5 (25.0)	6 (17.1)
History of cerebral infarction (%)	4 (7.3)	2 (10.0)	2 (5.7)
D-dimer $\geq$ 0.5 μg/mL (%)	36 (65.5)	16 (80.0)	20 (57.1)
Medication			
Antiplatelet drugs (%)	2 (3.6)	1 (5.0)	1 (2.9)

Note–Values are n (%) and median (range).
DEB = drug-eluting bead; HBV = hepatitis B virus; HCV = hepatitis C virus; MASH = metabolic dysfunction–associated steatohepatitis; PBC = primary biliary cholangitis; RA = radial artery; SCA = subclavian artery; TACE = transarterial chemoembolization; TAI = transarterial infusion; TRA = transradial access.

Other adverse events included minor subcutaneous hematomas around the puncture site in 3.6% (n = 2/55) of cases, which did not require additional intervention. Although there was no statistically significant difference, all cases of subcutaneous hematoma were observed in the latter group, showing a tendency to be more frequent than those in the former group. No radial artery occlusion was observed.

The mean catheterization time for the descending thoracic aorta via the left SCA was 123.2 seconds (SD ± 281.5), which was significantly longer in the former group (275.6 seconds [SD ± 433.9] vs 40.4 seconds [SD ± 24.6]; $P = .003$). Furthermore, the group with a left SCA angle of $\leq$50° relative to the horizontal plane showed a significantly longer mean catheterization time for the descending thoracic aorta via the left SCA (916.5 seconds [SD ± 609.7] vs 59.7 seconds [SD ± 95.4]; $P < 0.001$). Procedural details are summarized in Table 3.

Risk Factors of Silent Brain Infarction

The univariate analysis in the former group indicated that catheterization time for the descending thoracic aorta via the left SCA was significantly longer in the silent brain infarction group (575 seconds [SD ± 536.2] vs 57.9 seconds [SD ± 59.4]; $P = .008$). The cutoff value, sensitivity, and specificity of the catheterization time to the descending thoracic aorta were 58 seconds (sensitivity, 0.727; specificity, 0.875), with the corresponding area under the curve being 0.864 (Fig 3).

In addition, cases with a left SCA angle of $\leq$50° relative to the horizontal plane showed a significantly higher incidence of silent brain infarction (37.5% vs 0%; $P = .049$). No significant differences were observed between the 2 groups for the other factors. The results of the univariate analysis are presented in Table 4.

Table 2. Details of Cases with Silent Brain Infarction

Catheterization time for the descending thoracic aorta via the left SCA (s)	Angle of incidence of the left SCA in the horizontal direction (°)	Operator experience with TRA (procedures)	Cases in which a pigtail catheter was used	Location of DWI HISs	No. of DWI HSI	Operator	Type of TRA procedure	Procedural time (min)	Group	Age (y)	Case
58	73	10–100	–	Left frontal lobe	1	Consultant	cTACE	90	Former	87	1
42	86	<10	–	Right occipital lobe	1	Consultant	cTACE	130	Former	80	2
78	76	<10	–	Right corona radiata	1	Resident	cTACE	60	Former	71	3
121	85	10–100	–	Left hippocampus	1	Consultant	cTACE	100	Former	69	4
667	67	<10	Used	Right cerebellar hemisphere	1	Resident	cTACE	180	Former	88	5
993	28	10–100	Used	Left cerebellar hemisphere, left occipital lobe	4	Resident	DEB-TACE	130	Former	80	6
1,339	44	<10	Used	Right frontal and occipital lobes, left cerebellar hemisphere	4	Resident	DEB-TACE	210	Former	91	7
1,302	41	<10	Used	Right parietal lobe, left parietal and occipital lobes, left cerebellum	5	Resident	DEB-TACE	180	Former	87	8
112	73	10–100	–	Left occipital lobe	1	Consultant	cTACE	90	Latter	70	9

cTACE = conventional transarterial chemoembolization; DEB = drug-eluting bead; DWI = diffusion-weighted imaging; HSI = high signal intensity; SCA = subclavian artery; TACE = transarterial chemoembolization; TRA = transradial access.

Table 3. Comparison of the Procedural Outcomes between Former and Latter Groups

Outcome	All (N = 55)	Former group (n = 20)	Latter group (n = 35)	*P*
Puncture site				
Conventional RA	28 (50.9)	14 (70)	14 (40)	.050
Distal RA	27 (49.1)	6 (30)	21 (60)	.050
Procedural time (min)	100 (50–210)	100 (60–210)	90 (60–150)	**.027**
Catheterization time for the descending thoracic aorta via the left SCA (s)	38 (10–1,339)	58 (10–1,339)	32 (10–125)	**.003**
Catheterization time for the CA or SMA via the descending thoracic aorta (s)	98 (35–2,450)	95 (35–1,559)	98 (38–2,450)	.400
Total dose of heparin (U)	4,000 (2,500–7,000)	5,000 (2,500–5,000)	4,000 (2,500–7,000)	.325
Resident operator	17 (30.9)	7 (35)	10 (28.6)	.763
Type of TRA procedure				
Conventional TACE	43 (78.2)	14 (70)	29 (82.9)	.319
DEB-TACE	7 (12.7)	4 (20)	3 (8.6)	.242
TAI	4 (7.3)	1 (5)	3 (8.6)	1
Bland-TAE	1 (1.8)	1 (5)	0	.364
Hematoma	2 (3.6)	0 (0)	2 (5.7)	.529
Postprocedural complications				
Silent cerebral infarction	9 (16.4)	8 (40)	1 (2.9)	**<.001**

Note–Values are n (%) and median (range).
Bold values indicate statistical significance.
CA, celiac artery; DEB, drug-eluting beads; RA, radial artery; SCA, subclavian artery; SMA, superior mesenteric artery; TACE, transarterial chemoembolization; TAE, transarterial embolization; TAI, transarterial infusion.

Table 4. Risk Factors of the SBI following Transradial Intervention in the Former Group

Variable	SBI group (n = 8)	No-SBI group (n = 12)	*P*
Atrial fibrillation	1 (12.5)	0 (0)	.400
Hypertension	5 (62.5)	6 (50)	.670
Hyperuricemia	1 (12.5)	2 (16.7)	1.000
Diabetes	4 (50)	6 (50)	1.000
Smoking	4 (50)	2 (16.7)	.161
History of cerebral infarction	1 (12.5)	1 (8.3)	1.000
D-dimer $\geq$ 0.5 μg/mL	7 (87.5)	9 (75)	0.619
Resident operator	4 (50)	5 (41.7)	1.000
Angle of incidence of the left SCA in the horizontal direction $\leq$ 50°	3 (37.5)	0 (0)	**.049**
Catheterization time for the descending thoracic aorta via the left SCA (s)	575 (21–1,339)	58 (10–195)	**.008**
Catheterization time for the celiac artery or SMA via the descending thoracic aorta (s)	225 (50–762)	520 (35–1,559)	.601

Note–Values are n (%) and median (range).
Bold values indicate statistical significance.
SBI, silent brain infarction; SCA, subclavian artery; SMA, superior mesenteric artery.

DISCUSSION

This study revealed that the incidence of silent brain infarction following transradial hepatic intervention was 40%, which decreased to 2.9% by protocols excluding the patients with unfavorable arch anatomy and incorporating continuous heparinization and catheter perfusion. The 40% incidence of silent brain infarction observed in the former group of this study tended to be higher than the previously reported rates of 9.8%–34.8% in coronary and neuro-interventional procedures (18–23). This elevated rate may be attributed to the inclusion of cases with unfavorable aortic arch anatomy for TRA in the former group. Additionally, as shown in Table 3, more than half of the operators in the former group had performed fewer than 10 previous TRA cases, which may have also contributed to the increased incidence.

Silent brain infarction is an unavoidable adverse event in both TFA and TRA during coronary and neurointerventional procedures because catheter manipulation in the aortic arch is inevitable. In contrast, for hepatic interventions, the theoretical risk of silent brain infarctions with TFA is considered minimal, as catheter manipulation in the aortic arch is not required. Therefore, it is crucial to identify patient populations in whom TRA for hepatic interventions can be safely performed with minimal risk of brain infarction. Based on these considerations, this prospective observational study was designed.

Although abdominal intervention via TRA is gradually gaining popularity due to reduced patient burden and higher patient satisfaction (10–12), the unexpectedly high incidence of silent brain infarction in this study—which may contribute to long-term cognitive decline—emphasizes the need for careful patient selection and procedural optimization.

Regarding patient selection, preprocedural contrast-enhanced chest CT should be considered essential. Previous reports have indicated that the branching pattern of the left SCA from the aortic arch can influence the time required to guide the parent catheter into the celiac or superior mesenteric artery (31). However, this classification requires measurement of the common carotid artery diameter and creation of oblique CT reconstructions, which can be complex. In this study, based on a retrospective review of cases in authors' institutions, it was found that a steeper angle between the left SCA and horizontal plane was associated with greater difficulty in advancing the parent catheter into the descending aorta. Therefore, a simplified anatomical criterion of an SCA angle of $>50°$ was adopted. As there are few studies evaluating anatomical features of the aortic arch suited for TRA, further research is needed to establish more practical and refined criteria.

Regarding procedural modifications, strict heparinization with ACT monitoring and continuous flushing through the parent catheter were implemented in the latter group. Although ACT monitoring may not be available at all institutions, previous literature has reported heparin resistance despite standard dosing (32), indicating that ACT-based coagulation management is desirable when feasible. Continuous flushing from the parent catheter may not be necessary in cases where catheter manipulation in the aortic arch is minimal. However, in the absence of continuous flushing, there remains a risk of thrombus formation between the parent and microcatheter. Therefore, if continuous flushing is not performed, it is especially important to adhere to a basic precautionary step: withdrawing the microcatheter first, thoroughly flushing the parent catheter, and then removing it, in order to minimize embolic risk to the brain.

As an adverse event other than silent brain infarction, subcutaneous hematomas not requiring additional treatment were observed in 5.7% ($n = 2$) of patients in the latter group, whereas no such cases occurred in the former group. According to Posham et al (14), minor hematomas occurred in 0.86% of 1,512 TRA procedures, indicating a higher tendency for hematoma occurrence in this study. While strict heparinization is considered desirable to prevent silent brain infarction, caution is warranted regarding the potential for increased incidence of access site hematomas.

According to univariate analysis in the former group, this study identified the angle of incidence of the left SCA in the horizontal direction of $\leq 50°$ and prolonged catheterization time for the descending thoracic aorta via the left SCA as risk factors for silent brain infarction, with a cutoff value of 58 seconds. Previous studies on coronary and neurointerventional procedures have documented similar results in which a longer procedure or fluoroscopy time was identified as the risk factor for silent brain infarctions (19,21,33). Although the threshold of 58 seconds does not imply that operators should abandon TRA and convert to TFA once this time is exceeded, operators need to be aware that exceeding 58 seconds may increase the risk of silent brain infarction. In particular, when less experienced residents are performing the procedure, early involvement or takeover by a more experienced operator should be considered.

This study had several limitations. First, the inclusion criteria and procedural protocols were modified during patient enrollment, resulting in a heterogeneous study population. It is remarkable that these modifications led to a decrease in the incidence of silent brain infarction; however, it is challenging to determine precisely which factors (angle of LSCA origin, catheterization time, use of pigtail catheter) contributed to this reduction. Second, this was a single-arm trial without a comparison with TFA. Although the theoretical risk of silent brain infarction with TFA is considered minimal, a randomized controlled trial comparing the TRA and TFA remains a subject for future investigation. Third, the incidence of silent brain infarction might have decreased in part by the accumulating experience of the operators. To minimize the influence of operators and institutions, this study was conducted as a multicenter prospective study. Finally, the plaque characteristics and degree of stenosis of the left SCA, which could be a potential source of embolism, were not evaluated. Although patients with severe stenosis of the left SCA were excluded based on preprocedural CT, the lack of assessment of plaque burden and stability represents a major limitation of this study and may have impacted the results.

In conclusion, this study demonstrated a 40% incidence of silent brain infarction after hepatic intervention with TRA. A protocol excluding patients with unfavorable anatomy and involving continuous catheter perfusion and heparinization was shown to reduce the risk to 2.9%. Preprocedural CT evaluation of the aortic arch anatomy is desirable to select suitable cases where parent catheter advancement from the left SCA to descending thoracic aorta can be easily achieved. Even if a patient prefers TRA, it may be more appropriate to recommend treatment via TFA in cases with unfavorable aortic arch anatomy.

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AUTHOR INFORMATION

From the Department of Diagnostic and Interventional Radiology (YujiK., K.T., Y.O., N.T.), Osaka University, Osaka, Japan; Department of Diagnostic Radiology (M.S., S.K., S.S., Y.A., M.K.), National Cancer Center Hospital, Tokyo, Japan; Department of Diagnostic Radiology (Yoshihisa K.), Keiyukai Sapporo Hospital, Hokkaido, Japan; and Department of High Precision Image-guided Percutaneous Intervention (H.H., Yasushi K.), Osaka University, Osaka, Japan. Received February 4, 2025; final revision received April 29, 2025; accepted May 14, 2025. Address correspondence to Y.K., Department of Diagnostic and Interventional Radiology, Osaka University, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan; E-mail: korestune-yuji@radiol.med.osaka-u.ac.jp

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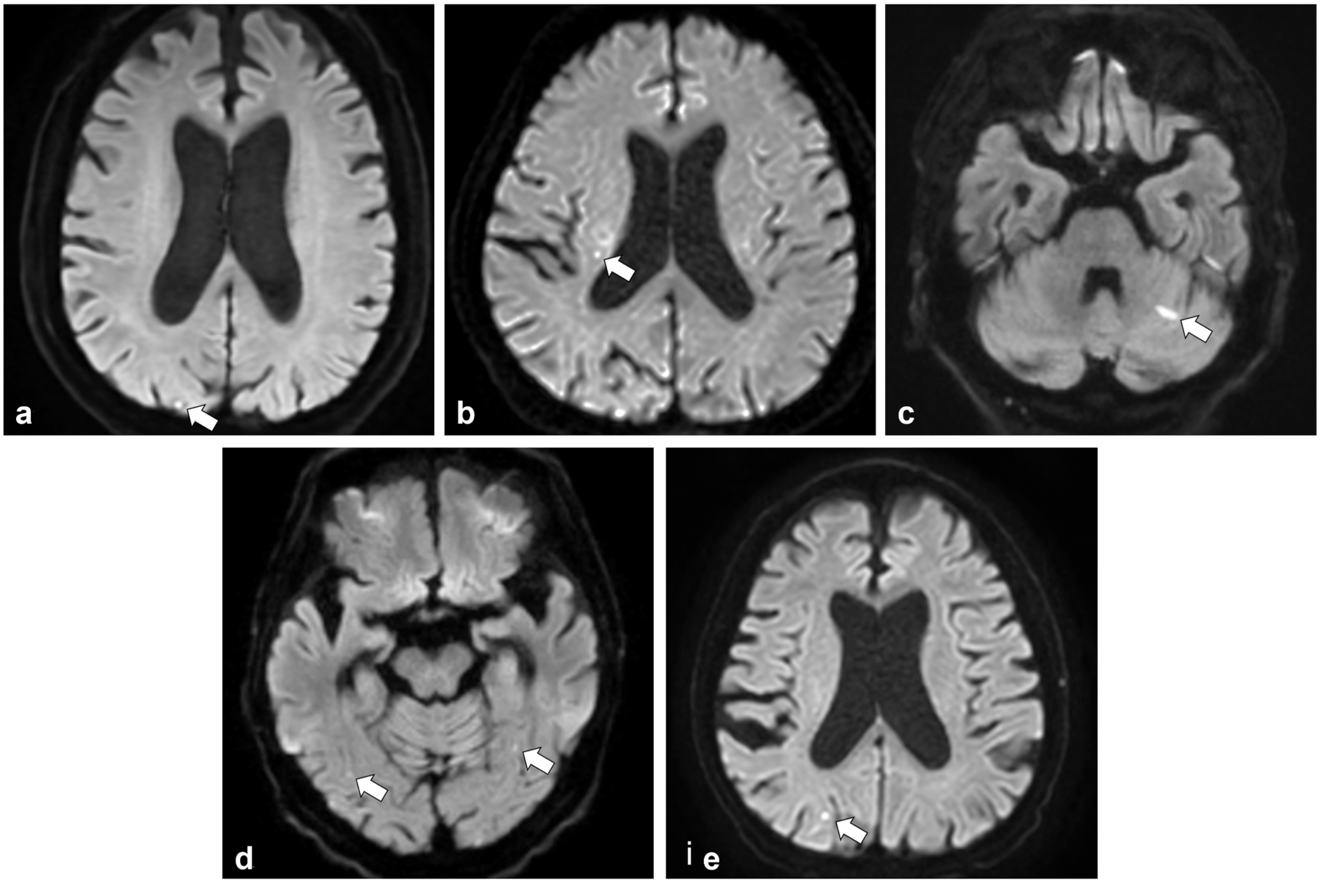

Figure E1. Diffusion-weighted imaging magnetic resonance (MR) images of patients with silent brain infarctions. Figure parts **(a)**, **(b)**, **(c)**, **(d)**, and **(e)** represent to patients 2, 3, 5, 8, and 9, respectively, in Table 2. Arrows in each image indicate punctate lesions of high signal intensity suspected to represent microemboli.