

A randomised comparison of transradial and transfemoral approach for carotid artery stenting: RADCAR (RADial access for CARotid artery stenting) study

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KEYWORDS

- carotid stenosis
- carotid stenting
- radial approach

Abstract

Aims: Limited data exist on radial access in carotid artery stenting. This multicentre prospective randomised study was performed to compare the outcome and complication rates of transradial and transfemoral carotid artery stenting.

Methods and results: The clinical and angiographic data of 260 consecutive patients with high risk for carotid endarterectomy, treated between 2010 and 2012 by carotid stenting with cerebral protection, were evaluated. Patients were randomised to transradial (n=130) or transfemoral (n=130) groups and several parameters were evaluated. Primary combined endpoint: major adverse cardiac and cerebral events, rate of access-site complications. Secondary endpoints: angiographic outcome of the procedure, fluoroscopy time and X-ray dose, procedural time, crossover rate to another puncture site and hospitalisation in days. Procedural success was achieved in all 260 patients (100%), the crossover rate was 10% in the TR and 1.5% in the TF group (p<0.05). A major access-site complication was encountered in one patient (0.9%) in the TR group and in one patient (0.8%) in the TF group (p=ns). The incidence of major adverse cardiac and cerebral events was 0.9% in the TR and 0.8% in the TF group (p=ns). Procedure time (1,620 [1,230-2,100] vs. 1,500 [1,080-2,100] sec, p=ns) and fluoroscopy time (540 [411-735] vs. 501 [378-702] sec, p=ns) were not significantly different, but the radiation dose was significantly higher in the TR group (195 [129-274] vs. 148 [102-237] Gy*cm², p<0.05) by per-protocol analysis. Hospitalisation days were significantly lower in the TR group (1.17±0.40 vs. 1.25±0.45, p<0.05). By intention-to-treat analysis there was a significantly higher radiation dose in the TR group (195 [130-288] vs. 150 [104-241], p<0.05), but no difference in major events (0.9 vs. 0.8, p=ns) and length of hospitalisation in days (1.4±2.6 vs. 1.25±0.45, p=ns).

Conclusions: The transradial approach for carotid artery stenting is safe and efficacious; however, the crossover rate is higher with transradial access. There are no differences in the total procedure duration and fluoroscopy time between the two approaches but the radiation dose is significantly higher in the radial group, and the hospitalisation is shorter with the use of transradial access by per-protocol analysis. By evaluating the patient data according to intention-to-treat analysis we found no difference in major adverse events and hospitalisation. In both groups, vascular complications rarely occurred.

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Abbreviations

CAS	carotid artery stenting
CCA	common carotid artery
CEA	carotid endarterectomy
CFA	common femoral artery
CT	computer tomography
DAP	dose area product
ECA	external carotid artery
FA	femoral artery
GW	guidewire
ICA	internal carotid artery
ITT	intention-to-treat
MACCE	major adverse cardiac and cerebral events
MACE	major adverse cardiac events
MRI	magnetic resonance imaging
NASCET	North Atlantic Society of Endovascular Therapy
PAD	peripheral artery disease
PP	per-protocol
RAO	radial artery occlusion
RAS	radial artery spasm
SA	subclavian artery
TB	transbrachial
TC	transcervical
TCD	transcranial Doppler
TF	transfemoral
TR	transradial

Introduction

Carotid artery stenting (CAS) has become an increasingly tenable alternative to carotid endarterectomy (CEA) for occlusive disease in

high-risk patients^{1,2}. The concept of CAS is to lower the mortality in surgically high-risk patients and to be an effective treatment alternative. Therefore, avoiding or managing complications becomes crucial in CAS. The results are constantly improving because of the introduction of new embolic protection devices and small calibre stenting systems. The conventional approach to access the common carotid artery (CCA) during endovascular interventions is through the femoral artery (FA); however, this approach is not always feasible because of vessel pathology or aberrant anatomy of the iliofemoral arteries and the aortic arch. The transbrachial (TB)³ and the direct transcervical (TC)⁴ approaches are alternative access sites for CAS when femoral access is not available. The rationale for the TR approach was to attempt to reduce the incidence of bleeding complications at the vascular access site and to avoid the necessity for prolonged bed rest. Several pilot studies have confirmed the safety and efficacy of transradial CAS⁵⁻⁸ but no randomised prospective trial exists comparing the transfemoral (TF) and transradial (TR) approach for CAS. Our multicentre prospective randomised study is the first to compare the outcome and complication rate between TR and TF access for carotid artery stenting (CAS).

Materials and methods

STUDY POPULATION (Figure 1)

The clinical and angiographic outcomes of 265 consecutive patients with high risk for CEA⁹ treated by CAS with cerebral protection were evaluated in a prospective randomised multicentre study between 2010 and 2012. Five patients were excluded from the study due to unmet angiographic inclusion criteria. One hundred and fifty-eight symptomatic patients with >70% carotid stenosis and 102 asymptomatic patients with >80% stenosis were enrolled. Patients were

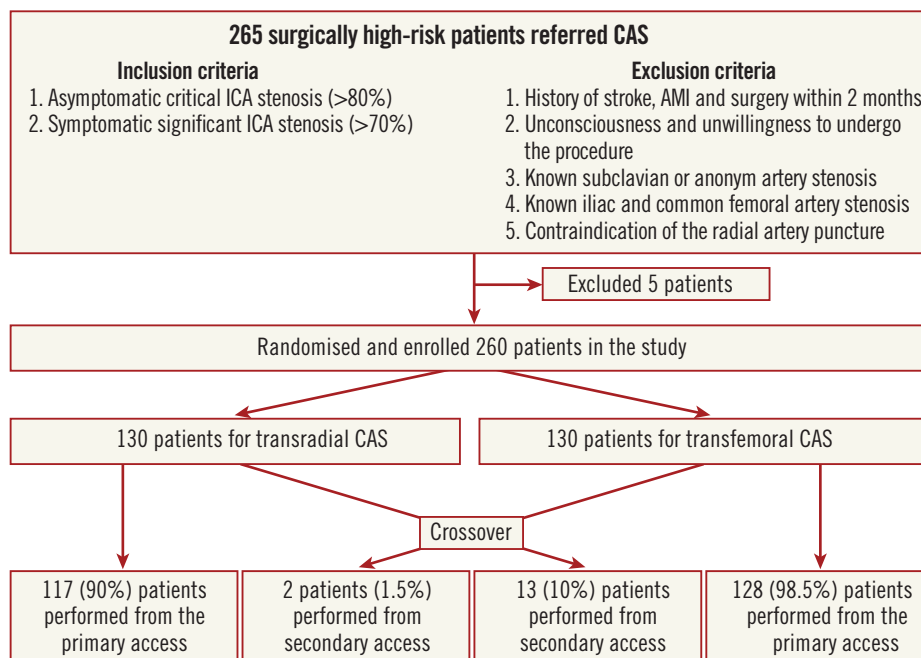


Figure 1. Process of screening, exclusion/inclusion, randomisation and crossover.

randomised to TR (n=130) or TF (n=130) groups. Randomisation was performed blindly using previously sealed envelopes. TR cases were performed by three skilled transradial operators. All femoral access sites were closed with a femoral closure device.

ENDPOINTS

The following parameters were applied to evaluate the potential advantages of TR access:

- Primary endpoint: major adverse cardiac and cerebral events (MACCE), rate of major and minor access-site complications.
- Secondary endpoints: angiographic outcome of the CAS, and consumption of the angioplasty equipment, fluoroscopy time and X-ray dose, procedural time, crossover to another puncture site and hospitalisation days.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria were: 1) symptomatic (history of stroke or transient ischaemic attack within six months) internal carotid artery stenosis (>70%) determined by magnetic resonance imaging (MRI) or computer tomography (CT), and 2) critical asymptomatic (80%) ICA stenosis by MRI or CT.

Exclusion criteria were: 1) history of acute or recent stroke (<2 months), myocardial infarction, and surgery or trauma within the preceding two months, 2) unconsciousness or unwillingness to undergo the procedure, 3) known subclavian or brachiocephalic artery stenosis, 4) known iliac or common femoral stenosis, and 5) contraindications of the transradial access (negative Allen test, non-palpable radial artery).

ANTITHROMBOTIC REGIMEN

All patients were on dual antiplatelet therapy for two months (aspirin 100 mg and clopidogrel 75 mg per os) started at least three days before the procedure. An intra-arterial cocktail (2.5 mg verapamil, 5,000 IU sodium heparin, 250 mcg nitroglycerine) was given directly in the radial artery through the sheath. Additional Na-heparin was given up to 100 IU/kg.

VASCULAR ACCESS AND PROCEDURE

For the radial approach, an ischaemic Allen's test contraindicated the procedure. After local anaesthesia (1% lidocaine), the modified Seldinger technique was used for cannulating the radial artery with a 4-5 Fr dedicated transradial sheath (10 cm, 4-5 Fr; Terumo Co., Tokyo, Japan). The sheath was changed for a 6 Fr long kinking resistant guiding sheath or for a 7 Fr short sheath. After the procedure, the sheath was removed immediately and haemostasis was achieved with a tourniquet for six hours. We did not apply a dedicated haemostatic device. Despite radial artery access the patients were immobilised in the intensive care unit for six hours.

For the femoral approach, after local anaesthesia the femoral artery was punctured with a 19-gauge needle through which a J-wire was advanced into the femoral artery. In all cases a 5 Fr short sheath was introduced initially, then the procedure was performed using a 6 Fr 90 cm long sheath. The sheath was removed immediately after

the procedure and a closure device (Angio-Seal™; St. Jude Medical, St. Paul, MN, USA) was used. A mechanical compression bandage was used for four hours and the patients were mobilised afterwards.

ANGIOPLASTY PROCEDURE

CAS was performed under local anaesthesia without sedation. Blood pressure, pulse and oxygen saturation were continuously monitored throughout the procedure and neurologic assessment was performed by experienced nursing staff.

Transfemoral CAS was performed according to the standard clinical practice with a guiding sheath, using the Carotid WALLSTENT (Boston Scientific Corporation, Natick, MA, USA), Cristallo Ideale (Medtronic-Invatec, Frauenfeld, Switzerland), and Precise (Cordis Corporation, Bridgewater, NJ, USA) stents. In all procedures we used either the Filter wire (Boston Scientific Corp.) or Emboshield (Abbott Vascular, Santa Clara, CA, USA) cerebral protection device. Post-dilation, to the diameter of the internal carotid artery (ICA), was performed in all patients. Completion angiography was then performed, and a closure device was used to achieve haemostasis in all cases.

TRANSRADIAL CAS

After the sheath insertion (5 Fr; Terumo), diagnostic angiography was performed with a 5 Fr Simmons 1 (Cook Medical, Bloomington, IN, USA) diagnostic catheter with the "pullback and rotate" technique. First, an aortography was performed in LAO 30 projection with small contrast volume (15 ml at 10 ml/s) to visualise the aortic arch, then the non-symptomatic or non-severely stenotic carotid artery was cannulated. Secondly, the diseased common carotid artery (CCA) was deeply engaged with the Simmons 1 catheter (**Figure 2**, **Figure 3**). A long J-tip guidewire (GW) was advanced in the external carotid artery (ECA) under "road map" guidance and the CCA was cannulated with a 7 Fr guiding catheter or with a 6 Fr guiding sheath. If the guiding catheter technique was used, the 5 Fr radial sheath was exchanged for a 7 Fr short sheath and a 7 Fr XF 40 (Boston Scientific Corp.) guiding catheter was used for cannulation of the CCA. If the guiding sheath technique was used, a 6 Fr kinking resistant (Cook, Bloomington, IN, USA) guiding sheath was used for the CCA cannulation. In the case of insufficient guiding or sheath support, firstly a buddy wire was used to advance the system forward in the CCA. In failed cases when the guiding catheter or the sheath jumped out in the aortic arch, the telescoping technique was used with the Simmons catheter inside the XF 40 guiding catheter. In case of a failed telescoping attempt, we changed to the loop technique (the guiding catheter was pushed ahead while the guidewire was kept strongly in the operator's hand creating a loop [loop technique], **Figure 4**). The stenting was performed the same way as for the femoral CAS, using distal protection.

ANGIOGRAPHIC ANALYSIS

Carotid angiography was obtained in a routine manner using at least two different projections. The vessels and lesions were analysed by a computerised quantitative analysis system (Siemens Hicor and

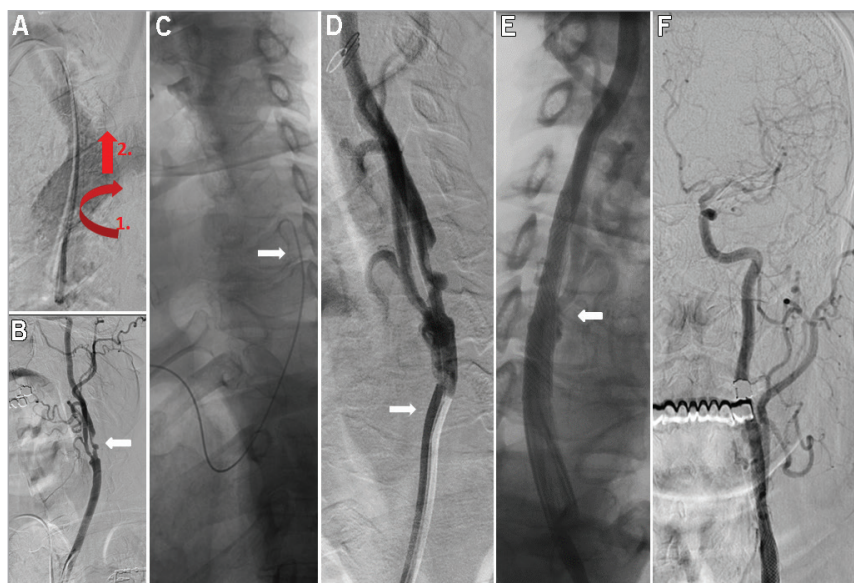


Figure 2. Left ICA stenting in aortic arch type I. Digital subtraction image of the aortic arch shows aortic arch type I (A). The Simmons catheter was pulled back with clockwise rotation (pull and rotate technique - red arrows) (A) and the left CCA was cannulated (B). Angiography from the left CCA shows significant ICA stenosis (B, white arrow). The 260 cm long GW is shown in the left CCA (C, white arrow), followed by the cannulation of the left CCA with a 7 Fr XF 40 guiding catheter (D, white arrow). Final angiographies show no residual stenosis after stenting (E & F).

General Electric) according to previously described and validated edge-detection algorithms using the North Atlantic Society of Endovascular Therapy (NASCET) criteria¹⁰. Minimum lumen diameter, reference vessel diameter and percent diameter stenosis were measured before and after angioplasty.

Definitions

CRITERIA FOR A SUCCESSFUL ANGIOPLASTY

A successful angioplasty was defined as no more than 30 percent post-intervention stenosis by NASCET criteria, and an improvement of at least 20 percent in the degree of stenosis¹⁰.



Figure 3. Right ICA stenting in aortic arch type II. Aortography pictures of a 65-year-old patient with right-sided ICA stenosis and aortic arch II. The Simmons catheter was pulled back in the right CCA with anticlockwise rotations (A). Critical stenosis at the origin of the right ICA (B, white arrow). The Starter™ 260 cm long 0.035 GW (Boston Scientific) was advanced deeply in the ECA (C, white arrow) and an XF guiding catheter was advanced in the right CCA (D, white arrow). Angiography after Filter wire advancement and stenting (E, white arrow). Final angiography shows good stent expansion and cerebral flow with patent cerebral arteries (E & F).

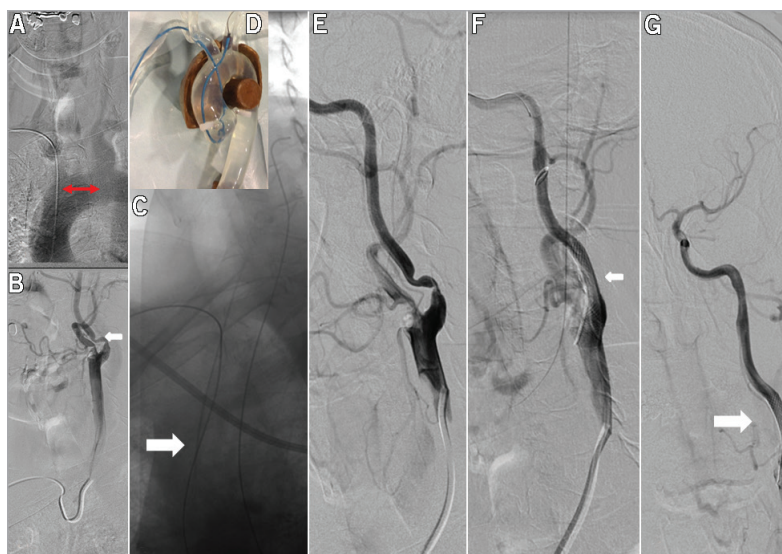


Figure 4. Left ICA stenting in aortic arch type I (loop technique). A 67-year-old patient with level I aorta and left-sided CCA stenosis. Angiography performed with a Simmons I diagnostic catheter revealed a high grade calcified left ICA and ECA lesion (A & B, white arrow). The GW and the XF 40 7 Fr guiding advancement was unsuccessful due to the wide distance between the origin of the left CCA (red arrow). Therefore, the “loop technique” was used with pushing the GW against resistance creating a loop in the aortic arch (C, white arrow). D) shows the loop technique in aortic demonstration model. E) shows the guiding catheter and stent in the left CCA and ICA (white arrow). The left ICA before and after stenting (F & G, white arrow).

ACCESS-SITE BLEEDING

Access-site bleeding was defined as major if associated with a haemoglobin loss of at least 2 mmol/l, administrations of blood transfusions, vascular repair and prolonged hospitalisation, and minor if bleeding at the vascular access site only resulted in haematoma formation and did not require specific therapy.

MAJOR ADVERSE CARDIAC AND CEREBRAL EVENTS (MACCE)

MACCE were assessed as the composite of stroke, death, non-fatal acute myocardial infarction, repeated revascularisation of the target vessel by PTA or vascular operation during the hospital stay and at 30 days.

STROKE

Stroke was defined as an acute neurological event with focal symptoms and signs lasting >24 hrs. Stroke was considered a complication of carotid revascularisation if it occurred within 30 days of the procedure. Independent certified personnel performed baseline and post-procedure neurological assessments on all patients.

Follow-up

Follow-up included a clinical examination during the hospital stay and at one month. All patients without radial artery pulse underwent vascular ultrasound examination.

Statistical analysis

All statistical analysis was performed with the commercially available software STATISTICA version 8.0 (StatSoft Inc., Tulsa, OK, USA). Categorical variables were presented as absolute numbers

and percentages, and continuous variables were expressed as mean±standard deviation or median (with interquartile range) as appropriate. The Shapiro-Wilk test was used for testing the distribution of the data. Proportions were compared using the chi-square test or Fisher's exact test, and continuous variables were compared by t-test or the Mann-Whitney U test as appropriate. Per-protocol (PP) and intention-to-treat (ITT) analysis was performed in the examined population. Probability values lower than 0.05 were considered to be significant.

Results

Two hundred and sixty-five patients were selected for the study, but five patients were excluded because the ICA stenosis severity did not reach the inclusion criteria. Baseline demographic and clinical characteristics of the total study population (n=260) are shown in **Table 1**. Most of the demographic data did not differ significantly between the two groups.

ANGIOGRAPHIC DATA (Table 2)

Angiographic data are summarised in **Table 2**. Arch type III occurred more frequently in the TR group ($p<0.05$), but the stenosis location was not different.

VASCULAR ACCESS AND CROSSOVER (Table 2 and Figure 1)

Successful puncture was achieved in 128 (98.5%) patients in the TR and in 130 patients (100%) in the TF group ($p=ns$). Procedural success was achieved in all patients (100%). The crossover rate was 10% in the TR group (two failed punctures, one radial artery spasm, one radial artery loop, one subclavian artery stenosis, one subclavian

Table 1. Demographic and clinical data.

Demographic and clinical data of all study patients			
	Radial group (n=130)	Femoral group (n=130)	p-value
Age	66.8±8.9	66.7±10.2	0.856
Male (%)	60.8	65.4	0.441
Hypertension (%)	77.7	88.5	0.021
Hyperlipidaemia (%)	56.2	47.7	0.172
Diabetes mellitus (%)	36.2	36.9	0.898
Obesity (%)	14.6	34.6	0.0003
Smoker (%)	28.5	26.9	0.889
Peripheral artery disease (%)	13.9	13.8	1.000
Coronary artery disease (%)	24.6	24.6	0.776
Positive family history (%)	6.9	9.2	0.495
Dialysis (%)	6.2	3.1	0.237

artery tortuosity and six cannulation problems) and 1.5% in the TF group (two iliac artery stenoses) ($p<0.05$). The cannulation failed in the TR group in six patients (5.12%) due to severe angulation of the right CCA origin from the SA (two/six cases) and to severe angulation of the left CCA (three/six cases) or wide distance of the origin of the left CCA from the innominate artery (one/six cases). All crossover patients were successfully treated from the alternative access. The crossover rate proved to be significantly more frequent from the radial than from the femoral artery ($p<0.05$). All TR interventions ($n=130$) were started from the right radial or ulnar artery (129 radial, one ulnar), and TF interventions were performed from the right femoral access in 126 patients (97%) and from the left femoral access in four patients (3%). Crossover examples from the study population are summarised in **Figure 5**.

CAROTID ANGIOPLASTY PROCEDURAL DATA AND EQUIPMENT (Table 2)

Procedure time (1,620 [1,230-2,100] vs. 1,500 [1,080-2,100] sec, $p=ns$) and fluoroscopy time (540 [411-735] vs. 501 [378-702] sec,

$p=ns$) were not significantly different, but the radiation dose was significantly higher in the TR group (195 [129-274] vs. 148 [102-237] Gy*cm², $p<0.05$) by PP analysis. By ITT analysis there was a significantly higher radiation dose in the TR group (195 [130-288] vs. 150 [104-241], $p<0.05$), but no difference in major events (0.9 vs. 0.8, $p=ns$). **Table 3** shows the subgroup analysis of the procedural data in different aortic configurations and right and left-sided lesions. The consumption of diagnostic catheters, guiding catheters and buddy wires was significantly higher in the TF group by both PP and ITT analysis. The consumption of balloon catheters and carotid stents proved to be the same for the two groups (**Table 2**). Hospitalisation days by PP analysis were significantly lower in the TR group (1.17±0.40 vs. 1.25±0.45, $p<0.05$), but by ITT analysis there was no significant difference between the two groups.

Complications

MAJOR ADVERSE CARDIAC AND CEREBRAL EVENTS (Table 3)

The MACCE rate was 0.9% in the TR and 0.8% in the TF group ($p=ns$). A transient neurological deficit that resolved completely within 12 hours was noted in 1/128 patients (0.8%) in the femoral group. No periprocedural TIA was observed in the radial artery group, but one patient (0.9%) died as a result of a major stroke 20 days after the procedure. The rate of MACCE in the total population was not different either by PP or by ITT analysis.

RATE OF ACCESS-SITE COMPLICATIONS (Table 4)

A major access-site complication was encountered in one patient (0.9%) in the TR group (one symptomatic radial artery occlusion in a patient with Buerger's disease) and in one patient (0.8%) in the TF group (one pseudoaneurysm treated successfully with thrombin injection) ($p=ns$). Minor access-site complications occurred in nine patients (7%) in the TR and in six patients (4.7%) in the TF group. The cause of minor vascular complications was small forearm haematoma in one patient (0.8%), and asymptomatic RAO in eight patients (6.8%). There was no occurrence of compartment syndrome in the TR group. There were no instances of peripheral nerve

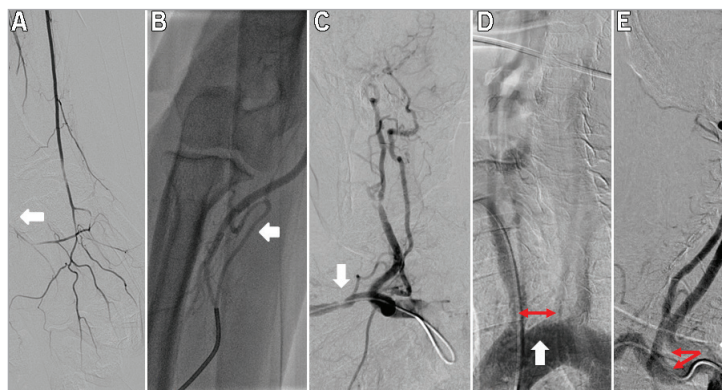


Figure 5. Crossover cases. Radial artery occlusion (A, white arrow), severe radial artery loop (B, white arrow), borderline stenosis in the tortuous SA and sharp angulation between the CCA and the SA (C, white arrow), wide distance between the innominate artery and left CCA (D, red and white arrows), sharp angulation (E, red and white arrows).

Table 2. Angiographic and procedural data.

Angiographic data by per-protocol analysis		Radial group (n=117)	Femoral group (n=128)	p-value
Aortic arch morphology	Arch type I, n (%)	79 (67.5)	108 (84.4)	0.002
	Arch type II-III, n (%)	38 (32.5)	20 (15.6)	0.073
Stenosis localisation	Left-sided, n (%)	50 (42.7)	75 (58.6)	0.013
	Right-sided, n (%)	67 (57.3)	53 (41.4)	
Reference diameter (ICA) (mm)		5.7±0.9	5.7±0.9	0.854
Stenosis diameter (%)		81.9	84.1	0.286
Angiographic data by intention-to-treat analysis		Radial group (n=130)	Femoral group (n=130)	p-value
Aortic arch morphology	Arch type I, n (%)	86 (66.2)	108 (83.1)	0.001
	Arch type II-III, n (%)	44 (33.8)	22 (16.9)	
Stenosis localisation	Left-sided, n (%)	57 (43.8)	76 (58.5)	0.018
	Right-sided, n (%)	73 (56.2)	54 (41.5)	
Reference diameter (ICA) (mm)		5.7±0.9	5.7±0.9	0.592
Stenosis diameter (%)		0.8±0.1(82.6)	0.8±0.1 (84.0)	0.216
Procedural data by per-protocol analysis				
Successful puncture in all patients, n (%)		128 (98.5)	130 (100.0)	0.156
Successful cannulation, n (%)		119 (91.5)	129 (99.2)	0.003
Successful procedure from primary access, n (%)		117 (90.0)	128 (98.5)	0.003
Crossover, n (%)		13 (10.0)	2 (1.5)	0.003
Puncture time (sec)		20 (10-30)	20 (15-30)	0.249
Cannulation time (sec)		62 (30-180)	60 (60-120)	0.842
Procedure time (sec)		1,620 (1,230-2,100)	1,500 (1,080-2,100)	0.298
X-ray dose (mGy)		195 (129-274)	148 (102-237)	0.004
Fluoroscopy time (sec)		540 (411-735)	501 (378-702)	0.160
Contrast volume (ml)		120 (80-149)	103 (81-134)	0.115
Hospitalisation days		1.17±0.40	1.25±0.45	0.006
Procedural data by intention-to-treat analysis				
Puncture time (sec)		20 (10-30)	20 (15-30)	0.457
Cannulation time (sec)		62 (30-180)	60 (60-120)	0.992
Procedure time (sec)		1,650 (1,200-2,100)	1,500 (1,080-2,235)	0.298
X-ray dose (mGy)		195 (130-288)	150 (104-241)	0.003
Fluoroscopy time (sec)		543 (403-759)	513 (378-716)	0.165
Contrast volume (ml)		120 (80-150)	104 (82-137)	0.180
Hospitalisation days		1.4±2.6	1.25±0.45	0.158
Consumption of devices by per-protocol analysis				
Diagnostic catheter/procedure (%)		122 (104.3)	110 (85.9)	0.011
Guide catheter/procedure (%)		108 (92.3)	77 (60.2)	<0.001
Guiding sheath (%)		9 (7.7)	51 (39.8)	<0.001
Buddy wire (%)		45 (38.5)	69 (53.9)	0.016
Balloon/procedure (%)		128 (109.4)	147 (114.8)	0.355
Stent used/procedure (%)		112 (95.7)	126 (98.4)	0.204
Consumption of devices by intention-to-treat analysis				
Diagnostic catheter/procedure (%)		142 (109)	113 (86.9)	0.196
Guide catheter/procedure (%)		119 (91.5)	78 (60.0)	<0.001
Guiding sheath (%)		11 (8.5)	52 (40.0)	<0.001
Buddy wire (%)		75 (57.7)	30 (23.1)	<0.001
Balloon/procedure (%)		142 (109.2)	150 (115.4)	0.748
Stent used/procedure (%)		125 (96.2)	128 (98.5)	0.250

Table 3. Procedural data in different aortic configurations and right- and left-sided lesions.

	Radial group (n=130)		Femoral group (n=130)		p-value
Arch type I (n=194)	Crossover, n (%)	7 (8.1)	Crossover, n (%)	0 (0.0)	0.003
	Procedure time (sec)	1,590 (1,200-2,100)	Procedure time (sec)	1,500 (1,095-2,100)	0.298
	X-ray dose (mGy)	198 (140-288)	X-ray dose (mGy)	140 (105-236)	0.002
	Fluoroscopy time (sec)	540 (400-779)	Fluoroscopy time (sec)	513 (378-696)	0.245
Arch type II-III (n=66)	Crossover, n (%)	6 (13.6)	Crossover, n (%)	2 (0.9)	0.594
	Procedure time (sec)	1,690 (1,260-2,100)	Procedure time (sec)	1,850 (1,035-2,430)	0.995
	X-ray dose (mGy)	181 (123-292)	X-ray dose (mGy)	201 (90-320)	0.854
	Fluoroscopy time (sec)	548 (430-744)	Fluoroscopy time (sec)	495 (373-1,174)	0.634
Right-sided lesion (n=127)	Crossover, n (%)	6 (8.2)	Crossover, n (%)	1 (1.9)	0.120
	Procedure time (sec)	1,560 (1,200-2,100)	Procedure time (sec)	1,500 (1,065-2,100)	0.260
	X-ray dose (mGy)	174 (130-286)	X-ray dose (mGy)	150 (105-252)	0.071
	Fluoroscopy time (sec)	549 (426-719)	Fluoroscopy time (sec)	507 (387-685)	0.303
Left-sided lesion (n=133)	Crossover, n (%)	7 (12.2)	Crossover, n (%)	1 (1.3)	0.009
	Procedure time (sec)	1,700 (1,350-2,100)	Procedure time (sec)	1,500 (1,200-2,280)	0.561
	X-ray dose (mGy)	200 (126-290)	X-ray dose (mGy)	150 (102-230)	0.014
	Fluoroscopy time (sec)	540 (369-851)	Fluoroscopy time (sec)	513 (368-784)	0.366

injury. In the TF group haematoma occurred in six patients (4.7%). The rates of major and minor vascular complications by PP analysis in the total population including the crossover cases were not significantly different (TF group: 2.3% major and 4.6% minor; TR group: 1.5% major and 7.8% minor) (p=ns).

Discussion

TR access was chosen for CAS for patients with severe peripheral artery disease (PAD), iliac artery tortuosity and in cases of difficult CCA cannulation, as in bovine arch; however, many pilot studies have also confirmed the safety and high success rate of the TB³ and TR⁵⁻⁸ access in a non-selected population.

TRANSFEMORAL ACCESS

TF access is the optimal approach for CAS because the catheter engagement is coaxial and therefore cannulation is easy and safe. Another advantage is that TF access allows the use of all proximal and distal protection systems. Despite this easy access route, the femoral access has many limitations and disadvantages. Significant iliac artery tortuosity and stenosis compromise the responsive movement of GWs and catheters, and the precise implantation of the stents. TF access is also difficult in obese patients and in patients with aortic aneurysm. The rates of major and minor vascular complications are still high after transfemoral CAS¹¹. Another limitation is the prolonged immobilisation after the intervention, resulting in decreased patient comfort. Femoral closure devices were introduced into clinical practice to reduce vascular access complications, and to reduce bed rest, but no significant difference in the rate of vascular complications was observed when compared to manual compression¹². Whereas crossing the diseased iliac system has its own risks and challenges, the pathway to the carotid

artery via the aortic arch is where the risks begin to include stroke, the very condition the intervention is intended to prevent. Selective cannulation of the arch vessels is technically the most challenging and critical portion of CAS procedures, and it is especially difficult in level II-III aortic arch, bovine arch, tortuous brachiocephalic artery and ostial stenosis. Catheter manipulations in these cases can cause distal plaque disruption and embolisation. Reducing the risk of stroke during CAS requires a combination of proper patient selection and impeccable technique. Transcranial Doppler (TCD) data from multiple studies have shown that there are emboli to the middle cerebral artery during all phases of the procedure¹³. Faggioli et al found that, during TF, CAS silent cerebral embolisations assessed with diffusion-weighted MRI (DW-MRI) occurred in 57.6% patients both in the contralateral and in the ipsilateral hemisphere (82% contralateral and 18% ipsilateral), suggesting that these embolisations are related not only to the stenting procedure, but also to the cannulation itself¹⁴. Difficult cannulation and anatomically high-risk CAS are associated with an increased number of periprocedural strokes¹⁵, and the majority of the strokes occur during the cannulation.

TRANSBRACHIAL ACCESS

As an alternative route, brachial and axillary access was introduced at first, but these approaches have been associated with a relatively high risk of vascular and nerve complications^{3,16}.

ADVANTAGES OF RADIAL ACCESS

TR access was first introduced by invasive cardiologists for coronary angiography and angioplasty (PCI), and in many centres this is now the first access line for PCI because of a low vascular complication rate, better patient comfort and immediate mobilisation¹⁷⁻¹⁹.

Table 4. Complications.

MACCE by intention-to-treat analysis	Radial group (n=130)	Femoral group (n=130)	p-value
MACCE, n (%)	2 (1.5)	1 (0.8)	0.561
Death	2 (1.5)	0 (0.0)	0.156
Myocardial infarction	0 (0.0)	0 (0.0)	1.000
Reintervention	0 (0.0)	0 (0.0)	1.000
Neurological events (all)	1 (0.8)	1 (0.8)	1.000
Stroke	1 (0.8)	0 (0.0)	0.316
TIA	0 (0.0)	1 (0.8)	0.316
Vascular complications by intention-to-treat analysis			
Minor, n (%)	10 (7.7)	6 (4.6)	0.302
Spasm	0 (0.0)	0 (0.0)	1.000
Haematoma	2 (1.5)	5 (3.8)	0.250
Asymptomatic RAO	8 (6.2)	0 (0.0)	0.004
Other	0 (0.0)	1 (0.8)	0.316
Major, n (%)	2 (1.5)	1 (0.8)	0.561
Symptomatic RAO	1 (0.8)	0 (0.0)	0.316
Bleeding and compartment syndrome	1 (0.8)	1 (0.8)	1.000
Other	0 (0.0)	0 (0.0)	1.000
Total vascular complications, n (%)	12 (9.2)	7 (5.4)	0.234
MACCE by per-protocol analysis	Radial group (n=117)	Femoral group (n=128)	p-value
MACCE, n (%)	1 (0.9)	1 (0.8)	0.949
Death	1 (0.9)	0 (0.0)	0.295
Myocardial infarction	0 (0.0)	0 (0.0)	1.000
Reintervention	0 (0.0)	0 (0.0)	1.000
Neurological events (all)	1 (0.9)	1 (0.8)	0.949
Stroke	1 (0.9)	0 (0)	0.295
TIA	0 (0)	1 (0.8)	0.295
Vascular complications by per-protocol analysis			
Minor, n (%)	9 (7.7)	6 (4.7)	0.327
Spasm	0 (0.0)	0 (0.0)	1.000
Haematoma	1 (0.9)	6 (4.7)	0.072
Asymptomatic RAO	8 (6.8)	0 (0.0)	0.003
Other	0 (0.0)	0 (0.0)	1.000
Major, n (%)	1 (0.9)	1 (0.8)	0.949
Symptomatic RAO	1 (0.9)	0 (0.0)	0.295
Bleeding and compartment syndrome	0 (0.0)	1 (0.8)	0.338
Other	0 (0.0)	0 (0.0)	1.000
Total vascular complications, n (%)	10 (8.6)	7 (5.5)	0.344

The most important advantage of TR access is the low rate of vascular complications, because post-procedural bleeding after acute coronary interventions and in an older population is associated with an increased risk for short- and long-term recurrent bleeding, MACE, and all-cause mortality²⁰. Despite these positive results in acute coronary angioplasty, the association of bleeding complications and

MACE was not investigated during TF CAS. Another advantage of TR access during CAS is the easy cannulation of the left CCA in a patient with bovine aorta or in a patient with an elongated left CCA. The right CCA can be easily cannulated from the right radial access as well, but left CCA cannulation might be difficult⁵⁻⁸. By reducing the amount of manipulation required in the aortic arch, the risk of access-related strokes can be reduced. Etzegeioen et al⁶ published the results of the right radial approach for CAS in 382 patients. The crossover rate was 9% and the stroke rate was 0.13% (two major and three minor strokes). Another advantage of the TR technique is increased comfort due to the ability to sit up after the procedure and the fast mobilisation which results in shortened hospitalisation. Shortened hospitalisation was observed by PP analysis in our radial patients; however, by ITT analysis this benefit of the RA access disappeared, because the patients converted to TF were immobilised longer.

DISADVANTAGES AND COMPLICATIONS OF RADIAL ACCESS

Several complications were reported after TR intervention, including radial artery spasm (RAS), occlusion (RAO), perforation and compartment syndrome, pseudoaneurysm formation, and distal embolisation^{21,22}. RAS is a common problem and in most cases can be prevented with intra-arterial vasodilators and/or hydrophilic guidewires. In our patient population, severe RAS was responsible for crossover in only one case despite sheath upsizing for a 6-7 Fr sheath. Forearm compartment syndrome followed by radial artery perforation can be a serious complication; however, immediate diagnosis and forearm bandage can prevent the occurrence of compartment syndrome in the vast majority of cases^{21,22}. In our study population, only one perforation occurred, and it was treated successfully with arm bandage. RAO is a frequent (1-3%) complication after transradial interventions and has no clinical importance if the palmar arch is complete²³. Asymptomatic RAO occurred in 10% of cases when a large (7-8 Fr) sheath was used in a small series^{24,25}; however, in our study population RAO occurred in only eight patients (6.15%) and only one patient was symptomatic. Uhlemann et al reported a significant increase in RAO when 6 Fr was used (RAO at 5 Fr=14.4% and at 6 Fr=33.1%, $p<0.01$)²⁵ compared with 5 Fr, and symptomatic RAO occurred in 7% of the cases. Of patients with RAO, 59% were treated with low molecular weight heparin (LMWH). The recanalisation rates were significantly higher in patients receiving LMWH compared with conventional therapy (55.6% vs. 13.5%, $p<0.001$) after a mean of 14 days. RAO is asymptomatic in most cases, but there are case reports of symptomatic RAO and successful radial artery recanalisations²⁶. Despite the low incidence of RAO, the radial artery must be preserved for further interventions, and in some cases for RA harvest and Cimino fistula surgery. For this reason, all preventive measures must be taken to prevent RAO, including fast and atraumatic puncture, intra-arterial administration of heparin and verapamil, and the use of a non-occlusive bandage²⁷.

An important disadvantage is the increased radiation exposure during TR access. In our patient population, the radiation dose

was 29% higher in the TR group by PP and 27% by ITT analysis. Mercuri et al²⁸ found that transradial coronary angiography was associated with increased radiation exposure to the patient (23% increase in DAP) when compared with femoral access, but the main criticism of the study was that the centre was not primarily a TR centre. Operator volume and learning curve issues are also powerful mediators of radiation exposure²⁹.

Limitations of transradial access

A limitation of TR access is that the puncture of the RA is sometimes difficult due to the small size of the artery. Another anatomical limitation is the RA loop or tortuosity which makes catheter advancement difficult. In difficult J-tip guidewire advancement, an early selective angiography and the use of a hydrophilic Terumo guidewire (Terumo Co.) solved the problem in most cases in our population. The main limitation of the technique is the difficult cannulation of the CCA which was related in right-sided lesions to the sharp angulation of the bifurcation between the CCA and the right subclavian artery and in left-sided lesions to type I and III aorta. In these situations, the use of a buddy wire and the use of the loop technique solved the problem in most cases. The loop technique failed when the 90 cm long sheath did not reach the CCA ostium and the aortic valve was not strong enough and therefore the sheath jumped in the left ventricle. In these cases, the TR technique was not forced and the procedure was finalised from a TF approach. In all cases using the loop technique, a “cough test” was performed before the intervention.

Study limitations

An important limitation of the study is that microembolisation was not assessed with TCD and diffusion-weighted MRI. Also, the cognitive test was not performed after the procedure. The fairly low number of the patient population may also limit our conclusions.

Take-home message

Radial artery access is recommended for patients with high bleeding risk (obese patients, concomitant peripheral artery disease) and for patients with difficult common carotid artery cannulation (aortoiliac disease or severe tortuosity, bovine arch and type II-III aortic arch). Femoral access should be addressed in patients with type I aortic arch and good femoral access.

Conclusions

The transradial approach for carotid artery stenting is safe and efficacious; however, the crossover rate is higher with transradial access. There are no differences in the total procedure duration and fluoroscopy time between the two approaches, but the radiation dose is significantly higher in the radial group and the hospitalisation is shorter with the use of transradial access by per-protocol analysis. By evaluating the patient data according to intention-to-treat analysis, we found no difference in major adverse events and hospitalisation. In both groups, vascular complications occurred rarely.

Impact on daily practice

We recommend the anatomy-related individualised access strategy for CAS after visualisation of the supra-aortic vessels with CT angiography. In type II-III aorta and in patients with severe PAD the radial access site is preferred but, in patients with type I aorta, the femoral access site is preferred. Despite these promising results, the authors suggest beginners in transradial technique should first start with diagnostic procedures to be familiar with the puncture and crossing the supra-aortic vessels, and should learn the proper cannulation of the CCA with the Simmons catheter.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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