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ORIGINAL ARTICLE

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Perfusion strategy using axillary or femoral cannulation for minimally invasive cardiac surgery: experience in 270 patients with computed tomography-based criteria

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Key question

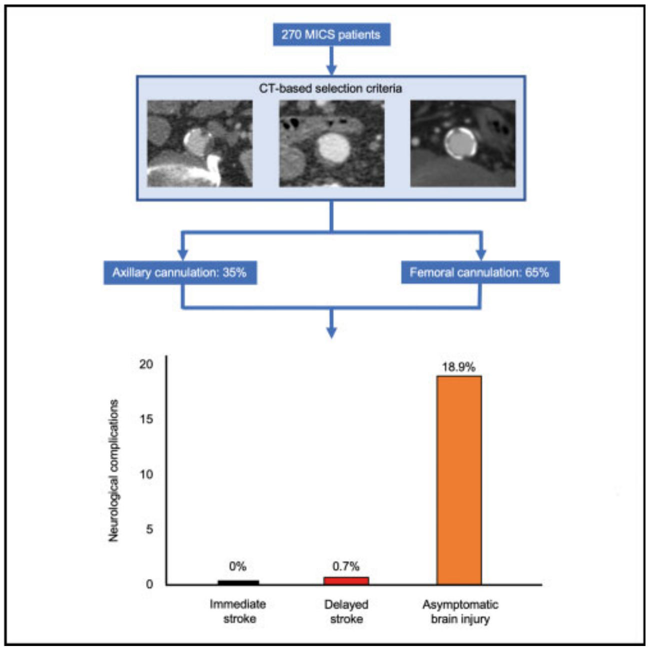
When should retrograde perfusion via femoral cannulation (FC) be avoided in MICS?

Key finding(s)

Using CT-based criteria to select axillary cannulation (AC) or FC, no strokes occurred within 48 h of MICS in 270 patients.

Take-home message

Using CT-based criteria to select AC or FC minimized brain embolisms. AC is a good alternative for patients with advanced atherosclerosis.



Abstract

OBJECTIVES: In patients with atherosclerotic disease, minimally invasive cardiac surgery using retrograde perfusion for cardiopulmonary bypass via femoral cannulation (FC) carries a higher risk of brain embolization compared with antegrade perfusion. However, guidelines for selecting antegrade versus retrograde perfusion do not exist. We developed a computed tomography (CT)-based perfusion strategy and assessed outcomes.

METHODS: We studied 270 minimally invasive cardiac surgery patients, aged 68 ± 13, 124 female, body surface area 1.6 ± 0.2 m^2. Antegrade perfusion using axillary cannulation (AC) was selected if any of the following preoperative enhanced CT scan criteria were satisfied anywhere in the aorta or iliac arteries: thrombosis thickness >3 mm, thrombosis >one-third of the total circumference and calcification present in the total circumference. FC was selected otherwise. Asymptomatic brain injury was assessed by diffusion-weighted magnetic resonance imaging.

RESULTS: AC and FC were selected in 95 (35%) and 175 patients, respectively. AC patients were 10 years older ($P < 0.001$) and had higher EuroSCORE II (2.7 ± 3.4 vs 1.7 ± 1.9, $P = 0.002$). The median cardiopulmonary time and cross-clamp times were not significantly different.

No patients died in hospital. There was no immediate stroke in either group during 48 h after surgery. Asymptomatic brain injury was detected in 25 (26%) and 27 (15%) AC and FC patients, respectively, $P = 0.03$.

CONCLUSIONS: We believe our CT-based perfusion strategy using AC or FC minimized brain embolic rates. AC can be a good alternative to prevent brain embolization for minimally invasive cardiac surgery patients with advanced atherosclerotic disease.

Keywords: Minimally invasive cardiac surgery • Axillary cannulation • Femoral cannulation • Retrograde perfusion • Stroke • Asymptomatic brain injury

ABBREVIATIONS

ABI	Asymptomatic brain injury
AC	Axillary cannulation
CI	Confidence interval
CPB	Cardiopulmonary bypass
CT	Computed tomography
EuroSCORE	European System for Cardiac Operative Risk Evaluation
FC	Femoral cannulation
MICS	Minimally invasive cardiac surgery
MRI	Magnetic resonance imaging
MV	Mitral valve
OR	Odds ratio

INTRODUCTION

Femoral cannulation (FC) for cardiopulmonary bypass (CPB) is a straightforward technique and the most commonly used cannulation in minimally invasive cardiac surgery (MICS) through right minithoracotomy [1, 2]. However, in patients with atherosclerotic disease such as intravascular thrombus or severe calcification, retrograde perfusion via FC carries a higher risk of brain embolization compared with antegrade perfusion [3–5]. However, there are no established guidelines on when to select antegrade or retrograde perfusion for CPB in MICS. Our institution developed uniform criteria based on preoperative enhanced computed tomography (CT) for choosing between antegrade and retrograde perfusion, and have applied them for the past 4 years. Axillary cannulation (AC) was always used to establish antegrade perfusion while FC was used for retrograde perfusion. The aim of the present study was to analyse impact of our perfusion strategy to select either AC or FC on surgical success and brain embolization rates by magnetic resonance imaging (MRI).

PATIENTS AND METHODS

Patients

This study was approved by the institutional review board. All patients provided written consent preoperatively. This was a retrospective study of data collected from 273 MICS patients who underwent postoperative MRI between July 2015 and July 2018. During this period, 33 patients who had MICS were excluded from this study. The reasons were as follows: consent was not obtained, or MRI could not be performed on the 5th day after surgery as per protocol. Reasons for the latter were early patient discharge from the hospital, existence of epicardial pacing wire/pre-existing implanted pacemaker, or patient still being on oxygen.

In the same period, patients who had severe atherosclerotic disease in the ascending aorta, poor cardiac function (left ventricular ejection fraction < 30%), severe renal dysfunction (estimated glomerular filtration rate < 30 ml/min/1.73 m^2), history of right thoracotomy, or poor lung function (forced expiratory volume during the first second < 1 l) were excluded as candidates for MICS. We note that 5 patients with severe atherosclerotic disease in the ascending aorta were excluded; however, patients who had severe atherosclerosis in arteries other than the ascending aorta were not excluded. Three MICS patients who required bilateral FC, FC plus AC, and ascending aortic cannulation to maintain minimum perfusion (2.2 l/m^2) were excluded. The remaining 270 patients were included in this study. They received either right-sided AC or unilateral FC (mainly the right side) for perfusion during CPB. To analyse the impact of our perfusion strategy on surgical success and complication rates, we investigated hospital mortality, postoperative complications, and neurological complications including asymptomatic brain injury (ABI) using MRI. In addition, we split patients into those receiving AC and FC, and compared patient characteristics, intraoperative data, postoperative results and MRI findings.

Perfusion strategy

Preoperative enhanced CT scanning was performed in all patients. Axial images with slice thickness of 1.0 mm and sagittal images of 5.0 mm with thickness of 5.0 mm were used, and atherosclerotic disease of the entire aorta and iliac arteries was evaluated. Either AC for antegrade perfusion or FC for retrograde perfusion was selected by applying the same systematic selection criteria. AC was selected if any of the following criteria were satisfied in the aorta or an iliac artery at any point: (i) thickness of the thrombosis is > 3 mm (Fig. 1A); (ii) thrombosis is more than one-third of total circumference (Fig. 1B); and (iii) calcification present in the total circumference (Fig. 1C). FC was selected in the remaining patients. No other preoperative factors were considered for selection criteria.

Magnetic resonance imaging study

To detect ABI, all patients received 2 MRI studies including diffusion-weighted imaging sequences the day before and 5 days after the surgery. A high field-strength (3T) MRI unit was used. Images studied included axial T2-weighted images, axial T2-weighted FLAIR images, trace diffusion-weighted images, and apparent diffusion coefficient images. All images were evaluated by a diagnostic radiologist. When lesions were detected, neurosurgeons were consulted. Our definition of perioperative stroke included any new temporary or permanent symptomatic neurological deficit. Immediate stroke was defined as stroke which occurred up to 48 h postoperatively, while delayed stroke was defined as stroke which occurred later than 48 h. ABI was defined

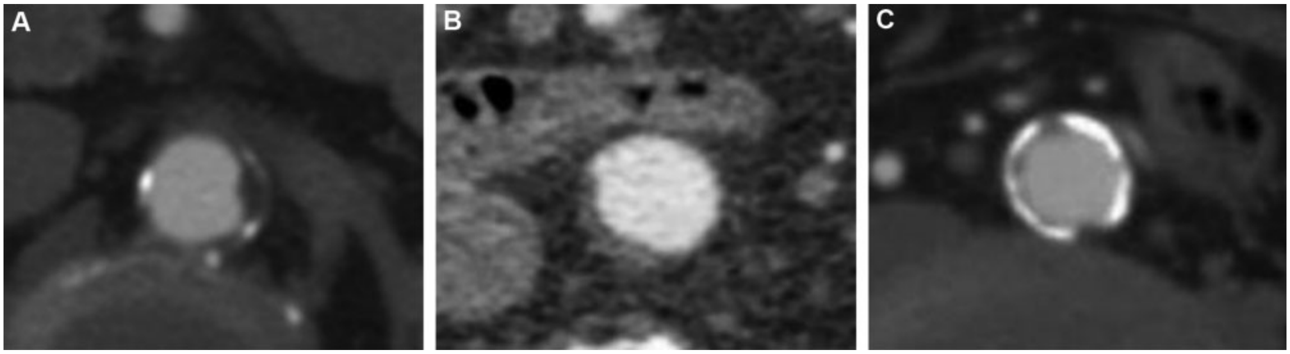


Figure 1: Representative computed tomographic images of selection criteria. (**A**) Thickness of the thrombosis is >3 mm in the aorta or iliac artery; (**B**) thrombosis is more than one-third of total circumference of the aorta or iliac artery; (**C**) calcification present in the entire circumference of the aorta or iliac artery.

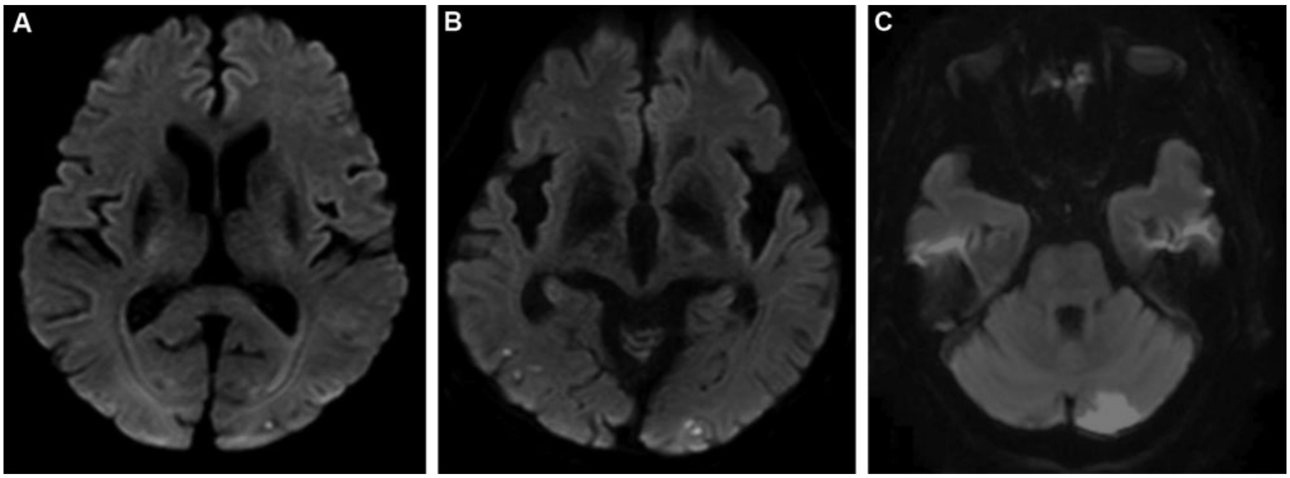


Figure 2: Examples of images of asymptomatic brain injury (ABI) in 3 categories. (**A**) 1–3 ABIs < 10 mm, (**B**) >3 ABIs < 10 mm, (**C**) any ABI > 10 mm.

as new focal diffusion abnormalities detected as bright lesions by postoperative MRI (diffusion-weighted image) unaccompanied by any neurological deficit. In addition, ABI was categorized following the example of Platz *et al*. [6] as follows: (A) 1–3 ABIs < 10 mm, (B) > 3 ABIs < 10 mm, (C) any ABI > 10 mm (Fig. 2).

Statistical analysis

Continuous data are presented as mean ± standard deviation and were analysed using a Student's *T*-test for independent samples. Categorical variables are given as frequencies and percentages and were compared using χ^2 or Fisher's exact tests. Two-sided *P*-values were used and $P < 0.05$ was considered statistically significant. Logistic regression analysis was performed to identify factors that were associated with ABI. The univariable model included preoperative patients' characteristics, cross-clamp time and CPB time, and AC. Variables were entered into the multivariable model based on the *P*-value of 0.157, excepting AC and cross-clamp time, which were included based on clinical relevance [7]. The least significant variables were then eliminated and variables at the 0.05 level were retained. All data were analysed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Surgical procedure

After general anaesthesia with differential lung ventilation, patients were placed in a 30–40° left lateral position with a pillow under the right thorax. A right lateral minithoracotomy, 5–6 cm in length, was performed in the 4th intercostal space, with the incision placed 2–3 cm lateral to the nipple in males, and in the sub-mammary crease in females. After dissecting the space under the pectoralis major muscle anteriorly, a thoracotomy incision was made through the 3rd intercostal space in aortic valve replacement procedures and in the 4th intercostal space in all other procedures. When selection criteria of AC were met, CPB was established by right axillary artery (cannula PCKC-A, MERA, Tokyo, Japan) and percutaneous femoral vein (cannula HLS Cannulae, Maquet, Rastatt, Germany) cannulations. For femoral artery cannulation, the right artery was used in the majority of cases. The axillary artery was exposed through a 3-cm skin incision made from the caudal to a point roughly two-thirds lateral of the clavicle. The pectoralis major muscle was separated along its fibre orientation, and then the pectoralis minor was incised. The artery was gently retracted from the surrounding tissue with a tape. If the selection criteria of AC were not met, the femoral artery (cannula PCKC-A, MERA, Tokyo, Japan) and femoral vein (cannula HLS Cannulae, Maquet, Rastatt, Germany) were cannulated through a 3-cm skin incision in the groin. Both FC and AC were performed by modified Seldinger technique via a purse-string suture. The femoral venous cannulation was performed under transoesophageal echocardiography guidance. Vacuum assistance was used for venous drainage. Perfusion was controlled between 2.2 and 2.6 l/m^2. The lowest blood temperature during CPB was 32°C. After insertion of the aortic root cannula, the ascending aorta was cross-clamped using a Cygnet flexible clamp (Vitalitec Inc., Plymouth, MA, USA) through the main incision. All procedures were performed under direct vision with thoracoscopic assistance. All sutures were tied down with the aid of a knot pusher. In all cases, antegrade cardioplegia was delivered through a root cannula into the aortic root through an aortic root needle. CO_2 insufflation into the right thoracic cavity was performed with a flow of 5 l/min. In cases of aortic valve surgery, air removal was performed through vents that was placed in the aortic root and left ventricle, and in mitral valve (MV) surgery, with a vent in the aortic root. Air removal was continued until all air bubbles inside the left heart chambers were gone. All patients were transferred to the intensive care unit where they were extubated. The chest drains were removed when the discharge decreased to <50 ml per 12 h.

RESULTS

Patient characteristics

Baseline patient characteristics are summarized in Table 1. Mean age was 68 ± 13 years old. Mean EuroSCORE II (European System for Cardiac Operative Risk Evaluation) was 2.1 ± 2.6. AC was selected in 95 (35.2%) patients (AC group), while FC was selected in the remaining 175 (64.8%) patients (FC group). Compared to the FC group, patients in the AC group were 10 years older on average (75 ± 8 vs 65 ± 14, $P < 0.001$) and EuroSCORE II was significantly higher (2.7 ± 3.4 vs 1.7 ± 1.9, $P = 0.002$). With the exception of a significantly higher prevalence of hypertension [65 (68%) vs 90 (51%), $P = 0.005$] and chronic kidney disease [18 (19%) vs 14 (8%), $P = 0.008$] in the AC group, no significant differences were found in risk factors between the 2 groups.

Intraoperative data

Intraoperative data are summarized in Table 2. Isolated aortic valve replacement and isolated MV surgery (repair/replacement) comprised 83% (223/270) of all procedures. Double-valve surgery and triple-valve surgery were 12% (33/270) and 1% (3/270), respectively. Twenty-one percent (33/270) of patients underwent concomitant procedures (Maze procedure, patent foramen closure, left atrial appendage closure). Compared to the FC group, the AC group had more isolated aortic valve replacement [51 (54%) vs 66 (38%), $P = 0.008$] and less isolated MV surgery [29 (31%) vs 78 (38%), $P = 0.02$]. There were no differences between the 2 groups in other procedures performed. There was no conversion to sternotomy in either group. Procedure time, CPB time and cross-clamp time were not significantly different between the 2 groups.

Postoperative data

Postoperative data are summarized in Table 3. There was no in-hospital mortality overall. The AC group had 1 respiratory failure (1.1%). Acute kidney failure occurred in 4 (4.2%) patients in the AC group and 5 (2.9%) patients in the FC group. Rates of atrial fibrillation were 20% and 14% in the AC and FC groups, respectively. There were no significant differences in the postoperative complications. While significantly more chest tube output ($P = 0.02$) was observed in the AC group, timing of the chest tube removal was not different. Significantly longer postoperative ventilation time ($P = 0.004$) and higher prevalence of blood transfusion was seen in the AC group ($P < 0.001$). There was no complication associated with the cannulation itself except for one superficial infection in each group.

Neurological complications and asymptomatic brain injury in magnetic resonance imaging study

There was no immediate stroke in either group (Table 4). There were 2 (0.7%) delayed strokes overall. The FC group experienced no delayed strokes. The AC group had 2 (2.1%) delayed strokes, which occurred on postoperative day 3. Both patients had bouts of paroxysmal atrial fibrillation several times during the 6 h before their stroke, and PT-INR had not reached therapeutic range even though oral anticoagulation with a vitamin K antagonist had already been commenced on postoperative day 1. Intravenous heparin had not yet been commenced at that time,

Table 1: Patient characteristics

	All ($n = 270$)	AC ($n = 95$)	FC ($n = 175$)	P-value
Age (years)	68 ± 13	75 ± 8	65 ± 14	<0.001
Female	124 (45.9)	41 (43.1)	83 (47.4)	0.27
BSA (m^2)	1.6 ± 0.2	1.5 ± 0.1	1.6 ± 0.2	0.07
Hypertension	155 (57.4)	65 (68.4)	90 (51.4)	0.01
NYHA class III or IV	99 (36.7)	37 (38.9)	62 (35.4)	0.33
Diabetes	35 (13.0)	16 (16.8)	19 (10.9)	0.11
History of cerebral infarction	11 (4.1)	5 (5.2)	6 (3.4)	0.33
COPD	8 (3.0)	2 (2.1)	6 (3.4)	0.42
Atrial fibrillation	32 (11.9)	9 (9.4)	23 (13.1)	0.25
Chronic kidney disease	32 (11.9)	18 (18.9)	14 (8.0)	0.01
Infective endocarditis	7 (2.6)	2 (2.1)	5 (0.3)	0.53
LVEF (%)	68 ± 10	64 ± 10	66 ± 10	0.08
Prior cardiac surgery	5 (1.9)	3 (3.2)	2 (1.1)	34
EuroSCORE II (%)	2.1 ± 2.6	2.7 ± 3.4	1.7 ± 1.9	0.002

Values for continuous variables are presented as mean ± standard deviation and values for categorical variables are presented as *n* (%).

AC: axillary cannulation; BSA: body surface area; COPD: chronic obstructive pulmonary disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; FC: femoral cannulation; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Table 2: Intraoperative data

	All (*n* = 270)	AC (*n* = 95)	FC (*n* = 175)	*P*-value
Primary surgical procedure				
Isolated AVR	116 (43.0)	51 (53.7)	66 (37.8)	0.01
Isolated MV surgery	107 (40.0)	29 (30.5)	78 (38.3)	0.02
Repair	92 (34.0)	23 (24.2)	69 (37.3)	0.23
Replacement	15 (5.6)	6 (6.3)	9 (6.0)	
Double valve	32 (11.9)	12 (12.6)	20 (11.4)	0.46
MV surgery + AVR	9 (3.3)	5 (5.6)	4 (2.3)	0.24
MV surgery + TAP	23 (8.5)	7 (7.4)	16 (9.1)	
Triple valve (AVR + MV surgery + TAP)	3 (1.1)	2 (2.1)	1 (0.6)	0.28
ASD closure	6 (2.2)	1 (1.1)	5 (2.9)	0.67
Myxoma resection	5 (1.9)	0	5 (2.9)	0.11
Concomitant procedure	57 (21.1)	21 (22.1)	36 (17.1)	0.44
Maze	33 (12.2)	11 (11.6)	22 (12.6)	0.79
PFO closure	9 (3.3)	4 (4.2)	5 (2.9)	
Left atrial appendage closure	15 (5.6)	6 (6.3)	9 (6.0)	
Conversion to sternotomy	0	0	0	NA
Cannula size (French)	16.6 ± 1.1	16.5 ± 1.0	16.7 ± 1.6	0.23
Side branch	6 (2.2)	1 (1.1)	5 (2.9)	0.67
Procedure time (min)	218 ± 49	222 ± 50	215 ± 50	0.3
CPB time (min)	135 ± 38	140 ± 35	132 ± 39	0.11
Cross-clamp time (min)	105 ± 35	108 ± 32	103 ± 37	0.25

Values for continuous variables are presented as mean ± standard deviation and values for categorical variables are presented as *n* (%).

AC: axillary cannulation; ASD: atrial septal defect; AVR: aortic valve replacement; CPB: cardiopulmonary bypass; FC: femoral cannulation; MV: mitral valve; NA: not assessed; PFO: patent foramen ovale; TAP: tricuspid annuloplasty.

Table 3: Postoperative data

	All (*n* = 270)	AC (*n* = 95)	FC (*n* = 175)	*P*-value
Hospital mortality	0	0	0	NA
Complication				
Low cardiac output syndrome	0	0	0	NA
Myocardial infarction	0	0	0	NA
Re-exploration	2 (0.7)	0	2 (1.1)	0.42
Respiratory insufficiency	1 (0.4)	1 (1.1)	0	0.35
Gastrointestinal bleeding	0	0	0	NA
Acute kidney injury	9 (3.3)	4 (4.2)	5 (2.9)	0.4
Atrial fibrillation	41 (15.2)	16 (20.0)	25 (14.2)	0.15
Complication associated with cannulation				
Vascular injury	0	0	0	NA
Extremity compartment syndrome	0	0	0	NA
Superficial infection	2 (0.7)	1 (1.1)	1 (0.5)	0.65
Aortic dissection	0	0	0	NA
Seroma	0	0	0	NA
Ventilation time (h)	9.5 ± 5.8	10.9 ± 6.4	8.8 ± 5.4	0.004
Chest tube output (in 24 h) ml	192 ± 183	233 ± 207	171 ± 165	0.02
Timing of chest tube removal (day)	1.7 ± 1.1	1.9 ± 1.3	1.6 ± 1.0	0.09
Blood transfusion	69 (25.6)	35 (36.8)	34 (19.4)	<0.001

Values for continuous variables are presented as mean ± standard deviation and values for categorical variables are presented as *n* (%).

AC: axillary cannulation; FC: femoral cannulation; NA: not assessed.

because the patients had not met institutional criteria for receiving heparin. Therefore, we deemed their strokes as likely due to the atrial fibrillation.

In contrast to the low rate of stroke, comparison of pre- and postprocedural MRI revealed an overall ABI rate of 18.9% (51/270). A significantly higher incidence of ABI was seen in the AC group (26% vs 15%, $P = 0.03$). As for localization of lesions, roughly 3% of both AC and FC patients had bilateral lesions. Laterality of lesions was skewed, with left hemisphere involvement (bilateral count + left hemisphere only count) more common in AC patients and right hemisphere involvement (bilateral count + right hemisphere only count) more common in FC patients (X^2 = 4.45, $P = 0.04$). Most patients were categorized as A (45/51, 88.2%). There was no significant difference in number of patients in each category between the AC and FC groups. Predictors of ABI on logistic regression analysis included age over 70 years [odds ratio (OR) 2.08, 95% confidence interval (CI) 1.02–4.27, $P = 0.01$], diabetes (OR 2.55, 95% CI 1.16–5.58,

Table 4: Neurological complications and asymptomatic brain injury

	All (*n* = 270)	AC (*n* = 95)	FC (*n* = 175)	*P*-value
Stroke	2 (0.7)	2 (2.1)	0	0.12
Immediate	0	0	0	NA
Delayed stroke (after 48 h)	2 (0.7)	2 (2.1)	0	0.12
ABI	51 (18.9)	25 (26.3)	26 (15.4)	0.03
Laterality of ABI				
Bilateral hemisphere	9 (3.3)	3 (3.2)	6 (3.4)	0.03
Right hemisphere	19 (7.0)	6 (6.3)	13 (7.4)	
Left hemisphere	23 (8.5)	16 (16.8)	7 (4.0)	
Right hemisphere involvement	28 (10.4)	9 (9.5)	19 (10.9)	0.04
Left hemisphere involvement	32 (11.8)	19 (20.0)	13 (7.4)	
Category of ABI				
A (1–3 ABIs <10 mm)	45 (16.7)	21 (22.1)	24 (13.7)	0.34
B (>3 ABIs <10 mm)	4 (1.4)	2 (2.1)	2 (1.1)	
C (single ABI >10 mm)	2 (0.7)	2 (2.1)	0	
Asymptomatic subdural haematoma	1 (0.3)	0	1 (0.6)	1.00

Values for categorical variables are presented as *n* (%).
ABI: asymptomatic brain injury; AC: axillary cannulation; FC: femoral cannulation; NA: not assessed.

Table 5: Logistic regression analysis to identify predictors of asymptomatic brain injury

Variables	Univariable Odds ratio (95% CI)	*P*-value	Mutivariable Odds ratio (95% CI)	*P*-value
Age over 70 years	2.52 (1.36–4.69)	0.004	2.08 (1.02–4.27)	0.01
Male	1.25 (0.71–2.21)	0.44		
Hypertension	2.16 (1.17–3.98)	0.01	1.84 (0.97–3.50)	0.06
Diabetes	2.98 (1.42–6.27)	0.004	2.55 (1.16–5.58)	0.02
COPD	2.05 (0.48–8.84)	0.33		
Chronic kidney disease	1.08 (0.46–2.53)	0.86		
Infective endocarditis	4.70 (1.02–21.55)	0.04	5.87 (1.14–30.32)	0.04
Atrial fibrillation	1.57 (0.74–3.32)	0.24		
EuroSCORE II	1.03 (0.93–1.14)	0.59		
Axillary artery cannulation	1.51 (0.84–2.70)	0.17	0.99 (0.51–1.96)	0.99
Cross-clamp time >120 min	1.62 (0.81–3.26)	0.18	1.39 (0.63–3.06)	0.41
Cardiopulmonary bypass time >150 min	1.50 (0.76–2.97)	0.24		

CI: confidence interval, COPD: chronic obstructive pulmonary disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation.

P = 0.02) and infective endocarditis (OR 5.87, 95% CI 1.14–30.32, *P* = 0.04) (Table 5).

DISCUSSION

MICS using systematic perfusion strategy to select either AC or FC was associated with excellent surgical outcomes and low risk of neurological complications including ABI. According to our selection criteria, roughly a third of patients were assigned to antegrade perfusion by AC, and the remaining patients to retrograde perfusion by FC. Symptomatic sequelae were limited to 2 strokes in the AC patient group at 3 days postoperatively, both of which were likely due to paroxysmal atrial fibrillation rather than CPB use. We believe our study is unique on several points. Firstly, we found FC to be a relatively safe cannulation procedure using our criteria for when to avoid employing FC. There were no strokes in FC, and ABI was seen in 15%. That is not to say that FC could not have been safely employed in some of our AC cases. What we are saying is that our FC selection criteria set a minimal standard of when it is safe to employ FC. Secondly, outcomes of AC were not as poor as might be expected from the higher atherosclerotic state of the subpopulation selected to receive AC. Thirdly, we were able to demonstrate hitherto speculated laterality in ABI distribution, with left hemisphere more common in AC, based on 270 postprocedure MRI comparisons.

In the decade since 2010, several reports showed that MICS using retrograde perfusion had higher rates of neurological complications compared to conventional sternotomy [2, 3, 8, 9]. A consensus statement of the International Society of Minimally Invasive Coronary Surgery 2010 reported that the risk of stroke in MV surgery was higher with MICS versus conventional surgery (2.1% vs 1.2%) [2]. Thereafter, several high-volume centres began to use antegrade perfusion by direct ascending aortic cannulation [3, 5]. Murzi *et al.* [5] showed that retrograde perfusion by FC was associated with a higher incidence of stroke (5 vs 1%; *P* = 0.002) and postoperative delirium (14 vs 5%, *P* = 0.001). However, they also reported that no significant difference in stroke rate was observed when limiting data to patients younger than 70 years (OR 0.85; $P = 0.24$) [8]. Similarly, Grossi *et al.* [3] reported that MICS with retrograde perfusion was associated with increased risk of neurological complication in older patients. The same team reported that retrograde perfusion was associated with an increased risk of stroke in patients with peripheral vascular disease and diseased aorta [4]. Through these experiences, it became clear that patient selection was critically important for MICS using retrograde perfusion. However, no specific criteria have been developed for avoiding retrograde perfusion in MICS. At most institutions, it is up to each surgeon to determine cannulation site for individual patients [5, 10, 11, 12]. This is the first report to address systematic criteria for selecting antegrade or retrograde perfusion in MICS. We have employed these selection criteria since 2014. We selected the criteria based on our experience with 1100 thoracic aortic surgeries with CPB using FC, AC or both, over a period of 10 years. In thoracic aortic surgery, retrograde perfusion was often contraindicated due to atherosclerosis of the aortoiliac system; we had aggressively used AC in such cases. In the beginning, however, we had not used systematic criteria to select the cannulation site. It was left to each surgeon to determine cannulation site for individual patients based on experience and preference, and stroke rate was 5%. Nevertheless, over this decade, our surgeons gradually came to have similar views on when it was risky to use FC. This led to a meeting and construction of a uniform set of CT criteria for cannulation site selection. In this report, we retrospectively assessed the impact of our systematic criteria on MICS. We believe these criteria will be useful to others to prevent neurological complications and help surgeons to plan surgical strategy in MICS.

According to our selection criteria, rate of AC candidacy was 35%. Modi and Chitwood [13] suggested in their perspective article that grades IV/V atherosclerotic disease (using grading by Ribakove *et al.* [14]) anywhere along the aortoiliac system could increase the risk of stroke; however, they did not show any supporting clinical data. The grading reported by Ribakove *et al.* [14] was as follows. Atherosclerotic disease of the aorta was graded by transoesophageal echocardiography in patients undergoing open heart surgery: grade I = minimal intimal thickening; II = extensive intimal thickening; III = sessile atheroma; IV = protruding atheroma; and V = mobile atheroma (Ribakove). Our CT-based selection criteria for assignment to AC approximate Ribakove's grades III, IV and V. In their report, prevalence of grades III, IV and V totalled 30.2%, and is similar to rate of patients who received AC (35%) in our report.

The prevalence of ABI as assessed by MRI was 19% in our study patients. Although the clinical impact of ABI on intrahospital course is negligible, ABI should not be overlooked in regard to long-term neurological function. Several studies have demonstrated that ABI is correlated with postoperative cognitive deterioration and dementia [15–17]. A review article made a simple calculation of the incidence of ABI after cardiac surgery through median sternotomy using data from 13 published reports, and the result was 29% [15]. Even after coronary angiography and stenting, the prevalence has been reported to be 29% [18]. Compared to these previous studies, the prevalence of ABI was low in this study. One reason may be that patients who had severe atherosclerosis in the ascending aorta were excluded as MICS candidates. We speculate also that in MICS, CO_2 accumulates in the right pleural cavity compared with median sternotomy, and this prevents intracardiac air and therefore air embolism to the brain.

The AC group had significantly higher incidence of ABI than the FC group (26% vs 15%). However, AC was not found to be a significant risk factor for ABI on univariate analysis. We believe this is because the CT-based selection criteria led to more patients with advanced atherosclerotic disease being assigned to the AC group. Multivariable analysis showed that age over 70 years, hypertension, diabetes, and infective endocarditis were independent risk factors of ABI. Most of them were consistent with risk factors for atherosclerotic disease.

If patients in the AC group had been assigned to FC, we surmise that ABI and stroke rates would have been even higher. MICS through right minithoracotomy is performed in the left decubitus position. Therefore, intracardiac air and small light debris may travel easily into the right cranial hemisphere through the brachiocephalic artery after declamping. Interestingly, however, laterality of ABI lesions was skewed with the AC group producing more ABI in the left hemisphere. We believe the reason for the difference is that the embolism due to air or debris from the heart can be blocked by backward flow inside the brachiocephalic artery in patients with AC. AC is an uncommon cannulation site in MICS, and its safety relative to FC has not been fully investigated. In thoracic aortic surgery, AC has been commonly used for patients with atherosclerotic disease in the aorta to prevent brain embolization [19–22]. It has been speculated that AC has haemodynamic effects that prevent stroke in the right hemisphere in several publications [19, 20]. In addition, our complication rate in AC was low; only one superficial infection occurred in this study. We believe therefore, that AC can be safely and effectively used to prevent brain embolization in MICS patients with advanced atherosclerotic disease. We do not use AC for lower risk MICS patients (those without advanced atherosclerotic disease) because there are 3 disadvantages of AC. Firstly, we need to make an incision in the pectoralis minor, which is more invasive than for FC, and exposing the axillary artery creates a scar on the anterior surface of the chest which is a part of the body more likely to be seen in public. Secondly, in AC, femoral vein cannulation is percutaneous. In some patients, the femoral vein is located behind the femoral artery, making percutaneous cannulation technically difficult compared to exposing the femoral vein and cannulating it from a skin incision in the groin. Thirdly, in FC, one operator can be working on the minithoracotomy, while another is exposing the femoral artery, but in the case of AC, the minithoracotomy and axillary artery exposure have to be done sequentially, and this adds to procedure time. Therefore, we recommend FC as the first choice for low-risk patients.

Limitations

There are several limitations to this study. It was a nonrandomized retrospective observational study. The baseline characteristics of the patients differed between AC and FC, with AC patients being older and having higher atherosclerotic burden. The surgical procedures for which the patients received MICS were not evenly distributed over AC and FC, with AC patients having more isolated aortic valve surgery and FC patients having more isolated MV surgery. For ethical reasons, we did not have a patient group who received FC despite having advanced atherosclerosis, so we were unable to prove that AC resulted in better outcomes for such patients. Lastly, we compared the results of 2 different groups treated with 2 different strategies in our study, so the interpretation of the results is not straightforward. For example, our results cannot be used to compare the relative benefits of AC versus FC directly and say which is better, However, we feel it is clinically useful to know that good outcomes both obvious (stroke incidence) and hidden (ABI) can be obtained with AC in patients with advanced atherosclerosis as defined by CT criteria.

CONCLUSIONS

Surgical outcomes and brain embolization rate were satisfactory in MICS patients using our perfusion strategy based on preoperative CT to select either AC or FC. AC can be a good alternative to prevent brain embolization for MICS patient with advanced atherosclerotic disease.

Conflict of interest: none declared.

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Author contributions

Yoshitsugu Nakamura: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Visualization; Writing—original draft; Writing—review & editing. **Shuhei Nishijima:** Data curation; Investigation; Writing—review & editing. **Miho Kuroda:** Data curation. **Taisuke Nakayama:** Data curation. **Ryo Tsuruta:** Data curation. **Daiki Yoshiyama:** Data curation. **Yuto Yasumoto:** Data curation. **Yujiro Ito:** Data curation.

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REFERENCES

[1] Lamelas J, Williams RF, Mawad M, LaPietra A. Complications associated with femoral cannulation during minimally invasive cardiac surgery. Ann Thorac Surg 2017;103:1927–32.

[2] Cheng DC, Martin J, Lal A, Diegeler A, Folliguet TA, Nifong LW *et al.* Minimally invasive versus conventional open mitral valve surgery: a meta-analysis and systematic review. Innovations (Phila) 2011;6: 84–103.

[3] Grossi EA, Loulmet DF, Schwartz CF, Solomon B, Dellis SL, Culliford AT *et al.* Minimally invasive valve surgery with antegrade perfusion strategy is not associated with increased neurologic complications. Ann Thorac Surg 2011;92:1346–9.

[4] Grossi EA, Loulmet DF, Schwartz CF, Ursomanno P, Zias EA, Dellis SL *et al.* Evolution of operative techniques and perfusion strategies for minimally invasive mitral valve repair. J Thorac Cardiovasc Surg 2012; 143:S68–70.

[5] Murzi M, Cerillo AG, Miceli A, Bevilacqua S, Kallushi E, Farneti P *et al.* Antegrade and retrograde arterial perfusion strategy in minimally invasive mitral-valve surgery: a propensity score analysis on 1280 patients. Eur J Cardiothorac Surg 2013;43:e167–72.

[6] Platz J, Wagner M, Güresir E, You SJ, Konczalla J, Rochemont RM *et al.* Early diffusion-weighted MRI lesions after treatment of unruptured intracranial aneurysms: a prospective study. J Neurosurg 2017;126: 1070–8.

[7] Heinze G, Dunkler D. Five myths about variable selection. Transpl Int 2017;30:6–10.

[8] Murzi M, Cerillo AG, Gasbarri T, Margaryan R, Kallushi E, Farneti P *et al.* Antegrade and retrograde perfusion in minimally invasive mitral valve surgery with transthoracic aortic clamping: a single-institution experience with 1632 patients over 12 years. Interact CardioVasc Thorac Surg 2017;24:363–8.

[9] Gammie JS, Zhao Y, Peterson ED, O'Brien SM, Rankin JS, Griffith BP. Less-invasive mitral valve operations: trends and outcomes from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Ann Thorac Surg 2010;90:1401–8.

[10] Sakaguchi T. Minimally invasive mitral valve surgery through a right mini-thoracotomy. Gen Thorac Cardiovasc Surg 2016;64:699–706.

[11] Algarni KD, Suri RM, Schaff H. Minimally invasive mitral valve surgery: does it make a difference? Trends Cardiovasc Med 2015;25:456–65.

[12] Nakajima H, Takazawa A, Tounaga C, Yoshitake A, Tochii M, Hayashi J *et al.* Comparison of the efficacy of transthoracic cannulation into the ascending aorta versus femoral artery cannulation in minimally invasive cardiac surgery. Innovations (Phila) 2019;14:537–44.

[13] Modi PW, Chitwood JR. Retrograde femoral arterial perfusion and stroke risk during minimally invasive mitral valve surgery: is there cause for concern? Ann Cardiothorac Surg 2013;2:E1.

[14] Ribakove GH, Katz ES, Galloway AC, Grossi EA, Esposito RA, Baumann FG *et al.* Surgical implications of transesophageal echocardiography to grade the atheromatous aortic arch. Ann Thorac Surg 1992;53:758–63.

[15] Sun X, Lindsay J, Monsein LH, Hill PC, Corso PJ. Silent brain injury after cardiac surgery: a review: cognitive dysfunction and magnetic resonance imaging diffusion-weighted imaging findings. J Am Coll Cardiol 2012;60: 791–7.

[16] Vermeer SE, Prins ND, den Heijer T, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and the risk of dementia and cognitive decline. N Engl J Med 2003;348:1215–22.

[17] Knipp SC, Matatko N, Wilhelm H, Schlamann M, Massoudy P, Forsting M *et al.* Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neuropsychological assessment and diffusion-weighted magnetic resonance imaging. Eur J Cardiothorac Surg 2004;25: 791–800.

[18] Göksülük H, Güleç S, Özyüncü N, Kürklü ST, Vurgun VK, Candemir B *et al.* Comparison of frequency of silent cerebral infarction after coronary angiography and stenting with transradial versus transfemoral approaches. Am J Cardiol 2018;122:548–53.

[19] Kim J-H, Lee SH, Lee S, Youn Y-N, Yoo K-J, Joo H-C. Axillary artery cannulation reduces early embolic stroke and mortality after open arch repair with circulatory arrest. J Thorac Cardiovasc Surg 2020;159:772–8.

[20] Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H *et al.* 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The task force for the diagnosis and treatment of aortic diseases of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2873–926.

[21] Numata S, Ogino H, Sasaki H, Hanafusa Y, Hirata M, Ando M *et al.* Total arch replacement using antegrade selective cerebral perfusion with right axillary perfusion. Eur J Cardiothorac Surg 2003;23:771–5.

[22] Carino C, Mori M, Pang PYK, Singh M, Elkinany S, Tranquilli M *et al.* Direct axillary cannulation with open Seldinger-guided technique: is it safe? Eur J Cardiothorac Surg 2018;53:1279–81.