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Silent brain infarction after minimally invasive cardiac surgery with retrograde perfusion

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Abstract

Background and Aim: There is no report on silent brain infarction (SBI) after minimally invasive cardiac surgery (MICS) with retrograde perfusion. Thus, the current study aimed to investigate the incidence of SBI after MICS using magnetic resonance imaging (MRI).

Methods: This study included 174 patients who underwent MICS with retrograde perfusion between July 2014 and July 2018. Preoperative computed tomography (CT) angiography was routinely performed and vascular pathology was evaluated for patient selection. Postoperative MRI was performed to investigate the occurrence of SBI.

Results: Out of the total 174 patients, 26 (14.9%) presented with SBI. A total of 61 SBI lesions were found in the 26 patients; of these, 34 (56%) SBI lesions were in the right hemisphere and 27 (44%) in the left hemisphere. SBIs were primarily observed in the posterior cerebral artery territory. Multivariate analysis revealed aortic stenosis to be the only risk factor of SBI.

Conclusions: Retrograde perfusion via femoral cannulation may not increase the incidence of SBI in selected MICS patients based on preoperative CT findings.

KEYWORDS

cardiovascular research, perfusion, valve repair/replacement

1 | INTRODUCTION

Some studies have discussed the significance of silent brain infarction (SBI) after cardiac surgery; SBI reportedly poses a risk of postoperative delirium and cognitive dysfunction.[1] Roach et al[2] reported that cognitive deterioration after coronary bypass surgery was associated with increased morbidity and mortality. Vermeer et al[3] showed that the risk of dementia increased with spontaneous SBI, accompanied by a steep decline in cognitive function. The incidence rates of SBI were 29% after median sternotomy[1] and 29% after coronary angiography and stenting.[4] Thus, the clinical meaning of SBI was significant, moreover, its incidence was not low. However, there are no reports providing detailed information on SBI after minimally invasive cardiac surgery (MICS) with retrograde perfusion via femoral cannulation. In this study, the detailed characteristics of SBI after MICS with retrograde perfusion via femoral cannulation were evaluated using head magnetic resonance imaging (MRI) without contrast.

2 | MATERIALS AND METHODS

2.1 | Patient selection and data collection

After obtaining approval from the review board of Chiba-Nishi General Hospital, we performed a prospective, observational study of data collected from patients who underwent MICS with right minithoracotomy, at the Chiba-Nishi General Hospital between July 2014 and July 2018. All patients were diagnosed based on

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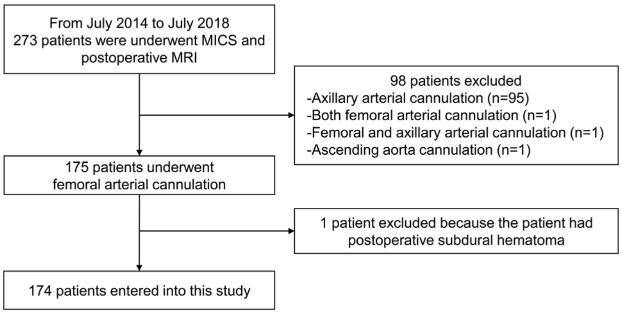

FIGURE 1 Flowchart of patient selection for analyses. MICS, minimally invasive cardiac surgery; MRI, magnetic resonance imaging

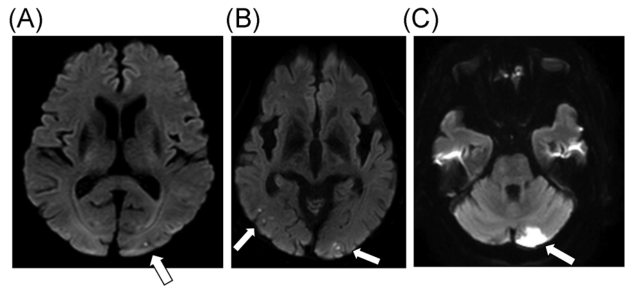

FIGURE 2 Categorization of lesion detected on diffusion-weighted imaging (DWI). A, 1 to 3 DWI spots measuring less than 10 mm. B, Greater than 3 DWI spots measuring less than 10 mm. C, Single DWI lesion measuring greater than 10 mm. White arrows represent DWI lesions

echocardiography findings. During the study period, there were 273 patients who underwent MICS and MRI without contrast, including diffusion-weighted imaging (DWI) sequences, 1 day before and 5 days after surgery. We selected the femoral artery for retrograde perfusion and the axillary artery or ascending aorta for antegrade perfusion. Preoperative computed tomography (CT) angiography was routinely performed, and vascular pathology was evaluated.

The femoral artery was chosen as the cannulation site if the patients met the following criteria: (a) absence of entire circumference calcification in any part of the aorta, (b) thrombosis in less than one-third of the aorta in any part of the aorta, and (c) thrombosis in any part of the aorta with a thickness of less than 3 mm. In patients who did not meet the criteria, antegrade cannulation was performed.

Of 273 patients, 175 (64.1%) underwent femoral arterial cannulation for cardiopulmonary bypass (CPB) and 95 (34.8%) axillary arterial cannulation. Moreover, one patient (0.37%) had both femoral arterial cannulations, one patient (0.37%) had femoral and axillary arterial cannulations, and the remaining one patient (0.37%) had ascending aorta cannulation. Patients who underwent axillary arterial cannulation, both femoral arterial cannulations, femoral and axillary arterial cannulations, and ascending aorta cannulation were excluded. Moreover, one patient who presented with a subdural hematoma 3 days after the surgery was excluded. Finally, 174 patients were included in the study (Figure 1).

Patients who were scheduled for MICS underwent MRI, including DWI sequences, 1 day before and 5 days after surgery. SBIs detected via DWI were categorized as follows: (a) 1 to 3 DWI spots measuring less than 10 mm, (b) greater than 3 DWI spots measuring less than 10 mm, and (c) single DWI lesion measuring greater than 10 mm (Figure 2).

A high field strength (3T) MRI unit was used. The protocol included axial T2-weighted imaging, axial T2-weighted fluid attenuation inversion recovery imaging, axial trace-weighted DWI, and apparent diffusion coefficient mapping.

All patients were diagnosed with SBI by a diagnostic radiologist using relevant images. When lesions were detected, neurosurgeons were consulted. Renal failure was defined as the requirement of hemodialysis or an elevated creatinine level at 2.0 mg/dL, which is twice the preoperative baseline level. Thirty-day mortality was defined as all deaths within 30 days after surgery regardless of where the patients died (in- or out-of-hospital).

2.2 | Use of anesthetics, surgical technique, and postoperative management

MICS was performed via a 5- to 6-cm lateral right thoracotomy. The surgical approaches used were through the third intercostal space in aortic valve surgery and the fourth intercostal space in mitral valve surgery.

In case of retrograde perfusion, we cannulated the femoral artery via a small skin incision in the inguinal region with the direct cannulation technique. The femoral vein was cannulated with a venous cannula, and transesophageal echocardiography was performed to assess the guide wire and cannula in the bicaval view.

Cross-clamping was performed directly through the incision. In both the aortic and mitral valves, antegrade cardioplegia was delivered into the aortic root.

The removal of air was performed using a vent placed in the aortic root and left ventricle in aortic valve surgery and via a vent in the aortic root in mitral valve surgery.

In our hospital, CPB was initiated with a perfusion index of 2.6 L/min/m^2 and was conducted with a systemic temperature of 32°C.

The procedures were performed under direct visualization with thoracoscopic guidance. CO_2 insufflation into the right thoracic cavity was performed with a flow rate of 5 L/min during the procedure.

2.3 | Statistical analysis

Continuous data were presented as mean and standard deviation within the normal range. These data were analyzed using Student's and independent-sample *t* test or Mann-Whitney *U* test. Meanwhile, categorical variables were expressed as counts and percentages, and

TABLE 1 Preoperative characteristics of 174 patients who underwent MICS and postoperative MRI, which were stratified according to SBI

	Patients			
Demographic characteristics of the participants	Total (n = 174)	Without SBI (n = 148)	SBI (n = 26)	P value
Age, y	65.0 ± 14.2	64.1 ± 14.6	70.0 ± 9.96	.007
Male	92 (52.9)	81 (54.7)	11 (42.31)	.289
Body surface area, m^2	1.57 ± 0.21	1.57 ± 0.22	1.55 ± 0.18	.319
Hypertension	90 (51.7)	72 (48.7)	18 (66.67)	.0584
Diabetes mellitus	19 (10.9)	15 (10.1)	4 (14.8)	.492
CKD	14 (8.1)	13 (8.8)	1 (3.7)	.697
Hemodialysis	1 (0.57)	1 (0.68)	0 (0)	1
COPD	6 (3.45)	4 (2.7)	2 (7.41)	.22
History of chronic arterial fibrillation	22 (12.6)	5 (3.38)	2 (7.69)	.536
History of paroxysmal atrial fibrillation	5 (2.87)	20 (13.5)	0 (0)	1
History cerebrovascular disease	7 (4.02)	5 (3.38)	2 (7.69)	.281
Euro SCORE II	1.70 ± 2.00	1.71 ± 2.06	1.67 ± 1.59	.449
AS (n)	38 (21.84)	27 (18.24)	11 (42.31)	.00995
AR (n)	27 (15.52)	22 (14.86)	5 (19.2)	.562
MR (±TR, n)	87 (50.00)	78 (52.70)	9 (34.62)	.136

Note: The values were presented as n (%) or median (interquartile range).
Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MICS, minimally invasive cardiac surgery; MRI, magnetic resonance imaging; SBI, silent brain infarction.

they were analyzed using χ^2 test or Fisher's exact test. Univariate and multivariate logistic regression analyses were conducted to determine the risk factors for SBI after MICS. $P \leq .05$ was considered statistically significant. Statistical analysis was conducted using the Statistical Package for the Social Sciences software version 25.0 (IBM, NY).

3 | RESULTS

3.1 | Patient characteristics and operative data

The mean age of the patients was 65.0 ± 14.2 years, and 92 men (52.9%) were included in the study. Moreover, seven patients (4.0%) had a history of stroke (Table 1).

The procedures comprised single valve surgeries (*n* = 143, 82.2%), double valve surgeries (*n* = 20, 11.5%), and other cardiac surgeries (*n* = 11, 6.3%). Single valve surgeries comprised aortic valve replacements (*n* = 66, 37.9%) and mitral valve procedures (*n* = 77, 44.2%). The mitral valve procedures included mitral valve repairs (*n* = 69, 39.6%) and mitral valve replacements (*n* = 8, 4.6%). The double valve procedures comprised aortic and mitral valve surgeries (*n* = 4, 2.3%) and mitral and tricuspid valve surgeries (*n* = 16, 9.2%).

The median times taken to perform aortic cross-clamping and CPB were 102.9 ± 37.5 and 132.7 ± 38.6 minutes, respectively (Table 2).

3.2 | Outcomes

The postoperative outcomes are shown in Table 3. There was no mortality, and none of the patients had a stroke (Table 3). In total, 26 (14.9%) patients were diagnosed with SBI based on the postoperative MRI findings. The incidence of SBI after each surgery is shown in Table 4. Two (7.7%) patients had a history of stroke. The patients were categorized according to severity: (a) 1 to 3 DWI spots measuring less than 10 mm (n = 22) and (b) greater than 3 DWI spots measuring less than 10 mm (n = 4).

The total number of SBI lesions in 26 patients was 61. Based on the shape and size of the lesion, the etiology of SBI was interpreted as embolism due to microdebris and air by MRI image reading. The anatomical location and number of SBIs were summarized in Table 5. The location of ischemic foci was divided into cerebrovascular territories, including watershed regions. In total, 34 (56%) SBI lesions were in the right hemisphere and 27 (44%) in the left hemisphere. Most SBIs were observed in the posterior cerebral artery territory.

In the univariate analysis, the patients with SBI were older than those without SBI ($P < .05$), and the number of patients with aortic stenosis (AS) was higher than that of patients without SBI ($P < .05$; Table 1). Meanwhile, the multivariate analysis revealed that the risk factor for postoperative SBI was aortic valve replacement for AS (odds ratio: 2.668; 95% confidence interval: 1.054-6.754; $P = .038$; Table 6). There was no recorded death among the patients diagnosed with SBI who were discharged from the hospital.

TABLE 2 Operative details of 174 patients who underwent MICS and postoperative MRI

	Patients (n = 174)
Isolated aortic valve replacement	66 (37.9)
Isolated mitral valve surgery	77 (44.2)
Isolated mitral valve repairs	69 (39.6)
Mitral valve replacements	8 (4.6)
Double valves	20 (11.5)
Aortic/mitral valve	4 (2.3)
Mitral/tricuspid valve	16 (9.2)
Other cardiac surgeries	11 (6.3)
Procedure time, min	215 (±49.6)
Aortic cross-clamping time, min	102.9 (±37.5)
Cardiopulmonary bypass time, min	132.7 (±38.6)
Ventilation time, h	8.8 (±5.4)
Intensive care unit stay, h	57.6 (±26.4)

Note: The values were presented as n (%) or median (interquartile range).
Abbreviations: MICS, minimally invasive cardiac surgery; MRI, magnetic resonance imaging.

TABLE 3 Postoperative outcome of 174 patients who underwent MICS and postoperative MRI

Outcomes	Patients (n = 174)
Thirty-day mortality	0
Symptomatic stroke	0
Re-exploration	2 (1.1)
Renal failure	5 (2.9)
Reintubation	1 (0.5)
Surgical site infection	1 (0.5)
Sepsis	0
Pneumonia	0
Aortic dissection	0
Femoral artery trauma	0
Postoperative atrial fibrillation	25 (14.3)
Lower extremity compartment syndrome	0
Intensive care unit readmission	0
Chest tube output (total or within 24 h), mL	171 (±165)
Timing of chest tube removal, d	1.6 (±1.0)
Blood transfusion	34 (±19.4)
Length of hospital stay, d	9.4 (±7.5)

Note: The values were presented as n (%) or median (interquartile range).
Abbreviations: MICS, minimally invasive cardiac surgery; MRI, magnetic resonance imaging.

TABLE 4 The number and percentage of silent brain infarction in each procedure

Procedures associated with SBI	n = 26 (14.8)
Isolated aortic valve surgery	16 (61.5)
Isolated mitral valve surgery	7 (26.9)
Mitral valve repairs	5 (19.2)
Mitral valve replacements	2 (7.7)
Double valve surgery	2 (7.7)
Aortic and mitral valve	0 (0)
Mitral and tricuspid valve	2 (7.7)
Other cardiac procedures (ASD/tumor)	1 (3.8)

Note: The values were expressed as number and percentage (%), unless otherwise specified.
Abbreviations: ASD, atrial septal defect; SBI, silent brain infarction.

4 | DISCUSSION

4.1 | Incidence of SBI

The incidence rate of SBI was 14.9% in patients who underwent MICS with retrograde perfusion. According to a previous study, SBI is common in cardiac surgeries or catheterization.[5] Compared with previous reports about SBI after median sternotomy, the incidence of SBI in this study was low. In the study by Sun et al,[1] the incidence rate of SBI after median sternotomy was 29%. A detailed review of this report revealed that the incidence rates were 45% after on-pump coronary artery bypass grafting (CABG),[6] 47% after valve surgery,[7] 31% after off-pump CABG,[8] 22% after catheterization of aortic valves,[9] 10.2% after coronary angiography,[10] 29% after angiographic and percutaneous coronary interventions,[4] and 34.7% after urgent percutaneous coronary intervention.[11]

The two possible reasons for the low incidence of SBI in our institution are as follows: first, patient selection using our criteria for

TABLE 5 Occurrence of the lesion according to the vascular region

	Hemisphere		
Vascular region	Right	Left	Total
ACA	1	0	1
MCA	8	4	12
PCA	13	8	21
Watershed	6	7	13
AICA	0	1	1
PICA	6	7	13
Total	34 (56%)	27 (44%)	

Abbreviations: ACA, anterior cerebral artery; AICA, anterior inferior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebral artery.

TABLE 6 Risk factors for postoperative silent cerebral infraction after minimally invasive cardiac surgery in the multivariate logistic regression model

Variables	Odds ratio	95% CI	Wald	*P* values
AVR for AS	2.668	1.054-6.754	4.286	.038
Hypertension	1.904	0.781-4.643	2.004	.157
Age over 70 y	2.184	0.876-5.446	2.808	.094

Abbreviations: AS, aortic stenosis; AVR, aortic valve replacement; CI, confidence interval.

femoral cannulation might have led to the incidence of SBI. At our institution, all patients underwent whole-body contrast-enhanced CT scan before surgery, and vascular properties were evaluated using our criteria. As retrograde perfusion is not used in patients with poor vascular properties and is used only in those with comparatively good vascular properties, our patient with severe atherosclerosis was excluded as an MICS candidate. The second possible reason for the low incidence of SBI may be with the presence of CO_2 in the thoracic cavity at the time of surgery. It may be advantageous to reduce the effect of air embolism.[12]

4.2 | Location of SBI

In this study, all lesions were small and focal; therefore, they were presented as grade A or B lesions. Based on the shape and size of the lesion, the SBI etiology was considered to be embolism due to the presence of microdebris and air by MRI image reading.

Based on the evaluation of SBI location, a high number of lesions were localized in the right hemisphere. We speculated the possible causes of SBI in the right hemisphere, which were as follows: first, MICS is performed while the patients are in the left lateral decubitus position at our institution, and this might have made it easier for debris and air to reach the right vasculature area. Floyd et al[13] reported a similar tendency on MRI after median sternotomy. In the reports of Knipp et al[7] and Barbut et al,[14] the percentage of embolic lesions in the posterior cerebral circulation was high. However, the actual cause of the localization of lesions in these studies was not identified. Second, the brachiocephalic artery, which is the first artery from the heart other than the coronary artery, is the final point of blood flow in retrograde perfusion. Therefore, air and debris in the heart are most likely to burst out when cardiac beating begins after the release of the aortic clamp, and the brachiocephalic artery becomes the boundary between retrograde perfusion and cardiac output. Then, the air and debris can flow to the brachiocephalic artery.

4.3 | Risk factor of SBI

In the univariate analysis, age and AS were considered the risk factors of SBI. Meanwhile, the multivariate analysis revealed that AS was a risk factor. In aortic valve replacement for AS, the possible cause of embolic lesions is the presence of debris generated when resecting aortic valves, and this debris may be responsible for brain infarcts, including emboli, after releasing the aortic clamp.

4.4 | Study limitations

The current study had several limitations. First, this study was a nonrandomized prospective study with no control group. Second, the timing of occurrence of SBI was not accurately confirmed. MRI was performed on postoperative day 5; thus, we can only state that SBI occurred at some point from mid-surgery or postoperative day 5. Some SBI might have occurred postoperatively and not during the surgery. Finally, postoperative delirium and cognitive function were not quantified. We believe further research and follow-up are required for patients with postoperative SBI.

5 | CONCLUSIONS

Retrograde perfusion via femoral cannulation may not increase the incidence of SBI in selected MICS patients based on preoperative CT scan findings. The right and posterior regions were vulnerable to SBI probably due to the nature of retrograde perfusion.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Manuscript draft: SN; writing editing: YN; data collection: DY, YY, MK, TN, RT, YI; statistics: FS; data analysis: TT, NK.

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REFERENCES

1. 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(9):791-797.
2. Roach GW, Kanchuger M, Mangano CM, et al. Adverse cerebral outcomes after coronary bypass surgery. *N Engl J Med*. 1996;335(25):1857-1863.
3. 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(13):1215-1222.
4. Göksülük H, Güleç S, Özyüncü N, et al. Comparison of frequency of silent cerebral infarction after coronary angiography and stenting with transradial versus transfemoral approaches. *Am J Cardiol*. 2018;122(4):548-553.
5. Indja B, Woldendorp K, Vallely MP, Grieve SM. Silent brain infarcts following cardiac procedures: a systematic review and meta-analysis. *J Am Heart Assoc*. 2019;8(9):e010920.

6. Knipp SC, Matatko N, Wilhelm H, 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(5):791-800.
7. Knipp SC, Matatko N, Schlamann M, et al. Small ischemic brain lesions after cardiac valve replacement detected by diffusion-weighted magnetic resonance imaging: relation to neurocognitive function. *Eur J Cardiothorac Surg*. 2005;28(1):88-96.
8. Friday G, Sutter F, Curtin A, et al. Brain magnetic resonance imaging abnormalities following off-pump cardiac surgery. *Heart Surg Forum*. 2005;8(2):E105-E109.
9. Omran H, Schmidt H, Hackenbroch M, et al. Silent and apparent cerebral embolism after retrograde catheterisation of the aortic valve in valvular stenosis: a prospective, randomised study. *Lancet*. 2003; 361(9365):1241-1246.
10. Kim MJ, Lim YC, Oh SY, Kim BM, Kim BS, Shin YS. Thromboembolic events associated with electrolytic detachment of Guglielmi detachable coils and target coils: comparison with use of diffusion-weighted MR imaging. *J Korean Neurosurg Soc*. 2013;54(1):19-24.
11. Murai M, Hazui H, Sugie A, et al. Asymptomatic acute ischemic stroke after primary percutaneous coronary intervention in patients with acute coronary syndrome might be caused mainly by manipulating catheters or devices in the ascending aorta, regardless of the approach to the coronary artery. *Circ J*. 2008;72(1):51-55.
12. Murzi M, Cerillo AG, Gasbarri T, 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(3):363-368.
13. Floyd TF, Shah PN, Price CC, et al. Clinically silent cerebral ischemic events after cardiac surgery: their incidence, regional vascular occurrence, and procedural dependence. *Ann Thorac Surg*. 2006;81(6): 2160-2166.
14. Barbut D, Grassineau D, Lis E, Heier L, Hartman GS, Isom OW. Posterior distribution of infarcts in strokes related to cardiac operations. *Ann Thorac Surg*. 1998;65(6):1656-1659.

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