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Neurologic Outcomes of Preoperative Acute Silent Cerebral Infarction in Patients with Cardiac Surgery

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Background: Acute cerebral infarction is a major risk factor for postoperative neurologic complications in cardiac surgery. However, the outcomes associated with acute silent cerebral infarction (ASCI) have not been not well established. Few studies have reported the postoperative outcomes of these patients in light of preoperative Diffusion-weighted magnetic resonance imaging (DWI). We studied the postoperative neurologic outcomes of patients with preoperative ASCI detected by DWI. ***Methods:*** We retrospectively studied 32 patients with preoperative ASCI detected by DWI. None of the patients had preoperative neurologic symptoms. The mean age at operation was 68.8±9.5 years. Five patients had previous histories of stroke. Four patients had been diagnosed with infective endocarditis. Single cerebral infarct lesions were detected in 16 patients, double lesions in 13, and multiple lesions (>5) in three. The median size of the infarct lesions was 4 mm (range, 2 to 25 mm). The operations of three of the 32 patients were delayed pending follow-up DWI studies. ***Results:*** There were two in-hospital mortalities. Neurologic complications also occurred in two patients. One patient developed extensive cerebral infarction unrelated to preoperative infarct lesions. One patient showed sustained delirium over one week but recovered completely without any neurologic deficits. In two patients, postoperative DWI confirmed that no significant changes had occurred in the lesions. ***Conclusion:*** Patients with preoperative ASCI showed excellent postoperative neurologic outcomes. Preoperative ASCI was not a risk factor for postoperative neurologic deterioration.

Key words: 1. Cerebral infarction
2. Neurologic outcome
3. Thoracic surgery

INTRODUCTION

Neurologic complications are a major problem in cardiac surgery. Preoperative acute cerebral infarction is a significant risk factor for postoperative neurologic complications [1]. Preoperative acute cerebral infarction can be exacerbated after cardiac surgery [1,2]. Intraoperative hypotension during cardiopulmonary bypass (CPB) may aggravate ischemic damage and potentiate cerebral edema by disrupting the blood-brain barrier [1]. Additionally, the hemorrhagic transformation of cerebral infarctions can be caused by systemic heparinization [1].

In acute cerebral infarctions without clinical neurologic symptoms, such as silent cerebral embolism and transient ischemic attacks, postoperative neurologic outcomes are improved [3,4]. However, another study has suggested that even silent cerebral infarctions can be exacerbated postoperatively [5].

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Diffusion-weighted magnetic resonance imaging (DWI) is a very useful imaging modality for the early detection of acute cerebral infarction. Its sensitivity and specificity are 85% and 100%, respectively [6]. Acute infarct lesions show maximal intensity after 48 to 72 hours from the onset of infarction, and their intensity starts to decrease after one week [6].

There is a considerable literature about perioperative neurologic outcomes using DWI. However, studies of neurologic outcomes in patients with preoperative acute silent cerebral infarction (ASCI) using DWI are rare. The neurologic outcomes of patients with ASCI are also not well established. We studied the postoperative neurologic outcomes of patients with preoperative ASCI detected by DWI.

METHODS

From January 2010 to July 2013, 362 consecutive patients underwent cardiac surgery in Saint Carollo General Hospital. We routinely performed preoperative neurologic evaluations with DWI in patients aged over 50 years if the patient's condition was suitable. Preoperative DWI was not performed in 117 patients because of unsuitable preoperative conditions, emergency situations, or young age. A total of 245 patients underwent DWI preoperatively. Among them, we retrospectively reviewed the medical records of 32 patients who were diagnosed with acute cerebral infarction on preoperative DWI imaging and were without any neurologic symptoms. The mean age at operation was 68.8±9.5 years. Sixteen patients (50%) were male. The preoperative cardiac diseases were valvular heart disease in 13 patients, coronary arterial disease in 13 patients, thoracic aortic disease in two patients, and infective endocarditis in four patients. To evaluate the risk of embolic infarction, we reviewed preoperative variables including age, sex, hypertension, diabetes mellitus, renal insufficiency, atrial fibrillation, smoking, history of cerebrovascular disease, and the time interval between coronary angiography and the DWI scan. This study was approved by review board of Saint Carollo General Hospital, which waived informed consent due to the retrospective nature of this study (SCH 2014-042).

1) Magnetic resonance imagery

Magnetic resonance imagery examinations were carried out with a 1.5 Tesla system (SignaHDx; GE Healthcare, Milwaukee, WI, USA). The imaging protocol included a diffusion-weighted, single-shot, spin echo echoplanar sequence (diffusion gradient b values of 0 and 1,000 s/mm^2, 9,000 ms repetition time, minimal echo time, 5 mm slice thickness with a 1 mm intersection gap, 128×128 pixel matrix, and 260 mm field of view), turbo fluid-attenuated inversion recovery, and T2-weighted turbo spin echo sequences. For DWI, the diffusion gradients for total acquisition were successively and separately applied in three orthogonal directions for a total acquisition time of 80 seconds. Trace images were then generated and apparent diffusion coefficient maps calculated with a dedicated software tool. The DWI scan results were considered abnormal if the scan revealed an area of hyperintensity on DWI and hypointensity on apparent diffusion coefficient maps relative to the normal brain, signifying cerebral ischemia. The lesions on the magnetic resonance imaging and DWI findings were evaluated by two experienced neuroradiologists masked to the clinical and neuropsychological data.

2) Preoperative cerebral infarct lesions

Of the 32 patients with preoperative acute cerebral infarctions on DWI imaging, 16 patients had a single lesion, 13 patients had two lesions, and three patients had multiple lesions (>5). The median size of the lesions was 4 mm (range, 2 to 25 mm). Three of the patients with two lesions had large infarction lesions (>15 mm).

There were 60 infarct lesions found on preoperative DWI, of which 44 (73%) were supratentorial and 16 (27%) were infratentorial. Most of the supratentorial lesions were located in the cerebral cortex (68%) and the others were in the white matter (basal ganglia, thalamus, centrum semiovale, hippocampus, corpus callosum, and corona radiata). Most of the infratentorial lesions were in the cerebellum (81%) and the others were in the pons (19%).

3) Operation

All patients except one underwent a standard median sternotomy for surgical exposure. One patient underwent a post-

erolateral thoracotomy for the replacement of their descending thoracic aorta. Twenty-five patients underwent operations under CPB. In most cases, mild hypothermia (32°C) was maintained during CPB. One patient underwent an aortic dissection type B under deep hypothermic total circulatory arrest. The mean arterial pressure was maintained between 60 and 70 mmHg during CPB. Histidine-tryptophan-ketoglutarate solution or blood cardioplegia was used for myocardial protection. The types of operations are listed in Table 1. Two patients underwent a biatrial maze operation using concomitant radiofrequency. The mean CPB time and aortic cross-clamp time was 135.1±53.9 and 97.7±46.2 minutes, respectively.

Table 1. Types of operation

Cardiac surgery	No.
Valve (n=16)	
AVR	7
AVR+MVR	3
MVR	1
MVR+TAP	2
MVP+TAP	1
TAP	1
Tricuspid valve replacement	1
CABG (n=13)	
Off-pump	7
On-pump	6
Valve+CABG (n=1)	
AVR+CABG	1
Aorta (n=2)	
AVR+ascending aorta replacement	1
Descending aorta replacement	1

AVR, aortic valve replacement; MVR, mitral valve replacement; TAP, tricuspid annuloplasty; CABG, coronary artery bypass graft.

4) Operative timing

Twenty-nine patients underwent cardiac surgery within 3 days after preoperative DWI. All but one of the patients showed single or double infarct lesions on preoperative DWI. One patient who showed multiple cerebral infarct lesions underwent elective cardiac surgery due to an unstable preoperative condition. Three patients delayed cardiac surgery by 10, 11, and 14 days, respectively. Two of these patients had multiple infarct lesions and one patient had the largest infarct lesion (25 mm) in our study. All three of these patients underwent operation after a follow-up DWI study. On the follow-up DWI, the previous cerebral infarct lesions of two patients had improved (Fig. 1), but one patient who was diagnosed with infective endocarditis showed newly developed acute cerebral infarctions.

5) Statistical analysis

Continuous variables are expressed as mean±standard deviation or median values. Comparisons between the two groups were made with the Student t-test for continuous variables and with the chi-square test or Fisher's exact test for categorical variables. A p-value less than 0.05 was considered stat-

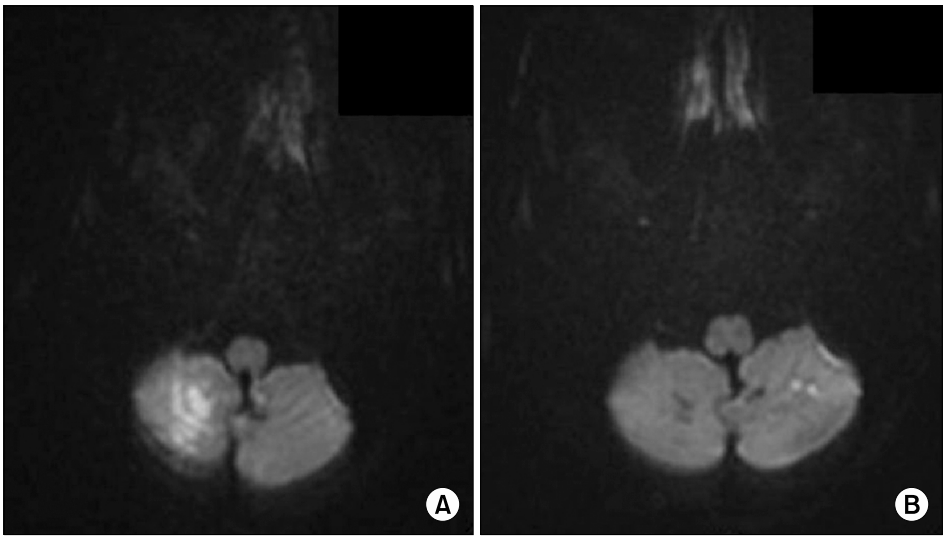

Fig. 1. (A) The initial DWI image showed a 25 mm acute infarction in the right cerebellar hemisphere. (B) A follow-up DWI image taken 11 days later showed the regression of the acute right cerebellar infarction and a new acute small left cerebellar infarction. DWI, diffusion-weighted magnetic resonance imaging.

Table 2. Patients characteristics compare to ASCI absent group

Characteristic	Present ASCI (n=32)	Absent ASCI (n=213)	p-value
Age (yr)	68.8±9.5	64.9±13.3	0.047
Sex (male)	16 (50)	126 (59.2)	0.328
Hypertension	16 (50)	86 (40.4)	0.303
Diabetes mellitus	11 (34.4)	38 (17.8)	0.029
Renal insufficiency	0	6 (2.8)	0.336
History of cerebrovascular attack	4 (12.5)	16 (7.5)	0.337
Atrial fibrillation	3 (9.4)	47 (22.1)	0.097
Smoking	6 (18.8)	41 (19.2)	0.947
Coronary angiography within 14 days	21 (65.6)	95 (44.6)	0.026

ASCI, acute silent cerebral infarction.

Table 3. Postoperative outcomes compare to ASCI absent group

Postoperative variable	Present ASCI (n=32)	Absent ASCI (n=213)	p-value
Neurologic complications	2/32 (6.25)	6/213 (2.81)	0.308
Mean ventilator time (hr)	35.1±95.3	23.5±74.1	0.192
Mean intensive care unit stay (day)	4.4±4.6	3.9±6.5	0.871

Values are presented as number (%) or mean±standard deviation.
ASCI, acute silent cerebral infarction.

istically significant. Analyses were performed with PASW SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Table 2 summarizes preoperative demographic variables compared to patients without acute cerebral infarction lesions on DWI. Patients with ASCI tended to be older and have a higher incidence of diabetes mellitus and a significantly higher rate of coronary angiography within the 14 days before the DWI scans.

There were two in-hospital mortalities. One patient underwent a descending thoracic aorta replacement for acute type B aortic dissection because of uncontrolled hypertension and intractable pain. He died of brain death 24 days after surgery. He was under total circulatory arrest during the operation and postoperative brain computed tomography imaging showed extensive cerebral infarction unrelated to preoperative infarction lesions. The other patient who underwent off-pump coronary artery bypass grafting died of sudden ventricular arrhythmia 35 days after surgery. Postoperatively, he developed acute renal failure and required an extensive period of hemodialysis.

Two patients including the above-mentioned brain death case developed postoperative neurologic complications. One patient showed postoperative delirium sustained over one week. On her postoperative brain computed tomography finding, there was no evidence of infarction or hemorrhage. She recovered completely and was discharged without any neurologic problems.

The median postoperative ventilator time was seven hours (range, 2 to 497 hours) and the median stay in the intensive care unit was three days (range, 1 to 26 days). There were no patients who required prolonged ventilator support or an extended stay in the intensive care unit because of neurologic deterioration except for the two patients with neurologic complications.

Neurologic complications occurred in six patients (2.81%) without preoperative ASCI. All six of these patients developed symptomatic multifocal cerebral infarctions postoperatively. These results did not show statistically significant differences in comparison with the patients who received a preoperative ASCI (6/213, 2.81% vs. 2/32, 6.25%; p=0.308). Other postoperative variables such as ventilator time and time in the intensive care unit did not show significant differences between

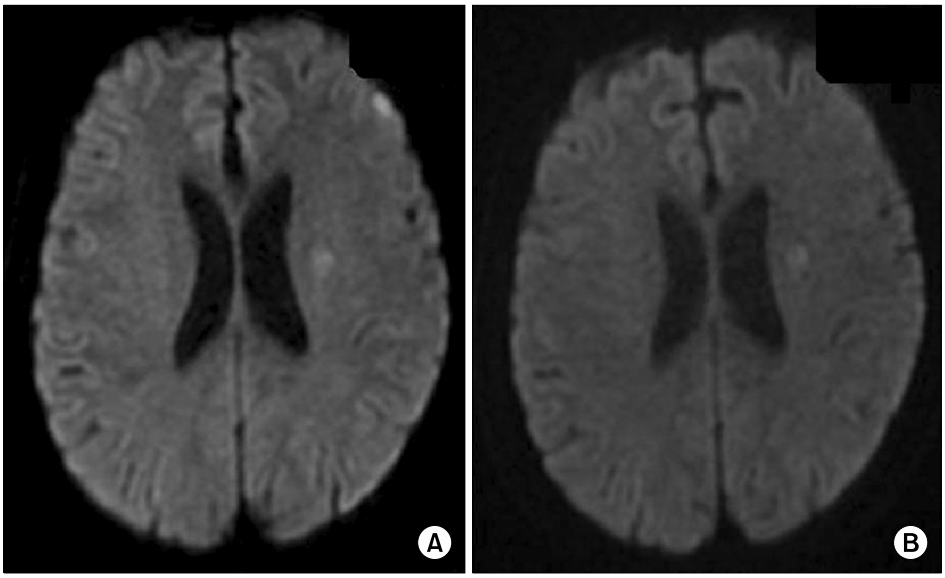

Fig. 2. (A) A preoperative DWI image showed acute infarctions in the left frontal cortex and corona radiata. (B) A postoperative DWI image showed mildly decreased signal intensity at the same infarct area. DWI, diffusion-weighted magnetic resonance imaging.

the two groups (Table 3).

Postoperative DWI was performed in two of the 32 patients with preoperative ASCI. One patient who had two infarct lesions in the left frontal cortex and corona radiata on preoperative DWI showed severe dizziness postoperatively. The other patient with multiple preoperative infarct lesions did not show any specific neurologic symptoms postoperatively. On the postoperative DWI, both had similar findings and no evidence of exacerbation (Fig. 2).

DISCUSSION

A silent cerebral infarct is defined as certain brain abnormalities identified by a magnetic resonance imaging scan that lack clinically overt stroke-like symptoms. These infarcts are associated with subtle deficits in physical and cognitive function that commonly go unnoticed [7]. They have been shown to occur in up to 20% of healthy elderly people [7]. In the present study, the incidence of preoperative ASCI identified by DWI was 13%. Most lesions were small but large or multiple infarct lesions were also observed. The patients with ASCI tended to be older, have a higher incidence of diabetes mellitus, and have a higher rate of coronary angiography within the 14 days before DWI scans. Age and diabetes mellitus are known significant risk factors of silent cerebral infarcts that have been reported in several studies [5,7]. Paradoxical embolism is also an important pathogenesis of silent cerebral infarcts [5,7,8]. Preoperative coronary angiography might be a source of paradoxical embolism. Recent studies demonstrated that asymptomatic embolic cerebral infarction could be detected in 2.2% to 22% of patients using DWI after left-sided cardiac catheterization [9,10]. The other important finding of this study was the distribution of infarct lesions. Most silent infarct lesions are located in white matter areas [7]. However, cortical lesions were most prevalent in our study. Kim et al. [8] demonstrated that paradoxical embolism may play an important role in the development of silent brain infarcts outside the perforating artery territory, such as in the cortical area. These findings indicated that embolism may be an important cause of ASCI.

Preoperative acute cerebral infarction is a major risk factor for postoperative neurologic complications. It can be exacerbated after cardiac surgery because of intraoperative hypotension and CPB-induced systemic heparinization. Eishi et al. [1] reported that the exacerbation rate of cerebral infarctions was 45.5% when operated on within 24 hours, 16.7% when operated on between eight and 14 days, and 2.3% when operated on even after four weeks. They suggested that the major risk factor of neurologic exacerbation was the severity of preoperative cerebral infarction [1]. In the case of preoperative ASCI, postoperative neurologic outcomes have been shown to be better than the case of preoperative symptomatic cerebral

infarction [3,4]. Thuny et al. [3] reported that no neurologic deaths occurred in patients with preoperative acute silent infarction or transient ischemic attacks [3]. However, another report does indicate that even ASCI can be exacerbated postoperatively [5]. According to that study, one patient with preoperative silent infarction developed dysarthria and right hemiparesis postoperatively and his postoperative DWI demonstrated an increased preoperative infarct size [5]. Their finding supports the conclusion that it would be helpful to evaluate preoperative neurologic DWI studies to prepare for unexpected postoperative neurologic complications.

In our study, neurologic complications developed in two patients with preoperative ASCI. One patient showed sustained delirium and the other patient developed a major cerebral infarction postoperatively. These neurologic complications were unrelated to the preoperative infarct lesions because these two patients had single or double infarct lesions preoperatively. That is, these complications were not the result of the exacerbation of preoperative ASCI.

There is some controversy about the timing of operations in patients with preoperative acute cerebral infarction. According to the European Society of Cardiology guidelines on infective endocarditis, operations should be delayed by at least four weeks to prevent hemorrhagic exacerbation or preoperative cerebral hemorrhage [11]. In acute cerebral infarction, no definite criterion exists regarding the timing of the operation. However, in the case of silent cerebral infarction or transient ischemic attack, delaying the surgery is not recommended because the risk of postoperative neurologic deterioration is low [11]. Even though silent cerebral infarction is a minor risk factor for postoperative neurologic complications, multiple or large lesions can result in increased risk [12,13]. Goto et al. [12] have reported that preoperative multiple small infarctions or large infarctions ($>$15 mm) significantly increase the risk of postoperative neurologic dysfunction.

In this study, 29 patients underwent elective cardiac surgery and three patients underwent delayed operations. When ASCI showed multiple lesions ($>$5) or a large lesion ($>$20 mm), the operation was delayed if the patient's condition required it.

There were several limitations to our study. Our study was a retrospective, single-center study, and the total number of patients in the study was too small to draw definitive conclusions. We were not able to evaluate the patients' cognitive function, although several studies have documented that patients with silent cerebral infarction showed cognitive dysfunction [5,7]. A more exact neurologic evaluation should compare preoperative and postoperative cognitive function. In addition, postoperative DWI was not performed in all study patients. Thus, we cannot be sure whether all infarct lesions were exacerbated postoperatively.

In conclusion, ASCI detected by preoperative DWI occurred with some frequency in older patients. Patients with preoperative ASCI showed excellent postoperative neurologic outcomes. There was no neurologic deterioration related to preoperative infarct lesions, and preoperative ASCI was not a risk factor for postoperative neurologic deterioration.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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