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ORIGINAL ARTICLE

A functional evaluation of cerebral perfusion for coronary artery bypass grafting patients

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Abstract
We evaluate the utility of providing a pulsatile blood flow by applying off-pump coronary artery bypass grafting (CABG) or intra-aortic balloon pumping (IABP) with conventional CABG to prevent perioperative stroke in patients with cerebral hypoperfusion on single-photon emission-computed tomography (SPECT). A total of 286 patients underwent isolated CABG with a cerebral magnetic resonance angiography (MRA) evaluation between 2006 and 2015. Seventy-five had significant stenosis and/or occlusion of craniocervical vessels; the other 211 had no significant stenosis. Cerebral SPECT was performed for 49 (SPECT group) of the 75 patients. The SPECT group was further divided into a normal perfusion (NP) ($n = 37$); and a hypoperfusion (HP) ($n = 12$). In the present study we compared the NP group and the 211 patients with no significant stenosis (as a control group) to the HP group. No strokes occurred in the HP group, and 1 stroke occurred at the time of operation in the control group. Postoperative stroke within 30 days occurred in 3 patients in the control group; the difference was not statistically significant. The long-term stroke-free rates of the HP and Control group did not differ to a statistically significant extent. The functional evaluation of cerebral perfusion by SPECT is important when patients have significant stenotic lesions on cerebral MRA. Maintaining an adequate pulsatile flow by off-pump CABG or IABP with conventional CABG will help prevent perioperative stroke, even if cerebral hypoperfusion is detected by SPECT.

Keywords Coronary artery bypass grafting · Cerebral perfusion single photon emission computed tomography · Perioperative stroke · Intra-aortic balloon pumping

Introduction

A considerable number of coronary artery bypass grafting (CABG) patients are known to have concomitant extracranial carotid and/or intracranial artery disease. Perioperative stroke remains a serious adverse complication after cardiac surgery. Neurological events are associated with substantial increases in mortality and morbidity and an extended length of hospitalization [1–3], and are also responsible for additional costs [1, 2]. To avoid perioperative neurologic complications, CABG patients may undergo preoperative duplex ultrasonography of the extracranial carotid and vertebral arteries [4, 5] or magnetic resonance angiography (MRA) [6]. These examinations are useful for the morphological evaluation of the craniocervical vessels (intracranial and extracranial arteries) but cannot functionally evaluate cerebral perfusion. As an alternative, the quantification of the regional cerebral blood flow (rCBF) using I-123 iodoamphetamine and cerebral perfusion single photon emission computed tomography (SPECT) is useful for the functional evaluation of the cerebral perfusion in patients with significant stenosis or occlusion of the craniocervical vessels on MRA.

Regarding the details of our surgical approach, our strategy is based on the following hypotheses: (1) cerebral hypoperfusion is the most critical risk factor for intraoperative stroke; (2) maintaining the pulsatile blood flow is essential for preventing a reduction in cerebral blood flow; and (3) significant stenosis of the craniocervical vessels is not a critical risk factor for stroke so long as the rCBF remains normal. In the present study we address these hypotheses by

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retrospectively reviewing our CABG cases and evaluate the feasibility of our surgical strategy for preventing perioperative stroke.

The strategy of surgical intervention for patients with significant stenosis of the craniocervical vessels

All patients undergoing elective cardiac surgery at our institution receive brain MRA unless contraindicated. The strategy of surgical treatment is driven by the MRA findings. In patients found to have significant stenosis of an extracranial carotid and/or intracranial artery disease on preoperative MRA, SPECT is principally performed to evaluate the cerebral blood perfusion. If SPECT reveals abnormal hypoperfusion, we routinely consult with neurosurgeons about prophylactic cerebrovascular intervention and perform such intervention before the coronary intervention. However, if cerebrovascular intervention is difficult or urgent CABG is required, CABG is performed cautiously. In such cases, we select off-pump CABG (OPCAB) as the first choice and conventional CABG with intra-aortic balloon pumping (IABP), which creates a pulsatile flow, as the second choice. For patients with normal SPECT findings, even those with significant stenosis of the craniocervical vessels on MRA, any type of CABG procedure can be applied. We also routinely evaluate the ascending aortic wall by intraoperative epiaortic ultrasonography (EUS) and decide whether or not to perform cardiopulmonary bypass (CPB). In patients with a normal aorta or mild atherosclerosis, any type of CABG procedure can be applied. However, OPCAB is the first choice for patients with moderate or severe atherosclerotic change or mobile plaque in the ascending aorta (Fig. 1).

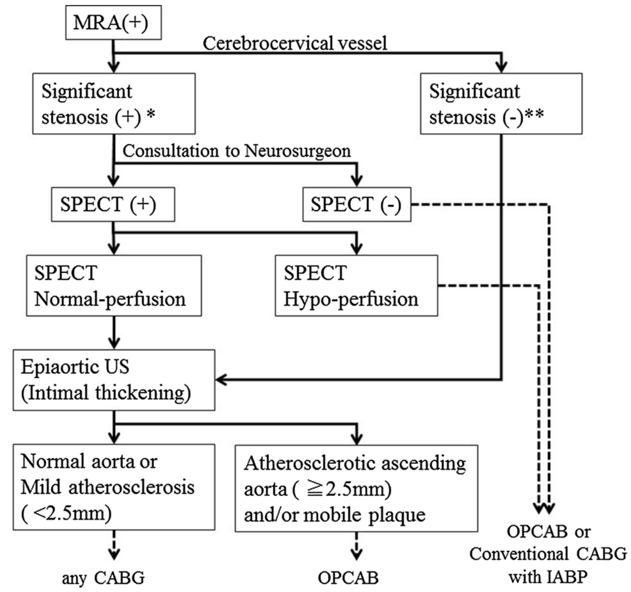

Fig. 1 Operative strategy. *US* ultrasonography. Asterisk: intracranial artery and/or carotid artery and/or vertebral artery severe stenosis (≥ 75%), occlusion (100%), or complex moderate stenosis. Double asterisk: cerebral vessel normal or mild–moderate stenosis (< 75%)

Materials and methods

Patients and study design

The protocol was approved by the Institutional Review Board of Toyota Kosei Hospital. Between September 1, 2006, and July 31, 2015, 390 consecutive patients underwent isolated CABG procedures in our institution. Among these, 293 patients underwent MRA before surgery, while another 94 patients did not undergo MRA because of an urgent situation, the use of IABP, or because they were having a pacemaker implanted, and 3 patients were excluded from the present study because of posterolateral thoracotomy, postoperative cardiac arrest, or cardiogenic shock requiring cardiopulmonary resuscitation.

Of the 293 patients who underwent MRA, 82 had significant stenosis or occlusion of the craniocervical vessels. Of these 82 patients, 7 underwent cerebrovascular intervention before CABG. Three patients had hypoperfusion according to SPECT without acetazolamide (ACZ). Carotid endarterectomy (CEA) was performed for these 3 patients. Another three had normal perfusion according to SPECT, and the cerebrovascular reactivity was reduced on SPECT using ACZ. The cerebrovascular interventions included CEA ($n=1$), carotid artery stenting (CAS) ($n=1$), and superficial temporal artery (STA)-middle cerebral artery (MCA) bypass ($n=1$). The one remaining patient had normal perfusion and normal cerebrovascular reactivity; however, prophylactic cerebrovascular intervention was required due to the progression of severe common carotid artery (CCA) stenosis. This patient underwent CAS before CABG. These seven patients were excluded from the present study because their cerebral blood flow was considered to have been maintained. The other 75 patients had significant stenosis on MRA. Among the patients suspected of having brain ischemia on MRA, 49 underwent cerebral perfusion SPECT before CABG (SPECT group). In the SPECT group, 37 patients had normal perfusion (SPECT NP group) and 12 had hypoperfusion (SPECT HP group). The other 211 patients showed no significant stenotic lesions on MRA and did not undergo SPECT (Fig. 2).

The cerebrovascular interventions in the 12 patients in the SPECT HP group included STA-MCA bypass at 6 months after CABG ($n=1$), and CAS at 3 months after CABG ($n=1$). A comparison between the SPECT HP group and the SPECT NP with other 211 patients as a control group were performed. SPECT NP group in which normal rCBF

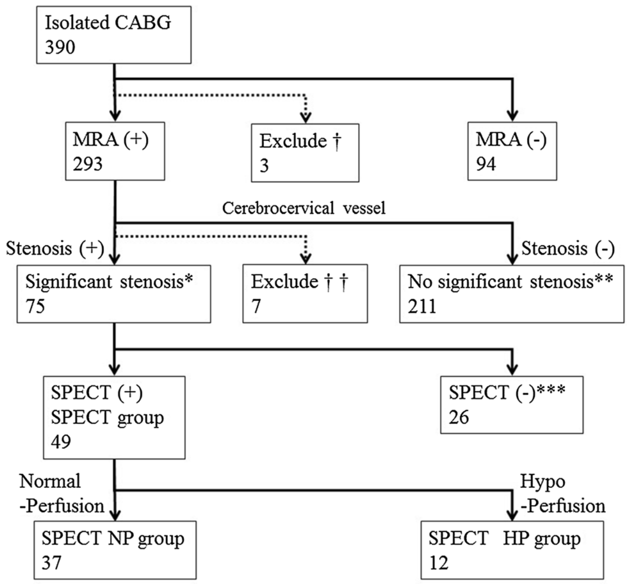

Fig. 2 Patients and study design. Dagger: two patients with postoperative cardiac arrest because of severe coronary spasm and another patient with reoperation via posterolateral thoracotomy were excluded from this study. Double dagger: seven patients underwent cerebrovascular intervention before CABG. These patients were excluded from the present study. Asterisk: intracranial artery and/or carotid artery and/or vertebral artery severe stenosis (≥ 75%), occlusion (100%), or complex moderate stenosis. Double asterisk: cerebral vessel normal or mild–moderate stenosis (< 75%). Triple asterisk: these patients did not undergo SPECT because a radioisotope examination could not be scheduled, OPCAB had been planned previously, or for some other unknown reason

with significant stenosis of the craniocervical vessels reveals some collateral flow to stenotic region might maintain the cerebral blood flow. That's why we combined SPECT NP group and 211 patients with no significant stenosis to the control group.

MRA

The MRA findings obtained within 1 year before surgical intervention using an Intera, Acheva 1.5 T (PHILIPS, Amsterdam, Holland) were evaluated. The preoperative imaging of the intracranial and extracranial cervical arteries was obtained by three-dimensional time-of-flight MRA. For the intracranial arteries, we evaluated the intracranial internal carotid artery (ICA), anterior cerebral artery (ACA), MCA, and basilar artery. For the extracranial arteries, we evaluated the extracranial ICA, CCA, and vertebral artery. We classified stenosis as normal (no stenosis), mild to moderate (< 75%), severe (75–99%), and total occlusion (100%). All images were evaluated by our team and an experienced radiologist. We designated moderate multiple complex stenosis, severe stenosis, and occlusion as significant stenosis.

Cerebral perfusion SPECT

Cerebral perfusion SPECT (Infinia; GE Healthcare Japan, Tokyo, Japan) was performed for patients who had significant stenosis, such as moderate multiple complex stenosis, severe stenosis, or occlusion on MRA. *N*-isopropyl-*p*-iodine-123-iodoamphetamine ([^{123}I] IMP) was used to quantify the rCBF by SPECT. We applied rCBF measurement using a graph plot analysis, as reported by Okamoto et al.[7]. At our institution, rCBF of < 35 ml/100 g brain/min was considered to be abnormally low. When cerebral hypoperfusion was diagnosed, it was confirmed by the cerebrovascular reactivity using ACZ on SPECT if possible. A < 10% increase in rCBF or < 35 ml/100 g brain/min of cerebrovascular reactivity was considered to indicate a reduced cerebral perfusion reserve. If the cerebrovascular reactivity was normal, we operated as we would in a patient without cerebral ischemia.

Operative strategy

We routinely evaluate the ascending aorta using epiaortic ultrasonography (EUS). We performed conventional CABG with CPB whenever possible; however, when the ascending aorta had mobile atheroma or > 2.5 mm of intimal thickening, OPCAB was principally performed. In such patients, we used the aortic no-touch technique and a suture device on the healthy aorta (confirmed by EUS). OPCAB was also selected for patients with malignancy or simple anatomy, such as those with single-vessel disease of the left anterior descending artery. CPB was used in a standardized fashion with a membrane oxygenator and a centrifugal pump with non-pulsatile flow. All conventional CABG procedures were performed with moderate hypothermia and antegrade cold cardioplegic solution.

As mentioned above, OPCAB was the first-choice procedure for the SPECT HP group. In the SPECT HP group, conventional CABG was also applied with IABP using pulsatile flow (80-bpm internal pulsation of IABP during aortic cross-clamping).

Neurological assessment

Perioperative stroke was defined as any focal or global new neurologic deficit at admission. Stroke was diagnosed by neurologists or neurosurgeons and was confirmed by brain computed tomography (CT) or magnetic resonance imaging (MRI). When we encountered a newly developed neurological abnormal finding in patients after discharge or in the midterm or long term, neurologists or neurosurgeons diagnosed stroke based on brain CT or MRI.

Study endpoints

Baseline demographic and clinical data were available for all patients. Initial data were collected from medical records. The primary endpoint was stroke. Early stroke was defined as perioperative stroke and stroke that occurred within 1 month after surgery. Late stroke was defined as readmission because of newly developed stroke. We investigated the postoperative patients who were followed up in a hospital or clinic. When patients the late survival or stroke incidence of a patient had not been assessed, a telephone interview was performed to obtain details. The mean observation period for freedom from stroke was 81.6 months in the SPECT group and 102.7 months in the control group.

Statistical analyses

All data were retrospectively reviewed. All continuous variables were presented as the mean ± SD. A comparative analysis was performed between the different patient groups. Categorical variables were shown as the percentage of the sample. An unpaired two-tailed *t* test was used for univariate comparisons of continuous variables, and an χ^2 test or two-sided Fisher's exact test was for univariate comparisons of categorical variables. The Kaplan–Meier method was used to assess long-term survival and freedom from stroke. The survival curves were compared using a log-rank test. p values of < 0.05 were considered to indicate statistical significance in all of the analyzes. All statistical analyzes were performed using the SPSS software program (version 25.0, IBM Corp. Armonk, NY, USA).

Results

Comparison of the SPECT HP and control groups

The characteristics of the 12 patients in the SPECT HP group and the 248 patients in the control group are shown in Table 1. The prevalence of atrial fibrillation (AF) (33.3% vs. 1.6%), chronic obstructive pulmonary disease (COPD) (25.0% vs. 4.0%), peripheral vascular disease (58.3% vs. 21.1%), and history of cerebrovascular accident (41.7% vs. 11.7%) were higher in the SPECT HP group than in the control group. The Logistic Euro SCORE in the SPECT HP group was higher than that in the control group (6.50 ± 2.71 vs. 4.57 ± 2.71). The perioperative variables and outcomes of the SPECT HP and control groups are shown in Table 2. The rate of OPCAB in the SPECT HP group was significantly higher than that in the control group (83.3% vs. 39.5%). The operation time, CPB time, and cross clamp time were not markedly different between the two groups. Similarly, the number of distal anastomoses was not markedly different between the two groups. The rate of new-onset postoperative atrial fibrillation (POAF) was not markedly different between the two groups. Intraoperative stroke occurred in one patient in the control group and no patients in the SPECT HP group. Early stroke within 30 days (1–30 days after surgery) occurred in 3 patients (1.2%) in the control group and no patients in the SPECT HP group. Late stroke (more than 1 month) occurred in 7 patients (2.8%) in the control group and 1 patient (8.3%) in the SPECT HP group.

Table 1 Patient characteristics in the SPECT HP group vs. the control group

Variable	SPECT HP group ($n = 12$)	Control group ($n = 248$)	p value
Age, years	71.7 ± 11.6	67.3 ± 8.7	0.097
Gender (% male)	11 (91.7%)	189 (76.2%)	0.306
Diabetes mellitus	8 (66.7%)	131 (53.0%)	0.392
Hyperlipidemia	11 (91.7%)	199 (80.2%)	0.472
Hypertension	10 (83.3%)	198 (80.2%)	1.000
Atrial fibrillation	4 (33.3%)**	4 (1.6%)	< 0.001**
Chronic kidney disease	1 (8.3%)	12 (4.9%)	0.468
COPD	3 (25.0%)*	10 (4.0%)	0.017*
Peripheral vascular disease	7 (58.3%)**	52 (21.1%)	0.007**
Cerebrovascular accident	5 (41.7%)*	29 (11.7%)	0.012*
Logistic Euro SCORE	6.50 ± 2.71*	4.57 ± 2.71	0.017*
LVEF (%)	55.9 ± 15.0	60.4 ± 12.1	0.216

Continuous variables are expressed as the mean ± standard deviation

COPD chronic obstructive pulmonary disease, *LVEF* left ventricular ejection fraction

*$p < 0.05$, **$p < 0.01$

Table 2 Perioperative variables and outcomes in the SPECT HP group vs. the control group

Variable	SPECT HP group ($n=12$)	Control group ($n=248$)	p value
Ratio of OPCAB	10 (83.3%)	98 (39.5%)	0.005**
Operation time (min)	271 ± 67	293 ± 142	0.583
CPB time (min)	125 ± 6	109 ± 30	0.428
Cross clamp time (min)	107 ± 2	87 ± 25	0.267
Number of distal anastomoses	3.1 ± 1.4	3.5 ± 1.3	0.326
New-onset POAF	2 (16.7%)	40 (16.1%)	1.000
Stroke < 1 day	0 (0.0%)	1 (0.4%)	1.000
Stroke 1–30 days	0 (0.0%)	3 (1.2%)	1.000
Stroke > 1 month	1 (8.3%)	7 (2.8%)	0.318

Continuous variables are expressed as the mean ± standard deviation

OPCAB off-pump coronary artery bypass grafting, *CPB* cardiopulmonary bypass, *POAF* postoperative atrial fibrillation

**$p < 0.01$

Early and late stroke

The perioperative stroke data are shown in Table 3. In the present study, no patients in the SPECT HP group had early stroke. Four patients in the control group had early stroke. In the SPECT NP group, two patients had early stroke without any intraoperative stroke. One patient in the SPECT NP group had watershed-type stroke on postoperative day (POD) 3, probably due to postoperative hypotension. The other patient had stroke with thromboembolism on POD 9, probably due to cardiac embolism during paroxysmal atrial fibrillation or atheromatous embolism of vulnerable plaque in the carotid artery. Early stroke occurred in 2 of the 211 patients without significant stenosis. One patient suffered a stroke at the time of operation. The patient had undergone brain MRI/MRA in a medical check-up, and could not receive re-MRA due to urgent CABG. The patient had mild–moderate stenosis on MRA 1 year before CABG; however, progression of cerebral atherosclerosis had been noted on postoperative MRA. The cause of stroke might have been atheromatous thrombosis and/or intraoperative hypoperfusion of the moderately stenotic ACA. The other patient was diagnosed with atheromatous thromboembolic stroke on POD 9. Among the 26 patients who did not undergo SPECT, 2 had early stroke. One patient had atheromatous thrombotic stroke on POD 6, the other had stroke with thromboembolism on POD 12, probably due to atheromatous embolism of vulnerable plaque in the carotid artery.

Among the eight cases of late stroke, four were diagnosed with atheromatous thrombotic stroke, another two were diagnosed with watershed-type stroke, and the remaining two were diagnosed with thromboembolic stroke due to atrial fibrillation without anticoagulation therapy.

Freedom from stroke

Figure 3a shows the stroke–free curves of the SPECT HP and control groups. The results of log-rank tests ($p = 0.390$) did not support a significant difference in stroke between the two groups in the Kaplan–Meier survival analysis. The mean observation period of the patient with freedom from stroke was 82.0 months in the SPECT HP group and 101.9 months in the control group. The stroke free rate at 5 years was 91.7% in the SPECT HP group and 94.5% in the control group. Figure 3b shows the stroke-free curves of the SPECT NP and SPECT HP

Table 3 Perioperative stroke data

Case	Age/sex	Group	SPECT	POD	CPB	Preoperative MRA	Reason for stroke	Type of stroke
1	56/M	Control (SPECT NP)	Normal perfusion	3	On	ICA severe stenosis	Watershed-type	Transient
2	71/M	Control (SPECT NP)	Normal perfusion	9	Off	ICA severe stenosis	Cardiac or CA thromboembolism	Transient
3	72/F	Control (Other 211 pt)	No significant stenosis	0	On	ACA mild–moderate stenosis	Atheroma thromboembolism and intraoperative hypoperfusion	Permanent
4	69/M	Control (Other 211 pt)	No significant stenosis	9	Off	CCA moderate stenosis	Atheroma thromboembolism	Transient
5	75/F	Significant stenosis (no SPECT 26 pt)	Not performed[a]	6	On	ICA severe stenosis	Atheroma thromboembolism	Permanent
6	71/M	Significant stenosis (no SPECT 26 pt)	Not performed[b]	12	Off	CCA severe stenosis	Atheroma thromboembolism	Transient

POD postoperative day, *SPECT* single-photon emission computed tomography, *CPB* cardiopulmonary bypass, *MRA* magnetic resonance angiography, *ACA* anterior cerebral artery, *CCA* common carotid artery, *ICA* internal carotid artery

[a]The patient did not undergo SPECT because a radioisotope examination could not be scheduled before CABG

[b]The patient was detected severe calcification of ascending aorta by preoperative computed tomography. The patient did not undergo SPECT because OPCAB with single-vessel disease of the left anterior descending artery had been planned previously

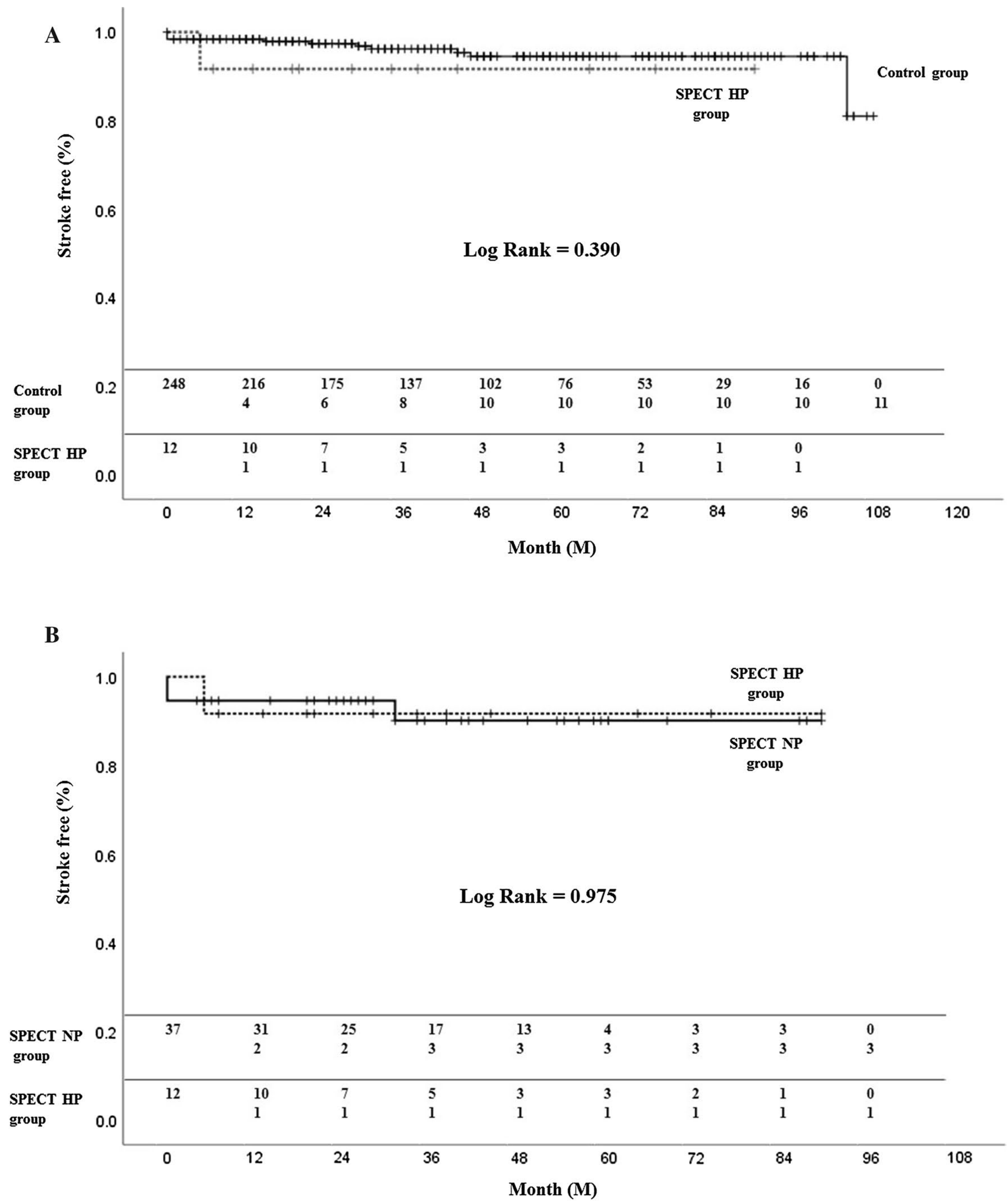

Fig. 3 A. Kaplan–Meier stroke-free curves for the SPECT HP and control groups. B Kaplan–Meier stroke-free curves for the SPECT NP and HP groups

groups. The mean observation period of the patient with freedom from stroke was 81.6 months in the SPECT NP group and 82.0 months in the SPECT HP group. The stroke-free curves of the two groups did not differ to a statistically significant extent ($p = 0.975$; log-rank test).

Discussion

Stroke is a devastating complication in the perioperative period after CABG and can prolong the intubation time and extend the length of intensive-care unit stay and the overall hospital stay. It is also associated with increased rates of morbidity and mortality [1–4]. In previous reports, the incidences of perioperative stroke in patients undergoing CABG ranged from 0.42 to 5.7% [1, 4, 8–13].

Many independent predictors of perioperative stroke have been identified, including moderate-to-severe proximal aortic atherosclerosis, age ≥ 70 years, usage of IABP, a history of pulmonary disease, peripheral vascular disease, cerebral vascular disease, hypertension, diabetes mellitus, previous cardiac surgery, urgent operation, CPB time > 2 h, the need for intraoperative hemofiltration, a high transfusion requirement, the presence of carotid bruit, and cerebral atherosclerosis [1, 4, 8, 9].

Elid et al. showed that an increased carotid intima-media thickness is an independent predictor of new-onset atrial fibrillation, suggesting that subclinical atherosclerosis may predispose patients to future atrial fibrillation [14]. Barr et al. reported that COPD and emphysema were distinctly and independently associated with subclinical atherosclerosis in the carotid arteries and peripheral circulation [15]. In the present study, all patients in the SPECT HP group had significant stenosis or occlusion of the craniocervical vessels. As a result, the rate of AF, COPD, peripheral vascular disease, and the history of cerebrovascular accident in the SPECT HP group might have been higher than those in the control group.

The main causes of stroke were considered to be perioperative thromboembolism and intraoperative hypoperfusion. Likosky et al. created the following classifications for the underlying mechanism of postoperative ischemic stroke after CABG: hemorrhage, thromboembolism (embolic, thrombotic, lacunar), hypoperfusion, other, multiple (≥ 2 competing mechanisms), or unclassified (unknown mechanism) [16]. The incidence rates of these mechanisms were as follows: embolism (62.1%), multiple etiologies (10.1%), and hypoperfusion (8.8%). The severity of stenosis in the craniocervical vessels was not necessarily related to the occurrence of atheromatous thromboembolism. Momjian-Mayor et al. reported that combined hemodynamic and embolic mechanisms may be involved in cortical watershed infarcts when small emboli lodge in the distal fields [17]. In present study, one patient in the SPECT NP group had a watershed-type stroke. In this patient, no prophylactic cerebrovascular intervention for ICA stenosis and intracranial atherosclerotic stenosis (ICAS) was performed, because preoperative SPECT using ACZ detected normal cerebrovascular reactivity. Abildstrom et al. reported that the postoperative global cerebral blood flow (gCBF) was significantly decreased on POD 5–7 even in CABG patients without previous stroke and clinically important carotid stenosis [18]. Furthermore, they argued that the decrease in gCBF could be related to perioperative neuron loss as a consequence of either the diffuse distribution of microemboli in the cerebral circulation, or irreversible damage caused by cerebral ischemia. In other words, we thought that the watershed stroke case might have occurred due to combined postoperative hemodynamic impairment and microembolization in the ischemic area. Yi et al. reported that the administration of either low-molecular-weight heparin or dual antiplatelet therapy was more effective than aspirin alone for the prevention of early neurological deterioration [19]. In the stroke patient of the SPECT NP group, anticoagulant therapy with heparin might have prevented the onset of postoperative microembolic stroke. We, therefore, should have administered anticoagulant therapy with heparin in the present study to prevent embolic stroke, even when such patients do not demonstrate AF, especially for those patients in the SPECT group.

Tarakji et al. furthermore reported that the instantaneous risk of postoperative stroke peaked at 40 h after surgery [9]. Likosky et al. reported that most strokes occurred on the first postoperative day (41.7%), and that an additional 20.4% occurred on the second postoperative day [16]. However, in the present study, one stroke occurred at the time of operation in the Control group, while the other three cases occurred from POD 3 to 9.

In the present study, patients who underwent CABG had routinely used aspirin within the past 24 h. Van Gelder et al. reported that subclinical AF duration > 24 h was associated with a significantly increased risk of subsequent stroke or systemic embolism [20]. Eight patients in the SPECT group were undergoing anticoagulant therapy with unfractionated heparin and/or warfarin were as follows (SPECT HP group, $n=3$; SPECT NP group, $n=5$). If the duration of sustained AF or recurrent paroxysmal AF was longer than 24 h, we administered anticoagulant therapy within 48 h in present study. However, one patient who did not receive anticoagulant therapy might have suffered early stroke caused by paroxysmal AF within 24 h. Horwich et al. reported that new-onset atrial fibrillation after CABG could predict a higher risk of stroke or death after discharge [10]. Late stroke caused by atrial fibrillation without anticoagulation occurred in two patients: one case was caused by paroxysmal atrial fibrillation without anticoagulation; the other patient was diagnosed as cholesterol crystal embolic (CCE) syndrome before surgery. In the CCE syndrome case, anticoagulation with warfarin was not recommended and even suggested to be potentially harmful. Endo et al. reported that concomitant left atrial appendage amputation/ligation at the time of OPCAB reduces the incidence of postoperative stroke in patients who develop atrial fibrillation without an increase in time, cost, or risk [11]. For patients with preoperative AF, left atrial appendage amputation/ligation might be reasonable if anticoagulation therapy is contraindicated.

Among the 12 patients in the SPECT HP group, 10 underwent MRI after discharge. Seven suffered no stroke, while 2 suffered from a silent brain infarct (SBI) in the ischemic area. One suffered a symptomatic stroke caused by chronic atrial fibrillation without anticoagulation. Vermeer et al. reported that elderly people with SBI have > threefold increase in the risk of stroke in comparison to those without infarcts on MRI [21]. In the present study, two patients with SBI did not develop recurrent symptomatic stroke.

Cerebral perfusion SPECT was considered a superior evaluation method to MRA. Imasaka et al. reported that brain perfusion SPECT was very likely to enable the prevention of hemodynamic ischemic stroke during cardiac surgery in patients with obstructive carotid and/or intracranial artery disease [12]. When any significant stenosis of the intracranial and extracranial arteries is detected by MRA, we principally perform SPECT. For patients in the SPECT HP group, we directly consulted with neurosurgeons to assess the severity of the disease, the risk of perioperative stroke, and the possibility of endovascular or surgical intervention for these diseases. In the present study, 11 patients had low rCBF at rest according to SPECT without ACZ. Of these 11 patients, 2 patients who underwent SPECT using ACZ had normal cerebral perfusion reserve. In the other 9 patients in the SPECT HP group, we performed CABG while maintaining the pulsatile blood flow and no patients experienced perioperative stroke.

Kakkos et al. reported that progressive asymptomatic carotid stenosis identified a subgroup of patients whose risk of suffering ipsilateral stroke was approximately twice that of patients without progression [22]. In the patient with intraoperative stroke, the progression of cerebral atherosclerosis had been noted on postoperative MRA. Prophylactic cerebrovascular intervention was technically impossible in the patient who had ACA distal stenosis. However, if preoperative MRA and SPECT had been performed, then maintaining the pulsatile flow during CABG might have prevented the occurrence of intraoperative hemodynamic stroke.

Nakamura et al. reported that the combination of a preoperative examination (MRA, duplex ultrasonography, three-dimensional CT, four-vessel angiography, SPECT) and prophylactic cerebrovascular interventions reduced the prevalence of postoperative stroke in 238 patients from 2.8 to 0.42% [13], while cerebral perfusion was reduced in 11 patients. Seven of the patients in this report received prophylactic cerebrovascular intervention, but such intervention was technically impossible in four patients. Unfortunately, one of the patients who underwent STA-MCA bypass developed acute myocardial infarction after the cerebral procedure. Whether to give priority to coronary perfusion or cerebral perfusion should be discussed further to prevent such events.

Our strategy is based on the following hypotheses: (1) cerebral hypoperfusion might be the most critical risk factor for intraoperative stroke; (2) maintaining the pulsatile blood flow may be essential for preventing a reduction in cerebral blood flow; and (3) significant stenosis of the craniocervical vessels might not be a critical risk factor for stroke so long as the rCBF remains normal. The feasibility of these hypotheses was reviewed in the present study.

We believe that maintaining the pulsatile flow might be useful for preventing cerebral hypoperfusion. OPCAB is an ideal procedure for maintaining the pulsatile blood flow when a certain blood pressure is preserved. IABP is another method that can be used to ensure pulsatile blood flow during any kind of CABG when the descending aorta and access route shows less atherosclerotic change. Kowalewski et al. reported that OPCAB was associated with a significant reduction in the odds of cerebral stroke in comparison to conventional CABG [23]. In our strategy, OPCAB was the first-choice procedure for the SPECT HP group. Kleisli et al. reported that complete revascularization improved the 5-year survival, while off-pump techniques did not affect survival [24]. Complete revascularization should be performed whenever possible. In the SPECT HP group, two patients underwent conventional CABG with IABP due to a heavily atheromatous coronary vessel and small target vessels. Serraino et al. demonstrated the effect of IABP in an automatic 80-bpm mode during cross-clamping in patients undergoing CABG. IABP-induced pulsatile perfusion achieved a better multi-organ response and endothelial protection during CPB than continuous perfusion [25]. Salameh et al. showed, based on the results of histological examinations, that laminar flow during CPB produced significant cellular edema in the kidney and hippocampus. In addition, the markers of hypoxia and apoptosis were elevated in the hippocampus and proximal tubules of the kidney after continuous flow during CPB, suggesting that the pulsatile flow might provide better organ protection—particularly for the hippocampus—than continuous perfusion [26]. In the present study, there were no cases of intraoperative stroke in the SPECT HP group, even in patients with hypoperfusion. This may suggest that maintaining pulsatile blood flow to ensure adequate cerebral blood flow during operation has a strong preventive effect.

Limitations

The present study is associated with several limitations. First, this study was a single-institution, retrospective, small-sized study. In the present study, the other 26 patients who had significant stenosis without SPECT showed a high prevalence of perioperative stroke. In these patients, the prevalence of diabetes mellitus (80.8% vs. 55.3%, $p = 0.024$) and chronic hemodialysis (19.2% vs. 2.0%, $p = 0.017$) were significantly higher than those in the SPECT group. These patients who had multiple risk factors were observed to have macro and microvascular disease. ICAS of a major intracranial artery is one of the most common causes of stroke. Therefore, these patient characteristics might have differed from the control group, and the possibility of a selection bias could not be denied. Larger randomized and prospective studies will, therefore, be necessary to confirm our findings. Second, we did not routinely perform postoperative MRI. MRI was performed for patients who had had any new focal or global neurologic deficit after surgery. Thus, the silent stroke could not be detected as intraoperative or postoperative stroke. Third, SPECT is too costly to be perform widely performed. Each instance of cerebral perfusion SPECT costs approximately $600, while each instance of MRA costs approximately $140. If CABG patients were to undergo both preoperative MRA and SPECT, the cost would be increased to more than $740 per person. However, Salazar et al. reported on the profound impact of stroke after cardiac surgery, noting that it doubled the length of stay in the intensive care unit and the postoperative stay, and that it was associated with a $30,000 increase in total hospital charges [3]. Such overall costs might need to be considered when evaluating the preoperative risk of CABG patients. Finally, in our institution SPECT is a semi-quantitative modality that is performed using the IMP-Graph plot method [7]. These methods are useful; however, we hope to further improve the performance and precision of the medical equipment in the future.

Conclusion

The functional evaluation of cerebral perfusion by SPECT is important when patients have significant stenotic lesions on MRA. If cerebral hypoperfusion or low cerebrovascular reactivity is detected on SPECT, strategies for preventing perioperative stroke may need to be implemented. Our surgical strategy involves maintaining the pulsatile flow by OPCAB or IABP during aortic cross-clamping, an approach that might be feasible for preventing intraoperative stroke in patients with cerebral hypoperfusion. Otherwise normal findings of rCBF may be associated with a low risk of intraoperative stroke, even in patients with significant disease of the craniocervical vessels. Cerebral perfusion SPECT indeed detected hypoperfusion, which was treated successfully by maintaining pulsatile blood flow, but the performance of MRA and SPECT did not prevent thromboembolic stroke. The incidence of perioperative stroke in the SPECT HP and control groups in perioperative stroke did not differ to a statistically significant extent. Thus, the prevention of perioperative stroke based on SPECT findings is deemed important.

Compliance with ethical standards

Conflict of interest All authors declared that they have no potential conflict of interest.

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