



Preoperative brain magnetic resonance imaging and postoperative delirium after off-pump coronary artery bypass grafting: a prospective cohort study

Imagerie préopératoire par résonance magnétique du cerveau et délirium postopératoire après pontage coronarien à cœur battant: une étude prospective de cohorte

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Abstract

Background Delirium after cardiac surgery is a serious complication, increasing morbidity and mortality. Despite its high expectations, off-pump coronary artery bypass grafting (OPCAB) has largely failed to reduce the incidence of postoperative neurological complications. To further investigate the reasons for this failure, we used perioperative brain magnetic resonance imaging (MRI) to determine the relation between MRI findings and postoperative delirium.

Methods Altogether, 98 patients undergoing elective OPCAB were enrolled in this prospective observational study. Patients underwent brain MRI and magnetic resonance angiography (MRA) before and after surgery to identify cerebral infarction, white matter lesions, and

intracranial artery stenosis. Postoperative delirium in the intensive care unit was measured using the delirium rating scale. The relation between postoperative delirium and MRI findings was examined using logistic regression.

Results Magnetic resonance imaging and MRA was completed in 88 (90%) of the patients. New ischemic lesions were present in seven (7.9%) patients. Delirium rating scale scores of 0, 1–7, and ≥ 8 were found in 25 (31%), 48 (60%), and seven (9%) patients, respectively. Multivariate logistic regression analysis revealed that new ischemic lesions (odds ratio [OR] 11.07, 95% confidence interval [CI]: 1.53 to 80.03; $P = 0.017$), carotid artery stenosis (OR 7.06, 95% CI: 1.59 to 31.13; $P = 0.010$), history of myocardial infarction (OR 3.78, 95% CI: 1.05 to 13.65; $P = 0.043$), and deep subcortical white matter hyperintensity (OR 3.04, 95% CI: 1.14 to 8.12; $P = 0.027$) were significantly associated with postoperative delirium.

Conclusions Magnetic resonance imaging findings of new cerebral ischemic lesions, carotid stenosis, and deep subcortical white matter hyperintensity correlated significantly with postoperative delirium in patients who had undergone OPCAB surgery.

Author contributions Hiroki Omiya was involved in patient recruitment and writing the manuscript. Kenji Yoshitani was involved in patient recruitment and data collection. Naoki Yamada was involved in review of the brain magnetic resonance images. Yosuke Kubota was involved in patient recruitment and data collection. Kanae Takahashi was involved in study design and data analysis. Junjiro Kobayashi assisted with editing of the manuscript, particularly for the surgical procedure. Yoshihiko Ohnishi was involved in overall supervision and management of the study.

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Résumé

Contexte La survenue d'un délirium après chirurgie cardiaque est une complication grave, augmentant la morbidité et la mortalité. En dépit des fortes attentes, le pontage coronarien à cœur battant (OPCAB) a largement échoué à démontrer qu'il pouvait réduire l'incidence des complications neurologiques postopératoires. Pour approfondir l'étude des raisons de cet échec, nous avons utilisé une imagerie par résonance magnétique (IRM) périopératoire du cerveau pour déterminer la relation entre les constatations de l'IRM et le délirium postopératoire.

Méthodes Un ensemble de 98 patients subissant un OPCAB électif a été inclus dans cette étude observationnelle prospective. Les patients ont subi une IRM cérébrale et une angiographie par résonance magnétique (ARM) avant et après l'intervention chirurgicale afin d'identifier un infarctus cérébral, des lésions de la substance blanche et une sténose d'une artère intracrânienne. Le délirium postopératoire a été mesuré dans l'unité de soins intensifs au moyen de l'échelle d'évaluation du délirium. La relation entre le délirium postopératoire et les constatations de l'IRM a été analysée par régression logistique.

Résultats L'imagerie par résonance magnétique et l'ARM ont été effectuées chez 88 (90 %) patients. De nouvelles lésions ischémiques ont été retrouvées chez sept (7,9 %) patients. Les scores de l'échelle d'évaluation du délirium étaient de 0, 1 à 7, et ≥ 8 chez, respectivement, 25 (31 %), 48 (60 %), et 7 (9 %) patients. Analyse de régression logistique multifactorielle a révélé que les nouvelles lésions ischémiques (rapport de cotes [RC] 11,07, intervalle de confiance [IC] à 95 %: 1,53 à 80,03; $P = 0,017$), une sténose carotidienne (RC 7,06, IC à 95 %: 1,59 à 31,13; $P = 0,010$), un antécédent d'infarctus du myocarde (RC 3,78, IC à 95 %: 1,05 à 13,65; $P = 0,043$), et une hyperintensité de la substance blanche sous-corticale profonde (RC 3,04, IC à 95 %: 1,14 à 8,12; $P = 0,027$) étaient significativement associés au délirium postopératoire.

Conclusions La constatation par imagerie cérébrale par résonance magnétique de nouvelles lésions ischémiques cérébrales, d'une sténose carotidienne et d'une hyperintensité de la substance blanche sous-corticale profonde est significativement corrélée au délirium postopératoire chez des patients ayant subi une intervention pour OPCAB.

number of elderly patients with a similarly increasing number of comorbidities are able to safely undergo cardiac surgery. Although mortality after cardiac surgery has decreased, neurologic complications remain an important and widespread issue in an ever-aging surgical population. Delirium, reflecting acute changes in cognition and attention, is common after cardiac surgery, occurring in 9-52% of patients.^{1,2} In particular, recent studies have revealed that postoperative delirium may have more than transient effects, and can negatively affect long-term morbidity and mortality.^{1,3-5} Therefore, understanding the risks for postoperative delirium is an important consideration for surgeons and anesthesiologists.

Cardiopulmonary bypass (CPB) may result in neurological injury caused by emboli, systemic inflammation, and unpredictable intraprocedural hypoperfusion.⁶ In an attempt to avoid these adverse CPB sequelae, off-pump coronary artery bypass grafting (OPCAB) was introduced during the early 1990s. This technique was expected to reduce postoperative neurological complications, but recent studies largely failed to show any significant benefit.⁷⁻⁹

Microembolization has been considered a significant contributor to postoperative delirium.^{10,11} However, relatively few studies have investigated the relation between the brain lesions that would be expected to result from a significant embolic load and postoperative delirium. Indeed, studies of cerebral emboli in conventional on-pump coronary artery bypass surgery (CABG) using transcranial Doppler (TCD) have failed to show any significant association with postoperative delirium.¹² In regard to OPCAB, however, there are a few reports investigating the relation between cerebral embolia and postoperative delirium. Importantly, not all of the cerebral emboli detected by TCD would be expected to induce a clinically apparent ischemic lesion. Therefore, magnetic resonance diffusion-weighted imaging (DWI) might provide more information about the more subtle ischemic lesions caused by cerebral emboli.

With respect to carotid artery lesions, we previously reported that carotid artery stenosis was significantly associated with postoperative stroke and delirium.¹³ Embolic signals measured using TCD were even observed in patients with asymptomatic carotid artery stenosis, resulting in silent cerebral infarction.^{14,15} Significant atherosclerosis, manifesting as carotid stenosis or ascending aortic plaque, was also associated with delirium after CABG.¹⁶ Therefore, evaluation of carotid artery stenosis and ascending aortic plaque to identify its relation to both postoperative delirium and new magnetic resonance imaging (MRI)-detectable ischemic lesions may provide important information on the pathophysiology of these neurological abnormalities.

As a result of continuing improvements in surgical techniques and cardiovascular anesthesia, an increasing

The principal aim of the present study was to investigate the relation between postoperative delirium and new ischemic lesions detected by MRI-DWI after OPCAB. The impact of magnetic resonance angiographic (MRA) detectable intracranial artery stenoses that could result in cerebral hypoperfusion was also explored. Finally, as recent studies have reported that white matter hyperintensities may predict postoperative delirium with conventional on-pump CABG,¹⁷⁻¹⁹ we assessed whether these white matter lesions were associated with postoperative delirium after OPCAB.

Methods

Patients

The institutional review board of our hospital approved this study (September 2008). All participants provided written informed consent prior to enrolment. From February 2009 to July 2011, consecutively consenting patients undergoing elective OPCABG who were more than 20 yr old were enrolled. Exclusion criteria included patients with contraindications to MRI (e.g., claustrophobia or anxiety) or who had psychiatric disease (depression) or Kawasaki's disease.

Brain MRI

Brain MRI was performed using two 1.5-T systems (MAGNETOM Vision or MAGNETOM Sonata; Siemens Healthcare, Tokyo, Japan). All patients underwent preoperative MRI within three days of surgery, with postoperative MRI being performed within two weeks after removal of the temporary pacing leads. Preoperative MRI was performed using T2-weighted imaging (T2WI) with TR/TE of 5400/99 msec or 5400/85 msec; T2*-weighted imaging (T2*WI) with TR/TE of 736/20 msec and a flip angle of 30°; fluid-attenuated inversion recovery (FLAIR) with TR/TE/TI of 9000/105/2400 msec; diffusion-weighted imaging (DWI) with TR/TE of 4000/100 msec and b of 1000 sec-mm⁻² and MRA. A slice thickness of 4 mm with a slice interval of 2 mm was used for T2WI, T2*WI, FLAIR, and DWI. Postoperative MRI was performed using the same sequences as for preoperative MRI. MRA was not performed postoperatively.

Abnormal lesions were diagnosed as follows. Preoperative cerebral infarction was detected using preoperative FLAIR and DWI. A significant intracranial arterial stenosis was defined as > 50% stenosis on MRA in one or more of the intracranial carotid, vertebral, basilar, first and second portions of the anterior cerebral, and/or the

horizontal portion of the middle cerebral arteries. Using DWI and FLAIR, new postoperative ischemic lesions were defined as cerebral lesions > 2 mm that were not present before surgery. Minor intracranial bleeding was diagnosed using T2*WI. White matter lesions were defined as periventricular hyperintensity (PVH) and deep subcortical white matter hyperintensity (DSWMH). They were graded (grades 0-3) according to the Fazekas scale: 0, absence; 1, cap of pencil-thin PVH or punctate focal DSWMH; 2, smooth halo PVH or early confluence of focal DSWMH; 3, irregular PVH extending into the deep white matter or large confluent areas of DSWMH.²⁰ An experienced neuroradiologist blinded to the patients' preoperative and postoperative clinical status read the MR images. Preoperative carotid artery duplex scanning was performed to assess the severity of the carotid stenosis, which was quantified as present (stenosis > 50%) or absent (stenosis < 50%).²¹ Transesophageal echocardiography was performed in all patients to evaluate the severity of aortic atherosclerosis (using the Katz score).²²

Delirium assessment

All patients were assessed for delirium six to 24 hr after extubation by a nurse trained to use the delirium rating scale R98 (DRS-R98). The DRS-R98 is composed of a 16-item clinician-rated scale. It includes three severity items and three diagnostic items, for a maximum total score of 46 points.²³ The DRS-R98 divides delirium into three categories based on severity: no delirium (total points 0), subclinical delirium (total points 1-7), and delirium (total points ≥ 8).²⁴

Operative procedure

All patients underwent standard OPCAB using an aortic "no-touch" technique, avoiding aortic side clamping and manipulation of the ascending artery to minimize the risk of stroke. Vein grafts were anastomosed with an assist device where indicated, using either the Enclose 2 (Novare Surgical Systems, Inc. Cupertino, CA, USA) or the PAS PORT system (Cardiac Inc., Redwood City, CA, USA). Surgical procedures, operative times, and use of anesthetic and narcotics were obtained from the operative record. We selected potential risk factors of postoperative delirium from a review of the literature. Candidate variables included age, body weight, history of smoking, hypertension, hyperlipidemia, heart failure, diabetes, perioperative atrial fibrillation, myocardial infarction, cerebral infarction, chronic obstructive pulmonary disease, chronic kidney disease, duration of the operation and anesthesia, intubation time, and MRI findings.

Statistical analysis

Our initially planned sample size was based on an expected delirium incidence of 12% in patients without carotid stenosis. Using a power of 80%, a 5% two-sided significance level, and a 2.5 ratio of patients with carotid artery stenosis to patients without carotid artery stenosis, with a 2.0 relative risk of delirium in those with carotid stenosis,¹³ our final sample size was estimated to be 370.

Continuous variables are presented as the mean (SD), and discrete variables are presented as the frequency and percentages. Univariate analysis with the proportional odds model was used to evaluate risk factors for postoperative delirium. The proportional odds ratio (OR) was assumed to be equal between the two groups' comparisons (i.e., DRS score between 0 and 1-7; as well as between 1-7 and ≥ 8) in this model. In addition, we conducted a multivariate analysis that included risk factors with a univariate $P < 0.3$. The model was selected by the Akaike's information criterion (AIC),²⁵ with low AIC values being preferred. ORs and 95% confidence intervals (CI) were also determined. Postoperative outcome, length of stay (LOS) in the intensive care unit (ICU), intubation, and hospital LOS were tested between patients with or without delirium using the non-parametric Jonckheere-Terpstr test. P values < 0.05 (two-sided) were considered to indicate significance. Statistical analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

Because patient recruitment was slower than expected, we ceased enrolment after a convenience sample of 105 eligible patients (Figure). Before the baseline data collection, seven patients were excluded for claustrophobia, anxiety, or refusing informed consent. Ten patients were further excluded from analysis because of either the MRI or carotid artery ultrasonography not being completed. We thus analyzed 88 patients. The patients' preoperative characteristics and intraoperative parameters are shown in Table 1. MRI findings are shown in Table 2. Preoperative MRA revealed intracranial artery lesions in 24 (27%) of the 88 patients. PVH was found in 71 (81%) patients and DSWMH in 76 (86%) patients. Postoperative DWI or FLAIR MRI detected new ischemic lesions in seven (7.9%) patients. Overall, 25 (32%), 48 (60%), and seven (8%) patients had total DRS scores of 0, 1-7, and ≥ 8 , respectively.

Table 3 shows the univariate analysis of factors correlated with postoperative delirium. Older age (≥ 70 yr), preoperative myocardial infarction, new ischemic lesions on MRI, new white matter disease (WMD; i.e., DSWMH or PVH) had a significant association with postoperative delirium. Multivariate analysis demonstrated a significant association

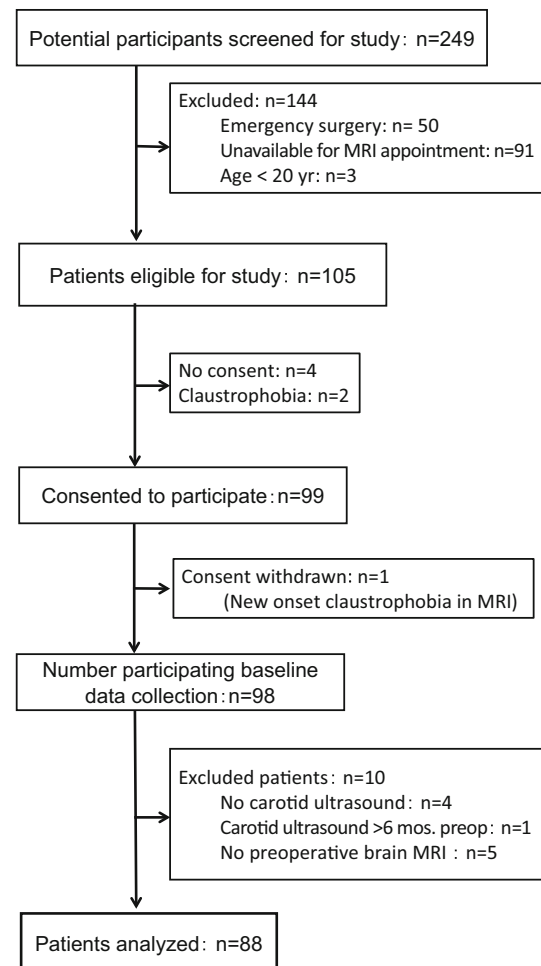


Figure Patient enrolment and outcomes. MRI = magnetic resonance imaging

with new ischemic lesions (OR 11.07, 95% CI 1.53 to 80.03; $P = 0.017$), carotid artery stenosis (OR 7.06, 95% CI 1.59 to 31.31; $P = 0.010$), myocardial infarction (OR 3.78, 95% CI 1.05 to 13.65; $P = 0.043$), and WMD (OR 3.04, 95% CI 1.14 to 8.12; $P = 0.027$) (Table 4). As the DRS advanced from 1-7 to ≥ 8 , the ICU LOS was significantly greater in patients with postoperative delirium than in those without delirium (Table 5).

There was no significant association between new ischemic lesions detected by MRI and carotid artery stenosis, cerebral artery stenosis, or the degree (determined by the Katz score) of aortic atherosclerosis.²²

Discussion

This prospective observational study examined whether brain MRI findings and previously reported risk factors for postoperative delirium were associated with delirium following OPCABG surgery. Our main finding was that

Table 1 Patients' characteristics and intraoperative parameters ($n = 88$)

Age (yr)	69 (7)
Height (cm)	162 (8)
Weight (kg)	63 (11)
Hypertension	75 (85%)
Smoking	11 (13%)
Diabetes mellitus	47 (53%)
Hyperlipidemia	65 (74%)
History of myocardial infarction	29 (33%)
angina pectoris	8 (9%)
heart failure	10 (11%)
atrial fibrillation	2 (2%)
cerebral infarction	17 (19%)
Carotid artery stenosis (>50%)	20 (23%)
Operating time (min)	290 (56)
Transfusion (mL)	1330 (1316)
Bleeding (mL)	1793 (1325)
Fluid administration (mL)	5069 (1948)
Urine output (mL)	1773 (972)
Lowest hemoglobin concentrations (g·dl ⁻¹)	8.6 (0.9)
Katz score*	
I	7 (8%)
II	25 (28%)
III	32 (36%)
IV	19 (22%)
V	2 (2%)

Data represent mean (SD) or number (%), as indicated

*Katz score;²²

I: Normal to mild intimal thickening; II: Severe intimal thickening without protruding atheroma; III: Atheroma protruding < 5 mm into lumen; IV: Atheroma protruding \geq 5 mm into lumen; V: Any thickness with mobile component or components

new ischemic lesions seen on MRI, carotid artery stenosis > 50%, and DSWMH were independently associated with postoperative delirium. We also demonstrated a relation between delirium and myocardial infarction.

The incidence of new ischemic lesions detected by brain MRI in our study was 7.9%. This contrasts with on-bypass cardiac surgery studies in which a high number of postoperative lesions were detected by MRI: 47% after valvular surgery²⁶ and 30% after on-pump CABG.²⁷ In a prior study of OPCAB, although the patient number was small ($n = 13$), no postoperative embolic ischemic events were observed.²⁸ Thus, in comparison to reports of on-pump cardiac surgery, the incidence of injuries related to brain embolism following OPCAB was relatively low. The difference in the rates of DWI-defined ischemic lesions between the on-bypass and off-bypass cases might be explained by the numbers of cerebral emboli that occurred. For example, Liu *et al.* also found that avoiding CPB

Table 2 Findings of brain magnetic resonance imaging ($n = 88$)

Intracranial artery lesion	24 (27%)
ICA stenosis	16 (18%)
ICA occlusion	2 (2%)
M1 stenosis	5 (6%)
M1 occlusion	1 (1%)
A1 stenosis	7 (8%)
Basilar artery stenosis	1 (1%)
Basilar artery occlusion	1 (1%)
Vertebral artery stenosis	4 (4%)
Vertebral artery occlusion	2 (2%)
Fazekas scale	
PVH	
grade 0	17 (19%)
grade 1	49 (56%)
grade 2	21 (24%)
grade 3	1 (1%)
DSWMH	
grade 0	12 (14%)
grade 1	59 (67%)
grade 2	16 (18%)
grade 3	1 (1%)
T2* positive	14 (16%)
History of cerebral infarction	17 (19%)
New ischemic lesion in MRI	7 (8%)

ICA = internal carotid artery; M1 = M1 segment of middle cerebral artery; A1 = A1 segment of anterior cerebral artery; PVH = periventricular hyper intensities; DSWMH = deep subcortical white matter hyper intensities; T2* = T2 star weighted image MRI = magnetic resonance imaging

during CABG decreased the number of postoperative cerebral microemboli measured with bilateral TCD ultrasonography.²⁹

There are several mechanisms by which ischemic lesions could result in delirium. For example, in an animal study, cholesterol cerebral emboli altered the permeability of the blood-brain barrier, activated microglia, and caused cognitive dysfunction in rats.³⁰ After microglia returned to their resting state, the rats recovered from the cognitive decline, suggesting that inflammation due to emboli may have influenced cognitive function. Neuroinflammation may also be associated with delirium. Proinflammatory cytokines have been shown to lead to synaptic and neuronal dysfunction and to subsequent neurobehavioural and cognitive symptoms that are characteristic of delirium.³¹ Although the incidence of embolic events was low, it is possible that emboli contributed to the postoperative delirium given that the theories regarding the pathogenesis of delirium – neuronal aging, oxidative stress, neurotransmitter and

Table 3 Univariate analysis of risk factors of postoperative delirium

DRS	0 (n = 25)	1-7 (n = 48)	>8 (n = 7)	Odds ratio	95% CI	P value
Age > 70	8	23	6	2.98	1.17 to 7.59	0.022
DM	8	12	1	0.63	0.23 to 1.70	0.361
HT	8	10	2	0.68	0.25 to 1.86	0.452
Anemia	1	1	1	2.24	0.21 to 24.28	0.509
HLP	1	1	1	2.12	0.20 to 23.01	0.536
CKD	1	7	1	2.45	0.57 to 10.50	0.227
COPD	1	3	1	1.69	0.26 to 11.20	0.585
Smoking	5	8	2	1.07	0.35 to 3.28	0.912
AMI	3	21	2	2.83	1.04 to 7.71	0.042
HF	1	8	0	1.66	0.40 to 6.88	0.485
AF	0	2	0	2.24	0.12 to 40.60	0.586
Carotid AS	2	14	2	2.87	0.93 to 8.87	0.067
Cerebral AS	4	14	2	1.82	0.64 to 5.14	0.262
Operation time > 5 hr	17	31	5	0.967	0.38 to 2.44	0.944
Bleeding > 1500 mL	12	24	4	1.173	0.49 to 2.82	0.721
Katz Score				1.26	0.83 to 1.92	0.283
I	4	2	0			
II	10	11	2			
III	6	21	1			
IV	3	13	3			
V	2	0	0			
New lesions in MRI	1	3	3	8.73	1.51 to 50.66	0.016
DSWMH				3.21	1.36 to 7.59	0.008
Grade 0	5	5	0			
Grade 1	18	34	3			
Grade 2, 3	2	9	4			
PVH				2.65	1.34 to 5.26	0.005
Grade 0	9	6	1			
Grade 1	12	31	1			
Grade 2	4	10	5			
Grade 3	0	1	0			

DRS = delirium rating scale; CI = confidence interval; DM = diabetes mellitus; HT = hypertension; HPL = hyper lipidemia; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; AMI = acute myocardial infarction; HF = heart failure; AF = atrial fibrillation; Carotid AS = carotid artery stenosis; Cerebral AS = cerebral artery stenosis; MRI = magnetic resonance imaging; DSWMH = deep subcortical white matter hyper intensities; PVH = periventricular hyper-intensity. Odds ratio means between DRS = 0 and 1-7; 1-7 and > 8

Table 4 Multivariate analysis of risk factors of postoperative delirium

	Odds ratio	95% CI	P value
New ischemic			
Lesion in MRI	11.07	1.53 to 80.03	0.017
Carotid AS	7.06	1.59 to 31.13	0.010
MI	3.78	1.05 to 13.65	0.043
DSWMH	3.04	1.14 to 8.12	0.027

CI = confidence interval; MRI = magnetic resonance imaging; Carotid AS = carotid artery stenosis; MI = myocardial infarction; DSWMH = deep subcortical white matter hyper intensities

neuroendocrine dysfunction, network disconnectivity – are complementary rather than competing.³²

The presence of carotid artery stenosis > 50% implies the presence of chronic cerebral hypoperfusion and systemic arteriosclerosis. Symptomatic carotid artery stenosis also plays an important role in other cerebrovascular diseases, such as stroke, cognitive impairment, and dementia.^{33,34} Carotid stenosis is also associated with white matter lesions.³⁵ A recent study indicated that asymptomatic internal carotid atherosclerosis is associated with large white matter hyperintensities, low total brain volume, and poor neuropsychological performance.³⁶ The patients in our

Table 5 Relationship between delirium and duration of ICU and hospital stay

ICU stay (hr)	Median	25% tile	75% tile	<i>P</i> value
DRS				
0	22	19	42	
1-7	43	22	89	
8 >	67	46	73	0.002
Hospital stay (days)	Median	25% tile	75% tile	<i>P</i> value
DRS				
0	19	16	22	
1-7	20	18	24	
8 >	21	20	25	0.078

DRS = delirium rating scale; ICU = intensive care unit

study who had carotid stenosis > 50% were most likely asymptomatic because at our institute carotid endarterectomy and carotid artery stenting are prioritized over CABG in patients with symptomatic carotid stenosis. Our finding that both carotid artery stenosis and white matter lesions had a significant association with postoperative delirium is compatible with the findings of previous studies.

White matter lesions appear as hyperintensities on T2-weighted MRI images. In the general population, the prevalence of white matter hyperintensities ranges from 11 to 21% in adults around 64 yr of age to 94% at age 82 yr.^{37,38} Previous studies reported a significant association between white matter lesions and postoperative delirium.^{17,18} Hatano *et al.* retrospectively investigated whether white matter hyperintensities predicted delirium after cardiac surgery.¹⁷ Although the incidence of postoperative delirium might have been underestimated because of the nature of their retrospective chart review using the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition, severe DSMH had a significant OR (OR 3.9, 95% CI: 1.2 to 12.5; *P* = 0.02) in the multivariate logistic regression analysis. The population of the above study¹⁷ included patients with valve replacement or repair and with OPCAB, making it difficult to determine whether the effects of CPB were significant. In contrast, our study enrolled only OPCAB patients, and delirium was prospectively assessed with the DRS-98, likely resulting in more accurate findings.

Although we used the DRS-98 in the ICU, the Confusion Assessment Method-ICU (CAM-ICU) is arguably used more commonly for screening and diagnosis of delirium. However, the CAM-ICU is a categorical assessment, and thus the incidence of postoperative delirium might be underestimated by missing patients with less severe manifestations of delirium. Indeed, we examined specific

score ranges to ensure that symptoms of postoperative delirium were not overlooked.

This study has several limitations. First, the number of patients studied was smaller than that of our initially calculated sample size, thus weakening the study's statistical power. However, we obtained significant results that were compatible with those of previous studies. Second, the delirium assessment was performed only once, between six and 24 hr after extubation. Because of its fluctuating nature, we might have missed some patients who manifested delirium after the one-time assessment. In our institute, most patients are transferred to the ward of the cardiac surgical division the day after surgery. As a result, we were able to evaluate delirium status only in the ICU. Thus, delirium may have been underestimated if it occurred after patients moved to the ward. The duration of the ICU stay, however, had a significant association with postoperative delirium, meaning that the one-time assessment may have had clinical significance. Third, there was uncertainty as to what happens with these white matter lesions over the long term, although white matter lesions could indirectly predict an increased risk of stroke, dementia, and mortality.¹⁹ Fourth, we made an assumption that emboli are the key etiologic factors in all the lesions described, but we do not have any objective measurement of emboli, such as with TCD ultrasonography. Thus, we cannot rule out hypoperfusion or inflammation playing a significant role in the lesions that we described.

In conclusion, in patients undergoing OPCAB surgery, carotid artery stenosis of > 50% and the presence of white matter lesions were significantly associated with postoperative delirium in the ICU. Although MRI detected a lower incidence of new ischemic lesions than were seen in prior on-pump CABG studies, they were significantly associated with postoperative delirium.

Conflicts of interest None declared.

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