Incidence and impact of silent brain lesions after coronary artery bypass grafting

Check for updates

Hitoshi Tachibana, MD,[a] Arudo Hiraoka, MD, PhD,[a] Kazuya Saito, PT,[b] Yoshitaka Naito, OT,[b] Genta Chikazawa, MD, PhD,[a] Kentaro Tamura, MD,[a] Toshinori Totsugawa, MD, PhD,[a] Hidenori Yoshitaka, MD, PhD,[a] and Taichi Sakaguchi, MD, PhD[a]

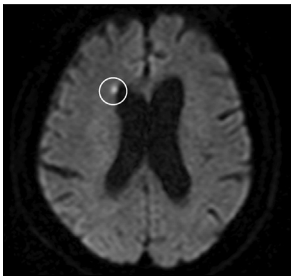
ABSTRACT

Objective: Silent brain lesions are known to occur after coronary artery bypass grafting (CABG). The aim of this study was to seek the incidence rate, the influence of procedures, and their impact on the postoperative course.

Methods: From July 2016 to April 2018, 104 consecutive patients undergoing elective and isolated first-time CABG (65 off-pump and 39 on-pump) were enrolled. New brain lesions were evaluated by brain magnetic resonance imaging both before and after CABG. Postoperative outcomes, including cognitive function, were compared between patients with and without brain lesions.

Results: The overall incidence of new brain lesions was 20.1% (21/104). Excluding one symptomatic stroke case, silent brain lesions were revealed in the remaining patients. The percentage of on-pump CABG (61.9% [13/21] vs 31.3% [26/83], $P = .019$) and aortic clamp (52.4% [11/21] vs 24.1% [20/83], $P = .014$) were significantly greater in patients with brain lesions. Brain lesions were observed in 12.3% and 15.8% of patients in the off-pump and anaortic CABG. The Katz Index of Independence in Activities of Daily Living was significantly lower in patients with brain lesions (from 5.8 ± 0.9 to 5.4 ± 1.2 vs from 5.9 ± 0.5 to 5.9 ± 0.6, $P = .013$). In patients with new lesions, postoperative cognitive dysfunction (POCD) was observed only in multiple lesions, and the maximum size was significantly greater in patients with POCD.

Conclusions: Magnetic resonance imaging of the brain frequently detected postoperative silent brain lesions after CABG in off-pump and aorta non-touch groups. Multiple and larger new brain lesions were associated with the development of POCD. (J Thorac Cardiovasc Surg 2021;161:636-44)



Brain magnetic resonance imaging in typical cases of silent brain lesions.

Central Message

Silent brain lesions were frequently observed even in off-pump and anaortic coronary artery bypass grafting. Multiple and large lesions were associated with cognitive dysfunction.

Perspective

New brain lesions were observed in 12.3% and 15.8% of the off-pump coronary artery bypass grafting (OPCAB) and aorta non-touch groups. Anaortic OPCAB could not absolutely avoid silent brain lesions, and multiple and larger brain lesions were associated with postoperative cognitive dysfunction. More accurate evaluation is required to know whether these brain lesions are really "silent" or not.

See Commentaries on pages 645, 647, and 649.

Coronary artery bypass grafting (CABG) is one of the most common surgical procedures. Despite advances in surgical technique, anesthesia management, and postoperative intensive care, postoperative stroke remains a major complication after CABG, and the incidence rate ranges from 0.4% to 13.8%.[1,2] The potential causes of stroke reported are cerebral and carotid artery disease, atherosclerotic change of the aorta, air embolism, hypotension, and reactive thrombocytosis.[3-5] Regarding techniques of surgical revascularization, investigators in the first large-scale Veterans Affairs Randomized On/Off Bypass (ROOBY) trial and the CABG Off or On Pump Revascularization Study (CORONARY) found no significant difference between off-pump and on-pump CABG (OPCAB and ONCAB) in 30-day rate of mortality and stroke.[6,7]

From the Departments of [a]Cardiovascular Surgery and [b]Rehabilitation, The Sakakibara Heart Institute of Okayama, Okayama, Japan.

Read at the 2018 American Heart Association Scientific Sessions, Chicago, Illinois, November 10-12, 2018.

Received for publication May 21, 2019; revisions received Sept 27, 2019; accepted for publication Sept 27, 2019; available ahead of print Oct 16, 2019.

Address for reprints: Taichi Sakaguchi, MD, PhD, Department of Cardiovascular Surgery, The Sakakibara Heart Institute of Okayama, 2-5-1 Nakaicho, Kita-ku, Okayama, 700-0804, Japan (E-mail: ts472@tuba.ocn.ne.jp).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.09.162

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
DWI	= diffusion-weighted imaging
Katz ADL	= Katz Index of Independence in Activities of Daily Living
MRI	= magnetic resonance imaging
ONCAB	= on-pump coronary artery bypass grafting
OPCAB	= off-pump coronary artery bypass grafting
POCD	= postoperative cognitive dysfunction
TE	= echo time
TR	= repetition time

However, manipulation of the ascending aorta, including cannulation for cardiopulmonary bypass, aortic cross-clamping, and proximal anastomosis, was directly associated with a greater incidence of postoperative stroke in several studies.[8-13] These reports indicated side-clamping in OPCAB can be a risk for stroke in high-risk patients, and the aortic "no-touch" technique was associated with nearly 60% lower risk of postoperative cerebrovascular events.[12,13]

In contrast, silent cerebral infarction in the asymptomatic population after cardiac surgeries has been documented. Notably, silent brain lesions were observed in cardiac surgeries without cardiopulmonary bypass, and the incidence rate was similar between ONCAB (16%-45%) and OPCAB (31%).[14,15] In addition, the new lesions, expected as "silent" on magnetic resonance imaging (MRI) scans, appeared to cause postoperative cognitive dysfunction (POCD); therefore, it is important to evaluate silent brain lesions to improve clinical outcomes. However, there is still only a small number of studies with small samples. The aim of this study is to elucidate the incidence of perioperative stroke, including silent lesions in patients undergoing elective and isolated CABG with the use of MRI of the brain, and to evaluate the impact on postoperative physical and cognitive function.

PATIENTS AND METHODS

Cohort and Data Collection

This was a single-center, prospective study. From July 2016 to April 2018, a cohort of 108 consecutive patients undergoing elective and isolated first-time CABG at the Sakakibara Heart Institute of Okayama, Japan, were enrolled. After excluding 4 patients with contraindications for MRI of the brain (eg, pacemaker or claustrophobia), the remaining 104 patients were enrolled.

The overall mean patient age was 69 (range, 48-85) years, of whom 30.8% (32/104) were female. The cohort included 65 (62.5%) OPCAB and 39 (37.5%) ONCAB cases. In the OPCAB group, median full sternotomy and left thoracotomy approaches was selected in 18 and 47 patients, respectively. In the ONCAB group, on-pump beating and arrest CABG was performed in 9 and 30 patients, respectively. The aim of this prospective study was to seek the incidence of stroke, including silent brain lesions after CABG, and evaluate the influence on the postoperative course. We compared perioperative data between patients with and without new brain lesions after CABG. This study was approved by the Sakakibara Hearty Institute of Okayama Institutional Review Board on June 30, 2016, in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Individual patient consent for entry into this prospective study was obtained from all patients.

Anesthesia and Surgical Procedures

Midazolam, remifentanil, and rocuronium were administered intravenously and isoflurane was used to maintain the sedation level. In ONCAB, CPB was established by using ascending aortic cannulation and bicaval drainage. Heparin was administrated to obtain an activated clotting time of ≥400 seconds. When cardiopulmonary bypass support was required, on-pump arrest CABG is the first choice. Myocardial protection was achieved by using cold modified St Thomas' solution. On-pump beating CABG was selected for patients with ongoing ischemia. ONCAB was performed in mild hypothermia (34°C-36°C). In OPCAB cases, a suction stabilizer (Octopus; Medtronic Inc, Minneapolis, Minn) was used to expose and stabilize the target lesions. Vein grafts were anastomosed by using the side aortic clamp or proximal anastomosis device (Enclose II, Novare Surgical system; Cardiac Inc, Redwood City, Calif) based on the condition of the ascending aorta. Heparin was administrated to obtain an activated clotting time of ≥350 seconds.

ADULT

MRI of the Brain Protocol

An MRI of the brain was performed in all patients pre- and postoperatively on a 1.5-Tesla whole-body system (Excelart Vantage; Toshiba Medical Systems Corporation, Tokyo, Japan). The magnetic resonance protocol included the following sequences: (1) T1-weighted imaging with repetition time (TR)/echo time (TE) of 450/12 milliseconds, (2) T2-weighted imaging with TR/TE of 4400/105 milliseconds, (3) fluid-attenuated inversion recovery with TR/TE/TI 9000/105/2400 milliseconds, and (4) diffusion-weighted imaging (DWI) with TR/TE/TI of 4800/100 milliseconds and b value of 1000 sec $\times$ mm^{-2}. A slice thickness of 6 mm with slice interval of 1.5 mm was used for T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery, and DWI. Preoperative cerebrovascular evaluation was performed by brain MRI, and cerebral and cervical magnetic resonance angiogram. Preoperative MRI findings included old cerebral infarction in 91 patients (87.5%) and chronic ischemic change in 7 patients (6.7%). There were 6 patients (5.8%) without abnormal findings. Postoperative MRI of the brain was performed within 2 weeks after CABG to detect stroke, and new lesions in DWI were independently evaluated by experienced radiologists. MRI was performed within 1 week in 15 patients. Silent brain lesions were defined as new lesions detected by postoperative DWI in asymptomatic patients.

Evaluation of the Atheromatous Level of the Aorta

The thickness of the ascending aorta was evaluated by preoperative enhanced computed tomography. Severity of the atheromatous level was scored based on the intimal thickness (1, normal; 2, nonprotruding intimal thickening >2 mm; 3, atheroma <4 mm; 4, atheroma ≥4 mm).[16]

Assessment of Physical and Cognitive Function

Both of pre- and postoperative evaluation could be performed in 76 patients by physical test and 47 patients by cognitive tests. To assess physical function, standing balance, gait speed, and the Short Physical Performance Battery were used. To evaluate pre- and postoperative patients' activities of daily living, the Katz Index of Independence in Activities of Daily Living (Katz ADL <6 points, not frail; 6 points, frail) was used.[17]

To evaluate cognitive function, the Mini-Mental Status Examination, Montreal Cognitive Assessment, Trail-Making Test A, and Trail-Making Test B were performed before and after surgery. After surgery, the results of these tests were evaluated from 5 to 7 days after the patients were returned from the intensive care unit to the general ward. POCD was defined as a decline of score >20% from baseline in 2 or more neuropsychological tests or as incomprehensibility and discontinuance of 1 or more tests that were performed before surgery.

Statistical Analysis

Continuous data are presented as mean ± standard deviation. Continuous data were compared with a Mann–Whitney *U* test. Categorical variables are given as a count and percentage of patients and were compared using the χ^2 test. When any expected frequency was less than 1, or 20% of expected frequencies were less than or equal to 5, the Fisher exact test was used. Changes in physical and cognitive parameters between patients with and without new brain lesion were analyzed by mixed linear model (restricted maximum likelihood approach). New lesions (+) or (–) and the timing of cognitive test were included as variables. Individual was used as the random effect. A *P* value less than .05 was considered to be statistically significant. All data were analyzed using the Statistical Analysis Systems software JMP 8.0 (SAS Institute Inc, Cary, NC).

RESULTS

Incidence of New Brain Lesions After CABG

The overall incidence of new brain lesions after CABG was 20.1% (21/104). Symptomatic stroke occurred in 2 patient who underwent OPCAB. In this case, a proximal anastomosis device (Enclose II) was used. Greater functional impairment and aphasia remained after surgery (Figure 1, *A* and *B*). In contrast, postoperative MRI detected silent brain lesions in 20 patients (Figure 2, *A-C*). The locations of postoperative new brain lesions detected by MRI were supratentorial in 15 cases (71%), infratentorial in 4 cases (19%), and infra-and-supratentorial in 2 cases (10%). A single lesion was found in 11 cases (52%), and multiple lesions were found in 10 cases (48%). There was no significant difference in the percentage of MRI timing <1 week between patients with and without new brain lesions (14% [3/21] vs 18% [15/83], *P* = 1.00). Data of patients with brain lesions are summarized in Table 1.

Comparison of Patient Characteristics

We compared perioperative data between patients with (n = 21) and without (n = 83) new brain lesions. There were no significant differences in the percentage of diabetes mellitus, previous stroke, smoking, renal dysfunction on dialysis, or neck vessel disease. The percentage of patients with hypertension and dyslipidemia was significantly greater in patients without brain lesions (62% [13/21] vs 84% [70/83], *P* = .031 and 33% [7/21] vs 71% [59/83], *P* = .002, respectively). The score of atheromatous change in the ascending aorta was significantly greater in patients with brain lesions (1.7 ± 1.0 vs 1.2 ± 0.9, *P* = .024), and the percentage of intra- and extracranial vascular disease was tended to be greater in patients with brain lesions (62% [13/21] vs 40% [33/83], *P* = .09 and 24% [5/21] vs 8% [7/83], *P* = .06, respectively). There were no patients with atrial fibrillation in both groups. Table 2 shows a comparison of preoperative data.

Comparison of Operative Data

In patients with new brain lesions, the percentage of ONCAB was significantly greater (61.9% [13/21] vs 31.3%

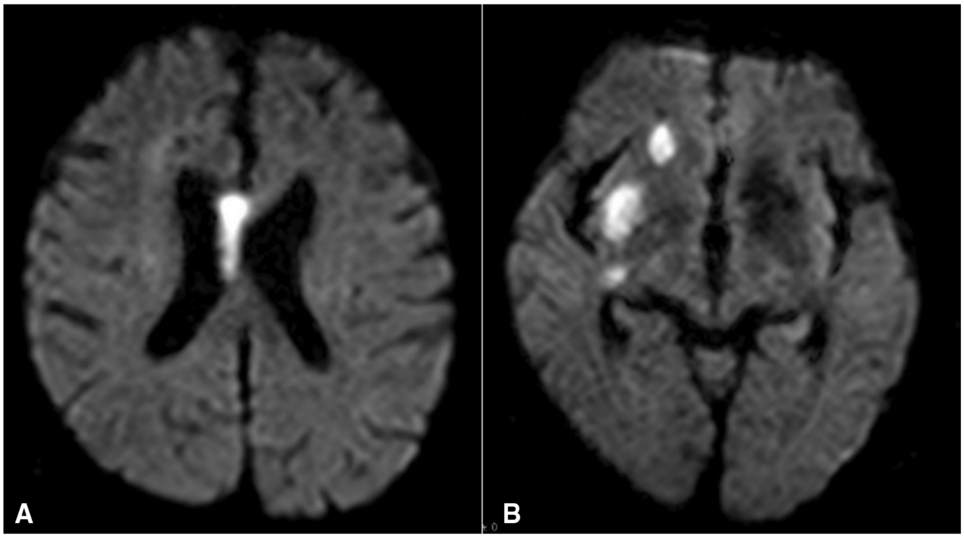


FIGURE 1. A case of symptomatic stroke. A 58-year-old man with a diagnosis of angina pectoris and occluded bilateral internal carotid arteries is shown. The patient underwent off-pump coronary artery bypass grafting using a suture device for proximal anastomosis. Postsurgery, he suffered greater brain dysfunction and aphasia from multiple brain infarctions. Postoperative diffusion-weighted imaging showed brain infarction on the temporal lobe (A) and cingulate gyrus (B).

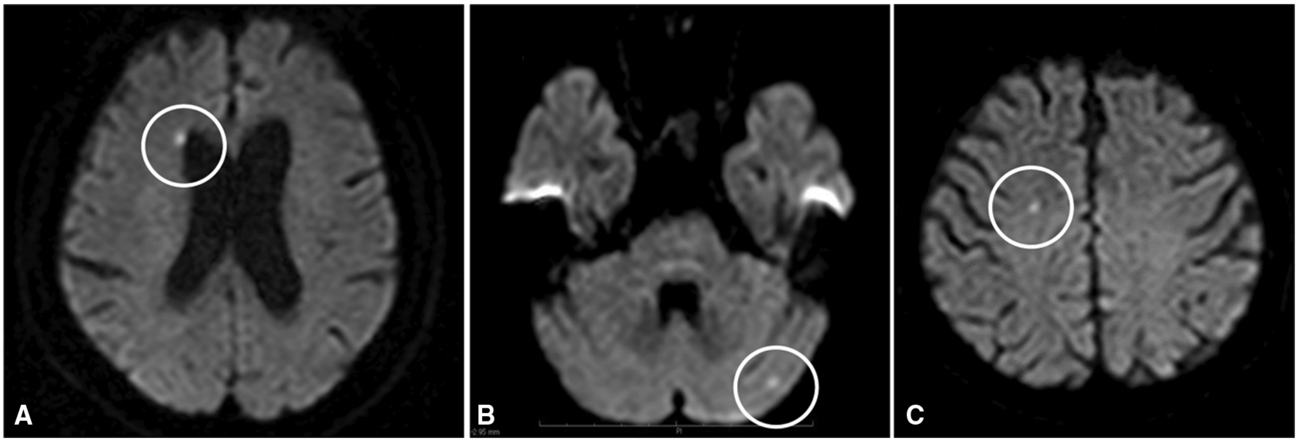


FIGURE 2. Magnetic resonance imaging of the brain in typical cases of silent brain lesions. A, Single lesion at the periventricular white matter in a 70-year-old man (*white circle*). B, Single lesion at the left cerebrum matter in a 71-year-old man (*white circle*). C, Single lesion at the right frontal lobe matter in a 70-year-old man (*white circle*).

[26/83], $P = .019$). Aortic clamp rate including partial and crossclamping was significantly greater in patients with brain lesions (52.4% [11/21] vs 24.1% [20/83], $P = .014$). There were no significant differences in the percentage of suture device use and aorta non-touch cases (Table 3). However, the data show that brain lesions were observed in 12.3% (8/65) of patients in the OPCAB group. Of the 8 patients with new lesions detected by MRI of the brain, 7 cases (87.5%) were silent brain lesions. In addition, silent brain lesions were detected in 15.8% of patients of the aorta non-touch group (3/19).

Comparison of Postoperative Clinical Results

There were no hospital deaths in either group. No significant differences were observed in the incidence of reoperation for bleeding, deep sternal infection, prolonged

TABLE 1. Patients with new brain lesions after coronary artery bypass grafting

Patient no.	Age, y	Sex	Location	Number of lesions	Maximum size of lesion, mm
1	75	Male	Brain stem	1	5.5
2	71	Male	Left cerebellum and left frontal lobe	1	5.5
3	69	Female	Periventricular white matter	1	8.0
4	76	Male	Bilateral cerebrum	3	35.2
5	60	Female	Right basal ganglia	1	7.1
6	55	Male	Right frontal lobe	1	4.9
7	48	Male	Left frontal lobe	1	5.1
8	70	Male	Right frontal lobe	1	4.3
9	70	Male	Periventricular white matter	2	4.8
10	59	Male	Periventricular white matter	2	4.9
11	79	Male	Right basal ganglia and left parietal lobe	2	5.5
12	66	Male	Right cerebrum	1	4.8
13	71	Female	Periventricular white matter	3	7.5
14	80	Male	Left occipital lobe and right cerebellum	2	6.1
15	58	Male	Right island, temporal and cingulate gyrus	3	33.8
16	78	Male	Right frontal lobe	1	6.0
17	66	Male	Right basal ganglia and left frontal lobe	2	6.1
18	64	Female	Right cerebellum	1	2.6
19	75	Male	Right frontal lobe	1	20.9
20	79	Male	Right occipital lobe and parietal lobe	2	5.5
21	80	Female	Right radiate crown	1	4.4

ADULT

TABLE 2. Comparison of patient characteristics between patients with and without new brain lesions

	Brain lesion (+) (n = 21)	Brain lesion (–) (n = 83)	*P* value
Age, y	69.0 ± 9.0	69.0 ± 8.6	.93
Male	16 (76.2%)	56 (67.5%)	.43
BSA, m^2	1.60 ± 0.04	1.56 ± 0.02	.38
Hypertension	13 (61.9%)	70 (84.3%)	.03
Dyslipidemia	7 (33.3%)	59 (71.1%)	.002
Previous stroke	4 (19.1%)	14 (16.9%)	.81
Smoke	1 (4.8%)	15 (20.0%)	.07
Hemodialysis	3 (14.3%)	8 (9.6%)	.55
LVEF, %	53.3 ± 13.5	59.1 ± 10.7	.09
BNP, pg/mL	482 ± 903	128 ± 237	.001
Score of atheromatous aortus	1.7 ± 1.0	1.2 ± 0.9	.024
Intracranial vascular disease	13 (61.9%)	33 (39.8%)	.09
Extracranial vascular disease	5 (23.8%)	7 (8.4%)	.06
Japan mortality score (%)	3.5 ± 3.4	1.6 ± 1.4	.06

BSA, Body surface area; *LVEF*, left ventricular ejection fraction; *BNP*, brain natriuretic peptide.

ventilation, hemodialysis, and hospital stay. In addition, there were no significant differences in the percentage of postoperative atrial fibrillation or flutter, use of postoperative heparin, anticoagulant, and antiplatelet agent. The postoperative clinical results are shown in Table 4.

Comparison of Postoperative Physical and Cognitive Function

Regarding physical function, postoperative standing balance and gait speed did not change from preoperative data in either group. The Short Physical Performance Battery score significantly improved only in patients without new brain lesions (from 9.9 ± 3.2 to 9.9 ± 3.5, $P = .43$ and from 10.2 ± 2.8 to 10.8 ± 2.6, $P = .023$) (Figure 3, *A-C*). With respect to unaided walking, there were no significant differences in start date (7.1 ± 3.8 vs 7.4 ± 2.6, $P = .15$) and percentage of patients in with and without brain lesions (14.3% [3/21] vs 4.8% [4/83], $P = .14$). The percentage of those with dysphagia was equivalent (4.8% [1/21] vs 3.6% [3/83], $P = 1.00$). Katz ADL index did not significantly change within the groups of patients with and without new brain lesions (from 5.8 ± 0.9 to 5.4 ± 1.2, $P = .09$ and from 5.9 ± 0.5 to 5.9 ± 0.6, $P = .10$); however, the change between the groups was significant ($P = .013$) (Figure 3, *D*).

To evaluate cognitive function, there were no significant differences in change of Mini-Mental Status Examination (from 27.1 ± 2.2 to 26.3 ± 2.1, $P = .39$ and from 27.3 ± 2.4 to 27.7 ± 2.3, $P = .44$) ($P = .88$, $R^2 = 0.001$), Montreal Cognitive Assessment (from 25.0 ± 4.3 to 24.9 ± 3.0, $P = .85$ and from 26.5 ± 10.6 to 25.1 ± 3.8,

TABLE 3. Comparison of operative data between patients with and without new brain lesions

	Brain lesion (+) (n = 21)	Brain lesion (–) (n = 83)	*P* value
On-pump CABG	13 (61.9%)	26 (31.3%)	.019
Number of grafts	3.5 ± 0.87	3.2 ± 1.1	.28
Operative time, min	329.9 ± 46.9	321.4 ± 86.8	.51
Bleeding, mL	1904.1 ± 1078.8	1403.3 ± 1214.4	.020
Aortic crossclamp	11 (52.4%)	20 (24.1%)	.014
Suture device	5 (23.8%)	36 (43.4%)	.09
Partial aortic clamp	1 (4.76%)	11 (13.3%)	.24
Aorta non-touch	3 (14.3%)	16 (19.1%)	.59

CABG, Coronary artery bypass grafting.

TABLE 4. Comparison of clinical results between patients with and without new brain lesions

	Brain lesion (+) (n = 21)	Brain lesion (–) (n = 83)	*P* value
Hospital mortality	0	0	–
Hospital stay, d	30.3 ± 30.4	23.4 ± 19.6	.33
Reoperation for bleeding	0	0	–
Deep sternal infection	1 (4.8%)	3 (4.0%)	.88
Prolonged ventilation (>72 h)	0	1 (1.3%)	.48
Renal failure requiring hemodialysis	0	0	–
Atrial fibrillation or flutter	1 (4.8%)	12 (16.9%)	.12
Heparin	14 (66.7%)	49 (62.0%)	.69
Anticoagulation	18 (85.7%)	59 (74.7%)	.27
Antiplatelet agent	21 (100%)	83 (100%)	–

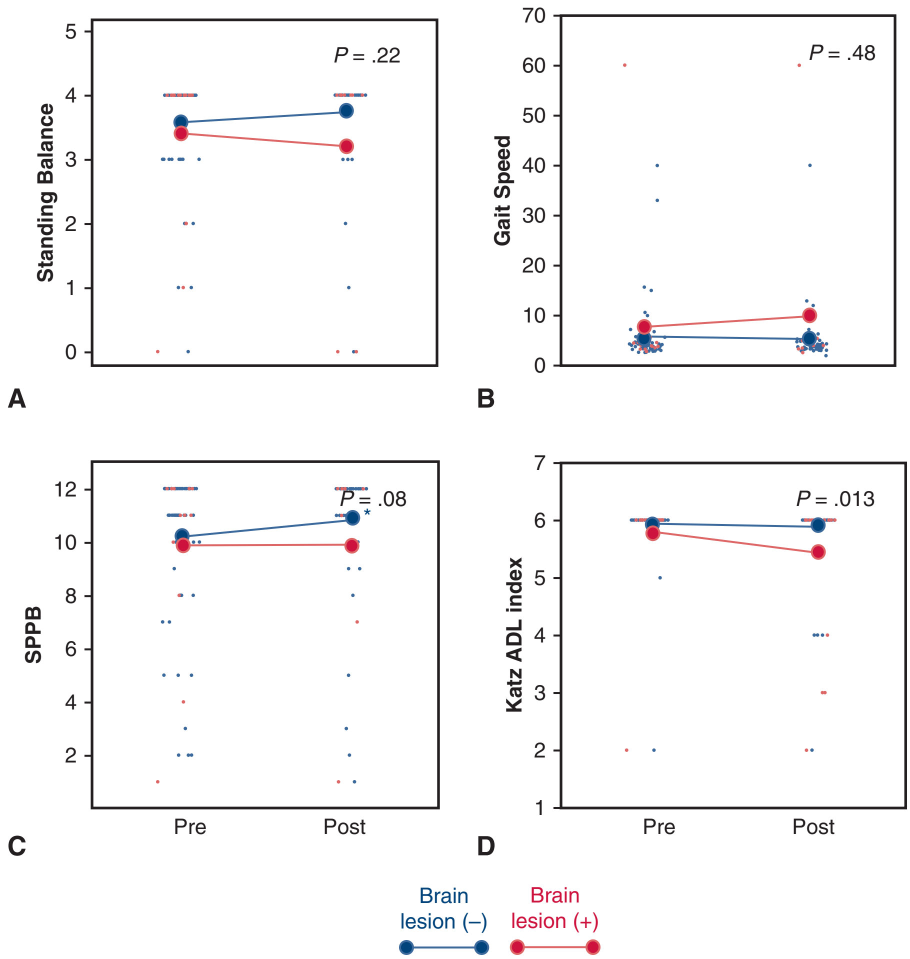


FIGURE 3. Comparison of change of physical function between patients with and without brain lesions. *$P = .023$. A, Standing balance; B, gait speed; C, Short Physical Performance Battery; D, Katz Index of Independence in Activities of Daily Living. *SPPB*, Short Physical Performance Battery; *Katz ADL*, Katz Index of Independence in Activities of Daily Living.

$P = .48$) ($P = .70$, $R^2 = 0.004$), Trail-Making Test-A (from 168 ± 93 to 155 ± 82, $P = .90$ and from 134 ± 48 to 134 ± 60, $P = .94$) ($P = .16$, $R^2 = 0.028$), and Trail-Making Test-B (from 187 ± 121 to 151 ± 112, $P = .08$ and from 168 ± 66 to 203 ± 114, $P = .16$) ($P = .63$, $R^2 = 0.009$) between pre- and postoperative data in either of the patients with and without new brain lesions (Figure 4, *A-D*). In patients with new brain lesions, POCD was observed only in patients with multiple lesions, and the maximum size of lesions was significantly greater in patients with POCD (19.7 ± 20.0 mm vs 5.0 ± 1.3 mm, $P = .032$).

DISCUSSION

We documented the incidence and impact of new brain lesions after CABG. First, the incidence of postoperative new brain lesions detected by MRI was 20.2% (21/104). Excluding a symptomatic case, the brain lesions were silent in the remaining 20 patients. Second, ONCAB and aortic clamping were risk factors for new brain lesions. There were no significant differences in the percentage of suture device use and aorta non-touch cases. However, brain lesions were observed in 12.3% of patients in the OPCAB group and 15.8% of patients of the aorta non-touch group. Finally, new brain lesions had no significant impact on postoperative physical function. However, Katz ADL index was significantly decreased in patients with brain lesions, and POCD was significantly observed in patients with multiple and larger lesions (Figure 5).

Several randomized studies comparing OPCAB and ONCAB failed to show an advantage in avoidance of postoperative stroke; however, a number of large retrospective studies showed that OPCAB was associated with reduction of incidence of postoperative stroke compared with ONCAB. The main mechanism of new brain lesions after CABG is microembolism due to CPB, aortic cannulation, clamping, and declamping.[18-20] Several investigators have revealed embolic showers by transcranial Doppler, and the occurrence of microembolism was associated with neuropyschologic impairments.[21,22] Moss and

ADULT

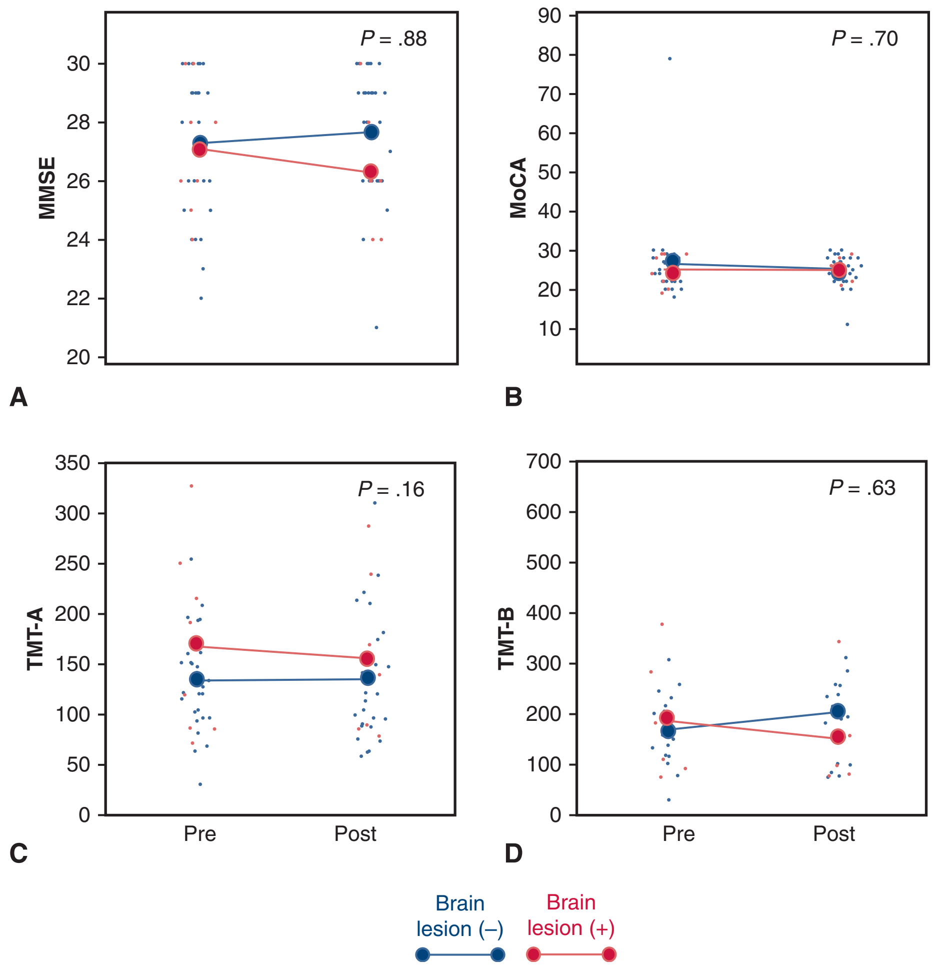


FIGURE 4. Comparison of change of cognitive function between patients with and without brain lesions. A, Mini-Mental Status Examination (*MMSE*); B, Montreal Cognitive Assessment (*MoCA*); C, Trail-Making Test-A (*TMT-A*); and D, Trail-Making Test-B (*TMT-B*).

colleagues[10] demonstrated that any aortic manipulation was likely to increase the risk of postoperative stroke regardless of severity of aortic atherosclerotic change, and Zhao and colleagues[13] showed that anaortic OPCAB without any manipulation of the aorta was associated with a reduction of 78% and 66% in the 30-day risk of stroke compared with conventional CABG and OPCAB with partial clamping.

Albert and colleagues[23] reported that the incidence of postoperative stroke was 4 of 4485 patients after anaortic OPCAB technique, and anaortic OPCAB was an effective tool to minimize the risk of early stroke. In the present study, ONCAB and aortic clamping were risk factors for brain injury as previously reported. There was no significant association of aorta non-touch operation with the incidence of postoperative brain lesions, and silent brain lesions were detected in 15.8% of patients of the aorta non-touch group. The findings revealed an unexpected high rate of silent brain lesions in CABG and indicated that anaortic OPCAB could not absolutely avoid the new brain lesions. The mechanism and origin of brain lesions cannot fully be demonstrated, and anaortic OPCAB tended to be selected for patients with atheromatous change; therefore, perioperative hemodynamics change and low perfusion may be a cause of new spot lesions. Since various preoperative statuses of hemodynamics and conditions of vessels directly influence the selection of procedures, it is still difficult to clarify the true mechanism of new brain lesions after CABG.

In several studies, postoperative brain lesions without focal neurologic deficits was detected by MRI after cardiac surgery.[14,15,24] Bendszus and Stoll[24] represented embolic phenomena as "fingerprints of invasive medical procedures." In population-based studies, a strong association was found between silent brain infarction and prevalent cognitive dysfunction and dementia.[25,26] Barber and colleagues[27] reported that cognitive decline was associated

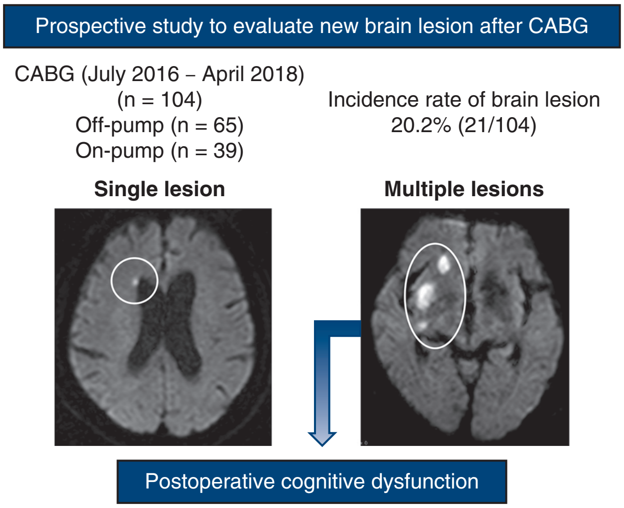


FIGURE 5. The incidence of postoperative new brain lesions detected by magnetic resonance imaging was 20.2% (21/104) after coronary artery bypass grafting (*CABG*). Postoperative cognitive dysfunction was significantly observed in patients with multiple and larger lesions.

with perioperative cerebral ischemic lesions on diffusion-weighted imaging in patients undergoing cardiac valve surgery. Sun and colleagues[14] reviewed previous studies on silent brain injury and POCD after CABG. Bendszus and colleagues[28] reported there were no patients with POCD after ONCAB, but most reports showed the incidence of POCD in patients with silent brain lesions after ONCAB.[29-33] In contrast, silent brain lesions with POCD were observed in OPCAB,[14] and influence of silent brain lesions on POCD is still controversial. In this study, POCD was significantly observed in patients with multiple and larger lesions, and the Katz ADL index was significantly lower in patients with brain lesions. Excluding single small lesions, new brain lesions were associated with POCD, and they may be a cause of degradation of the postoperative ADL and have the potential to decrease long-term quality of life. Therefore, pre- and postoperative cognitive function should be evaluated routinely. However, the POCD test is significantly affected by postoperative pain, sedation, and other clinical recovery issues, and this fact makes it difficult to objectively evaluate the influence of postoperative brain lesions. To discover whether silent brain lesions are really ‘‘silent’’ or not, more accurate evaluation method and protocol are required.

Study Limitations

The present study has several limitations, as well as a small sample size. One, the selection of procedure was by surgeon's preference; therefore, selection bias was present in distribution of OPCAB and ONCAB. Two, assessment of pre- and postoperative physical and cognitive function could not be performed in all patients, and these tests were performed at different time point. Therefore, the statistic power of evaluation of physical and cognitive function was likely insufficient. Finally, there is no internationally accepted definition of POCD, and the difference between neuropsychological test batteries and POCD criteria was not defined in many previously published reports. Therefore, different definitions of POCD may lead to different results.

CONCLUSIONS

MRI of the brain detected postoperative new brain lesions in 20.2% of patients after CABG. Although ONCAB and aortic clamping were risk factors for brain lesions, silent brain lesions were observed in more than 10% of patients in the OPCAB and aorta non-touch groups. Although silent brain lesions did not affect postoperative physical function after CABG, multiple and larger lesions increased POCD and degraded the Katz ADL index.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

ADULT

References

1. Selnes OA, Goldsborough MA, Borowicz LM, McKhann GM. Neurobehavioral sequelae of cardiopulmonary bypass. *Lancet*. 1999;353:1601-6.
2. Roach G, Kanchuger M, Mangano C, Newman M, Nussmeier N, Wolman R, et al. Adverse cerebral outcomes after coronary bypass surgery. *N Engl J Med*. 1996;335:1857-63.
3. Hartman G, Yao F, Bruefach M, Barbut D, Peterson J, Charlson M, et al. Severity of aortic atheromatous disease diagnosed by transesophageal echocardiography predicts stroke and other outcomes associated with coronary artery surgery: a prospective study. *Anesth Analg*. 1996;83:701-8.
4. Barbut D, Gold J. Aortic atheromatosis and risks of cerebral embolization. *J Cardiothorac Vasc Anesth*. 1996;10:24-30.
5. Crowley J, Hannigan M, Daly K. Reactive thrombocytosis and stroke following cardiopulmonary bypass surgery: case report on three patients. *Eur Heart J*. 1994;15:1144-6.
6. Shroyer A, Grover F, Hattler B, Collins J, McDonald G, Kozora E, et al. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med*. 2009;361:1827-37.
7. Lamy A, Devereaux P, Prabhakaran D, Taggart D, Hu S, Paolasso E, et al. Off-pump or on-pump coronary-artery bypass grafting at 30 days. *N Engl J Med*. 2012;366:1489-97.
8. Calafiore AM, Di Mauro M, Teodori G, Di Giammarco G, Cirmeni S, Contini M, et al. Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. *Ann Thorac Surg*. 2002;73:1387-93.
9. Antunes PE, de Oliveira JF, Antunes MJ. Predictors of cerebrovascular events in patients subjected to isolated coronary surgery. The importance of aortic cross-clamping. *Eur J Cardiothorac Surg*. 2003;23:328-33.
10. Moss E, Puskas JD, Thourani VH, Kilgo P, Chen EP, Leshnower BG, et al. Avoiding aortic clamping during coronary artery bypass grafting reduces postoperative stroke. *J Thorac Cardiovasc Surg*. 2015;149:175-80.
11. Kowalewski M, Pawliszak W, Malvindi PG, Bokszanski MP, Perlinski D, Raffa GM, et al. Off-pump coronary artery bypass grafting improves short-term outcomes in high-risk patients compared with on-pump coronary artery bypass grafting: meta-analysis. *J Thorac Cardiovasc Surg*. 2016;151:60-77.
12. Pawliszak W, Kowalewski M, Raffa GM, Malvindi PG, Kowalkowska ME, Szwed KA, et al. Cerebrovascular events after no-touch off-pump coronary artery bypass grafting, conventional side-clamp off-pump coronary artery bypass, and proximal anastomotic devices: a meta-analysis. *J Am Heart Assoc*. 2016;5:e002802.

13. Zhao DF, Edelman JJ, Seco M, Bannon PG, Wilson MK, Byrom MJ, et al. Coronary artery bypass grafting with and without manipulation of the ascending aorta: a network meta-analysis. *J Am Coll Cardiol*. 2017;69:924-36.
14. Sun X, Lindsay J, Monsein LH, Hill PC, Corso PJ. Silent brain injury after cardiac surgery: a review: cognitive dysfunction and magnetic resonance imaging diffusion-weighted imaging findings. *J Am Coll Cardiol*. 2012;60:791-7.
15. Friday G, Sutter F, Curtin A, Kenton E, Caplan B, Nocera R, et al. Brain magnetic resonance imaging abnormalities following off-pump cardiac surgery. *Heart Surg Forum*. 2005;8:E105-9.
16. Wilson MJ, Boyd SY, Lisagor PG, Rubal BJ, Cohen DJ. Ascending aortic atheroma assessed intraoperatively by epiaortic and transesophageal echocardiography. *Ann Thorac Surg*. 2000;70:25-30.
17. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA*. 1963;185:914-9.
18. Wareing TH, Davila Roman VG, Barzilai B, Murphy SF, Kouchoukos NT. Management of severely atherosclerotic ascending aorta during cardiac operations: a strategy for detection and treatment. *J Thorac Cardiovasc Surg*. 1992;103:453-62.
19. Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke*. 1994;25:1393-9.
20. Barbut D, Hinton RB, Szatrowski TP, Hartman GS, Bruefach M, Williams-Russo P, et al. Cerebral emboli detected during bypass surgery are associated with clamp removal. *Stroke*. 1994;25:2398-402.
21. Diegeler A, Hirsch R, Schneider F, Schilling LO, Falk V, Rauch T, et al. Neuromonitoring and neurocognitive outcome in off-pump versus conventional coronary bypass operation. *Ann Thorac Surg*. 2000;69:1162-6.
22. Guerrieri Wolf L, Abu-Omar Y, Choudhary BP, Piggot D, Taggat DP. Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary artery surgery: the effect of an aortic side-biting clamp ant two clampless devices. *J Thorac Cardiovasc Surg*. 2007;133:485-93.
23. Albert A, Ennker J, Hegazy Y, Ullrich S, Petrov G, Akhyari P, et al. Implementation of the aortic no-touch technique to reduce stroke after off-pump coronary surgery. *J Thorac Cardiovasc Surg*. 2018;156:544-54.
24. Bendszus M, Stoll G. Silent cerebral ischemia: hidden fingerprints of invasive medical procedures. *Lancet Neurol*. 2006;5:364-72.
25. Vermeer SE, Prins ND, den Heijer T, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and the risk of dementia and cognitive decline. *N Engl J Med*. 2003;348:1215-22.
26. Vermmer SE, Longstreth WT Jr, Koudstaal PJ. Silent brain infarction: a systemic review. *Lancet Neurol*. 2007;6:611-9.
27. Barber PA, Hach S, Tippett LJ, Ross L, Merry AF, Milsom P. Cerebral ischemic lesions on diffusion-weighted imaging are associated with neurocognitive decline after cardiac surgery. *Stroke*. 2008;39:1427-33.
28. Bendszus M, Reents W, Franke D, Müllges W, Babin-Ebell J, Koltzenburg M, et al. Brain damage after coronary bypass grafting. *Arch Neurol*. 2002;59:1090-5.
29. Restrepo L, Wityk RJ, Grega MA, Borowicz L Jr, Barker PB, Jacobs MA, et al. Diffusion- and perfusion-weighted magnetic resonance imaging of the brain before and after coronary artery bypass grafting surgery. *Stroke*. 2002;33:2909-15.
30. Knipp SC, Matatko N, Wilhelm H, Schlamann M, Massoudy P, Forsting M, et al. Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neurological assessment and diffusion-weighted magnetic resonance imaging. *Eur J Cardiovasc Surg*. 2004;25:791-800.
31. Djaiani G, Fedorko L, Borger M, Mikulis D, Carroll J, Cheng D, et al. Mild to moderate atheromatous disease of the thoracic aorta and new ischemic brain lesions after conventional coronary artery bypass graft surgery. *Stroke*. 2004;35:e356-8.
32. Knipp SC, Matatko N, Wilhelm H, Schlamann M, Thielmann M, Lösch C, et al. Cognitive outcomes three year after coronary artery bypass surgery: relation to diffusion-weighted magnetic resonance imaging. *Ann Thorac Surg*. 2008;85:872-9.
33. Gerriets T, Schwarz N, Bachmann G, Kaps M, Kloevekorn WP, Sammer G, et al. Evaluation of methods to predict early long-term neurobehavioral outcome after coronary artery bypass grafting. *Am J Cardiol*. 2010;105:1095-101.

Key Words: coronary artery bypass grafting, stroke, silent brain lesions, magnetic resonance imaging, off-pump coronary artery bypass grafting, anaortic coronary artery bypass grafting, postoperative cognitive dysfunction