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Relationship between Deep White Matter Hyperintensities on Magnetic Resonance Imaging and Postoperative Cognitive Function Following Clipping of Unruptured Intracranial Aneurysm

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Abstract

To evaluate the effects on cognitive function of deep white matter hyperintensities (DWMHs) on magnetic resonance imaging (MRI) in patients treated surgically for unruptured intracranial aneurysms (UIAs). The subjects were 106 patients in whom a Wechsler adult intelligence scale-revised (WAIS-R) examination was performed 1 week before and 1 month after clipping surgery for asymptomatic UIAs. DWMH severity was evaluated on preoperative MR images by Fazekas scale, as follows: none (absence), mild (punctate foci), moderate (beginning confluence of foci), or severe (large confluent areas). A decrease of 7 or more points in intelligence quotient (IQ) postoperatively was considered deterioration. Fazekas score was none in 41 (none group), mild in 42 (mild group), moderate in 21, and severe in 2 patients (moderate/severe group). Patient characteristics, surgical factors, IQ change, and abnormal findings on postoperative MRI were compared among the groups. Although there was no statistically significant deterioration in IQ postoperatively in any group, the percentage of deteriorated patients was significantly higher in the moderate/severe group (34.8%) than in the other groups (4.9% in the none group, 7.1% in the mild group; $p < 0.01$, $p < 0.05$, respectively). Brain injury was observed more frequently on postoperative MR images in the moderate/severe group (17.4%) compared with the none group (2.4%; $p = 0.052$). The presence of moderate/severe DWMHs was an independent prognostic factor for postoperative cognitive dysfunction. In conclusion, the presence of moderate/severe DWMHs was a prognostic factor for postoperative cognitive dysfunction after surgery for UIAs.

Keywords: deep white matter hyperintensity, unruptured intracranial aneurysm, clipping surgery, cognitive function

Introduction

The results of surgery for unruptured intracranial aneurysms (UIAs) have recently been evaluated by assessment of neuropsychological function, in addition to neurological function, using the Glasgow Outcome Scale (GOS) and the modified Rankin Scale (mRS).[1] The effects of clipping surgery on cognitive function in patients with UIAs have been studied previously.[2–19] A greater tendency for deterioration in cognitive function has been reported in patients who undergo clipping compared with those treated with coils.[2] Therefore, knowledge of the incidence of and risk factors for cognitive deterioration in patients who undergo clipping may enable its reduction by considering the operative indications and procedures.

The reported prognostic factors for cognitive dysfunction include age,[4,9,15,16,19] aneurysm location,[4,9,15] and systemic disease.[9] Brain injury following surgical manipulation,[7] the surgical approach,[9] and long operative time[15] have also been reported to affect cognitive function.

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Deep white matter hyperintensities (DWMHs), which are observed as bright foci on T2-weighted or fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI), occur commonly in the elderly, in cognitively healthy subjects, and in those with mild cognitive impairment and a variety of dementias, including Alzheimer's disease (AD).[20–23] It has been reported that the severity of DWMHs generally increases with the severity of cognitive impairment, from no cognitive impairment to probable AD, and the severity of DWMHs at baseline is associated with the rate of progression of cognitive impairment.[20,24,25] Relationships have been reported between DWMHs and surgical results as well as with other diseases.[26–29] Therefore, it is considered that patients with severe DWMHs on preoperative MRI may show deterioration of cognitive function after clipping surgery. As the relationship between DWMHs on MRI and cognitive function following craniotomy has not been reported, the present study evaluated the effects of DWMHs on cognitive function in patients treated surgically for UIAs.

Methods

A total of 130 clipping surgeries for UIAs (130 patients) were performed at our institution between January 2002 and December 2009. Of these, 106 patients in whom the Japanese translation of the Wechsler adult intelligence scale-revised (WAIS-R) examination[30] was performed 1 week before and 1 month after clipping surgery were admitted to the study. The intelligence quotient (IQ) was obtained from the total of the verbal IQ (VIQ) and the performance IQ (PIQ). As the standard deviation (SD) of the IQ is 3.02, a ≥7-point decrease in IQ (more than 2 SD) postoperatively was considered deterioration, a ≥7-point increase in IQ postoperatively was considered improvement, and a <7-point change in IQ postoperatively was considered no change. In addition, this indicates that a subject shows IQ score within 2 SD in 19 of 20 examinations.

MR and computed tomography (CT) images were obtained before surgery, within a few days after surgery, and 1 month after surgery. MRI was performed using a 1.5-T scanner (Signa Excite HD 23, GE Healthcare, Waukesha, WI, USA), as follows: T1-weighted imaging (slice thickness 6 mm, repetition time (TR) 450 msec, echo time (TE) 8 msec, matrix 25 × 256), T2-weighted imaging (slice thickness 6 mm, TR 3500 msec, TE 105 msec, matrix 512 × 512), FLAIR imaging (slice thickness 6 mm, TR 9002 msec, TE 122 msec, matrix 512 × 512), and diffusion-weighted (DW) imaging (slice thickness 6 mm, TR 4000 msec, TE 85 msec, matrix 256 × 256). The presence of DWMHs was defined as bright foci on FLAIR or bright foci on T2-weighted images, and no foci on T1-weighted images.

DWMH severity was evaluated on preoperative MRI using the grading scale of Fazekas et al.,[31] as follows: none (absence), mild (punctate foci), moderate (beginning confluence of foci), or severe (large confluent areas). The postoperative MR and CT images were evaluated for abnormal findings such as brain injury, subdural fluid collection, and cerebral infarction due to the operative procedure. Brain injury detected on two slices of FLAIR performed within a few days after surgery was considered positive. Cerebral infarction was assessed on DW imaging performed within a few days after surgery. A subdural fluid collection showing mass effect or of thickness ≥1 cm on CT or MRI performed within a few days and 1 month after surgery was considered positive. MR images were evaluated by radiologists and neurosurgeons, and the WAIS-R examinations were performed by speech therapists. The evaluators were blinded to the patients' clinical histories.

DWMHs were evaluated as none in 41 patients, mild in 42, moderate in 21, and severe in 2. As only two patients had severe DWMHs, the patients were divided into three groups: none, mild, and moderate/severe DWMHs. Patient characteristics, postoperative changes in IQ, abnormal findings on postoperative MRI or CT, and mRS were evaluated in each group. Univariate analysis was performed using the Mann–Whitney U test for differences in age and preoperative IQ between groups; and Fisher's exact test for the following: prevalence of underlying disease, aneurysm size, aneurysm location, number of aneurysms, surgical approach, procedure, operative time, bleeding volume, temporary clip usage, percentage of patients with decreased and increased IQ, abnormal findings on MRI, the rate of patients showing mRS ≥1 in each group or univariate analysis between groups with and without IQ deterioration; paired *t*-test was used to analyze change in IQ between these groups. Multivariate analysis was performed to identify prognostic factors for cognitive dysfunction. In addition to preoperative DWMHs and IQ, factors suspected to affect cognitive function according to previous reports were selected for multivariate analysis. A p value less than 0.05 was considered significant.

Informed consent was obtained from all study participants. This study was approved by the Clinical Research Ethics Review Committee of Ehime University Hospital (#1806010).

Results

Patient and surgical characteristics

Table 1 lists the patient characteristics. Patients with any degree of DWMH were significantly older than those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.01$), and there was no statistically significant difference in age between the mild group and the moderate/severe group. Patients with any degree of DWMH had a lower IQ than those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.01$), a lower VIQ than those without DWMHs (none vs. mild; $p < 0.05$, none vs. moderate/severe; $p < 0.05$), and a lower PIQ than those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.05$). There was no statistically significant difference in IQ, VIQ, or PIQ between the mild group and the moderate/severe group. There was no statistically significant difference among the groups in terms of the prevalence of underlying disease, aneurysm size, aneurysm location, or number of aneurysms.

Table 2 lists the surgical characteristics. There was no statistically significant difference among the groups in terms of surgical approach, procedure, operative time, bleeding volume, or temporary clip usage. Premature aneurysmal rupture did not occur in any surgery.

Postoperative change in IQ, MRI findings, and mRS score

Table 3 lists the postoperative changes in IQ, MRI findings, and outcome. In comparison with the preoperative values, there was no statistically significant decrease in IQ, VIQ, or PIQ postoperatively in any group; IQ, VIQ, and PIQ showed a significant increase postoperatively in the none group ($p < 0.01$), and PIQ showed a significant increase postoperatively in the mild group ($p < 0.05$).

With regard to individual cases in each group, a greater proportion of patients in the moderate/severe group suffered a deterioration of IQ than in the other groups (vs. none, $p < 0.01$; vs. mild, $p < 0.05$).

Brain injury was seen more frequently in the moderate/severe group compared with the none group, but the difference was not significant ($p = 0.052$). Of the four patients with brain injury in the moderate/severe group, deterioration in IQ was recognized in three. Of the two patients with subdural fluid collection in the moderate/severe group, deterioration in IQ was recognized in one patient (a 76-year-old patient with ACoA aneurysm). On MR images obtained several months after clipping surgery, subdural fluid collection had completely resolved in two patients, and transformed to hematoma requiring irrigation surgery in three patients. Although MRI performed a few days after surgery revealed cerebral infarction in the perforating artery territory region, the infarctions were asymptomatic in all of these patients.

The mRS score at 6 months after surgery was 0 for 104 patients; and 1 for 2 patients, both of whom were in the none group, and who suffered from visual disturbance on the operative side after clipping of paraclinoid ICA aneurysms. None of the 12 patients with postoperative IQ deterioration showed a worsened mRS score at 6 months after surgery.

Prognostic factors for postoperative IQ deterioration

Table 4 summarizes the results of univariate analysis comparing patients with IQ deterioration and without IQ deterioration (no change, improvement). Age ≥70 years, preoperative moderate/severe DWMHs, and postoperative brain injury were factors affecting IQ deterioration. Multivariate analysis revealed age ≥70 years and the presence of moderate/severe DWMHs as independent prognostic factors for postoperative IQ deterioration (Table 5).

Discussion

Numerous studies have reported the effects of clipping surgery on cognitive function in patients with UIAs. Some studies reported cognitive dysfunction in some patients postoperatively,[2,4-7,9,11,12,14–17,19] whereas others reported no postoperative cognitive dysfunction in any patients.[8,10,13,18] The incidence of cognitive dysfunction may depend on the type of analysis (group-based or event-based), the examination combination, evaluation criteria, and the timing of examinations after surgery (1 week or 6 months postoperatively). WAIS-R was selected for examining cognitive function because it is the international standard for evaluating holistic intelligence; and because it scores IQ relative to age, thus enabling IQ to be compared regardless of age. Group-based and event-based analyses were performed at 1 month after surgery when postsurgical effects such as wound pain and anxiety had disappeared.

The prognostic factors for cognitive deterioration after surgery have been reported previously.[4,7,9,15,16,19] These include age ≥65 years,[4,9,15,16,19] ACoA aneurysm,[4,9,15] systemic disease such as hypertension,[9] interhemispheric surgical approach,[9] operative time ≥5 hours,[15] and the presence of brain damage preoperatively.[7] In the present study, the severity of DWMHs on preoperative MRI was related to cognitive function in patients treated surgically for UIAs. We found a decrease in IQ of ≥7 points in 4.9% of patients in the none group, 7.1% in the

Table 1 Patient characteristics

Severity of DWMHs	Total	None	Mild	Moderate/severe
Number of patients	106	41	42	23
Male/female	42/64	20/21	13/29	9/14
Age (mean ± SD)	59.6 ± 9.4	55.2 ± 10.2	61.9 ± 6.6**	63.2 ± 9.5**
Preoperative IQ (mean ± SD)	100.7 ± 13.0	105.6 ± 13.6	97.1 ± 12.5**	98.4 ± 10.1**
VIQ (mean ± SD)	99.3 ± 12.8	102.5 ± 14.6	97.2 ± 11.9*	97.7 ± 9.9*
PIQ (mean ± SD)	101.2 ± 14.2	107.0 ± 13.1	96.7 ± 14.3**	99.0 ± 12.7*
Underlying disease				
Hypertension	70 (66.0%)	25 (61.0%)	28 (66.7%)	17 (73.9%)
Diabetes mellitus	12 (11.3%)	3 (7.3%)	5 (11.9%)	4 (17.4%)
Dyslipidemia	21 (19.8%)	6 (14.6%)	10 (23.8%)	5 (21.8%)
Ischemic heart disease	15 (14.2%)	4 (9.8%)	6 (14.3%)	5 (21.8%)
Cerebral infarction	14 (13.2%)	4 (9.8%)	5 (11.9%)	5 (21.8%)
Aneurysm diameter				
Mean diameter (range) (mm)	5.5 (2–18)	5.5 (2–13)	5.6 (2–18)	5.3 (3–8)
0–4.9 mm	51	23	20	8
5–6.9 mm	43	10	20	13
7–9.9 mm	19	6	9	4
10–14.9 mm	8	4	4	0
15–24.9 mm	2	1	1	0
Location of aneurysm				
ACoA	28 (22.8%)	10 (22.7%)	10 (18.5%)	8 (32.0%)
Distal ACA	5 (4.1%)	3 (6.8%)	2 (3.7%)	0 (0.0%)
MCA	47 (38.2%)	16 (36.4%)	21 (38.9%)	10 (40.0%)
ICA	38 (30.9%)	15 (34.1%)	18 (33.3%)	5 (20.0%)
BA	3 (2.4%)	0 (0.0%)	2 (3.7%)	1 (4.0%)
PCA	2 (1.6%)	0 (0.0%)	1 (1.9%)	1 (4.0%)
Number of aneurysms				
Single	93	38	34	21
Multiple	2, n = 9; 3, n = 4	2, n = 3	2, n = 4; 3, n = 4	2, n = 2

Locations of multiple aneurysms were as follows: None group: ACoA+MCA: 1, MCA (2): 2 Mild group: ICA+MCA: 3, ICA+—BA: 1, ICA (2)+MCA: 1, ACoA+MCA (2): 1, ICA+MCA (2): 1, ICA+MCA+distal ACA: 1 Moderate/severe group: ICA+MCA: 1, BA+MCA: 1 Patients with any degree of DWMH were significantly older than those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.01$). In patients with any degree of DWMH, IQ was lower than in those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.01$), VIQ was lower than in those without DWMHs (none vs. mild; $p < 0.05$, none vs. moderate/severe; $p < 0.05$), and PIQ was lower than in those without DWMHs (none vs. mild; $p < 0.01$, none vs. moderate/severe; $p < 0.05$). ACA: anterior cerebral artery, ACoA: anterior communicating artery, BA: basilar artery, DWMHs: deep white matter hyperintensities, ICA: internal cerebral artery, IQ: intelligence quotient, MCA: middle cerebral artery, PCA: posterior cerebral artery, PIQ: performance IQ, VIQ: verbal IQ.

mild group, and 34.8% in the moderate/severe group. Thus, IQ decreased in a greater proportion of patients in the moderate/severe group than in the other groups, and multivariate analysis confirmed the presence of moderate or severe DWMHs and age as prognostic factors regarding preoperative cognitive function. To the best of our knowledge, this is the first study to show that preoperative severity of DWMHs on MRI is related to cognitive function after clipping surgery.

The etiology of DWMHs has been most frequently ascribed to normal aging and cerebrovascular disease,

Table 2 Surgical characteristics

Severity of DWMHs	Total	None	Mild	Moderate/severe
Surgical approach				
Lt-pterional	31 (29.0%)	10 (24.4%)	13 (30.2%)	8 (34.8%)
Rt-pterional	62 (57.9%)	26 (63.4%)	25 (58.1%)	11 (47.8%)
Interhemispheric	12 (11.2%)	5 (12.2%)	4 (9.3%)	3 (13.0%)
Rt-subtemporal	1 (0.9%)	0 (0.0%)	1 (2.3%)	0 (0.0%)
Lt-subtemporal	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (4.4%)
Procedure				
Clipping	115 (93.5%)	42 (95.5%)	49 (90.7%)	24 (96.0%)
Others (coating)	8 (6.5%)	2 (4.5%)	5 (9.3%)	1 (4.0%)
Operative time				
Mean ± SD (min)	346 ± 125	360 ± 141	335 ± 122	341 ± 100
Number of operations (<300 min)	48 (45.3%)	18 (43.9%)	20 (47.6%)	10 (43.5%)
Number of operations (300 min≤)	58 (54.7%)	23 (56.1%)	22 (52.4%)	13 (56.5%)
Bleeding volume (mL)				
Mean ± SD (mL)	233 ± 146	227 ± 179	240 ± 119	231 ± 131
Number of operations (<400 mL)	96 (90.6%)	38 (92.7%)	38 (90.5%)	20 (87.0%)
Number of operations (400 mL≤)	10 (9.6%)	3 (7.3%)	4 (9.5%)	3 (13.0%)
Temporary clip usage	8 (7.5%)	4 (9.8%)	4 (9.5%)	0 (0%)

DWMHs: deep white matter hyperintensities.

even among subjects with dementia diagnosed with probable AD.[32–34] It is generally considered that they are produced by chronic ischemia or by brief and repeated ischemic insults of moderate severity that occur in the subcortical white matter.[35] Histologically, these hyperintensities reflect myelin pallor and dilatation of perivascular spaces, and small lacunar infarcts occasionally coexist with these histologic changes.[36] There is growing evidence that neurodegeneration or associated processes such as gliosis, microglial infiltration, inflammation, and amyloid angiopathy may also result in DWMHs.[34,37–40]

Although the reason for the high incidence of postoperative cognitive deterioration in patients with moderate or severe DWMH was not clear, previous reports have suggested that the severity of DWMH may be related to a functional vulnerability of the brain. The severity of DWMHs showed a general increase with the severity of cognitive impairment in a cross-sectional study,[20] and longitudinal studies have also shown an association of the severity of DWMHs at baseline with the rate of progression of cognitive impairment.[24,25,41] Several studies have reported a relationship between the severity of pre-existing white matter hyperintensities (WMHs) and cognitive dysfunction after vascular or cardiac surgery.[26–29] Boulouis et al. determined the influence of WMH burden on functional outcome, rate of symptomatic intracerebral hemorrhage, and procedural success in patients with acute ischemic stroke who were treated by mechanical thrombectomy with current stentriever/aspiration devices. Their results showed that patients demonstrated increasingly worse outcomes with increasing WMH volumes, although WMH severity was not associated with symptomatic intracerebral hemorrhage rate, nor did it influence recanalization success.[26] Yoshida et al. reported that pre-existing WMHs on MRI adversely affected cognitive improvement after carotid endarterectomy; that is, improvement of patients' cognitive function after carotid endarterectomy was worse in those with a large area of pre-existing WMHs than in those with a small area of WMHs.[29] Omiya et al. assessed the relationship between preoperative MRI findings and delirium after off-pump coronary artery bypass grafting. Multivariate logistic regression analysis revealed that new ischemic lesions, carotid artery stenosis, history of myocardial infarction, and deep subcortical WMH were significantly associated with postoperative delirium.[28] Cerebral small vessel disease markers including WMHs, lacunes, cerebral microbleeds, and perivascular spaces cause cognitive impairment.[42,43] Among these, WMHs were shown to

Table 3 Postoperative changes in IQ, MRI findings, and mRS score

Severity of DWMHs	Total	None	Mild	Moderate/severe
Postoperative IQ				
IQ (mean ± SD)	102.5 ± 14.6	109.1 ± 15.3**	98.8 ± 12.9	97.3 ± 12.0
VIQ (mean ± SD)	100.6 ± 14.4	105.2 ± 16.4**	97.8 ± 12.7	97.5 ± 11.4
PIQ (mean ± SD)	103.8 ± 15.3	111.4 ± 14.6**	99.7 ± 13.8*	97.4 ± 13.8
Number of patients showing change in IQ				
IQ decrease	13 (12.3%)	2 (4.9%)**	3 (7.1%)*	8 (34.8%)
No change	70 (66.0%)	27 (65.8%)	31 (73.8%)	12 (52.2%)
IQ increase	23 (21.7%)	12 (29.3%)	8 (19.1%)	3 (13.0%)
Postoperative MRI finding				
Brain injury	7 (6.6%)	1 (2.4%)	2 (4.8%)	4 (17.4%)
SDFC	5 (4.7%)	1 (2.4%)	2 (4.8%)	2 (8.7%)
Cerebral infarction	5 (4.7%)	2 (4.8%)	2 (4.8%)	1 (4.3%)
mRS score				
0	104	39	42	23
1	2	2	0	0

No statistically significant decrease was found in postoperative IQ, VIQ, or PIQ in comparison with the preoperative scores in any group. Compared with the preoperative values, postoperative IQ, VIQ, and PIQ in the none group increased significantly ($p < 0.01$), and postoperative PIQ in the mild group increased significantly ($p < 0.05$). Examining individual cases in each group, IQ deteriorated in a greater proportion of patients in the moderate/severe group than in the other groups (versus none, $p < 0.01$; versus mild, $p < 0.05$). DWMHs: deep white matter hyperintensities, IQ: intelligence quotient, MRI: magnetic resonance imaging, mRS: modified Rankin Scale, PIQ: performance IQ, SDFC: subdural fluid collection, VIQ: verbal IQ.

predict cognitive decline following stroke or transient ischemic attack. Molad J et al.[42] evaluated the relationship between cognitive performances at 1 year post-stroke, and previously suggested total cerebral small vessel disease burden score. Significant negative associations were then found between WMHs and cognition. Adding other small vessel disease markers (i.e., lacunes, cerebral microbleeds, perivascular spaces) to WMHs did not improve prediction of post-stroke cognitive performances.

In the present study, brain injury was more frequent in the moderate/severe DWMH group compared with the none group, although the difference was not statistically significant ($p = 0.052$). As there were no differences in surgical characteristics among each group, brains with moderate/severe DWMHs may be easily injured by surgical manipulation; for example, contusion of cerebral parenchyma due to use of a spatula, or ischemia following compression of cerebral vessels. Previous studies have clarified the structural vulnerability of brains with WMH by investigating the relationship between the blood–brain barrier (BBB) and WMH,[44–46] and by assessing the adverse effects of WMH in patients with intracerebral hematoma[47,48] and carotid artery stenosis.[47] Li et al. found that higher BBB permeability was associated with higher WMH burden and cognitive decline.[44] Lou et al. found that severe WMHs were associated with larger intracerebral hemorrhage volumes, and with hematoma growth to a lesser extent.[48] Maggio et al. concluded that the treated side and pre-existing white matter damage are risk conditions for brain micro-embolism during carotid artery stenting.[49]

In the present study, 12 patients with IQ deterioration at 1 month postoperatively did not show worsening mRS score at 6 months. Because we evaluated cognitive function at 1 month after surgery, it could be inferred that some of these patients have long-term cognitive dysfunction. Ohue et al. reported that only 67% and 40% of patients who showed deterioration in the Kana-hiroi and Miyake memory tests, respectively, at 1 month after surgery showed full recovery 6 months later. As those patients were all evaluated as "good" on GOS, the cognitive impairment did not influence their outcomes.[9] It may be more accurate to state that cognitive dysfunction was recognized in patients showing good outcome; that is, that ordinary evaluation such as mRS and GOS may be inadequate for evaluating postsurgical function in patients with UIAs. The present results may be of assistance when considering the operative indications for performing perfect clipping of UIAs, with no complications, in patients

Table 4 Univariate analysis between IQ deterioration and no IQ deterioration

	Deterioration	No deterioration	p value
Age			p = 0.0135*
<70 years	8	84	
≥70 years	5	9	
Preop. IQ			p = 0.6991
<90	3	16	
≥90	10	77	
Hypertension			p = 0.7593
(+)	8	62	
(–)	5	31	
Diabetes mellitus			p = 1.000
(+)	1	11	
(–)	12	82	
Hyperlipidemia			p = 0.7185
(+)	3	18	
(–)	10	75	
Heart disease			p = 0.3903
(+)	3	12	
(–)	10	81	
Aneurysm size			p = 1.000
<7 mm	10	67	
≤7 mm	3	26	
Aneurysm location			
ACoA	5	23	p = 0.3215
other	8	70	
Number of aneurysms			p = 1.000
multiple	1	12	
single	12	81	
Preop. DWMH			p = 0.0010**
moderate or severe	8	15	
none or mild	5	78	
Preop. cerebral infarction			p = 1.000
(+)	1	13	
(–)	12	80	
Surgical approach			p = 1.000
Interhemispheric	1	11	
Other	12	83	
Operative time			p = 0.3746
<300 min	4	44	
≤300 min	9	49	
Bleeding volume			p = 0.3538
<400 mL	11	85	
≤400 mL	2	8	

Table 4 Univariate analysis between IQ deterioration and no IQ deterioration (Continued)

	Deterioration	No deterioration	p value
Temporary clip usage			p = 0.5916
(+)	0	8	
(–)	13	85	
Abnormal findings on postoperative MRI			
Brain injury			p = 0.0383*
(+)	3	4	
(–)	10	89	
Subdural fluid collection			p = 0.4872
(+)	1	4	
(–)	12	89	
Cerebral infarction			p = 1.000
(+)	0	5	
(–)	13	88	

Statistically significant difference was found for age (*p <0.05), DWMHs on preoperative MRI (**p <0.01), and brain injury on postoperative MRI (*p <0.05) (Fisher's exact test). ACoA: anterior communicating artery, DWMHs: deep white matter hyperintensities, IQ: intelligence quotient, MRI: magnetic resonance imaging, Preop.: preoperative.

Table 5 Multivariate analysis of potential predictors of cognitive dysfunction

	p value	Odds ratio	95% CI	
			Lower	Upper
Age ≥70 years	0.047*	4.42	1.02	19.21
ACoA aneurysm	0.561	0.64	0.14	2.88
Preoperative DWMH	0.007**	6.81	1.70	27.34
Cerebral infarction	0.514	0.44	0.04	5.12
Brain injury	0.159	4.38	0.56	34.34
Size of aneurysm	0.440	1.18	0.77	1.82
Preoperative IQ	0.615	0.98	0.92	1.05

Age ≥70 years and presence of moderate/severe DWMHs were independent prognostic factors for postoperative deterioration in IQ (*p <0.05; **p <0.01). ACoA: anterior communicating artery, DWMHs: deep white matter hyperintensities, IQ: intelligence quotient.

aged ≥70 years with moderate or severe DWMHs on preoperative MRI.

Study Limitations

The limitations of this study are as follows: (1) As we evaluated cognitive function only at 1 month after surgery, longer-term examination is necessary. No conclusion can be reached concerning follow-up results over the long term; indeed, some studies have reported full recovery,[4,5] whereas others did not.[9,17–19] (2) The severity of DWMHs was evaluated because manipulation during aneurysm surgery affects mainly the subcortical white matter in the frontal and temporal lobes. However, periventricular hyperintensity is also related to cognitive dysfunction, the relationship between periventricular hyperintensities and cognitive function after clipping surgery should also be studied. (3) The patients in our study underwent surgery more than a decade ago, between January 2002 and December 2009. However, as operative techniques and monitoring systems have not changed substantially since then, we consider that the data reported from those years would be little different to those obtained at the present time.

Conclusions

The presence of moderate/severe DWMHs may be a prognostic factor for postoperative cognitive dysfunction after clipping surgery.

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Conflicts of Interest Disclosure

The authors declare no conflicts of interest concerning the materials or methods used in this study, or the findings specified in this paper.

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