



Original Article



Clinical efficacy of early microsurgical clipping of tumor neck in the treatment of cerebral aneurysm rupture and bleeding and its impact on oxidative stress response and prognosis of patients

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Abstract



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Cerebral aneurysm can rupture a blood vessel and cause bleeding in the brain. Microsurgical clipping of the tumor neck has been reported to be effective in treating cerebral aneurysm rupture and bleeding. This research attempted to clarify the clinical efficacy of early microsurgical clipping of tumor neck for treating cerebral aneurysm rupture and bleeding, and its impact on the prognosis of patients. One hundred patients with cerebral aneurysm rupture and bleeding patients were treated. They were selected and divided into experimental group (n=25) and control group (n=25) according to surgical time. All patients underwent microsurgical clipping of tumor neck for therapy. The control group chose to undergo surgery 72 hours after the onset of cerebral aneurysm rupture and bleeding, while the experimental group chose to undergo complete surgery within 72 hours after the onset of cerebral aneurysm rupture and bleeding. Primary outcome measures were incidence of complications, cognitive function scores, prognosis, surgical indicators, oxidative stress response and quality of life. Results showed that compared to the control group, the incidence of complications in experimental group exhibited depletion ($P<0.05$), the prognosis in experimental group exhibited elevation ($P<0.05$), the hospitalization time in experimental group exhibited depletion ($P<0.05$), the nomination, abstraction, language, orientation, attention, delayed recall and visual and executive function scores and total scores in experimental group exhibited elevation ($P<0.05$), serum levels of oxidative stress-related indicators in experimental group exhibited depletion ($P<0.05$) and the quality of life in experimental group exhibited elevation ($P<0.05$). In conclusion, early microsurgical clipping of the tumor neck can reduce the risk of complications and cognitive impairment in patients with cerebral aneurysm rupture and bleeding.

Keywords: Cerebral aneurysm rupture and bleeding, Microsurgical clipping of tumor neck, Oxidative stress, Prognosis

1. Introduction

Cerebral aneurysm (CA) is a common disease in clinical neurosurgery. When patients' lesion tissue ruptures and bleeds, it will accelerate disease progression [1–3]. If patients' bleeding problem is not resolved in a timely manner, it will directly damage brain nerve function as the disease progresses and cannot reverse, increasing secondary bleeding rate of CA, affecting patients' prognosis, and in severe cases, it can lead to patients' death [4, 5]. Research has demonstrated that the pathogenesis of CA patients is complex; usually, major pathogenic factor for patients is proliferation of arterial walls or occurrence of degenerative changes in arteries; once tumor ruptures and bleeds, it is rapidly affected by disease development, which will increase rate of subarachnoid hematoma formation [6]. Oxidative stress plays an important role in the pathological process of CA. CA can aggravate oxidative stress and lipid peroxidation, promote vascular endothelial damage and endothelial cell apoptosis, and thus induce

CV rupture and bleeding [7]. Currently, clinical practice advocates for surgery to quickly stop bleeding in patients with such conditions, whereas timing of surgery has not been determined. Research has demonstrated that early surgery can effectively control degree of brain tissue damage in patients during acute attacks, elevating survival rate [8]. Simultaneously, there are also relevant clinical reports that improper early surgical treatment can increase the risk of brain edema in patients and cause other brain injuries, which cannot achieve the expected surgical effect and affect prognosis [9]. Thus, choosing appropriate surgical timing is of great significance.

With the widespread application of clinical microsurgical techniques in neurosurgery, for patients with CA rupture and bleeding, microsurgical clipping of the tumor neck can be applied to remove hematoma, reducing stimulation response of pathological products to patients' cerebrovascular system, which is an effective plan to reduce the risk of complications and has been confirmed by rele-

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vant research [10].

Based on this, this research attempted to clarify the clinical efficacy of early microsurgical clipping of tumor neck for treating CA rupture and bleeding, and its impact on oxidative stress response and prognosis of patients. The following report is presented.

2. Materials and methods

2.1. General data

The 100 patients with CA rupture and bleeding treated in our hospital from November 2020 to November 2022 were selected as research subjects. All patients underwent microsurgical clipping of the tumor neck for therapy. Patients received division into early therapy group (experimental group; EG) and late therapy group (control group; CG) according to surgical time, with 25 cases in each group. The research achieved approval of the Ethics committee of our hospital, and all patients and their family members signed informed consent.

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

All patients were diagnosed with CA rupture and bleeding through imaging examinations such as CT angiography (CTA) and digital subtraction angiography (DSA), and there was spontaneous subarachnoid hemorrhage; there were symptoms of varying degrees of coughing, vomiting, headache, cold sweating, emotional anxiety, visual impairment, and even coma and disturbance of consciousness.

2.2.2. Exclusion criteria

Those with symptoms such as blood system diseases, coagulation disorders, malignancies, and heart failure; those with communication barriers or mental illnesses; women during lactation or pregnancy.

2.3. Methods

Both groups underwent microsurgical clipping of the tumor neck. Specific method: Patients underwent CTA or DSA examination before surgery to determine specific situation of CA, including tissue location, size, bleeding, hematoma, and whether or not there were symptoms of cerebrovascular spasm. Surgery risk assessment received conduction, and contraindications received exclusion based on previous medical history data. During surgery, patients were placed in a supine position and subjected to general anesthesia. The patients' heads were fixed, and conventional disinfection and tissue placement received performance. The scalp was cut open from the point of the affected wing as surgical entry point, completely exposing tumor and surgical area of the tumor neck. Combined with surgical microscope, the arachnoid membrane and blood vessels on affected side received separation, and cerebral cistern was opened to present cerebral artery ring. After separating cerebral artery ring from tumor neck, a suitable model of tumor clamp was taken to completely clip blood supply artery and paid attention to adjust tumor clamp to appropriate position. On the premise of ensuring smooth flow of tumor carrier artery, multiple tumor clamps can receive selection to ensure complete clipping of blood supply artery, and blood clots found in surgical field were cleaned up. After thorough hemostasis of patients' bleeding site, dural suture received performance. If swelling of patients' brain tissue was obvious, bone flap reduction did

not receive performance. On the contrary, direct reduction and bone flap fixation received performance. After suturing scalp layer by layer, drainage tubes were placed. After the wound was sutured, sterile dressing continued to cover surgical incision, and surgery was completed. After surgery, targeted treatment should be given to patients based on their physical condition, such as dehydration to reduce intracranial pressure, anti-vasospasm, anti-infection, monitoring of neurological changes, and monitoring of vital signs. Cerebral angiography should also be performed for reexamination.

On the basis of above surgery, CG chose to undergo surgery 72 h after the onset of CA rupture and bleeding, while EG chose to undergo surgery early, that is, complete surgery within 72 h after the onset of CA rupture and bleeding. Postoperative follow-up was conducted to record patients' oxidative stress response and prognosis and evaluate surgical efficacy.

2.4. Observation indicators

(1) Complications: Complications include aneurysm re-rupture, cerebrovascular spasm, hydrocephalus, intracranial infection, etc.

(2) Cognitive function scores. Two weeks after surgery, patients' cognitive function received evaluation through the Montreal Cognitive Assessment (MoCA) [11] with a total score of 30 points, including multiple cognitive domains such as attention and concentration, executive function, memory, language, visual structural skills, abstract thinking, computation, directional ability, etc. A score of ≥ 26 points indicates normal cognitive function, while a score of < 26 points indicates abnormal cognitive function.

(3) Prognosis. The Glasgow Outcome Scale (GOS) [12] received application to evaluate patients' prognosis. 1 point indicated death, 2 points indicated a vegetable state, 3 points indicated conscious but severely disabled, 4 points indicated conscious and self-care but moderately disabled, and 5 points indicated conscious and self-care but mildly disabled. Additionally, grade V indicates that patients have the ability to fully take care of themselves in daily life; grade IV indicates that patients can basically take care of themselves; grade III indicates that patients have moderate disability and difficulty taking care of themselves; grade II indicates that patients have severe disability and a vegetative state of survival; grade I indicates death. Among them, grades I, II, and III indicate poor prognosis of patients, while grades IV and V indicate excellent and good prognosis of patients. Excellent and good prognosis rate = (grade IV + grade V) cases / total cases $\times 100\%$.

(4) Surgical indicators. Surgical indicators include surgical time, intraoperative bleeding, and hospitalization time.

(5) Oxidative stress response. Patients' oxidative stress response received evaluation through comparing serum soluble vascular cell adhesion molecule-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), and malondialdehyde (MDA) levels between both groups before operation and 2 weeks after operation. The 3 mL of fasting venous blood received was collected from patients and centrifugation at 3000 r/min for 5 min. The serum received separation followed by detection through enzyme-linked immunosorbent assay (ELISA, R&D Systems, Minneapolis, USA).

(6) The short form 36 health survey questionnaire (SF-

36) was used to evaluate patients' quality of life with a score ranging from 0 to 100. The higher the score, the better the quality of life was.

2.5. Statistical analysis

SPSS 27.0 statistical software (IBM, Armonk, New York, USA) received applications for analyzing data. The measurement data received representation by (x ± s), with intergroup comparison through t-test. The count data received representation by [n (%)], with intergroup comparison through χ² test. P<0.05 indicated difference with statistical significance.

3. Results

3.1. Comparison of general data between both groups

No statistical significance was discovered in clinical data containing gender, age, aneurysm site, and Hunt-Hess grading between both groups (P>0.05; Table 1), which was comparable.

3.2. Comparison of incidence of complications between both groups

The incidence of complications in EG was 8.0%, exhibited depletion relative to that of 24.0% in CG, indicating statistical significance (P<0.05; Table 2).

3.3. Comparison of prognosis between both groups

Two weeks after operation, GOS scores in EG were (4.12±0.3) points, exhibiting elevation relative to those of (2.23±0.45) points in CG, indicating statistical significance (P<0.05; Figure 1). The excellent and good prognosis rate in EG was 88.0%, exhibited elevation relative to that of 60.0% in CG, indicating statistical significance (P<0.05; Table 3).

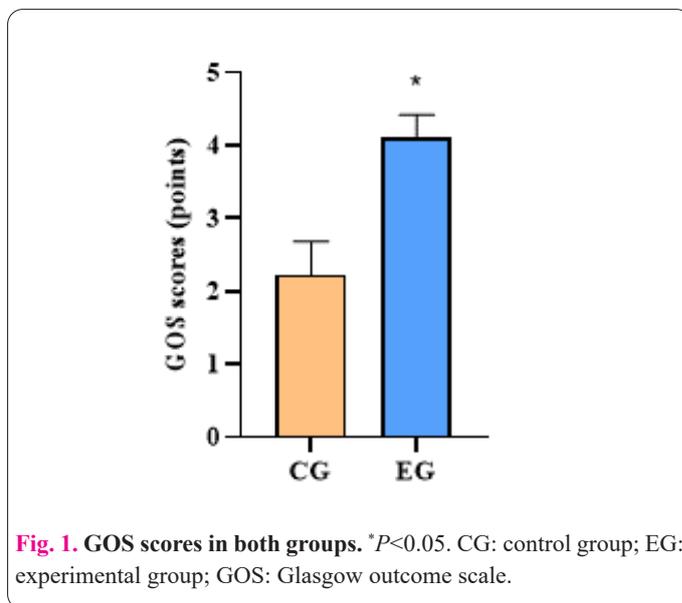


Fig. 1. GOS scores in both groups. *P<0.05. CG: control group; EG: experimental group; GOS: Glasgow outcome scale.

gnosis rate in EG was 88.0%, exhibited elevation relative to that of 60.0% in CG, indicating statistical significance (P<0.05; Table 3).

3.4. Comparison of surgical indicators between both groups

No statistical significance in surgical time and intraoperative bleeding between both groups (P>0.05). The hospitalization time in EG was (11.31±0.65) d, exhibited depletion relative to that of (15.69±1.21) d in CG, indicating statistical significance (P<0.05; Figure 2).

Table 1. General data in both groups (x ± s)/[n (%)].

Groups	N	Gender		Age	Aneurysm site			Hunt-Hess grading				
		Male	Female		Anterior cerebral aneurysm	Middle cerebral aneurysm	Posterior communicating aneurysm	I	II	III	IV	V
CG	50	28 (56.0)	22 (44.0)	50.75±3.65	17 (34.0)	15 (30.0)	18 (36.0)	11 (22.0)	13 (26.0)	9 (18.0)	8 (16.0)	9 (18.0)
EG	50	26 (52.0)	24 (48.0)	51.58±4.10	20 (40.0)	12 (24.0)	18 (36.0)	13 (26.0)	12 (24.0)	10 (20.0)	8 (16.0)	7 (14.0)
χ ² /t		0.322		0.207	1.153			1.019				
P		0.57		0.837	0.562			0.907				

Note: CG: control group; EG: experimental group.

Table 2. Incidence of complications in both groups [n (%)].

Groups	N	Aneurysm re rupture	Cerebrovascular spasm	Hydrocephalus	Intracranial infection	Total complication occurrence rate (%)
CG	50	2 (4.0)	3 (6.0)	3 (6.0)	4 (8.0)	12 (24.0)
EG	50	0 (0.0)	2 (4.0)	0 (0.0)	2 (4.0)	4 (8.0)
χ ²		/	/	/	/	9.524
P		/	/	/	/	0.002

Note: CG: control group; EG: experimental group.

Table 3. Excellent and good prognosis rate in both groups [n (%)].

Groups	N	I	II	III	IV	V	Total excellent and good prognosis rate (%)
CG	50	0 (0.0)	12 (24.0)	8 (16.0)	14 (28.0)	16 (32.0)	30 (60.0)
EG	50	0 (0.0)	2 (4.0)	4 (8.0)	20 (40.0)	24 (48.0)	44 (88.0)
χ ²		/	/	/	/	/	20.374
P		/	/	/	/	/	<0.001

Note: CG: control group; EG: experimental group.

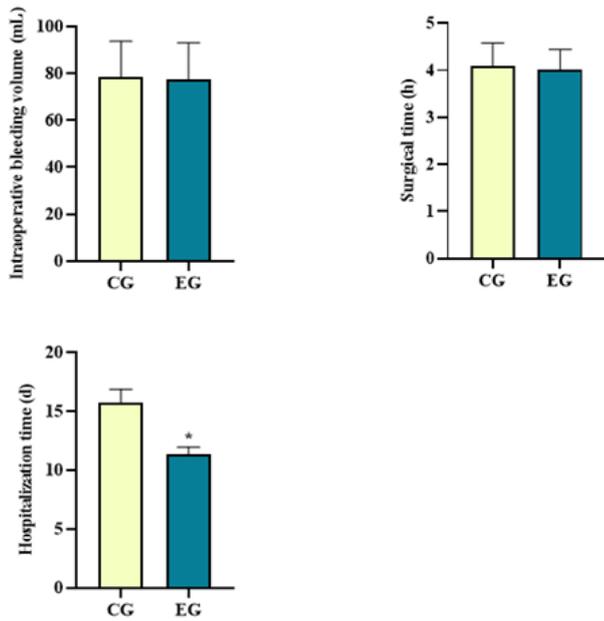


Fig. 2. Surgical indicators in both groups. * $P<0.05$. CG: control group; EG: experimental group.

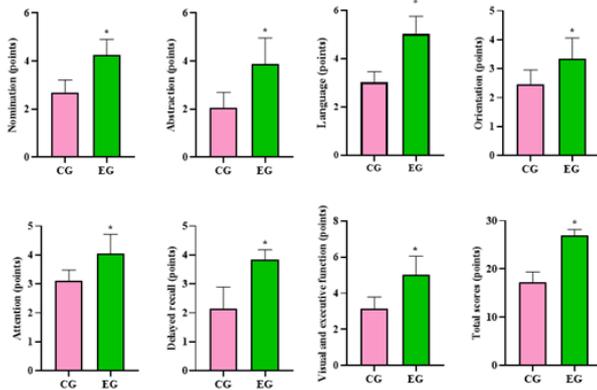


Fig. 3. MoCA scores in both groups. * $P<0.05$. CG: control group; EG: experimental group.

3.5. Comparison of MoCA scores between both groups

The nomination, abstraction, language, orientation, attention, delayed recall, visual and executive function scores and total scores in EG were (4.25 ± 0.65 points, 3.88 ± 1.08 points, 5.03 ± 0.73 points, 3.34 ± 0.72 points, 4.05 ± 0.66 points, 3.85 ± 0.33 points, 5.02 ± 1.04 points and 26.89 ± 1.33 points) exhibited elevation relative to those of (2.69 ± 0.52 points, 2.07 ± 0.63 points, 3.02 ± 0.44 points, 2.45 ± 0.51 points, 3.12 ± 0.36 points, 2.14 ± 0.75 points, 3.15 ± 0.64 points and 17.24 ± 2.15 points) in CG, indicating statistical significance ($P<0.05$; Figure 3).

3.6. Comparison of serum sVCAM-1, sICAM-1 and MDA levels between both groups

No difference was discovered in serum sVCAM-1, sICAM-1 and MDA levels between 2 groups before operation ($P>0.05$). Two weeks after the operation, serum sVCAM-1, sICAM-1 and MDA levels in both groups declined, and those in EG were (365.58 ± 44.56 ng/mL, 201.51 ± 34.47 ng/mL and 1.15 ± 0.1 nmol/mL), exhibited depletion relative to those of (462.14 ± 48.47 ng/mL, 281.14 ± 36.44 ng/mL and 1.62 ± 0.12 nmol/mL) in CG ($P<0.05$; Figure 4).

3.7. Quality of life in both groups

Two weeks after the operation, the physical function, emotional function, role function, social function and overall health scores of patients in EG were (81.25 ± 8.14 points, 80.87 ± 8.09 points, 81.43 ± 8.15 points, 80.57 ± 8.07 points and 81.32 ± 8.14 points), presented higher than those of (73.65 ± 7.43 points, 72.24 ± 7.23 points, 73.25 ± 7.36 points, 70.24 ± 7.05 points and 72.16 ± 7.25 points) in CG ($P<0.05$, Figure 5).

4. Discussion

CA rupture bleeding, as a common critical and severe condition in clinical neurosurgery, has a rapid onset and development, and is more common in middle-aged females [13]. The onset of CA rupture is due to damage and aging of patients' arterial wall caused by congenital weakness of cerebral artery, brain injury, or arteriosclerosis, leading to local vascular proliferation and formation of a cystic tumor; nevertheless, when the tumor is not ruptured, patients basically have no obvious symptoms [14, 15]. If patients experience abnormal emotional excitement or excessive physical exertion, the tumor may receive stimulation by the body's stress response, leading to rupture and bleeding. In the early stage, major symptoms

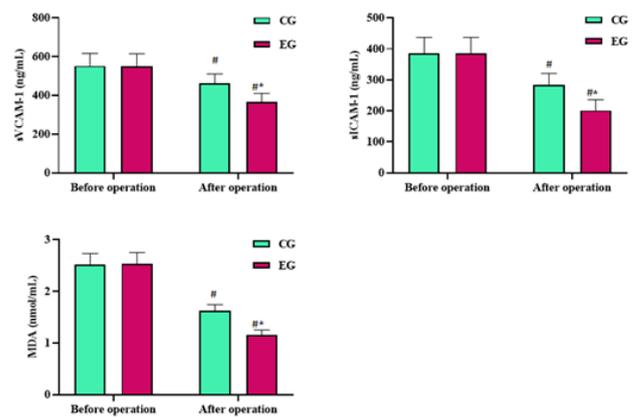


Fig. 4. Serum sVCAM-1, sICAM-1 and MDA levels in both groups. # $P<0.05$, compared with before operation, * $P<0.05$, compared with control group. CG: control group; EG: experimental group; sVCAM-1: soluble vascular cell adhesion molecule-1; sICAM-1: soluble intercellular adhesion molecule-1; MDA: malondialdehyde.

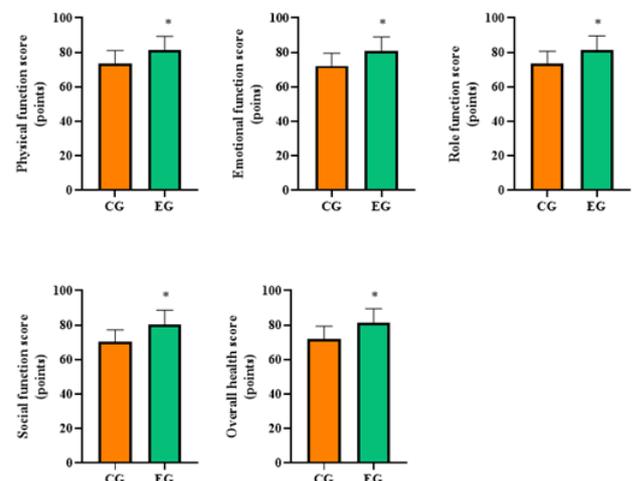


Fig. 5. Quality of life in both groups. * $P<0.05$. CG: control group; EG: experimental group.

include vomiting, elevated body temperature, headache, neck stiffness, and pain in back and loin; as the condition progresses, consciousness disorders and coma may occur. If effective measures are not taken in a timely manner to solve problem of intracranial hemorrhage in patients, late mortality rate can reach 30%, and disability rate is high, which reduces quality of life of patients and threatens their safety [16]. For patients with CA rupture and bleeding, if conventional conservative therapy is difficult to achieve a hemostatic effect, it is recommended to combine Hunt-Hess grading to decide whether to undergo surgery. Among them, grade I and II patients require immediate surgery, while > grade II patients need to decide whether to undergo surgery based on their condition after bleeding situation stabilizes, in order to minimize degree of damage caused by surgery to patients' body and brain tissue [17]. Nevertheless, research has indicated that after CA rupture and bleeding of patients, the peak stage of secondary bleeding occurs within 4-9 days, indirectly elevating patients' mortality rate [18]. Additionally, if patients miss optimal treatment opportunities while waiting for surgical therapy, it will elevate the difficulty of completely eliminating subarachnoid hemorrhage, and CA is also susceptible to external stimuli, resulting in a high risk of rupture and bleeding, which will not only affect prognosis of patients but also increase incidence of cerebrovascular spasm and attenuate their quality of life. Thus, clinical emphasis should be placed on treating patients' symptoms, and timing of surgery should be early treatment. Early surgery can receive performance if patients are not in a state of imminent death or with dilated pupils within 3 days after bleeding, which exerts a positive impact on improving surgical efficacy and prognosis.

With the vigorous promotion of minimally invasive concepts in clinical neurosurgery, there are also more options for surgical procedures for patients with CA rupture and bleeding. Early endovascular intervention, as one of the treatment options for patients with CA rupture and bleeding, can effectively treat multiple aneurysms at once with minimal trauma and easy operation; nevertheless, postoperative follow-up results have demonstrated that patients have a high rate of rebleeding within one year after surgery, indirectly elevating the risk of disability and death, and overall efficacy still needs further research and verification [19]. Microsurgical clipping of tumor neck, as a minimally invasive surgery, receives application in treating patients with CA rupture and bleeding can completely clip ruptured aneurysms of patients in a short period under the clear surgical field presented by microscope, control lesion site, reduce risk of re-rupture and bleeding, facilitate recovery of cerebral hemodynamics, and repair brain nerve function, whose overall effect is remarkable. Moreover, microsurgical clipping of tumor neck surgery can effectively remove intracerebral hemorrhage points and edema in patients, avoid inducing delayed cerebrovascular spasm after surgery, markedly downregulate patients' disability rate, and elevate survival rate [20, 21]. Herein, the incidence of complications in EG exhibited depletion relative to that in CG. Two weeks after the operation, GOS scores in EG exhibited elevation relative to those in CG, and excellent and good prognosis rate in EG exhibited elevation relative to that in CG. No statistical significance in surgical time and intraoperative bleeding between both groups, whereas hospitalization time in EG exhibited de-

pletion relative to that in CG, indicating that early surgery will not increase intraoperative bleeding in patients, and can effectively enhance treatment effectiveness under the premise of safety assurance, and early surgery can shorten hospitalization time of patients with CA rupture and bleeding. Consistently, Wang *et al.* [22] have indicated that the treatment of CA rupture and bleeding at the early stage by microsurgical clipping may predict a favorable prognosis.

Research has demonstrated that both problems of CA rupture and bleeding and invasive surgical procedures, can damage structure and function of patients' cerebral cortex, leading to cognitive problems such as language, memory, execution, reaction speed, and decreased attention, affecting patients' physical and mental health and safety [23]. Herein, nomination, abstraction, language, orientation, attention, delayed recall and visual and executive function scores and total scores in EG exhibited elevation relative to those in CG. At the same time, the physical function, emotional function, role function, social function and overall health scores of patients in EG presented higher than those of in CG. All these outcomes suggested that early surgery will not excessively damage patients' cognitive function; on the contrary, it will also alleviate cognitive dysfunction, timely control patients' disease progression, avoid irreversible dysfunction problems, and thereby elevate the quality of life. In line with our findings, Germanò *et al.* [24] have proposed that early aneurysm surgery, coupled with microsurgical clipping is associated with a good neurological outcome and a full recovery of cognitive and neuropsychological performances in patients.

After CA rupture and bleeding, body is in a hypercoagulable state, and brain tissue presents hypoxia, which is prone to oxidative stress response, producing a large amount of oxygen free radicals and consuming a large amount of antioxidant substances; in oxidative reaction, lipid peroxidation substance MDA receives production; if without treatment in a timely manner and inhibiting oxidative stress response, risk of secondary bleeding in patients exhibits elevation, and mortality rate increases accordingly [25]. Herein, serum sVCAM-1, sICAM-1 and MDA levels in EG two weeks after the operation exhibited depletion relative to those before the operation, and EG exhibited depletion relative to CG, suggesting that early surgery can attenuate oxidative stress response of patients with CA rupture and bleeding, which was consistent with previous studies [26].

There are some limitations to our study. First, the sample size of our study was relatively small. Second, this study is a single-center study, which may affect the external validity of the findings and applicability to other hospitals.

In conclusion, early microsurgical clipping of the tumor neck is the preferred treatment option for patients with CA rupture and bleeding, which can enhance effectiveness of surgical treatment and downregulate the risk of complications and cognitive impairment, which is worthy of clinical promotion and application.

Conflict of interest

The authors report that there is no conflict of interest.

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