Preventing Cerebral Vasospasm After Aneurysmal Subarachnoid Hemorrhage with Aggressive Cisternal Clot Removal and Nicardipine

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■ BACKGROUND: **A subarachnoid clot is the strongest predictor of cerebral vasospasm. Our purpose was to analyze the relationship between the number of postoperative cisternal clots and cerebral vasospasm and to assess the efficacy of surgical clot removal.**

■ METHODS: **The subjects were 158 patients with aneurysmal subarachnoid hemorrhage. All patients underwent clipping with cisternal clot removal. The preoperative and postoperative number of clots was analyzed semiquantitatively using computed tomography, and cerebral vasospasm and its severity were analyzed using magnetic resonance angiography in a blind fashion. Factors related to cerebral vasospasm and poor outcome were analyzed retrospectively. Poor outcome was defined as modified Rankin Scale (mRS) score of 3 or greater.**

■ RESULTS: **Symptomatic cerebral vasospasm (SCV) was observed in 6 patients (3.8%). Angiographic vasospasm (AVS) was observed in 38 patients (24.1%). One year after the operation, 82.9% of patients had an mRS score of 0–2. The postoperative number of clots was significantly ($P < 0.005$) related to SCV (adjusted odds ratio [OR], 6.447; 95% confidence interval [CI], 2.063–20.146), AVS (OR, 2.634; 95% CI, 1.467–4.728), and poor outcome (OR, 2.103; 95% CI, 1.104–4.007). Poor outcome was also related to age over 65 (OR, 6.658; 95% CI, 2.389–18.559) and World Federation of Neurosurgical Societies scale grade (OR, 1.732; 95% CI, 1.248–2.403).**

■ CONCLUSIONS: **Surgically removing as many clots as possible in the acute stage can decrease SCV and reduce AVS severity. Irrigation should be performed on all approachable cisterns.**

INTRODUCTION

Cerebral vasospasm following aneurysmal subarachnoid hemorrhage (SAH) is a leading cause of mortality and morbidity.[1-3] The strongest predictor of cerebral vasospasm is the number of subarachnoid clots present on initial computed tomography (CT).[4-10] Blood degradation products from these clots trigger molecular cascades that lead to cerebral vasospasm.[11-13] Although complete removal of subarachnoid clots would be ideal for preventing cerebral vasospasm, it has been considered technically difficult and disadvantageous. Hence, alternative ways to induce clot fibrinolysis[14-17] or to prevent molecular cascades have been studied, and some effective drugs have been developed.[18-22] However, vasospasm still occurs in 12%–30% of patients.[23]

Key words
- Angiographic vasospasm
- Aneurysmal subarachnoid hemorrhage
- Cisternal clot removal
- Clipping
- Nicardipine
- Symptomatic vasospasm

Abbreviations and Acronyms
ACA: Anterior cerebral artery
AVS: Angiographic vasospasm
CI: confidence interval
CT: Computed tomography
CTA: Computed tomography angiography
DSA: Digital subtraction angiography
IVH: Intraventricular hemorrhage
MRA: Magnetic resonance angiography
mRS: modified Rankin scale
OR: Odds ratio
SAC: Sum of scores for all cisterns
SMC: Sum of scores for major cisterns
SAH: Subarachnoid hemorrhage
SCV: Symptomatic cerebral vasospasm
TOF: Time-of-flight
WFNS: World Federation of Neurosurgical Societies

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We reported effective cisternal clot removal with continuous low-dose nicardipine in 2015, and symptomatic cerebral vasospasm (SCV) was observed in only 2.9% of patients.[24] However, that study was not focused on the number of clots. The present study's purpose was to analyze the relationship between the postoperative number of clots and angiographic vasospasm (AVS) and to assess the efficacy of surgical clot removal.

MATERIALS AND METHODS

Patient Population

Sapporo Teishinkai Hospital's Institutional Research Board approved this retrospective study. We included patients with aneurysmal SAH that was diagnosed using CT or lumbar puncture and treated surgically. We excluded those who died of initial brain damage from SAH (n = 4) or received endovascular treatment (n = 1). We enrolled 158 patients between April 2012 and March 2016. The patients' demographic, clinical, and outcome data were collected from hospital charts, and radiographic data were analyzed retrospectively. A neurologic and general medical evaluation was performed by a neurosurgeon. Modified Rankin Scale (mRS) scores were measured at discharge and at 3 and 12 months after SAH using medical charts or telephone interviews. We defined death or poor outcome as an mRS score of 3–6.

Definition of the Cerebral Vasospasm

Using 1.5-T MAGNETOM Essenza (Siemens Healthcare, Erlangen, Germany) and 3.0-T MAGNETOM Skyra (Siemens Healthcare, Erlangen, Germany) magnetic resonance angiography (MRA) systems, 3-dimensional time-of-flight (TOF) MRA examinations were performed on all subjects. For consistent MRA assessment result, the same model was always used. MRA was analyzed by 2 neurosurgeons blinded to the patient's preoperative and postoperative CT and medical history.

SCV was defined as either a new infarction on diffusion-weighted imaging that was not visible immediately after operation or clinical deterioration or neurologic deficit attributable to vascular narrowing on MRA, computed tomography angiography (CTA), or digital subtraction angiography (DSA). AVS was defined solely through angiographic analysis as vascular narrowing with or without neurologic symptoms. MRA was performed 1 day after the operation to establish a baseline control and to identify early vasospasm. MRA was performed every 2–3 days until day 14 if no AVS was detected. If, however, AVS was identified, MRA was performed daily and continued until AVS was resolved. CT and CTA were performed before and immediately after the operation. CTA and DSA were not routinely used for identifying AVS. Rather, they were performed if AVS was suspected and the neurologist believed that MRA was unsuitable for analyzing the spasm or that endovascular treatment was necessary.

AVS was analyzed in each major anterior vessel on both sides, including the internal carotid arteries, A1 arteries, proximal M1 arteries, distal M1 arteries, proximal M2 arteries, distal middle cerebral arteries, and distal anterior cerebral arteries (ACAs). The surgical clip artifact caused a signal defect around the treated vessel; therefore, AVS could not be assessed around it. AVS was classified into 3 groups. In the AVS1 group, the affected vessel angiographically exhibited a width one third narrower than that detected in baseline control MRA. In the AVS2 group, the width was narrowed by 2 thirds. The AVS3 group exhibited no signal under MRA and was further subdivided into the AVS3A subgroup, which still exhibited distal blood flow, and the AVS3B group, which did not. We defined severe AVS as AVS2 or AVS3.

MRAs performed in the post-acute stage (>21 days) were compared with the baseline control MRAs to detect early vasospasms. Sometimes patients became restless during MRI scanning, making it difficult to analyze the vasospasm. We categorized patients exhibiting such restlessness as having AVS if the situation happened twice.

Radiographic Measurement of Subarachnoid Clot

Head CT was performed using a 320-row CT scanner Aquilion One Vision Edition (Toshiba Medical Systems, Tochigi, Japan). CT was performed on admission and immediately after the operation. All scans were analyzed in their original format with a 5-mm slice thickness scaled to Level 40/Window 80. CT scans were analyzed by 2 different neurosurgeons who were blinded to the patient's MRA and medical history.

We analyzed clots in 16 cisterns including the (1) premedullary, (2) prepontine, (3) interpeduncular, (4, 5) both ambient, (6) quadrigeminal, (7, 8) both suprasellar, (9, 10) both basal Sylvian, (11, 12) both lateral Sylvian, (13, 14) both distal Sylvian, (15) basal interhemispheric, and (16) distal interhemispheric cisterns. The 10 cisterns with major arteries running through were defined as "major cisterns," these being (1) the basal interhemispheric, (2, 3) both suprasellar, (4, 5) both basal Sylvian, (6, 7) both lateral Sylvian, (8, 9) both distal Sylvian, and (10) distal interhemispheric cisterns.

Each cistern was scored using a modified version of the Hidjura classification.[4] A score of 0 indicates no clots. A score of 1 means different things for different cisterns. For the suprasellar, basal interhemispheric, basal Sylvian, interpeduncular, and ambient cisterns, it indicates isodensity or mild high-density of clots. For the lateral Sylvian, distal Sylvian, and distal interhemispheric cisterns, it indicates clots with thicknesses less than 1 mm. For the premedullary, prepontine, and quadrigeminal cisterns, it indicates clots that are partly filled or isodensity to mild high-density. A score of 2 also means different things for different cisterns. For the suprasellar, basal interhemispheric, basal Sylvian, interpeduncular, and ambient cisterns, it indicates high-density clots. For the lateral Sylvian, distal Sylvian, and distal interhemispheric cisterns, it indicates clots with thicknesses greater than 1 mm. For the premedullary, prepontine, and quadrigeminal cisterns, it indicates high-density full-packed clots. The number of clots was analyzed semiquantitatively by summating scores for different cisterns. The 2 major sums calculated were the sum of scores for all cisterns (SAC) and the sum of scores for major cisterns (SMC). Interventricular hemorrhage (IVH) was separately analyzed whether or not it was full-packed.

Clinical Management

Patients were treated in a stroke care unit, and neurologic symptoms were assessed at least every 6 hours. The baseline treatment was nicardipine continuously administered at 0.25–0.5 μg/kg/min through a central venous catheter to avoid phlebitis. The dose was adjusted for the patient's blood pressure to avoid hypotension. If SCV or AVS were observed, the dose was increased up to 1 μg/kg/min as long as hypotension did not occur. Patients also received intravenous fasudil (30 mg) 3 times a day for 14 days. We did not perform triple-H