Postoperative Subdural Air Collection Is a Risk Factor for Chronic Subdural Hematoma after Surgical Clipping of Cerebral Aneurysms

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Abstract

The precise mechanism of the development of chronic subdural hematoma (CSDH) as a postoperative complication after aneurysmal clipping remains unclear. The purpose of this study was to identify the independent risk factors for CSDH after craniotomy for aneurysmal clipping and to elucidate the relationship between CSDH and subdural air (SDA) collection immediately after surgery. The medical records and radiologic data of 344 patients who underwent surgical clipping of unruptured aneurysms from July 2010 to July 2016 were retrospectively evaluated. Patient characteristics, aneurysm characteristics, and operation data were statistically analyzed to reveal their relationships with CSDH development. Among the 344 patients, 46 (13.4%) developed CSDH and 13 (3.8%) required subsequent burr-hole surgery for evacuation and irrigation. Multivariate analyses showed that advanced age (P < 0.0001), male sex (P = 0.035), and surgical clipping of multiple aneurysms (P = 0.037) were independent preoperative predictors of CSDH development. Advanced age (P = 0.0005) and postoperative SDA after clipping surgery (P < 0.0001) were independent postoperative predictors of CSDH development. Postoperative SDA and CSDH were not associated with the individual surgeon or operation time. Postoperative severe SDA was significantly associated with the ipsilateral development of CSDH, irrespective of the side of craniotomy. Postoperative SDA is an independent risk factor for CSDH after surgical clipping of unruptured aneurysms and is as important as advanced age, male sex, and surgical clipping of multiple aneurysms in predicting CSDH.

Key words: cerebral aneurysm, clipping, subdural hematoma, subdural air

Introduction

Chronic subdural hematoma (CSDH) is a known complication of neurosurgical procedures, especially surgical clipping of unruptured aneurysms.¹ Most CSDHs resolve spontaneously, but some persist and may convert to symptomatic CSDH. Symptomatic CSDH can require burr-hole drainage; even asymptomatic CSDH can require cessation of antiplatelet or anticoagulant therapy. Therefore, both asymptomatic and symptomatic CSDH can cause serious problems.

The risk factors for the development and recurrence of traumatic CSDH are well known and include advanced age, male sex, antiplatelet therapy, and postoperative subdural air (SDA).²-⁴ However, the risk factors for CSDH after aneurysmal clipping have been sporadically reported and remain unclear because of their low incidence.²-⁶

The purpose of this study was to identify the independent risk factors for CSDH after aneurysmal clipping. Because the causes of postoperative SDA immediately after surgical clipping and the association between SDA and the development of CSDH are less thoroughly understood than other factors, we focused on the perioperative factors related to SDA and the relationship between postoperative CSDH and SDA.

Materials and Methods

Study population

From July 2010 to July 2016, 466 patients underwent surgical clipping of unruptured intracranial aneurysms of the anterior circulation in our hospital.
We excluded 74 patients who were treated via an interhemispheric approach and 48 patients who did not undergo postoperative follow-up computed tomography (CT) scans. The remaining 344 patients were evaluated in this study. All patients were treated through a pterional approach.

We retrospectively reviewed patients’ medical records and radiologic data. The following data were collected: age, sex, medical history, aneurysm location, surgeon, operation time (<188 or ≥188 min), diameter of SDA collection (<10 or ≥10 mm), and CSDH. We defined multiple aneurysms as those located in different arteries: the internal cerebral artery (ICA) and middle cerebral artery (MCA), ICA and anterior cerebral artery (ACA), and MCA and ACA.

**CSDH and postoperative SDA collection**

Brain CT scans were routinely performed 1 day postoperatively and 4–8 weeks postoperatively. If the CT scan revealed CSDH, we carefully followed the patient until CSDH resolution.

Chronic subdural hematoma was evaluated based on CT findings of 4–8 weeks postoperatively. Lesions with a thickness of >10 mm and with high density compared with the cerebrospinal fluid (CSF) were diagnosed as CSDH. This size cut-off has been used previously to define CSDH. Bilateral SDA (ipsilateral and contralateral to the craniotomy) was identified and assessed according to the maximal distance between the inner table of the skull and the cerebral cortex on CT 1 day postoperatively. The median distance and time were used as cut-off values to create two groups for the analysis of SDA and operation time, respectively. The SDA collection was classified as mild (<10 mm) or severe (≥10 mm). Surgeons were classified as chief doctor (N.S.) or others to create two groups for analysis.

**Statistical analysis**

The χ²-test was performed as appropriate. Univariate analyses were performed to identify potential variables associated with CSDH and postoperative SDA. Clinical variables with a P-value of <0.10 in univariate analysis were entered into a multivariate logistic regression model. A P-value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed with JMP software, version 10.0 (SAS Institute, Cary, NC, USA).

**Results**

**Risk factors for CSDH**

Among the 344 patients analyzed, 46 (13.4%) developed CSDH and 13 (3.8%) required burr-hole surgery. All 46 patients with CSDH had good outcomes. Clinical characteristics of the patients, characteristics of the aneurysms, and operation data are summarized in Table 1. The mean patient age was 61.5 ± 10.1 years; 255 patients (74%) were female. Univariate analyses indicated that advanced age, surgical clipping of multiple aneurysms, and postoperative SDA were significantly associated with CSDH (P = 0.0046, 0.0065, and <0.0001, respectively). The mean diameter of postoperative SDA was 8.7 ± 2.7 mm among those who did not develop CSDH and 12.6 ± 2.8 mm among those who developed CSDH (P < 0.0001). The chief doctor had a significantly higher percentage of operation times <188 min than other doctors (86% versus 21%; P < 0.0001). However, neither operation time nor surgeon was associated with the development of CSDH. Total of 17 patients with multiple aneurysms, two had ICA and ACA aneurysms, 10 had ICA and MCA aneurysms, and five had MCA and ACA aneurysms. Among these, CSDH occurred in two (100%), one (10%), and three (60%) patients, respectively. Multivariate analyses of parameters for the preoperative prediction of CSDH development showed that advanced age (P = 0.0030), male sex (P = 0.035), and surgical clipping of multiple aneurysms (P = 0.033) were independently associated with CSDH (Table 2). Multivariate analyses of parameters for the postoperative prediction of CSDH development showed that advanced age and severe postoperative SDA were independently associated with CSDH.

**Risk factors for postoperative SDA**

The risk factors for severe postoperative SDA are summarized in Table 3. The number of patients with severe SDA was 164 (48%). Surgical clipping of multiple aneurysms was not associated with severe SDA. Moreover, neither operation time nor surgeon was associated with SDA. The significant risk factors for SDA accumulation in univariate analysis were advanced age (P = 0.027), male sex (P = 0.026), and the absence of a history of subarachnoid hemorrhage (P = 0.018). Multivariate analyses indicated that advanced age (P = 0.0010), male sex (P = 0.0073), and the absence of a history of subarachnoid hemorrhage (P = 0.0043) were independently associated with SDA.

**Relationship between distribution of CSDH and postoperative SDA**

The CSDH was ipsilateral to the craniotomy in 29 patients, contralateral to the craniotomy in 10 patients, and bilateral in seven patients. In total, 36 CSDHs occurred ipsilateral to the craniotomy.
and 17 occurred contralaterally; the number of CSDHs on either side included seven bilateral CSDHs. Among 164 patients with severe SDA, the SDA was ipsilateral to the craniotomy in 125 patients and contralateral to the craniotomy in 118 patients; these numbers include 79 patients with bilateral severe SDA. Univariate analysis showed that CSDH ipsilateral to the craniotomy was associated with ipsilateral SDA ($P = 0.033$) and that CSDH contralateral to the craniotomy was associated with contralateral SDA ($P = 0.032$). These results are summarized in Table 4.

The mean diameter of ipsilateral postoperative SDA in patients with ipsilateral CSDH was 11.4 ± 3.3 mm; this value was 7.6 ± 3.5 mm in patients without ipsilateral CSDH. The mean diameter of contralateral postoperative SDA in patients with contralateral CSDH was 13.0 ± 2.5 mm; this value

| Table 1  | Characteristics of patients, aneurysms, and operations |
|----------|--------------------------------------------------------|
| Characteristic | Total | CSDH | $P$-value |
| Patients | 344 | 46 (13) | 0.0046 |
| Age in years | | | |
| ≥65 | 147 | 32 (23) | |
| <65 | 197 | 14 (7) | |
| Sex | | | 0.054 |
| Male | 99 | 18 (18) | |
| Female | 255 | 28 (11) | |
| Medical history | | | |
| History of SAH | 19 | 2 (11) | 0.70 |
| Antiplatelet therapy | 31 | 3 (10) | 0.53 |
| Anticoagulant therapy | 5 | 2 (40) | 0.078 |
| Aneurysm location | | | 0.59 |
| ICA | 102 | 14 (14) | |
| MCA | 185 | 23 (12) | |
| ACA | 40 | 3 (8) | |
| Multiple aneurysms | 17 | 6 (35) | 0.0065 |
| Surgeon | | | 0.40 |
| Chief doctor | 162 | 19 (12) | |
| Others | 182 | 27 (15) | |
| Operation time (≥188 min) | 156 | 26 (17) | 0.16 |
| Postoperative SDA | | | <0.0001 |
| Mild (<10 mm) | 180 | 4 (2) | |
| Severe (≥10 mm) | 164 | 42 (26) | |

ACA: anterior cerebral artery, ICA: internal cerebral artery, MCA: middle cerebral artery, SAH: subarachnoid hemorrhage, SDA: subdural air. Data are presented as $n$ or $n$ (%). Bold face type indicates statistical significance.

| Table 2  | Pre- and postoperative predictors of chronic subdural hematoma in multivariate regression models |
|----------|-----------------------------------------------------------------------------------------|
| Variables | Preoperative model | Postoperative model |
|          | OR (95% CI) | $P$-value | OR (95% CI) | $P$-value |
| Advanced age | 3.90 (1.98–8.06) | <0.0001 | 3.61 (1.73–7.90) | 0.0005 |
| Male sex | 2.17 (1.06–4.38) | 0.035 | 1.88 (0.86–4.10) | 0.11 |
| Multiple aneurysms | 3.54 (1.09–10.7) | 0.037 | 3.57 (0.91–14.1) | 0.067 |
| Anticoagulant therapy | 2.25 (0.27–15.4) | 0.42 | 1.74 (0.19–13.4) | 0.40 |
| Severe postoperative SDA | 13.7 (5.26–46.9) | <0.0001 |

CI: confidence interval, OR: odds ratio, SDA: subdural air. Bold face type indicates statistical significance.
was 7.0 ± 4.1 mm for patients without contralateral CSDH. Receiver operating characteristic curve analysis of postoperative SDA was performed to determine the cut-off value for predicting the occurrence of CSDH. Analysis revealed that a postoperative SDA threshold of 12.0 mm separated patients with versus without CSDH for both ipsilateral and contralateral sides (ipsilateral side: sensitivity, 72%; specificity, 91% [area under curve = 0.82]; contralateral side: sensitivity, 82%; specificity, 88% [area under curve = 0.91]).

Bilateral CSDH developed in five patients with bilateral severe SDA (5/79, 6.3%); the remaining two patients who developed bilateral CSDH did not have bilateral severe SDA (2/265, 0.8%). This result indicates that bilateral CSDH was associated with bilateral SDA ($P = 0.002$). Among 13 patients with symptomatic CSDH requiring burr-hole surgery, the

### Table 3  Risk factors for postoperative subdural air

| Characteristic                  | Total $n = 344$ | Severe SDA $n = 164$ | Univariate analysis | Multivariate analysis |
|--------------------------------|----------------|---------------------|---------------------|-----------------------|
|                                |                |                     | $P$-value           | OR (95% CI)           | $P$-value |
| Age                            |                |                     |                     |                       |          |
| ≥65                            | 147            | 79 (54)             | 0.051               | 1.79 (1.15–2.81)      | 0.0010   |
| <65                            | 197            | 85 (43)             |                     |                       |          |
| Male                           | 94             | 54 (58)             | 0.026               | 1.98 (1.20–3.25)      | 0.0073   |
| Female                         | 250            | 110 (44)            |                     |                       |          |
| History of SAH                 | 19             | 4 (21)              | 0.018               | 0.22 (0.059–0.64)     | 0.0043   |
| Antiplatelet therapy           | 31             | 14 (45)             | 0.85                |                       |          |
| Anticoagulant therapy          | 5              | 4 (80)              | 0.20                |                       |          |
| Location                       |                |                     | 0.60                |                       |          |
| ICA                            | 102            | 50 (49)             |                     |                       |          |
| MCA                            | 185            | 89 (57)             |                     |                       |          |
| ACA                            | 40             | 16 (40)             |                     |                       |          |
| Multiple aneurysms             | 17             | 9 (53)              | 0.80                |                       |          |
| Surgeon                        |                |                     | 0.96                |                       |          |
| Chief doctor                   | 162            | 77 (48)             |                     |                       |          |
| Others                         | 182            | 87 (48)             |                     |                       |          |
| Operation time (≥188 min)      | 156            | 75 (48)             | 0.83                |                       |          |

ACA: anterior cerebral artery, ICA: internal cerebral artery, MCA: middle cerebral artery, SAH: subarachnoid hemorrhage. Bold face type indicates statistical significance. Continuous variables are shown as mean ± standard deviation, and categorical variables are shown as $n$ or $n$ (%).

### Table 4  Relationship between distribution of CSDH and postoperative subdural air collection in 164 patients with severe postoperative subdural air

| Characteristic                  | Total | Ipsilateral CSDH | P-value | Contralateral CSDH | P-value |
|--------------------------------|-------|------------------|---------|--------------------|---------|
| Patients                       | 164   | 32               |         | 17                 |         |
| Ipsilateral SDA                |       |                  |         |                    |         |
| Severe                         | 125   | 29 (23)          | 0.033   | 12 (10)            | 0.56    |
| Mild                           | 39    | 3 (8)            |         | 5 (13)             |         |
| Contralateral SDA              |       |                  |         |                    |         |
| Severe                         | 118   | 25 (21)          | 0.39    | 16 (14)            | 0.032   |
| Mild                           | 46    | 7 (15)           |         | 1 (2)              |         |

CSDH: chronic subdural hematoma, SDA: subdural air. Bold face type indicates statistical significance. Categorical variables are shown as $n$ or $n$ (%).
CSDH was ipsilateral to craniotomy in 10, contralateral in two, and bilateral in one.

**Discussion**

In this study, we investigated the incidence of and risk factors for CSDH and postoperative SDA after aneurysmal clipping, with adjustment for demographic characteristics of patients, clinical characteristics of aneurysms, and operation data. We also assessed the relationship between CSDH and postoperative SDA. The results showed that advanced age, male sex, and surgical clipping of multiple aneurysms were independent preoperative predictors of CSDH development; advanced age and postoperative SDA after clipping surgery were independent postoperative predictors of CSDH development. Advanced age, male sex, and the absence of a history of subarachnoid hemorrhage were independent risk factors for postoperative SDA. Additionally, the distribution of SDA was significantly associated with that of CSDH. In contrast, the surgeon and operation time were not associated with the development of CSDH or postoperative SDA. These results indicate that the risk of CSDH is not associated with the surgical procedure but instead is related to preoperative brain characteristics, extensive arachnoid dissection, and postoperative SDA. This is the first report focusing on the role of postoperative SDA immediately after surgical clipping of unruptured aneurysms.

In a retrospective study of 6613 patients, the incidence of postoperative CSDH after brain tumor removal was 0.4% and that after surgical clipping was 2.4%.\(^2\) The CSDH is a postoperative complication known to occur more frequently after surgical clipping than other surgical procedures. The reported incidence of CSDH requiring surgical intervention after aneurysmal clipping ranges from 1.9% to 4.7%.\(^1,5,7\) One previous study reported an incidence of CSDH, including asymptomatic CSDH, of 19.2%.\(^6\) In the present study, the overall incidence of CSDH was 12.4% and the incidence of CSDH requiring surgical intervention was 4.5%; these incidence rates are comparable with those in previous studies.

**Risk factors for development of CSDH**

The risk factors for the development and recurrence of traumatic CSDH, such as advanced age, male sex, anticoagulant therapy, antiplatelet therapy, and postoperative SDA, are well known.\(^2,4,8\) However, the risk factors for CSDH after aneurysmal clipping have remained unclear. Since 2013, a few studies have investigated the risk factors for CSDH after aneurysmal clipping; reported predisposing risk factors include unruptured aneurysms, advanced age, male sex, antiplatelet therapy, anticoagulant therapy, and postoperative subdural fluid at the 1-week CT examination.\(^5,7,8\) In a 2016 retrospective study, CSDH was reported to be associated with aneurysm locations requiring extensive arachnoid dissection (such as the MCA and ACA).\(^5\) Arachnoid plasty has been reported to be useful for the prevention of CSDH.\(^9,10\) The present study also found that extensive arachnoid dissection was a likely risk factor for CSDH. The relationship between CSDH and extensive arachnoid dissection supports our understanding of the mechanism of CSDH development. CSF leakage through an arachnoid membrane torn during surgery is thought to initiate CSDH development and induce subdural bleeding as a result of stretching of the bridging vein.\(^11\) This mechanism of CSDH development resulting from extensive subarachnoid dissection helps to explain the etiology of CSDH that is ipsilateral to the craniotomy; however, it does not fully explain how CSDH develops on the contralateral side.

Advanced age and male sex were risk factors for CSDH in the present study. Advanced age has been shown to be associated with brain atrophy, brain surface elastance, and poor re-expansion capacity.\(^12\) The degree of age-related brain atrophy is reportedly greater in men than in women.\(^13,14\) These findings suggest that advanced age and male sex are associated with preoperative physical brain characteristics, and that either factor could cause brain atrophy, which is predominantly responsible for massive postoperative SDA.

**Relationship between CSDH and SDA**

In previous studies, the presence of SDA was a cause of recurrent traumatic CSDH.\(^3,15,16\) In one of these randomized studies of traumatic CSDH, the incidence of postoperative fluid reaccumulation was reduced by placing the tip of the drainage catheter in the frontal convexity and by removing subdural air during or after surgery.\(^3\) In traumatic CSDH, massive accumulation of air postoperatively is considered the major factor leading to pressure imbalance across the inner membrane, which induces prolonged widening of the subdural space and disturbs the adhesion between the inner and outer membranes.\(^3\) In another study, the incidence of CSDH was lower after clipping of ruptured aneurysms versus unruptured aneurysms, a difference explained by the effect of brain swelling following subarachnoid hemorrhage, which decreases the subdural space and prevents the accumulation of air or CSF.\(^5\) This result also suggests that SDA is related to the development of CSDH. In the present...
study, SDA was independently associated with the development of CSDH. Furthermore, the distribution of CSDH was significantly related to that of SDA, irrespective of the side of craniotomy. This finding indicates that the presence of SDA itself plays an important role in the development of CSDH; that is, the presence of SDA can compress the adjacent brain tissue and prevent re-expansion as well as reflect physical brain characteristics. This can describe how CSDH develops on the contralateral side.

**Risk factors for SDA**

In the present study, SDA accumulation was not associated with the surgeon or operation time. This finding indicates that the risk of SDA and subsequent CSDH is not associated with the characteristics of microsurgical procedures, such as application of intraoperative pressure on the brain surface with spatulas, because the duration of pressure application is thought to be longer when the operation time is longer. Moreover, this study indicated that advanced age, male sex, and the absence of a history of subarachnoid hemorrhage were independent risk factors for postoperative SDA. These results indicate that the development of postoperative SDA is strongly dependent upon preoperative physical brain characteristics and that it might be difficult to reduce the accumulation of SDA. Replacing the air in the subdural space with artificial CSF and patching the dura mater to ensure watertight closure is a basic technique that is generally performed; however, more careful execution of this step might reduce SDA accumulation and the risk of CSDH. Placing the tip of the drainage catheter in the frontal convexity and removing SDA may be useful to reduce the incidence of CSDH.

Although most patients with CSDH have good outcomes, careful attention to the potential development of CSDH is important in patients with advanced age, male sex, and multiple aneurysms at the time of clipping surgery and in patients with advanced age and severe SDA after clipping surgery.

**Limitations**

This study has several limitations. First, this was a single-center retrospective study. Although the results of several evaluations in our study were statistically significant, such observations should be validated in larger populations and across multiple centers in the future. Second, the volume of CSDH and SDA may provide more reliable results than their maximum diameter. However, we did not use volume data because an additional study would have been needed to perform volume calculations. Nevertheless, our results suggest that the maximal diameter of SDA accumulation on CT images could help to predict postoperative CSDH. Finally, only the pterional approach was evaluated in this study; we did not evaluate other approaches. Some aneurysms located in the ACA were excluded from this study because they were treated via the interhemispheric approach.

**Conclusions**

Advanced age, male sex, multiple aneurysms, and severe postoperative SDA are independent risk factors for CSDH after surgical clipping of unruptured aneurysms. The distribution of SDA after craniotomy closure significantly coincides with the distribution of postoperative CSDH. Further studies of the risk factors for and etiology of CSDH after neurosurgical procedures, especially studies focusing on SDA, are required to improve our understanding and to reduce the incidence of CSDH.

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**Conflicts of Interest Disclosure**

None.

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