A Less Invasive Strategy for Ruptured Cerebral Aneurysms with Intracerebral Hematomas: Endovascular Coil Embolization Followed by Stereotactic Aspiration of Hematomas Using Urokinase

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Objective: Aneurysm clipping and simultaneous hematoma evacuation through open craniotomy is traditionally recommended for ruptured cerebral aneurysms accompanied by intracerebral or intrasylvian hemorrhages. We report our experience of adapting a less invasive treatment strategy in poor-grade patients with intracerebral or intrasylvian hemorrhages associated with ruptured cerebral aneurysms, where the associated ruptured cerebral aneurysms were managed by endovascular coil embolization, followed by stereotactic aspiration of hematomas (SRH) using urokinase.

Materials and Methods: We retrospectively analyzed 112 patients with ruptured cerebral aneurysms. There were accompanying intracerebral or intrasylvian hemorrhages in 36 patients (32.1%). The most common site for these ruptured aneurysms was the middle cerebral artery (MCA) (n = 15; 41.6%). Endovascular coil embolization followed by SRH using urokinase was performed in 9 patients (25%).

Results: In these 9 patients, the most common site of aneurysms was the MCA (n = 3; 33.4%); the hematoma volume ranged from 19.24 to 61.68 mL. Four patients who were World Federation of Neurological Surgeons (WFNS) grade-IV on admission, achieved favorable outcomes (Glasgow Outcome Score [GOS] 4 or 5) at 6-months postoperatively. In the five patients who were WFNS grade-V on admission, one achieved a favorable outcome, whereas 4 achieved GOS scores of 2 or 3, 6-months postoperatively. There was no mortality.

Conclusion: If immediate hematoma evacuation is not mandated by clinical or radiological signs of brain herniation, a less invasive strategy, such as endovascular coil embolization followed by SRH using urokinase, may be a good alternative in poor-grade patients with intracerebral or intrasylvian hemorrhages associated with ruptured cerebral aneurysms.

Keywords: Endovascular coil embolization, Intracerebral hemorrhage, Intrasylvian hemorrhage, Ruptured cerebral aneurysm, Stereotactic aspiration of hematoma

INTRODUCTION

Although ruptured aneurysms usually present with
subarachnoid hemorrhages (SAH), they can present with intracerebral hemorrhages (ICH) or intrasylvian hemorrhages (ISH). This presentation is not rare and carries an unfavorable prognosis; in 1966, Locksley reported a 90% mortality rate within 3 days.28)

Conservative management15)16)40) or only hematoma evacuation52) has poor outcomes in ruptured aneurysms with ICH or ISH. Hence, an open craniotomy with aneurysm clipping and simultaneous hematoma evacuation is recommended in these cases, having demonstrated better outcomes than seen with the previous strategies.1)15)16)38)40)47)52) However, this technique entails the risks of retraction injuries and aggravation of vasospasm, edema, and ischemia, which could result in poor outcomes.

Alternative methods with better outcomes have been reported by Niemann et al.,35) who introduced endovascular treatment for ruptured aneurysms followed by hematoma evacuation, and Chung et al.,9) who introduced endovascular treatment for ruptured anterior communicating artery (A-com) aneurysms, followed by burr-hole trephination, catheterization, and hematoma drainage. In both studies, the patients did not show signs of deterioration, and did not need immediate surgical decompression. We believed that the technique used by Chung et al.9) to treat the ruptured A-com aneurysms could be applied to treat other ruptured aneurysms with ICH or ISH. Hence, we adapted this less-invasive strategy of endovascular treatment for ruptured aneurysms, followed by stereotactic aspiration of hematoma (SRH; stereotactic removal of hematoma) using urokinase, to all types of ruptured aneurysms. Here we report our experience of managing ruptured cerebral aneurysms with ICH in poor-grade patients through endovascular coil embolization followed by SRH using urokinase.

Materials and Methods

Patient characteristics

This study was approved in January 2017, by the Institutional Review Board (IRB) of our hospital, South Korea, with a waiver for informed consent. A retrospective analysis was performed in 112 patients with ruptured cerebral aneurysms, who were managed by surgical clipping or endovascular coil embolization, between January 2013 and December 2014 at our hospital. Subarachnoid hemorrhage with the ruptured aneurysms was noted on computed tomography (CT) scans or magnetic resonance imaging (MRI) scans of the brain. The aneurysmal rupture was confirmed by using conventional cerebral angiography, CT angiography (CTA), or magnetic resonance angiography (MRA). The aneurysmal rupture was accompanied by ICH or ISH in 36 patients (32.1%). Patient age ranged from 33 to 79 years (mean ± standard deviation = 55.92 ± 12.36 years), and there were 13 male and 23 female patients. The most common site of the aneurysms was the middle cerebral artery (MCA) (n = 15; 41.6%), followed by the anterior cerebral artery (ACA) (n = 13; 36.1%) (Table 1). The most common location of the hematoma was the frontal lobe (n = 17; 47.2%), followed by the temporal lobe (n = 12; 33.3%) and the sylvian fissure (n = 5; 13.9%) (Table 2).

Management in 36 patients with ruptured aneurysms with ICH or ISH

Endovascular coil embolization alone was performed in 15 patients (41.7%) and the surgical clipping alone in 1 patient (2.8%) (Table 3). In these cases,
Table 2. The locations of hematomas in 36 patients with ruptured aneurysms with intracerebral hemorrhages or intrasylvian hemorrhages

| Hematoma locations | No. of patients |
|--------------------|----------------|
| Frontal lobe       | 17 (47.2)      |
| Temporal lobe      | 12 (33.3)      |
| Sylvian fissure    | 5 (13.9)       |
| Basal ganglia      | 2 (5.6)        |

Values are presented as number (%).

Table 3. Management in 36 patients with ruptured aneurysms with intracerebral hemorrhages or intrasylvian hemorrhages

| Strategies                          | No. of patients |
|-------------------------------------|----------------|
| Endovascular coil embolization + Conservative care | 15 (41.7) |
| Surgical clipping + Conservative care  | 1 (2.8)       |
| Surgical clipping + Hematoma evacuation | 11 (30.5)    |
| Endovascular coil embolization + SRH* | 9 (25)        |

Values are presented as number (%).

*Stereotactic aspiration of hematoma using urokinase

Data analysis

The patients' medical records were reviewed by 2 neurosurgeons, and the imaging studies were evaluated by a neuro-radiologist and a neurosurgeon. These experts evaluated the clinical status of the patients, the location of the aneurysms, and the location and size of the hematomas.

RESULTS

Clinical outcomes

In 9 patients managed by endovascular coil embolization followed by SRH using urokinase, the most common site for the aneurysms was the MCA (n = 3; 33.4%), followed by the internal carotid-posterior communicating artery (IC-PCom) (n = 2; 22.2%) (Table 6). The most common location of the hematoma was the temporal lobe (n = 4, 44.5%), followed by the frontal lobe (n = 3; 33.3%) and the sylvian fissure (n = 1; 11.1%) (Table 7). The hematoma volume ranged from 19.24 to 61.68 mL (mean ± standard deviation = 35.2 ± 14.8 mL).

Table 4. World Federation of Neurological Surgeons (WFNS) grading system

| Glasgow Coma Score | Motor deficit* | Grade |
|--------------------|----------------|-------|
| 15                 | Absent         | 1     |
| 13-14              | Absent         | 2     |
| 13-14              | Present        | 3     |
| 7-12               | Present or Absent | 4   |
| 3-6                | Present or Absent | 5   |

*Where a motor deficit refers to a major focal deficit

the hematoma size was small (< 15 mL). Surgical clipping with simultaneous hematoma evacuation was performed in 11 patients (30.5%). Endovascular coil embolization followed by SRH using urokinase was performed in 9 patients (25%); these patients had no clinical or radiological evidence of brain herniation. Additional signs evaluated were no anisocoric pupil, no decorticate or decerebrate rigidity, and no signs of active bleeding in the brain on CTA or digital subtraction angiography (DSA). Each patient's clinical status was evaluated using World Federation of Neurological Surgeons (WFNS) grading system on admission and the Glasgow Outcome Scale (GOS) scores at 6-months (Table 4, 5).20)49)
Table 5. Glasgow Outcome Scale scores

| Score | Description |
|-------|-------------|
| 1     | Death       |
| 2     | Persistent Vegetative State  
Patient exhibits no obvious cortical function. |
| 3     | Severe Disability (Conscious but disabled)  
Patient depends upon others for daily support due to mental or physical disability or both |
| 4     | Moderate Disability (Disabled but independent)  
Patient is independent as far as daily life is concerned. The disabilities found include varying degrees of dysphasia, hemiparesis, or ataxia, as well as intellectual and memory deficits and personality changes |
| 5     | Good Recovery  
Resumption of normal activities even though there may be minor neurological or psychological deficits |

In the 9 patients managed by endovascular coil embolization followed by SRH using urokinase, 4 patients (44.4%) were WFNS grade-IV on admission, and 5 patients (55.6%) were WFNS grade-V on admission. The 4 patients who were WFNS grade-IV on admission achieved favorable outcomes (GOS score 4 or 5), 6-months postoperatively (Fig. 1). Among the 5 patients who were WFNS grade-V on admission, one patient achieved a favorable outcome, and 4 patients achieved GOS scores of 2 or 3 at 6-months postoperatively (Fig. 2). There was no mortality (Table 8).

Illustrative cases

Case 1

A 41-year-old female patient presented in our hospital with mental stupor and left-hemiparesis (motor grades I and II) of 5-hours duration. Her clinical status was compatible with WFNS grade-IV (GCS E2/V2/M4). She had a history of hyperlipidemia and gastric ulcer, which had been properly managed. Her brain CT scan revealed a diffuse subarachnoid hemorrhage and a large ICH and ISH in the right perisylvian area, with an estimated volume of 55 mL (Fig. 1A). Her brain CTA and DSA revealed a 5 mm ruptured right-MCA aneurysm (Fig. 1B). She underwent endovascular coil embolization using 6 coils (Fig. 1C: preoperative, Fig. 1D: postoperative), which was followed by SRH using urokinase (Fig. 1E: postoperative, Fig. 1F: postoperative 14 days). Four weeks later, the patient showed a drowsy mental state and an improvement in the left-hemiparesis (motor grade-II). She was transferred to a rehabilitation center. At 3-months postoperatively, the patient showed a confused mental state and an improvement in the left-hemiparesis (motor grades III or IV-). At 6-months postoperatively, the patient showed an alert mental state with mild memory impairment, and a further improvement in the left-hemiparesis (motor grade-IV+). This was compatible with a GOS of 5 (good recovery).

Table 6. The locations of aneurysms in 9 patients managed by endovascular coil embolization followed by stereotactic aspiration of hematoma using urokinase

| Aneurysm locations | No. of patients |
|--------------------|----------------|
| MCA                | 3 (33.4)       |
| ACA                | 1 (11.1)       |
| IC-Pcom            | 2 (22.2)       |
| ICBIF              | 1 (11.1)       |
| IC-Ophthalmic      | 1 (11.1)       |
| BA-SCA             | 1 (11.1)       |

Values are presented as number (%).  
MCA = middle cerebral artery; ACA = anterior cerebral artery; IC-Pcom = internal cerebral artery-posterior communicating artery; IC-BIF = internal carotid artery bifurcation; IC-Ophthalmic = internal carotid artery-Ophthalmic artery; BA-SCA = basilar artery-Superior cerebellar artery

Table 7. The locations of hematomas in 9 patients managed by endovascular coil embolization followed by stereotactic aspiration of hematoma using urokinase

| Hematoma locations | No. of patients |
|--------------------|----------------|
| Frontal lobe       | 3 (33.3)       |
| Temporal lobe      | 4 (44.5)       |
| Sylvian fissure    | 1 (11.1)       |
| Basal ganglia      | 1 (11.1)       |

Values are presented as number (%).
Case 2

A 39-year-old female patient presented to our hospital in a deep stupor mental status of two hours duration. Her clinical status was compatible with WFNS grade-V (GCS E1/V1/M4). According to her family, she did not have any significant past medical history. Her brain CT scan revealed a diffuse IVH, and a large ICH in the left prefrontal area with an estimated volume of 56 mL (Fig. 2A). Her brain CTA and DSA revealed a 12 mm ruptured right-IC-Ophthalmic aneurysm (Fig. 2B). She underwent endovascular coil embolization using 7 coils (Fig. 2C: preoperative, Fig. 2D: postoperative), which was followed by SRH and EVD (Fig. 2E: postoperative). Seven days later, a brain CT scan revealed a significant decrease in ICH and IVH (Fig. 2F: postoperative 7 days). She was transferred to a rehabilitation center. At 6-months postoperatively, the patient still showed a stupor mental state, which was compatible with a GOS of 2 (persistent vegetative state).

**DISCUSSION**

On the basis of autopsy and angiography studies, the prevalence of aneurysmal rupture is 0.4-6%. 44) The incidence of ICH or ISH with aneurysmal ruptures is known to be 12-34%, 13)38-40)50) the prevalence range is higher at autopsy (33-60%). 10)19)31)43) The ICH or ISH is most common with ruptured MCA aneurysms,38)40) accompanying 23.8% of the ruptured MCA aneurysms.38)42) Moreover, if the aneurysms are located between the cortices, involving the ACA or the MCA, their rupture can present with ICH. In our study, the most common site for the aneurysms was the MCA (41.6%), followed by the ACA (36.1%) (Table 1). A previous intracranial hemorrhage may be one of the predisposing factors for ICH, because the previous hemorrhages could have created adhesions and changing
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Fig. 2. A 39-year-old female patient with ruptured right IC-ophthalmic aneurysm. (A) Brain CT scan revealed a diffuse IVH, and a large ICH in the left prefrontal area with an estimated volume of 56 mL. (B) Brain CTA and DSA revealed a 12 mm ruptured right IC-ophthalmic aneurysm. (C-E) She underwent endovascular coil embolization using 7 coils (C: preoperative, D: postoperative), which was followed by SRH and EVD (E: postoperative). (F) Seven days later, a brain CT scan revealed a significant decrease in ICH and IVH. CT = computed tomography; IVH = intraventricular hemorrhage; ICH = intracerebral hemorrhage; CTA = CT angiography; DSA = digital subtraction angiography; SRH = stereotactic aspiration of hematomas; EVD = extra-ventricular drainage.

the subarachnoid structure. Even if there is no past history of a hemorrhage, if the dome of the aneurysm is adherent to the cerebral cortex, a ruptured aneurysm could result in ICH.

The ICH or ISH with aneurysmal rupture is a poor prognostic factor. It may worsen the rebleeding rate, vasospasm, cerebral edema, and hydrocephalus. The ruptured aneurysms associated with ICH or ISH are associated with higher Hunt-Hess (HH) grades on admission, and poor GOS at 6-months follow-up. Abbed et al. have reported favorable outcomes (based on GOS) in 37% patients with ruptured aneurysms with ICH versus 61% in patients without ICH, during 6 months of follow-up. Similarly, many authors have focused on the initial clinical status. In 2007, Prat et al. have reported that an ICH due to aneurysmal rupture with anisocoria shows poor clinical outcomes. In 2013, Bohnstedt et al. have reported on using the HH grade on admission as a primary prognostic factor, with poor outcomes in the pa-
Table 8. Clinical outcomes in 9 patients managed by endovascular coil embolization followed by stereotactic aspiration of hematoma using urokinase at 6-months postoperatively

| Admission WFNS grade | GOS 4-5 | GOS 2-3 | Death | Total |
|----------------------|---------|---------|-------|-------|
| I-III                | 0       | 0       | 0     | 0     |
| IV                   | 4 (100) | 0       | 0     | 4 (44.4) |
| V                    | 1 (20)  | 4 (80)  | 0     | 5 (55.6) |
| Total                | 5 (55.6)| 4 (44.4)| 0     | 9 (100)  |

Values are presented as number (%).
WFNS = World Federation of Neurological Surgeons; GOS = Glasgow Outcome Scale

Table 8. Clinical outcomes in 9 patients managed by endovascular coil embolization followed by stereotactic aspiration of hematoma using urokinase at 6-months postoperatively

| Admission WFNS grade | GOS 4-5 | GOS 2-3 | Death | Total |
|----------------------|---------|---------|-------|-------|
| I-III                | 0       | 0       | 0     | 0     |
| IV                   | 4 (100) | 0       | 0     | 4 (44.4) |
| V                    | 1 (20)  | 4 (80)  | 0     | 5 (55.6) |
| Total                | 5 (55.6)| 4 (44.4)| 0     | 9 (100)  |

Values are presented as number (%).
WFNS = World Federation of Neurological Surgeons; GOS = Glasgow Outcome Scale

There are many opinions regarding the prognostic factors. Brott et al. have focused on the extent of hemorrhage and have reported that the extent of hemorrhage is an important prognostic factor in the patients with aneurysmal ICH. Yoshimoto et al. have agreed with this opinion and have reported that the size of hemorrhage larger than 30 mm (maximum diameter) correlates with poor clinical outcomes in patients with ruptured MCA aneurysm with ICH. Another prognostic factor is the timing of surgery: in 2008, Guresir et al. have reported that the timing of surgery is the most important prognostic factor, and that an early surgical intervention within 6 to 12 hours may result in good clinical outcomes. They have reported that this is especially important in patients with poor-grades on admission, such as WFNS grade IV or V. In 1986, Pasqualin have reported a 44% mortality rate and 44% favorable outcomes in patients with HH grade-IV undergoing early hematoma evacuation; however, they have also reported a 79% mortality rate and only 4% favorable outcomes in patients with HH grade-IV undergoing delayed hematoma evacuation. In the group with HH grade-V, 15% favorable outcomes were noted in patients with early hematoma evacuation, whereas the favorable outcomes were only 2% with delayed hematoma evacuation.

There are several options for the management of ICH or ISH associated with a ruptured aneurysm: conservative management, open craniotomy and surgical clipping with simultaneous hematoma removal, endovascular coil embolization followed by open craniotomy and hematoma removal, and endovascular coil embolization followed by SRH using urokinase. With conservative management of the aneurysmal SAH with accompanying ICH or ISH, the reported mortality rate is 84.2-100%. With only acute hematoma evacuation, the results are similar, with the mortality rate of 75-100%. Hence, aneurysmal obliteration is considered an essential part of the management strategy. Open craniotomy and aneurysmal clipping with simultaneous hematoma evacuation has been traditionally recommended in the patient with ICH in case of a severe mass effect. Sometimes, this procedure is performed on the basis of a brain CTA alone, in the absence of a DSA, to save time to surgical intervention in patients with impending or acute herniation. This strategy has shown better outcomes compared with the conservative management or only hematoma evacuation. The mortality rates are reported as 18.6-85% and the favorable outcomes (modified Rankin 0-2) are reported as 13-48%. However, this surgical procedure can be very difficult to perform because of the increased intracranial pressure, abnormal autoregulation, aggravated edema, and adhesions in the
arachnoid space. Moreover, for aneurysmal clipping, arachnoid dissection and proximal control need to be performed, during which cortical contusion may occur due to retraction and dissection procedures; this could result in poor outcomes. Shimoda et al. have reported contusions and injuries with retractor use in 13 out of 27 (48%) patients with ruptured aneurysm with ICH. Additionally, the manipulation and temporary clipping of the vessel may result in vasospasm and aggravation of cerebral ischemia.

When the size of the hemorrhage is large enough to require evacuation, but if the clinical state does not mandate an immediate hematoma evacuation, we may choose less invasive options. In a spontaneous ICH, the volume of hemorrhage is a strong prognostic factor, regardless of the hemorrhage location, patient's age, or the neurological status. An ICH may increase the intracranial pressure (ICP), and decrease the cerebral perfusion. Moreover, the blood breakdown products may cause edema and neurotoxicity. Thus, the volume reduction of ICH (including hematoma evacuation) can reduce the ICP, maintain the cerebral perfusion, and prevent secondary injury from the blood breakdown products.

In 2003, Niemann et al. tried endovascular treatment of ruptured aneurysm followed by hematoma evacuation in patients who did not show rapid deterioration and did not need immediate surgery. They reported better outcomes: The mortality rate was 24%, and there were 44% favorable outcomes. In 2007, Jeong also tried the same management, and reported experiencing better outcomes, with no mortality and 57% favorable outcomes. The endovascular treatment of ruptured aneurysm followed by hematoma evacuation has some advantages: earlier protection from aneurysmal rebleeding; no need for dissection and retraction; possibly a simpler, safer, and quicker surgical procedure; and a shorter time for aneurysmal obliteration, which is especially good in the elderly or poor-grade patients.

In the management of a spontaneous ICH, many surgeons agree on an urgent surgical decompression being mandatory in patients (especially in younger patients) with impending or acute brain herniation. However, it is also true that many randomized, controlled trials have shown that a craniotomy for hematoma evacuation is not superior to conservative management in terms of the outcomes. Some authors have reported that a less-invasive surgery (including SRH using urokinase) can reduce the surgical morbidity and improve the clinical outcomes, compared with only conservative management. Since Doi et al. introduced SRH using direct instillation of urokinase, many authors have reported favorable results with this method. In 2008, Kim et al. have reported using a less-invasive strategy in patients with ruptured A-com aneurysms. Endovascular treatment of a ruptured A-com aneurysm followed by SRH (burr hole trephination, catheterization, and hematoma drainage) were tried, but the outcomes were not-favorable. In 2009, Chung et al. reported trying the same strategy in patients with ruptured A-com aneurysms. In this series, they reported better outcomes: there was no mortality, and the favorable outcomes were 66.7%. They have suggested that this strategy is a good alternative, but only for A-com aneurysms with ICH, and not for other aneurysms. They believe that the MCA aneurysms with ICH or ISH can have a massive mass effect and induce brain herniation easily, in which case a craniotomy is the better choice.

In our series, ICH or ISH associated with ruptured aneurysms were noted in 36 patients (32.1%), which is consistent with the previously reported studies. We adapted the less-invasive strategy (endovascular treatment of ruptured aneurysm followed by SRH using urokinase) to not only A-com aneurysms with ICH, and not for other aneurysms. They believe that the MCA aneurysms with ICH or ISH can have a massive mass effect and induce brain herniation easily, in which case a craniotomy is the better choice.
managed by endovascular coil embolization followed by SRH using urokinase, the most common sites for the aneurysms were the MCA (33.4%) and the IC-PCom (22.2%), with the hematoma volume of at least 19 mL. This is consistent with the previously reported studies, in which the surgical criterion of ICH is 10-15 mL.3)(28)(33)(46)

This kind of less-invasive strategy (endovascular treatment of ruptured aneurysm followed by SRH using urokinase) would be best done in a hybrid operating room, which is a surgical theatre that is equipped with advanced medical imaging devices such as cerebral angiographic machine. Recently a hybrid operating room began to be used gradually. Our hospital doesn't have a hybrid room either, but someday the hybrid room will be widely used, and then this less-invasive strategy might be widely used more easily. Although our study has the limitations of being a retrospective analysis, with a small patient population and the absence of a control group, the outcomes are comparable with previously reported studies: there was no mortality, and the favorable outcomes were 55.3%.

CONCLUSION

Craniotomy and surgical clipping with simultaneous hematoma evacuation may be the best recommendation for patients with ruptured aneurysmal SAH with ICH or ISH, who show rapid clinical deterioration due to a mass effect. Sometimes, it is not easy to perform the surgery due to edema, worsening of ischemia, or a high risk of rebleeding.

If the patient does not show the clinical or radiological signs of brain herniation that mandate emergency hematoma evacuation, we may choose less invasive surgical methods for hematoma evacuation. Endovascular coil embolization followed by hematoma evacuation has been tried and has shown good results. Endovascular coil embolization followed by SRH using urokinase has been tried in patients with ruptured A-com aneurysms with ICH, and has resulted in good outcomes. We have adapted endovascular coil embolization followed by SRH using urokinase to not only treat the ruptured A-com aneurysm, but also to manage ruptured aneurysms in other arteries. The results are comparable with those of previous reports. Endovascular coil embolization followed by SRH using urokinase is a less invasive technique and may be a good alternative in the poor-grade patients, with ICH associated with different ruptured cerebral aneurysms.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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