Original Article

Significance of endoscopic hematoma evacuation in elderly patients with spontaneous putaminal hemorrhage

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ABSTRACT

Background: The efficacy of endoscopic surgery for spontaneous intracerebral hemorrhages (ICH) has been previously reported, but differences in the effect between early and late elderlies remain unclear.

Methods: Ninety-seven patients diagnosed with putaminal hemorrhage (age, ≥ 65 years; hematoma volume, ≥ 30 mL) were included in this retrospective analysis and separated into three treatment groups: craniotomy surgery (CR), endoscopic surgery (EN), and non-surgical (NS) groups. The patients were additionally subdivided into two groups according to age: patients aged 65–74 years ("early elderlies") and patients aged ≥ 75 years ("late elderlies"). Their clinical data and outcomes at discharge were compared using statistical analyses.

Results: The CR and the EN groups were associated with lower mortality rates ($P < 0.001$), lower modified Rankin Scale (mRS; $P = 0.007$), and lower National Institutes of Health Stroke Scale (NIHSS; $P = 0.029$) compared to the NS group. Early elderlies in the CR and EN groups with ICH scores of 3 also had significantly better outcomes ($P = 0.001$). The proportion of patients with mRS ≤ 4 was highest in the early elderlies of the EN group ($P = 0.553$). Although significant differences in the change of NIHSS scores between the early and late elderlies was not observed, significantly improved NIHSS scores were observed in the EN group compared to the NS group, even in the late elderlies ($P = 0.037$).

Conclusion: The evacuation of deep-seated intracranial hematomas using the endoscope might improve functional outcomes and mortality, regardless of age.

Keywords: Aging society, Endoscope, Minimally invasive surgery, Putaminal hemorrhage, Spontaneous intracerebral hemorrhage

INTRODUCTION

The aging of society has progressed to become one of the most prominent challenges in Japan. For elderly patients, it is important to consider the most suitable treatment. Minimally invasive surgery (MIS) has attracted attention as a treatment option for various conditions due to its broad application in elderly patients. Spontaneous intracerebral hemorrhage (ICH) accounts for approximately 15% of all strokes and is associated with high rates of morbidity and mortality.[19] The optimal treatment for ICH remains debatable; treatment options include hematoma removal with conventional craniotomy and MIS-like stereotactic evacuation with endoscopic surgery.[8,13,20] As a promising type of MIS, the effect of endoscopic surgery in ICH

appears favorable in some studies.[7,15,24-26] Since it is less invasive, endoscopic surgery has been considered as the most convenient treatment for ICH,[27] and its use is currently being validated in the INVEST trial.[4] Results of recent studies support the use of endoscopic surgery,[7,11,15,26] but, to the best of our knowledge, to date, there are no reports focusing on elderly patients, especially comparing the difference between "early" and "late" elderly patients.

The aim of this study was to analyze our institutional cases of putaminal hemorrhage and evaluate the effectiveness of endoscopic surgery, with a focus on the differences between early and late elderlies.

MATERIALS AND METHODS

Patient characteristics

This study was approved by the Ethics Committee of Institutional Review Board (Ethics No-675, the requirement for informed consent was waived). We reviewed our institutional cases of putaminal hemorrhage that was diagnosed using computed tomography (CT) imaging and had been treated at our hospital between 2005 and 2016. Eligible patients were aged 65 years or older; we defined those under 75 years of age as "early elderlies," and the remainder as "late elderlies." Hematoma volume was calculated using CT imaging with the formula ABC/2,[14] and patients with ≥30 mL hematoma volume were enrolled in this study. Patients requiring vasopressor drugs, those on respiratory support, and those with irreversibly dilated pupils bilaterally upon arrival were excluded from the study. CT angiography was routinely performed in all cases, and non-spontaneous ICH cases (e.g. due to venous thrombosis, ischemic stroke, or vascular lesions including arteriovenous malformations, moyamoya disease, or aneurysms) were excluded from the study. Surgical indications were selected with reference to the Japanese Guideline for the Management of Stroke 2015;[10,18] thus, no surgery was performed on patients with only mild hemiparesis without disturbance of consciousness. Besides, when patients or their families refused any surgical intervention, only medical treatment was provided as described below. Endoscopic surgery was the first line surgical intervention, and conventional surgery with a frontotemporal craniotomy was performed in the following instances: for patients managed by a surgeon without a certified license by the Japanese Society of Neuroendoscopy; when a decision was made that craniotomy was advantageous in a specific patient; or when there was a predicted difficulty in achieving hemostasis using the endoscopic technique, for example, due to an irregularly shaped hematoma or the use of anti-coagulant drugs by the patient.

A total of 97 cases of putaminal hemorrhage were enrolled in this study. These cases were differentiated into three groups: a conventional surgery group with craniotomy surgery group (CR group, *n* = 34), an endoscopic surgery (EN group, *n* = 38), and a non-surgical group (NS group, *n* = 25).

Endoscopic surgery

The endoscopic surgery was performed by two expert neuroendoscopists who were certified by the Japanese Society of Neuroendoscopy. Three surgical instruments were used for this endoscopic procedure [Figures 1a and b]: a rigid endoscope (Karl Storz, Tuttlingen, Germany) with a diameter of 2.7 mm, a suction tube designed for endoscopic surgery which can be connected to a monopolar coagulation system for hemostasis, and a clear guide sheath (Machida Endoscope Co., Ltd., Tokyo, Japan) that is an acrylic tube with an inner diameter of 6 mm and outer diameter of 8 mm.

The patient's head was positioned in a neutral position under general anesthesia. A single burr hole was usually made at Kocher's point for entry of the endoscope. The clear guide sheath was carefully inserted into the hematoma cavity. Both the endoscope and the suction tube were inserted into the sheath, and the hematoma clot was evacuated under endoscopic guidance by manipulating them [Figure 1c]. Hemostasis was achieved by coagulating the bleeding vessels using an energized suction tube. Continuous irrigation by artificial cerebrospinal fluid can be useful as a hemostasis technique. With our surgical strategy, intracranial pressure reduction is prioritized; thus, partial evacuation of the hematoma was accepted in patients with hard hematoma clots. However, over 90% of hematoma volume was evacuated on average (data not shown).[9] Finally, a drainage tube was left in the surgical cavity to help monitor for rebleeding.

Hematoma removal with conventional craniotomy

In our craniotomy surgery approach, the putaminal hemorrhage was removed through a conventional frontotemporal approach. The transsylvian fissure approach or trans-middle temporal gyrus approach was used to remove the hematoma. In all cases, the microscope was used during intracerebral procedures.

Conservative treatments

All cases enrolled in this study received the best medical treatment, which included blood pressure control under 140 mmHg with nicardipine hydrochloride, and tranexamic acid was used as a hemostatic agent immediately following putaminal hemorrhage diagnosis using CT scan. In some cases, glycerol was used in the presence of widespread cerebral edema. Although airway management and respiratory support were used if required, all cases were subsequently independent of respiratory support except mortal cases. In addition, all cases received anti-thrombotic management using calf pumps, rehabilitation therapy, and
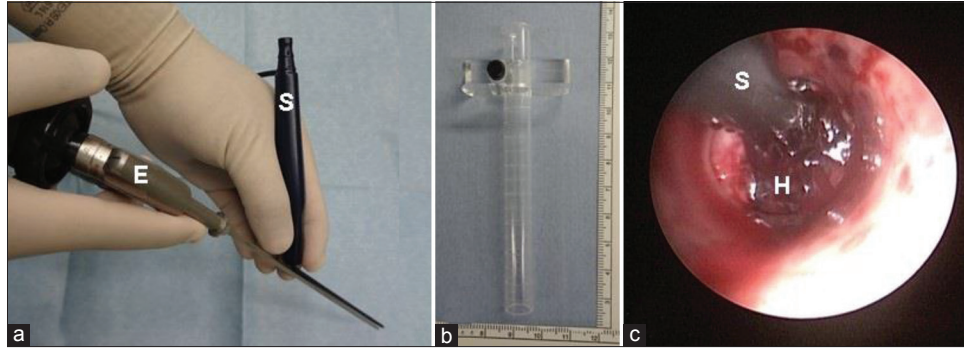
Figure 1: Surgical instruments and endoscopic view (a and b) The rigid endoscope (E) in the left hand and the suction tube (S) in the right hand handled in the clear guide sheath (B). (c) Endoscopic view showing a hematoma clot (H) gently evacuated by suction tubing (S) under endoscopic guidance.

nutritional management as early as possible, depending on their neurological deficit. If patients exhibited symptomatic delayed hydrocephalus, a ventriculoperitoneal (VP) shunt surgery was performed.

Statistical analysis

All statistical analyses in this study were performed using SPSS version 22 (SPSS IBM Corp., Armonk, NY, USA). Statistical comparisons were performed using one-way analysis of variance (ANOVA), Pearson's Chi-square test, Mann–Whitney U test, and the Kruskal–Wallis test, where appropriate. In this study, statistical significance was confirmed when the $P < 0.05$. Modified Rankin Scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) scores were used to compare outcomes in patients. The changes in NIHSS score between admission and discharge were calculated by subtracting the NIHSS score at discharge from that at admission. Each analysis was performed separately for each age group to evaluate the difference between the early and late elderly groups. In addition, we compared outcomes for each ICH score group.

RESULTS

Patient background

The baseline patient characteristics are shown in [Table 1]. The values of each parameter are described as number, mean ± standard deviation, or median ± interquartile range. The mean patient age was 72.2 ± 6.4 years in the CR group, 73.2 ± 6.4 years in the EN group, and 76.4 ± 7.9 years in the NS group. There was a non-significant tendency for the older patients to receive conservative management ($P = 0.060$). The mean hematoma volumes of the CR, EN, and NS groups were 68.1 ± 29.5 mL, 63.3 ± 26.1 mL, and 53.2 ± 17.5 mL, respectively. These were not significantly different, but hematoma volumes in the NS group were slightly lower than those in the surgical groups ($P = 0.090$). NIHSS and

Glasgow Coma Scale (GCS) scores on admission were also not significantly different between the treatment groups ($P = 0.523$ and $P = 0.309$, respectively), but the ICH score was higher in the NS group compared to the other groups ($P = 0.033$). The frequency of intraventricular hematoma (IVH) was slightly higher in the NS group but was not significantly different ($P = 0.189$).

Outcome

The results of the comparison of outcomes are shown in [Table 2]. Both the CR and EN groups showed better outcomes than the NS group, with statistical significance in the mRS and NIHSS scores at discharge ($P = 0.007$ and $P = 0.029$, respectively). The mortality rate, owing to cerebral hematoma, was significantly higher in the NS group compared to the CR and EN groups ($P < 0.001$). No significant difference in mortality from complications was observed ($P = 0.818$), and most of the complications were infections such as pneumonia. The EN group had the highest percentage of mRS T 3 cases (10.5%), although this trend did not reach statistical significance ($P = 0.151$). The lengths of hospitalization were evaluated, excluding mortal cases, and did not show a significant difference between groups ($P = 0.526$). Rebleeding within 1 week of surgery was determined to be postoperative rebleeding, and there was no difference in the frequency of either asymptomatic or symptomatic rebleeding between the CR and EN groups ($P = 0.223$ and 0.271, respectively). There was no significant difference in the frequency with which VP shunt was required ($P = 0.497$).

[Figure 2] shows the distribution of mRS scores at discharge for each treatment group, subdivided into age groups. As mentioned above, the CR and EN groups showed lower mRS scores than the NS group, and this trend remained when dividing patients into age groups. In particular, the EN group had the highest proportion of patients with mRS score c4 in the early elderlies, although it did not reach statistical significance ($P = 0.553$).

Table 1: Patient characteristics.

Characteristics	CR group (*n*=34)	EN group (*n*=38)	NS group (*n*=25)	*P* value
Age (years)				
Mean	72.2±6.4	73.2±6.4	76.4±7.9	0.058*
Early elderlies (65–74)	24 (70.6)	24 (63.2)	10 (40.0)	0.060†
Late elderlies (≥75)	10 (29.4)	14 (36.8)	15 (60.0)	-
Sex (male: female)	23:11	22:16	17:8	0.611†
Median GCS score	10 (7–11.75)	10 (8–13)	9 (6–11)	0.309‡
Median NIHSS score	18 (13.25–2 4.5)	17 (13–23)	18 (16–24)	0.523‡
Hematoma volume				
Mean (mL)	68.1±29.5	63.3±26.1	53.2±17.5	0.090*
30–79	28 (82.4)	32 (84.2)	22 (88.0)	-
≥80	6 (17.6)	6 (15.8)	3 (12.0)	-
IVH	15 (44.1)	21 (55.3)	17 (68.0)	0.189*
ICH score				
Median	3 (2–3)	3 (2–3)	3 (3–4)	0.033‡
1	7 (20.6)	7 (18.4)	2 (8.0)	-
2	10 (29.4)	8 (21.1)	4 (16.0)	-
3	14 (41.2)	19 (50.0)	11 (44.0)	-
4	3 (8.8)	4 (10.5)	8 (32.0)	-

P values show the relationship between treatment groups and clinical characteristics. Bold indicates statistical significance (*P*<0.05). Data are shown as mean (±SD), median (interquartile range), or *n* (%), *ANOVA, †Chi-square test, and ‡Kruskal–Wallis test were used to calculate the *P* value. CR: Craniotomy surgery, EN: Endoscopic surgery, GCS: Glasgow coma scale, ICH: Intracerebral hemorrhage, IVH: Intraventricular hemorrhage, NIHSS: National institutes of health stroke scale, NS: Non-surgical
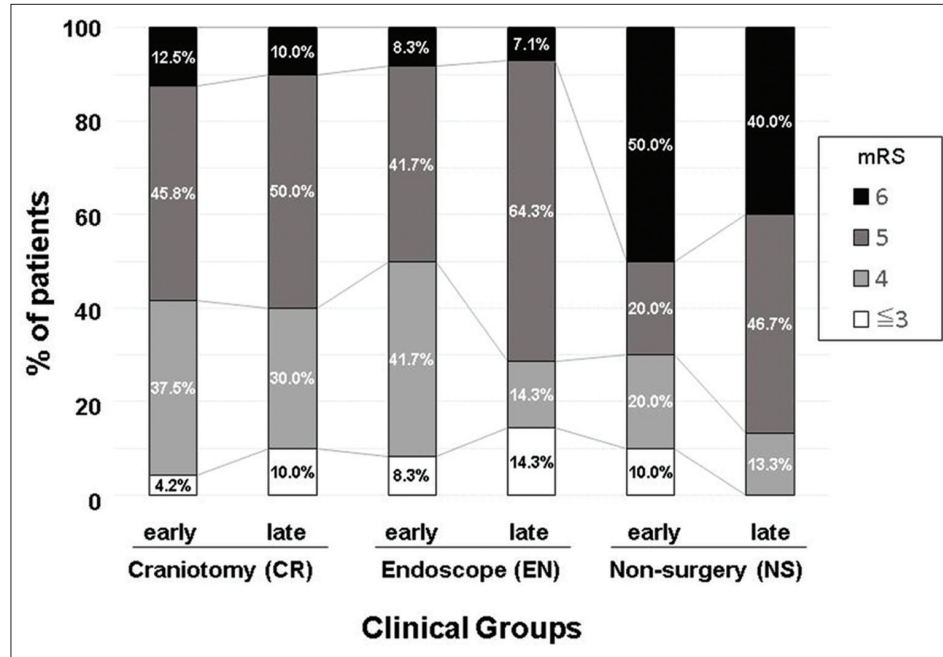
Table 2: Clinical outcomes.

Variable	CR group (*n*=34)	EN group (*n*=38)	NS group (*n*=25)	*P* value
mRS				
Median	5 (4–5)	5 (4–5)	5 (5–6)	0.007*
0–3	2 (5.9)	4 (10.5)	1 (4.0)	0.151†
4	12 (35.3)	13 (34.2)	4 (16.0)	-
5	16 (47.1)	18 (47.4)	9 (36.0)	-
6 (=Mortality rate)	4 (11.8)	3 (7.9)	11 (44.0)	<0.001†
Died of disease	2 (5.9)	0 (0)	10 (40)	<0.001†
Died of complications	2 (5.9)	3 (7.9)	1 (4.0)	0.818
Median NIHSS score	15 (11–23.5)	13 (10–23.5)	22 (15–40)	0.029*
Mean hospitalization period (days)	44.6±21.6	40.0±22.3	37.7±20.0	0.526‡
Postoperative rebleeding				
Asymptomatic	3 (9.7)	1 (2.7)	-	0.223†
Symptomatic	1 (3.2)	0 (0)	-	0.271†
VP shunt	1 (2.9)	2 (5.3)	0 (0)	0.497†

P values show the relationship between treatment groups and outcomes. Bold indicates statistical significance (*P*<0.05). Data are shown as mean (±SD), median (IQR), or *n* (%), *Kruskal–Wallis test, †Chi-square test, and ‡ANOVA were used to calculate the *P* value. CR: Craniotomy surgery, EN: Endoscopic surgery, IQR: Interquartile ratio, mRS: Modified Rankin Scale, NIHSS: National institutes of health stroke scale, NS: Non-surgical, VP: Ventriculoperitoneal

In addition, we performed statistical analysis according to each ICH score; the results are listed in [Table 3]. In the early elderlies group, no statistical differences were observed in the groups of patients with an ICH score of 1, 2, or 4; however, in patients with an ICH score of 3, both the CR and EN groups had significantly better outcomes than the NS group (*P* = 0.005). In the late elderlies group,

no statistical differences were identified in any of the ICH score groups.

Finally, the comparisons of the changes in NIHSS scores between admission and discharge are shown in [Figure 3]. Overall, the CR and EN groups showed significant improvements compared to the NS group (*P* = 0.017). In each treatment group, there was no significant difference in the amount of change in NIHSS

Figure 2: Clinical outcome by mRS. Distribution of mRS at discharge. Bar graphs are shown by treatment and age groups. The CR and EN groups had lower mRS scores than the NS group, even after dividing patients into each age group. CR: Craniotomy surgery group, EN: Endoscopic surgery group, mRS: Modified Rankin Scale, NS: Non-surgical group.
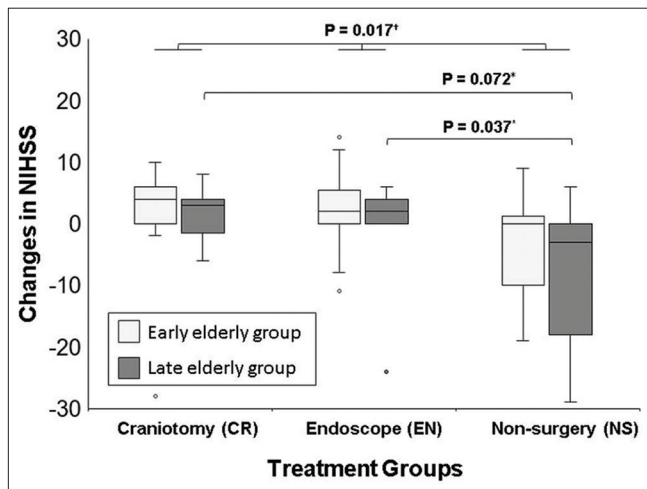
Figure 3: Comparison of improvement in the NIHSS score following treatment. Box and whisker plot showing changes in NIHSS from admission to discharge for each treatment and age group. The center lines denote the median value, while the boxes contain the 25th–75th percentiles of data. The whiskers mark the largest value within 1.5 times the IQR above the 75th percentile, or the smallest value within 1.5 times the IQR below the 25th percentile. Outliers are marked as dots. The changes in NIHSS were statistically different in each group (*P*=0.017). In the late elderly group, the improvement of NIHSS in the EN group was significantly greater than that in the non-surgical group (*P*=0.037). *Mann–Whitney U test, †Kruskal–Wallis test. CR: Craniotomy surgery group, Early: Early elderly group, EN: Endoscopic surgery group, Late: Late elderly group, NIHSS: National institutes of health stroke scale, IQR: Interquartile range.

Table 3: Comparison of outcomes according to ICH score in the early and late elderlies.

ICH score	Treatment group	Early elderlies mRS	Early elderlies P value	Late elderlies mRS	Late elderlies P value
	CR	4 (4–5)		3.5 (3.25–3.75)	
1	EN	4 (4–4.5)	0.571	-	-
	NS	4 (3.5–4.5)		-	
	CR	5 (4–5)		4 (4–4)	
2	EN	4 (4–4)	0.197	4 (4–4)	0.368
	NS	4 (4–4)		5 (4.5–5.5)	
	CR	5 (4–5)		5 (4.75–5)	
3	EN	5 (4.5–5)	0.005	5 (4–5)	0.527
	NS	6 (6–6)		5 (5–6)	
	CR	-		5 (5–5.5)	
4	EN	6 (6–6)	-	5 (5–5)	0.488
	NS	-		5 (5–6)	

Data are shown as median (interquartile ratio) mRS score. *P* value was calculated using the Kruskal–Wallis test. Bold indicates statistical significance (*P*<0.05). CR: Craniotomy surgery, EN: Endoscopic surgery, ICH: Intracerebral hemorrhage, mRS: Modified Rankin Scale, NS: Non-surgical

score between the early and late elderlies. Both the CR and EN groups showed larger changes than the NS group, and only the EN group showed a statistically significant difference in the late elderlies, relative to the NS group (*P* = 0.037).

DISCUSSION

Surgical indication for ICH

At present, a benefit for surgery with conventional craniotomy for ICH has not been demonstrated; for example, the STICH I and II trials showed almost identical outcomes in surgically and medically managed cases.[16,17] In some reports, it has been suggested that the trauma of the normal brain around a hematoma might contribute to the unfavorable outcomes of conventional open surgery.[3,22] Our results showed that the CR group improved their mRS scores and mortality and suggest that an ICH score of 3 in early elderlies may be a good indicator for both conventional craniotomy surgery and endoscopic surgery, although the improvement of outcomes in the CR group was generally less than that observed in the EN group. Meanwhile, the EN group showed better outcomes not only with regard to mortality and mRS scores but also in the change in NIHSS scores in the late elderlies; this result suggests the possibility that endoscopic surgery might contribute to functional improvements in this group of patients. MIS should be less invasive and damaging to the normal brain with regard to physical brain trauma. Recently, Sun *et al.* reported that endoscopic surgery with a keyhole craniotomy was associated with a decrease in postoperative brain edema, an increase in hematoma clearance rate, and improved postoperative activities of daily life scores.[22]

Advantages of endoscopic surgery in MIS

The MISTIE III trial, a representative randomized control trial using MIS,[9] has reported that lower residual hematoma volumes are associated with the rates of independence following ICH; endoscopic surgery was reported to show excellent performance in terms of hematoma removal rates.[22] These data suggest that, if endoscopic surgery was selected as the MIS modality, MISTIE III could have exhibited more encouraging results.

In addition, endoscopic surgery looks more advantageous with regard to hemostasis. More postoperative rebleeding was identified in 32% of MIS group patients in MISTIE III study, although it was limited to asymptomatic cases, while MIS did not increase symptomatic patients. Similar to previous findings, our current study showed that endoscopic surgery did not increase the frequency of postoperative bleeding compared to conventional open surgery.[1,15] Accurate comparison was not possible in this study since patients with hemorrhagic tendency were excluded from EN group. However, our results illustrate the benefit of hemostasis, as postoperative hemorrhage occurred in only 2.7% of the patients in the EN group, and all of the cases were asymptomatic. One reason for this hemostatic advantage is that endoscopic surgery enables the surgeon to visualize bleeding points and coagulate them safely. This suggests that

the endoscopic surgical is superior to other MIS modalities in terms of hematoma removal rates and hemostatic ability, except in patients with a high risk for bleeding tendency such as those excluded from the present study.

There are other advantages to endoscopic treatment, one of which is its potential application in hemorrhages in other locations. In the present study, the rate of IVH was the highest in the EN group; nevertheless, outcomes were better in the EN group, and this may be collateral evidence that endoscopic treatment is effective for IVH as well. Previous reports have shown the efficacy of endoscopic surgery for thalamic hemorrhage, cerebellar hemorrhage, and IVH.[5,21,25] These results may imply that endoscopic surgery can be used for putaminal hemorrhages combined with thalamic or IVHs. This wide-ranging indication is an advantage of endoscopic surgery. Another benefit of endoscopic surgery is the shorter operative time, which has been previously reported.[25] Endoscopic surgery is essentially a burr hole operation, which reduces the time to remove the hematoma, thereby contributing to a better neurological outcome. Although endoscopic surgery requires time to set up the endoscope and monitor, we address this issue by ensuring that two surgeons always participate in the operation. Furthermore, endoscopic surgery has been reported to reduce the duration of hospitalization.[23] This is presumably due to the lower invasiveness of endoscopic surgery, which is considered one of the major benefits of MIS. Shortening hospitalization periods in emergency medical centres can be cost-effective, but most importantly, they will allow patients to move quickly to an environment where rehabilitation can be received more intensively. Early transition to active rehabilitation is an important aspect that may improve the outcomes of patients with ICH.[2] Although our results did not show a reduction in the hospitalization period of these patients, patients who underwent endoscopic surgery seemed to recover more quickly and were more actively participating in rehabilitation in general, compared to those who underwent conventional open surgery. Since enhancement of social management and collaboration between other neighboring hospitals are also important for the early transfer to rehabilitation facilities, reinforcing them is essential and they should be implemented in the future.

Application of endoscopic surgery for late elderlies

Age is an important factor in the prognosis of ICH patients.[12,28] In Japan and across the world, aging societies are constantly experiencing changes in the epidemiology of stroke. Recently, an observational study from Japan (Hisayama study) showed that the incidence of ICH has been decreasing.[6] This result was associated with a decrease in smoking and alcohol consumption, perhaps in response to increasing health concerns and good management of

hypertension. According to this study, the putamen was once the most frequent location in ICH, but the incidence of putaminal hemorrhage is now decreasing, whereas the incidence thalamic hemorrhage is relatively increasing. The number of patients in their 60s is declining, and the percentage of seniors over 80 years of age is increasing; this indicates that the peak age of ICH incidence is being shifted from the early to the late elderlies. In Japan, elderly individuals are continually working and live actively, thereby postponing retirement age. In short, the healthy late elderlies will become the predominant group of ICH patients. Therefore, palliative therapies, which had been used in elderlies, may require reconsideration. Our current study suggests that endoscopic surgery has a broad application in the increasing number of elderlies, which in part may be due to the lower invasiveness of endoscopic surgery. Appropriate treatment for late elderlies warrants further investigations, and we believe that endoscopic surgery is one of the most appropriate treatments for ICH in all age groups.

Limitations

One critical limitation of this study is that this study incurred a selective bias as this is a retrospective study, and the final decision on the surgical method was made by the neurosurgeon in charge of each patient. However, we suspect that the greatest cause of the selective bias is that family members of the more severe patients were more likely to refuse surgical intervention. The NS group showed higher median age, hematoma volume, frequency of IVH, and ICH score, but lower GCS score. In addition, the case numbers were relatively small. In total, 97 cases were enrolled in this study, yet more data are required to subdivide and analyze them accurately. Finally, long-term follow-up was not available in this study; thus, the improvement in the outcomes of patients following surgery may have been overlooked. Therefore, prospective studies are warranted to accumulate larger clinical datasets over a longer period of time, including follow-up.

CONCLUSION

We performed a retrospective analysis of 97 cases of putaminal hemorrhage. From this analysis, both conventional surgery with craniotomy and endoscopic surgery might contribute for better mortality rates as well as mRS and NIHSS scores, especially when patients are early elderlies with an ICH score of 3. Moreover, the late elderlies did not have different outcomes from early elderlies; therefore, late elderlies could deserve to undergo surgical intervention as well as early elderlies, and endoscopic surgery might be the best option for this group. Further research is warranted to accurately assess the effect of endoscopic surgery in this group.

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