Abstract

Background

Aneurysmal subarachnoid hemorrhage (aSAH) in the elderly often has a poor prognosis even after surgical treatment in the acute phase. Additionally, subarachnoid clots are the strongest predictors of cerebral vasospasm and tend to be thicker and heavier due to cerebral atrophy. We aimed to compare the conventional surgical treatment in such patients and identify the independent predictors of a favorable outcome after aggressive surgical clot removal.

Methods

We included 40 patients with aSAH aged 70 or more years. Each patient underwent aneurismal clipping. We used the modified Rankin Scale to assess the primary outcome of neurological status at discharge. We performed univariate analysis using the following factors: sex, age, neurologic and general medical condition, radiographic data, aneurysm location, treatment approach, and timing of the aneurysm surgery. We divided the patients into the irrigation group and the non-irrigation group. We focused mainly on subarachnoid clots and analyzed them semi-quantitatively using computed tomography (CT).

Results

Clot removal was significantly greater in the irrigation group (n = 21) than in the non-irrigation group (n = 19). The period of intrathecal drainage was significantly shorter in the irrigation group ($p=0.002$). The rate of occurrence of new low-density areas on CT scans was higher in the non-irrigation group. Outcomes were better in the irrigation group ($p=0.010$).

Conclusion

In elderly patients with aSAH in the acute phase, aggressive surgical clot removal after clipping showed favorable outcomes by facilitating early out-of-bed mobilization.

Introduction

Opportunities to treat aneurysmal subarachnoid hemorrhage (aSAH) in elderly patients are expected to increase in Japan, which largely comprises a super-aging society. However, surgeons often select conservative treatments rather than acute surgical intervention due to the advanced age of the patients, which is a significantly poor prognostic factor.[1] Additionally, perioperative management is known to have a greater impact on outcomes in elderly patients.[2] However, this decision is subjective and differs among treatment facilities. Considering this, there is room for further improvement in the prognosis of such patients.

In the elderly patients at our institute, we apply clipping as soon as possible regardless of the disease severity and simultaneously perform aggressive intraoperative clot removal, except in cases in which the intracranial pressure (ICP) is extremely high and treatment is not desired. The necessity of intraoperative clot removal was not mentioned in the 2015 Japanese stroke guidelines[3]; however, we have introduced this method in February 2017 as cisternal clot removal could prevent prolonged intrathecal drainage management and cerebral vasospasm, which causes prolonged bed rest. In this study, we examined patient outcomes before and after introducing an aggressive intraoperative irrigation procedure for clot removal in our hospital and described its effects on the recovery of elderly patients with aSAH.

Materials and Methods

Study design and patient population

Shimane University's institutional ethics committees approved this retrospective study. Informed consent was obtained in the opt-out format on the website. Those who declined consent were excluded. We included patients 70 or more years of age who were diagnosed with aSAH and underwent clipping between April 2014 and March 2019. We have a policy of performing clipping for aneurysms in anterior circulation for high curability, and in posterior circulation, if possible. We excluded patients with fatal ICPs and those with insufficient medical records.

Patient characteristics

We used hospital charts to record patient sex, age, neurological and general medical condition, radiographic data, aneurysm location, treatment approach, outcome, and timing of the aneurysm surgery. Two neurosurgeons who were blinded to the patients' clinical data analyzed the radiographs. We classified the timings of intervention as follows: (1) ultra-early: treatment within 24 hours; (B) early: treatment between 24-72 hours; and (C) mid-late: treatment more than 72 hours after diagnosis of SAH. Primary brain damage (PBD) was defined as the presence of intracranial hemorrhage or severely high ICP.

Treatment groups

In this study, we divided the patients into two groups based on the surgical treatment method: (1) the irrigation group, in which we performed aggressive irrigation for clot removal after clipping, and (2) the non-irrigation group, in which we performed conventional clipping only.

We defined aggressive irrigation as the removal of clots in opened cisterns around the bilateral internal carotid arteries, basilar artery, sylvian fissure on the side of the surgical approach, and contralateral basal sylvian fissure (Figure 1). We performed intraoperative irrigation using a Suction Plus device (Johnson and Johnson, Tokyo, Japan) and a 0.9% saline solution with urokinase (120,000 units/1000 mL) as the irrigation fluid. The duration of this procedure was over 30 minutes after clipping. The details of this procedure are shown in the video. Figure 2 illustrates the standard clot removal method. In contrast to the irrigation group, the non-irrigation group performed removal of clot only in the process up to clipping and did not perform aggressive irrigation after clipping.

Clinical management

We treated the individuals in both groups according to the institutional standard of care. We controlled the patients' hemodynamics at normotension, normovolemia, and normohydration in the perioperative period. The patients received 30 mg of intravenous fasudil three times a day for 14 days from the first day after securing the ruptured aneurysm. We administered early rehabilitation treatment that started with range-of-motion exercises from the day after surgery and performed gait training as soon as the patients' conditions allowed. In cases with an intrathecal tube in place, we allowed drainage until the ICP normalized.

We performed CT immediately after the surgery and on the day after surgery. We routinely used magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) or CT and computed tomography angiography (CTA) to identify asymptomatic abnormalities during days 7-10 after surgery. Additionally, if we suspected symptomatic cerebral vasospasm (SCV) or perioperative cerebral ischemia (PCI), we conducted the appropriate radiological examinations. SCV was defined as new neurological symptoms appearing in days 4-14, no other causes (intracranial disease, systemic complications), and the cause of the symptoms proven by radiological examinations, including vascular evaluations. PCI was defined when we observed low-density lesions on CT or high-signal intensity on MRI diffusion-weighted images, with or without symptoms, within 14 days after onset of aSAH. We inserted ventriculoperitoneal shunts (VPSs) or lumboperitoneal shunts (LPSs) in patients with secondary hydrocephalus during hospitalization.

Patient outcomes

We measured the modified Rankin Scale (mRS) scores at discharge and defined 0-2 as a good score and 3-6 as a poor score.

Radiographic measurement of subarachnoid clot

In this study, we analyzed clots in 16 cisterns, including the (1) interpeduncular, (2,3) both ambient, (4) quadrigeminal, (5,6) both suprasellar, (7,8) both basal Sylvian, (9,10) both lateral Sylvian, (11,12) both distal Sylvian, (13) basal interhemispheric, (14) distal interhemispheric, (15) premedullary, and (16) prepontine cisterns. We scored each cistern using a modified version of the Hidjura classification[4] as the subarachnoid clot (SAC) index. A score of 0 indicated no clots, 1 indicated a barely visible clot, 2 represented a level intermediate between 1 and 3, and 3 indicated full-packed clots. For anatomically narrow cisterns, including the ambient, quadrigeminal, and distal sylvian cisterns (except for the distal interhemispheric cistern), a score of 0 indicated no clots, 1 represented a change intermediate between scores 0 and 2, and 2 indicated full-packed clots. We classified the SAC index scores of 0-20 as the mild group and 21-42 as the severe group. We recorded SAC indices before the surgery and on the day after surgery and defined them as preoperative-SAC (PreSAC) and postoperative-SAC (PostSAC), respectively.

Statistical methods

We performed all statistical analyses with EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan) and a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions that are frequently used in biostatistics.[5] To analyze the differences between the two groups, we used Fisher's exact test for categorical variables, and Welch t-tests for quantitative variables. We examined nonparametric data using the Wilcoxon-Mann-Whitney test. The statistical significance was defined as $p < 0.05$.

Results

Baseline characteristics

Cohort characteristics for the irrigation (n=21) and non-irrigation (n=19) groups are shown in Table 1. The sex, age, Hunt and Kosnik grade (H&K grade), Fisher group, size and location of aneurysm, timing of the surgery, presence of PBD, and PreSAC index did not differ significantly between the groups.

Clinical outcome

Clinical outcomes of the irrigation and non-irrigation groups are shown in Table 2. We performed clipping in all patients during the ultra-early and early treatment periods, except in 2 cases, one of whom had a delayed medical examination due to mild symptoms and the other was in an extremely poor condition with an unidentifiable aneurysm at the first visit. The surgical duration, number of placed intrathecal drainage tubes, and number of cases of secondary hydrocephalus requiring treatment did not differ significantly between the groups.

The PostSAC index in the irrigation group showed significantly milder scores than that of the non-irrigation group (p=0.017). Cases that shifted from the severe PostSAC group to the mild group were 14 in the irrigation group and 2 in the non-irrigation group (Figure 3).

We observed SCV in 2 patients in the irrigation group and 7 in the non-irrigation group (p=0.058) and found PCI in 3 irrigation patients and 9 non-irrigation patients (p=0.035). We observed 3 cases of meningitis (p=0.098) and 4 cases of respiratory or cardiovascular complications (p=0.042) in the non-irrigation group; all 7 cases had poor mRS scores. The period of intrathecal drainage was significantly shorter in the irrigation group than in the non-irrigation group (4.2±2.1 vs. 14.6±7.0, p=0.002).

The mRS scores at discharge are shown in Figure 4; scores of good and poor were 12 and 9 in the irrigation group, and 3 and 16 in the non-irrigation group, respectively (p=0.010). The 3 patients who died during the study period were: (1) one patient with severe intracranial hypertension that was not detected before surgery in the irrigation group, (2) one patient with occurring hemorrhagic cerebral infarctions after arterial infusion of fasudil, and (3) one patient with central diabetes insipidus due to extensive cerebral infarction in the non-irrigation group.

The effect of changes in SAC index before and after surgery in the irrigation group

We examined patients with mild (n=14) and severe (n=3) PreSAC index scores. The clinical data and outcomes of the patients with severe PreSAC index scores in the irrigation group are shown in Table 3. The age, sex, H&K grade, Fisher group, number of placed intrathecal drainage tubes, period of intrathecal drainage, and number of cases of secondary hydrocephalus that required treatment did not differ significantly between the groups.

In the severe PostSAC index group, we found SCV and PCI in 2 (p=0.008) and 2 cases (p=0.022), respectively. The mRS scores at discharge are shown in Figure 5; scores of good and poor were 9 and 5 in the mild PostSAC index group, and 0 and 3 in the severe PostSAC index group, respectively (p=0.047). Excluding PBD, scores of good and poor were 8 and 1 in the mild group and 0 and 2 in the severe group, respectively (p=0.011, data not shown).

Discussion

The adverse characteristics of elderly aSAH patients include the likely occurrence of rebleeding, acute hydrocephalus, and severe cerebral vasospasm. The ratio of poor-grade (defined as H&K grades IV and V) to all grades is as high as 33.8% to 38.2%.[2,6,7] In this study, 24 cases (60%) were poor H&K grade, a higher number than those reported previously. The prognostic factors for poor outcomes are age, H&K grade IV and V, Fisher group 3-4, the occurrence of SCV or PCI, and prolonged bed rest.[8,9,10,11] Our study makes a novel suggestion that the postoperative residual amount of subarachnoid clots is associated with the patient outcome at discharge.

Aggressive intraoperative irrigation for clot removal shortens the bed rest period

Prolonged bed rest in elderly aSAH patients is a poor prognostic factor, and previous studies recommend early mobilization even in the acute phase.[11,12] Focal symptoms due to SCV or PCI and perioperative management using intrathecal drainage are the main causes of prolonged bed rest in aSAH patients. First, paralysis occurs due to focal symptoms, and poor awakening causes prolonged ventilation management and aspiration pneumonia, which inhibit the early out-of-bed mobilization of the patient. Then, there is also a report of a method called “cisternal irrigation therapy” [13,14] that removes hematoma more strongly than management using intrathecal drainage, but both prevent early mobilization and cause an increased risk of meningitis. Therefore, the drainage period should be kept as short as possible.

Cerebral atrophy in elderly patients is an important factor in irrigation procedures for clot removal. The subarachnoid clot in such patients tends to be thicker and heavier due to cerebral atrophy,[15] resulting in prolonged withdrawal from drain management. However, a previous study reported that cerebral atrophy makes it easier to obtain a surgical field with good visibility.[16] In the current study, we safely performed irrigation for clot removal over a wide surgical area with good visibility. Good visibility probably contributed to the prevention of perforator infarction during surgery.

The results of this study suggest that intraoperative aggressive removal of clots can be safely performed in elderly patients and can shorten the bed rest period. However, insufficient clot removal is ineffective and carries an inherent risk of complications, such as brain contusion, cerebral aneurysm rebleeding, and injury to perforating arteries.[17] Thus, it is imperative to learn this surgical technique skillfully.

Aggressive clot removal in the acute phase improves the outcome of poor-grade patients

Previous reports state that severe elderly aSAH patients have a poor prognosis even after acute surgical treatment[18,19] and that aggressive medical treatment is not recommended in Japan.[3,20] However, sometimes the consciousness level of pure-SAH-type patients, i.e., those with no intracerebral hemorrhage, may improve with time even if they were initially diagnosed as poor-grade patients.[21,22] Interestingly, in our study, 4 out of 5 pure-SAH poor-grade patients who underwent aggressive clot removal in the acute phase had good outcomes (data not shown). Although there is no evidence about the proper timing of surgery for such cases, it is known that elderly patients have a high rebleeding rate of 70%, especially in severe cases.[23] Therefore, rapid surgical intervention is extremely important for obtaining good outcomes.

Ota *et al*. reported that surgically removing as many clots as possible in the acute phase can decrease the incidence of SCV.[12] While their study documented that this effect was inferior in outcome among patients aged 65 and over, it lacked a control group. Our results emphasized that performing aggressive clot removal contributes to improving outcomes in the elderly, not only due to prevention of SCV and PCI but also by shortening periods of bed rest by improving drain management.

It may be worth mentioning here that coil embolization, which was assessed in The International Subarachnoid Aneurysm Trial (ISAT) study, reported to have better outcomes than clipping.[24] During the same period of our study, eight cases of coil embolization were performed at our institution for patients 70 years of age or more. Three cases were poor-grade, five cases were poor-outcome, and five cases were located on the posterior circulation (data not shown). As the number of these procedures performed at this facility is small and the grade as well as localization of aneurysms are significantly different from those of the clipping group, we could not include them in this study. However, Ohkuma and Joshua agree that the reported outcome of clipping is superior to that of coil embolization among the elderly.[2,25] The outcome of clipping and aggressive irrigation of present study was superior to the reported outcomes of coil embolization,[26,27] and indicate that it may be more effective, especially in severe cases.

Conclusion

We concluded that applying rapid surgical clipping treatments in elderly patients with aSAH and performing aggressive surgical clot removal in the acute phase of the disease resulted in good patient outcomes. Additionally, we found that even in patients with poor-grade prognoses, our recommended treatment may lead to a favorable outcome; therefore, surgeons should not default to conservative treatments simply because the patient is elderly and should explore aggressive treatments as well.

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Disclosure of Interest

The authors have no conflicts of interest directly relevant to the content of this manuscript.

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Figure Legends

Figure 1.

A, B: Intraoperative photograph demonstrating the subarachnoid clot (A) and its clear removal using irrigation and suction (B). The operative fields were obtained via right side pterional approach and were placed at the same scope angle under the operating microscope.

#1: suprasellar cistern (chiasmatic cistern)

#2: left basal sylvian cistern

ON: optic nerve

Figure 2.

Preoperative and postoperative computed tomography (CT) of a woman in her 80s with a ruptured right-sided internal carotid artery posterior communicating artery aneurysm. Her Hunt & Kosnik grade was 4 and she underwent surgical treatment with a right-sided pterional approach. An external ventricular drain was placed during the first surgery and left in place for 3 days. She showed no symptomatic vasospasm or other major complications. She was subsequently discharged to go home.

A, B, C: Preoperative CT showing thick subarachnoid clots in almost all major cisterns. The preoperative SAC index was 38.

D, E, F: Postoperative CT showed good clot removal. The postoperative SAC index was 7.

Figure 3. Changes in the SAC index before and after surgery.

Asterisk indicates a significant difference ($P<0.05$).

Figure 4. Distribution of modified Rankin Scale (mRS) scores at discharge.

Asterisk indicates a significant difference ($P<0.05$).

Figure 5. Distribution of modified Rankin Scale (mRS) scores at discharge in the irrigation group.

Asterisk indicates a significant difference ($P<0.05$).

Figure 1

A B

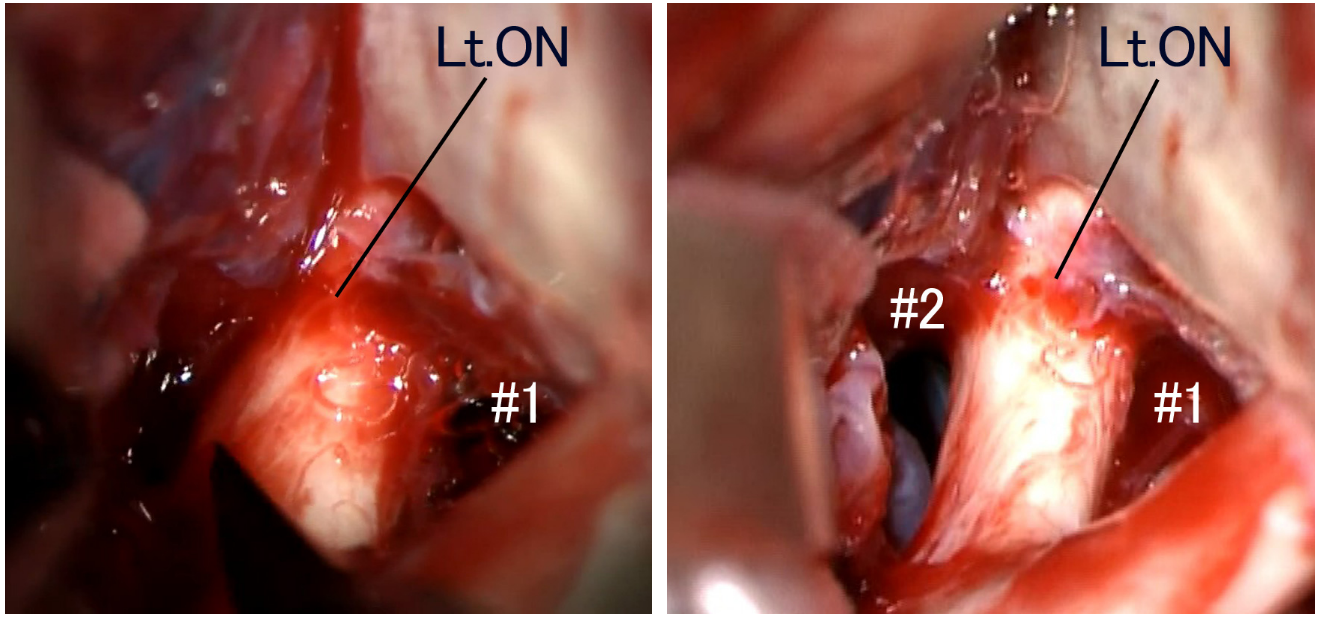


Figure 2

A B C
D E F

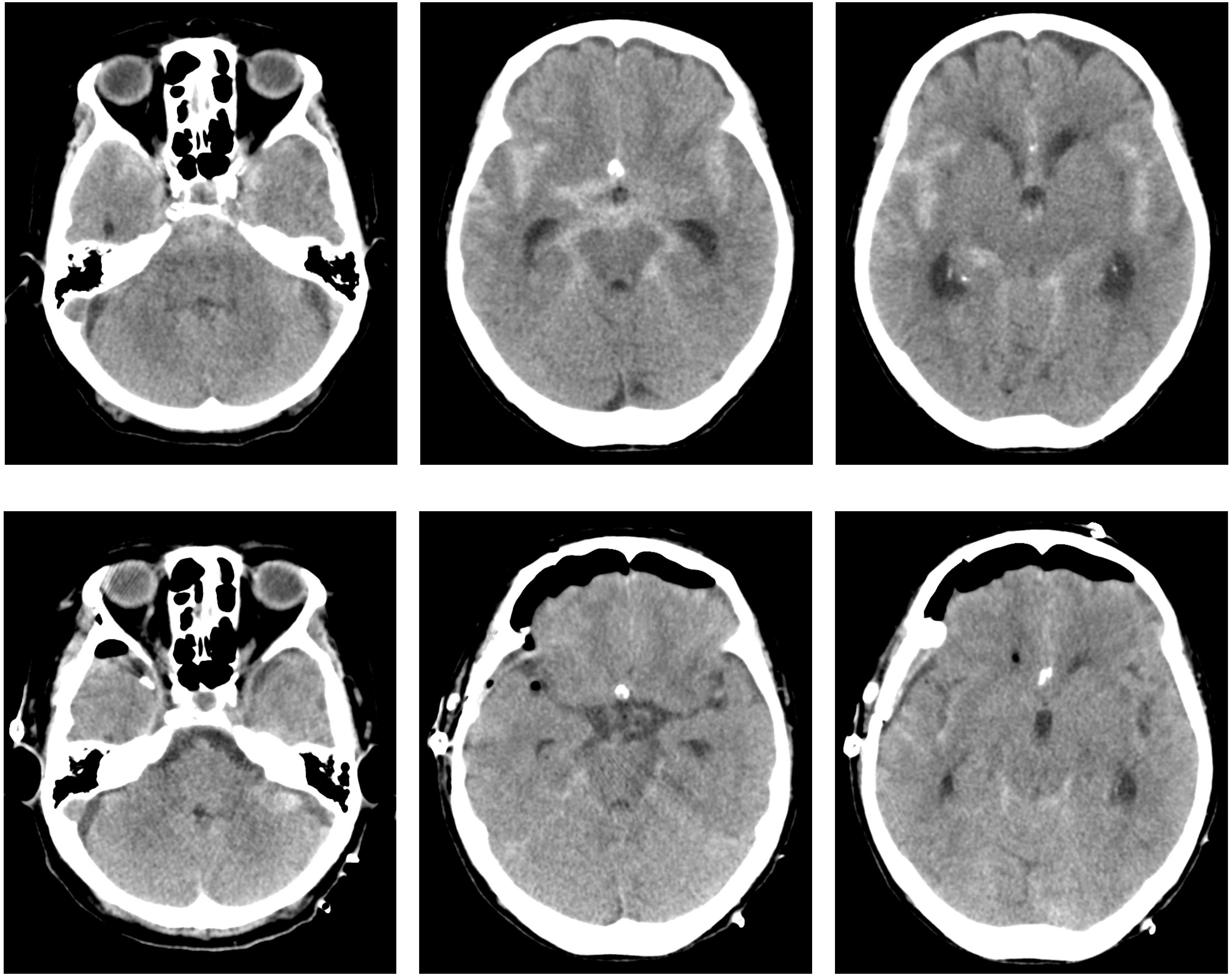
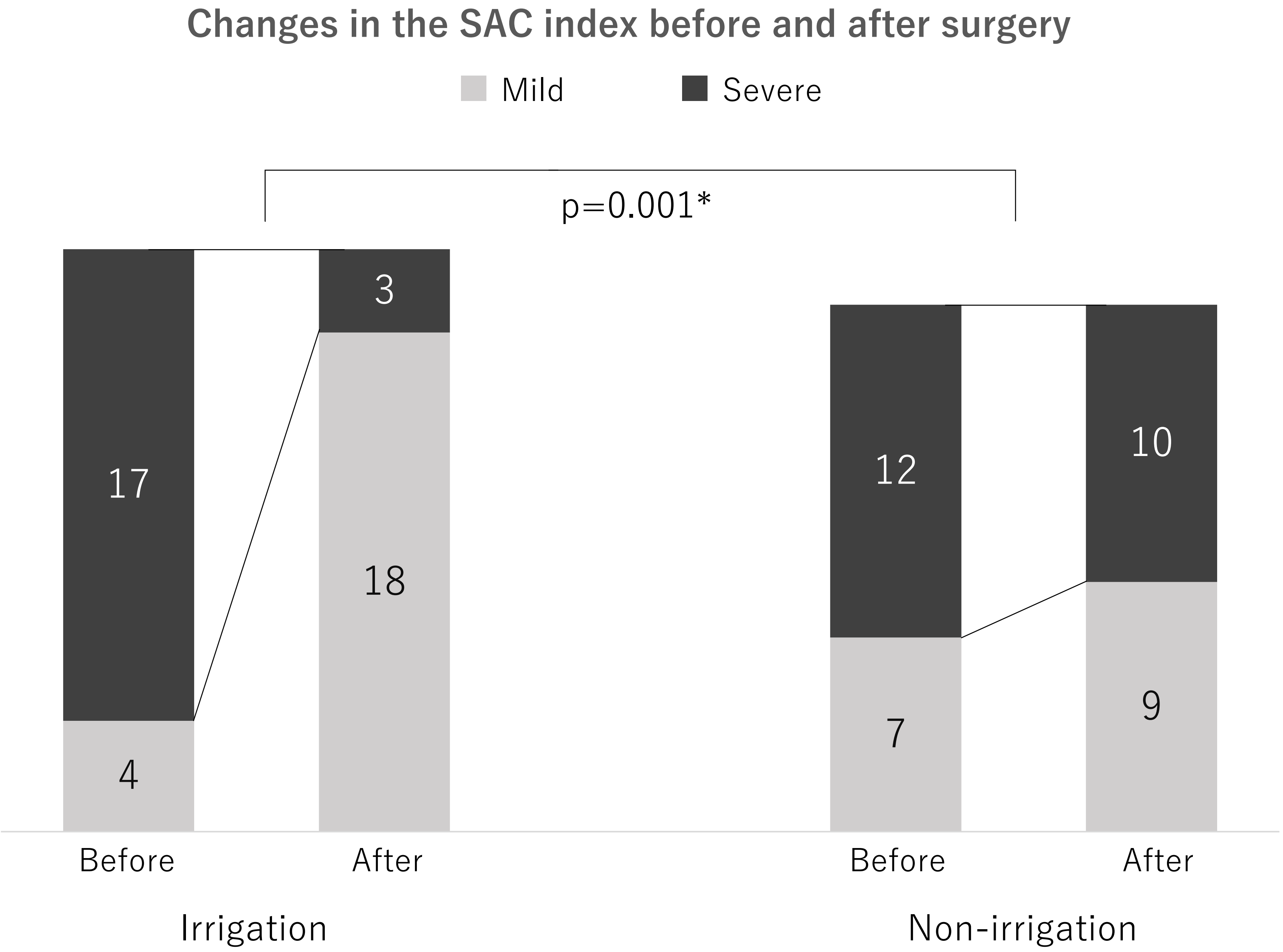


Figure 3



Changes in the SAC index before and after surgery
Mild
Severe
p=0.001*
17
4
3
18
12
7
10
9
Before
After
Before
After
Irrigation
Non-irrigation

Figure 4

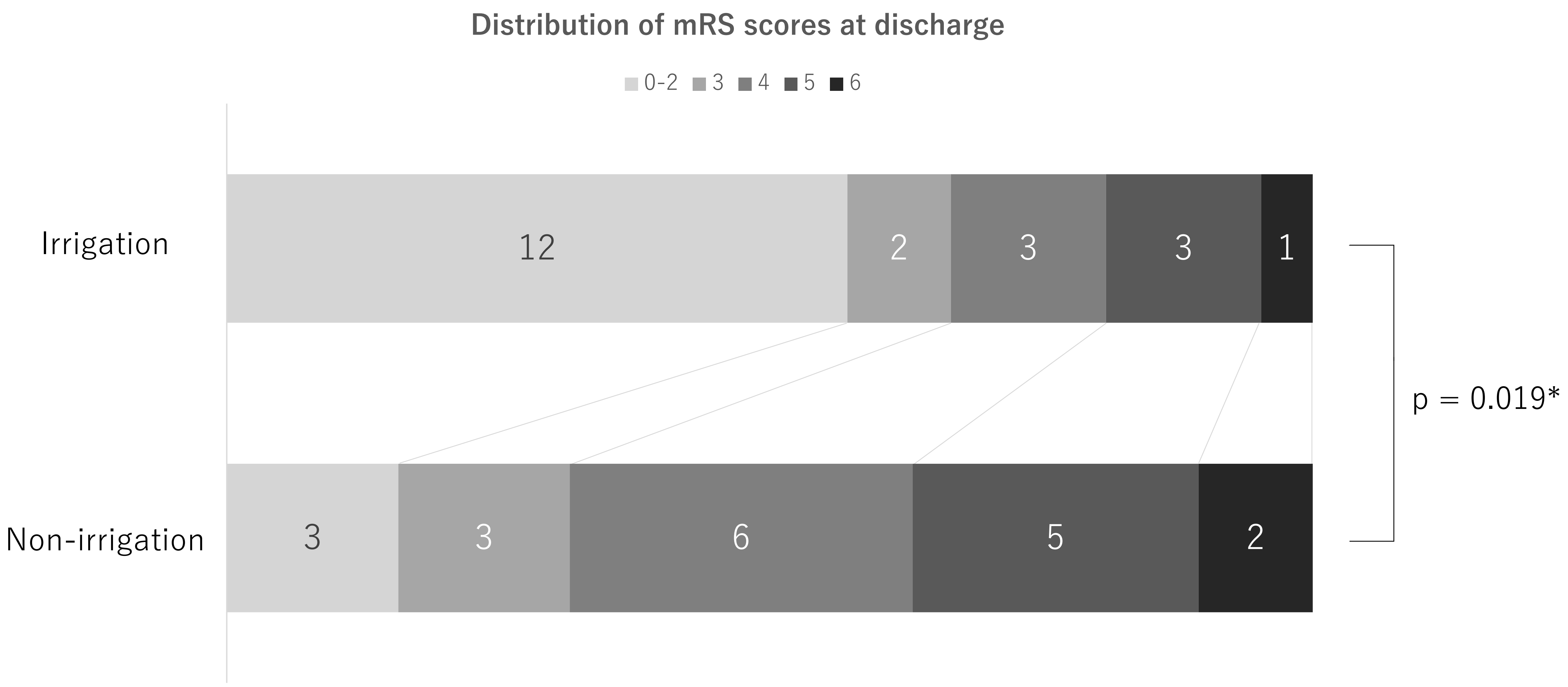
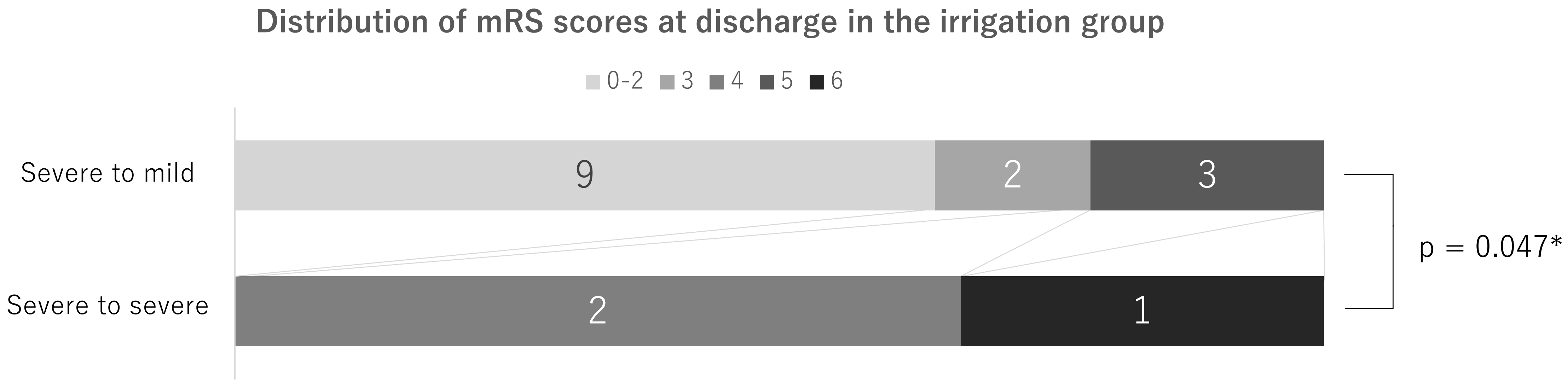

Distribution of mRS scores at discharge
0-2
3
4
5
6
Irrigation
12
2
3
3
1
Non-irrigation
3
3
6
5
2
p = 0.019*

Figure 5



	Severe → mild	Severe → Severe	p value
Distribution of mRS score, no.			
0-2	9	0	0.047*
3	2	0	
4	0	2	
5	3	0	
6	0	1	

Table 1 Background and clinical characteristics of the treatment groups

	Irrigation	Non-irrigation	p value
Men: women, no	3 : 18	4 : 15	0.689
Age(year)			
Range	70-91	70-91	0.193
Average	79.4 ± 6.7	82.3 ± 7.0	
Distribution of H&K grade, no.			
I	0	0	
II	2	4	
III	7	3	0.854
IV	5	4	
V	7	8	
Fisher group			
I	0	1	
II	1	4	0.723
III	13	6	
IV	7	8	
Aneurysm location, no.			
Anterior circulation	20	18	1
Posterior circulation	1	1	
Aneurysm size(mm)	7.1 ± 4.4	8.4 ± 4.3	0.355
Timing of aneurysm surgery			
Ultra-early	20	14	
Early	1	2	0.118
Mid-late	0	3	
Primary brain damage, no.	8	8	1
Preoperative SAC index, no.			
0-20 (mild)	4	7	0.293
21-42 (severe)	17	12	

Table 2　Comparison of the irrigation group vs. the non-irrigation group

	Irrigation	Non-irrigation	p value
Surgical time	332.0 ± 99.8	349.1 ± 147.5	0.673
Postoperative SAC index, no.			
0-20 (mild)	18	9	0.017*
21-42 (severe)	3	10	
Symptomatic vasospasm, no. †	2	7	0.058
Cerebral infarction, no.	3	9	0.035*
Meningitis, no.	0	3	0.098
Severe pneumonia or Heart failure, no.	0	4	0.042*
VPS or LPS placement, no. ‡	6	10	0.188
Period of CSF drainage(day)	4.21	14.58	0.002*
Distribution of mRS score, no.			
0-2	12	3	0.010*
3-6	9	16	

Table 3 Comparison of mild and severe postoperative SAC and preoperative severe SAC in the irrigation group

	Severe → mild	Severe → Severe	p value
Men : women, no.	2 : 12	0 : 3	0.486
Distribution of H&K grade, no.			
I	0	0	
II	0	0	
III	6	1	0.946
IV	3	1	
V	5	1	
Fisher group			
I	0	0	
II	0	0	1
III	9	2	
IV	5	1	
Change SAC index	19.4 ± 7.8	7.3 ± 5.8	0.040*
Symptomatic vasospasm, no. [†]	0	2	0.008*
Cerebral infarction, no.	0	2	0.022*
VPS or LPS placement, no. [‡]	3	2	0.083
CSF drainage placement, no.	11	2	1
Period of CSF drainage(day)	4.0 ± 1.9	6.5 ± 2.1	0.318