



THE EFFECTS OF ULTRA-EARLY CLIPPING ON SURVIVAL AND NEUROLOGICAL OUTCOME IN POOR-GRADE ANEURYSMAL SUBARACHNOID HAEMORRHAGE

Osman ŞİMSEK, Ahmet Tolgay AKINCI

Trakya University, Department of Neurosurgery, Edirne, Turkey



English

<https://doi.org/10.18071/isz.75.0325>

www.elitmed.hu

AZ ULTRAKORAI KLIPELÉS HATÁSA A TÚLÉLÉSRE ÉS A NEUROLÓGIAI KIMENETEKRE SÚLYOS STÁDIUMÚ, ANEURYSMARUPTURA OKOZTA SUBARACHNOIDEALIS VÉRZÉS ESETÉN

Şimsek O, MD; Akinci AT, MD

Idegggyogy Sz 2022;75(9–10):325–332.

Background and purpose

– European Stroke Organisation guidelines advise treating aneurysmal subarachnoid haemorrhage (aSAH) as early as possible. However, the optimum timing along with its beneficial effects is controversial. Therefore, we aimed to investigate the effects of ultra-early clipping on neurological outcomes and survival in poor-grade aneurysmal subarachnoid haemorrhages.

Methods – This retrospective study included all poor-grade aneurysmal subarachnoid haemorrhage patients treated by ultra-early surgical clipping at Trakya University Hospital between January 1, 2001, and December 31, 2020. We analysed the outcome and mortality data of these patients. Specifically, we evaluated the effects of ultra-early clipping on outcomes, defined as within six hours of the onset of symptoms.

Results – From 813 records, 212 met our inclusion criteria. Of these, 117 (55.2%) were female and 95 (44.8%) male. The mean age was 58.3 ± 13.7 years. Glasgow Outcome Scale scores differed significantly between age groups, subarachnoid haemorrhage grades, those who did and did not rebleed, and those who did or did not suffer from vasospasms. A beneficiary relationship was found between ultra-early clipping and mortality among patients. Furthermore, favourable outcomes were significantly more frequent in the ultra-early clipping group.

Conclusion – The aSAH patients treated at our hospital who received ultra-early clipping had significantly lower mortality rates and more favourable outcomes. The difference was significant among those treated during the last decade and among patients younger than 50.

Keywords: cerebral aneurysm, outcome, subarachnoid haemorrhage, timing, treatment

Háttér és cél – A European Stroke Organisation irányelвеi szerint az aneurysmaruptura okozta subarachnoidealis vérzést (aSAH) a lehető leghamarabb kezeln kell. Mindazonáltal, a beavatkozás optimális ideje, és az általa elérhető előnyök egyelőre még nem tisztázottak. Célunk ezért az volt, hogy megvizsgáljuk az ultrakorai kliplés hatását a túlélésre és a neurológiai kimenetekre súlyos stádiumú, aneurysmaruptura okozta subarachnoidealis vérzések esetén.

Módszerek – Retrospektív vizsgálatunkba bevontuk mindeneket a súlyos stádiumú, aneurysmaruptura okozta subarachnoidealis vérzésben szenvedő betegeket, akiket 2001. január 1. és 2020. december 31. között a Trakya Egyetemi Kórházban ultrakorai klipléssel kezeltek. Elmeztük a bevont betegek neurológiai kimeneteit és mortalitási adatait. Értékeltük az ultrakorai kliplés (definíció szerint a tünetek jelentkezése utáni 6 órán belüli beavatkozás) kimenetekre gyakorolt hatását.

Eredmények – 813 beteg közül 212 felelt meg a bevonási kritériumoknak. A bevont betegek 55,2%-a nő (n=117), 44,8%-a férfi (n=95) volt. Az átlagos életkor $58,3 \pm 13,7$ volt. A Glasgow Kimeneti Skála pontszámai szignifikánsan különböztek az életkorú csoportok, a subarachnoidealis vérzés súlyossága, az ismételt vérzés, illetve a vasospasmus előfordulása szerint. Az ultrakorai kliplés hatására csökkent a mortalitás, és a többi kedvező kimenet is szignifikánsan gyakoribb volt ebben a csoportban.

Következtetés – Azon aSAH-betegek körében, akiket kórházunkban ultrakorai klipléssel kezeltünk, szignifikánsan alacsonyabb mortalitás alakult ki, és egyéb kimeneteik is szignifikánsan jobbak lettek. A különbség szignifikáns volt a legutóbbi évtizedben (2010–2020) kezeltek és az 50 évesnél fiatalabbak esetén.

Kulcsszavak: cerebralis aneurysma, kimenet, subarachnoidealis vérzés, időzítés, kezelés

Correspondent: Dr. Ahmet Tolgay AKINCI, Trakya University, Department of Neurosurgery, Edirne 22130/ Turkey.

E-mail: ahmettolgayakinci@gmail.com. Phone: +90 543 415 06 78, +90 284 235 76 41.

Érkezett: 2022. április 2.

Elfogadva: 2022. július 18.

Aneurysmal subarachnoid haemorrhages (aSAH) are major neurological emergencies, with a yearly incidence of 2–32 per 100,000 people. The prevalence of cerebral aneurysms is between 0.4% and 6%^{1–3}. It is a life-threatening condition, with first-day mortality rates of 25%, in-hospital mortality rates of 35%, and overall mortality reaching 50%^{4, 5}. Amongst those who survive, one-third have been found to have a poor quality of life at one-year follow-up. Over 90% of employed aSAH patients never return to work⁶. In poor-grade aSAH, the mortality and morbidity are even higher. A poor grade is defined as World Federation of Neurological Surgeons (WFNS) grade IV or V^{7, 8}.

Rebleeding is the leading complication associated with in-hospital mortality. It primarily occurs in the first six hours after admission^{9, 10}. European Stroke Organisation guidelines suggest treating aSAH as early as possible, or at least in the first 72 hours^{11–13}. However, the optimum timing of intervention and the beneficial effects of early surgery in poor-grade aSAH are still debated^{8, 14, 15}. The trend for more aggressive treatments and the decline in mortality over the last five decades suggests that early intervention might be vital for poor-grade aSAH patients^{16–20}.

Trakya University Health Centre for Medical Research and Practice is the primary treatment centre for aSAH patients in the Trace region. The vast majority of patients are referred to our institution as it is the only centre in the area with the resources and expertise to manage aSAH, including digital subtraction angiography (DSA), endovascular treatment and aneurysm clipping surgery. Our institutional experience and resources have developed and improved over time. Our treatment protocol for aSAH has evolved into securing aneurysms as early as possible. Before we had the computerised tomography angiography (CTA) equipment, emergency surgery was only performed for cerebral conditions such as midline shift or haematoma. However, we have had access to CTA around the clock for the last decade, which subsequently facilitated the ultra-early clipping. This study defines ultra-early clipping as immediately after initial resuscitation within six hours of the onset of symptoms associated with the initial bleeding.

This retrospective study aimed to investigate the effects of ultra-early clipping on neurological outcomes and survival in poor-grade aSAH.

Materials and methods

ETHICS STATEMENT

This study was conducted in accordance with the tenets of the Declaration of Helsinki 1964 and approved by the ethics committee of Trakya University Health Centre for Medical Research and Practice (approval no. TUTF-GOKAEK 2021/51). Given the retrospective and anonymous nature of the analysis, written informed consent was waived by the ethics committee.

STUDY POPULATION

We retrospectively reviewed the electronic records of all patients admitted to Trakya University Hospital between January 1, 2001, and December 31, 2020.

CLINICAL MANAGEMENT

Before 2011, patients in respiratory distress and those with a Glasgow Coma Scale (GCS) score of 8 or less were intubated after initial evaluation in the emergency department. Once vitals were stabilised, a CT scan was performed. DSA was performed on grade I-III aSAH patients during working hours when the Interventional Radiology Department was accessible. Grade IV-V patients were followed up in the intensive care unit, and DSA was performed on those whose condition improved to grade I-III. For those whose condition was not improved, no intervention was made. Emergency surgery was only performed for haematomas causing midline shifts greater than 5 mm.

In 2011, a different algorithm was adopted, allowing emergency surgery. This change in protocol was due to the hospital's acquisition of CTA equipment and its availability around the clock. Following the implementation of the new algorithm, those with GCS scores of 8 and under were sedated and intubated. Those with GCS over eight were intubated if in respiratory distress. If systolic blood pressure was above 160 mmHg, it was reduced. If subarachnoid haemorrhage (SAH) was observed on CT, a single dose of tranexamic acid was administered, and CTA was performed. Surgical clipping treatments performed within the first six hours after bleeding were defined as ultra-early clipping. Surgical techniques used with high-grade aSAH patients include large craniotomy,

aggressive cisternal lavage, clipping and lamina terminalis opening. In a minority of cases, decompressive craniectomy was also performed.

All cases received steroids, antiepileptics, nimodipine, sedatives, analgesics and laxatives. Clinical management included haemodilution, preventing hyponatraemia, maintaining normovolemia, appropriate support of systolic blood pressure and intermittent cerebrospinal fluid (CSF) drainage via lumbar puncture or external ventricular drainage during the vasospasm period. If rebleeding or vasospasm were suspected, confirmation was obtained through clinical diagnosis, and then confirmed radiologically. All patients were followed up for at least six months. Glasgow Outcome Scale (GOS) scores obtained at the six-month follow-ups were used as the outcome measure in this study.

DATA COLLECTION

The demographic, clinical and radiological data of patients with diagnosis of subarachnoid haemorrhage were accessed via three sources: 1. Electronic Health Records System (ENLIL) 2. Patient files (Trakya University, Neurosurgery Department, clinical archive) and 3. The picture archiving and communication system.

The study inclusion criteria were: 1) A diagnosis of aneurysmal subarachnoid haemorrhage confirmed by computed tomography; 2) A poor WFNS grade of aneurysmal subarachnoid haemorrhage (grade 4 or 5); 3) Treatment by surgical clipping; 4) Availability of complete documentation of patient data.

The study exclusion criteria were: 1) Non-aneurysmal causes of subarachnoid haemorrhage such as trauma or arteriovenous malformation; 2) A good WFNS grade of aneurysmal subarachnoid haemorrhage (grade 1, 2 or 3); 3) Treatment by endovascular coiling; 4) Incomplete documentation of patient data.

STATISTICAL DESIGN

The descriptive statistics for continuous variables were expressed as mean \pm standard deviation or median (interquartile range) based on the distribution. Shapiro-Wilk tests were used to evaluate the normality of continuous variables. The statistical tests used to determine relationships between variables were t-tests, Pearson chi-square tests and Fisher-Freeman-Halton exact tests. A *p*-value below

0.05 was considered significant. Using Jamovi v. 1.2, Gpower v. 3.1, and IBM SPSS v. 21.0 software, statistical analyses were performed. An *a priori* power analysis for $\alpha = 0.05$, power $(1 - \beta) = 0.80$ and effect size = 0.3 (medium) was used to determine the minimum sample size, which was 143.

Results

Our institution's database found 813 records for SAH patients hospitalised between January 1, 2001, and December 31, 2020. Amongst these, 212 patients met our inclusion criteria. 117 (55.2%) were female and 95 (44.8%) male. The mean age was 58.3 ± 13.7 years. The demographic, clinical and outcome parameters from the two decades were compared. These comparisons are summarised in **Table 1**.

There was no difference in outcomes between patients of different sexes or Fisher grades. Conversely, GOS scores differed significantly between age groups and WFNS grades ($p < 0.001$). GOS scores also differed significantly between those who did and did not rebleed and those who did and did not suffer vasospasms ($p < 0.001$). The results of these analyses and the outcome distributions are presented in **Table 2**.

The distribution of surgical clipping timing among patients was homogenous between sexes but heterogeneous between age groups and WFNS and Fisher grades ($p = 0.553$, $p < 0.001$, $p < 0.001$ and $p = 0.002$, respectively). In addition, the timing of intervention led to significant differences in the occurrence of both rebleeding and vasospasms ($p < 0.001$ and $p = 0.018$, respectively). Parameter comparison data are summarised in **Table 3**.

The ultra-early intervention had no significant effect on mortality between 2001 and 2010; nevertheless, the effect was significant in the 2011–2020 period ($p = 0.167$ and $p = 0.002$, respectively). Overall, the ultra-early clipped group was found to have significantly lower mortality ($p < 0.001$, **Table 4**). Logistic regression analyses for the overall and 2011–2020 periods showed that ultra-early clipping led to lower mortality rates ($p < 0.001$ and $p = 0.001$, respectively, **Table 5**).

Similarly, there was no significant difference between favourable and unfavourable outcomes during the 2001–2010 period, but ultra-early clipping significantly increased favourable outcomes during the 2011–2020 period and throughout the

Table 1. Descriptives & demographics

N (%)	2001 – 2010 N = 150	2011 – 2020 N = 62	2001 – 2020 N = 212	p (Phi or Cramer's V)
Females	87 (58.0)	30 (48.4)	117 (55.2)	0.200
Age (year, mean ± sd)	58.8 ± (13.2)	56.9 ± (14.9)	58.3 ± 13.7	0.338
Age ≤ 49	35 (23.3)	21 (33.9)	56 (26.4)	0.262
50 – 64	60 (40.0)	23 (37.1)	83 (39.2)	
≥ 65	55 (36.7)	18 (29.0)	73 (34.4)	
WFNS Grade 1*	193	184	377	
WFNS Grade 2*	97	41	138	
WFNS Grade 3*	33	11	44	
WFNS Grade 4	91 (60.7)	33 (53.2)	124 (58.5)	0.317 (Grade 4 vs 5)
WFNS Grade 5	59 (39.3)	29 (46.8)	88 (41.5)	
Fisher Grade 3	77 (51.3)	25 (40.3)	102 (48.1)	0.144
Fisher Grade 4	73 (48.7)	37 (59.7)	110 (51.9)	
Rebleeding –	86 (57.3)	57 (91.9)	143 (67.5)	<0.001
Rebleeding +	64 (42.7)	5 (8.1)	69 (32.5)	(0.336)
Vasospasm –	134 (89.3)	56 (90.3)	190 (89.6)	0.830
Vasospasm +	16 (10.7)	6 (9.7)	22 (10.4)	
GOS 1	118 (78.7)	35 (56.5)	153 (72.2)	<0.001
GOS 2	2 (1.3)	0 (0.0)	2 (0.9)	(0.311)
GOS 3	7 (4.7)	6 (9.7)	13 (6.1)	
GOS 4	20 (13.3)	11 (17.7)	31 (14.6)	
GOS 5	3 (2.0)	10 (16.1)	13 (6.1)	
Favourable (GOS 4 and 5)	23 (15.3)	21 (33.9)	44 (20.8)	0.002
Unfavourable (GOS 1, 2 and 3)	127 (84.7)	41 (66.1)	168 (79.2)	(0.208)

WFNS Grade: World Federation of Neurological Surgeons, GOS: Glasgow outcome scale

*WFNS Grade 1, 2 and 3 patients are not included in the study

Table 2. Overall outcomes

N (%)	GOS 1 N = 153	GOS 2 N = 2	GOS 3 N = 13	GOS 4 N = 31	GOS 5 N = 13	Total N = 212	p (Phi or Cramer's V)
Females	89 (76.1)	1 (0.9)	9 (7.7)	12 (10.3)	6 (5.1)	117 (100)	0.203
Males	64 (67.4)	1 (1.1)	4 (4.2)	19 (20.0)	7 (7.4)	95 (100)	
Age ≤ 49	31 (55.4)	1 (1.8)	5 (8.9)	11 (19.6)	8 (14.3)	56 (100)	<0.001
50 – 64	58 (69.9)	0 (0)	6 (7.2)	16 (19.3)	3 (3.6)	83 (100)	(0.233)
≥ 65	64 (87.7)	1 (1.4)	2 (2.7)	4 (5.5)	2 (2.7)	73 (100)	
WFNS Grade 4	77 (62.1)	1 (0.8)	10 (8.1)	26 (21.0)	10 (8.1)	124 (100)	<0.001
WFNS Grade 5	76 (86.4)	1 (1.1)	3 (3.4)	5 (5.7)	3 (3.4)	88 (100)	(0.276)
Fisher Grade 3	74 (72.5)	0 (0)	4 (3.9)	18 (17.6)	6 (5.9)	102 (100)	0.354
Fisher Grade 4	79 (71.8)	2 (1.8)	9 (8.2)	13 (11.8)	7 (6.4)	110 (100)	
Rebleeding –	88 (61.5)	2 (1.4)	11 (7.7)	29 (20.3)	13 (9.1)	143 (100)	<0.001
Rebleeding +	65 (94.2)	0 (0)	2 (2.9)	2 (2.9)	0 (0)	69 (100)	(0.347)
Vasospasm –	136 (71.6)	2 (1.1)	9 (4.7)	30 (15.8)	13 (6.8)	190 (100)	0.076
Vasospasm +	17 (77.3)	0 (0)	4 (18.2)	1 (4.5)	0 (0)	22 (100)	
Clipping –	112 (96.6)	0 (0)	2 (1.7)	2 (1.7)	0 (0)	116 (100)	<0.001
Clipping +	41 (42.7)	2 (2.1)	11 (11.5)	29 (30.2)	13 (13.5)	96 (100)	(0.601)

WFNS Grade: World Federation of Neurological Surgeons

whole period studied ($p=0.292$, $p=0.003$ and $p<0.001$, respectively). Moreover, while favourable results were higher in the ultra-early intervened

patients under 50, there was no significant difference between the 50–64 and 65+ age groups ($p<0.001$, $p=0.264$ and $p=0.127$ respectively, **Table 6**).

Table 3. Clipping timing

N (%)	< 6 hours N = 34	6 – 72 hours N = 35	> 72 hours N = 27	No Clipping N = 116	Total N = 212	p (Phi or Cramer's
Females	16 (47.1)	18 (51.4)	14 (51.9)	69 (59.5)	117 (55.2)	0.553
Males	18 (52.9)	17 (48.6)	13 (48.1)	47 (40.5)	95 (44.8)	
Age ≤ 49	15 (44.1)	9 (25.7)	9 (33.3)	23 (19.8)	56 (26.4)	<0.001
50 – 64	11 (32.4)	21 (60.0)	11 (40.7)	40 (34.5)	83 (39.2)	(0.225)
≥ 65	8 (23.5)	5 (14.3)	7 (25.9)	53 (45.7)	73 (34.4)	
WFNS Grade 4	15 (44.1)	26 (74.3)	25 (92.6)	58 (50)	124 (58.5)	<0.001
WFNS Grade 5	19 (55.9)	9 (25.7)	2 (7.4)	58 (50)	88 (41.5)	(0.328)
Fisher Grade 3	7 (20.6)	16 (45.7)	17 (63.0)	62 (53.4)	102 (48.1)	0.002
Fisher Grade 4	27 (79.4)	19 (54.3)	10 (37.0)	54 (46.6)	110 (51.9)	(0.258)
Rebleeding –	34 (100)	29 (82.9)	21 (77.8)	59 (50.9)	143 (67.5)	<0.001
Rebleeding +	0 (0)	6 (17.1)	6 (22.2)	57 (49.1)	69 (32.5)	(0.412)
Vasospasm –	32 (94.1)	26 (74.3)	24 (88.9)	108 (93.1)	190 (89.6)	0.018
Vasospasm +	2 (5.9)	9 (25.7)	3 (11.1)	8 (6.9)	22 (10.4)	(0.229)

WFNS Grade: World Federation of Neurological Surgeons

Table 4. The effects of ultra-early clipping on mortality

N (%)	Mortality in 6th Month	Ultra-early Clipping –	Ultra-early Clipping +	Total	p (Phi or Cramer's V)
2001 – 2010	Alive	29 (20.3)	3 (42.9)	32 (21.3)	0.167
	Dead	114 (79.7)	4 (57.1)	118 (78.7)	
2011 – 2020	Alive	9 (25.7)	18 (66.7)	27 (43.5)	0.002
	Dead	26 (74.3)	9 (33.3)	35 (56.5)	
Total	Alive	38 (21.3)	21 (61.8)	59 (27.8)	<0.001
	Dead	140 (78.7)	13 (38.2)	153 (72.2)	(0.331)

Table 5. Regression results

	B	Standard Error	Wald statistics	Degree of freedom	Significance	Exp(B)
2001–2020	Ultra Early Surgery	-1,784	0,397	20,135	1	0,000
	Constant	1,304	0,183	50,826	1	0,000
2011–2020	Ultra Early Surgery	-1,754	0,562	9,729	1	0,002
	Constant	1,061	0,387	7,524	1	0,006

B: coefficient, Exp(B): exponential value of B

Figure 1 summarises the results of ultra-early clipping, giving details on external ventricular drainage (EVD) and shunt necessity, mortality, Glasgow Outcome Scale and modified Glasgow Outcome Scale scores at the six-month follow-ups.

Discussion

Our results suggest that our institutional outcomes have improved over time. We found that patients' age, WFNS grade, Fisher grade, rebleeding, vasospasm and ultra-early surgical clipping of the

aneurysm affected the outcome. The ultra-early clipping might be the primary factor leading to lower mortality rates and more favourable outcomes in our institution in the last decade.

Poor-grade aSAH patients have been reported to have worse outcomes due to a higher incidence of aSAH-associated complications such as rebleeding, hydrocephalus and vasospasm^{8, 19, 21, 22}. Up until a few decades ago, intervention was not provided for this subgroup of patients until their neurological status improved²³. Since recent guidelines recommend aSAH intervention as early as possible, most centres currently follow much more aggressive

Table 6. The effects of ultra-early clipping on the favourable outcome

N (%)	Ultra Early Clipping – N = 178	Ultra Early Clipping + N = 34	Total N = 212	p (Phi or Cramer's V)
2001 – 2010	Favourable 21 (14.7) Unfavourable 122 (85.3)	2 (28.6) 5 (71.4)	23 (15.3) 127 (84.7)	0.292
2011 – 2020	Favourable 6 (17.1) Unfavourable 29 (82.9)	15 (55.6) 12 (44.4)	21 (33.9) 41 (66.1)	0.003 (0.402)
Total	Favourable 27 (15.2) Unfavourable 151 (84.8)	17 (50) 17 (50)	44 (20.8) 168 (79.2)	<0.001 (0.315)
≤ 49 years	Favourable 8 (19.5) Unfavourable 33 (80.5)	11 (73.3) 4 (26.7)	19 (33.9) 37 (66.1)	<0.001 (0.503)
50 – 64 years	Favourable 15 (20.8) Unfavourable 57 (79.2)	4 (36.4) 7 (63.6)	19 (22.9) 64 (77.1)	0.264
≥ 65 years	Favourable 4 (6.2) Unfavourable 61 (93.8)	2 (25) 6 (75)	6 (8.2) 67 (91.8)	0.127
Total	Favourable 27 (15.2) Unfavourable 151 (84.8)	17 (50) 17 (50)	44 (20.8) 168 (79.2)	<0.001 (0.315)

Favourable: Glasgow outcome scale 4 and 5, Unfavourable: Glasgow outcome scale 1, 2 and 3

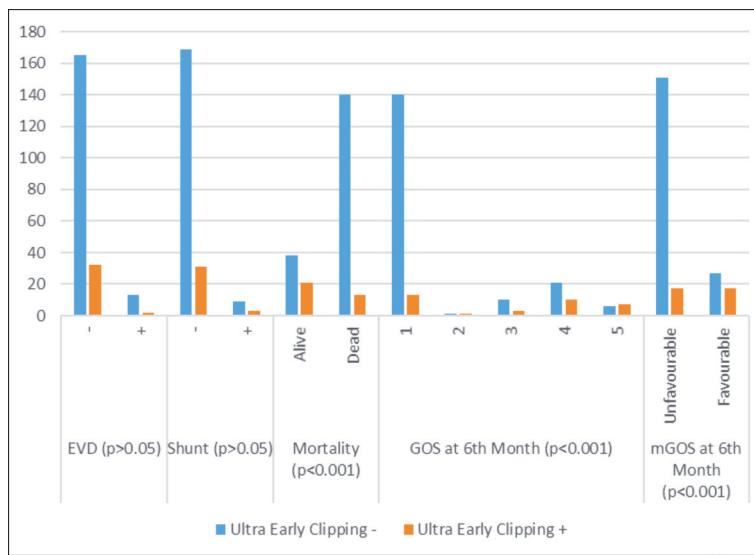


Figure 1. Summary of the results of ultra-early clipping, details on external ventricular drainage and shunt necessity, mortality, Glasgow Outcome Scale and modified Glasgow Outcome Scale scores at the six-month follow-ups

EVD: external ventricular drainage, GOS: Glasgow outcome scale, mGOS: Modified Glasgow outcome scale

management strategies and endeavour to provide medical intervention in the first 72 hours^{11,13,21}. Yet, if earlier interventions lead to better outcomes, this raises the question of whether the earliest, most aggressive intervention possible is the best approach for every patient. While there is still no consensus on this, there is an undeniable trend towards earlier, more aggressive intervention. In

addition, the plethora of new technologies available, such as CT angiography and endovascular interventions, have also affected the management strategies used with aSAH patients.

Several systematic reviews have shown that mortality rates among aSAH patients have declined significantly over the last three decades^{2,5,21}. However, over the last two decades, there have been no discernible changes in the demographic characteristics of aSAH patients. The introduction of CT angiography, paving the way for ultra-early surgery, is likely to have played a large part in the improved mortality, outcome and rebleeding rates.

Increased intracranial pressure (ICP > 20 mmHg) is prevalent in aSAH and can worsen complications²³. The leading causes of increased ICP are initial bleeding, hydrocephalus, global cerebral oedema and vasospasm²³. This list overlaps considerably with the list of aSAH complications.

One of the best-known predictors of aSAH prognosis is neurological status at admission, with lower grade aSAH patients having better outcomes²⁴. Correspondingly, our results show better outcomes among grade 4 than grade 5 patients. Also, according to the literature, the overall outcomes were worse for older patients, those who suffered rebleeding, and those who received no interven-

tion²⁴. There was no Fisher grade 1 or 2 patients included in the study. The overall outcome distributions between Fisher grades and vasospasm groups did not reach significance; nevertheless, the differences were distinguishable when patients were grouped according to rebleeding and surgical clipping.

Comorbidities and anticoagulants are critical obstacles to early surgery in elderly patients²⁵. Our results show that ultra-early surgery in our clinic was mainly performed on patients under 50. It was also observed that patients with higher Fisher grades received an ultra-early clipping and that rebleeding and vasospasm were less common with ultra-early clipping.

We admit that some contributing, mediating, or even confounding variables affect our results. One example might be the bleeding amount. There is a great deal of bleeding in high-grade aSAH patients, which can directly or indirectly increase ICP by disrupting CSF circulation²³. In this patient series, aggressive cisternal lavage and lamina terminalis fenestration were performed during microvascular clipping. Reducing blood by-products and opening CSF pathways during early surgery may decrease ICP and help mitigate the deleterious effects of vasospasm and delayed cerebral ischemia²⁶. Over the last decade, angiography has made ultra-early surgical intervention feasible in our institution, resulted in improvements to clinical outcomes. Therefore, availability of the endovascular procedures in the period 2010-2020 constitutes another significant limitation of the study. In developing countries, it is often not possible to provide 24/7 endovascular intervention, especially in provincial hospitals. Consequently, we think our results supporting ultra-early surgery's positive effects on low-grade SAH patients' outcomes are noteworthy.

LIMITATIONS

This study was limited by relatively small sample size, retrospective data collection and single-centre design.

Conclusion

This retrospective study assessed the effects of ultra-early clipping on survival and neurological outcomes in poor-grade aneurysmal subarachnoid hemorrhages. Our institution's outcomes have improved over time. In this study, aSAH patients who received an ultra-early clipping had a lower mortality rate and more favourable outcomes than those who received later or no surgical clipping. We found that ultra-early clipping positively affected survival and neurological outcome. We believe that proactive and aggressive medical management and surgical intervention provided as early as possible provide considerable amelioration of the deleterious effects of aSAH.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

ACKNOWLEDGEMENTS

The Turkish Neurosurgical Society partly supported the preparation for the publication of this article.

CONFLICTS OF INTEREST

The authors certify that they have no affiliations with, or involvement in, any organisation or entity with any financial or non-financial interest in this study's subject matter, data, or findings.

REFERENCES

1. Linn FH, Rinkel GJ, Algra A, van Gijn J. Incidence of subarachnoid hemorrhage: role of region, year, and rate of computed tomography: a meta-analysis. *Stroke* 1996;27: 625-9. PubMed PMID: 8614919. <https://doi.org/10.1161/01.STR.27.4.625>
2. Rinkel GJ, Djibuti M, Algra A, van Gijn J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke* 1998;29:251-6. PubMed PMID: 9445359. <https://doi.org/10.1161/01.STR.29.1.251>
3. Simsek O, Akinci AT, Delen E, Süt N. Spontaneous subarachnoid haemorrhage incidence among hospitalised patients in Edirne, Turkey. *Acta Neurochir (Wien)* 2019;161: 2381-7. PubMed PMID: 31494729. <https://doi.org/10.1007/s00701-019-04036-7>
4. Long B, Koyfman A, Runyon MS. Subarachnoid hemorrhage: updates in diagnosis and management. *Emerg Med Clin North Am* 2017;35:803-24. PubMed PMID: 28987430. <https://doi.org/10.1016/j.emc.2017.07.001>
5. Lovelock CE, Rinkel GJE, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: population-based study and systematic review. *Neurology* 2010;74:1494-501. PubMed PMID: 20375310; PubMed Central PMCID: PMC2875923. <https://doi.org/10.1212/WNL.0b013e3181dd42b3>
6. Taufique Z, May T, Meyers E, et al. Predictors of Poor quality of life 1 year after subarachnoid hemorrhage. *Neurosurgery* 2016;78:256-64. PubMed PMID: 26421590. <https://doi.org/10.1227/NEU.0000000000001042>
7. Hutchinson PJ, Power DM, Tripathi P, Kirkpatrick PJ.

- Outcome from poor grade aneurysmal subarachnoid haemorrhage – which poor grade subarachnoid haemorrhage patients benefit from aneurysm clipping? *Br J Neurosurg* 2000;14:105-9. PubMed PMID: 10889881.
<https://doi.org/10.1080/02688690050004516>
8. Gupta SK, Ghanta RK, Chhabra R, et al. Poor-grade subarachnoid hemorrhage: is surgical clipping worthwhile? *Neurol India* 2011;59:212-7. PubMed PMID: 21483120.
<https://doi.org/10.4103/0028-3886.79144>
 9. Stienen MN, Germans M, Burkhardt J-K, et al. Predictors of In-hospital death after aneurysmal subarachnoid hemorrhage: analysis of a nationwide database (swiss sos swiss study on aneurysmal subarachnoid hemorrhage). *Stroke* 2018;49:333-40. PubMed PMID: 29335333.
<https://doi.org/10.1161/STR.0000000000000169>
 10. Starke RM, Connolly ES. Rebleeding after aneurysmal subarachnoid hemorrhage. *Neurocrit Care* 2011;15:241-6. PubMed PMID: 21761274.
<https://doi.org/10.1007/s12028-011-9581-0>
 11. Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2012;43:1711-37. PubMed PMID: 22556195.
<https://doi.org/10.1161/STR.0b013e3182587839>
 12. Diringer MN, Bleck TP, Claude Hemphill J, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. *Neurocrit Care* 2011;15:211-40. PubMed PMID: 21773873. <https://doi.org/10.1007/s12028-011-9605-9>
 13. Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G. European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovasc Dis* 2013;35:93-112. PubMed PMID: 23406828. <https://doi.org/10.1159/000346087>
 14. Choudhry A, Murray D, Corr P, et al. Timing of treatment of aneurysmal subarachnoid haemorrhage: are the goals set in international guidelines achievable? *Ir J Med Sci* 2021. PubMed PMID: 33599919.
 15. Robbert M, Germans MR, Hoogmoed J, et al. Time intervals from aneurysmal subarachnoid hemorrhage to treatment and factors contributing to delay. *J Neurol* 2014; 261:473-9. PubMed PMID: 24366653.
<https://doi.org/10.1007/s00415-013-7218-2>
 16. Naidech AM, Janjua N, Kreiter KT, et al. Predictors and impact of aneurysm rebleeding after subarachnoid hemorrhage. *Arch Neurol* 2005;62:410-6. PubMed PMID: 15767506. <https://doi.org/10.1001/archneur.62.3.410>
 17. Lawton MT, Vates GE. Subarachnoid Hemorrhage. *N Engl J Med* 2017;377:257-66. PubMed PMID: 28723321.
<https://doi.org/10.1056/NEJMcp1605827>
 18. Goldberg J, Schoeni D, Mordasini P, et al. Survival and outcome after poor-grade aneurysmal subarachnoid hemorrhage in elderly patients. *Stroke* 2018;49:2883-9. PubMed PMID: 30571422.
<https://doi.org/10.1161/STROKEAHA.118.022869>
 19. Hoogmoed J, Coert BA, van den Berg R, et al. Early treatment decisions in poor-grade patients with subarachnoid hemorrhage. *World Neurosurg* 2018;119:e568-e573. PubMed PMID: 30077026.
<https://doi.org/10.1016/j.wneu.2018.07.212>
 20. Schwartz C, Pfefferkorn T, Ebrahimi C, et al. Long-term neurological outcome and quality of life after world federation of neurosurgical societies grades iv and v aneurysmal subarachnoid hemorrhage in an interdisciplinary treatment concept. *Neurosurgery* 2017;80:967-74. PubMed PMID: 28327912.
<https://doi.org/10.1093/neuros/nyw138>
 21. Han Y, Ye F, Long X, et al. Ultra-early treatment for poor-grade aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. *World Neurosurg* 2018;115: e160-e171. PubMed PMID: 29649648.
<https://doi.org/10.1016/j.wneu.2018.03.219>
 22. Macdonald RL, Schweizer TA. Spontaneous subarachnoid haemorrhage. *Lancet* 2017;389:655-66.
[https://doi.org/10.1016/S0140-6736\(16\)30668-7](https://doi.org/10.1016/S0140-6736(16)30668-7)
 23. Alotaibi NM, Wang JZ, Pasarikovski CR, et al. Management of raised intracranial pressure in aneurysmal subarachnoid hemorrhage: time for a consensus? *Neurosurg Focus* 2017;43:E13. PubMed PMID: 29088956.
<https://doi.org/10.3171/2017.7.FOCUS17426>
 24. van Donkelaar CE, Bakker NA, Birks J, et al. Prediction of Outcome After Aneurysmal Subarachnoid Hemorrhage. *Stroke* 2019;50:837-44. 118.023902. PubMed PMID: 30869562.
<https://doi.org/10.1161/STROKEAHA.118.023902>
 25. Scotti P, Séguin C, Lo BWY, Guise E de, Troquet J-M, Marcoux J. Antithrombotic agents and traumatic brain injury in the elderly population: hemorrhage patterns and outcomes. *J Neurosurg* 2019;133:1-10. PubMed PMID: 31277068.
<https://doi.org/10.3171/2019.4.JNS19252>
 26. Diringer MN, Zazulia AR. Aneurysmal Subarachnoid Hemorrhage: Strategies for Preventing Vasospasm in the Intensive Care Unit. *Semin Respir Crit Care Med* 2017 Dec;38(6):760-7. Epub 2017 Dec 20. PMID: 29262433.
<https://doi.org/10.1055/s-0037-1607990>