Acta Neurochirurgica

Survival and outcome in patients with aneurysmal subarachnoid hemorrhage in Glasgow Coma Score 3-5 --Manuscript Draft--

Manuscript Number:	ANCH-D-19-01134R2
Full Title:	Survival and outcome in patients with aneurysmal subarachnoid hemorrhage in Glasgow Coma Score 3-5
Article Type:	Original Article
Keywords:	Aneurysmal subarachnoid hemorrhage; Comatose; Hunt and Hess grade V; outcome; Poor grade; Survival
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Abstract:	<p>Background: Outcome of early, aggressive management of aneurysmal subarachnoid hemorrhage (aSAH) in patients with Hunt and Hess grade V is hitherto limited and we therefore present our results.</p> <p>Methods: Retrospective study analyzing the medical data of 228 aSAH patients in Glasgow Coma Score 3-5 admitted at our hospital during the years 2002-2012. Background and treatment variables were registered. Outcome was evaluated after three and twelve months.</p> <p>Results: We intended to treat 176 (77.2%) patients, but only 146 went on to aneurysm repair. Of 52 patients managed conservatively, 27 had abolished cerebral circulation around arrival and 25 were deemed unsalvageable. One-year overall mortality was 65.8% and most (84.7%) of the fatalities occurred within 30 days. One-year mortality was higher in patients >70 years. Without aneurysm repair, mortality was 100%. After one year, 21.9% of all patients lived independently and 4.8% lived permanently in an institution. Outcome in the 78 survivors (34.2%) was favorable in 64.1% in terms of modified Rankin Scale score 0-2 and 85.9% of survivors were able to live at home. Return to work was low for all 228 patients with 14.0% of those employed prior to the hemorrhage having returned to paid work, and respectively, 26.3% in the subgroup of survivors.</p> <p>Conclusions: Even with aggressive, early treatment, one-year mortality is high in comatose aSAH patients with 65.8%. A substantial portion of the survivors have a favorable outcome at one year (64.1%, corresponding to 21.9% of all patients admitted) and 85.9% of the survivors could live at home alone or aided.</p>

Survival and outcome in patients with aneurysmal subarachnoid hemorrhage in Glasgow Coma Score 3-5.

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Abbreviations

aSAH: aneurysmal subarachnoid hemorrhage
CPP: cerebral perfusion pressure
CSF: cerebrospinal fluid
CT: computed tomography
CTA: computed tomography angiography
EVD: external ventricular drain
GCS: Glasgow Coma Scale
GHQ-30: Global Health Questionnaire
GOS: Glasgow Outcome Scale
ICP: intracranial pressure
ICU: intensive care unit
IVH: intraventricular hemorrhage
MAP: mean arterial pressure
mRS: modified Rankin Scale
SF-36: the 36-item Short Form Health Survey
TCD: transcranial Doppler ultrasonography
WFNS: World Federation of Neurological Surgeons

Abstract

Background: Outcome of early, aggressive management of aneurysmal subarachnoid hemorrhage (aSAH) in patients with Hunt and Hess grade V is hitherto limited and we therefore present our results.

Methods: Retrospective study analyzing the medical data of 228 aSAH patients in Glasgow Coma Score 3-5 admitted at our hospital during the years 2002-2012. Background and treatment variables were registered. Outcome was evaluated after three and twelve months.

Results: We intended to treat 176 (77.2%) patients, but only 146 went on to aneurysm repair. Of 52 patients managed conservatively, 27 had abolished cerebral circulation around arrival and 25 were deemed unsalvageable. One-year overall mortality was 65.8% and most (84.7%) of the fatalities occurred within 30 days. One-year mortality was higher in patients >70 years. Without aneurysm repair, mortality was 100%. After one year, 21.9% of all patients lived independently and 4.8% lived permanently in an institution. Outcome in the 78 survivors (34.2%) was favorable in 64.1% in terms of modified Rankin Scale score 0-2 and 85.9% of survivors were able to live at home. Return to work was low for all 228 patients with 14.0% of those employed prior to the hemorrhage having returned to paid work, and respectively, 26.3% in the subgroup of survivors.

Conclusions: Even with aggressive, early treatment, one-year mortality is high in comatose aSAH patients with 65.8%. A substantial portion of the survivors have a favorable outcome at one year (64.1%, corresponding to 21.9% of all patients admitted) and 85.9% of the survivors could live at home alone or aided.

Keywords: Aneurysmal subarachnoid hemorrhage, Comatose, Hunt and Hess grade V, Outcome, Poor grade, Survival

Introduction

Depending on hospital referring patterns, patients with non-traumatic aneurysmal subarachnoid hemorrhage (aSAH) in Glasgow Coma Score 3-5 (Hunt and Hess [13] grade V) comprise 4% - 24% of aSAH patients admitted to neurosurgical departments [1,2,18,26,30,36,48]. Traditionally, this particular aSAH subgroup was offered conservative treatment [13,48,54] with extremely high mortality rates [15,45]. Over time, outcome in aSAH patients improved in general [34], so that some institutions changed to a more offensive attitude towards treatment of poor grade patients. Eventually, promising results in poor grade patients undergoing early aneurysm repair and receiving full-scale intensive care were [1,19,26] published. Acknowledging the high frequency of early rebleeds in comatose aSAH patients, Laidlaw and Siu [23,24] routinely performed early aneurysm repair in this subgroup (i.e. within 24 hours after SAH and 85% of them within 12 hours). With half of their surgically treated World Federation of Neurological Surgeons (WFNS) grade V patients surviving (65.3% of them with a favorable outcome at three months), they revealed the feasibility of routine early aneurysm repair with potentially good outcome regardless of clinical grade.

Ultimately, current European guidelines for the management of aSAH now also recommend treatment of poor grade aSAH cases with early surgery: "...aneurysm should be treated as early as logistically and technically possible to reduce the risk of rebleeding; if possible it should be aimed to intervene at least within 72 h after onset of first symptoms. This decision should not depend on grading" [51]. American guidelines give this class I recommendation: "Surgical clipping or endovascular coiling of the ruptured aneurysm should be performed as early as feasible in the majority of patients to reduce the rate of rebleeding after aSAH" and this class IIb, level of evidence C recommendation: "Endovascular coiling may receive increased consideration in the elderly (>70 years of age), in those presenting with poor-grade (WFNS grade IV/V) aSAH" [6]. Hence, even though there is some consensus regarding active treatment of poor grade patients, it remains highly unclear how to triage Hunt and Hess grade V patients upon their arrival to a Neurosurgical unit and how their further course develops dependent on this selection. To this end, we present the data and outcome of 228 Hunt and Hess grade V patients from a single center that were either allocated to conservative treatment, or to ultra-early aneurysm repair including management equivalent to those admitted in grades I-IV.

Methods

Patients

This retrospective study comprises all patients admitted to the Neurosurgical Department, Rikshospitalet, Oslo University Hospital, Oslo, Norway, with aSAH and in Hunt and Hess grade V [13] prior to intubation/aneurysm repair. Due to a tendency of intubating aSAH patients at higher levels of consciousness prior to transport to a neurosurgical center in the later years, this study includes only patients admitted between the years 2002 to 2012.

Patients were considered to be in Hunt and Hess grade V when their level of consciousness was scored to be stable between Glasgow Coma Score (GCS) 3-5 and not obviously caused by a seizure.

Patients were excluded if their GCS was 6 or higher just prior to aneurysm repair or prior to intubation and sedation. We also excluded patients that could not unequivocally be considered Hunt and Hess grade V and those that were intubated and sedated so quickly after the ictus that their true status remained vague (including those intubated shortly after a generalized epileptic seizure).

Patients with cerebral arteriovenous malformation where the aSAH was caused by a flow-related aneurysm were also excluded.

The present study is part of the projects entitled “Treatment of patients in poor clinical grade following aneurysmal subarachnoid hemorrhage”, and “Effect of early rehabilitation following aneurysmal subarachnoid hemorrhage”, approved by the Regional Committee for Medical Research Ethics, Southeast Norway in January 2012, archive number 2011/2189.

This study was approved as a quality project by the institutional data protection officer (number 2011/20184) and did not require informed consent.

Methods

Standard institutional aSAH management principles

Oslo University Hospital, Rikshospitalet, is a tertiary medical center solely responsible for the management of all non-traumatic aSAH patients in the South-Eastern Norway Health Region. It is the sole hospital in the Nation performing organ transplants. The hospital serves a population of 2.7 million within a catchment area of 111.500 km². The vast distances from the site of ictus to the neurosurgical department often necessitate admission to a local hospital

where the patient is stabilized and undergoes cerebral computed tomography (CT) prior to further transport to our center.

We practice low threshold, ultra-early, rigorous treatment of aSAH patients, including those in poor clinical grade, patients with comorbidities and the elderly. There is a 24/7 availability of both surgical and endovascular aneurysm repair which is performed by dedicated vascular teams. Patients are treated in accordance with our standardized guidelines [50]. They receive intravenous Tranexamic acid every six hours until the aneurysm is repaired as swiftly as possible. Intravenous/oral Nimodipine is administered for three weeks after the ictus. Following aneurysm repair, cerebral perfusion pressure (CPP) is maintained >70 mmHg and we aim at lowering the intracranial pressure (ICP) towards 0 mmHg. To this end, we practice liberal cerebrospinal fluid (CSF) drainage, establishing CSF drainage shortly after arrival in most patients and draining at low resistance once the aneurysm is repaired. Poor grade aSAH patients remain on invasive mechanical ventilatory support as long as needed with respect to intracranial pressure and we perform decompressive craniectomy if ICP is not controllable otherwise. We readily perform early percutaneous tracheotomy in order to ease patient awakening and reduce the use of sedative drugs [42]. Cerebral CT angiography (CTA) is performed the day after aneurysm repair and seven days after the ictus, given that the patient is stable enough to allow transport to the radiological suite. Transcranial Doppler ultrasonography (TCD) [28,29] is performed frequently from day four after the ictus. If severe cerebral vasospasm is diagnosed, the CPP threshold is elevated to >90 mmHg by means of volume expansion, further lowering of the ICP even to negative values through aggressive CSF drainage and, if needed, by pharmacological increase of the mean arterial blood pressure (MAP). If this strategy is insufficient, we may deepen sedation with Thiopentone, actively cool the patients and/or administer angiographical intra-arterial Nimodipine. Upon unsuccessful gradual weaning of CSF diversion, a permanent CSF shunt is implanted. When no longer in need of neurosurgical management, the patients are transferred to their local intensive care units (ICUs) if still on mechanical respiratory support or their local neurological/rehabilitation departments.

Entrance- and treatment variables registered

We registered the following background variables: age, gender, co-morbidity, relevant medication and occupational status.

Relevant points in the patient`s timeline was time from ictus to neurosurgical admission, time from admission to aneurysm repair (if performed), time on mechanical ventilatory support, length of stay, and time to death. We also registered any clinical and/or radiological evidence of rebleeding prior to aneurysm repair and the occurrence of pupillary dilatation regardless of duration (i.e. including reversible pupillary dilatation). Cerebral CT/CTA was performed in all patients. From these scans, we obtained the amount of subarachnoid hemorrhage expressed by the modified Fisher score [5] and the amount of intraventricular hemorrhage (IVH) using a modified LeRoux score [27] with zero points indicating that no IVH was present. CTA was also used to determine the location and size of the ruptured aneurysm. Ventricular score [32] was acquired from the first available CT scan. We further registered the mode of aneurysm repair and the use/amount of CSF drainage.

Outcome

Mortality was defined as death of any cause within one year after the ictus. We registered the juridical time of death as set in the death certificate, which is the time of observed cardiac arrest or, in patients on mechanical ventilatory support, the time of documented cerebral circulatory arrest.

Patients receive routinely follow-up at our department at three and twelve months after the ictus. Global functional status was scored using the Glasgow Outcome Scale (GOS) [17] and the modified Rankin Scale (mRS) [57]. Housing and occupational status prior to the ictus and after one year was also registered.

Statistics

Statistical analysis was performed in SPSS v 25.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows and Macintosh, Version 25.0. Armonk, NY: IBM Corp). Normally distributed continuous variables are presented by mean with standard deviation, and independent samples t-test was used to compare differences between groups. Continuous variables which were not normally distributed are presented with median and range, and Mann Whitney U test was used to compare differences between groups. Categorical variables are presented by frequencies or percentages, and Chi square test was used to compare differences between groups. For survival, we used Kaplan-Meier-plots and subgroups were tested for significance using the Mantel-Cox test. A significance level of 5% was adopted.

Results

A total of 1220 patients with aSAH were admitted to our department during the years 2002-2012. Of these, 971 had a GCS ≥ 6 . Among the remaining 249 patients, 21 were excluded because their true status remained vague. Hence, 228 patients (18.7%) met the inclusion criteria for the present study. Fig. 1 displays the course of the 228 patients.

Patients selected for treatment

We intended to treat 176/228 patients: in 29 of these 176 patients, treatment was initiated with CSF diversion, but the patients did not go on to aneurysm repair because of uncontrollable increase in ICP (n=12), fatal rebleed prior to or during aneurysm repair (n=10), MRI showing severe anoxic brain damage resulting in withdrawal of further treatment (n=4), and complex/multiple aneurysms in a very old patient (n=3). Another patient bled at our hospital the night before elective aneurysm surgery; aneurysm repair was attempted immediately, but the patient died on the table. Hence, 146/176 patients went on to aneurysm repair (64.0%, 75 surgical -and 71 endovascular repairs, Fig. 1). Aneurysm repair was performed within six hours after the ictus in 60.3% of the 146 patients and within twelve and 24 hours in 79.5% and 93.8%, respectively. The time from arrival at the neurosurgical department to aneurysm repair was significantly shorter when performed surgically (median 1 hour 36 min versus 6 hours 34 min, $p < 0.001$, Fig. 1). All but six of the 146 patients that underwent aneurysm repair received an EVD. The six patients that were managed without CSF drains underwent surgical aneurysm repair, including opening of the lamina terminalis and removal of large hematomas. Three of them developed malignant ICP increases and quickly succumbed to their hemorrhage. Forty-three of the 75 patients with surgical aneurysm repair had their EVD inserted in conjunction with the craniotomy, whereas the other 26 had their CSF drain placed in a separate procedure prior to aneurysm repair. Every patient undergoing endovascular aneurysm repair received a temporary CSF drain prior to the endovascular procedure. Thirteen patients received a temporary CSF drain more than 24 hours prior to the aneurysm repair. In twelve of them, the delayed aneurysm repair was caused by significant vasospasm at admission, inability to identify the aneurysm, failed first attempt of aneurysm repair, or need of medical stabilization of the patient (for instance dialysis).

Table 1 shows the localization of aneurysms and method of aneurysm repair: for aneurysms on the internal carotid artery (ICA), there was no difference in surgical versus endovascular repair; whereas all middle cerebral artery (MCA) aneurysm repairs were performed surgically. Endovascular repair prevailed in aneurysms in the vertebro-basilar

circulation as well as the anterior cerebral artery (ACA) complex, and failure to go on/complete the aneurysm repair was most common in these two locations (Table 1).

Patients managed conservatively

Fifty-two patients were selected for conservative management: in 27/52 cerebral circulatory arrest was diagnosed by TCD and/or cerebral CTA after arrival or after aneurysm rebleed occurring shortly after arrival. The remaining 25 patients were managed conservatively due to: severe clinical brainstem dysfunction with irreversible bilateral pupillary dilatation and abolished cornea reflex (n=12); deep and very large hematomas including the basal ganglia with midline-shift and signs of herniation (n=4, thereof one with a giant MCA aneurysm); the combination of old age and very large hemorrhage (n=4; ages 76, 77, 77, and 79 years); comorbidity: one was critically ill at our hospital's ICU because of fungal sepsis at the time of hemorrhage and another patient was hemiplegic after an earlier aSAH and had a triple cardiac bypass and an Y-graft; MRI showing global ischemic damage (n=2); brainstem hematoma and basilar-tip giant aneurysm of 3 cm (n=1).

When not selected for treatment, patients were either extubated shortly after the decision was made or they remained on mechanical ventilatory support for organ preservation until they went on to organ donation or were extubated.

Patients selected for treatment versus those managed conservatively

Table 1 shows demographic and medical variables in all 228 patients combined and in those we intended to treat versus those managed conservatively. The time from ictus to arrival was somewhat longer in those that were chosen for treatment. Middle cerebral artery aneurysms were more common in the conservatively managed patients, whereas aneurysms on the ACA complex were more common in those we intended to treat (Table 1). Intracerebral hematomas and midline-shifts were significantly larger in patients managed conservatively than in those we intended to treat (Table 1). There was no difference in intraventricular hemorrhage in the two groups.

Bilateral pupillary dilatation was significantly more common in those managed conservatively ($p < 0.001$); however, as shown in Fig. 2, even 16% of those chosen for treatment had bilaterally dilated pupils at some point of time and for some duration. Unilateral pupillary dilatation was similar in the two groups.

Survival

In hospital mortality was 118/228 (51.8%), whereas 30-day mortality was 127/228 (55.7%), 90-day mortality 144/228 (63.2%) and 1-year mortality was 150/228 (65.8%). Beyond one year, and during the observation period of median 2932.5 days (1168-5149 days), two deaths occurred at 511 and 1198 days post hemorrhage. Hence, most fatalities occurred early, within 30 days (84.7%) as illustrated in accordance to age categories 0-45, 46-69, and ≥ 70 years, respectively in Fig. 3, upper. There was no significant difference in mortality between age groups during the first 60 days (Fig. 3, lower); thereafter a significant difference emerged, leading to patients ≥ 70 years showing a higher one year mortality ($p=0.029$).

Among the patients we intended to treat, 78/176 (44.3%) were alive one year after the ictus. Mortality was not significantly different within categories of pupillary dilatation in those we intended to treat (none: 52.0%, unilateral: 59.6%, bilateral: 63.0%, $p=0.492$).

As shown in Fig. 1, there was no difference in mortality between those undergoing surgical versus endovascular repair and none of the 82 patients that did not undergo aneurysm repair survived. All conservatively managed patients died.

Functional outcome

At discharge from our hospital, 34 patients were in a poor condition, showing no response or merely opened their eyes on command (regardless of sedative drugs administered and intubation status). Twenty-two of these 34 patients died at a median of 36 days (6.2 – 2749.2 days); whereas 12 were still alive beyond one year after the ictus. Eleven of these 12 were dependent one year after the ictus, although five of them were able to live at home with help of caretakers. After three months, one patient was vegetative and 4.4% of the 228 patients were in mRS5. After one year, none was vegetative and 2.2% were in mRS5.

There was a significant improvement in functional outcome from three months to one-year among the survivors (Wilcoxon signed ranks test: GOS: $Z=-4.147$, $p<0.001$ and mRS: $Z=-3.590$, $p<0.001$; Fig. 4). At one year, 50/78 (64.1%) lived independently (mRS score 0-2: 64.1% and GOS score 4-5: 70.5%). This corresponds to 50/228 (21.9%) individuals from the entire cohort of grade V patients admitted to our hospital living independently one year after the hemorrhage.

Among the 28 that were dependent (mRS 3-5) at one year, 17 lived at home with help from others, whereas 11 lived permanently at an institution (4.8% of the entire cohort and 14.1% of the survivors; median age 54 years; range 44-71). Cognitive impairment was the cause of dependency in 6 of the dependent patients while the remaining 5 were wheelchair-

bound due to hemiparesis. Hence, 67 of the survivors (85.9%) and correspondingly 29.4% of all 228 patients admitted lived at home at 1-year follow-up.

Occupational status prior to hemorrhage and one year after is shown in Figure 5. At 1-year follow-up, 14.0% of all individuals being employed prior to the hemorrhage had returned to paid work, and respectively, 26.3% in the subgroup of survivors. Mortality in individuals working full-time prior to the ictus was significantly lower than within the other categories of occupational status (46.3% versus 79.7%, $p < 0.001$, Fig. 5).

Discussion

The core finding of this retrospective, single center study on 228 Hunt and Hess grade V aSAH patients was that 34.2% survived and 21.9% lived independently one year after the ictus. Without aneurysm repair, mortality was 100%. Most fatalities occurred within 30 days (84.7%). Functional outcome in survivors was good, with 64.1% of survivors being mRS 0-2, and 70.5% being GOS 5-4, respectively. Return to work was 14.0% for all individuals being employed prior to the hemorrhage, and respectively, 26.3% in the subgroup of survivors.

Survival

When comparing the treatment periods 1980-1995 with 2005-2014, Konczalla et al. [19] found a six-month mortality in all grade V SAH patients submitted of 94% during the early period versus 49% during the later period. Bailes et al. [1] evaluated grade V patients admitted during the years 1986-1988 and found an overall mortality of 65.6%, which is in the same magnitude as the 60.2% reported by LeRoux et al. [26] for patients admitted between 1983-1993 and the 65.8% found in the present study. These numbers consider mortality only in those that actually reach a hospital. Pre-hospital mortality due to aSAH is usually estimated to be between 12-15% [46], but the true numbers may be as high as 26% [20]. The incidence of pre-hospital death caused by aSAH will vary with the availability of medical attention and the frequency of autopsies performed, and is hence likely to be underestimated. Mortality in all grade V hemorrhages may therefore be closer to 85%.

Swift attention of pre-hospital services capable of resuscitation and intubation may increase the chance to reach a hospital and potentially influence the chance of survival [49]. Active treatment, in particular aneurysm repair, increases the chance of survival in aSAH patients [6,51]. Vice versa, the chances to survive are poorer with conservative management, and will in grade V patients almost throughout result in death within hours or few days [16,19,23,26,33,59]. Also in the present study, all conservatively managed patients died.

Mortality in the subgroup of those actively treated including aneurysm repair is lower with 32-57%: one year survival in those that underwent aneurysm repair (53%, n=78/146) was presently lower than that reported by Wostrack et al. [59] at 3 months in WFNS grade V patients (67%, n=69/103) and Konczalla et al. [19] at 6 months in Hunt and Hess grade V patients (68%, n=94/139), but similar to that of Laidlaw and Siu [23] at 3 months in WFNS V patients (50%, n=50/99) and Inamasu et al. [16] at 3 months in GCS 3 patients (57%, n=29/51). Le Roux et al. [26] on the other hand, reported a somewhat lower survival at 6 months in their Hunt and Hess grade V patients (42%, n=33/78), as did Mocco et al. [33] at 1 year (43%, n=23/53). Use of different clinical scoring systems (Hunt and Hess versus WFNS) and different time periods from ictus to score of outcome may explain some of these differences. A common feature of the above-mentioned studies is that the vast majority of fatalities occurred within days/few weeks following ictus, which could reflect that a portion of those receiving maximum treatment actually were unsalvageable. It would also explain the present finding that age had no impact on survival during the first 60 days after aneurysm repair; i.e. the devastating force of the hemorrhage in these cases outweighed any effect of age. Mortality beyond 60 days was higher in our patients older than 70 years, which corroborates with the finding of higher mortality in patients older than 60 years in the grade V subgroup of SAH [19,59].

Along with the fear of producing heavily dependent survivors, the economic burden of extensive ICU care and prolonged rehabilitation efforts in poor grade aSAH patients is an important argument behind conservative management protocols [7,41], as the cost of a grade V patient is about twice that of a grade 1 patient [7]. Presently, the majority of deaths in patients undergoing early aneurysm repair occurred early; median time to death was 12 days, and 84.7% of fatalities occurred within 30 days. Delayed aneurysm repair on the other hand, results in increased rebleed rates [23,49]. With rebleeding being the most important factor for poor outcome in aSAH, a study analysing the costs of aSAH recommended that all efforts should be directed at reducing the risk of rebleeding and aneurysm repair should be initiated early [41].

Functional outcome

Full or nearly full recovery is nowadays anticipated in good grade aSAH patients, whereas poor grade patients are generally alleged to have a much worse prognosis [38]. Large numbers of dependent survivors have thus been a feared consequence of an aggressive aneurysm repair policy in primarily comatose aSAH patients. Laidlaw et al. [23] studied

1 outcome in 391 consecutive patients selected for aggressive treatment regardless of clinical
2 grade and age, and they found 2.9% vegetative patients at three months in their WFNS V
3 cohort. In the study of Konczalla et al. [19], outcome was not reported in GOS, but 11.9% of
4 grade V patients actively treated were in mRS 5 at 6 months, which is somewhat higher than
5 our finding of 5.7% in mRS 5 in those we intended to treat and correspondingly 4.4% in the
6 entire cohort at three months. Wostrack et al. [59] reported 18.5% of actively treated SAH
7 patients in GCS 3-6 surviving to a vegetative state at median 20 months after the hemorrhage.
8 The discrepancy to our finding of none of the patients being in a vegetative state after one
9 year, may possibly be explained by a higher mortality in our series (46.6% mortality in those
10 with aneurysm repair as compared to 33% in Wostracks series); i.e. the frailest of our patients
11 seem not to have survived until follow-up.
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20 Among all our grade V patients admitted, 21.9% survived to a favorable outcome
21 (mRS 0-2) at one year. This concurs well with the 23% favorable outcome (mRS 0-2) six
22 months after the ictus in grade V SAH patients reported by Konczalla et al. [19]. Their
23 outcome in grade V SAH patients was significantly better than the corresponding 3.4%
24 favorable outcome at 6-12 months in patients treated with decompressive craniectomy due to
25 MCA infarction [19]. Wostrack et al. [59] reported that 26% of their actively treated grade V
26 patients were in GOS 5 and 4 at last follow-up (at median 20 months) and they concluded
27 from this that refraining from treating WNFS grade V patients no longer is acceptable.
28 Likewise, Laidlaw et al. [23] found 23.6% good outcome (GOS 5 and 4) in all their WFNS
29 grade V patients admitted and they recommend early aneurysm repair throughout all clinical
30 grades of aSAH, with poor grade patients presumably benefitting the most due to the high risk
31 of rebleeding in that subgroup. Early aneurysm rebleed has been shown to occur at higher
32 rates in poor grade patients and within the first six hours after the ictus [25,53]. Sorteberg et
33 al. [49] have recently shown that the frequency of early aneurysm rebleed increases almost
34 exponentially with Hunt and Hess grade, reaching a 6.5% hourly rebleed rate in grade V
35 patients. Presently, there was a high rebleeding rate of 25%, and patients selected for
36 aneurysm repair died due to fatal rebleeding in the time period between arrival and aneurysm
37 occlusion although we practice an ultra-early management policy [50].
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53 When investigating outcome in terms of cognitive functioning and health-related
54 quality of life one year after the ictus, Haug et al. [11] found that more than half of Hunt and
55 Hess grade V survivors had good cognitive and physical function, at a quality of life not
56 significantly different from the population mean. Their findings were later confirmed by
57 several larger studies on comatose aSAH patients that also were managed rigorously with
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early intervention [16,19,59]. Despite many patients recovering to a good functional outcome after aSAH, many have permanent residual symptoms impairing their daily live and ability to return to work [10]. Powell et al. [39] investigated psychosocial outcome in WFNS I and II patients with good outcome 18 months after the ictus and found it remarkable that despite being physically intact and cognitively functioning within normal limits, the patients showed low levels of productive employment-related activities. Including the entire range of aSAH patients, also others found that return to work is relatively low and a major issue [10,37]. In a selected cohort of grade V survivors, return to work was 34.8% [11], which corresponds to the 26.3% found in the present subgroup of survivors.

Patient selection for aneurysm repair

The proper selection of comatose aSAH patients to aneurysm repair is challenging due to the limited insight in risk factors and predictors of favorable outcome in these patients. It is well established that neurological status at admission alone is not the optimal selection criterion for active treatment [1,4,33,48,56]. Comatose aSAH patients often present with increased ICP and may harbour intracranial blood clots (parenchymal, ventricular and/or subdural), which could be responsible for the clinical presentation, but can potentially improve the clinical status considerably upon removal [9,12,14,21,22,47,55,58]. Large intracerebral hemorrhages have been associated with MCA aneurysms, and led in the present study rather to conservative management. Some institutions base selection to aneurysm repair on clinical improvement after ventriculostomy, with a controllable ICP [1,14,35,44,48,52,56]. This “wait-and-see” policy can avoid overtreatment of unsalvageable cases; however, it also carries the danger of aneurysm rebleed with fatal consequences in a patient that otherwise could be saved [24]. The frequency of our patients actively treated with unilateral and bilateral pupillary dilatation corresponds well to that reported by Wostrack et al. [59]. Pupillary dilatation has been proposed as a grading tool in poor grade patients [8]. There seems to be, however, a certain time frame where even bilateral pupillary dilatation can be reversible without long-term sequelae [40,43]. This notion is supported by the lack of relation between pupillary dilatation and mortality in the patients we intended to treat. Nonetheless, it remains obscure which time period of bilateral pupillary dilatation is compatible with meaningful survival.

Wostrack et al. [59] propose that treatment of grade V SAH patients with intraventricular hemorrhage and in old patients should be performed more restrictive because their prognosis is particularly poor. In their material, unfavorable outcome in GOS 3 and 2

was much more common in those >60 years of age than in the younger patients (54% versus 34%) [59]. Konczalla et al. [19] recommend that SAH guidelines should favor early treatment in comatose patients younger than 61 years. This corroborates with our finding of higher mortality in patients >70 years of age.

Limitations and strengths

The main weakness of our study is its retrospective design. A randomised, controlled trial allocating patients to aneurysm repair versus conservative treatment would be ethically not justifiable, knowing that conservative treatment of Hunt and Hess grade V patients almost invariably leads to death. The decision process of offering active treatment or conservative management was presently in the hands of the vascular team on call, and hence not only regulated by our institutional guidelines, but also by the individual consideration of how salvageable a patient was and if active treatment was meaningful. Our guidelines instruct on ultra-early aneurysm repair regardless of clinical grade, and therefore, we included basically all patients with the exception of those presenting with cerebral circulatory arrest confirmed by TCD and/or CTA, those with abolished brain stem reflexes, and those with deep and very large hematomas also affecting the basal ganglia and causing midline-shift with signs of herniation. This is reflected in the significantly larger size of intracerebral hematomas and midline-shifts in those we managed conservatively. LeRoux et al. [26] also managed patients without brainstem-reflexes conservatively but allocated all other poor grade patients to treatment. Presently, global ischemic hypoxia on cerebral MRI led to the choice of conservative treatment in two cases, but could give cause to withdraw further active treatment if such was initiated. Our selection to treatment widely concurs with that described by Konczalla et al. [19] and therefore their and our rates of cases undergoing aneurysm repair within all grade V patients admitted is similar (64% versus 68.5%). One could, however, argue whether the cases we managed conservatively due to comorbidity also should have been offered active treatment. The bias regarding patient selection limits the applicability of our findings into guidelines for treatment of grade V SAH patients, but they add some more information to the hitherto limited knowledge about proper selection and treatment algorithms within this patient cohort. Future studies in this patient group should aim at identifying markers for survival and establish a prognostic scoring system for this aSAH subpopulation.

The present study is one of the largest analysing exclusively Hunt and Hess V patients, within the larger cohort of “poor grade patients”. A concern of studies on this topic often involves the question whether the patients truly were grade V. With regard to this, a strength

of the study is that it spans the years 2002-2012, a time period when patients were not always intubated as early as they are today, i.e. pre-emptively, at a higher level of consciousness [31,49]. One could hence anticipate that the patient's poor clinical presentation was precisely and properly assessed, i.e. the study included only true Hunt and Hess grade V aSAH patients. Patients with obvious epileptic fits and patients where there was any doubt about their state of consciousness were also excluded from this study. Furthermore, the patients were admitted swiftly after the ictus and received CSF diversion almost immediately after arrival, thus the chance of their coma being caused by mainly hydrocephalus is negligible. Another strength is the 24/7 availability of both surgical and endovascular teams provided at our center, avoiding bias related to only a surgical or endovascular treatment option.

Conclusions

One year mortality in aSAH patients in GCS 3-5 admitted to our department was high with 65.8%. Without aneurysm repair, mortality was 100%. Most of the fatalities (84.7%) occurred within 30 days. After one year, 21.9% of all patients lived independently and 4.8% lived permanently in an institution. Outcome in survivors was favorable (mRS 0-2) in 64.1% and 85.9% of survivors were able to live at home after one year.

Funding: No funding was received for this research.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: For this type of study formal consent is not required.

Comments:

Treatment of patients with poor grade aneurysmal subarachnoid hemorrhage (aSAH) has changed in the last two decades. Where previously this group of patients has traditionally been offered conservative treatment, several studies have now been published in support of treatment of these patients. Not coincidentally, these new studies have been published since the rise of endovascular treatment of cerebral aneurysms. Lashkarivand et al present here their institutional experience with treatment of patients with Hunt and Hess Grade V aSAH from 2002-2012. Among the 228 patients with Grade V aSAH, 146 underwent aneurysm repair, while 82 did not. Patients who were not treated included those with large, deep hematoma in the dominant hemisphere, signs of permanent brain dysfunction and those with evidence of severely deranged or abolished intracranial circulation. Unsurprisingly, those who did not

receive aneurysmal treatment died. Of those who did undergo aneurysm repair, approximately half underwent surgical repair, while the other half underwent endovascular repair. Of all treated patients, approximately 53% were alive one year after ictus, with the majority (50/78) with good functional status (modified Rankin Scale 0-2). Neither survival outcomes nor functional outcomes stray from previously published data in this patient population. This is one of the largest series on outcomes of patients who present with Hunt and Hess grade V aSAH. The authors should be commended on their large series and patient outcomes. This addition to the literature only furthers the notion that many of the patients with a devastating high grade aSAH, if selected properly for treatment, can recover to be functionally independent at one year after presenting with aSAH.

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References

1. Bailes JE, Spetzler RF, Hadley MN, Baldwin HZ (1990) Management morbidity and mortality of poor-grade aneurysm patients. *Journal of neurosurgery* 72:559-566. doi:10.3171/jns.1990.72.4.0559
2. Cesarini KG, Hardemark HG, Persson L (1999) Improved survival after aneurysmal subarachnoid hemorrhage: review of case management during a 12-year period. *Journal of neurosurgery* 90:664-672. doi:10.3171/jns.1999.90.4.0664
3. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40:373-383. doi:10.1016/0021-9681(87)90171-8
4. Chiang VL, Claus EB, Awad IA (2000) Toward more rational prediction of outcome in patients with high-grade subarachnoid hemorrhage. *Neurosurgery* 46:28-35; discussion 35-26
5. Claassen J, Bernardini GL, Kreiter K, Bates J, Du YE, Copeland D, Connolly ES, Mayer SA (2001) Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: the Fisher scale revisited. *Stroke* 32:2012-2020
6. Connolly ES, Jr., Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, Hoh BL, Kirkness CJ, Naidech AM, Ogilvy CS, Patel AB, Thompson BG, Vespa P, American Heart Association Stroke C, Council on Cardiovascular R, Intervention, Council on Cardiovascular N, Council on Cardiovascular S, Anesthesia, Council on Clinical C (2012) Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 43:1711-1737. doi:10.1161/STR.0b013e3182587839
7. Dodel R, Winter Y, Ringel F, Spottke A, Gharevi N, Muller I, Klockgether T, Schramm J, Urbach H, Meyer B (2010) Cost of illness in subarachnoid hemorrhage: a German longitudinal study. *Stroke* 41:2918-2923. doi:10.1161/STROKEAHA.110.586826
8. Fung C, Inglin F, Murek M, Balmer M, Abu-Isa J, Z'Graggen WJ, Ozdoba C, Gralla J, Jakob SM, Takala J, Beck J, Raabe A (2016) Reconsidering the logic of World Federation of Neurosurgical Societies grading in patients with severe subarachnoid hemorrhage. *Journal of neurosurgery* 124:299-304. doi:10.3171/2015.2.JNS14614
9. Guresir E, Beck J, Vatter H, Setzer M, Gerlach R, Seifert V, Raabe A (2008) Subarachnoid hemorrhage and intracerebral hematoma: incidence, prognostic factors, and outcome. *Neurosurgery* 63:1088-1093; discussion 1093-1084. doi:10.1227/01.NEU.0000335170.76722.B9
10. Haug Nordenmark T, Karic T, Roe C, Sorteberg W, Sorteberg A (2019) The post-aSAH syndrome: a self-reported cluster of symptoms in patients with aneurysmal subarachnoid hemorrhage. *Journal of neurosurgery*:1-10. doi:10.3171/2019.1.JNS183168

11. Haug T, Sorteberg A, Finset A, Lindegaard KF, Lundar T, Sorteberg W (2010) Cognitive functioning and health-related quality of life 1 year after aneurysmal subarachnoid hemorrhage in preoperative comatose patients (Hunt and Hess Grade V patients). *Neurosurgery* 66:475-484; discussion 484-475. doi:10.1227/01.NEU.0000365364.87303.AC
12. Heros RC (1989) Acute hydrocephalus after subarachnoid hemorrhage. *Stroke* 20:715-717
13. Hunt WE, Hess RM (1968) Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *Journal of neurosurgery* 28:14-20. doi:10.3171/jns.1968.28.1.0014
14. Hutchinson PJ, Power DM, Tripathi P, Kirkpatrick PJ (2000) Outcome from poor grade aneurysmal subarachnoid haemorrhage--which poor grade subarachnoid haemorrhage patients benefit from aneurysm clipping? *British journal of neurosurgery* 14:105-109
15. Inagawa T, Takahashi M, Aoki H, Ishikawa S, Yoshimoto H (1988) Aneurysmal subarachnoid hemorrhage in Izumo City and Shimane Prefecture of Japan. Outcome. *Stroke* 19:176-180
16. Inamasu J, Nakae S, Ohmi T, Kogame H, Kawazoe Y, Kumai T, Tanaka R, Wakako A, Kuwahara K, Ganaha T, Hirose Y (2016) The outcomes of early aneurysm repair in World Federation of Neurosurgical Societies grade V subarachnoid haemorrhage patients with emphasis on those presenting with a Glasgow Coma Scale score of 3. *J Clin Neurosci* 33:142-147. doi:10.1016/j.jocn.2016.03.035
17. Jennett B, Bond M (1975) Assessment of Outcome after Severe Brain-Damage - Practical Scale. *Lancet* 1:480-484
18. Kassell NF, Torner JC, Haley EC, Jr., Jane JA, Adams HP, Kongable GL (1990) The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: Overall management results. *Journal of neurosurgery* 73:18-36. doi:10.3171/jns.1990.73.1.0018
19. Konczalla J, Seifert V, Beck J, Guresir E, Vatter H, Raabe A, Marquardt G (2018) Outcome after Hunt and Hess Grade V subarachnoid hemorrhage: a comparison of pre-coiling era (1980-1995) versus post-ISAT era (2005-2014). *Journal of neurosurgery* 128:100-110. doi:10.3171/2016.8.JNS161075
20. Korja M, Lehto H, Juvela S, Kaprio J (2016) Incidence of subarachnoid hemorrhage is decreasing together with decreasing smoking rates. *Neurology* 87:1118-1123. doi:10.1212/WNL.0000000000003091
21. Kosteljanetz M (1985) Pressure-volume conditions in patients with subarachnoid and/or intraventricular hemorrhage. *Journal of neurosurgery* 63:398-403. doi:10.3171/jns.1985.63.3.0398
22. Kusske JA, Turner PT, Ojemann GA, Harris AB (1973) Ventriculostomy for the treatment of acute hydrocephalus following subarachnoid hemorrhage. *Journal of neurosurgery* 38:591-595. doi:10.3171/jns.1973.38.5.0591
23. Laidlaw JD, Siu KH (2002) Ultra-early surgery for aneurysmal subarachnoid hemorrhage: outcomes for a consecutive series of 391 patients not selected by grade or age. *Journal of neurosurgery* 97:250-258; discussion 247-259. doi:10.3171/jns.2002.97.2.0250
24. Laidlaw JD, Siu KH (2003) Poor-grade aneurysmal subarachnoid hemorrhage: outcome after treatment with urgent surgery. *Neurosurgery* 53:1275-1280; discussion 1280-1272
25. Larsen CC, Astrup J (2013) Rebleeding after aneurysmal subarachnoid hemorrhage: a literature review. *World Neurosurg* 79:307-312. doi:10.1016/j.wneu.2012.06.023
26. Le Roux PD, Elliott JP, Newell DW, Grady MS, Winn HR (1996) Predicting outcome in poor-grade patients with subarachnoid hemorrhage: a retrospective review of 159 aggressively managed cases. *Journal of neurosurgery* 85:39-49. doi:10.3171/jns.1996.85.1.0039
27. LeRoux PD, Haglund MM, Newell DW, Grady MS, Winn HR (1992) Intraventricular hemorrhage in blunt head trauma: an analysis of 43 cases. *Neurosurgery* 31:678-684; discussion 684-675
28. Lindegaard KF, Bakke SJ, Sorteberg W, Nakstad P, Nornes H (1986) A non-invasive Doppler ultrasound method for the evaluation of patients with subarachnoid hemorrhage. *Acta Radiol Suppl* 369:96-98
29. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P (1988) Cerebral vasospasm after subarachnoid haemorrhage investigated by means of transcranial Doppler ultrasound. *Acta Neurochir Suppl (Wien)* 42:81-84
30. Longstreth WT, Jr., Nelson LM, Koepsell TD, van Belle G (1993) Clinical course of spontaneous subarachnoid hemorrhage: a population-based study in King County, Washington. *Neurology* 43:712-718. doi:10.1212/wnl.43.4.712
31. Luoma A, Reddy U (2013) Acute management of aneurysmal subarachnoid haemorrhage. *Continuing Education in Anaesthesia Critical Care & Pain* 13:52-58. doi:10.1093/bjaceaccp/mks054
32. Mataro M, Poca MA, Sahuquillo J, Cuxart A, Iborra J, de la Calzada MD, Junque C (2000) Cognitive changes after cerebrospinal fluid shunting in young adults with spina bifida and assumed arrested hydrocephalus. *J Neurol Neurosurg Ps* 68:615-621. doi:DOI 10.1136/jnnp.68.5.615

33. Mocco J, Ransom ER, Komotar RJ, Schmidt JM, Sciacca RR, Mayer SA, Connolly ES, Jr. (2006) Preoperative prediction of long-term outcome in poor-grade aneurysmal subarachnoid hemorrhage. *Neurosurgery* 59:529-538; discussion 529-538. doi:10.1227/01.NEU.0000228680.22550.A2
34. Nieuwkamp DJ, Setz LE, Algra A, Linn FH, de Rooij NK, Rinkel GJ (2009) Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. *Lancet Neurol* 8:635-642. doi:10.1016/S1474-4422(09)70126-7
35. Nowak G, Schwachenwald R, Arnold H (1994) Early management in poor grade aneurysm patients. *Acta Neurochir (Wien)* 126:33-37
36. Ogden JA, Utley T, Mee EW (1997) Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. *Neurosurgery* 41:25-34. doi:10.1097/00006123-199707000-00008
37. Passier PE, Visser-Meily JM, Rinkel GJ, Lindeman E, Post MW (2011) Life satisfaction and return to work after aneurysmal subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis* 20:324-329. doi:10.1016/j.jstrokecerebrovasdis.2010.02.001
38. Pegoli M, Mandrekar J, Rabinstein AA, Lanzino G (2015) Predictors of excellent functional outcome in aneurysmal subarachnoid hemorrhage. *Journal of neurosurgery* 122:414-418. doi:10.3171/2014.10.JNS14290
39. Powell J, Kitchen N, Heslin J, Greenwood R (2004) Psychosocial outcomes at 18 months after good neurological recovery from aneurysmal subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 75:1119-1124. doi:10.1136/jnnp.2002.000414
40. Ritter AM, Muizelaar JP, Barnes T, Choi S, Fatouros P, Ward J, Bullock MR (1999) Brain stem blood flow, pupillary response, and outcome in patients with severe head injuries. *Neurosurgery* 44:941-948. doi:10.1097/00006123-199905000-00005
41. Roos YB, Dijkgraaf MG, Albrecht KW, Beenen LF, Groen RJ, de Haan RJ, Vermeulen M (2002) Direct costs of modern treatment of aneurysmal subarachnoid hemorrhage in the first year after diagnosis. *Stroke* 33:1595-1599. doi:10.1161/01.str.0000016401.49688.2f
42. Rosseland LA, Narum J, Stubhaug A, Kongsgaard U, Sorteberg W, Sorteberg A (2015) The effect of tracheotomy on drug consumption in patients with acute aneurysmal subarachnoid hemorrhage: an observational study. *BMC Anesthesiol* 15:47. doi:10.1186/s12871-015-0029-5
43. Sakas DE, Bullock MR, Teasdale GM (1995) One-year outcome following craniotomy for traumatic hematoma in patients with fixed dilated pupils. *Journal of neurosurgery* 82:961-965. doi:10.3171/jns.1995.82.6.0961
44. Sasaki T, Sato M, Oinuma M, Sakuma J, Suzuki K, Matsumoto M, Kodama N (2004) Management of poor-grade patients with aneurysmal subarachnoid hemorrhage in the acute stage: Importance of close monitoring for neurological grade changes. *Surg Neurol* 62:531-535; discussion 535-537. doi:10.1016/j.surneu.2004.01.015
45. Saveland H, Hillman J, Brandt L, Edner G, Jakobsson KE, Algers G (1992) Overall outcome in aneurysmal subarachnoid hemorrhage. A prospective study from neurosurgical units in Sweden during a 1-year period. *Journal of neurosurgery* 76:729-734. doi:10.3171/jns.1992.76.5.0729
46. Schievink WI, Wijdicks EF, Parisi JE, Piepgras DG, Whisnant JP (1995) Sudden death from aneurysmal subarachnoid hemorrhage. *Neurology* 45:871-874. doi:10.1212/wnl.45.5.871
47. Schuss P, Konczalla J, Platz J, Vatter H, Seifert V, Guresir E (2013) Aneurysm-related subarachnoid hemorrhage and acute subdural hematoma: single-center series and systematic review. *Journal of neurosurgery* 118:984-990. doi:10.3171/2012.11.JNS121435
48. Seifert V, Trost HA, Stolke D (1990) Management morbidity and mortality in grade IV and V patients with aneurysmal subarachnoid haemorrhage. *Acta Neurochir (Wien)* 103:5-10
49. Sorteberg A, Bredmose PP, Hansen AE, Sorteberg W (2019) The path from ictus to Neurosurgery: chronology and transport logistics of patients with aneurysmal subarachnoid haemorrhage in the South-Eastern Norway Health Region. *Acta Neurochir (Wien)* 161:1497-1506. doi:10.1007/s00701-019-03971-9
50. Sorteberg W, Slettebo H, Eide PK, Stubhaug A, Sorteberg A (2008) Surgical treatment of aneurysmal subarachnoid haemorrhage in the presence of 24-h endovascular availability: management and results. *British journal of neurosurgery* 22:53-62. doi:10.1080/02688690701593553
51. Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G, European Stroke O (2013) European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovasc Dis* 35:93-112. doi:10.1159/000346087
52. Steudel WI, Reif J, Voges M (1994) Modulated surgery in the management of ruptured intracranial aneurysm in poor grade patients. *Neurological research* 16:49-53

53. Tang C, Zhang TS, Zhou LF (2014) Risk factors for rebleeding of aneurysmal subarachnoid hemorrhage: a meta-analysis. *PLoS One* 9:e99536. doi:10.1371/journal.pone.0099536
54. Testa C, Andreoli A, Arista A, Limoni P, Tognetti F (1985) Overall results in 304 consecutive patients with acute spontaneous subarachnoid hemorrhage. *Surg Neurol* 24:377-385. doi:10.1016/0090-3019(85)90294-0
55. Torne R, Rodriguez-Hernandez A, Romero-Chala F, Arikan F, Vilalta J, Sahuquillo J (2016) Prognosis of patients in coma after acute subdural hematoma due to ruptured intracranial aneurysm. *J Clin Neurosci* 26:126-129. doi:10.1016/j.jocn.2015.06.028
56. Ungersbock K, Bocher-Schwarz H, Ulrich P, Wild A, Perneczky A (1994) Aneurysm surgery of patients in poor grade condition. Indications and experience. *Neurological research* 16:31-34
57. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J (1988) Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 19:604-607
58. Wan A, Jaja BNR, Schweizer TA, Macdonald RL, collaboration obotS (2016) Clinical characteristics and outcome of aneurysmal subarachnoid hemorrhage with intracerebral hematoma. *Journal of neurosurgery* 125:1344-1351
59. Wostrack M, Sandow N, Vajkoczy P, Schatlo B, Bijlenga P, Schaller K, Kehl V, Harmening K, Ringel F, Ryang YM, Friedrich B, Stoffel M, Meyer B (2013) Subarachnoid haemorrhage WFNS grade V: is maximal treatment worthwhile? *Acta Neurochir (Wien)* 155:579-586. doi:10.1007/s00701-013-1634-z

Figure legends

Figure 1: Flow-chart illustrating the course of the 228 Hunt and Hess grade V patients included in the study. : surgical aneurysm repair, : endovascular aneurysm repair, †: mortality.

Figure 2: Pupillary dilatation regardless of duration in patients we intended to treat (left columns, n=176), and in those managed conservatively (right columns, n=52). Blue: no pupillary dilatation, orange: unilateral pupillary dilatation, gray: bilateral pupillary dilatation.

Figure 3: One-year survival (upper) and 90-day survival (lower) in the 228 patients for age categories 0-45 (green), 46-69 (red), and ≥ 70 years (blue). There was no significant difference between age groups during the first 60 days; however, in patients ≥ 70 years mortality was higher at 90 days and 1-year.

Figure 4: Glasgow Outcome Scale score (GOS, left) and modified Rankin Scale score (mRS, right) at three months (upper bars) and at one-year after the ictus (lower bars). Green color shades indicate independent functional outcome, whereas yellow/orange color shades represent dependent functional outcome. Black: dead.

Figure 5: Occupational status prior to ictus (light blue columns) and at one year (green columns) in the 228 patients. The hatched area indicates dead individuals within each category of occupational status.