2023

Retrospective analysis of prospectively collected data from the multicentric Poor-grade aneurysmal subarachnoid hemorrhage Study Group (POGASH) registry of consecutive patients treated from January 1, 2015, to June 30th, 2021. Grading was defined as pretreatment World Federation of Neurological Surgeons grading scale IV-V. Ultra-early vasospasm (UEV) was defined as luminal narrowing of intracranial arteries not due to intrinsic disease. Rebleeding was defined as clinical deterioration with evidence of increased hemorrhage on subsequent computed tomography scans, fresh blood from the external ventricular drain, or deterioration before neuroradiological evaluation. The outcome was assessed by the modified Rankin Scale.

Among 443 consecutive World Federation of Neurological Surgeons grades IV-V patients with aSAH treated within a median of 5 (IQR 4-9) hours since onset, rebleeding occurred in 78 (17.6%). UEV (adjusted odds ratio [OR] 6.8, 95% CI 3.2-14.4; P < .001) and presence of dissecting aneurysm (adjusted OR 3.5, 95% CI 1.3-9.3; P = .011) independently predicted rebleeding while the history of hypertension (adjusted OR 0.4, 95% CI 0.2-0.8; P = .011) independently reduced its chances. 143 (32.3) patients died during hospitalization. Rebleeding emerged, among others, as an independent predictor of intrahospital mortality (adjusted OR 2.2, 95% CI 1.2-4.1; P = .009).

Ultra-early vasospasm (UEV) and the presence of dissecting aneurysms are the strongest predictors of aneurysmal rebleeding. Their presence should be carefully evaluated in the acute management of poor-grade aSAH [1)].

A study aimed to develop a stable nomogram model for predicting adverse outcomes at 6 months in patients with aSAH, and thus, aid in improving the prognosis.

Method: The clinical data and imaging findings of 150 patients with poor-grade aSAH treated with microsurgical clipping of intracranial aneurysms on admission from December 2015 to October 2021 were retrospectively analyzed. The least absolute shrinkage and selection operator (LASSO), logistic regression analyses, and a nomogram were used to develop the predictive models. Receiver operating characteristic (ROC) curves and Hosmer-Lemeshow tests were used to assess discrimination and calibration. The bootstrap method (1,000 repetitions) was used for internal validation. Decision curve analysis (DCA) was performed to evaluate the clinical validity of the nomogram model.

Result: LASSO regression analysis showed that age, Hunt-Hess grade, Glasgow Coma Scale (GCS), aneurysm size, and refractory hyperpyrexia were potential predictors for poor-grade aSAH. Logistic regression analyses revealed that age (OR: 1.107, 95% CI: 1.056-1.116, P < 0.001), Hunt-Hess grade (OR: 8.832, 95% CI: 2.312-33.736, P = 0.001), aneurysm size (OR: 6.871, 95% CI: 1.907-24.754, P = 0.003) and refractory fever (OR: 3.610, 95% CI: 1.301-10.018, P < 0.001) were independent predictors of poor outcome. The area under the ROC curve (AUC) was 0.909. The calibration curve and Hosmer-Lemeshow tests showed that the nomogram had good calibration ability. Furthermore, the DCA curve showed better clinical utilization of the nomogram.

This study provides a reliable and valuable nomogram that can accurately predict the risk of poor prognosis in patients with poor-grade aSAH after microsurgical clipping. This tool is easy to use and can help physicians make appropriate clinical decisions to improve patient prognosis significantly [2)].

During the 5-year period, 415 patients with intracranial aneurysm were admitted to our institution. Patients with poor-grade aneurysmal SAH accounted 31.08% (n = 132) of the total number of ruptured aneurysms. Interventional treatment was predominantly in the form of surgery, whereas conservative treatment included medication and external ventricular drainage. Final outcome was assessed with a modified Rankin score (mRs). Statistical analysis was performed using SPSS version 23.0 with a significance level set to 5% (α = 0.05). Results The majority of patients (57.6%) were in the age range of 51 to 69 years. Twenty-five patients (18.9%) had an HH score of 4, whereas 107 patients (81.1%) had an HH score of 5. Depending on the location, the majority of patients (n = 43) had an aneurysm on the medial cerebral artery (MCA). The final aneurysm occlusion was performed in 71 patients, of whom 94.36% were treated surgically. A positive outcome (mRs 0-4) was found in 49.25% of patients who underwent primary surgical, treatment with a mortality of 42.3%. Although the outcome was better in patients with an HH score of 4, both groups benefited from surgical treatment. Poor-grade aneurismal SAH is a condition of middle and older age, with most patients with an HH 5 score and a deep comatose state. There was a better outcome in patients with an HH score of 4 compared to an HH score of 5 and both groups benefited from surgical treatment, which resulted in a positive outcome in almost 50% of surgically treated patients [3)].

Decompressive craniectomy is an option to decrease elevated intracranial pressure in poor-grade aneurysmal subarachnoid hemorrhage (SAH) patients. The aim of the study of Vychopen et al. was to analyze the size of the bone flap according to approach-related complications in patients with poor-grade SAH. They retrospectively analyzed poor-grade SAH patients (WFNS 4 and 5) who underwent aneurysm clipping and craniectomy (DC or omittance of bone flap reinsertion). Postoperative CT scans were analyzed for approach-related tissue injury at the margin of the craniectomy (shear bleeding). The size of the bone flap was calculated using the De Bonis equation. Between 01/2012 and 01/2020, 67 poor-grade SAH patients underwent clipping and craniectomy at our institution. They found 14 patients with new shear bleeding lesions in postoperative CT scans. In patients with shear bleeding, the size of the bone flap was significantly smaller compared to patients without shear bleeding (102.1 ± 45.2 cm2 vs. 150.8 ± 37.43 cm2, p > 0.0001). However, we found no difference in mortality rates (10/14 vs. 23/53, p = 0.07) or number of implanted VP shunts (2/14 vs. 18/53, p = 0.2). They found no difference regarding the modified Rankin Scale (mRS) 6 months postoperatively. In poor-grade aneurysmal SAH, the initial planning of DC-if deemed necessary -and enlargement of the flap size seems to decrease the rate of postoperatively developed shear bleeding lesions [4)].

The aim was to study the course of body temperature in the acute phase of poor-grade aneurysmal subarachnoid hemorrhage (aSAH) in relation to the primary brain injury, cerebral physiology, and clinical outcome.

Methods: In this observational study, 166 patients with aSAH treated at the neurosurgery department at Uppsala University Hospital in Sweden between 2008 and 2018 with temperature, intracranial pressure (ICP), and microdialysis (MD) monitoring were included. The first 10 days were divided into the early phase (days 1-3) and the vasospasm phase (days 4-10).

Results: Normothermia (temperature = 36-38 °C) was most prevalent in the early phase. A lower mean temperature at this stage was univariately associated with a worse primary brain injury, with

higher Fisher grade and higher MD glycerol concentration, as well as a worse neurological recovery at 1 year. There was otherwise no association between temperature and cerebral physiological variables in the early phase. There was a transition toward an increased burden of hyperthermia (temperature > 38 °C) in the vasospasm phase. This was associated with concurrent infections but not with neurological or radiological injury severity at admission. The elevated temperature was associated with higher MD pyruvate concentration, a lower rate of an MD pattern indicative of ischemia, and a higher rate of poor neurological recovery at 1 year. There was otherwise no association between temperature and cerebral physiological variables in the vasospasm phase. The associations between temperature and clinical outcome did not hold true in multiple logistic regression analyses.

Conclusions: Spontaneously low temperature in the early phase reflected a worse primary brain injury and indicated a worse outcome prognosis. Hyperthermia was common in the vasospasm phase and was more related to infections than primary injury severity but also with a more favorable energy metabolic pattern with better substrate supply, possibly related to hyperemia [5)]

2019

A total of 104 consecutive patients with poor-grade aSAH from the Department of Neurosurgery, The Second Hospital of Shandong University, Jinan, were enrolled between January 2010 and December 2017. All these patients underwent early microsurgical clipping or endovascular coiling within three days after onset. Microsurgical clipping or endovascular coiling was selected according to aneurysm patterns, patient clinical status, interdisciplinary consultation, and the decision-making of the family. The individual prognosis was evaluated using the modified Rankin scale (mRS), while the prognostic factors were analyzed using multivariate logistic regression analysis.

There were 58 patients with grade IV aSAH and 46 patients with grade V aSAH. Microsurgical clipping was performed in 71 cases, while endovascular coiling was performed in 33 cases. According to the statistical results, microsurgical clipping was preferred by patients with CT Fisher grade III-IV, WFNS grade V, cerebral hernia, intracranial hematoma and preoperative rebleeding. At six months after onset, the overall rate of favorable outcome (mRS ≤ 2) was 36.5%. Furthermore, the favorable outcome rate was 56.9% in grade IV patients and 11.1% in grade V patients. Moreover, the univariate and multivariate logistic regression analyses revealed that CT Fisher grade I-II, WFNS grade IV, and endovascular coiling were associated with a favorable prognosis, while the CT low-density area was slightly correlated to a poor prognosis.

The treatment of aSAH at the early stage by microsurgical clipping or endovascular coiling should be highlighted, especially for patients with WFNS grade IV. CT Fisher grade I-II, WFNS grade IV and endovascular coiling may predict a favorable prognosis, and the CT low-density area appeared to be a possible risk factor for poor prognosis [6)].

2018

Goldberg et al., performed a retrospective analysis of the Bernese SAH database for poor-grade (World Federation of Neurosurgical Societies grade IV and V) elderly patients (age ≥60 years) suffering from aSAH admitted to our institution from 2005 to 2017. Patients were divided into 3 age groups (60-69, 70-79, and 80-90 years). Survival analysis was performed to estimate mean survival and hazard ratios for death. Binary logarithmic regression was used to estimate the odds ratio for favorable (modified Rankin Scale score of 0-3) and unfavorable (modified Rankin Scale score of 4-6) outcome. Results- Increasing age was associated with an increasing risk of death after aSAH. The

hazard ratio increased by 6% per year of age (P<0.001; hazard ratio, 1.06; 95% CI, 1.03-1.09) and 76% per decade (P<0.001; hazard ratio, 1.76; 95% CI, 1.35-2.29). Mean survival was 56.3±8 months (patients aged 60-69 years), 31.6±7.6 months (70-79 years), and 7.6±5.8 months (80-90 years). Unfavorable outcomes 6 to 12 months after aSAH were strongly related to older age. The odds ratio increased by 11% per year of age (P<0.001; odds ratio, 1.11; 95% CI, 1.05-1.18) and 192% per decade (P<0.001; odds ratio, 2.92; 95% CI, 1.63-5.26). Conclusions- Risk for death and unfavorable outcome increases markedly with older age in elderly patients with poor-grade aSAH. Despite a high initial mortality, treatment resulted in a reasonable proportion of favorable outcomes up to 79 years of age and only a small number of patients who were moderately or severely disabled 6 to 12 months after aSAH. Mean survival and proportion of favorable outcomes decreased markedly in patients older than 80 years [7)].

2016

During the period 2004-2014, 248 patients with poor-grade SAH were treated in our institution. Poor-grade SAH was defined as World Federation of Neurological Surgeons grades IV-V on admission. Data including patient characteristics, treatment modality, radiologic features, and functional neurologic outcome were assessed and further analyzed. Outcome was assessed according to the modified Rankin Scale after 6 months and stratified into favorable (modified Rankin Scale score 0-2) versus unfavorable (modified Rankin Scale score 3-6). A multivariate analysis was performed to identify predictors of functional outcome.

A favorable outcome was achieved in 24% of patients with poor-grade SAH. Patients with a favorable outcome were significantly younger (P = 0.005), harbored significantly smaller aneurysms (P = 0.004), and had a lower initial World Federation of Neurological Surgeons grade (P < 0.0001). An unfavorable outcome was significantly more frequent in patients with additional space-occupying hematoma compared with patients without additional space-occupying hematoma (P = 0.0009). On multivariate analysis, patient age, World Federation of Neurological Surgeons grade V, signs of cerebral herniation, aneurysm size, and presence of space-occupying hematoma were identified as significant predictors of unfavorable outcome in patients with poor-grade SAH.

A favorable outcome was achieved in 24% of severely ill patients with poor-grade SAH. Therefore, treatment of patients with poor-grade SAH should not be omitted. Careful individualized decision making is necessary for each patient [8)].

2015

118 patients with World Federation of Neurosurgical Societies (WFNS) grades IV and V underwent surgical treatment. Ultra-early surgery was defined as surgery performed within 24 h of aSAH, and delayed surgery as surgery performed after 24 h. Outcome was assessed by modified Rankin Scale (mRS). The mean time of follow-up was 12.5±3.4 months (range 6-28 months).

47 (40%) patients underwent ultra-early surgery, and 71 (60%) patients underwent delayed surgery. Patients with WFNS grade V (p=0.011) and brain herniation (p=0.004) more often underwent ultra-early surgery. Postoperative complications were similar in ultra-early and delayed surgery groups. Adjusted multivariate analysis showed the outcomes were similar between the two groups. Multivariate analysis of predictors of poor outcome, ultraearly surgery was not an independent predictor of poor outcome, while advanced age, postresuscitation WFNS V grade, intraventricular

haemorrhage, brain herniation and non-middle cerebral artery (MCA) aneurysms were associated with poor outcome.

Although patients with WFNS grade V and brain herniation more often undergo ultra-early surgery, postoperative complications and outcomes in selected patients were similar in the two groups. Patients of younger age, WFNS grade IV, absence of intraventricular haemorrhage, absence of brain herniation and MCA aneurysms are more likely to have a good outcome. Ultra-early surgery could improve outcomes in carefully selected patients with poor-grade aSAH [9)].

Data for 97 patients with poor-grade SAH (World Federation of Neurosurgical Societies Grade IV or V) were retrospectively analyzed from a single-center, prospective, observational cohort database. Ultra-early surgical clipping, removal of hematoma, external decompression for brain swelling, and prevention of vasospasm by cisternal irrigation with milrinone were combined as an aggressive treatment. Characteristics and clinical courses of SAH with ISH were identified. The authors also evaluated any correlations between poor admission-grade SAH and ISH with good functional outcomes.

Results: Patients with poor admission-grade SAH and with ISH were more likely to have initial cerebral edema ($p < 0.001$, Mann-Whitney U-test), which significantly resolved over time ($p < 0.001$, Mann-Whitney U-test). These patients had a better chance of functional survival (modified Rankin Scale scores of 1-3; OR 5.75; 95% CI 1.36-24.3; $p = 0.017$) at 6 months after hospital discharge, after adjustment for potential confounders such as younger age and better initial neurological grade by multivariable analysis.

Intrasylvian hematoma (ISH) predicted good functional recovery from poor-grade aneurysmal SAH [10)].

Patients with poor-grade SAH were randomized within 24 hours of admission to early treatment or treatment after neurologic recovery. If a patient was randomized to early treatment, the aneurysm was treated endovascularly within 24 hours of randomization. Recruitment rate, safety profile, and functional outcome at the time of discharge and at 6 months were assessed.

Fourteen of the 51 patients screened were eligible for the trial. Of these 14, 8 patients were randomized (57%). All patients in the early coiling arm received treatment within 24 hours of randomization. There was no treatment-related complication. Overall, good outcomes occurred in 25% of patients; the mortality rate was 75%. Patients in the early treatment arm ($n = 5$) had a good outcome rate of 20%, while those in treatment after the neurologic recovery arm ($n = 3$) had a good outcome rate of 33.3%.

This was a feasibility study that demonstrated that recruitment and randomization for comparing management strategies in poor-grade SAH are feasible. The recruitment rate among eligible patients was encouraging (57%), though a number of patients had to be excluded due to ineligibility. A multicenter study is necessary to recruit the numbers required to compare the clinical outcomes of these management strategies [11)].

2014

The purpose of a study was to undertake a single-center randomized controlled feasibility trial comparing a strategy of early endovascular aneurysm treatment with treatment after neurologic recovery in this group of patients.

Patients with poor-grade SAH were randomized within 24 hours of admission to early treatment or treatment after neurologic recovery. If a patient was randomized to early treatment, the aneurysm was treated endovascularly within 24 hours of randomization. Recruitment rate, safety profile, and functional outcome at the time of discharge and at 6 months were assessed.

Fourteen of 51 patients screened were eligible for the trial. Of these 14, 8 patients were randomized (57%). All patients in the early coiling arm received treatment within 24 hours of randomization. There was no treatment-related complication. Overall, good outcome occurred in 25% of patients; the mortality rate was 75%. Patients in the early treatment arm (n = 5) had a good outcome rate of 20%, while those in treatment after neurologic recovery arm (n = 3) had a good outcome rate of 33.3%.

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2013

Timing of surgery for poor-grade aneurysmal subarachnoid hemorrhage is still controversial, therefore this study aimed to identify the optimal time to operate on patients admitted in poor clinical condition.

Ninety-nine patients meeting the inclusion criteria were randomly assigned into three treatment groups. The early surgery group received operation within 3 days after onset of subarachnoid hemorrhage (day of SAH = day 1); the intermediate surgery group received operation from days 4 to 7, and surgery was performed on the late surgery group after day 7. Follow-up was performed 1, 3, and 6 months after aneurysm clipping. Primary indicators of outcome included the Extended Glasgow Outcome Scale and the Modified Rankin Scale, while secondary indicators of outcome were assessed using the Barthel Index and mortality.

This was the first prospective, single-center, observer-blinded, randomized controlled trial to elucidate optimal timing for surgery in poor-grade subarachnoid hemorrhage patients. The results of this study will be used to direct decisions of surgical intervention in poor-grade subarachnoid hemorrhage, thus improving clinical outcomes for patients [13]

2004

A prospective investigation was conducted in 149 patients with SAH (mean age 50.9 +/- 12.9 years); these patients were studied for 162 +/- 84 hours (mean +/- standard deviation). Lesions were classified as low-grade SAH (WFNS Grades I-III, 89 patients) and high-grade SAH (WFNS Grade IV or V, 60 patients). After approval by the local ethics committee and consent from the patient or next of kin, a microdialysis catheter was inserted into the vascular territory of the aneurysm after clip placement. The microdialysates were analyzed hourly for extracellular glucose, lactate, lactate/pyruvate (L/P)

ratio, glutamate, and glycerol. The 6- and 12-month outcomes according to the Glasgow Outcome Scale and functional disability according to the modified Rankin Scale were assessed. In patients with high-grade SAH, cerebral metabolism was severely deranged compared with those who suffered low-grade SAH, with high levels ($p < 0.05$) of lactate, a high L/P ratio, high levels of glycerol, and, although not significant, of glutamate. Univariate analysis revealed a relationship among hyperglycemia on admission, Fisher grade, and 12-month outcome ($p < 0.005$). In a multivariate regression analysis performed in 131 patients, the authors identified four independent predictors of poor outcome at 12 months, in the following order of significance: WFNS grade, patient age, L/P ratio, and glutamate ($p < 0.03$).

Microdialysis parameters reflected the severity of SAH. The L/P ratio was the best metabolic independent prognostic marker of 12-month outcome. A better understanding of the causes of deranged cerebral metabolism may allow the discovery of therapeutic options to improve the prognosis, especially in patients with high-grade SAH, in the future [14)].

2003

A prospectively audited, nonselected series of 177 consecutive poor-grade (i.e., World Federation of Neurological Surgeons Grades IV and V) patients with aneurysmal subarachnoid hemorrhage managed during a 9-year period was analyzed. A management policy of aggressive ultraearly surgery (not selected by age or by grade) was followed. Coiling was not available. Outcomes were assessed at 3 months.

Despite the aggressive management policy, surgery could be performed in only 132 poor-grade patients (75%). Twenty percent of all patients were 70 years of age or older (15% of the surgical cases). All surgery was performed within 12 hours of subarachnoid hemorrhage (majority <6 h). Preoperative rebleeding occurred within the first 12 hours (>85% within 6 h) in 20% of the patients, which is four times the rate found in good-grade patients managed according to the same policy. Outcome assessment performed at 3 months in the 132 poor-grade surgical patients revealed that 40% were independent, 15% were dependent, and 45% had died. There was no significant difference in outcomes for young and old (70+ yr) poor-grade surgical patients ($P > 0.05$).

The high ultraearly rebleeding rate indicates a need to urgently secure the ruptured aneurysm by performing surgery or coiling, and this indication is more pronounced for poor-grade patients than for good-grade patients. The outcome results of ultraearly surgery indicate that a nonselective policy does not lead to a large number of dependent survivors, even among elderly poor-grade patients [15)].

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