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Outcome and hospitalization costs after aneurysmal subarachnoid hemorrhage: a single center retrospective analysis

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Abstract: Aneurysmal subarachnoid hemorrhage (aSAH) has a highly variable clinical outcome. Extended ICU and hospital stay often result in increased healthcare related costs. This study aimed to examine the relationship between aSAH severity, hospital costs and functional outcome in patients who required urgent or semi-urgent endovascular repair.

Patients treated with endovascular repair after experiencing aSAH from January 2017 until September 2018 were included in this retrospective single center study. aSAH severity upon admission was classified by the World Federation of Neurosurgical Societies (WFNS) grade, dichotomized into WFNS grade 1-2, 'low grade aSAH' and WFNS grade 3-5, 'high grade aSAH'. Functional outcome was assessed at ICU discharge and 1 year post aSAH by utilizing the modified Rankin Scale (mRS) and converted to quality adjusted life years (QALY) for the latter time point. Healthcare related costs during index hospital stay were analyzed.

A total of 69 patients were included with 44 (63,8%) suffering from low grade aSAH and 25 (36,2%) from high grade aSAH. Median utility scores at 1 year were 0,93 (IQR 0,83-0,93) for low grade aSAH and 0,42 (IQR 0-0,83) for high grade aSAH ($p<0{,}001$). Mean total costs were 56.150 euro (IQR 25.572-62.060) in high grade and 26.288 euro (IQR 18.893-29.993) in low grade aSAH ($p=0{,}003$). Cost per 0.1 QALY gain in high grade aSAH was 13.233 euro (IQR 2.803-23.072) and higher than in low grade aSAH 3.497 euro (IQR 2.200-3.344) ($p=0{,}027$). Short term healthcare related costs strongly depend on aSAH severity. ICU stay and ICU related complications were important cost driving factors.

High grade aSAH is also accompanied by lower functional outcomes at 1 year and decreased cost-effectiveness in comparison to low grade aSAH.

Keywords: aneurysmal subarachnoid hemorrhage; cost analysis; WFNS; QALY; Critical Care.

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) has an estimated annual incidence of 6 cases per 100.000 persons and a case fatality rate up to 50% (1-3). Despite advances in medical and interventional therapy, patient outcomes still vary greatly from full recovery to severe disability or death (4). Management of aSAH invariably requires ICU admission. This is often characterized by neurologic and systemic complications including hydrocephalus, vasospasm, delayed cerebral injury, respiratory and cardiovascular failure, leading to prolonged intensive care unit (ICU) and hospital stay. Because of the complex clinical presentation and possible complications, prediction of outcome in aSAH has been a daunting challenge. Since their development, outcome score systems such as the World Federation of Neurosurgical Societies score (WFNS) have been widely implemented in aSAH management in order to grade aSAH severity. On the other hand, their clinical relevance is questioned (5).

Healthcare related costs can also be high and have previously been linked to prolonged hospitalization and clinical grade at admission (6-9). However detailed cost analysis data after endovascular repair in aSAH are scarce and there seems to be a great regional and country based

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variation due to differences in methods of cost calculation or estimates (10). Improvements in aSAH management cost prediction, could be of importance in optimization of resource allocation. In this retrospective single center study, we aimed to assess outcome and cost effectiveness in endovascular treatment of low and high grade aSAH. We tried to identify major cost drivers to provide a baseline for further research in cost allocation and quality improvement. We hypothesized that high grade aSAH results in reduced outcome, increased costs and thus decreased cost-effectiveness.

Materials and methods

Data collection

This retrospective single center study analyzed patients who experienced an aSAH, according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-M) codes and underwent endovascular treatment from January 2017 until September 2018 at the 'Ziekenhuis Oost-Limburg' ZOL, Genk, Belgium. From the total of 90 endovascular treated patients, 13 were excluded as they did not suffer from aneurysmal bleeding and had elective endovascular therapy, while 8 patients were lost to follow-up at 1 year (primary endpoint) after the endovascular therapy. Hence, 69 patients were included in the analysis. The study was approved by the independent Ethics Committee and adhered to the STROBE guidelines on retrospective analyses.

The endovascular therapies included coiling, deployment of a flow disruptor device and placement of a flow diverter. Hospital records were consulted for patient baseline characteristics such as sex and age, APACHE IV score, aneurysm location, type of endovascular therapy, Glasgow Coma Scale (GCS) and World Federation of Neurosurgical Societies (WFNS) grade at admission. As in routine clinical practice patients with aSAH were classified by the WFNS grade and dichotomized. WFNS grade 1 and 2 were combined as 'low grade' aSAH, while grade 3 to 5 as 'high grade' aSAH. APACHE IV scores were assessed by one trained physician (TM) for all patients at once.

Important brain related inpatient complications included (1) the presence of intracranial hypertension (defined as an intracranial pressure equal to or above 20 mmHg for more than 5 minutes), (2) cerebral vasospasm (measured with transcranial doppler by a specialist radiologist) or (3) delayed cerebral ischemia (DCI). DCI was defined as a decrease of 2 points on the GCS or the presence of a new focal deficit which continued for minimal two hours. Duration of mechanical ventilation, length of ICU and hospital stay were also registered. Treatment aggressiveness was assessed by the need for placement of ventricular drainage, the need for prolonged non-procedural sedation or decompressive craniectomy. Based on chart reviews we created an inventory of all complications not directly related to aSAH or its interventional procedure. These included thus complications of the respiratory, cardiac and urinary system, such as pneumonia and urinary tract infections. They were grouped as general complications during ICU stay.

Outcome measures

Functional outcome at ICU discharge and at one year (primary endpoint) was assessed by the modified Rankin Scale (mRS) and was categorized into 3 groups: good (mRS 0-2), moderate (mRS 3-4) and poor outcome (mRS 5-6). These scores were converted into QALYs using equivalents based on the study by Dijkland et al.(11)

All healthcare related costs during the entire index hospital stay were collected by the data warehouse system of the hospital according to their standard procedures. All direct, non-discounted index hospital stay costs, from a healthcare payer perspective, were included. No adjustment was made for inflation or price fluctuations of measured cost elements. All costs were reported in euro in mean with interquartile range (IQR).

Statistical analyses

All variables were tested for normality of data distribution. Normally distributed data were represented as mean (SD) and compared by the student's t-test/one-way ANOVA, while skewed data were represented as median (IQR) and compared using the Wilcoxon signed rank/Kruskal-Wallis test. Total costs were represented as mean (IQR) and compared by both parametric and non-parametric testing. The examination of drivers for costs was done by bootstrap forests to generate the contributions for patient characteristics (gender, age, WFNS score, aneurysm location, treatment, intracranial hypertension, vasospasm, delayed ischemic injury). This process was run three times and the average was taken.

Two-sided p-values of <0,05 were deemed statistically significant. Analyses were conducted in JMP, version 15.0.0 (SAS Institute Inc, Cary, NC, USA).

Results

Baseline characteristics

From January 2017 until September 2018, 69 patients underwent endovascular therapy for aSAH and completed a one year follow up. Mean age was 57,4 years (SD 14,5). Female to male patient ratio was 2,6 to 1. In both patient groups, the majority of aneurysms was located in the anterior circulation, however in the 'high grade' aSAH group we noted a higher number of posterior circulation aneurysms (28% vs 9,1%, p<0,019). There was no difference in the preferred method of endovascular intervention between low and high grade aSAH. Procedural complication rate was equivalent in both groups. These had no clinical implications (Table 1).

Table 1

Baseline characteristics

Variable		**Total N = 69**	
Age	years	57,4	(±14,5)
Female	n (%)	50	(73)
Aneurysm location			
ICA	n (%)	6	(9)
MCA	n (%)	7	(10)
ACOM	n (%)	33	(48)
PCOM	n (%)	11	(16)
Pericallosal artery	n (%)	3	(4)
PICA	n (%)	3	(4)
VBA	n (%)	6	(9)
Procedure			
Coiling	n (%)	46	(67)
Coiling and flow diverter	n (%)	1	(2)
Flow diverter	n (%)	2	(3)
Flow disruptor	n (%)	20	(29)
Procedural complications	n (%)	5	(7)
WFNS grade			
1-2	n (%)	44	(64)
3-5	n (%)	25	(36)
APACHE IV score	points	30	[40-75]

ICA, internal carotid artery; MCA, middle cerebral artery; ACOM, anterior communicating artery; PCOM, posterior communicating artery; PICA, posterior inferior cerebellar artery; VBA, vertebrobasilar artery; WFNS: World Federation of Neurosurgical Societies; APACHE, acute physiology and chronic health evaluation; IQR, interquartile range. Data are presented as median and interquartile range [IQR] or as an absolute number (n) with the percentage (%) of the whole (N).

WFNS grade and APACHE IV score

The low grade WFNS group consisted of 33 patients in grade 1 and 11 in grade 2. Grade 3, 4 and 5 had 5, 5 and 15 patients, respectively. All patients were classified for the APACHE IV as non-operative, neurologic, SAH, aneurysm (Table 1).

Complications

Neurologic complications occurred in 39 (56%) patients. Intracranial hypertension was present in low grade aSAH in 13,6% of cases, while one in four patients suffered from intracranial hypertension in the high grade aSAH group. Procedural sedation was needed in 5,8% of cases in low grade aSAH group versus 72% in high grade aSAH group (p<0,0001). Intracranial hypertension refractory to sedation and ventricular drainage therapy, necessitating decompressive craniectomy to control intracranial pressures occurred in only 4 patients in the high grade aSAH group. In the low grade aSAH group no patients required decompressive craniectomy. The occurrence of radiologically proven vasospasm appeared to be similar in both patient groups. Delayed cerebral ischemia (DCI) was more prevalent in high grade aSAH than in low grade aSAH (60% versus 18,2%, p<0,05).

General complication rate during ICU stay ratio was higher in high grade aSAH group in comparison to the low-grade group (73% versus 25%, p<0,001).

Duration of mechanical ventilation and ICU stay

Only 8 patients (18%) in the 'low grade' group required prolonged mechanical ventilation. The median time of mechanical ventilation in these patients was 13,9 hours (IQR 9,2-104). In contrast, in the 'high grade' group 21 patients (84%) needed mechanical ventilation with a median time of 115 hours (IQR 50-328).

Median ICU length of stay (LOS) in the 'low grade' group was 3,5 days (IQR 2-7,75) while median ICU LOS in the 'high grade' group was longer with 13 days (IQR 3-22). The mRS differed strongly at ICU discharge between low and high grade aSAH (p<0,0001) (Table 2).

Functional Outcome at one year

In 'low grade' aSAH, 34 patients (77%) had a good outcome and 6 patients (13%) had moderate outcome (Table 2). Mortality was 10%. In 'high

Table 2

Outcome

Variable		WFNS 1,2 (N = 44)		WFNS 3-5 (N = 25)		p-value
Vasospasm	n (%)	9	(21)	6	(24)	0,4778
Intracranial hypertension	n (%)	6	(14)	17	(68)	<0,0001
Delayed cerebral ischemia	n (%)	8	(18)	15	(60)	0,0006
Procedural complications	n (%)	4	(9)	1	(4)	0,41
General ICU related complications	n (%)	11	(25)	19	(76)	<0,0001
Procedural sedation	n (%)	4	(9)	18	(72)	<0,0001
External ventricular drainage	n (%)	9	(21)	20	(80)	<0,0001
Decompressive craniectomy	n (%)	0	(0)	4	(16)	0,015
ICU length of stay	days	3	[2 -6]	13	[3-2]	0,0015
Hospital length of stay	days	9	[2 -13]	16	[3-63]	0,03
One-year survival	n (%)	40	(90)	13	(52)	0,00013
Duration of mechanical ventilation	hours	0	[0 - 0]	107	[42-301]	<0,0001
mRS at ICU discharge	points	3	[2-3]	5	[4-5]	<0,0001
mRS at one year						0,0003
Good	n (%)	34	(77)	8	(32)	
Moderate	n (%)	6	(14)	5	(20)	
Poor	n (%)	4	(10)	12	(48)	
mRS at one year	points	1	[1-2]	4	[2-6]	<0,0001
Utility value at one year	points	0,93	[0,83-0,93]	0,42	[0,00-0,83]	<0,0001

ICU, intensive care unit; WFNS: World Federation of Neurosurgical Societies; mRS, modified Rankin Scale; IQR, interquartile range. Data are presented as median and interquartile range [IQR] or as an absolute number (n) with the percentage (%) of the whole (N).

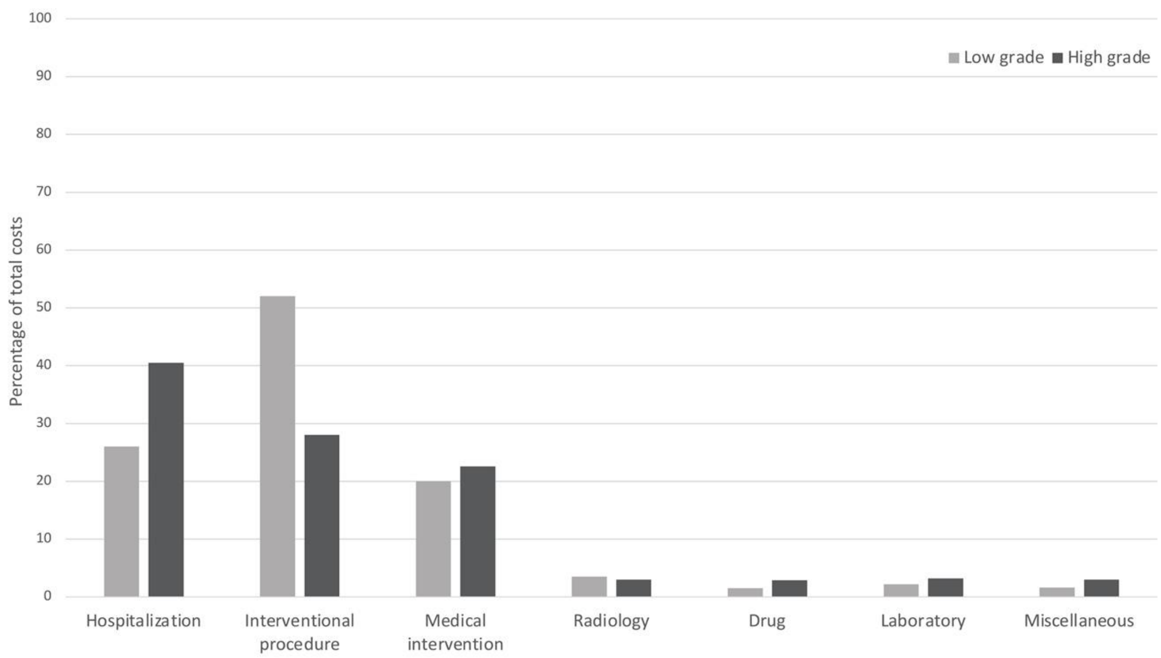

Figure 1. — Percentage of total costs. Bar graph representing percentage of total costs for the different cost categories in low and high grade aSAH.

Table 3

Costs per WFNS gradation

Variable		WFNS 1,2 (N = 44)		WFNS 3-5 (N = 25)		p-value
Total costs	euro	26.288	[18.893-29.993]	56.150	[25.572-62.060]	0,0004
Total costs deceased	euro	26.929	[17.434-40.119]	44.090	[26.038-53.909]	0,046
Cost per 0.1 QALY gain	euro	3.497	[2.200-3.344]	13.233	[2.802-23.073]	0,027
Hospitalization cost	euro	6.771	[1.610-7.047]	22.765	[2.192-31.508]	0,0022
Interventional procedure costs	euro	13.729	[9.394 -18.166]	15.661	[9.803-18.342]	0,29
Medical intervention costs	euro	5.233	[3.234-4.628]	12.685	[3.676-16.377]	0,0001
Radiology costs	euro	926	[538-1.158]	1.728	[800-2.234]	0,001
Drug costs	euro	408	[197-340]	1.649	[331-1.398]	0,03
Lab costs	euro	588	[228-582]	1.799	[263-2.581]	0,0007
Miscellaneous costs	euro	413	[75-154]	1.641	[75-236]	0,09

WFNS: World Federation of Neurosurgical Societies; QALY, quality-adjusted life-year; IQR, interquartile range. Data are presented as median and interquartile range [IQR] in euro.

grade' aSAH however, only 8 patients (32%) experienced good clinical outcome and 5 patients (20%) had moderate outcome. Mortality was 48%. Median mRS scores at one year for 'low grade' and 'high grade' aSAH were 1 (IQR 1-2) and 4 (IQR 2-6) respectively (p<0,0001).

Cost analysis

In the 'high grade' aSAH group the mean total cost (56.150 euro; IQR 25.572-62.060 euro) was higher than in the 'low grade' aSAH group (26.288 euro; IQR 18.893-29.993 euro) (Table 3). The cost of endovascular therapy was comparable in both groups. In the 'low grade' aSAH group however, this cost represented almost 50% of total cost and proportionally outweighed other costs especially in comparison to 'high grade' aSAH where interventional radiology accounted only for approximately 25% of costs (Figure 1).

Prolonged ICU and hospital length of stay in 'high grade' aSAH was also reflected in the higher mean hospital stay cost (22.765 euro; IQR 2.192-31.508 euro) in comparison to 'low grade' aSAH (6.771 euro; IQR 1.610-7.047 euro). Likewise, medical interventional, radiology, drug and lab costs were higher as well. The cost of providing therapy in patients who eventually died during hospital stay was higher in 'high grade' aSAH (44.090 euro; IQR 26.038-53.909 euro) in comparison to 'low grade' aSAH (26.929 euro; IQR 17.434-40.119 euro). Cost per QALY gain in 'high grade' aSAH (13.233 euro; IQR 2.803-23.072 euro) was higher than in 'low grade' aSAH (3.497 euro; IQR 2.200-3.344 euro) (p=0,027).

Table 4

Drivers for costs after aSAH

Drivers	Proportion contribution (%)
WFNS	28
Intracranial hypertension	27
Delayed cerebral ischemia	25,3
Aneurysm location	9,4
Age	3,9
Therapy	2,7
Gender	2,2
Vasospasm	1,6

Examination by bootstrap forests to generate the contributions for patient characteristics. This process was run three times and the average was taken. Data are presented as % of proportion of contribution. WFNS: World Federation of Neurosurgical Societies.

80,3% of total hospitalization costs could be explained by 3 factors: WFNS grade, the presence of intracranial hypertension and delayed cerebral ischemia (Table 4).

Discussion

Since its introduction in 1988 the WFNS scale has been widely adopted in critical care departments to predict outcome after aSAH.(12) In our retrospective analysis we showed that only half of 'high grade' aSAH group patients were alive after one year, confirming that -approximately thirty years after its introduction- the WFNS scale is still a useful instrument in early prognostication. However, cautious use is warranted since one in three patients in the 'high grade' aSAH group still had a good functional recovery at one year. This substantial proportion of 'high grade' patients with good functional recovery in our patient population could possibly be explained by three factors. Firstly, the timing of grading a patient according to the WFNS scale is crucial. WFNS gradation at admission has been shown to be less accurate in predicting outcome in comparison to gradation after initial neurological resuscitation. (13) Secondly, our decision to include WFNS grade 3 in the 'high grade' aSAH group could also be a contributing factor. However, previous WFNS outcome research stated no significance difference in outcome between WFNS grade 3 and 4 (13). Differentiation between grades is difficult; this is why we chose to group all patients with neurologic deficit as 'high grade' patients to be able to reach a clearer cut-off between groups. Thirdly, improved medical management of these patients in the last thirty years has likely occurred leading to better outcomes. Despite an equal incidence of cerebral vasospasm in both groups, the incidence of delayed cerebral injury was significantly higher in the 'high grade' group. This is remarkable and speaks in favor of the hypothesis that cerebral vasospasm is not the primary cause of DCI, but rather that DCI is a complex multifactorial syndrome possibly including micro-embolism and cortical spreading ischemia (14, 15) delayed cerebral ischemia (DCI The procedural cost of aneurysm occlusion by the interventional radiology team did not differ between both groups. However, the cost of intensive care therapy, including mechanical ventilation and medical therapy treating complications from both aSAH and ICU stay was higher in 'high grade' aSAH in comparison to the 'low grade' group. The mean total cost of hospitalization of 'high grade' patients was twice as high in comparison to the cost of the 'low grade' patients, while only 25% of this cost was directly related to the interventional therapy in the 'high grade' group. This is in contrast to 'low grade' aSAH, where half of the total cost was due to the interventional radiology procedure. Our findings are consistent with the previous work by Wilde and Roos et al, confirming that ICU stay and ICU related complications are important cost driving factors (8, 16). These play a major role in the significantly higher burden of cost in the 'high grade' group and are represented by a largely higher mean hospitalization cost and higher cost of medical interventions, radiology, drug and lab work. As a consequence, therapies which lead to decreased length of ICU stay will likely reduce total hospitalization costs. Calculating cost and cost effectiveness of medical therapy is important in hospital and disease management strategies and may pose a difficult economical and ethical conundrum. Despite the largely higher cost per 0,1 QALY gain, we were still able to achieve good functional outcome in a substantial part of 'high grade' patients.

Adjusting cost calculations to correct for the deceased patients, we could calculate a mean cost of 107.980 euro per patient leaving the unit alive. Despite the high cost, we believe this is still within society's willingness to pay (WTP) threshold in Belgium. According to the World Health Organization (WHO) recommendations, a country's WTP threshold is set at 1-3 times the gross domestic product per capita, which was approximately 44.000 USD in 2017 in Belgium. From both a financial and ethical perspective, continued aggressive medical therapy is warranted in all aSAH patients despite their initial WFNS grade. Our study's findings are concordant with the previous research from both Wostrack and Le Roux (17, 18). Comparing our results with other research concerning cost-effectiveness in aSAH is quite challenging and interpretation of results difficult. Martin et al. described an acute cost of 13.128 euro per patient and 4.679 euro per QALY gained in poor grade aSAH (19). In contrast Maud et al. reported $65.424 per overall QALY gain in aSAH after endovascular repair (20). To find an explanation for such differences we have to take into consideration the different data gathering and collection methods in different health care systems. If the projected data are based on actual billed health costs or based on estimates of expected costs. Increased methodological uniformity and cost transparency is needed in order to improve accuracy of cost prediction in aSAH.

There were several limitations in our study. Firstly, the retrospective nature and the limited number of patients included make definitive conclusions on cost-effectiveness in 'high grade' aSAH difficult. These results have to be confirmed in prospective larger multicenter studies. Secondly, the cost-effectiveness in aSAH may be influenced by other confounding factors which were not included in this dataset. Also, more accurate outcome prediction values could be possible by using the WFNS after initial neurological resuscitation (13), these were not available in this patient cohort though. Thirdly, total mean costs per patient only included hospital related costs, while out-of-hospital costs (e.g., rehabilitation costs) were not accounted for. This introduced an underestimation of the total healthcare costs within the first year after aSAH.

Conclusion

Our study confirmed that hospital costs are indeed affected by aSAH severity upon admission. In the 'high grade' aSAH group, mortality rate is higher and functional outcome scores are much lower in comparison to the 'low grade' group. Cost-effectiveness is noticeably lower in the 'high grade' group with a ratio of almost 4 to 1 per 0,1 QALY gain in the high versus low grade group. We identified WFNS grade, ICU stay, occurrence of intracranial hypertension and DCI as major cost drivers. Despite a high mortality in the high-grade group, one in three patients in this group still achieve reasonably good outcomes, suggesting aggressive medical therapy is still warranted in all patients irrespective of the admission WFNS score.

Author contributions

TM: Participated in the design of the study and analysis plan, checked the database for accuracy, drafted the manuscript.

WX: Conceived the study, participated in the design of the study and analysis plan, checked the database for accuracy, exported the data for statistical analysis, drafted the manuscript.

SL: Supervised patient recruitment, participated in the design of the study, revising the manuscript for important intellectual content.

DBT: Supervised patient recruitment, participated in the design of the study, revising the manuscript for important intellectual content.

GJ: Set-up of the cost database, revising the manuscript for important intellectual content.

LA: Set-up of the cost database, revising the manuscript for important intellectual content.

RS: Participated in the design of the study, revising the manuscript for important intellectual content.

PE: Provided all cost-data, participated in the design of the study, revising the manuscript for important intellectual content.

MD: Supervised study design and analysis plan, performed the statistical analyses, drafted the manuscript.

TM and WX contributed equally to the manuscript

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References

1. de Rooij N.K., Linn F.H.H., van der Plas J.A., Algra A. and Rinkel G.J.E. 2007. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry. 78: 1365-72.
2. van Gijn J., Kerr R.S. and Rinkel G.J.E. 2007. Subarachnoid haemorrhage. Lancet Lond Engl. 369: 306-18.
3. Linn F.H., Rinkel G.J., Algra A. and van Gijn J. 1996. Incidence of subarachnoid hemorrhage: role of region, year, and rate of computed tomography: a meta-analysis. Stroke. 27: 625-9.
4. Hop J.W., Rinkel G.J.E., Algra A. and van Gijn J. 1997. Case-Fatality Rates and Functional Outcome After Subarachnoid Hemorrhage.Stroke. 28: 660-4.
5. Fung C., Inglin F., Murek M., Balmer M., Abu-Isa J., Z'Graggen W.J. and Raabe A., et al. 2016. Reconsidering the logic of World Federation of Neurosurgical Societies grading in patients with severe subarachnoid hemorrhage. J Neurosurg. 124: 299-304.
6. Lekander I., Willers C., von Euler M., Lilja M., Sunnerhagen K.S., Pessah-Rasmussen H. and Borgström F. 2017. Relationship between functional disability and costs one and two years post stroke. PloS One. 12:e0174861.
7. Modi S., Shah K., Schultz L., Tahir R., Affan M. and Varelas P. 2019. Cost of hospitalization for aneurysmal subarachnoid hemorrhage in the United States. Clin Neurol Neurosurg. 182:167-70.
8. Wilde H., Twitchell S., Reese J., Guan J., Eli I.M., Karsy M. and Couldwell W.T., et al. 2020. Evaluation of disease severity and treatment intensity as cost drivers for ruptured intracranial aneurysms. Acta Neurochir (Wien). 162:157-67.
9. Elliott J.P., Le Roux P.D., Ransom G., Newell D.W., Grady M.S. and Winn H.R. 1996. Predicting length of hospital stay and cost by aneurysm grade on admission. J Neurosurg. 85: 388-91.
10. Yoon S., Yoon Jennifer C., Winkler E., Liu C. and Lawton Michael T. 2019. Nationwide Analysis of Cost Variation for Treatment of Aneurysmal Subarachnoid Hemorrhage. Stroke. 50: 199-203.
11. Dijkland S.A., Voormolen D.C., Venema E., Roozenbeek B., Polinder S., Haagsma J.A. and Lingsma H.F. et al. 2018. Utility-Weighted Modified Rankin Scale as Primary Outcome in Stroke Trials: A Simulation Study. Stroke. 49: 965-71.
12. Report of World Federation of Neurological Surgeons Committee on a Universal Subarachnoid Hemorrhage Grading Scale. 1988. J Neurosurg. 68: 985-6.

13. van Donkelaar C.E., Bakker N.A, Veeger N.J.G.M., Uyttenboogaart M., Metzemaekers J.D.M, Eshghi O and Van Dijk J.M.C., et al. 2017. Prediction of outcome after subarachnoid hemorrhage: timing of clinical assessment. J Neurosurg. 126: 52-9.
14. Francoeur C.L. and Mayer S.A. 2016. Management of delayed cerebral ischemia after subarachnoid hemorrhage. Crit Care Lond Engl. 20: 277.
15. de Oliveira Manoel A.L., Goffi A., Marotta T.R., Schweizer T.A., Abrahamson S. and Macdonald R.L. 2016. The critical care management of poor-grade subarachnoid haemorrhage. Crit Care Lond Engl. 20: 21.
16. Roos Y.B.W.E.M, Dijkgraaf M.G.W, Albrecht K.W., Beenen L.F.M., Groen R.J.M., de Haan R.J. and Vermeulen M. 2002. Direct costs of modern treatment of aneurysmal subarachnoid hemorrhage in the first year after diagnosis. Stroke. 33: 1595-9.
17. Wostrack M., Sandow N., Vajkoczy P., Schatlo B., Bijlenga P., Schaller K. and Meyer B. 2013. Subarachnoid haemorrhage WFNS grade V: is maximal treatment worthwhile? Acta Neurochir (Wien). 155: 579-86.
18. Le Roux P.D., Elliott J.P., Newell D.W., Grady M.S. and Winn H.R. 1996. Predicting outcome in poor-grade patients with subarachnoid hemorrhage: a retrospective review of 159 aggressively managed cases. J Neurosurg. 85: 39-49.
19. Wilby M.J., Sharp M.,Whitfield P.C., Hutchinson P.J., Menon D.K. and Kirkpatrick P.J. 2003. Cost-Effective Outcome for Treating Poor-Grade Subarachnoid Hemorrhage. Stroke. 34: 2508-2511
20. Maud A., Lakshminarayan K., Suri M.F.K., Vazquez G., Lanzino G. and Qureshi AI. 2009. Cost-effectiveness analysis of endovascular versus neurosurgical treatment for ruptured intracranial aneurysms in the United States. J Neurosurg. 110: 880-6.