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ORIGINAL ARTICLE

Outcome from spontaneous subarachnoid haemorrhage—results from 2007–2011 and comparison with our previous series

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Abstract

Objectives. The management of patients with spontaneous subarachnoid haemorrhage (SAH) has changed, in part due to interventions now being extended to patients who are older and in a worse clinical condition. This study evaluates the effects of these changes on a complete 5-year patient material.

Methods. Demographic data and results from 615 patients with SAH admitted from 2007 to 2011 were put together. Aneurysms were found in 448 patients (72.8%). They were compared with the aneurysm group ($n = 676$) from a previously published series from our centre (2001–2006). Linear regression was used to determine variables predicting functional outcome in the whole aneurysm group (2001–2011).

Results. Patients in the more recent aneurysm group were older, and they were in a worse clinical condition on admission. Regarding younger patients admitted in World Federation of Neurosurgical Societies SAH grading (WFNS) 3, there were fewer with a good outcome. In the whole aneurysm group 2001–2011, outcome was best predicted by age, clinical condition at admission, and the size of the bleeding, and not by treatment mode or localization of aneurysm.

Conclusion. It seems important for the outcome that aneurysms are treated early. The clinical course after that depends largely on the condition of the patient on admission rather than on aneurysm treatment method. This, together with the fact that older patients and those in worse condition are now being admitted, increases demands on neurointensive care. Further improvement in patient outcome depends on better understanding of acute brain injury mechanisms and improved neurointensive care as well as rehabilitation measures.

Key words: *Aneurysm, endovascular, outcome, neurointensive care, subarachnoid haemorrhage, surgery*

Introduction

Two major improvements in management of patients with subarachnoid haemorrhage (SAH) were the early treatment of the aneurysm and the introduction of neurointensive care units (NICU) (1). Modern NICU protocols target both the impact of the bleeding and complications such as hydrocephalus and vasospasm. General neurointensive care principles such as avoiding secondary insults are important as well (2).

Another significant advance in SAH treatment was the introduction and development of endovascular techniques and devices including the Gugliemi detachable coil (GDC, Boston Scientific/Target Therapeutics, Freemont, CA, USA) (3). There has been controversy concerning the relative merits of surgical and endovascular treatment of aneurysms. Randomized controlled studies performed to date all favour endovascular treatment (4-7), although surgery will still be required in a substantial percentage of cases.

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The development of endovascular techniques has enabled the treatment of patients judged to be in too poor condition or too old for open skull surgery. Advances in neurointensive care have also made it possible to treat older patients and those with more simultaneously occurring severe conditions. Extending treatment to more difficult cases puts a higher demand on clinical care, and it is expected that outcome for the whole group will be worse when patients who are older or in a worse clinical condition are treated.

In order to study the development of treatment methods and the impact this has had on patients treated in our department we evaluated our own results during 2007–2011 and compared them with a previously published material from 2001–2006 (1,8-10).

Material and methods

Patients

The study material comprised all patients admitted to the neurosurgical unit at Uppsala University Hospital with SAH, between 1 January 2007 and 31 December 2011. The great majority of the patients came from our own geographical referral area with approximately 2,000,000 inhabitants. The referring hospitals contacted the neurosurgeon on call as soon as a diagnosis of SAH was made, and the patient was transferred immediately unless considered terminally ill.

Altogether 647 patients with acute spontaneous SAH were treated. During 3 of the 5 years some SAH patients ($n = 70$) were transferred with intensive care helicopter to other university hospitals where the aneurysm was treated, since the interventional neuroradiologist could not cover every day of the year. After that the patients were brought back, usually within 24 hours. Another 14 patients had their haemorrhage while staying in the catchment areas of other neurosurgical departments, or even abroad, and their aneurysms were treated before they were transferred to us. Thirty-two patients with aneurysms treated in other hospitals were returned to us more than 2 days after the bleeding. They were excluded from the material since an important part of the intensive care period was spent elsewhere.

SAH treatment

Computerized tomography angiography (CTA) with 3D-reconstructions was carried out as soon as possible after admission. If CTA showed normal blood vessels and an aneurysm still was suspected, the investigation was completed with digital subtraction angiography (DSA). If both CTA and DSA were negative and the amount of blood on the first CT scan was regarded to be Fisher 3 or 4 (11), CT and/or DSA were repeated before discharge.

Normally, the aneurysm was treated as soon as possible during the usual day-time schedule. Surgery or coiling during the night was only performed if there were repeated bleedings or when it was necessary to remove a clot. All patients with SAH and suspected or proven aneurysm had bed-rest for 10 days, received nimodipine, and were kept normo-volemic. Patients with decreased consciousness were on mechanical ventilation and usually received a ventricular drain. Secondary insults (high intracranial pressure, low cerebral perfusion pressure, seizures, fever, hypoxia, and hypo/hyperglycaemia) were treated according to the unit's protocols for programmed care (12,13). The choice of surgical or endovascular treatment was made by the neurovascular team.

Statistics

The present patient material (2007–2011) was compared with our own data from the six previous years, i. e. 2001 to 2006 (8). Variables analysed in the study were age, gender, the amount of blood on first CT scan (11), clinical status at admission according to World Federation of Neurosurgical Societies SAH score (WFNS) (14), and treatment mode. Outcome was measured with Glasgow Outcome Scale (GOS) (15). This was done by a trained research nurse, through a telephone interview. Median follow-up time was 13 months with an interquartile range of 12–17 months. Outcome was further compared between the two time periods after stratifying for age (≤65 years and >65 years) and for clinical condition at admission (WFNS 1–2, WFNS 3, and WFNS 4–5).

Statistica 9.0 (Stat Soft, Inc., Tulsa, OK, USA) was used for descriptive and analytical statistics. Student's t test was used for comparing age since this was normally distributed. Chi-square test was used in order to compare the two time periods regarding the percentage of women and the distribution of clinical grades, outcome, angiographic findings, and aneurysm treatment. In order to evaluate the influence of demographic and clinical variables on the outcome we used a generalized linear model with a multinomial ordinal response and a logistic link function. The best subset of predictive variables was selected using Akaike's Information Criterion (AIC) (16). A p Value < 0.05 was considered statistically significant.

Ethics

The Uppsala University Regional Ethical Review Board for clinical research granted permission for the study.

Results

The study material consists of 615 patients. The mean age was 58 ± 13 years, and 65% were women. One- and six-month mortalities were 11% and 15%, respectively. A ruptured aneurysm was found in 448 patients (72.8%). Angiography was normal in 143 patients (23.2%). Other vascular pathological findings such as ruptured arteriovenous malformation (AVM) or vasculitis were found in 8 patients (1.2%). Angiography was not performed in the remaining 16 patients (2.6%).

When comparing the distribution of angiographic findings with the earlier time period we found that there were more patients in the 2001–2006 group who did not have any diagnostic angiography done. However, this difference did not attain statistical significance ($p = 0.090$). Regarding the other angiographic findings (see above), there were no differences.

The aneurysm group was analysed further. Mean age, gender distribution, Fisher grading, clinical condition at admission, outcome, and aneurysm treatment are shown for both time periods in Table I. Patients in the aneurysm group were older during 2007–2011 compared with 2001–2006. There were also more patients in a worse clinical condition at admission and fewer with a good outcome during 2007–2011. Furthermore, significantly more patients in the 2007–2011 aneurysm group did not receive any treatment, and fewer were treated with both coil and clip, compared with 2001–2006.

Since there were significant differences in age and in clinical condition at admission between the time periods we stratified the data according to clinical condition at admission (WFNS 1–2, 3, and 4–5) and age (≤65 and >65 years) when outcome was analysed (Table II). It was found that in the 2007–2011 group significantly more of the younger patients admitted in WFNS 3 had a severe outcome, and fewer had a favourable outcome.

Linear regression was done for the whole aneurysm patient material (2001–2011) in order to find the best subset of variables predicting a worse outcome. Variables entered into the analysis were gender, age, treatment with coil or clip, localization of aneurysm in anterior or posterior circulation, clinical condition at admission, and amount of blood on the first CT scan. The best subsets of variables predicting a worse outcome was higher age, worse clinical condition at admission, and more blood on the first CT scan.

Table I. Demographic data, clinical characteristics, and treatment alternatives for aneurysm patients during the 6 years 2001–2006 and the present 5-year material (2007–2011).

	2001–2006	2007–2011	*p* Value
n	676	448	
Mean age	57.0 ± 12.0	58.6 ± 12.7	< 0.03
	%	%	
Women	69	70	ns
WFNS 1–2	61	55	< 0.04
WFNS 3	5	4	ns
WFNS 4–5	34	41	< 0.01
Fisher 1–2	18	22	ns
Fisher 3–4	81	78	ns
GOS 1–2 (poor)	16	18	ns
GOS 3 (severe)	27	31	ns
GOS 4–5 (favourable)	57	51	< 0.03
Aneurysm treatment			
Surgery	29.4	31.4	ns
Endovascular	64.2	61.6	ns
Both surgery and endovascular	2.1	0.2	< 0.01
No treatment	4.3	7.1	< 0.04

Fisher refers to the grading of the amount of blood on the first CT scan (11).
WFNS = the World Federation of Neurosurgical Societies clinical grading of SAH (14); GOS = Glasgow Outcome Scale (15).

Discussion

Adding the results from the present material to previous publications (1,8) we now have a 30-year perspective on our centre's treatment of spontaneous SAH. During this time period there have been major improvements in the treatment of patients with ruptured aneurysms. There have also been significant changes in health care policies regarding the treatment of older patients as well as of those in a worse clinical condition.

Comparison with a previous study

In the present article we analysed aneurysm patients from 2007–2011 and compared them with those from 2001–2006 (8). The main difference was that the patients of the present group were older. This is in line with other observations, e.g. Nieuwkamp et al. (17) and Naval et al. (18). There were also fewer

Table II. Outcome for aneurysm patients after stratifying for age (≤65 years and >65 years) and clinical condition at admission (WFNS 1–2, WFNS 3, and WFNS 4–5). The results have been compared with a previously published series from our unit (2001–2006).

	2001–2006	2007–2011	*p* Value
≤65 Years:	%	%	
WFNS 1–2			
GOS 1–2 poor	4	4	ns
GOS 3 severe	16	18	ns
GOS 4–5 (favourable)	79	78	ns
WFNS 3			
GOS 1–2 poor	4	0	ns
GOS 3 severe	44	87	< 0.04
GOS 4–5 (favourable)	52	13	0.050
WFNS 4–5			
GOS 1–2 poor	20	27	ns
GOS 3 severe	40	42	ns
GOS 4–5 (favourable)	40	31	ns
>65 years:			
WFNS 1–2			
GOS 1–2 poor	28	21	ns
GOS 3 severe	21	30	ns
GOS 4–5 (favourable)	51	49	ns
WFNS 3			
GOS 1–2 poor	20	25	ns
GOS 3 severe	50	27	ns
GOS 4–5 (favourable)	30	27	ns
WFNS 4–5			
GOS 1–2 poor	40	45	ns
GOS 3 severe	45	38	ns
GOS 4–5 (favourable)	15	17	ns

patients in good clinical condition at admission, which is again consistent with previous literature (18).

Fewer patients with aneurysms had a good functional outcome in the present material compared with the earlier series. This was probably due to a combination of factors, one of which was a new routine requiring that almost every patient undergoes a CTA as soon as possible after admission. The effect was that some of the patients who previously would have been considered too old and/or too ill for a DSA were diagnosed as having an aneurysm, but did not receive treatment due to a poor clinical condition. This resulted in a larger group of patients diagnosed with aneurysmal subarachnoid haemorrhage who were on average older and in worse condition.

A second possible reason for the decline in outcome scores was that the follow-up in the newer material was done at an earlier time point. It has been shown that the outcome of SAH patients improves with time, especially for those in a poor condition (19). When comparing the current material (2007–2011) with the previous series (2001–2006), there was no significant change in outcome for the older patients (>65), but the younger patients admitted in WFNS 3 appeared to have a worse outcome in the current material. It is possible that the longer time to follow-up in our earlier series allowed for the younger group to recover sufficiently to return to work, an important factor in determining the Glasgow Outcome Score. Since the older group was past retirement age, return to work was not a factor, and the positive effects of the longer time to follow-up would probably have less of an impact on the outcome scores. This hypothesis is supported by the study by Wilson et al. (19) which showed that there could be a delayed recovery after poor grade SAH and that younger age was a predictor for improvement beyond 6 months.

When studying the literature regarding outcome there are difficulties in comparing different patient series. We have described the outcome on the whole material referred to us, and have a complete data set on all patients. However, other reports in which outcome was measured have further inclusion requirements, such as that the patient survive for at least 3 months (18), and restriction to specific age groups (20) or after certain treatments (4,21).

A combination of higher age and signs of a more severe disease predicted a worse outcome, while aneurysm location and treatment mode did not. This suggests that the most important treatment factor for outcome is that the aneurysm is treated early, which is now usually the case, and that the clinical course after that depends largely on the condition of the patient on admission rather than treatment factors.

Elderly patients and SAH

The introduction of endovascular techniques has made treatment an option for elderly patients who previously were treated conservatively (22,23).This is a positive development, but as discussed above it will naturally result in worse outcome scores for the overall patient group. Early closing of the aneurysm is of major importance for survival, but the final outcome depends on many other factors such as NICU treatment and rehabilitation measures.

The exclusion of the aneurysm is followed by a period during which cerebral as well as systemic complications can occur. The importance of NICU

care in elderly patients with SAH has been demonstrated (13,24). General policies regarding ICU treatment of elderly patients have also been studied (for references see (25)). One recommendation is that the grade of dependency should be considered before aneurysm treatment and intensive care are offered. The seriousness of the disease and any simultaneously occurring conditions are also important factors to be considered. Elderly patients are especially prone to kidney problems during ICU care (26), which can be a serious complication since the systemic effects of SAH often include infections and imbalances in fluid and salt levels and also infections. It should also be considered before choosing embolization for treating the aneurysm.

Limitations

One problem with this study is that follow-up was not done at the same time point in all patients. This seems to be a common problem in literature on SAH. However, in recent years our department has adopted a more consistent protocol for follow-up of functional outcome and of health-related quality of life, both of which are evaluated 1 year after SAH (10).

Conclusion

We show in this paper the results from treating patients with spontaneous SAH between 2007 and 2011. We compare the results with our previous series from 2001–2006. Aneurysms have been diagnosed in significantly more cases, which we attribute to a new routine in our clinic of doing CTA at admission. The results show that in the new series older patients and patients in a worse clinical condition and with more blood on the CT scan were admitted. Linear regression analysis showed that functional outcome was best predicted by age, clinical condition at admission, and the size of the bleeding, and not by treatment mode or location of the aneurysm. This suggests that the most important factor for outcome is that the aneurysm is treated early, which is now usually the case, and that otherwise the clinical course depends largely on the condition of the patient on admission rather than treatment factors.

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References

1. Cesarini KG, Hardemark HG, Persson L. Improved survival after aneurysmal subarachnoid hemorrhage: review of case management during a 12-year period. J Neurosurg. 1999;90: 664–72.
2. Ryttlefors M, Howells T, Nilsson P, Ronne-Engstrom E, Enblad P. Secondary insults in subarachnoid hemorrhage: occurrence and impact on outcome and clinical deterioration. Neurosurgery. 2007;61:704–14.
3. Guglielmi G, Vinuela F, Sepetka I, Macellari V. Electrothrombosis of saccular aneurysms via endovascular approach. Part 1: Electrochemical basis, technique, and experimental results. J Neurosurg. 1991;75:1–7.
4. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360:1267–74.
5. Molyneux AJ, Kerr RS, Yu LM, Clarke M, Sneade M, Yarnold JA, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet. 2005;366:809–17.
6. McDougall CG, Spetzler RF, Zabramski JM, Partov S, Hills NK, Nakaji P, et al. The barrow ruptured aneurysm trial. J Neurosurg. 2012;116:135–44.
7. Koivisto T, Vanninen R, Hurskainen H, Saari T, Hernesniemi J, Vapalahti M. Outcomes of early endovascular versus surgical treatment of ruptured cerebral aneurysms. A prospective randomized study. Stroke. 2000;31:2369–77.
8. Ronne-Engstrom E, Enblad P, Gal G, Norback O, Ryttlefors M, Cesarini KG, et al. Patients with spontaneous subarachnoid haemorrhage—presentation of a 10-year hospital series. Br J Neurosurg. 2009;23:499–506.
9. Ronne-Engstrom E, Enblad P, Lundstrom E. Outcome after spontaneous subarachnoid hemorrhage measured with the EQ-5D. Stroke. 2011;42:3284–6.
10. Ronne-Engstrom E, Enblad P, Lundstrom E. Health-related quality of life at median 12 months after aneurysmal subarachnoid hemorrhage, measured with EuroQoL-5D. Acta Neurochir. 2013;155:587–93.
11. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery. 1980;6:1–9.
12. Persson L, Enblad P. Neurointensive care of aneurysmal SAH. Acta Neurochir Suppl. 1999;72:73–80.
13. Ryttlefors M, Howells T, Ronne-Engstrom E, Nilsson P, Enblad P. Neurointensive care is justified in elderly patients with severe subarachnoid hemorrhage–an outcome and secondary insults study. Acta Neurochir. 2010;152:241–9.
14. Teasdale GM, Drake CG, Hunt W, Kassell N, Sano K, Pertuiset B, et al. A universal subarachnoid hemorrhage scale: report of a committee of the World Federation of Neurosurgical Societies. J Neurol Neurosurg Psych. 1988;51:1457.
15. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet. 1975;1:480–4.

16. Akaike H. A new look at the statistical model identification. IEEE Trans Automat Contr. 1974;19:716–23.
17. Nieuwkamp DJ, Setz LE, Algra A, Linn FH, de Rooij NK, Rinkel GJ. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. Lancet Neurol. 2009;8:635–42.
18. Naval NS, Chang T, Caserta F, Kowalski RG, Carhuapoma JR, Tamargo RJ. Improved aneurysmal subarachnoid hemorrhage outcomes: a comparison of 2 decades at an academic center. J Crit Care. 2013;28:182–8.
19. Wilson DA, Nakaji P, Albuquerque FC, McDougall CG, Zabramski JM, Spetzler RF. Time course of recovery following poor-grade SAH: the incidence of delayed improvement and implications for SAH outcome study design. J Neurosurg. 2013;119:606–12.
20. Karamanakos PN, Koivisto T, Vanninen R, Khallaf M, Ronkainen A, Parviainen I, et al. The impact of endovascular management on the outcome of aneurysmal subarachnoid hemorrhage in the elderly in eastern Finland. Acta Neurochir. 2010;152:1493–502.
21. Spetzler RF, McDougall CG, Albuquerque FC, Zabramski JM, Hills NK, Partovi S, et al. The Barrow Ruptured Aneurysm Trial: 3-year results. J Neurosurg. 2013;119:146–57.
22. Johansson M, Cesarini KG, Contant CF, Persson L, Enblad P. Changes in intervention and outcome in elderly patients with subarachnoid hemorrhage. Stroke. 2001;32:2845–949.
23. Ryttlefors M, Enblad P, Kerr RS, Molyneux AJ. International subarachnoid aneurysm trial of neurosurgical clipping versus endovascular coiling: subgroup analysis of 278 elderly patients. Stroke. 2008;39:2720–6.
24. Ryttlefors M, Enblad P, Ronne-Engstrom E, Persson L, Ilodigwe D, Macdonald RL. Patient age and vasospasm after subarachnoid hemorrhage. Neurosurgery. 2010;67:911–17.
25. Boumendil A, Guidet B. Elderly patients and intensive care medicine. Int Care Med. 2006;32:965–7.
26. Chronopoulos A, Rosner MH, Cruz DN, Ronco C. Acute kidney injury in elderly intensive care patients: a review. Int Care Med. 2010;36:1454–64.