Aneurismal subarachnoid hemorrhage: who remains for surgical treatment in the post-ISAT era?

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Abstract

Introduction: Although there have been a number of studies on changes and trends in the management of aneurismal subarachnoid hemorrhage (aSAH) since publication of the International Subarachnoid Aneurysm Trial (ISAT), no data exist on what category of patients still remains for surgical treatment. Our goal was to investigate the changes that occurred in the characteristics of a population of aSAH patients treated surgically in the post-ISAT period in a single neurosurgical center, with limited availability of endovascular service.

Material and methods: The study included 402 aSAH patients treated surgically in our unit between January 2004 and December 2011. Each year, data regarding number of admissions, age, aneurysm location and size, clinical and radiological presentation, outcome and mortality rates were collected and analyzed.

Results: The annual number of admissions more than halved in the study period (from 69 in 2004 to 32 in 2011). There were no linear trends regarding patients’ mean age, clinical presentation and outcomes, but the number of patients in Fisher grade 4 increased and mortality slightly decreased. An unexpected, statistically significant increase occurred in the incidence of anterior communicating artery aneurysms (from 36.2% to 50%) and medium size aneurysms (from 34.7% to 56.2%) treated surgically, with a corresponding decrease in the incidence of middle cerebral artery aneurysms (from 40.5% to 34.3%) and large aneurysms (from 21.7% to 12.5%).

Conclusions: Unexpected trends in characteristics of aSAH patients treated surgically could be related to treatment decision modality. Trend patterns could be properly expressed in the constant availability of endovascular services.

Key words: intracranial aneurysms, subarachnoid hemorrhage, trend, surgical clipping.

Introduction

Since the introduction of endovascular techniques in 1990 and their approval by the US Food and Drug Administration in 1995, treatment of intracranial aneurysms has been gradually modified. A number of clinical studies have revealed that endovascular coiling is an equal or even better alternative in aneurism treatment than surgery [1–5]. Following the publication of the results of the International Subarachnoid Aneurysm Trial (ISAT), a significant change in practice pattern occurred all over the world, with a constantly increasing number of aneurysms treated endovascularly [6]. Guidelines for the treatment of cerebral aneurysm have
been proposed and multidisciplinary teams have been formed to provide the best medical policy for the patients [7, 8]. However, in many centers there are still no endovascular services, and even if they exist they are not available on a permanent basis. Since the acute treatment of a ruptured aneurysm within the first 24 h seems to be the best option, the treatment decision is frequently made by neurosurgeons themselves [9, 10].

There have been a number of studies devoted to changes and trends in the field of management of aneurismal subarachnoid hemorrhage (aSAH) in the last decades, published on national and international levels [11–16]. Those studies usually covered both groups of patients treated by coiling and by clipping and focused on the overall data. However, the category of patients remaining for surgical treatment in the post-ISAT era is not specified. Therefore, the current study analyses only one subgroup, of those treated surgically.

The goal was to investigate what changes occurred in the population of aSAH patients treated by surgical methods in the post-ISAT period and to explore any possible trends in the successive years. We report data from a high-volume center (>35 aSAH cases per year) with limited availability of endovascular service.

Material and methods

Data collection

This study was conducted in the Department of Neurosurgery at Wroclaw Medical University, which serves a population of approximately 2.8 million. The staff of six attending neurosurgeons was available on call for 24 h to perform the clipping procedure. In contrast, the staff of two attending neuroradiologists, of whom only one performed endovascular coiling, was available twice a week during limited time. The treatment policy was to secure a ruptured aneurysm within the first 24 h.

The study period was selected to evaluate the changes and trends in the aSAH population treated by surgical clipping after the publication of the results of the ISAT trial in October 2002. Patients admitted to our unit between January 2004 and December 2011 with the diagnosis of aSAH and treated by surgical means were identified from a clinical database. Diagnostic code fields were screened for ICD-10 code I60.0-9 to identify adult patients with aneurismal SAH of a different source. Only the patients with the procedure code for aneurysm clipping ICD-9 39.51 were included in the study. We recorded details such as number of admissions per year, patient demographics, clinical grade at presentation, SAH severity, clinical outcome at discharge, mortality, aneurysm location and size. The clinical grade at presentation was assessed applying the Hunt-Hess (H-H) grade and Glasgow Coma Scale (GCS), where 4–5 H-H and 3–8 GCS were considered as poor grades. SAH severity was assessed by applying the Fisher grade. Clinical outcome at discharge was assessed using the Glasgow Outcome Scale (GOS), in which an outcome of 4–5 was considered to be good, whereas 1–3 was poor, including GOS 1 representing deaths. We selected several aneurysm locations such as the anterior communicating artery (ACoA), internal carotid artery (ICA), middle cerebral artery (MCA), posterior communicating artery (PCoA), posterior cerebral artery (PCA), anterior cerebral artery (ACA), basilar artery (BA), and anterior inferior cerebellar artery (AICA). Clipped aneurysms suspected of bleeding were divided into four size groups: small (1–5 mm), medium (6–10 mm), large (11–24 mm) and giant (≥25 mm).

Statistical analysis

We used the Cochran-Armitage test for categorical data and analysis of variance for continuous data to assess the trends in patients’ clinical grade at presentation, patients’ clinical outcome, SAH severity, mortality, aneurysm location and size in the successive years, from 2004 to 2011. The null hypothesis, that there is no linear trend, was true for a p-value ≤ 0.05; otherwise the alternative hypothesis, that there is a linear trend, was true. Due to the small sample size for some of the data (example: BA aneurysm localization), the result of statistical analysis was uncertain; therefore they were not considered. For the analysis of the trend in the number of patient admissions per year we used the χ² test for homogeneity. For the analysis of the trend in patients’ mean age we used Pearson’s correlation and Spearman’s rank correlation tests. All tests were performed using the R statistical package, version 2.8.0.

Results

Patients and surgical management

A total of 402 adult patients were admitted with the diagnosis of aSAH and treated by surgical clipping during the study period. The mean age of the patients was 53 years and 258 (64.1%) patients were females. The characteristics of the patients and clipped aneurysms are presented in Table I. On angiography or angio-CT 319 (79.4%) patients had a single aneurysm and 83 (20.6%) had multiple aneurysms (between 2 and 7). Table I shows the location and size of the aneurysms that were most likely to bleed. All of the patients underwent craniotomy and clipping of their aneurysms with concurrent evacuation of intracerebral hematoma (ICH) if present. Temporary clips were
Changes and trends in characteristics of aSAH patients

The annual number of admissions decreased in successive years from 69 in 2004 to 32 in 2011 (Table II). There was a statistically significant \((p < 0.001)\) trend toward a lower number of patients operated on annually. The highest number of patients was admitted in 2006 (82 patients), the lowest in 2008 (31 patients). The greatest decrease occurred in 2007, almost halving from 82 to 43 patients (Figure 1). The age range was 18–92 years. Pearson’s correlation and Spearman’s rank correlation revealed no linear trend in patient mean age in the study period. The biggest difference in the mean patients’ age appeared between 2007 and 2008, when it was 56.3 and 51.1 respectively (Figure 2). Sixty-seven percent of patients (271) were admitted in Hunt-Hess grade 1–3, which corresponds to 70.4% of patients (283) who achieved GCS 9-15 at presentation (Table I). There was no linear trend in the clinical presentation of the patients from 2004 to 2011 (Table II). However, the Cochran-Armitage test revealed that the number of patients with intracerebral or intraventricular hemorrhage (Fisher grade 4) tends to increase (Figure 3). In 2008 there was a lower number (9.6%) of patients in poor neurological grade (Hunt-Hess 4 and 5) as well as in Fisher grade 4 (35.4%). Overall, a favorable outcome (GOS 4 and 5) was achieved in 239 (59.4%) patients. The mortality rate was 20.1% (Table I). Although there was no linear trend in the overall outcomes, mortality slightly decreased over the study period (Figure 4). The highest percentage of favorable outcome occurred in 2008, with the lower mortality rate of 12.9% (Table II). Among the aneurysms that were more likely to bleed, 76.3% originated from the ACoA and MCA. Seventy-eight percent of aneurysms constituted those of small or medium size, i.e. equal to or less than 10 mm (Table I). There was a statistically significant increase in the percentage of patients with ACoA aneurysms (from 36.2% in 2004 to 50% in 2011), with a corresponding decrease in the percentage of patients with MCA aneurysms (from 40.5% to 34.3%) and ICA aneurysms (from 17.3% to 12.5%) (Table II, Figure 5). The percentage of patients with medium aneurysms (6–10 mm) also increased (from 34.7% in 2004 to 56.2% in 2011). In contrast, the percentage of patients with small (0–5 mm) aneurysms decreased

### Table I. Baseline patients’ characteristics

| Characteristics | No. \((n = 402)\) | Percent |
|-----------------|-----------------|---------|
| Age, median \([\text{years}]\) | 53.61 ±1.08 |         |
| Female gender | 258 | 64.1 |
| Aneurysm location: | | |
| ACoA | 155 | 38.5 |
| MCA | 152 | 37.8 |
| ICA | 68 | 16.9 |
| PCoA | 7 | 1.7 |
| PA | 13 | 3.2 |
| ACA | 1 | 0.2 |
| AICA | 1 | 0.2 |
| BA | 5 | 1.2 |
| Aneurysm size \([\text{mm}]\): | | |
| Mean | 9.12 ±6.8 |         |
| Small \((0–5)\) | 130 | 32.3 |
| Medium \((6–10)\) | 184 | 45.7 |
| Large \((11–24)\) | 63 | 15.6 |
| Giant \(\geq 25\) | 25 | 6.2 |
| GCS grade at presentation: | | |
| 3–8 | 119 | 29.6 |
| 9–12 | 60 | 14.9 |
| 13–15 | 223 | 55.4 |
| Hunt-Hess grade at presentation: | | |
| 1 | 55 | 13.6 |
| 2 | 94 | 23.3 |
| 3 | 122 | 30.3 |
| 4 | 65 | 16.1 |
| 5 | 66 | 16.4 |
| Fisher grade: | | |
| 1–3 | 205 | 51 |
| 4 | 197 | 49 |
| Outcome (discharge GOS): | | |
| 5 | 141 | 35.0 |
| 4 | 98 | 24.3 |
| 3 | 61 | 15.1 |
| 2 | 21 | 5.2 |
| 1 (death) | 81 | 20.1 |
Table II. Changes and trends in characteristics of aSAH patients, 2004–2011

| Characteristics                        | Years | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | \( \chi^2 \) | df | Value of \( p \) |
|----------------------------------------|-------|------|------|------|------|------|------|------|------|----------|-----|-----------------|
| Number of admissions                   | n     | 69   | 70   | 82   | 43   | 31   | 36   | 39   | 32   | 56.43    | 7   | < 0.0001        |
|                                       | %     | 17.16| 17.41| 20.40| 10.70| 7.71 | 8.96 | 9.70 | 7.96 |          |     |                 |
| Aneurysm location                      |       |      |      |      |      |      |      |      |      |          |     |                 |
| ACoA                                   | n     | 25   | 24   | 29   | 13   | 15   | 17   | 16   | 16   | 3.17     | 6   | 0.7868         |
|                                       | %     | 36.23| 34.29| 35.37| 30.23| 48.39| 47.22| 41.03| 50.00|          |     |                 |
| ICA                                    | n     | 12   | 12   | 14   | 9    | 4    | 3    | 10   | 4    | 5.24     | 7   | 0.5133         |
|                                       | %     | 17.39| 17.14| 17.07| 12.90| 8.33 | 7.41 | 10.43| 12.50|          |     |                 |
| MCA                                    | n     | 28   | 30   | 32   | 17   | 12   | 12   | 10   | 11   | 1.37     | 6   | 0.9677         |
|                                       | %     | 40.58| 42.86| 39.02| 39.53| 38.71| 33.33| 25.64| 34.38|          |     |                 |
| PCoA                                   | n     | 2    | 1    | 2    | 1    | 0    | 2    | 1    | 0    | (*)      | (*) | (*)            |
|                                       | %     | 2.90 | 1.43 | 2.44 | 2.33 | 0.00 | 0.00 | 0.00 | 0.00 |          |     |                 |
| PA                                     | n     | 0    | 2    | 3    | 3    | 2    | 0    | (*)  | (*)  | (*)      | (*) | (*)            |
|                                       | %     | 0.00 | 2.86 | 3.66 | 6.98 | 6.83 | 5.13 |      |      |          |     |                 |
| ACA                                    | n     | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | (*)      | (*) | (*)            |
|                                       | %     | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |      |      |          |     |                 |
| AICA                                   | n     | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | (*)      | (*) | (*)            |
|                                       | %     | 1.45 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |      |      |          |     |                 |
| death                                  | n     | 12   | 17   | 21   | 9    | 4    | 8    | 5    | 5    | 4.22     | 6   | 0.6466         |
|                                       | %     | 17.39| 24.29| 25.61| 20.93| 12.90| 22.22| 12.82| 15.62|          |     |                 |

(*) Values not established due to the small study sample.
from 34.7% in 2004 to 28.12% in 2011 and large (11–24 mm) aneurysms decreased from 21.7% to 12.5% (Table II, Figure 6). Due to the small study sample it was not statistically possible to establish the trend for PCoA, PA, ACA, AICA, BA and for giant aneurysms.

Discussion

Despite major technical advances in imaging and in endovascular treatment of cerebral aneurysms during the last two decades, there still exists a large group of “uncollapable aneurysms”
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and patients requiring surgical rather than endovascular intervention. They form the main bulk of surgical management after the ISAT study, which promoted endovascular coiling as a first-line treatment in patients with aSAH [6]. According to recent guidelines and data, for patients with MCA aneurysms or with very small and large/giant aneurysms, surgical treatment has tended to yield more favorable results [17–22]. However, in cases of vertebra-basilar aneurysms, especially in older patients, endovascular treatment has been gaining widespread acceptance based on several observational studies [23–28]. Early ICH evacuation has been shown to improve the outcome in this subgroup and provides arguments in favor of surgery for patients with large intracerebral hematomas in the course of aneurysm rupture [29]. Instead, patients with a poor neurological grade at presentation without parenchymal clots appear to benefit more from endovascular coiling [30].

Based on these assumptions, we hypothesized that the probable trend pattern in the characteristics of the aSAH population that remains for surgical treatment should move towards a higher proportion of older patients with MCA aneurysm, very small or very large/giant aneurysm. The percentage of patients with a Fisher grade of 4 should increase, which could influence the outcomes, because the occurrence of parenchymal clots is usually associated with a poor neurological grade. On the other hand, the percentage of patients with a poor neurological grade who do not require surgical intervention due to ICH should decrease, which is why the outcomes and mortality rate were rather unpredictable.

Seeking an answer to the question of who remains for surgical treatment in the post-ISAT era, we searched PubMed, but there were no data devoted to this subject. Although there are studies on trends and changes in the management of aSAH patients in the last decades, they refer to both groups, i.e. those treated surgically and endovascularly together, and even if there is a comparison between the two subgroups, it is quantitative rather than qualitative. This is somewhat incomprehensible, since in many European centers surgical clipping remains the main solution for intracranial aneurysm treatment due to economic reasons and the lack of experienced coilers. According to Bradac et al., endovascular service is not available in 40% of European centers that participated in the study, and among the remaining 60% there are still centers without permanent availability of this technique [31]. This situation probably applies to other countries outside Europe, but again we have found no published data.

In the current study the number of aSAH patients undergoing surgical treatment has decreased, which reflects the worldwide trend. In 2011 we operated on half the number of patients compared to 2004, while since 2006 the number of operations performed annually seems to have been constant. In other studies, that decrease was usually by one third or less [12–15]. The patients’ mean age differs in successive years but reveals no clear trend, although there are sparse reports on the regularly decreasing number of older patients treated by clipping [12]. There was also no visible trend in the clinical presentation of the patients (assessed by Hunt-Hess and GCS) and in the outcomes between 2004 and 2011. In some other studies there exist data which demonstrate a decrease in the number of patients in a good neurological state at presentation with a corresponding increase in the number of poor grade patients, although those data refer to patients treated with both surgical and endovascular methods [12, 14]. Although there was no outcome trend, the mortality rate revealed a tendency to decrease. We found two other reports on the decreasing mortality in a group of aSAH patients treated surgically [13, 14]. It is noteworthy that mortality and morbidity in aSAH patients depend mainly on non-modifiable factors (neurological state of patients on admission, age) while the surgical procedure of aneurysm clipping seems to be relatively safe and has no impact on the outcome [32–35]. However, there are reports on cerebrovascular accidents and systemic complications during this procedure [36, 37]. We also noted a slight trend of an increasing number of patients in Fisher grade four. There were some cases of posterior circulation aneurysm surgery, but due to the small sample size we did not take it into consideration in the statistical analysis. Surprisingly, there was a trend of an increasing number of ACoA aneurysms treated annually and a decrease in MCA aneurysms. This is in contrast to the study of Payner et al. and our original hypothesis [12]. We also observed a trend showing a higher number of small aneurysms treated, whereas the number of middle-size aneurysms remained stable and the number of large ones slightly decreased.

The authors attributed these unexpected trends related mainly to aneurysm characteristics to the limited availability of endovascular service, which is a serious problem facing a number of neurosurgical centers, especially in Central, Eastern and Southern Europe, according to the published data [31]. There are two points in the most recent guidelines for the management of aneurismal subarachnoid hemorrhage that cannot be followed simultaneously in those centers [7]. The first is that the management should be performed as early as feasible in the majority of patients to reduce the rate of rebleeding after aSAH, where-
as the other is that determination of aneurysm treatment should be a multidisciplinary decision based on the characteristics of the patient and the aneurysm. The neurosurgeons have to choose between an acute treatment, based on their own decision and their own skills, and a significantly delayed treatment (in some cases > 96 h), based on a multidisciplinary team decision. However, in the case of rebleeding, which could result in severe disability or patient’s death, the neurosurgeon will be held liable. The ultimate goal should be an early occlusion of a ruptured aneurysm, and although there is no prospective, randomized trial of the timing of ruptured aneurysm treatment, the majority of European centers provide this within 24 h by any methods available. In conclusion, although there was a trend indicating a lowering number of patients operated on annually in the post-ISAT period, the group of patients treated surgically remained stable in terms of age, clinical presentation and outcomes in successive years. The unexpected trends of the increasing number of ACoA aneurysms and the decreasing number of MCA aneurysms treated, together with the trend of the decreasing number of large aneurysm treated, could be related to the treatment decision modality. Trend patterns could be properly expressed in the constant availability of endovascular services.

Conflict of interest

The authors declare no conflict of interest.

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