RESULTS OF SURGICAL AND NON-SURGICAL TREATMENT OF ANEURYSMS IN IRAN

Mohammad Reza Rezvani[(1)], Kavian Ghandehari[(2)], Fahimeh Ahmadi[(3)], Azadeh Afzalnia[(3)]

Abstract

BACKGROUND: Direct surgery or endovascular procedures are an accepted way of treating patients with Aneurismal Subarachnoid Haemorrhage (SAH). However the impact of invasive methods of treatment on results in developing countries may differ from that in developed countries.

METHODS: This is a prospective clinical study of consecutive patients with Subarachnoid Haemorrhage (SAH) admitted in Ghaem hospital in Mashhad during 2005-2010. The initial diagnosis and investigations were carried out by neurologists. The patients were divided into two groups. One received surgical treatment whilst the other group was managed medically. The decision as to the choice of method of treatment was made by the neurosurgeons. The initial medical treatment was standardised for all the patients. The rate of complications and mortality was compared in both medical and surgical groups.

RESULTS: 120 SAH patients (52% females) with a mean age of 50.6 ± 7 years were evaluated. The angiography revealed the presence of an aneurysm in 62 patients. 63.5% of patients received medical treatment and 37.5% underwent aneurysmal surgery. Difference of rebleeding rate in two therapeutic groups was not significant; $\chi^2 = 0.014$, $P = 0.91$. The effect of rebleeding on mortality was not significant; $\chi^2 = 2.54$, $P = 0.14$. Within 62 SAH patients with cerebral aneurysm, the mortality rate in both therapeutic groups was also not significantly different; $\chi^2 = 0.16$, $P = 0.77$.

CONCLUSION: There is no significant difference in the mortality rate between the "surgical" and non "surgical" groups of patients with SAH. This could be due to delay in performance of surgery in neurovascular centers in Iran.

Keywords: Mortality, Subarachnoid, Surgery, Haemorrhage.

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Introduction

The outcome for patients with SAH remains poor, with mortality rates up to 45%, and there is significant morbidity among survivors.[1] The review of literature and prospective cohorts has shown that for untreated, ruptured aneurysms, there is at least a 3-4% risk of rebleeding in the first 24 hours and 1-2% per day in the first month.[2] Urgent investigation and treatment of patients with suspected SAH is therefore recommended.[2] The major complications following SAH are due to ischaemic deficit (27%) and hydrocephalus (12%).[3] However the most feared complication for survivors of the initial haemorrhage is recurrent bleeding, which occurs in 15-20% of the patients and is associated with a 40-78% mortality.[3] The definitive method for prevention of rebleeding is to secure the aneurysm as soon as possible.[2] Early surgery may not be appropriate for every patient with SAH but every attempt should be made to secure the aneurysm as soon as possible to prevent rebleeding.[3] Unfortunately in our country many patients with SAH are admitted to hospitals without facilities for catheter angiography, aneurysmal coiling, or direct aneurysmal surgery. Even in tertiary care hospitals with these facilities, many of the SAH patients are admitted after 3 days following the ictus and for this reason the surgical or endovascular treatment is delayed for up to 3 weeks post the event. Unfortunately there is no policy of urgency in the Emergency Departments to direct the patients with SAH for appropriate management. Additionally, some of our SAH patients refuse surgery on cultural or economic grounds. In this paper we report the first prospective study of aneurysmal surgery in patients with SAH in Iran.

1- Assistant Professor of Internal Medicine, Birjand University of Medical Sciences, Birjand, Iran.
2- Professor of Cerebrovascular Disease, Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
3- Resident of Neurology, Mashhad University of Medical Sciences, Mashhad, Iran.
Corresponding author: Kavian Ghandehari, Email: kavianghandehari@yahoo.com

Materials and Methods

Consecutive patients with Subarachnoid Hemorrhage (SAH) admitted in Ghaem hospital, Mashhad, during 2005-2010 were enrolled in a prospective clinical study. Our hospital is a University tertiary care center in north-east of Iran. Neurologists, neurosurgeons, and radiologists are available 24 hours per day and 7 days per week in the hospital. SAH patients who died before arriving to hospital were excluded from this study. The initial Hunt and Hess scale of each SAH patient on arrival to the hospital was recorded in both therapeutic groups. Diagnosis of SAH was based on a brain CT scan. Patients suspected to have a SAH but with normal brain CT scan underwent a FLAIR MRI scan and lumbar puncture.[4,5] Catheter cerebral angiography is a routine diagnostic investigation in our SAH patients and is performed by general radiologists. SAH patients with an initially normal cerebral angiography usually underwent a second angiography after 3 weeks. Patients who did not have cerebral angiography due to poor medical condition or early death in hospital or allergy to contrast material were excluded. Positive angiogram for aneurysm was found in 63.5% of our SAH patients. SAH patients were usually admitted for 3 weeks in either Neurology or Neurosurgery divisions. In our center, cerebral angiography followed by aneurysmal clipping is usually performed on patients with SAH within the first 72 hours post SAH. Patients who arrive to hospital after this time or were initially comatose were usually treated medically and diagnostic procedures and surgery if required were performed in this group of cases after 3 weeks post the event. SAH patients who underwent craniotomy and aneurysmal clipping were categorized as a surgical therapeutic group. Aneurysmal clipping is the usual type of surgical procedure in our hospital for these patients. Aneurysmal wrapping is not performed and endovascular coiling is not available. Patients who underwent ventricular shunting for hydrocephalus without aneurysmal clipping were included in the medical therapeutic group. Surgical decision of the patient for aneurysm was made by a neurosurgeon. General medical condition of the patients was assessed by anesthetists and patients with poor cardiopulmonary or medical condition were excluded. SAH patients with Hunt and Hess scale of 5 were also excluded. Despite neurosurgical recommendation, some of our patients refused surgery due to cultural aspects or lack of funds. The medical management received was standardized in both surgical and medical groups of SAH patients. Principles of medical management included; analgesia, Nimodipine, sedatives, laxatives, control of blood pressure and 3 litres of Normal Saline per day.[4,5] Demographic features, risk factors, cerebral CT findings, clinical manifestations and aneurysm characteristics were evaluated in all patients. Mortality and complications in SAH, including rebleeding, hydrocephalus and brain infarction due to vasospasm, were recorded in both medical and surgical groups of patients during hospitalization. The time was recorded and compared in each therapeutic group from SAH onset to hospital arrival, SAH onset to death, SAH onset to surgery (where applicable) and surgery (where applicable) to death in all patients. Chi-Square and Fisher tests were used for statistical analysis and $P < 0.05$ declared as significant. The research project was approved by the ethics committee of our hospital and an informed signed consent was taken from patients or their first degree relatives.

Results

The results of the treatment of one hundred and twenty SAH patients (63 females, 57 males) with a mean age 50.6 ± 7 years were prospectively evaluated. SAH was detected on cerebral CT in 95% of the cases. The patients were divided into two therapeutic groups. Among our SAH patients, 62.5% with mean age of 52.4 ± 5 received medical treatment and 37.5% with mean age of 49.7 ± 3 were subjected to surgery.

Hypertension, smoking, oral contraceptive medication, past trauma and over dosage of oral anticoagulation therapy were found in 41.6%, 19.1%, 0%, 0%, and 0.8% of patients respectively. Fifty six patients were subjected to surgery, of whom 45 underwent craniotomy and aneurysmal clipping, while 11 cases had CSF shunting without aneurysmal clipping and were included into the medically managed group. Overall mortality was 44.2% of all SAH patients (60.4% of females and 39.6% of males). There was no statistically significant difference in the death rate between the two therapeutic groups ($\chi^2 = 1.54$, df = 1, $P = 0.11$) and no significant difference between the females and males ($\chi^2 = 0.73$, df = 1, $P = 0.39$).

The mean SAH onset to admission time in whole of our SAH patients and in their medical and surgical groups were 66 ± 4, 84 ± 1 and 24 ± 7 hours respectively. The overall mean timing from the onset of SAH to death was 14.1 ± 2 days. In the surgical group, the mean length of time from onset of SAH to surgery was 8.4 ± 3 days and of those who died, the mean length of the time between surgery and death was 5.9 ± 3 days.

Table 1 compares the characteristics between surgical and medical groups. The effect of therapeutic type of aneurysm management on mortality was not

significant ($\chi^2 = 0.16$, P = 0.77). Rebleeding occurred in 4.4% of patients in the surgical group and 4% in the medical group and the difference was not statistically significant ($\chi^2 = 0.014$, P = 0.91). Among 5 SAH patients with rebleeding, 2 had an anterior communicating artery aneurysm and 3 had a "normal angiography". The influence of rebleeding on the overall mortality was not statistically significant ($\chi^2 = 2.54$, P = 0.14). None of the studied patients had rebleeding before admission to hospital. However rebleeding may have occurred in patients who died before arriving to the hospital and these were not included in this study. Hydrocephalus was found in 17 patients and its frequency was not significantly different in the two therapeutic groups ($\chi^2 = 5.58$, P = 0.03).

Out of 17 SAH patients with hydrocephalus, 13 (76%) died and the effect of hydrocephalus on the mortality of these patients was significant ($\chi^2 = 7.93$, P = 0.007). Cerebral infarction due to vasospasm occurred in 7 (5.8%) patients (4.4% of the surgical and 6.7% of the medical group).

The choice of aneurysmal therapeutic strategy on frequency of cerebral infarction was not significant ($\chi^2 = 0.25$, P = 0.71). Out of seven patients with brain infarction due to vasospasm, three cases died. The effect of cerebral infarction on the overall mortality of SAH patients was not significant ($\chi^2 = 0.005$, P = 1).

Table 2 represents distribution of complications in two therapeutic groups of our patients. Aneurysms were found in the angiography of 62 patients (45 in the surgical and 17 in the medical group). The distribution was as follows: Anterior communicating artery 41.9%, middle cerebral artery 23.1%, internal carotid artery 14.5%, basilar artery 4.8%, anterior cerebral artery 4.8%, posterior communicating artery 6.4%, and multiple aneurysms 3%. Among 62 SAH patients with aneurysm on angiography, 45 patients (72.6%) underwent aneurysm surgery and 17 cases (27.4%) received only medical management. Death was recorded in 48.9% of SAH patients with aneurysm who underwent aneurysm surgery (22/45) and 41.2% of patients with aneurysm who only received medical management (7/17).

High Hunt and Hess scale, poor general medical condition and refusal of patients constituted reason of excluding these 17 cases with aneurysm from surgical group in 58.8%, 29.4% and 11.7% respectively. Details of Hunt and Hess scales of these seventeen cases are presented in Table 1. The difference in the mortality rate in 62 SAH patients with angiographically confirmed aneurysms in two therapeutic groups was not statistically significant ($\chi^2 = 0.16$, P = 0.77).

Discussion

In aneurysmal surgery, delay in treatment is associated with increased rates of pre-operative rebleeding, in both retrospective and prospective studies.[2] Recently it has been associated with higher rates of poor outcome.[2,6] The International Co-operative Study on the Timing of Aneurysmal Surgery, analysed management of 3521 patients, of whom 83% underwent surgical repair of the ruptured aneurysm.[7] The timing of

Table 1. Clinical characteristics of surgical and medical groups of our SAH patients

Therapeutic group/H-H-S*	H-H-S 1	H-H-S 2	H-H-S 3	H-H-S 4	H-H-S 5	Death
Surgical (n:45) (F: 25, M: 20)	1	14	24	6	-	28 (62.2%)
Medical without aneurysm (n: 58) (F: 29, M:29)	1	12	26	11	8	18 (31%)
Medical with aneurysm (n:17) (F:9, M:8)	-	-	-	7	10	7 (41.2%)
Total (n:120) (F:63, M:57)	2	26	50	24	18	53 (44.2%)

H-H-S: Hunt Hess Scale

*: None of our SAH patients had Hunt Hess scale 0.

Table 2. Distribution of complications and outcome in two therapeutic groups of our SAH patients

Therapeutic group/	Rebleeding	Death due to rebleeding	Hydrocephaly	Ventricular shunting	Infarction due to vasospasm	Death
Surgical (n:45)	2 (4.4%)*	-	2 (4.4%)	2 (4.4%)	2 (4.4%)	28 (62.2%)
Medical (n:75)	3 (4%)	2 (2.7%)	15 (20%)	11 (14.7%)	5 (6.7%)	25 (33.3%)
Total (n:120)	5 (4.2%)	2 (1.7%)	17 (14.2%)	13 (10.8%)	7 (5.8%)	53 (44.2%)

* Rebleeding occurred before aneurysm clipping

surgery after SAH was significantly related to the likelihood of pre-operative rebleeding. Patients who underwent early surgery had a significantly lower pre-operative rebleed rate than those who underwent later surgery (3% versus 11%).[7] The mean time of onset to surgery in our SAH patients was 8 days which is longer than reported in western countries.[6] This significant delay in the timing of aneurysmal surgery in our patients, could be the main reason for failure to decrease mortality in our patients. During this period of delay a number of complications may occur in the surgical group. In recent years, there has been a trend towards early surgery for ruptured aneurysms, especially in good and moderate grade patients.[2,6] In addition, early surgery facilitates the possibility of aggressive therapy of vasospasm.[2] However, it is also reported that there were no overall differences in outcome in patients operated on early (0-3 days post SAH) or late (11-14 days post SAH).[6] Surgical mortality was higher with early surgery due to brain swelling, disturbed autoregulation and haemorrhage.[6] The treatment was most hazardous between days 7 and 10 due to the combined risks of rebleeding and vasospasm.[6] A prospective study, from three centers, indicates that despite attempts to do early surgery, rebleeding is still a significant problem, because only one half of the patients were operated on within 72 hours, and 35% of the patients with poor outcome had suffered rebleeding.[8,9] In addition, some SAH patients with acute hydrocephalus may benefit from early placement of a ventricular drain in the hospital.[10] Acute hydrocephalus is more frequent in patients with poor clinical grade. The clinical significance of acute hydrocephalus after SAH is uncertain because many patients are apparently asymptomatic and do not deteriorate.[2] There was no statistical significance between the type of management, mortality and complications in our patients. The impact of rebleeding despite presence of hydrocephalus on mortality was not significant in our patients. This is inconsistent with results in developed countries.[11] The late presentation of the SAH patients in our center, compared to developed countries is a local issue and this leads to late treatment. The logistic multivariate regression test is necessary, to access the exact influence of the therapeutic subtype of aneurysm, on in-hospital death in SAH patients. However, this type of analysis needs more than five hundred SAH cases, which is out of our reach in the near future. Meanwhile, we consider our work the first pilot study conducted in this field in Iran.

Conflict of Interests

Authors have no conflict of interests.

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