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Influence of Different Surgical Timing on Outcome of Patients with Aneurysmal Subarachnoid Hemorrhage and the Surgical Techniques During Early Surgery for Ruptured Intracranial Aneurysms

Anevrizmal Subaraknoid Kanamalı Hastalarda Farklı Cerrahi Zamanlamasının Sonuca Etkisi ve Rüptüre İntrakraniyal Anevrizmalar İçin Erken Cerrahi Sırasında Cerrahi Teknikler

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ABSTRACT

AIM: This study aims to investigate the influence of different surgical timing on outcome of patients with aneurysmal subarachnoid hemorrhage and to explore the surgical techniques for ruptured intracranial aneurysms

MATERIAL and METHODS: The clinical data were from 327 cases. 304 cases of the surgical group were further assigned to early surgery (89 cases), intermediate surgery(164 cases) and delayed surgery(51 cases) according to the surgical timing. The other 23 cases were the non-surgical group. The ultimate outcome of all cases was graded according to the Glasgow Outcome Scale. After the cases of the no-surgical group were re-assigned to different surgical subgroups according to the rebleeding time, the ultimate outcome was graded once more.

RESULTS: There was no significant difference among the 3 groups' pre-operative clinical data. After re-assigning the cases of no-surgical group to the different surgical subgroups, there was no significant difference among the 3 groups' preooperative clinical data, while the ultimate outcome grades of early surgery (3.6±1.8) and intermediate surgery (3.5±2.2) were superior to that of delayed surgery (2.9±2.8).

CONCLUSION: This retrospective study has demonstrated that early surgery can not only prevent re-rupture of aneurysm to decrease mortality rate but also improve the ultimate outcome.

KEYWORDS: Intracranial aneurysm, Subarachnoid hemorrhage, Early surgery, Outcome

ÖZ

AMAÇ: Bu çalışma, anevrizmal subaraknoid kanamalı hastalarda farklı cerrahi zamanlamasının sonuca etkisini araştırmayı ve rüptüre intrakraniyal anevrizmalar için cerrahi teknikleri incelemeyi hedeflemektedir.

YÖNTEM ve GEREÇLER: Klinik veriler 327 olgudan alınmıştır. Cerrahi gruptaki 304 olgu cerrahi zamanlamasına göre ayrıca erken cerrahi (89 olgu), orta dönemde cerrahi (164 olgu) ve gecikmiş cerrahi (51 olgu) olarak gruplara ayrılmıştır. Diğer 23 olgu cerrahi olmayan grubu oluşturdu. Tüm olguların son durumu Glasgow Sonuç Ölçeğine göre derecelendirildi. Cerrahi olmayan grubun olguları tekrar kanama zamanına göre farklı cerrahi alt gruplara tekrar tahsis edildikten sonra en sondaki sonuç tekrar derecelendirildi.

BULGULAR: Üç grubun preoperatif klinik verileri arasında önemli bir fark görülmedi. Cerrahi yapılmayan gruptaki olgular farklı cerrahi alt gruplara tekrar tahsis edildikten sonra 3 grubun preoperatif klinik verileri arasında önemli bir fark yokken erken cerrahi (3,6±1,8) ve orta dönemde cerrahi (3,5±2,2) son sonuç dereceleri gecikmiş cerrahiye göre daha iyi idi (2,9±2,8).

SONUÇ: Bu retrospektif çalışma, erken cerrahinin hem mortalite oranını azaltacak şekilde anevrizmanın tekrar rüptürünü önleyebileceğini hem de son sonucu daha iyi hale getirebileceğini göstermiştir.

ANAHTAR SÖZCÜKLER: İntrakraniyal anevrizma, Subaraknoid kanama, Erken cerrahi, Sonuç

INTRODUCTION

Despite the huge advance in the treatment of intracranial aneurysms over the past decades, aneurysmal subarachnoid hemorrhage is still a disastrous event with high morbidity and mortality (7, 22). Surgical clipping via craniotomy is still considered as the standard method for the treatment of ruptured intracranial aneurysms because of its durability and efficiency (15, 19, 24), although endovascular coiling can prevent some aneurysms from rebleeding with less invasiveness. The International Cooperative Study on the Timing of Aneurysm Surgery has shown that early surgery is

not associated with a better outcome than delayed surgery (8, 9). However, with the advance of microneurosuigical techniques in recent years, there has been a trend toward early surgery for ruptured intracranial aneurysms to decrease the aneurysm rebleeding risk before being repaired securely (17). Many retrospective and prospective studies have indicated that increased time to treatment is associated with increased rates of preoperative rebleeding and recently has been associated with higher rates of poor outcome (2, 18, 26). The above studies have shown that whether early surgery is able to improve the ultimate outcome of patients with aneurysmal subarachnoid hemorrhage is still controversial. Early surgery can not only prevent rebleeding by clipping aneurysms to decrease the mortality rate but can also improve the ultimate outcome by evacuating the subarachnoid clot and removing the bony flap, if needed, and therefore reduce the severity of vascular spasm and help patients survive the edema phase. Although early surgery has such advantages in theory, difficulties such as brain edema and swelling during early surgery lead to a high risk of brain injury and immature rupture that would offset its advantages. Analysis of the early studies on the effect of surgery timing on the patient outcome can help find the causes of this disappointing conclusion. Firstly, surgical experiences dealing with difficulties such as brain swelling during the early surgery were not available in the early studies; secondly, patients with poor outcome for which delayed surgery and rebleeding were responsible were excluded from delayed surgery when the ultimate outcome of early surgery and delayed surgery were calculated and compared. However, with the advanced microsurgical techniques and surgical experiences obtained in recent years, the difficulties during early surgery have been overcome gradually. Thus, we analysed retrospectively the clinical data of patients with aneurysmal subarachnoid hemorrhage treated by surgical clipping in the First Affiliated Hospital of Zhengzhou University in the last 3 years, and compared the influence of different surgical timing on the outcome of the cases. The goal of this study was to investigate whether early surgery was able to improve the ultimate outcome of patients with aneurysmal subarachnoid hemorrhage when the cases which die of rebleeding are included and some improved microsurgical techniques for early surgery are used. Meanwhile, we also developed some surgical techniques for clipping ruptured intracranial aneurysms successfully during early surgery.

PATIENTS and METHODS

Patients

A total 327 cases with aneurysmal subarachnoid hemorrhage were treated in the Neurosurgical Department of the First Affiliated Hospital of Zhengzhou University from Jan. 1st of 2009 to Dec. 31st of 2011. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the First Affiliated Hospital of Zhengzhou University. Written informed consent was obtained from all participants. All the cases were diagnosed as spontaneous subarachnoid hemorrhage by head CT scan, and the diagnosis of aneurysmal subarachnoid hemorrhage was established by CT angiography or digital subtraction angiography. 122 cases were male and the other 207 cases were female. The age of the cases was from 38 years to 79 years, with a mean of 64.8 and standard deviation of 14.6 years. On admission, the clinical grades of patients according to the Hunt-Hess Grade Scale were as follows: 13, 165, 96, and 34 cases were at grade 0, grade 1~2, grade 3 and grade 4~5 respectively, and 19 cases had brain herniation. The locations of the aneurysms responsible for the hemorrhage were as follows: 103 aneurysms were at the anterior communicating artery; 105 aneurysms were at the posterior communicating artery; 92 aneurysms were at the middle cerebral artery bifurcation; 5 aneurysms were at the ophthalmic artery; 7 aneurysms were at the pericallosal artery; 6 aneurysms were at the internal carotid artery bifurcation; 4 aneurysms were at the posterior cerebral artery, 3 aneurysms were at the basilar artery apex; 2 aneurysms were at the posterior inferior cerebellar artery. 34 of 327 patients had multiple intracranial aneurysms besides the responsible aneurysms.

Patient Assignments

The patients were assigned to surgery group or the no surgery group according to whether surgery was performed. Different surgical timing was determined for the surgical group cases mainly by the different time interval between the onset of hemorrhage and admission. The surgical timing was also determined by the patients' relative choice depending on their knowledge on the disease. The surgical timing was therefore determined objectively or randomly other than subjectively. The clinical data of the cases treated surgically were retrospectively analysed and the surgical timing groups were determined according to the pre-operative times. Cases treated surgically within 3 days after the onset of hemorrhage were assigned to the early surgery group, and those undergoing surgery between 3 and 14 days were assigned to the intermediate surgery group. Patients who were treated via craniotomy and clipping 14 days or more after the onset of hemorrhage were assigned to the delayed surgery group. There were also some patients who could not be operated as they were in critical condition or lost the surgical opportunity because of the aneurysm rebleeding during the hesitation time. These cases not treated surgically were assigned to the no surgery group.

Surgical Methods

All cases of the surgical group were treated surgically with the elementary goal of clipping the responsible aneurysms. According to the location of the responsible aneurysm, the pterional approach, anterior longitudinal fissure approach, subtemporal approach and basic extreme lateral approach were used. After the craniotomies were finished, the responsible aneurysms were explored and clipped by microsurgical techniques. Unruptured aneurysms that were not responsible for the hemorrhage were also explored and clipped if they could be demonstrated easily via the same

approach. The subarachnoid hemorrhage was irrigated off with saline water as much as possible while exploring aneurysms or after clipping the aneurysms. Intracerebral hemotomas were evacuated partially before exploring and clipping the aneurysms with the aim of relaxing the brain tissue, and they were removed as much as possible after the aneurysms were repaired successfully. The bony flaps were not replaced after the procedure if the patients were at or above grade 3 of the Hunt-Hess Scale or obvious brain edema was present. Ventricle puncture and external drainage via Paine's point was performed with the aim of relaxing the brain tissue and facilitating the procedure if acute hydrocephalus occurred. After the surgery was finished, routine post-operative therapeutic methods including dealing with brain edema, drainage of bloody CSF, and preventing vasospasm were applied according to the recommendation published by AHA in 2009 (1).

Evaluation of the Outcome

The outcome of the patients was evaluated 1 month after the surgeries were performed according to the Glasgow Outcome Scale. The results were digitally presented by a number from "1" to "5", i.e. from "death" to "normal" in the Glasgow Outcome Scale respectively.

Statistical Analysis

The data were processed by the statistical software SPSS 3.0. The count data were expressed as percent and the chi-square test was used for significance. Measurement data were expressed as mean±standard deviation. Variance analysis was used for significance among the 3 groups, and then the q-test was used for significance between 2 groups if significance among 3 groups was present. P value threshold of 0.05 was considered statistically significant.

RESULTS

Outcome of the No Surgery Group Cases

There were 23 cases in this group. 11 of the 23 cases fell in grade 5 immediately after the initial hemorrhage and 18 of 23 cases had a good grade after the initial hemorrhage but became grade 5 because of the second or third bleeding during the hesitation time. Of the 18 cases in whom rebleeding occurred, 3, 6 and 4 cases had rebleeding from aneurysm re-rupture within 3 days, at 3~7 days and 7~14 days after the initial hemorrhage respectively. All the cases in this no surgery group lost the surgical opportunity and were treated by conservative methods. 11 cases of this group died or developed brain death in the hospital. The other 12 cases left the hospital after abandoning treatment, follow-up proving they were dead.

Outcome of the Surgery Group Cases

There were 304 cases in this group. According to the surgical timing, 89, 164, and 51 cases were assigned to early surgery, intermediate surgery and delayed surgery respectively. Table I demonstrates the pre-operative, intra-operative and post-operative indexes of the 3 subgroups of this group.

On the basis of fact that there was no significant difference among the 3 groups' pre-operative indexes which had an important impact on the patient ultimate outcome including clinical grade, age, size and neck of the aneurysms as well as the rate of posterior circulation aneurysm, there was no significant difference among the immature rupture rate of the 3 groups, and the rates of removing of bony flap of early surgery (29.21%) and intermediate surgery (21.34%) were significantly higher than that of delayed surgery (7.84%), with the post-operative Glasgow Outcome Scale of early surgery (3.8±1.7) and intermediate surgery (3.9±2.1) being significantly lower than that of delayed surgery (4.1±0.8). There was no significant difference between the indexes of early surgery and intermediate surgery.

Overall Outcome of All Patients

Theoretically, the patients who died of the rebleeding of aneurysms could have survived if they had been operated timely to clip the aneurysms before the deadly rerupture. So, the fact that the surgery had not been performed timely was responsible for the death. On the basis of this theory, the no surgery cases dying of rebleeding were assigned to a different surgical subgroup according to the rerupture time. The re-assignments were as follows: half of the 8 cases in whom rebleeding occurred within 3 days after initial hemorrhage were assigned to early surgery and the other half were assigned to intermediate surgery; half of the 6 cases in whom rebleeding occurred 3~7 days after initial hemorrhage were assigned to intermediate surgery and the other half were assigned to delayed surgery; all the 4 cases in whom rebleeding occurred 7~14 days after initial hemorrhage were assigned to delayed surgery. After the above re-assignment, the ultimate outcome and mortality of the 3 subgroups were calculated again.

As shown in Table II, there was no significant difference among the 3 groups' indexes including pre-operative clinical grade, age, size and neck of the aneurysms as well as the rate of posterior circulation aneurysm, while the mortality rate of early surgery (6.45%) and intermediate surgery (7.01%) were significantly lower than that of delayed surgery (13.79%). The ultimate outcomes of early surgery (3.6±1.8) and intermediate surgery (3.5±2.2) were also superior to that of delayed surgery (2.9±2.8). There was no significant difference between the indexes of early surgery and intermediate surgery.

DISCUSSION

It has been indicated by many studies and clinical reports that the mortality rates of patients with intracranial aneurysms are as high as 30%, 60% and 100% after the initial hemorrhage, the second hemorrhage and the third hemorrhage respectively (3,23). Furthermore, the shorter the time from the initial hemorrhage, the higher the rebleeding rate. Many clinical studies have proven that the rerupture risk is the highest within the first week after the initial hemorrhage, with a peak at 4~9 days, and drops sharply after 3 weeks (4, 6, 10, 25). Delayed surgery therefore has a minor role in preventing the aneurysm

Table I: Surgical Group's Pre-Operative, Intra-Operative and Post-Operative Indexes

Index	Early surgery	Intermediate surgery	Delayed surgery
n	89	164	51
Age (yrs)	63±15.3	64±14.9▲	62±16.6▲
Clinical grade (Hunt-Hess)	2.5±1.4	2.3±1.6▲	2.1±1.8▮
Aneurysm diameter (mm)	6.5±2.2	7.1±1.9▲	6.7±2.1▮
Aneurysm neck (mm)	3.8±1.7	4.1±1.9▲	3.9±1.9▮
Posterior circulation/total (%)	3.37%	2.44%▲	3.92%▮
Immature rupture (%)	2.24%	2.44%▲	1.96%▮
Removing bony flap (%)	29.21%	21.34%▲	7.84%▮
Ultimate outcome (GOS)	3.8±1.7	3.9±2.1▲	4.1±0.8▮

▲ *stands for p >0.05, compared with early surgery.*
▮ *stands for p < 0.05, compared with early surgery.*

Table II: Surgical Group's Pre-Operative and Post-Operative İndexes After the Re-Assignment

Index	Early surgery	Intermediate surgery	Delayed surgery
n	89+4	164+7	51+7
Age (yrs)	62±15.6	63±14.7▮	62±16.9▮
Clinical grade (Hunt-Hess)	2.4±1.5	2.5±1.4▮	2.6±1.7▮
Aneurysm diameter (mm)	6.4±2.3	7.0±2.1▮	6.6±2.0▮
Aneurysm neck (mm)	3.9±1.8	4.0±1.7▮	4.2±1.9▮
Posterior circulation/total (%)	3.37%	2.44%▮	3.92%▮
Ultimate outcome (GOS)	3.6±1.8	3.5±2.2▮	2.9±2.8▮
Mortality rate	(2+4) /93=6.45%	(5+7) /171=7.01%▮	(1+7) /58=13.79%▮

▲ *stands for p >0.05, compared with early surgery.*
▮ *stands for p < 0.05, compared with early surgery.*

from rebleeding and early surgery is strongly recommended. Our surgical experiences have proven that the brain edema after subarachnoid hemorrhage is not severe until 3 days later and the severity of brain edema is less dependent on time than on the amount of subarachnoid hemorrhage and the pre-operative clinical grade. Surgery for patients with grade ≤3 on the Hunt-Hess scale and/or Fisher scale can therefore be performed relatively easily. The previous thought that early surgery was associated with a high risk of immature rupture of aneurysm is also obsolete, and a recent study has suggested early surgery does not always increase the risk of immature rupture (12). In fact, the intra-operative risk of aneurysm rupture is controllable with modern microsurgical techniques, and some intracranial aneurysms are intentionally punctured so that they can be visualized clearly and be clipped perfectly. For the above reasons, we propose that early surgery or at least intermediate surgery be performed for patients with clinical grade ≤3, which will cause an outcome not poorer than that of delayed surgery while the role of preventing deadly rerupture is obvious. As for the patients with clinical grade 3 or above, the outcome of patients treated by early surgery is actually poorer than those treated by delayed surgery, but the patients who have the opportunity to accept delayed surgery are those who survive the initial hemorrhage attack and have a high risk of rebleeding, and so the roles of preventing rebleeding and saving life of delayed surgery are very limited. The patient outcomes treated by early surgery are better than that of patients treated by delayed surgery if the cases who died because of not undergoing early surgery and then rebleeding are considered. Our study demonstrated that on the basis of the fact that some factors which have an important effect on the outcome including age, pre-operative clinical grade as well as aneurysm location and shape were similar among 3 groups, the ultimate outcomes of early surgery and intermediate surgery were not significantly different. Although the ultimate outcome of delayed surgery was better than that of early surgery and intermediate surgery, the patients who had the chance to accept delayed surgery were survivors with a high risk of rebleeding. The ultimate outcome and mortality rate of delayed surgery were obviously poorer than that of early surgery and intermediate surgery if the cases that did not have the opportunity to accept the delayed surgery and died were considered as shown in Table II. Our study also suggested that the differences of ultimate outcomes between early surgery and intermediate surgery were not statistically significant. The reason for this result is that surgical groups were determined and the cases in the no surgery group were re-assigned to different

surgical groups according to a relatively long time period, and thus the differences were weakened or concealed. The difference would have been significant if a relatively short time period were applied, suggesting that the earlier the surgery is performed, the better the ultimate outcome. For the above reasons, we propose that surgery be performed as soon as possible unless the patients are in critical situations and have no chance to survive even if surgery is performed successfully. The critical situations are as follows: 1- bilateral pupils are dilated and every physical reflex is lost; 2- automatic respiration is weak and blood pressure is decreased; 3-old age (≥ 75 years) or having severe organ complications.

It is a fact that the early surgery for ruptured aneurysms is much more difficult than delayed surgery. In this situation, some special strategies should be applied during early surgery so that the surgery can be performed successfully and help patients survive the post-operative critical phase. The greatest difficulty during early surgery for a ruptured aneurysm is facing the swollen and fragile brain tissue. In this situation of increased intracranial pressure, any crude dissection and forceful retraction will damage the brain severely. Our recommendation in dealing with this situation is to relax brain tissue by releasing CSF via some approaches. The first and the most effective method of relaxing brain tissue is later ventricle puncture and drainage via Paine's point when the pterional approach, which is indicated for most of the anterior circulation aneurysms, is used. Studies has shown that hydrocephalus develops to some extent in many patients with subarachnoid hemorrhage within several days (14, 20, 21), making the ventricle puncture and drainage easy. It has also been proven that ventricle puncture and drainage before repairing a ruptured aneurysm does not increase the rebleeding risk (5,13), and this method is therefore considered effective and safe. The second method of relaxing brain tissue is releasing CSF by opening sub-brain cisterns. This procedure may be difficult when the brain shows severe swelling, and thus resection of a small piece of frontal tissue covering the lateral fissure to approach the sub-brain cistern is recommended. Releasing CSF by lumbar puncture and drainage should be reserved as the last method when the above 2 methods are not be performed successfully, because it may cause deadly brain herniation in the situation of increased intracranial pressure. Intracerebral hematomas should be removed partially to decrease the intracranial pressure before retraction of brain tissue and exploring the aneurysms. Without decreased intracranial pressure, any procedure attempting to explore and clip aneurysms directly is dangerous, and has a high risk of causing immature aneurysm rupture and damaging brain tissue severely.

Early surgery can not only clip the aneurysm to prevent deadly rebleeding but also alleviate the attack caused by initial hemorrhage which will help patients survive the critical period. It is therefore recommended to open the subarachnoid cisterns widely and irrigate off the hemorrhage with saline water during surgery. It is also recommended to evacuate intracerebral hematomas as much as possible after the aneurysms are clipped. Ventricle external drainage or lamina terminalis fistula combining with subdural drainage are indicated for patients with intraventricular hemorrhage or hydrocephalus with the aims of alleviating cerebral vasospasm and reducing the risk of permanent shunt-dependent hydrocephalus (11,16). Bony flaps are not recommended to be replaced in cases with poor clinical grade for the purpose of decompressive craniotomy after the aneurysms are clipped, helping the patients survive the brain edema phase and preventing brain herniation. In our study, the rate of removing a bony flap was as high as 30% in patients undergoing early surgery and intermediate surgery, which accounted for most cases with a poor clinical grade, and the results demonstrated the effectiveness of improving the ultimate outcome.

CONCLUSION

This retrospective study has demonstrated that aneurysmal subarachnoid hemorrhage is a neurosurgical emergency, and the short term rebleeding rate and mortality rate after initial hemorrhage are very high. Thus, early surgery is strongly recommended in order to prevent deadly rebleeding and improve ultimate outcome. Our study has also indicated that early surgery can not only prevent re-rupture of the aneurysm to decrease the mortality rate but also improve ultimate outcome by evacuating the subarachnoid clot and removing bony flaps. To overcome the difficulties during early surgery, we recommend that some surgical methods including releasing CSF via ventricle external drainage, removing intracerebral hemotomas, as well as resection of part of the brain tissue be used to complete the surgery successfully.

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