Factors influencing the outcome after the operative treatment of cerebral aneurysms of anterior circulation

Zoran Roganović, Goran Pavličević

Military Medical Academy, Clinic of Neurosurgery, Belgrade

Background. The influence of various factors on the outcome after the operative occlusion of the cerebral aneurysm was to be defined through the retrospective study on 111 surgically treated patients with aneurysm of anterior cerebral circulation. Methods. Preoperative clinical condition was graded from 0 to V, according to Hunt & Hess. Postoperative outcome, defined as good or bad according to modified Glasgow Outcome Scale, was correlated in homogenous experimental groups with the following factors: gender, age, aneurysmal size, preoperative interval, nimodipine therapy, experience of surgical team and existence of chronic vascular diseases. Results. Surgical outcome was good in 74.4% of males and 71.4% of females (p>0.05); in 83.3% of patients with and 41.2% of patients without chronic diseases (p<0.01); in 71.4% of patients underwent early, 83.3% of ones underwent postponed and 85% of those underwent late surgery (p>0.05); in 81.5% of patients treated by nimodipine and in 41.7% of those untreated by the same drug (p<0.01); in 78.9% of patients operated by the experienced surgical team and in 40% of those operated by less experienced surgical team (p<0.01). In patients with both good and bad outcome, the mean age was 50.6 and 47.6 years (p>0.05), and the mean aneurysmal size was 12.3 mm and 13.3 mm, respectively (p>0.05). Before rupture, the mean size for aneurysms on the bifurcation of the middle cerebral artery was 14.3 mm, and for posterior communicating artery aneurysms only 9.7 mm (p<0.05). Conclusion. Surgical outcome was significantly influenced by the existence of chronic diseases, nimodipine therapy and experience of surgical team, whereas gender, age, timing for surgery and aneurysmal size were not of significant influence.

Key words: intracranial aneurysm; aneurysm, ruptured; anterior cerebral artery; middle cerebral artery; glasgow outcome scale; cerebral angiography; neurosurgical procedures; nimodipine; treatment outcome.

Introduction

Rupture of cerebral aneurysm is the most frequent and the most dangerous cause of subarachnoid hemorrhage (SAH). Total mortality from untreated rupture is 25% after one week, 50% after two months and 70% after one year, which makes surgical aneurysmal clipping an imperative (1). On the other hand, operative treatment is also risky, so only one third of all patients with ruptured aneurysm returns to previous lifestyle postoperatively (2).

Wanting to reduce mortality and morbidity, surgeons have investigated the factors influencing the treatment outcome, but there are still disputes in literature about the majority of such factors. No agreements have yet been reached about the ideal timing for surgery (3–5), nor about the dependence of the postoperative outcome correlated with aneurysmal size and location (6–8), patient’s gender and age (1, 2, 9, 10), chronic diseases (1, 10, 11), preoperative clinical condition (11–13), nimodipine therapy (14–16), vasospasm (1, 4, 11), aneurysmal intraoperative rupture and temporary clipping (17, 18).
Considering the cited dilemmas, we outlined the investigation on our own series of operated patients, based on the following hypothesis and objectives:

The hypothesis was that the outcome after an operative occlusion of cerebral aneurysms depended on: timing of surgery, characteristics of aneurysm and adjacent vessel (size, location, vasospasm), characteristics of the patient (gender, age, chronic diseases, clinical condition) and intra-operative and postoperative procedures (intraoperative rupture, temporary clipping, nimodipine therapy).

The aim was to test the influence of various factors on the operative aneurysmal occlusion outcome in homogenous experimental groups and to define the situations with the best chances for good outcome.

**Methods**

Retrospective study included 111 patients with 131 cerebral aneurysms of anterior circulation, operated in Neurosurgical Department of the Military Medical Academy.

Preoperative clinical condition was graded from 0 to V, according to Hunt & Hess grading scale (HHG) (19), and the treatment outcome was defined as good or bad on the basis of modified Glasgow Outcome Scale (19, 20).

The outcome was correlated with 7 factors: gender, age, aneurysmal size, duration of preoperative interval between SAH and operation, nimodipine therapy, experience of surgical team and existence of chronic vascular diseases (unstable hypertension, diabetic vasculopathy, cerebrovascular insufficiency). The correlation of the outcome with 6 more factors presented earlier was: aneurysmal location, preoperative clinical condition (20), intraoperative aneurysmal rupture, temporary clipping (21), ischemic complications (22) and vasospasm (23).

The correlation between the outcome and each individual factor was determined in experimental groups, homogenous in relation to other factors. The number of patients was different in different experimental groups (Table 1).

Aneurysmal location was defined as: a.carotis interna (ACI), a.cerebri media before or after bifurcation (ACM, M1 or M2 segment), a.communicans anterior (ACoA), a.cerebri anterior before or after communicating segment (ACA, A1 or A2 segment) and a.communicans posterior (ACoP).

Aneurysmal size, measured angiographically and/or intraoperatively, was analyzed separately for ruptured, unruptured symptomatic and asymptomatic aneurysms. Fusiform aneurysms and aneurysms in cavernous sinus were not included. In addition to correlation with the postoperative outcome, the size was also correlated with aneurysmal location, tendency for spontaneous and intraoperative rupture, vasospasm and the length of postoperative hospitalization.

Regarding the period elapsed from SAH, operation was defined as early (in the first 5 days), delayed (until the end of the second week), or late (in the third week or later) and the ideal time for surgery was estimated for different HHG groups.

Nimodipine was administrated before and/or after surgery intravenously (10 mg every 12 or 8 hours during 6 days) and/or per os (during 3–15 days).

Statistical significance of obtained differences was tested by calculating the standard error (σd) and standard deviation (Z) of the difference between two arithmetical averages, as well as by χ² test and contingency coefficient. In some situations, results were also checked by the regression analysis and nonparametric rank correlation test.

**Results**

The series consisted of 46.7% males and 53.3% females, and the mean preoperative HHG was similar both (2.4 ± 1.2 and 2.8 ± 1; σd=0.25; Z=1.64; p>0.05). Good postoperative outcome was obtained in 74.4% males and in 71.4% females (χ²=0.53; DF=1; p>0.05).

The average age of the total number of patients was 48.9 ± 11.5. Patients in bad clinical groups were older (Table 2), but the difference in age was significant between HHG=III and HHG=IV-V only (σd=2.93; Z=2.1; p<0.05).

**Table 1**

<table>
<thead>
<tr>
<th>Tested Factor</th>
<th>No of patients</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Aneurysmal size</td>
<td>86</td>
<td>103 aneurysms</td>
</tr>
<tr>
<td>Timing for surgery</td>
<td>65</td>
<td>ruptured aneurysms (I-V)</td>
</tr>
<tr>
<td>Nimodipine therapy</td>
<td>75</td>
<td>ruptured aneurysms (I-V)</td>
</tr>
<tr>
<td>Chronic diseases</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Location (20)</td>
<td>89</td>
<td>100 aneurysms (0-V)</td>
</tr>
<tr>
<td>Experience</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Preoperative condition (20)</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Intraoperative rupture (21)</td>
<td>72</td>
<td>ruptured aneurysms (I-V)</td>
</tr>
<tr>
<td>Temporary clipping (21)</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Brain ischemia (22)</td>
<td>72</td>
<td>HHG= 0-III</td>
</tr>
<tr>
<td>Vasospasm (23)</td>
<td>77</td>
<td>ruptured aneurysms (I-V)</td>
</tr>
</tbody>
</table>
Patients with bad outcome were older (50.6 ± 13.3 years), than patients with good outcome (47.6 ± 10.3 years of age), but the difference in age was not significant (αd=2.7; Z=1.11; p>0.05). Statistical significance of difference in age between patients with good and bad outcome existed only in patients with HHG=II (αd=4.9; Z=2; p<0.05) (Table 2).

Severity of clinical presentation after the rupture did not depend on aneurysmal size: aneurysms were smaller in patients with better clinical condition (11.1 ± 5.5 mm for HHG=I-II, 14 ± 6.1 mm for HHG=III and 15 ± 15.1 mm for HHG=IV-V), but the differences in size were not significant (p>0.05). Aneurysmal size did not significantly change the postoperative outcome, although aneurysms were smaller in patients with good outcome than in those with bad outcome (12.3 ± 3.9 mm and 13.3 ± 10.6 mm; αd=0.22; Z=0.46; p>0.05).

Aneurysms were larger in patients with intraoperative rupture (17.3 ± 12.9 mm) and in patients with vasospasm (17.3 ± 18.2 mm) than in patients without rupture and vasospasm (11.7 ± 6.4 mm and 12.2 ± 8.9 mm, respectively), but the differences in size were not significant (p>0.05). The length of postoperative hospitalization was longer for patients with aneurysms over than 9 mm in size (16.4 ± 11.5 days), than for patients with aneurysms smaller than 9 mm (11.9 ± 3.9 days), but the difference in hospitalization length was not significant (αd=3.05; Z=1.78; p>0.05). Such results were also confirmed after data processing by other statistical instruments: regression analysis revealed small correlation coefficient (r=−0.11) for regression equation (y=17.3−1.9x), pointing to weak direct correlation; small Spearman’s correlation coefficient (p=−0.027), obtained by nonparametric rank correlation test practically pointed out the absence of correlation.

Operations were performed usually in the first three days or after the end of the third week after SAH (Fig. 2). Early surgery was performed on 30.8% of patients, delayed one on 16.9%, while 52.3% of patients underwent late surgery.

The mean preoperative HHG was better for late operated patients (2 ± 1.1), than for those underwent to postponed (2.5 ± 1.1) and early surgery (3.2 ± 0.9), because, gradually, patients in bad condition died or passed into a better clinical group. The difference in preoperative HHG between the early and late operated patients was significant (αd=0.28; Z=4.24; p<0.05).

On average, operations were performed 16.2 ± 13.1 days after SAH and 7 ± 6.9 days after angiography. These intervals were similar among patients in various preoperative HHG (p>0.05) (Table 3). The average preoperative hospitalization lasted 5.7 days, but was twice longer for patients with good HHG than for ones with bad HHG.

### Table 2

<table>
<thead>
<tr>
<th>HHG</th>
<th>Good outcome</th>
<th>Bad outcome</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-I</td>
<td>43.8 ± 4.6</td>
<td>36.3 ± 12.1</td>
<td>41.5 ± 6.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>II</td>
<td>42.6 ± 10.4</td>
<td>52.6 ± 12.8</td>
<td>46.1 ± 12.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>III</td>
<td>53 ± 8.1</td>
<td>50.9 ± 7.9</td>
<td>52.1 ± 8.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>IV-V</td>
<td>61 ± 7.2</td>
<td>52.2 ± 13.3</td>
<td>54.1 ± 12.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Total</td>
<td>47.6 ± 10.3</td>
<td>50.6 ± 13.3</td>
<td>48.9 ± 11.5</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

HHG -preoperative clinical condition according to Hunt and Hess; p - probability

Chronic diseases existed in 19.1% of patients. Preoperative HHG was similar for those patients and the patients without chronic diseases (p>0.05). Good outcome existed in 83.3% of patients with chronic diseases and in 41.2% of those without such diseases. The difference in outcome was statistically significant (χ²=13.14; DF=1; p<0.01), with high contingency coefficient (C=0.36).

The mean aneurysmal size was 12.4 ± 10.5 mm for the whole analyzed series, 18.9 ± 12.1 mm for symptomatic unruptured aneurysms, 13 ± 10 mm for ruptured aneurysms, and 4.6 ± 2 mm for asymptomatic aneurysms. Differences in size were significant between ruptured and asymptomatic unruptured aneurysms (αd=0.13; Z=6.67; p<0.05), as well as between asymptomatic and symptomatic ones (αd=0.33; Z=4.37; p<0.05).

Aneurysms of ACI were significantly larger (19.3 ± 10.7 mm) than aneurysms of M1 (9.3 ± 7.9 mm; αd=0.44; Z=2.27; p<0.05) and A1A2 segments (9.4 ± 5 mm; αd=0.42; Z=2.34; p<0.05) (diagram 1). Before rupturing, ACI and M2 aneurysms were the largest (16.2 ± 9 mm and 14.3 ± 7 mm, respectively), and ACoP aneurysms were the smallest (9.7 ± 2.2 mm) (αd=0.18; Z=2.57; p<0.05) (Fig. 1).

![Fig. 1 – Average size (mm) of differently located aneurysms](image-url)
Timing of surgery in relation to SAH day

Fig. 2

Timing of surgery in relation to SAH day

Table 3

Average lengths of preoperative intervals (days)

<table>
<thead>
<tr>
<th>HHG</th>
<th>SAH / operation</th>
<th>Angiography / operation</th>
<th>Preoperative hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>18.7 ± 10.9</td>
<td>7.3 ± 7.1</td>
<td>7.5 ± 8.2</td>
</tr>
<tr>
<td>III</td>
<td>14.5 ± 13.2</td>
<td>6.4 ± 7.1</td>
<td>5.5 ± 7.1</td>
</tr>
<tr>
<td>IV-V</td>
<td>15.4 ± 13.4</td>
<td>7 ± 6.6</td>
<td>3.1 ± 6.9</td>
</tr>
<tr>
<td>Total</td>
<td>16.2 ± 13.1</td>
<td>7 ± 6.9</td>
<td>5.7 ± 7.6</td>
</tr>
</tbody>
</table>

HHG - preoperative clinical condition according to Hunt Hess;

Good outcome was obtained after 55% of early operations, 63.6% of delayed ones and 88.2% of late operations (Fig. 3). Differences in the outcome between the patients operated early and the ones that underwent the delayed surgery were statistically significant with high contingency coefficient ($\chi^2=8.97; \ p<0.01; \ C=0.38$). The average preoperative interval was significantly longer for the patients with good outcome (19.3 ± 12.9 days), than for the ones with bad outcome (11.5 ± 12.1 days; $\sigma d=3.14; \ Z=2.46; \ p<0.05$).

Fig. 3 – Correlation of good outcome with timing for surgery

In the circumstances of similar clinical preoperative condition (HHG=II-III), after the exclusion of the patients with HHG=I (absent among early operated) and the patients with HHG=IV-V (rarely present among late operated), good outcome was obtained after 71.4% of early, 83.3% of delayed and 85% of late surgery ($p>0.05$) (Fig. 3). The result after the early surgery was significantly better than in the control group, consisting of 17 unoperated patients with high contingency coefficient ($\chi^2=4.02; \ p<0.05; \ C=0.34$).

Nimodipine was used in 27 of 75 patients (36%) that underwent surgical occlusion of ruptured aneurysm. Good postoperative outcome was obtained in 81.5% of patients treated with nimodipine and in 41.7% of non-treated patients, and the difference in the outcome was significant ($\chi^2=10.73; \ DF=1; \ p<0.01$), with high contingency coefficient (C=0.36). Such difference was especially significant in patients with HHG=III ($\chi^2=4.49; \ DF=1; \ p<0.01; \ C=0.41$) (Fig. 4).

Fig. 4 – Good outcome in patients treated and not treated with nimodipine

Groups of patients operated by experienced or less experienced surgical teams were homogenous regarding preoperative clinical condition: the mean HHG was 1.9 ± 1.2 and 2.2 ± 1.5, respectively ($\sigma d=0.32; \ Z=1.04; \ p>0.05$).

Good postoperative outcome existed in 78.9% of patients operated by the experienced team and in 40% of patients operated by less experienced personnel. The difference in the outcome was significant ($\chi^2=11.54; \ DF=1; \ p<0.01$), with high contingency coefficient (C=0.37).

Discussion

Gender and age

Gender did not influence the outcome after the aneurysmal clipping (2, 4, 24, 25), which was confirmed by our results. Recently, aneurysms were frequently diagnosed in elderly persons: almost 70% of patients with verified aneurysm were older than 75 years of age (25). In such patients, the clinical presentation after the aneurysmal rupture was more severe, but vasospasm and rebleeding rates were the same as in the younger persons (25).

Some authors claim that the advanced age by itself does not preclude successful postoperative outcome and report similar results for patients in old and middle ages (24). However, even these authors are of the opinion that careful preoperative patients selection is necessary, especially for the age over 80. For such selection the physiological age, not biological, is of crucial importance (2, 4).
In our series, the postoperative result was worse among older patients, who also had more severe clinical presentation after rupture, which confirmed the claims of the majority of the authors that the advanced age diminished the chance for successful outcome, mostly because of the associated medical conditions (10, 11). Bad outcome could be expected in up to 60% of persons older than 70 years (25). Duong et al. (13) reported good outcome in 87% of patients older than 60 years, in 91% of those ranged between 30 and 59 years and in all the patients younger than 30 years of age. Advanced age was the risk factor especially for bad neuropsychological outcome (26). Among patients over 70 years of age postoperative results were particularly bad if aneurysm was large and/or located on ACM (27).

Unruptured aneurysms, frequently diagnosed in old patients by magnetic angiography and similar noninvasive techniques were the special problem. Some authors recommended the operation, because the awareness of the aneurysmal existence diminished quality of life, while, on the other hand, cumulative risk of rupture overestimated the risk of treatment (26.3% morbidity and 4% mortality), which was greater than for younger patients though not significantly (25, 28). General condition of the patient as well as the opinion of the patient and his/her family was also important for the decision (10). Other authors claimed that the age influenced the treatment outcome (6) and did not recommend the operation for patients older than 70 years of age, if aneurysm was small and asymptomatic (28).

Chronic vascular diseases

The majority of surgeons think that hypertension and arteriosclerosis neither aggravates postoperative outcome (4, 24), nor increases the rupture risk for unruptured aneurysms (12). Our results, as well as sparse literature data (13), refuted such position. In our series, the criteria for hypertension were strict (considering only the cases resistant to the usual therapy), so the incidence of chronic vascular diseases was about 19%, considerably less than 45–50%, usually cited in literature (4, 12, 13).

Aneurysmal size

It is indisputable that surgical occlusion of giant aneurysms caused greater operative difficulties than the treatment of smaller aneurysms, because of adhesions with adjacent structures and significantly changed local anatomy. On the other hand, the blood flow velocity in small aneurysms was similar to the velocity in the main artery, so the central pulse wave reached the aneurysmal wall, while the flow was slower in large aneurysms (29). More frequent intraoperative rupture in our patients with larger aneurysms was indirectly the cause of greater difficulties during microdissection.

The incidence of small aneurysms was different in various series. Up to 38% of ruptured aneurysms were smaller than 6 mm, while among unruptured ones 44.7% were smaller than 6 mm and 27% were larger than 25 mm (6, 7). Aneurysmal growing was an unpredictable process: visible enlargement usually occurred after several months or years, but this was not the rule, because, for example, enlargement from middle to giant size in the period shorter than three days had been reported for the ACoP aneurysm (8). According to our results, aneurysmal size depended on its location to a certain degree: the largest were the ACI and M2 aneurysms.

Principally, the risk for aneurysmal rupture is proportionate to its size: 1% per year for aneurysms over 10 mm in size and 6% for those larger than 25 mm (6). Nevertheless, aneurysmal size was not the only factor upon which the moment of rupture depended, thus in our series unruptured aneurysms were larger than the ruptured ones. The severity of clinical presentation after rupture did not depend on aneurysmal size.

Contrary to numerous literature reports (6, 7, 9), our results pointed out that aneurysmal size did not change postoperative outcome significantly. The cause of such disagreement was probably the fact that literature data compared mainly postoperative results of aneurysms smaller than 10 mm with the results after the occlusion of giant aneurysms, which were rarely present in our series. Slight influence of aneurysmal size on the surgical result was proved indirectly by good postoperative results of unruptured aneurysms, considerably larger in size than the ruptured ones. On the other hand, longer postoperative hospitalization and more frequent vasospasm in patients with larger aneurysms were the indirect signs of slower recovery.

Timing of surgery

Operative occlusion of recently ruptured aneurysm had been followed by high lethality and morbidity rates for a long time. On "angry, red, swollen brain", as it was operatively described, ischemic lesion, caused by brain retraction, was frequent and intraoperative aneurysmal rupture was a regular phenomenon. Because of such experiences many neurosurgeons did not perform surgery in the acute stage of SAH at all, even more so because the results after the postponed operations were excellent. The surgeons delayed operation for 8-10 days for patients with HHG=I-II and even longer for patients in even worse condition (3). In 1953 Norlen and Olivecrona reported mortality rate of only 3% for 100 patients with ACoA aneurysms, operated on at least 21 days after SAH (1). This report became mainstone and had been frequently cited in favor of the delayed operation strategy, inviolable until the seventies.

It was discovered than that the first two weeks after SAH were the most risky period for rebleeding and vasospasm, and that patients underwent postponed operation numbered only 50% of all hospitalized and 25% of all patients with aneurysmal SAH. In 1968 Hunt & Hess introduced a wellknown scale for clinical grading after SAH, facilitating the comparison of results after different methods of surgical treatment. Besides, the usage of microneurosurgical technique, modern neuroanesthesia and spinal drain-
age enabled good intraoperative visualization, minor operative trauma, good brain relaxation and minimal brain retraction.

All these things lead neurosurgeons to revise the analysis of the early operation as a therapeutical possibility. New strategy of medical treatment also demanded the early operation, because the induced hypertension and hypervolemia were safe only if aneurysm had been previously occluded.

Hunt and Miller reported survival rate of 72% among early operated patients. Afterwards, even better results were published by other European, Japanese and American authors, with good outcome in 52% of patients in III-IV grade and in 75% of all patients (1, 3, 5). According to Cooperative Study from the early eighties, there was no significant difference in morbidity and mortality rates between the early and late operated patients, and the same results were also reported by some new authors (4, 5).

Allegation that the early surgery increased the incidences of vasospasm and delayed ischemia was not correct, because it was based only on more frequent intraoperative visualization of vasospasm in the early operated, thus in the period already typical for vasospasm genesis. On the other hand, the claim that early operation and evacuation of subarachnoid hematomas prevented vasospasm, was not proved, either (30).

The surgical dilemma for each individual patient with ruptured aneurysm was: either to operate immediately, in spite of brain edema, and to prevent rebleeding, or to wait for the disappearance of consequences of initial hemorrhage. Both the early and the delayed surgery have advantages and disadvantages (31). During the operation in the acute stage, inadequate preoperative planning, premature intraoperative rupture, poor clips selection or undesirable occlusion or lesion of perforator vessels may be the problem (32).

The majority of authors think that the worldwide acceptance of early surgery in the last 10 years contributed considerably to decreasing rates of morbidity and mortality. Delayed surgery, once accepted throughout the world, is now being performed by small number of neurosurgeons (3). The incidence of early aneurysmal occlusion is different in various neurosurgical centers: about 26–95% of patients are hospitalized and 17–75% underwent surgery in the acute stage (4, 5, 33–35).

In our series, 30.8% of patients underwent early surgery, in accordance with the cited literature data, but preoperative intervals (SAH-angiography, angiography-surgery) were too long. For patients with HHG=IV-V delaying could have been explained by waiting for recovery, but for patients with HHG=I-II there were no medical excuses. Late referring from the regional centers was one of the reasons, but subjective weakness related to angiography and timing for surgery surely also existed (36).

Authors mostly agreed that the alert patients (HHG=I-III), without severe brain edema making difficult aneurysmal presenting, should be operated early (37, 38). Good outcome after the delayed surgery was possible in 88% of cases, with 5% mortality rate. However, if analysis also included the patients who rebelled waiting for operation, incidence of good outcome decreased to 68% and mortality rate increased to 26% (3).

In our series, the patients with HHG=II-III had similar outcome after both the early and the delayed operations, but, because of the rebleeding risk, it was not all the same when the operation was to be performed. Taking into consideration the rebleeding rate of 27% for the first week after SAH as well as rebleeding lethality rate of 70.6%, obtained in the same series for patients with HHG=II-III (39), the calculation should have been made as followed: Of 100 early operated, good outcome would exist in 71 patients (Fig. 3). On the other hand, of 100 patients prepared for the delayed operation, 81 would live long enough to be operated on, and good outcome would exist in 83.3% of operated persons (Fig. 3). Therefore, the whole number of 67 patients would have good outcome, which is lower than after an early operation.

The opinions for the ideal time of surgery for patients in bad clinical condition (HHG=IV-V) is still controversial. Supporters of early surgery claim that urgent operation and aggressive medical treatment enable good outcome in 51–64% of patients with mortality rate between 25 and 36%. On the other hand, only 25% of patients planned for delayed surgery would have good outcome (50% would die before the operation, because of rebleeding or brain infarction) (33, 35, 40–42). According to our results, early surgery was not superior to the delayed operative treatment in such kind of patients, but it should be mentioned that in our series medical treatment of such patients was mainly not sufficiently aggressive.

It was not proved that early surgery negatively influenced cognitive, neuropsychological and emotional recovery (43). As differences in the outcome after early and delayed surgery were not statistically significant, operation time had to be adapted to each individual patient.

**Nimodipine therapy**

Nimodipine emphasized the dilatation of parenchymal and leptomeningeal arterioles as well as deformability of erithrocytes, thus improving the collateral circulation towards ischemic brain regions (44, 45). It did not reverse the existing vasospasm, but decreased the incidence of symptomatic infarctions and improved the treatment outcome (14).

About 20–30% of patients had clinically visible vasospasm after SAH, but the clinical course could not had been predicted until several days of treatment have passed (13). Usual treatment protocol was intravenous application during 5–7 days in doses of 60 mg every 4 hours, and than oral application until the end of the 21st day (15, 16). However, in patients with HHG=I-III the treatment could have been discontinued without consequences after 15 days or less (15).

Favorable effect of nimodipine was more expressive if combined with hypervolemia and hypertension. Such pa-
tients stayed in hospital and in intensive care unit shorter and the period of invasive cardiac monitoring was shorter, too. For some authors the absence of prompt positive reaction to hypervolemic therapy was a reliable sign of subsequent bad postoperative outcome (11, 17, 18). Nimodipine therapy combined with ketamin and lignocaine was not more effective than monotherapy (16).

Our results also proved that nimodipine therapy significantly improved the final treatment outcome, especially in patients with HHG=III. In this group of patients, therapy without nimodipine had to be considered as erroneous.

Experience of surgical team

Good results in cerebrovascular surgery are impossible without sophisticated equipment and experienced personnel, although opposite opinions have also been sporadically reported (46). For hospitals performing more than 5, 1–5 and less than 1 craniotomies per year on the average, mortality rates after operative aneurysmal occlusion were 14.3%, 18.4% and 20.5%, respectively (47). For hospitals with more than 30 craniotomies per year, mortality rate after aneurysmal occlusion was 8.8%, but was almost doubled (15.5%) for those with lesser than 30 craniotomies per year (48). Our results also emphasized the importance of neurosurgeon's experience in all phases of therapeutic procedure: adequate operation planning, anticipation of potential intraoperative difficulties, quick and effective solving of incidental intraoperative situations and the adequate postoperative assessment.

Other factors

In addition to the mentioned, other factors also influence the outcome after the operative aneurysmal treatment, some of which were analyzed in previous papers (20, 21). It was concluded that the final outcome did not depend significantly (p>0.05) on: intraoperatively verified regional vasospasm (23), aneurysmal location (20), intraoperative aneurysmal rupture and temporary main artery occlusion for the period shorter than 8–10 minutes (21). On the contrary, postoperative outcome depended significantly (p<0.01) on postoperative brain ischemia and preoperative state of consciousness (passing from HHG=III to HHG=IV) (20).

The severity of SAH was also cited in literature as a risk factor for bad outcome. Fisher's grading from 0 to 4, based on bleeding distribution on CT in the first 72 hours, was usually used to estimate the severity of SAH (19). Some authors claimed that weakening of postoperative outcome start already with Fisher's grade 2 (diffuse subarachnoid hemathoma thinner than 1 mm) (4, 19), but the majority agreed that good outcome was not of lesser probability until Fisher's grade 4 (hemathoma in brain parenchyma or ventricles) (11, 17, 18).

Conclusion

On the basis of the obtained results, we may conclude the following:
The outcome after the operative treatment of cerebral aneurysms depended significantly (p<0.01) on: patient's preoperative clinical condition, existence of chronic vascular diseases, nimodipine therapy, intraoperative temporary main artery occlusion lasting longer than 8–10 minutes, postoperative brain ischemia and experience of the surgical team.

The outcome after operative treatment of cerebral aneurysms did not significantly depend on: patient's gender and age, timing for surgery, aneurysmal location, size and intraoperative rupture, temporary clipping and operatively verified regional vasospasm.

REFERENCES


The paper was received on April 18, 2001.

**A p s t r a k t**


**FAKTORI KOJI UTIČU NA ISHOD OPERATIVNOG LEČENJA MOŽDANIH ANEURIZMI PREDNJE CIRKULACIJE**

**Cilj.** Definisati uticaj pojedinih faktora na ishod operativne okluzije moždane aneurizme. **Metode.** Retrospektivna studija na 111 operisanih bolesnika sa aneurizmom prednje moždane cirkulacije. Preoperativno kliničko stanje je stepenovano od 0 do V, prema Hantu i Hessu. Ishod operacije, definisan kao dobar ili loš, na osnovu modifikovane Glazgovske skale ishoda, korelisan je u homogenim eksperimentalnim grupama, sa svakim od sledećih 7 faktora: pol, uzrast, veličina aneurizme, preoperativni interval, terapija nimodipinom, iskustvo hirurškog tima i prisustvo hroničnih vaskularnih oboljenja. **Rezultati.** Dobar ishod operacije je postojao: kod 74,4% muškaraca i 71,4% žena (p>0,05); kod 83,3% bolesnika sa i 41,2% bolesnika bez hroničnih oboljenja (p<0,01); kod 71,4% rano, 83,3% odloženo i 85% kasno operisanih bolesnika (p>0,05); kod 81,5% bolesnika lečenih i 41,7% bolesnika nelečenih nimodipinom (p<0,01); kod 78,9% operisanih od strane iskusnog i 40% operisanih od strane manje iskusnog hirurga (p<0,01). Kod bolesnika sa dobrim i sa lošim ishodom prosečna starost bila je 50,6 i 47,6 godina (p>0,05), a prosečna veličina aneurizme 12,3 mm i 13,3 mm (p>0,05). Pre rupture, aneurizme račve a. cerebri mediae imaju u proseku 14,3 mm, a aneurizme zadnje komunikantne arterije 9,7 mm (p<0,05). **Zaključak.** Na ishod operativnog lečenja značajno utiču: postojeće hronične oboljenja, primena nimodipina i iskustvo hirurga, dok uticaj pola i starosti bolesnika, vremena operativnog lečenja i dimenzija aneurizme nije značajan.

**K l u č n e r e č i:** aneurizma, intrakranijalna; aneurizma, rupture; a. cerebri anterior; a. cerebri media; ishod, glazgovska skala; angiografija mozga; neurohirurške procedure; nimodipin; lečenje, ishod.