Research Article

https://doi.org/10.23934/2223-9022-2022-11-1-31-41

The Role of Risk Factor in the Surgical Treatment of Hemorrhagic Stroke

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AIM OF STUDY To identify risk factors for adverse outcomes of surgical treatment of patients with HS.

MATERIAL AND METHODS A retrospective analysis of the results of surgical treatment of 500 patients operated on at the N.V. Sklifosovsky Institute from 1997 to 2020 for hypertensive intracerebral hematomas. The mean age of the patients was 53.1±12.2 years. There were 335 (67%) men and 165 (33%) women. The level of consciousness before the operation was clear in 176 (35.2%), stupor (11–14 score, GCS) — in 258 (53.6%), sopor (score 9–10, GCS) — in 38 (7.6 %), moderate coma (7–8 score, GCS) — in 10 (2%) patients, deep coma (score 6) — in 7 (1.4%) patients. ICHs were lobar in 218 (43.6%) patients, lateral in 212 (42.4%) patients, thalamic in 10 (2%) patients, mixed in 10 (2%) patients, cerebellar in 50 (10%) patients. The average volume of ICH was 46.5±25.1 cm3, supratentorial ICH – 49.6±24.5 cm^3 (from 4 to 147 cm^3), subtentorial — 18.7±6.4 cm^3 (from 5 to 36 cm^3). The average duration of the surgical intervention was 3.3±2.6 days. The following types of operations were performed: open removal of the ICH in 271 (54.2%) patients, puncture aspiration and local fibrinolysis of the ICH in 98 (19.6%) cases, endoscopic aspiration of the ICG in 131 (26.2%) patients.

RESULTS The risk factors for lethal outcome in HT surgery are the age of patients older than 50 years (χ^2=13.9, p<0.04), the volume of cerebral hemispheres more than 50 cm^3 (χ^2=7.8, p<0.01), the total volume of ICH and perifocal edema more than 100 cm^3 (χ^2=9.1, p<0.01), transverse dislocation of the median structures of the brain more than 5 mm (χ^2=32.2, p<0.0001), axial dislocation of the brain (χ^2=16 ,1, p<0.02), BP before surgery higher than 160 mm Hg (χ^2=21.9, p<0.002), presence of IVH (χ^2=36.9, p<0.00001), AOH (χ^2=28.0, p<0.0001), surgery time — the first day after hemorrhage (χ^2=64.4, p<0.00001), residual volume of ICH after surgery more than 15 cm^3 (χ^2=4.0, p<0.05) and recurrence of ICH (χ^2=33.1, p<0.00001). The outcomes correlate with the severity of the patient's condition before surgery (R=0.38, p<0.00001), and the risk factor for death is the depression of consciousness to deep stupor and below (χ^2=97.2, p<0.00001).

CONCLUSION Assessment of risk factors can help clarify the prognosis of the outcomes of surgical treatment and optimize the treatment tactics of patients.

Keywords: hemorrhagic stroke, surgical treatment, risk factors, duration of surgery, level of consciousness, ICH volume, brain dislocation, blood pressure, recurrent hemorrhage, occlusive hydrocephalus

For citation Dashyan VG, Godkov IM, Khamurzov VA, Kryachev RYu, Grin AA, Krylov VV. The Role of Risk Factor in the Surgical Treatment of Hemorrhagic Stroke. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2022;11(1):31–41. https://doi.org/10.23934/2223-9022-2022-11-1-31-41 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study has no sponsorship

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AOH – acute occlusive hydrocephalus
BP – blood pressure
BPdiast – diastolic blood pressure
BPsyst – systolic blood pressure
CT – computed tomography
EA – endoscopic aspiration
EH – essential hypertension
GCS – Glasgow Coma Scale
HS – hemorrhagic stroke
IVH – intraventricular hemorrhage
ICH – intracerebral hematoma
OH – occlusive hydrocephalus
OS – open surgery
PF – puncture aspiration and local fibrinolysis
VBR-2 – 2nd ventricular-brain ratio

Surgical treatment of patients with hemorrhagic stroke (HS) remains a problem associated with a high level of adverse and fatal outcomes [1–3]. Large retro- and prospective studies on HS surgery were mostly aimed at studying the outcomes and effect of surgery in general, comparing the results of surgical and conservative treatment of patients [1, 4–10]. However, the analysis of the literature shows that risk factors in the surgical treatment of patients with HS have not been studied enough: questions remain regarding the prediction of a particular outcome based on preoperative factors, safe timing of surgical intervention, the effect of radical removal and recurrence of intracerebral hematoma (ICH) on outcomes.

The aim of the work was to verify the risk factors for adverse outcomes of surgical treatment of patients with HS.

MATERIAL AND METHODS

A retrospective analysis of the results of surgical treatment of 500 patients operated at the N.V. Sklifosovsky Research Institute for Emergency Medicine from 1997 to 2020 for hypertensive ICH. Patients were included in the study by a continuous sample. The criterion for inclusion in the study was operations performed according to one of the three methods of ICH removal: 1) open surgery (OS), 2) puncture aspiration and local fibrinolysis (PF), and 3) endoscopic aspiration (EA). Patients who underwent only external ventricular drainage or third ventriculostomy for occlusive hydrocephalus (OH) as a complication of hemorrhage, or who underwent ICH removal using combined methods (endoscopic removal followed by local fibrinolysis), were not included in the study.

The mean age of the patients was 53.1±12.2 years. There were 335 (67%) men and 165 (33%) women. The patients were initially hospitalized or transferred to the N.V. Sklifosovsky Research Institute for Emergency Medicine from other hospitals within 1-3 days from the onset of the disease – in 403 cases (80.6%), on days 4-7 – in 57 cases (11.4%), on day 8 and later – in 40 cases (8%). The state of patients upon admission was assessed as satisfactory in 3 (0.6%) patients, moderate in 222 (44.4%) cases, severe in 265 (53.0%) cases, extremely severe in 9 patients (1, 8%). Consciousness was clear (15 points on the Glasgow Coma Scale (GCS) [11]) in 176 (35.2%) cases, stupor (11-14 points on the GCS) in 258 (53.6%) cases, sopor (9-10 GCS points) – in 38 (7.6%) patients, moderate coma (7-8 GCS points) – in 10 (2%) patients, deep coma (6 points) – in 7 patients (1.4%). Of the 500 patients, 445 (89%) suffered from hypertension, 55 (11%) did not have EH. Mean systolic

blood pressure (BPsyst) in the sample was 163±33 mm Hg, diastolic (BPdiast) – 92±19 mm Hg. Of the focal neurological disorders in patients, pyramidal insufficiency was most often detected – in 392 patients (78.4%), aphasia – in 191 (38.2%), mental disorders – in 35 (7%). Less significant symptoms of damage to the cerebral hemispheres were not taken into account in the analysis. Cerebellar disorders were observed in 44 patients (8.8%).

ICH was verified using computed tomography (CT) of the brain. The ICH volume was calculated using the formula A × B × C /2 [12]. According to the classification of the Institute of Neurology of the Academy of Medical Sciences, ICH was lobar – in 218 patients (43.6%), lateral – in 212 (42.4%), thalamic – in 10 (2%), mixed – in 10 (2%), cerebellar – in 50 (10%). The average volume of ICH was 46.5±25.1 cm3, supratentorial ICH – 49.6±24.5 cm3 (from 4 to 147 cm3), subtentorial – 18.7±6.4 cm3 (from 5 to 36 cm3).The total volume of ICH with perifocal edema in supratentorial location was 93.3±41.2 cm3, in subtentorial location – 45.4±25.4 cm3. Intraventricular hemorrhage (IVH) was revealed in 176 patients (35.2%) out of 500, on average 2.3±1.7 points (from 1 to 8 points) according to Graeb [13]. The transverse dislocation of the median structures of the brain averaged 5.0 ± 3.6 mm (from 0 to 21 mm), axial dislocation was observed in 125 patients (25%). The development of OH was verified in 42 patients (8.4%). In these patients, the 2nd ventricar-brain ratio (VBR-2) was 23.9±4.5%, in other patients it was 12.0±3.6%.

The average duration of surgical intervention was 3.3±2.6 days and did not depend on the surgical method used. The following types of operations were performed: open removal of the ICH in 271 patients (54.2%), puncture aspiration and local fibrinolysis of the ICH in 98 (19.6%), endoscopic aspiration of the ICH in 131 patients (26.2%). Operations were performed under general anesthesia.

The radicality of ICH removal was assessed according to the CT scan of the brain during the first day after the operation; the results were compared by the median and quartiles. Outcomes were assessed on the 30th day from the onset of the disease according to the modified Rankin scale (Modified Rankin Scale - mRS) [14].

RESULTS

The mRS outcomes in the total sample were as follows: type 0 – in 84 (16.8%), type 1 – in 37 (7.4%), type 2 – in 46 (9.2%), type 3 – in 38 (7.6%), type 4 – in 43 (8.6%), type 5 – in 142 (28.4%), type 6 – in 110 patients (22.0%) out of 500. Outcomes of treatment statistically significantly depended on the age of patients ($Z = 2.5$; $p < 0.02$), severity of the condition ($\chi 2 = 124.0$; $p < 0.00001$) and the level consciousness of patients before surgery ($\chi 2 = 97.2$; $p < 0.00001$), location ($\chi 2 = 189.0$; $p < 0.00001$), supratentorial ICH volume ($Z = 2.9$; $p < 0.01$), the total volume of supratentorial ICH and perifocal edema ($Z = 2.9$; $p < 0.01$); values of transverse dislocation of median structures in supratentorial ICH ($Z=2.9$; $p<0.005$), BPsyst ($Z=3.9$; $p<0.0001$) and diastolic blood pressure ($Z = 2.9$; $p < 0.01$) before surgery, breakthrough of blood into the ventricles of the brain ($\chi 2 = 13.4.0$; $p < 0.001$), development of occlusive hydrocephalus ($\chi 2 = 8.2$; $p < 0.05$), duration of surgery ($\chi 2 = 57.8$; $p < 0.00001$) and recurrence of hemorrhage after surgery ($\chi 2 = 33.1$; $p < 0.00001$).

AGE

Outcomes were statistically significantly dependent on the age of patients ($Z = 2.5$; $p < 0.02$). The mean age of surviving patients was 52.5±11.9 years, of those who died – 55.3±13.1 years (t-value =2.1; p =0.03). When comparing mRS outcomes in patients under the age of 50 years and older, we were able to find that in the second group there were fewer patients with type 3 and 4 outcomes, but higher mortality: mRS outcomes of types 0–2 were observed in 58 (33.3%) patients under the age of 50 years, in 109 patients (33.4%) aged 51 years and older, outcomes of types 3-4 – in 39 (22.4%) and 42 (12 .9%) cases, type 5 outcomes – in 50 (28.7%) and 92 (28.2%) patients, deaths – in 27 (15.5%) and 83 patients (25.5%) of the first and the second group, respectively ($\chi 2 = 13.9$; $p < 0.04$).

SEVERITY OF THE CONDITION, LEVEL OF CONSCIOUSNESS

The severity of the condition ($\chi 2 = 124.0$; $p < 0.00001$) and the level of consciousness ($\chi 2 = 97.2$; $p < 0.00001$) are risk factors affecting outcomes. If the level of consciousness was the result of a GCS assessment, then the severity of the condition, in addition to consciousness, was determined by focal neurological disorders, hemodynamic stability, and the presence and severity of concomitant diseases. Given the variety of factors that determine the severity of the patient's condition, in our opinion, the level of consciousness is a more representative criterion for presenting and comparing outcomes (Fig. 1). In patients with clear consciousness,

outcomes according to mRS were types 0-2 in 96 (54.5%), types 3–4 – in 27 (15.3%) cases, type 5 – in 32 (18, 2%) cases, type 6 – in 21 patients (11.9%) out of 176. In patients with stupor, outcomes according to mRS types 0-2 were observed in 66 (24.5%) cases, types 3-4 – in 48 (17.8%) cases, type 5 – in 92 (34.2%) cases, type 6 – in 63 patients (23.4%) out of 269. In patients with sopor, outcomes according to mRS 0-2 were observed in 5 (13.2%) cases, types 3-4 – in 4 (10.5%) cases, type 5 – in 15 (39.5%) cases, type 6 – in 14 patients (36.8%) out of 38. Patients in coma had no mRS outcomes of types 0-2, 2 (11.8%) had types 3-4, and 3 had type 5 (17.6%), and 12 patients (70.6%) out of 17 had type 6.

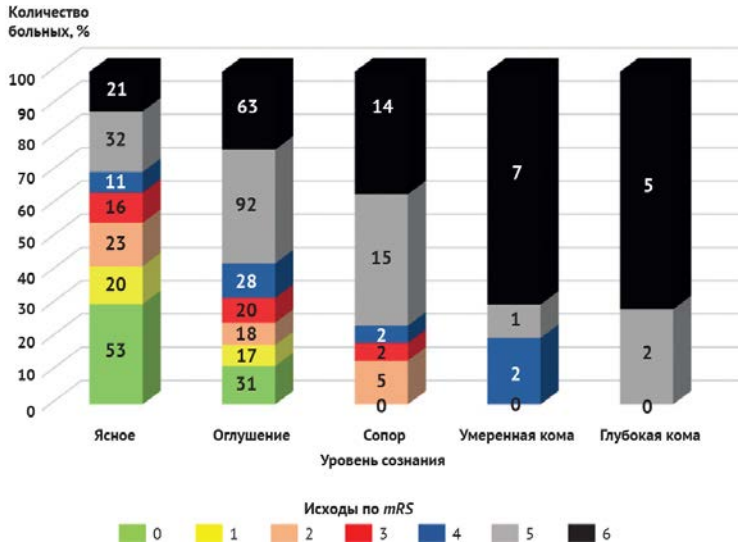

Fig. 1. Outcomes depending on the level of consciousness of patients before surgery

LOCATION OF INTRACEREBRAL HEMATOMAS

Outcomes were statistically significantly affected by ICH location ($\chi 2 = 189.0$; $p < 0.00001$). Lobar ICH had the lowest mortality, the best functional outcomes among patients with supratentorial hemorrhages: outcomes of types 0-2 according to mRS were observed in 127 (58.3%), types 3-4 – in 31 (14.2%), type 5 – in 36 (16.5%), fatal – in 27 patients (12.4%) out of 218.

With lateral, thalamic, and mixed ICH location, there were a small number of favorable outcomes (patients with severe neurological disorders predominated among the survivors), mortality was higher than with lobar ICH: 14 (6.0 %), types 3-4 – in 48 (20.7%) cases, type 5 – in 104 (44.8%) cases, fatal – in 66 patients (28.4%) out of 232.

With ICH of the cerebellum, there was a significant number of deaths. Along with this, in surviving patients with cerebellar ICH, outcomes with good recovery prevailed significantly: outcomes of types 0-2 according to mRS were observed in 29 (58.0%) cases, types 3-4 – in 2 (4.0%), 5 type – in 2 (4.0%), fatal – in 17 patients (34.0%) out of 50.

VOLUME OF INTRACEREBRAL HEMATOMA AND PERIFOCAL EDEMA

When analyzing the effect of ICH volume on outcomes, it was found that with supratentorial location of ICH in surviving patients, the average ICH volume was 47.6±22.9 cm3, in the deceased – 57.2 ± 28.9 cm3 (t-value=3.4; $p<0.01$) (Fig. 2). When comparing the outcomes in patients with ICH less than 50 cm 3 and more than 50 cm3, a statistically significant difference in mortality was revealed: with an ICH volume of up to 50 cm3, deaths occurred in 45 patients (16.3%) out of 277, with an ICH volume of 51 cm3 and more – in 47 patients (27.2%) out of 173 ($\chi 2=7.8$; $p<0.01$). In subtentorial location of ICH, no dependence of outcomes on ICH volume was found.

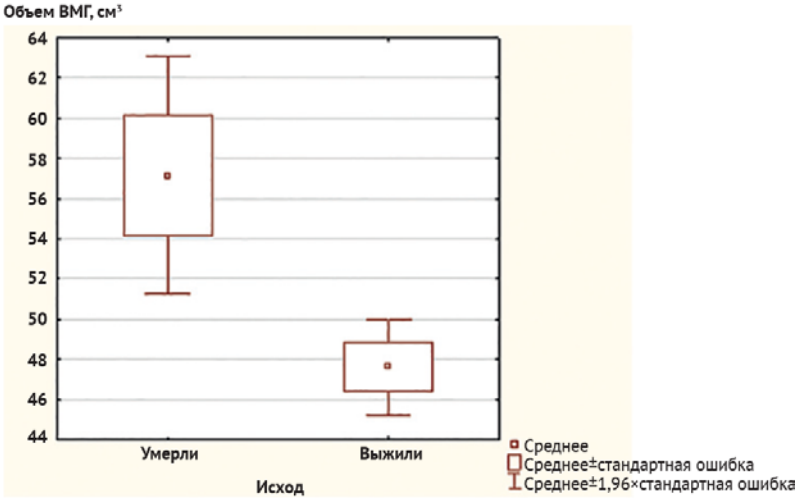

Fig. 2. Survival of patients depending on the volume of supratentorial intracerebral hematomas

With an increase in the period from the moment of hemorrhage, the volume of perifocal edema increased relative to the volume of IVH: on day 1-3, the ratio of the total volume (ICH + ischemic edema) and the volume of ICH was 2.1 ± 1.3, on day 4-7– 2.4±0.7, on day 8 and later – 3.2±1.8 (K.-W. – 16.6; p <0.001, statistically significant). The ratio of ICH volume to perifocal edema did not depend on ICH location. When analyzing the effect of the total volume of ICH and perifocal cerebral edema on outcomes with supratentorial location of ICH, it was found that in surviving patients, the average volume of ICH with perifocal ischemic brain edema was 89±36.6 cm3, in the deceased patients – 109.6±52.4 cm3 (t-value =3.9, p <0.001, statistically significant). In the group of patients with a total volume of ICH and edema-ischemia up to 100 cm3, 33 patients (15.6%) out of 212 died, in the group of patients with a total volume of ICH and edema-ischemia of 101 cm3 or more, deaths occurred in 41 patients (28.9%) of 142 ($\chi 2$ =9.1; p <0.01, statistically significant).

TRANSVERSE AND AXIAL DISLOCATION OF THE BRAIN

Of 450 patients with supratentorial ICH, transverse dislocation was counted in 411 cases. Lethality in supratentorial ICH depended on the size of the transverse dislocation of the median structures of the brain. In the group of surviving patients, the average value of the transverse dislocation was 5.2 ± 3.2 mm, in the deceased – 6.6 ± 4.1 mm (t-value = 3.2; p <0.002, statistically significant). With a transverse dislocation of up to 5 mm, deaths occurred in 32 (14.4%) of 222 cases, with a dislocation of 6-10 mm – in 37 (23.9%) of 155 cases, with a dislocation of 11 mm or more – in 12 cases (35 .3%) of 34 ($\chi 2$ =32.2; p <0.0001, statistically significant).

Axial dislocation was assessed by CT in 436 patients with supratentorial and 50 patients with subtentorial ICH. Out of 436 patients with supratentorial ICH, axial dislocation was in 89 (20.4%), out of 50 patients with subtentorial ICH – in 13 (26.0%). With supratentorial ICH, the development of axial dislocation led to a decrease in the number of outcomes with good recovery of neurological functions, an increase in the number of outcomes with severe neurological disorders and mortality ($\chi 2$ =16.1; p <0.02, statistically significant). In the absence of axial dislocation, outcomes of types 0-2 according to mRS were observed in 119 (34.3%) cases, types 3-4 – in 64 (18.4%) cases, type 5 – in 101 (29.1 %) cases, deaths – in 63 (18.2%) cases. With the development of axial dislocation, outcomes of types 0-2 according to mRS were observed in 15 (16.9%) cases, types 3-4 – in 15 (16.9%) cases, type 5 – in 35 (39.3 %) cases, deaths – in 24 (27.0%). In case of axial dislocation, a tendency of worsening outcomes in patients with cerebellar hemorrhage was found. Despite the fact that this relation is not statistically significant ($\chi 2$ =6.0; p =0.4), the results show a significant difference in patient outcomes. Patients with cerebellar ICH without axial brain dislocation had either favorable outcomes (type 0-1 according to mRS) or death. Type 0-1 outcomes according to mRS were achieved in 10 (76.9%) patients, deaths were registered in 3 patients (23.1%) out of 13. Patients with ICH of the cerebellum with the development of axial dislocation of the brain had higher mortality and worsening of functional outcomes in surviving patients: outcomes of type 0-4 were observed in 21 (56.8%) cases, type 5 – in 2 (5.4%) cases, deaths – in 14 patients (37.8%) of 37 (Fig. 3). Statistical analysis revealed a tendency for the

development of axial dislocation to depend on the volume of the cerebellar ICH (t-value =-1.9; p =0.07), in patients with axial dislocation, the average volume of the cerebellar ICH was 19.7±6.3 cm3.

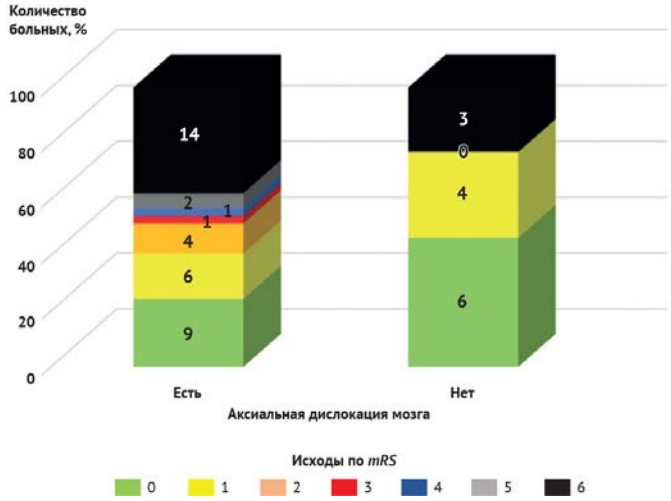

Fig. 3. Outcomes in patients with intracerebral hematoma of the cerebellum depending on the development of axial dislocation of the brain

BLOOD PRESSURE

Preoperative BP was analyzed in 301 patients. Both systolic and diastolic BP before surgery had a statistically significant effect on postoperative mortality. In surviving patients, BPsyst before surgery was 148.6±22.6 mm Hg, in deceased patients it was 164.2±31.5 mm Hg (t=4.7, p <0.00002). BPdiast in surviving patients was 87.3±10.5 mm Hg, in deceased patients it was 93.3±15.2 mm Hg (t =3.6; p <0.0004).

Out of 301 patients, systolic blood pressure exceeded 160 mm Hg. in 75 (24.9%), diastolic blood pressure was above 90 mm Hg in 68 patients (22.6%). When comparing outcomes between groups, it was found that in patients with systolic blood pressure of more than 160 mm Hg the number of adverse outcomes increased ($\chi 2$ =21.9; p <0.002). In this group of patients, outcomes of types 0-2 according to mRS were observed in 14 (18.7%) cases, types 3-4 – in 10 (13.3%) cases, type 5 – in 25 (33.3%) , deaths – in 26 patients (34.7%) out of 75. In patients with systolic blood pressure up to 160 mm Hg outcomes of types 0-2 according to mRS were observed in 90 (39.8%) cases, types 3-4 – in 41 (18.1%), type 5 – in 63 (27.9%), fatal outcomes – in 32 patients (14.2%) out of 75. When analyzing the dependence of mRS outcomes on the level of diastolic BP, only a trend of worsening outcomes was found in patients with diastolic BP more than 90 mm Hg ($\chi 2$ =10.5; p =0.1), however, when comparing mortality in groups of patients, a statistically significant difference was found: in patients with blood pressure diasts less than 90 mm Hg the mortality was 16.3% (38 out of 233 patients died), in patients with diastolic blood pressure less than 90 mm Hg the mortality reached 29.4% (20 out of 68 patients died) (χ 2 =5.8; p <0.02).

INTRAVENTRICULAR HEMORRHAGE

Intraventricular hemorrhage was verified in 176 (35.2%) of 500 patients and was a statistically significant independent risk factor influencing mRS outcomes ($\chi 2$ =36.9; p <0.00001). The frequency of IVH in lobar ICH was 26.6% (in 58 patients out of 218), in lateral ICH – 37.7% (in 80 patients out of 212), in thalamic ICH – 50.0% (in 5 patients out of 10), with mixed ICH – 70.0% (in 7 patients out of 10), with ICH of the cerebellum – 52.0% (in 26 patients out of 50). In patients without IVH , mRS outcomes of types 0-2 were observed in 129 (39.8%), types 3-4 – in 57 (17.6%), type 5 – in 83 (25.6%) %), deaths – in 55 patients (17.0%) out of 324. In patients with IVH, outcomes of types 0-2 according to mRS were observed in 38 (21.6%) cases, types 3-4 – in 24 (13.6%), type 5 – in 59 (33.5%), deaths – in 55 (31.3%) of 176 patients. On average, IVH corresponded to 2.4±1.7 according to Graeb scores and did not depend on the location of the ICH (varied from 2.1±1.7 to 2.4±1.8 for any location of the ICH). The analysis revealed only a trend towards an increase in mortality in patients with an increase in the degree of IVH according to Graeb (t-value = 1.8; p <0.08), however, IVH was a

statistically significant risk factor for the development of acute occlusive hydrocephalus (OH) ($\chi 2$ =14.3, p <0.001).

ACUTE OCCLUSIVE HYDROCEPHALUS

Acute occlusive hydrocephalus was verified according to CT data in 42 patients (8.4%) out of 500. Of the 42 cases, AOH developed in 6 cases in patients with supratentorial ICH and in 36 cases with cerebellar ICH ($\chi 2$ = 292.1; p <0.000001, statistically significant). In lobar ICH, the frequency of AOH was 0.9% (in 2 patients out of 218), 0.5% (in 1 patient out of 212) in lateral ICH, 20% (in 2 patients out of 10) in thalamic ICH, 10% in mixed ICH (in 1 patient out of 10), 72% (in 36 patients out of 50) in ICH of the cerebellum. AOH was a risk factor for worsening outcomes according to mRS ($\chi 2$ =28.0; p <0.0001): in patients without AOH, outcomes of types 0-2 according to mRS were observed in 145 (31.7%), 3-4- type 5 – in 80 (17.5%) cases, type 5 – in 139 (30.4%) cases, deaths – in 94 patients (20.5%) out of 458; in patients with AOH, outcomes of types 0-2 according to mRS were in 24 (57.1%), types 3-4 – in 1 (2.4%) case, type 5 – in 4 (7.1%) %) cases, deaths – in 16 patients (38.1%) out of 42.

OPERATION TERMS

When analyzing the outcomes in the total sample (500 patients), it turned out that with an increase in the duration of the operation, the treatment results were statistically significantly better ($\chi 2$ =64.4; p <0.00001). After operations performed on the 1st day after hemorrhage, deaths were observed in 36.4% (43 patients out of 118 died), and the number of outcomes of types 0-2 according to mRS was 18.6% (22 patients out of 118), after operations on day 2-3, the mortality rate was 20.4% (44 patients died out of 216), outcomes of types 0-2 according to mRS were observed in 29.6% (64 patients out of 216), after operations on day 4-7 the mortality was 17.4% (17 out of 98 patients died), outcomes of types 0-2 according to mRS – 49.0% (48 out of 98 patients), on day 8 and later the mortality was 8.8% (6 out of 68 patients died), favorable outcomes were observed in 48.5% (33 out of 68 patients). Thus, the least favorable for surgical intervention are the 1st day after the hemorrhage. Already from the 2nd day, postoperative mortality significantly decreased, and the best functional outcomes could be achieved when performing operations 3 days after the hemorrhage (Fig. 4).

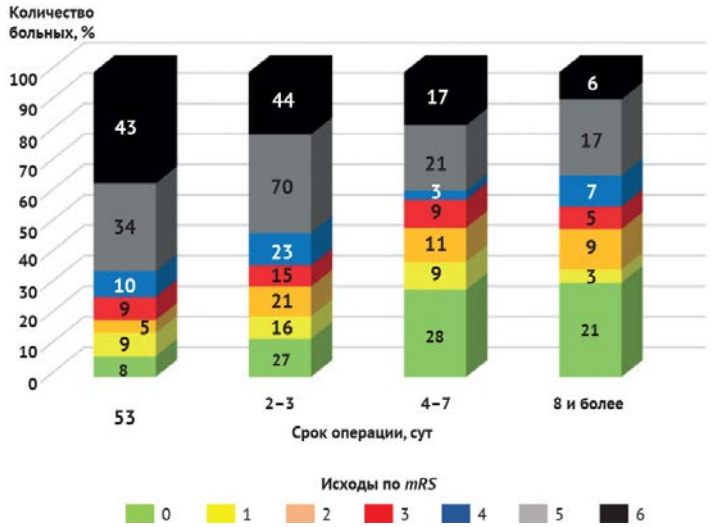

Fig. 4. Outcomes depending on the duration of the operation

RELAPSE AND RESIDUAL VOLUME OF INTRACEREBRAL HEMATOMAS

Treatment outcomes were statistically significantly influenced by factors such as residual volume and recurrence of ICH. When evaluating the effect of ICH volume on the outcome according to CT data after surgery, it was found that in surviving patients the average volume was 11.1±15.3 cm3, in the deceased – 20.5±25.2 cm3 (t-value = 4.2 , p <0.00003). When patients with recurrent ICH were excluded from the analysis, it was also confirmed that the residual volume of ICH affects the level of postoperative mortality. For intergroup analysis, we divided patients with supratentorial ICH into two subgroups: the first subgroup included patients in whom

the residual volume was less than 15 cm3, the second included patients in whom the volume of residual ICH was 15 cm3 or more. Mortality in the subgroups differed: in the first group it was 13.2% (29 out of 220 patients died), in the second group it was 23.0% (17 out of 74 patients died) ($\chi 2 = 4.0$; $p < 0.05$). In patients with subtentorial ICH, no effect of residual ICH volume on postoperative outcomes was found.

Of 500 patients, recurrence of ICH occurred in 74 (14.8%). Recurrent hemorrhages significantly worsened treatment outcomes, mainly increasing mortality ($\chi 2 = 33.1$; $p < 0.00001$). Relapses had a particularly noticeable effect on patients with supratentorial ICH: without relapses, mortality was 15.9% (61 patients out of 323 died), in patients with relapses – 47.0% (31 patients out of 66) ($\chi 2 = 33.5$; $p < 0.00001$). In patients with subtentorial ICH, relapses were also accompanied by an increase in the proportion of deaths (from 31.0 to 50.0%), however, the intergroup differences were statistically insignificant. It is noteworthy that ICH relapses not only led to an increase in mortality, but a decrease in the number of favorable functional outcomes.

Relapses most often occurred after PF – in 27.6% (in 27 patients out of 98), less often after EA – in 16.8% (in 22 out of 131 patients), most rarely after OS – in 9.2% (in 25 patients out of 271) observations ($\chi 2 = 19.7$; $p = 0.00005$, statistically significant). Differences in the frequency of relapses were found depending on the location of the ICH. With lateral ICH, the recurrence rate was the highest after PF (31.0% in 22 patients out of 71), and the lowest after OS (12.7% in 7 patients out of 55), after EA – in 20.9% (in 18 patients out of 86); in lobar ICH, the recurrence rate was the lowest after OS (5.7% in 10 out of 176 patients) and almost the same after PF (9.1% in 1 patient out of 11) and EA (9.7% in 3 patients out of 31); in cerebellar ICH, the recurrence rate practically did not differ after OO (18.4% – in 7 patients out of 38) and PF (20.0% – in 1 patient out of 5), and there were no relapses after EA.

The recurrence rate of ICH depended on the duration of the operation. The highest frequency of relapses was after operations performed on the 1st day after the hemorrhage, reaching 23.7% (in 28 patients out of 118). On days 2–7, the recurrence rate was 13.7% (in 43 patients out of 314), from the 2nd week it statistically significantly decreased to 4.4% (in 3 patients out of 68) ($\chi 2 = 8.1$; $p < 0.01$). An additional analysis of the frequency of relapses depending on the duration of the operation and the method of surgery revealed that their occurrence gradually decreases with an increase in the duration of the operation in OS and EA, but has a wavy frequency curve in PF. The maximum recurrence is observed after operations performed on the 1st day after a stroke: after OS – in 16.9% (in 12 patients out of 71), after PF – in 42.1% (in 8 patients out of 19), after EA – in 28.6% (in 8 out of 28 patients). After operations performed on the 2nd–3rd day, the recurrence rate decreases 2-fold with OS and PF, and 1.5-fold with EA, compared with the recurrence rate after surgery on the 1st day (table). After surgery on days 4–7 after OR and EA, the recurrence rate continues to decrease, after PF it increases. Starting with the day 8, OS was not complicated by relapses of ICH, after EA, relapses were very rare, and after PF, the recurrence rate remained at the level of 18.2%.

Table

The incidence of intracerebral hematoma recurrence depending on the method and duration of the operation

Operation time, days	Surgery methods and recurrence rate: there was a recurrence / total number of patients (% of relapse)			Number of patients
	OS	PF	EA	
1	12/71 (16.9)	8/19 (42.1)	8/28 (28.6)	118
2–3	10 / 114 (8.8)	10/47 (21.3)	10/55 (18.2)	216
4–7	3/55 (5.5)	7/21 (33.3)	3/22 (13.6)	98
8 or more	0 / 31 (0)	2/11 (18.2)	1/26 (3.9)	68
Total	25 / 271 (9.2)	27/98 (27.6)	22 / 131 (16.8)	500

Notes: ICH – intracerebral hematoma; OS - open surgery; PF - puncture aspiration and local fibrinolysis ; EA - endoscopic aspiration

DISCUSSION

The study of risk factors in HS surgery is of great practical importance. Risk factors can be used to assess the prospects for surgery, choose the optimal time, the method of ICH removal, and build prognosis scales. Previous large-scale studies made it possible to identify a number of risk factors for adverse outcomes in patients with HS, among which the most important were depression of consciousness to the point of stupor and coma,

supratentorial ICH volume more than 50 cm3, deep location of supratentorial ICH, subtentorial location of ICH, etc. [1, 2, 4, 6, 7, 21]. In this work, we were able to confirm the influence of these factors on postoperative mortality and to establish other pre- and postoperative factors that affect treatment outcomes. Factors that are not directly related to surgery (glycemia, blood electrolytes, coagulogram parameters, concomitant diseases), we deliberately did not include in this analysis, intending to devote a separate work to them.

Risk factors for poor outcomes in patients with HS are used in prognostic scales, which relevance is growing in the light of the long-standing discussion about the effectiveness of surgical treatment [15-17]. In the most well-known scales for predicting the outcome of HS, threshold values of age, level of consciousness of patients, IVH, volume of the ICH and its location relative to the cerebellar tentorium, established as a result of logistic regression analysis, are used as key parameters that affect the outcome [16, 17]. The age, level of consciousness of patients and the volume of ICH are presented on the scales as qualitative variables with interval values. In the Hemphill et al. (2001), 5 parameters are taken into account: age (up to 80 years and older), level of consciousness according to the GCS (3–4, 5–12, 13–15 points), location (supra- and subtentorial), volume of ICH (up to 30 cm3, 30–80 cm3, more than 80 cm3), the presence of IVH [16]. Ruiz-Sandoval et al. (2007) take into account the same 5 parameters, but with different threshold values: the age of patients (up to 44 years, 45–64 years, 65 years and older), the level of consciousness of patients (3–8, 9–12, 13–15 points according to GCS), location of ICH relative to the tentorium of the cerebellum, volume for supratentorial ICH (less than 40 cm3 , 40–70 cm3 , more than 70 cm3), volume for subtentorial ICH (less than 10 cm3, 10–20 cm3, more than 20 cm3) and the presence of IVH [17]. Both of these scales were created on the basis of an analysis of outcomes in patients with HS who were treated conservatively. Accordingly, the scales are poorly applicable to patients who are scheduled for ICH removal, as we saw when comparing the data obtained in our study. Thus, threshold age values of 80 years, as in the scale of Hemphill et al. (2001) [16], or 45 and 64 years, as in the Ruiz - Sandoval scale [17], did not show a corresponding difference in outcomes in the patients operated on by us: there were no patients older than 80 years in our sample, and the outcomes between groups of patients were less than 45 years and 45–64 years did not differ. In our study, we found that the difference in outcomes was noted when comparing patients under the age of 50 years and older. Mortality in the groups differed 1.7-fold (deaths were 15.5% and 25.5%, respectively).

When comparing outcomes depending on the level of consciousness of patients in our sample, an almost two-fold difference was found in the number of favorable outcomes (types 0–2 according to mRS), outcomes with severe disability in patients (type 5 according to mRS), and in the level of mortality already when comparing groups of patients in clear consciousness and stunning. Patients in sopor and coma of various depths showed a further increase in the level of mortality with a steady decrease in the number of favorable functional outcomes. Analysis of lethality showed that in patients in clear consciousness, the lethality was 11.9%, in moderate stupor – 15.6%, in deep stupor – 34.0%, sopor – 37.1%, in coma – 70.6%. In this regard, our study confirmed the validity of grouping patients into groups with comparable risks of death, as in the Ruiz - Sandoval scale: patients in clear consciousness and moderate stupor (Group 1), patients in deep group), patients in moderate and deep coma (group 3) [17]. At the same time, the grouping of patients according to the level of consciousness proposed by Hemphill et al. (2001) [16], contradicts the results of our study.

We were able to establish that BP was a preoperative factor influencing treatment outcomes. Outcomes were influenced to a greater extent by BPsyst : in surviving patients, BPsyst before surgery was 148.6 ± 22.6 mm Hg, in the deceased – 164.2 ± 31.5 mm Hg ($t = 4.7$, $p < 0.00002$, statistically significant). In patients with systolic blood pressure less than 160 mm Hg postoperative mortality was 14.2%, in patients with systolic blood pressure over 160 mm Hg –34.7%. Probably, this may be associated with violation of the mechanism of autoregulation of cerebral blood flow, which maintains a safe level of perfusion in BP within 160–170 mm Hg, especially in patients with long-term and untreated hypertension [18–20]. According to statistics, among our patients suffering from arterial hypertension with BPsyst more than 160 mm Hg, relapses occurred statistically significantly 2 times more often after ICH removal ($\chi 2 = 6.1$; $p < 0.02$). Given the strong statistical relationship between blood pressure levels and postoperative mortality, this factor is significant and can be taken into account when constructing a prognostic assessment.

In our sample, the analysis of the influence of the volume of ICH on the development of brain dislocation and outcome showed the following. In supratentorial ICH, the size of the transverse dislocation of the brain statistically significantly correlated with the volume of ICH ($R = 0.47$; $t = 11.1$; $p < 0.00001$). In surviving patients with supratentorial location, the average volume of ICH was 47.6±22.9 cm3, in the deceased –

57.2±28.9 cm3. With an ICH volume of not more than 50 cm3, postoperative mortality was 16.3%, with an ICH volume of more than 50 cm3 – 27.2%. Similar data were previously obtained in other works [1, 4, 6, 7, 21]. It is interesting that the interval values of supratentorial ICH volumes presented in the scales for predicting conservative treatment of patients [16, 17] differed from the values obtained in our work. This once again indicates that the course of the disease, prognosis and outcomes are likely to differ between surgical and conservative treatment.

In case of subtentorial location, no dependence of outcomes on ICH volume was found. In general, when comparing the results of treatment of patients with supra- and subtentorial ICH, it was found that after the removal of supratentorial ICH, mortality was 20.4%, and that of subtentorial ICH was 34.0%. However, the analysis of mortality depending on the surgical method used showed important nuances. In supratentorial ICH, the mortality varied depending on the location and method of ICH removal within 9.1–41.8%, but in subtentorial ICH after OS, the mortality rate was 44.7%, and there were no deaths after PF and EA ($\chi 2 = 8.1$, $p < 0.02$, statistically significant). Given this, in the future, with more active use of minimally invasive surgical methods, the subtentorial location of the ICH may not be taken into account as a risk factor for an unfavorable outcome.

The volume of perifocal edema depended on the volume of ICH, slightly increased in accordance with the period from the moment of hemorrhage, and had a statistically significant effect on the magnitude of the transverse dislocation of the brain ($R = 0.52$; $t = 10.7$; $p < 0.00001$). In turn, the outcomes of treatment depended on the size of the transverse and development of the axial dislocation of the brain. The larger the transverse dislocation, the higher the postoperative mortality. Axial dislocation was accompanied by worse outcomes on the 1st–3rd day and 2nd week after hemorrhage compared with patients without axial dislocation. At the same time, in patients operated on days 4-7, the outcomes did not depend on the presence of axial dislocation of the brain. In general, this period, according to our statistics, was the most favorable for achieving good outcomes of operations.

IVH, which occurs predominantly in subtentorial ICH, less often in medial and mixed ICH, is a risk factor leading to an increase in postoperative mortality. IVH is used in most scales for predicting outcomes in patients with HS as one of the aggravating factors [17]. In our sample, in patients with IVH, mortality was 1.8 times higher: without IVH, mortality was 17.0%, with IVH – 31.3%. The development of AOH is directly related to IVH and is a risk factor for death: in patients without AOH, mortality was 20.5%, with AOH – 38.1%. Considering that IVH was rarely large in our sample (on average, IVH corresponded to 2.4 ± 1.7 Graeb score), the increase in mortality in patients with IVH was associated with the development of AOH. Characteristically, AOH in the overwhelming majority of cases developed with cerebellar hemorrhage. This fact can explain why patients with AOH with a sufficiently high mortality had a significant proportion of favorable outcomes: with the timely resolution of AOH in patients with cerebellar hemorrhage, in most cases, good functional results can be achieved. Considering that AOH may be the direct cause of brain herniation in patients with HS, it can be considered as one of the significant factors in prognostic scales. The fear that the assessment of the development of AOH may be subjective [16] seems reasonable to us, however, in the future, this parameter may be taken into account when developing new prognostic scales.

Regarding the timing of surgery for HS, there are different approaches. Most researchers consider surgical intervention as early as possible, based on the biochemical mechanisms of the onset of the development of perifocal edema and degenerative changes in the brain tissue [7–9 , 21]. The works of some authors have shown that surgeries performed within the first 8 hours from the moment of hemorrhage offer great prospects for restoring neurological functions [5, 22–24]. Only the risk of ICH recurrence usually stops surgeons from performing operations within 8–24 hours after a hemorrhage [7, 8, 10, 25]. In our sample, the largest number of recurrences was after operations performed on the 1st day – 23.7%, subsequently their frequency decreased: after operations on the 2nd–7th day it was 13.7%, on the 8th day and later – 4.4%. In patients with recurrent ICH, the mortality rate reached 47.0%, without recurrence it was 15.9%. According to the literature and the results of our study, surgeries performed at a later date, within 48–72 hours [21, 25] and even within a week or more after a hemorrhage [1, 2, 26], can achieve good outcomes in patients with low recurrence rate of ICH.

Tactics, in which operations can be delayed, performed a day after the hemorrhage, can be explained. The goal of surgical treatment is to eliminate the volumetric and toxic effects of ICH. In fact, these are two tasks, somewhat separated in time. The volume effect of ICH is manifested already in the first minutes and hours after the hemorrhage, but it is not as detrimental as the effect on the substance of the brain of thrombin and blood decay products that determine the toxic effect of ICH. The toxic effect, which manifests itself in a local inflammatory

reaction, an increase in perifocal edema-ischemia of the brain, begins to fully manifest itself from the beginning of the second day and continues until the complete lysis of the ICH. To eliminate the toxic effect of the decay products of clotted blood, the operation can be performed within a period of days. The data obtained in our study demonstrate better overall outcomes and lower mortality after such interventions. At the same time, it is necessary to take into account the location of ICH. With ICH of the cerebral hemispheres, mortality was the highest after surgical interventions performed on the first day after hemorrhage, decreased 2-fold in the period from the 2nd to the 7th day. In our opinion, prospective randomized trials could provide a more accurate answer regarding the optimal timing of removal of supratentorial ICH, given that patients with HI often have comorbidities that aggravate their condition and increase the risks of surgery, especially in the early stages after hemorrhage. Also, it could clarify the possibilities of delayed surgery compared with conservative treatment of patients. Some prospective randomized trials did not allow demonstrating the advantage of surgical treatment over conservative treatment, however, it should be borne in mind that the condition for including patients in these studies was the early timing of surgery (up to 24-48 hours) and the almost absence of contraindications to surgical treatment due to age, severity of the patient's condition and volume, which did not allow them to identify patients in whom the potential benefit of the operation was higher than the perioperative risks [6, 8 , 27, 28].

In cerebellar hemorrhage, the largest number of deaths in our study was observed after operations performed on the 2nd–3rd day after hemorrhage, a smaller number of deaths were observed after operations performed on the 1st and days 4–7. Obviously, with ICH of the cerebellum, accompanied by a mass effect, compression of the basal cisterns and the fourth ventricle, the operation should be performed without delay.

Further study of the problem of surgery in patients with HS, prospective studies with a more rigorous selection of patients for surgery, development and implementation of scales for the prognosis of surgical treatment of patients, taking into account risk factors, can help optimize treatment tactics and further develop this area.

CONCLUSION

The risk factors for death in hemorrhagic stroke surgery are the age of patients older than 50 years, the volume of intracerebral hematomas of the cerebral hemispheres more than 50 cm3, the total volume of intracerebral hematomas and perifocal edema more than 100 cm3, transverse dislocation of the midline structures of the brain more than 5 mm, axial dislocation of the brain, systolic blood pressure before surgery more than 160 mm Hg and diastolic blood pressure before surgery more than 90 mm Hg, the presence of intraventricular hemorrhage and acute occlusive hydrocephalus before surgery, the duration of the operation is the first day after the hemorrhage, the residual volume of intracerebral hematomas after surgery is more than 15 cm3 and their recurrence. Outcomes correlate with the severity of the patient's condition before surgery, and the risk factor for death is depression of consciousness to a deep stupor and below. Assessment of risk factors can serve to clarify the prognosis of outcomes of surgical treatment and optimize treatment tactics.

FUNDING

1. The outcomes of surgical treatment of patients with HS depend on the severity of the condition before surgery, the age of the patients, the volume of the ICH, the severity of the transverse dislocation of the brain, the degree of depression of the level of wakefulness.

2. The most significant preoperative risk factors for a lethal outcome are age over 60 years, ICH volume more than 50 cm^3 , transverse dislocation more than 5 mm, depression of the level of wakefulness to stupor and coma, blood pressure system before surgery higher than 160 mm Hg, the presence of an axial dislocation and an IVH.

3. A postoperative risk factor for an unfavorable outcome is ICH recurrence: mortality in patients without relapses was 15.9% (61 patients died out of 323), with relapses – 47.0% (31 patients out of 66).

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Received on 29.04.2021

Review completed on 24.12.2021

Accepted on 27.12.2021