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Early predictors of conservative treatment for aneurysmal subarachnoid hemorrhage in low-income countries

Microsurgical and endovascular treatment for aneurysmal subarachnoid hemorrhage (SAH) is the gold standard for excluding ruptured intracranial cerebral arterial aneurysms (ICAA) from circulation and reducing rebleeding risk. However, conservative treatment remains an option in low-resource settings.

Objective — to identify early predictors of conservative treatment for SAH in low-resource settings.

Materials and methods. This retrospective, single-center cohort study included 212 patients with SAH treated between 2000 and 2023. Patients were divided into two groups: those receiving conservative treatment (n = 106) and those undergoing ICAA clipping within 14 days of their first rupture. Demographic data, clinical features, comorbidities, and radiographic/anatomical characteristics of ruptured ICAAs were analyzed.

Results and discussion. Of the 212 patients included in the study, 106 (Group 1) received conservative treatment, and 106 (Group 2) underwent ICAA clipping. The mean age was (56 ± 14) years in Group 1 and (50 ± 12) years in Group 2. Group 1 had a higher frequency of posterior circulation ICAA and multiple ICAAs. Although the mean size of ruptured ICAAs was similar (eight mm), Group 1 exhibited greater variability in ICAA size. Patient age, comorbidity burden, ICAA location and morphology, number of ICAA, and initial neurological condition are key determinants influencing the choice of conservative treatment over surgical clipping in low-resource settings.

Conclusions. Early predictors of conservative treatment for SAH in low-income countries include advanced age, high Charlson Comorbidity Index, anterior circulation ICAA, fusiform ICAA, multiple ICAA, and low-grade m-WFNS. These findings may help guide treatment decisions in settings with limited access to surgical interventions.

Keywords: cerebral aneurysm, subarachnoid hemorrhage, conservative treatment.

Surgical (endovascular and microsurgical) treatment for an aneurysmal subarachnoid hemorrhage (SAH) is considered the gold standard for excluding a ruptured intracranial cerebral arterial aneurysm (ICAA) from circulation and reducing the risk of recurrent ruptures [6, 13]. However, in low-income countries, limited resources may restrict immediate access to surgical treatment of aneurysmal SAH, making conservative management a last resort alternative [5]. In our study, conducted in such a setting, we analyzed factors influencing the choice of conservative treatment tactics. Important parameters such as advanced patient age, presence of comorbidities, and severity of the clinical picture were identified as determining the decision in favor of conservative therapy. Conservative therapy for poor-grade SAH in the elderly is associated with high mortality [2, 5, 7, 8, 14—16]. Surgical intervention even in poor preoperative clinical conditions significantly improves prognosis [2, 14, 16]. In such settings, where immediate access to surgical interventions may be limited, it is critical to understand the factors influencing the choice between conservative management and surgical treatment. By considering early clinical predictors, treatment protocols can be developed to help clinicians optimize aneurysmal SAH management and balance the limitations of available resources, particularly in low-income countries. This study aimed

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to identify early predictors of conservative treatment for SAH in low-resource settings.

Materials and methods

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Odesa National Medical University, protocol No.7, dated September 30, 2019. Informed consent was obtained from all participants included in this study.

This retrospective single-center cohort study was based on the analysis from the medical records of 212 patients treated for SAH in 2000—2023. This period corresponds to the years during which Ukraine was classified as a low-income country by the World Bank [19]. The study analyzed patients' medical data based on their treatment approach, and the patients were categorized into two groups. Group 1 consisted of patients who exclusively received conservative treatment as part of the retrospective observation. Group 2 consisted of patients who underwent ICAA clipping within 14 days of their first rupture.

The inclusion criteria for this study were (1) age over 18 years, (2) aneurysmal nature of SAH, (3) confirmation of ICAA on CT angiography, and (4) hospitalization in the first 14 days after the first ICAA rupture.

The exclusion criteria were (1) age under 18 years, (2) incomplete medical records; (3) absence of data on the date of the ICAA rupture; (4) other causes of SAH (trauma, presence of arteriovenous malformations, brain neoplasms, coagulopathy), (5) absence of ICAA on CT angiography, (6) hospitalization 14 days after the first ICAA rupture, and (7) ICAA trapping, endovascular surgery, and external ventricular drainage.

Patients who underwent endovascular surgery or required external ventricular drainage were excluded to avoid confounding variables related to newer surgical techniques and complications such as hydrocephalus. This allowed for a more focused analysis of early predictors in patients receiving conservative treatment. The study included a detailed analysis of patient demographics and clinical presentation, including clinical severity according to the modified World Federation of Neurosurgical Societies (mWFNS) scale grading system and symptoms of SAH upon admission.

The Charlson Comorbidity Index (CCI) is a widely used and validated tool for assessing the severity of comorbidities and predicting patient survival [12]. In our study, we calculated the CCI for each patient based on medical records to account for the impact of comorbidities on treatment decisions. Data on the following comorbidities were extracted from medical records. Patients were subsequently categorized into subgroups based on their CCI score: low risk (CCI 0—2), moderate risk (CCI 3—4), high risk (CCI 5—7) and very high risk (CCI ≥ 8). Additionally, radiological and anatomical parameters of ruptured ICAA were reviewed.

Descriptive statistics were used to analyze the data: calculation of mean values, standard deviations, medians, interquartile ranges, minimums, and maximums for continuous variables, as well as proportions and percentages for categorical variables. The normality of the distribution was tested using the Shapiro—Wilk test. The chi-square test was used to compare categorical variables, and the Mann—Whitney test was used to compare continuous variables. Binomial logistic regression was used to analyze the relationship between groups, with the results presented as odds ratios (OR) with 95 % confidence intervals (CI). Statistical significance was set at $p < 0.05$. All calculations were performed using JASP software version 0.19.3. Data visualization was performed using Python.

Results and discussion

Group 1 consisted of 106 patients who received conservative treatment: 43 (41 %) men and 63 (59 %) women. Group 2 also consisted of 106 patients who underwent surgical intervention, of which 58 (55 %) were men and 48 (45 %) were women. The mean age of the patients in Group 1 was 56 ± 14 years, with a median age of 56 ± 19 years, a minimum age of 19 years, and a maximum age of 85 years. In Group 2, the average age of patients was 50 ± 12 years, the median age was 51 ± 17 years, the minimum age was 18 years, and the maximum was 73 years.

The CCI distribution demonstrated notable differences between the studied patient groups. In both Group 1 and Group 2, the majority of patients fell into the low-risk category (CCI 0—2). However, Group 2 showed a significantly higher proportion of patients in the moderate-risk category (CCI 3—4), with 23 (22 %) patients compared to 15 (14 %) patients in Group 1, indicating that patients who underwent ICAA clipping generally had slightly more comorbidities. On the other hand, Group 1 had more high risk patients (n = 22 (19 %)) compared to Group 2 (n = 12 (12 %)), and a small percentage (n = 3 (3 %)) were very high risk, while no patients in Group 2 were classified as very high risk. This very likely influenced the treatment approach: patients with a higher CCI score and multiple comorbidities were often deemed less suitable for surgery due to the elevated risk of intraoperative and postoperative complications. Table 1 presents the baseline data and statistical comparisons between the studied groups.

The majority of patients with posterior circulation ICAA were in Group 1, representing 22 (21 %) patients, whereas Group 2 included only five patients (5 %). The detailed distribution of ICAA localization in the studied groups is shown in Fig. 1.

Multiple ICAA were more commonly observed in Group 1, with 23 patients (22%) compared to 12 (11 %) patients in Group 2. All patients with fusiform ICAA received conservative treatment. Although the mean size of ruptured ICAA in both groups was the same, at 8 mm, there was significantly greater size variation in Group 1. Hence, the variety of ICAA sizes required different treatment approaches. Fig. 2 shows

Table 1

Demographic and clinical characteristics

Parameter	Group 1	Group 2	χ^2/U statistic	p
Sex			$\chi^2 = 4.255$	0.039*
• Male, n (%)	43 (41)	58 (55)		
• Female, n (%)	63 (59)	48 (45)		
Age (mean ± SD)	56 ± 14	50 ± 12	U = 7059.000	0.001**
CCI:			U = 6875.500	0.003**
• Low risk (CCI 0-2)	68 (64)	70 (66)		
• Moderate risk (CCI 3-4)	15 (14)	23 (22)		
• High risk (CCI 5-7)	22 (19)	12 (22)		
• Very high risk (CCI ≥ 8)	3 (3)	0 (0)		
Type of hemorrhage:			$\chi^2 = 1.451$	0.694
• Isolated SAH, n (%)	43 (41)	50 (47)		
• SAH + ventricular, n (%)	30 (28)	23 (22)		
• SAH + parenchymal, n (%)	21 (20)	21 (20)		
• SAH + ventricular + parenchymal, n (%)	12 (11)	12 (11)		
ICAA localization:			$\chi^2 = 12.266$	0.001**
• Anterior circulation, n (%)	84 (79)	101 (95)		
• Posterior circulation, n (%)	22 (21)	5 (5)		
Number of ICAA:			U = 6232.000	0.033*
• Single ICAA, n (%)	83 (78)	94 (89)		
• Multiple ICAA, n (%)	23 (22)	12 (11)		
Size of ICAA (mm) (mean ± SD)	8 ± 6	8 ± 4	U = 6232.000	0.033*
Type of ICAA:			$\chi^2 = 10.462$	0.033*
• Saccular, n (%)	92 (87)	98 (92)		
• Fusiform, n (%)	5 (5)	0 (0)		
• Bilocular, n (%)	1 (1)	3 (3)		
• Multilocular, n (%)	0 (0)	2 (2)		
• Pseudoaneurysm, n (%)	8 (7)	3 (3)		
Modified WFNS Scale at admission:			U = 6546.000	0.027*
• Grade I, n (%)	45 (42)	55 (52)		
• Grade II, n (%)	11 (10)	19 (18)		
• Grade III, n (%)	23 (22)	19 (18)		
• Grade IV, n (%)	22 (21)	10 (9)		
• Grade V, n (%)	5 (5)	3 (3)		
Clinical presentation at admission				
Symptomatic epileptic seizure, n (%)	12 (11)	7 (7)	$\chi^2 = 1.445$	0.229
Meningeal syndrome, n (%)	87 (94)	86 (90)	$\chi^2 = 0.049$	0.825
Headache, n (%)	88 (83)	88 (83)	$\chi^2 = 0.024$	0.877
Ocular motor disturbances, n (%)	18 (17)	17 (16)	$\chi^2 = 0.061$	0.804
Hemiparesis, n (%)	18 (17)	18 (17)	$\chi^2 = 1.006$	0.605
Babinski reflex, n (%)	19 (18)	15 (14)	$\chi^2 = 0.517$	0.472

Note. *$p < 0.05$; **$p < 0.01$.

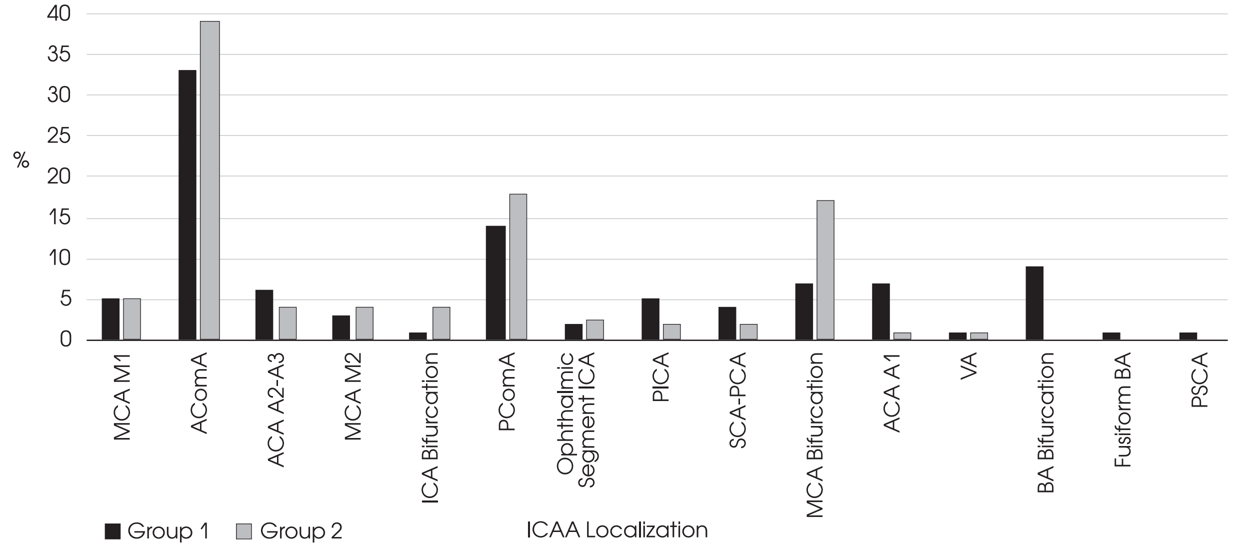

Fig. 1. *Distribution of ICAA localization in the studied groups*

MCA — middle cerebral artery; AComA — anterior communicating artery; ACA — anterior cerebral artery; ICA — internal carotid artery; PComA — posterior communicating artery; PICA — posterior inferior cerebellar artery; SCA — superior cerebellar artery — posterior cerebral artery junction; VA — vertebral artery; BA — basilar artery; AICA — anterior inferior cerebellar artery.

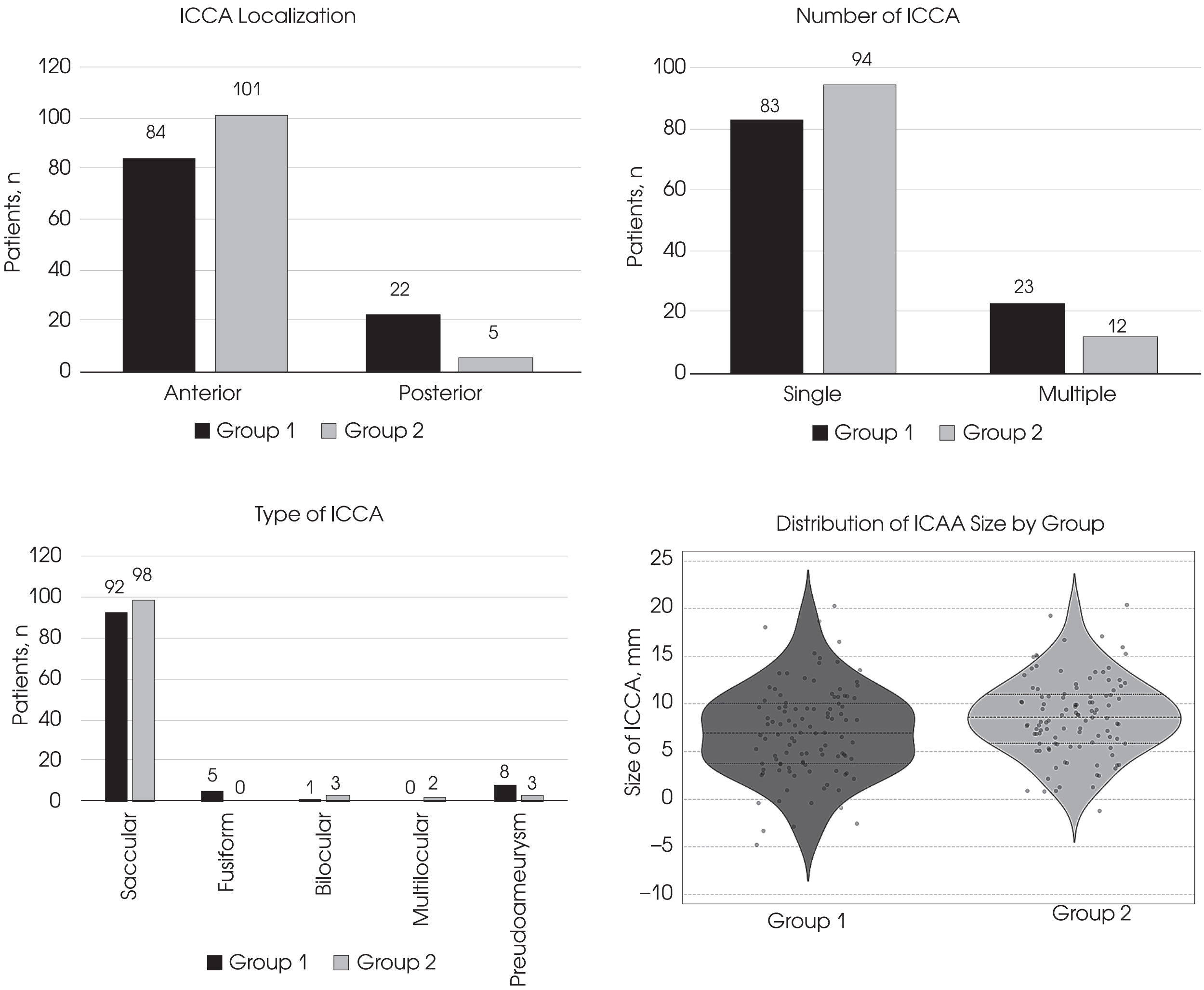

Fig. 2. *Comparison of groups by morphological parameters of ruptured intracranial arterial aneurysms*

ICAA — intracranial cerebral arterial aneurysm.

Table 2

Comparative analysis of early predictors in the studied groups

Variables	β (SE)	OR [95% CI]	P
Women—Men	0.571 (0.278)	1.770 [0.027; 1.116]	0.040*
Age	−0.036 (0.011)	0.965 [−0.057; −0.014]	0.001**
CCI	−0.223 (0.071)	0.800 [−0.363; −0.084]	0.002**
Type of hemorrhage			
SAH with ventricular component — Isolated SAH	−0.417 (0.347)	0.659 [−1.096; 0.263]	0.229
SAH with parenchymal component — Isolated SAH	−0.151 (0.372)	0.860 [−0.880; 0.579]	0.685
SAH with both components — Isolated SAH	−0.151 (0.458)	0.860 [−1.049; 0.747]	0.742
Posterior circulation — Anterior circulation	−1.666 (0.517)	0.189 [−2.679; −0.653]	0.001**
Number of ICAA	−0.724 (0.312)	0.485 [0.113; 1.335]	0.020*
Size of ICAA	0.003 (0.030)	1.003 [−0.056; 0.062]	0.915
Type of ICAA	−0.623 (0.466)	0.536 [−1.537; 0.291]	0.182
Modified WFNS Scale at admission	−0.266 (0.112)	0.767 [−0.485; −0.046]	0.018*
Symptomatic epileptic seizure	−0.591 (0.497)	0.554 [−1.565; 0.383]	0.234
Meningeal syndrome	0.098 (0.442)	1.103 [−0.769; 0.964]	0.825
Headache	0.057 (0.370)	1.059 [−0.669; 0.783]	0.877
Ocular motor disturbances	−0.092 (0.371)	0.912 [−0.819; 0.635]	0.804
Hemiparesis	0.065 (0.362)	1.068 [−0.644; 0.775]	0.856
Babinski reflex	−0.270 (0.377)	0.763 [−1.009; 0.468]	0.473

Note. *$p < 0.05$; **$p < 0.01$.*

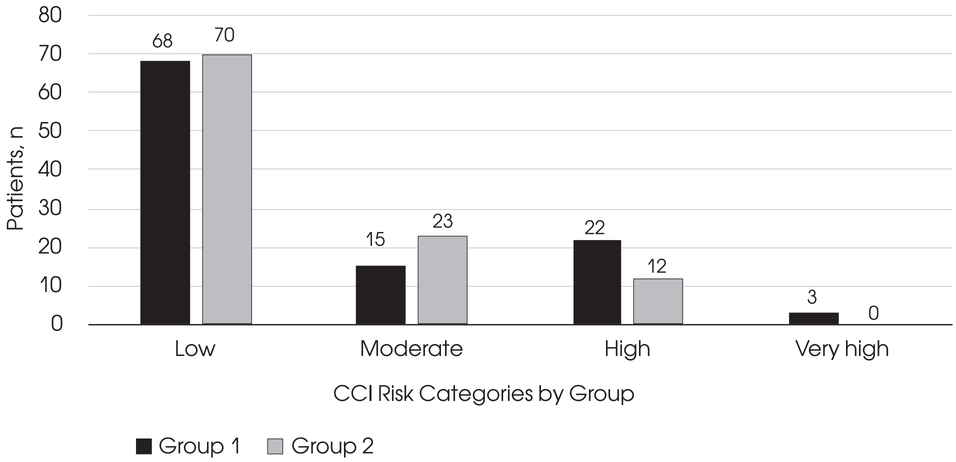

Fig. 3. *Distribution of CCI risk categories in the studied groups*

the comparison of groups by morphological parameters of ruptured ICAA.

Analysis showed the influence of demographic, clinical, radiological, and anatomical predictors on the choice between conservative treatment and ICAA clipping (Table 2).

The female gender and older age are statistically significant factors that influence the preference for conservative treatment. The probability of surgical intervention was almost two times lower in women (p = 0.040). Each additional year of life reduced the probability of surgical intervention by 3.5 % (p = 0.001). The CCI was a statistically significant factor in predicting the management strategy for patients with aneurysmal SAH (p = 0.002) (Fig. 3). Therefore an increase in CCI by 1 point, the probability of CAA clipping decreased by approximately 20 %.

The presence of complex forms of hemorrhages is related to a preference for conservative treatment. For ICAA characteristics, a significant relationship is observed in the localization of ICAA and their number. In our sample, patients with posterior circulation ICAA received conservative treatment approximately five times less often than ICAA clipping (p = 0.001). Furthermore, patients with multiple ICAA conservative treatment approximately two times less often than ICAA clipping (p = 0.020).

Patients with a high grade according to the m-WFNS scale are significantly less likely to receive surgical intervention (p = 0.018). In our study, we could not confirm whether clinical manifestations like symptomatic epileptic seizures, meningeal syndrome, headache, oculomotor disorders, hemiparesis, and Babinski reflex affected the treatment method.

The findings of this study may offer clinical value, particularly in healthcare settings with limited resources. Some results of our study are consistent with previous studies showing that advanced age reduces the likelihood of surgery [7, 14, 16]. To our knowledge, there has been limited research on how gender influences SAH treatment decision-making [4]. The preference for non-surgical treatment was twice as high among women. The presence of comorbidities is known to increase surgical risks and is associated with perioperative complications [7, 17]. However, this factor did not significantly influence decision-making regarding the extent of treatment. The critical factor that revealed a statistically significant difference between the groups was the clinical severity according to the m-WFNS scale. Patients with higher m-WFNS grades were more likely to receive conservative treatment, which is consistent with the results of other studies where the severity of the patient's condition is a major factor in determining treatment choices [5, 14, 15]. As demonstrated in previous studies, factors such as advanced age, comorbidities, and clinical severity are important determinants in treatment decision-making for patients with aneurysmal SAH, especially in areas where surgical interventions are not readily available [1, 5, 9—11]. In these settings, such as low-resource or rural healthcare systems, treatment protocols could be developed to assist clinicians in making informed decisions [1, 9—11].

Despite the substantial surgical complexity, ruptured posterior circulation ICAA is associated with a greater risk for poor prognosis and thus requires active surgical intervention [3, 18]. In addition, multiple ICAA significantly increase the likelihood of conservative treatment, which aligns with the previously published findings [18]. However, surgical obliteration of unruptured multiple ICAA from circulation is currently being used to prevent rebleeding in accordance with current guidelines [18]. Interestingly, none of the clinical symptoms alone influenced the decision to pursue conservative or surgical treatment. Thus, complex forms of hemorrhages did not significantly affect the early onset of focal neurological deficits or influence the selection of treatment approaches.

This study also revealed some inconsistencies. In particular, there were no significant differences in aneurysm type or size between the groups, which is contrary to other studies that suggest larger aneurysms are more likely to require surgery [2]. The extended time span of the study (200—2023) and relatively small annual patient numbers introduce a potential for bias. However, the patient sample was rigorously defined by inclusion and exclusion criteria, ensuring consistency in treatment practices throughout the study period. While the number of patients per year might appear low, this is reflective of the specific patient population selected based on these criteria, and the overall sample remains adequate for meaningful statistical analysis. A key strength of this retrospective study is its reliance on real-world data, which provides a comprehensive overview of clinical outcomes.

Conclusions

Our study underscores the importance of considering both clinical and socio-economic factors when making treatment decisions in healthcare systems with limited resources. Early predictors of conservative treatment for SAH in low-income countries include advanced age, high CCI score, anterior circulation ICAA, fusiform ICAA, multiple ICAA, and poor grade on the m-WFNS scale. These factors may help guide clinicians in resource-constrained settings, allowing for informed decisions when surgical options are limited.

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methodology, resources, writing — review & editing, supervision, project administration — Yu. S.

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К.О. ЯРОВА, Ю.О. СОЛОДОВНІКОВА

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Ранні предиктори консервативного лікування при аневризматичному субарахноїдальному крововиливі в країнах із низьким рівнем доходу

Мікрохірургічне й ендоваскулярне лікування аневризматичного субарахноїдального крововиливу (САК) є золотим стандартом для виключення розірваних церебральних артеріальних аневризм (ЦАА) і кровообігу та зниження ризику повторного розриву ЦАА. Консервативне лікування залишається варіантом в умовах обмежених ресурсів.

Мета роботи — визначити ранні предиктори консервативного лікування САК в умовах обмежених ресурсів.

Матеріали та методи. Проведено ретроспективне одноцентрове когортне дослідження 212 пацієнтів із САК, які отримували лікування в 2000—2023 рр. Пацієнтів розподілили на дві групи залежно від методу лікування (консервативне лікування (n = 106) та кліпування ЦАА упродовж 14 днів після їхнього розриву. (n = 106)). Проаналізовано демографічні дані, клінічні особливості, супутні захворювання та радіологічні/анатомічні характеристики розірваних ЦАА.

Результати та обговорення. Середній вік у групі консервативного лікування становив (56 ± 14) років (19—85 років), у групі кліпування ЦАА — (50 ± 12) років (18—73 роки). У першій групі зареєстровано вищу частоту ЦАА задньої циркуляції та множинних ЦАА. Хоча середній розмір розірваних ЦАА в обох групах був подібним (8 мм), у групі консервативного лікування була більша варіабельність розміру ЦАА. Установлено, що вік пацієнта, супутні захворювання, локалізація та морфологія ЦАА, кількість ЦАА і вихідний неврологічний стан є ключовими детермінантами, що впливають на вибір консервативного лікування замість хірургічного кліпування в умовах обмежених ресурсів.

Висновки. Ранніми предикторами консервативного лікування САК у країнах із низьким рівнем доходу є похилий вік, високий індекс коморбідності Чарлсон, ЦАА переднього кровообігу, веретеноподібні ЦАА, множинні ЦАА та низький ступінь за модифікованою шкалою World Federation of Neurosurgical Societies. Отримані результати можуть допомогти в прийнятті рішень щодо лікування в умовах з обмеженим доступом до хірургічних втручань.

Ключові слова: церебральна аневризма, субарахноїдальний крововилив, консервативне лікування.

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