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ARTICLE

Natural course of subarachnoid hemorrhage is worse in elderly patients

A história natural da hemorragia subaracnóide é pior em pacientes idosos

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ABSTRACT

Aging is a major risk factor for poor outcome in patients with ruptured or unruptured intracranial aneurysms (IA) submitted to treatment. It impairs several physiologic patterns related to cerebrovascular hemodynamics and homeostasis. **Objective:** Evaluate clinical, radiological patterns and prognostic factors of subarachnoid hemorrhage (SAH) patients according to age. **Method:** Three hundred and eighty nine patients with aneurismal SAH from a Brazilian tertiary institution (Hospital do Servidor Público Estadual de São Paulo) were consecutively evaluated from 2002 to 2012 according to Fisher and Hunt Hess classifications and Glasgow Outcome Scale. **Results:** There was statistically significant association of age with impaired clinical, radiological presentation and outcomes in cases of SAH. **Conclusion:** Natural course of SAH is worse in elderly patients and thus, proper recognition of the profile of such patients and their outcome is necessary to propose standard treatment.

Keywords: subarachnoid hemorrhage, aneurysm, age, outcome, treatment.

RESUMO

A idade é considerada fator de risco de mau prognóstico em pacientes com aneurismas intracranianos rotos ou não-rotos; com o aumento da idade, ficam prejudicados vários padrões fisiológicos relacionados à hemodinâmica cerebral e homeostase. **Objetivo:** Estudar o quadro clínico, os dados radiológicos e o prognóstico nos pacientes com hemorragia subaracnóide aneurismática em relação à idade. **Método:** Foram avaliados consecutivamente, de 2002 a 2012, 389 pacientes com hemorragia subaracnóide aneurismática oriundos de uma instituição terciária brasileira. **Resultados:** Houve associação da idade com pior quadro clínico, radiológico e prognóstico nos pacientes com hemorragia subaracnóide aneurismática. **Conclusão:** O curso natural da hemorragia subaracnoidea é pior em pacientes idosos. O reconhecimento adequado do perfil desses pacientes e seu prognóstico é importante para estabelecer um tratamento adequado.

Palavras-chave: hemorragia subaracnóide, aneurisma, idade, prognóstico, tratamento.

Aging is a major risk factor for poor outcome in patients with ruptured or unruptured intracranial aneurysms (IA) submitted to treatment[1,2,3,4,5].

In those patients, there is increased impairment of consciousness, thick subarachnoid clot, intraventricular hemorrhage, acute hydrocephalus and higher probability of rebleeding after subarachnoid hemorrhage (SAH)[4]. In the case of unruptured aneurysms, early and late complications are usually more severe in older patients, due to association with systemic morbidities and loss of adequate physiologic homeostasis[2,3].

We present our series and report nuances in the characterization and outcome of patients with IA.

METHOD

Three hundred and eighty nine patients who suffered subarachnoid hemorrhage from a Brazilian tertiary institution (Hospital do Servidor Público Estadual de São Paulo) were consecutively evaluated from 2002 to 2012. Our analysis is a retrospective discussion, based in medical records.

Although the concept of elder patient varies (most developed countries consider over 65 years old and World Health Organization warrants over 60 years old), we have chosen the cutoff of 70 years old, which is the most addressed threshold in pertinent guidelines as a landmark for therapeutic decision of IA[1,2].

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Inclusion criteria: all patients diagnosed with ruptured intracranial aneurysms submitted to treatment based in surgical approach and/or endovascular approach.

Exclusion criteria: unruptured intracranial aneurysms.

SAH patients were divided in two groups. Group 1 was composed of patients 70 years old or above and group 2 was composed of patients below 70 years. They were submitted to complete neurological examination during hospitalization. At admission they were classified according to Fisher and Hunt-Hess (HH) classification. Treatment modalities were classified as surgical or endovascular. At discharge, they were classified according to Glasgow Outcome Scale (GOS).

This study was approved by *Hospital do Servidor Público Estadual de São Paulo* Ethics Committee and informed consent was obtained from each patient.

Statistics

In this study, numerical data are presented as mean± standard deviation or median with range when appropriate. Categorical data are presented as percentages. To determine the distribution of our data, the Kolmogorov-Smirnov Test was used. Statistical analysis was performed by Student's *t*-test and Chi-Square test when appropriate. Multiple logistic regression analysis was used to evaluate outcome in GOS. When comparing groups, the level of significance is considered when $p<0.05$.

RESULTS

Characterization of patients

Three hundred and eighty nine patients have suffered SAH. Seventy two (18.5%) were 70 years old or above (group 1) and 317 (81.5%) were below 70 years old (group 2) (Table 1).

Fisher classification

Thirty one patients (43%) in group 1 presented with Fisher 1 or 2. 41 (57%) patients in the same group presented with Fisher 3 or 4. In group 2, 213 patients (67%) presented with Fisher 1 or 2 and 104 (33%) with Fisher 3 or 4. The distribution of the Fisher strata was different between groups (p=0.0002) (Figure 1).

Table 1. Features of 389 subarachnoid hemorrhage (SAH) patients (age, gender, Fisher classification, Hunt Hess classification and treatment modality).

Age (years)	<70 81.5%	= or >70 18.5%			
Gender	female	male			
	74%	26%			
Fisher	I	II	III	IV	
	32%	14%	22%	32%	
Hunt Hess	I	II	III	IV	V
	28%	38%	15%	5%	14%
Treatment	surgery	endovascular			
	90.7%	9.3%			

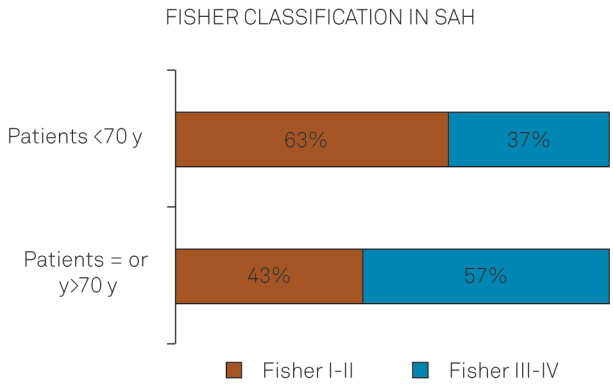

Figure 1. Fisher classification of subarachnoid hemorrhage (SAH) patients according to age.

Hunt Hess classification

Twenty nine patients (40%) in group 1 presented with Hunt Hess of 4 or 5, and 43 patients (60%) presented with HH of 1, 2 or 3. In group 2, 48 patients (15%) were HH 4 or 5 and 269 (85%) were HH 1, 2 or 3. The distribution of the Fisher strata was different between groups ($p<0.0001$) (Figure 2).

Treatment modality

The majority of patients in our sample (90.7%) was submitted to surgical treatment, while few cases underwent endovascular management (9.3%) (Table 1).

Outcome in SAH

In group 1, 58 out of 72 patients (80.5%) developed GOS of 1, 2 or 3 and 14 patients 4 or 5 (19.5%). In group 2, 124 (39%) developed GOS 1, 2 or 3 and 193 (61%) 4 or five ($p<0.0001$) (Figure 3).

One hundred and three patients (26.5%) were discharged in GOS 1, 2 and 3. Two hundred and eighty six (73.5%) were discharged in GOS 4 or 5. Forty patients (38.8%) discharged

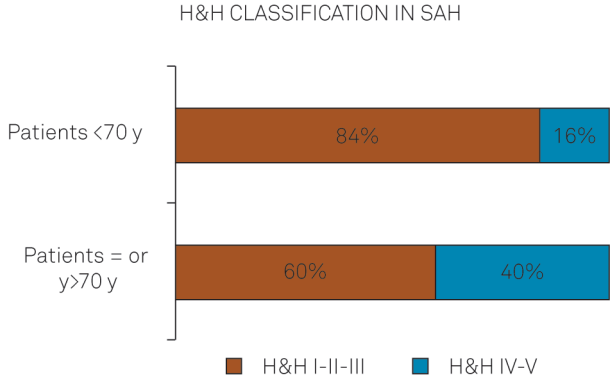

Figure 2. Hunt-Hess (HH) classification of subarachnoid hemorrhage (SAH) patients according to age.

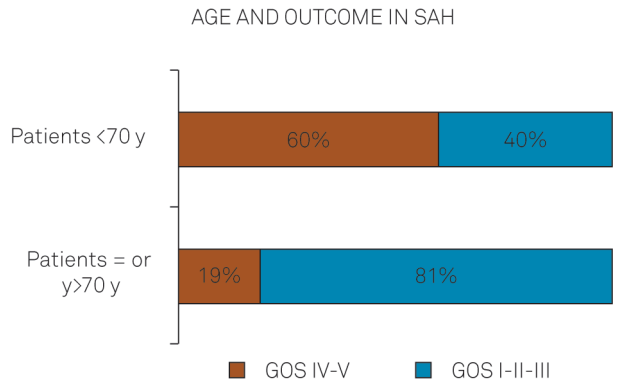

Figure 3. Age and glascow outcome scale (GOS) outcome in subarachnoid hemorrhage (SAH) patients.

with GOS 1, 2 and 3 presented initially with HH of 1, 2 or 3 and 63 patients (62.2%) with 4 or 5. Among patients discharged with GOS 4 or 5, 275 (96%) presented initially with HH 1, 2 or 3 and 11 patients (4%) with HH of 4 or 5 ($p<0.0001$).

In group 1, 50 patients (69.5%) were discharged in GOS 1, 2 or 3 and 22 (30.5%) in GOS 4 or 5. Among GOS 1, 2 or 3 group, 22 (44%) were HH 1, 2 or 3 and 28 (56%) were HH 4 or 5. Among GOS 4 or 5 group, 21 (95.5%) were HH 1, 2 or 3 and 1 (4.5%) was HH 4. The distribution of the Fisher strata was different between groups ($p<0.0001$).

In group 2, 51 patients (16%) were discharged in GOS 1, 2 or 3 and 264 (84%) in GOS 4 or 5. Among GOS 1, 2 or 3 group, 18 (35%) were HH 1, 2 or 3 and 35 (65%) were HH 4 or 5. Among GOS 4 or 5 group, 254 (96%) were HH 1, 2 or 3 and 10 (4%) was HH 4 ($p<0.0001$).

Patients submitted to surgical treatment presented with better GOS ($p<0.05$). Two hundred and fifty four patients submitted to surgery (72%) were discharged in GOS 4 or 5. 28% were discharged in GOS 1, 2 or 3. In endovascular group, 81% (29 patients) were discharged in GOS 1, 2 or 3 and 19% in GOS 4 or 5.

Female patients were 74% of the sample. There was no difference in GOS according to gender. When evaluating all variates together in multiple regression analysis, age, Fisher, Hunt Hess and treatment modality were associated with worse outcome. Age and Hunt Hess revealed the strongest association with worse GOS (Table 2).

Table 2. Statistical analysis in multiple logistic regression.

Variate	Odds ratio	Confidence interval (95%CI)	p-value
Age (years)	7.5	5.3-10.6	$p<0.0001$
Gender	1.2	0.7-1.4	$p>0.05$
Fisher	2.4	1.9-2.8	$p<0.01$
Hunt Hess	5.1	3.6-7.3	$p<0.001$
Treatment modality	1.6	1.2-1.9	$p<0.05$

DISCUSSION

Our sample illustrates the strong association between age and poor outcomes when treating ruptured intracranial aneurysms. In summary, there was statistically significant association of age with impaired clinical and radiological presentation in cases of SAH and outcomes were worse in SAH patients. When age was analysed together with initial HH as an outcome predictor, age presented stronger impact with statistical significance.

Although most of our patients were female, there was no association of gender with clinical, radiological and/or outcome. Other factors like clinical comorbidities, may indeed interfere with presentation and outcomes.

The incidence of intracranial aneurysms rises with age, and the same behavior is true regarding SAH[1,2,3,4,5]. As a general rule, unruptured aneurysms have a 1% per year probability of bleeding. Thus, unruptured aneurysms greater than 10 mm should be treated at any age, due to risk of rupture. Aneurysms between 5-10 mm should be considered in a particular basis, once age and clinical morbidities may interfere with treatment[2,3]. Below 5 mm, a more conservative approach is usually advocated. When SAH is present, these rationales are abandoned and prompt treatment must be achieved independently of aneurysm size[1].

Several factors impact evaluation, treatment strategies and outcomes in intracranial aneurysmal disease. Aging probably is one of the most significant independent factors. It impairs several physiologic patterns related to cerebrovascular hemodynamics and homeostasis[6,7,8,9,10,11,12].

There is a decline in cerebral blood flow velocity with age, which may be associated with certain changes as: decreased cerebral blood flow (CBF) or metabolic demands; vessel changes like progressive kinking, calcifications (Figure 4), elongation, stenosis and lower cardiac output[1,2,3,11,13,14,15]. It is also associated with a 20% to 30% decrease in CBF in healthy individuals between the ages of 20 and 80 years

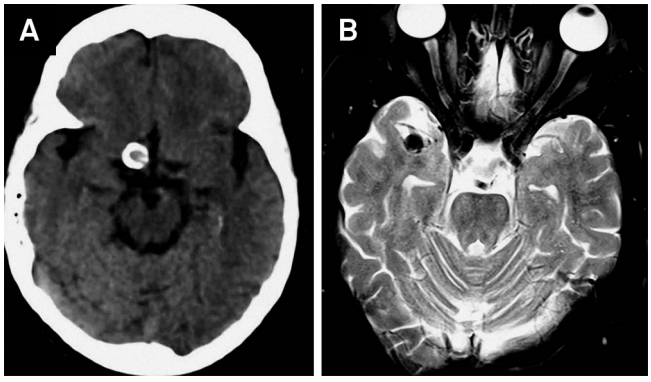

Figure 4. Two examples of calcified aneurysms in elderly patients.

and with dilatation of major extracranial arteries and reduction of flow within parenchymal vessels[1,13,14,15].

All those statements justify that elderly usually present with more severe SAH than younger patients, characterized by higher Fisher and Hunt Hess grades. After treatment, elderly are also prone to face severe neurological and systemic complications, like vasospasm, hydrocephalus, brain and heart ischemic insults and others[6,7,8,9,10].

Cerebral vasospasm (VSP) is the major complication associated with aneurysmal SAH that results in delayed ischemic deficits in up to 25% of all cases. Although it is associated with hypercholesterolemia, chronic hypertension and atherosclerosis, there is lower incidence of VSP in older patients, probably secondary to the age-related impairment of contractility and elasticity of the muscle wall of small arteries and arterioles. However, the severity of VSP in such patients is pronounced as the margin between adequate CBF and the ischemic threshold may become especially narrow[13,14,15].

Several limitations should be pointed out. Our report was a simplified analysis of outcome related to the age of patients and restricted to general classification according to Fisher and Hunt Hess scores and GOS. The association between age and adverse outcome is almost a constant in any disease. This is why most investigations adjust for age, but do not primarily investigate its effects. This fact may bias but not invalidate our analysis.

Then, discharge outcomes are biased because the follow-up times are highly variable between patients and post-discharge outcomes were not assessed. Additionally, the age of 70 years old was chosen because it is a landmark in the most important trials in literature, above what management strategies are substantially changed towards endovascular approaches.

We did not disclose important details like associated clinical morbidities, Glasgow Coma Scale, aneurysm topography, size, shape and presence of aneurysmal calcifications. We also did not discuss presence of hydrocephalus and vasospasm in our sample.

Our endovascular sample was biased, once patients submitted to endovascular treatment were already in worse clinical conditions, changing outcomes. Randomization of surgical and endovascular groups would potentially disclose different results. All those factors may surely bias our findings and interfere with inferences from the study, but not invalidate it.

Therefore, solid experimental and clinical evidence already points to similar findings and corroborate the need of evaluating aneurysmal disease in elderly with caution. A special issue that must be addressed is the increasing application of endovascular treatment in elderly, due to lower perioperative risk, similar treatment results and potential better outcomes[1,2].

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