



Identification of clinical and paraclinical findings predictive for headache occurrence during spontaneous subarachnoid hemorrhage



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ABSTRACT

Objectives: Headache is recognized as the main but unwarranted symptom of subarachnoid hemorrhage (SAH). There are no enough findings identified as predictive for headache occurrence in SAH. We evaluated the clinical and paraclinical factors predictive for headache occurrence in SAH.

Patients and methods: We retrospectively analyzed medical records of 431 consecutive non traumatic SAH patients (264 females and 167 males), ages from 19 to 91 years, presenting with headache (70.3%) and without headache (29.7%) during period of 11 years.

Results: Among all tested parameters, as negative predictors for headache occurrence were recognized: patients' ages (OR 0.97 [95%CI: 0.96–0.99], $p = 0.025$), persistence of coagulation abnormality (OR 0.23 [95% CI: 0.08–0.67], $p = 0.006$), atrial fibrillation (OR 0.23 [95% CI: 0.09–0.59], $p = 0.002$), chronic renal failure (OR 0.26 [95% CI: 0.09–0.76], $p = 0.014$) and more diseases (OR 0.11 [95% CI: 0.04–0.32], $p < 0.0001$), as higher clinical score (OR 0.94 [95% CI: 0.90–0.99], $p = 0.018$) including positive neurological findings (OR 0.34 [95% CI: 0.21–0.55], $p < 0.001$) and loss of consciousness (OR 0.22 [95% CI: 0.12–0.39], $p < 0.001$) at the SAH onset, while the complaint of neck stiffness was identified as its positive predictor (OR 1.93 [95%CI: 1.19–3.10], $p = 0.007$).

Conclusions: Although diagnosis based solely on clinical presentation is not reliable and speculative, our findings could provide physicians with evidence to consider SAH not only in conditions of its headache occurrence but also in those with headache absence.

1. Introduction

Non traumatic (spontaneous) subarachnoid hemorrhage (SAH) represents about 5% of cerebrovascular pathology and it is associated with the significant rate of complications such as rebleeding (within first four weeks), with significant mortality (up to half of patients die within three weeks) and long term disability (a third of survivors remain dependent) [1–3]. Unfortunately, the initially presenting symptoms of SAH are manifold and can be subtle and overlap with commonly frequent conditions, such as coexisting patients' diseases or its complications. The earliest, accurate diagnosis and therapy are important for the clinical outcome improvement.

Although suddenly occurred and severe headache is considered as the main clinical feature suggestive to SAH in general, it is well known that headache is not presented in a third to quarter of SAH patients [4,5]. The headache appears as only symptom in about a third of

patients with SAH, but among all patients presenting to general practice with sudden, severe headache alone, only one in ten cases turns out to be SAH. The rest patients have benign thunderclap headache and other primary and secondary headache syndromes [6,7]. It suggests that the lack of other signs and symptoms cannot be used to rule out the SAH in cases when headache having features suggestive for SAH appears as sole symptom. Adversely, other patients' diseases as well as symptoms and signs of SAH is being developed, may be recognized as a more common cause of the headache, wherefore, headache might be mistakenly referred as a secondary to these causes so far neglecting the existence of SAH. That is why all clinical and paraclinical attributes must be carefully taken in the clinical differentiating SAH presented with headache against SAH without headache in the clinical presentation. In that sense, some clinical decision rules that include clinical findings have been proposed to help identify SAH patients among all patients having headache suggestive to SAH, have been defined [8,9].

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Again, there are no identified predictive findings for the headache occurrence in SAH, in relations to patients' characteristics and other SAH symptoms and signs, among all SAH patients (including those clinically presented without headache).

The authors are in belief that detecting of those predictive factors for headache occurrence could provide and help identify SAH patients and could improve care of SAH patients by directing testing for those at high risk who might otherwise not be adequately investigated.

Hence, we retrospectively assessed clinical and paraclinical characteristics of patients having non traumatic SAH in order to determine which of tested attributes might be predictive for headache occurrence during SAH pathogenesis.

2. Patients and methods

2.1. Study design and data collection

The study was performed as a retrospective clinical study that was carried out in strictly accordance with the principles of the Declaration of Helsinki as revised in 2000, ensuring full patients' anonymity.

We retrospectively screened the medical records of all consecutive patients treated to the Clinic for Neurology, Clinical Centre of Nis, having as the main final diagnosis – non traumatic SAH, between January 2005 and December 2015. Our Clinical Center serves as unique tertiary care teaching hospitals in south-east part of Serbia for population of about 2 million people. Thus, practically all patients above 18 years of age diagnosed as non traumatic SAH were enrolled in the study.

Completed data were organized as unique document based on presence or absence of each of tested study attributes and other relevant findings accompanied to the non traumatic SAH. Patients with non traumatic SAH having inefficient or inconclusive data were deemed to be a missed eligible patient. These data are not shown and were not included in the statistics.

2.2. Study patients

Four hundred thirty one patients, entered into this study, were referred to the Clinic for Neurology Clinical Centre of Nis because of acute developed signs and symptoms such as headache, positive neurological findings, loss of consciousness, neck pain, complaint of neck stiffness, etc. Patients were mostly referred directly by general practitioners, by doctors from the other secondary hospitals which are directed to the CC Nis but quite frequently patients were brought directly from their home to the Clinical Centre of Nis by their relatives or by ambulance.

All study patients met the following criteria – age above 18 years, there is no head trauma, admitted at the hospital within 24 h after main symptoms onset, which was defined as the point at which the patient or his/her family reported that he/she was no longer in a normal/health condition, having as main final diagnosis on hospital discharge – non traumatic SAH. Patients were excluded from the study if they had traumatic etiology of SAH, or had non traumatic SAH with positive findings on brain scans other than SAH, such as cerebral infarction, subdural/extradural/intracerebral hemorrhage, carotid or vertebral-basilar dissection, intracranial venous thrombosis, vasculitis, hydrocephalus, idiopathic intracranial hypertension, intracranial tumors, pituitary apoplexy, infection, etc.

2.3. Clinical evaluation

All the patients underwent routine blood tests (including screening of coagulation), electrocardiography, ultrasound tomography of carotid and vertebral arteries and repeated neurological examinations. The patients' comorbidities were verified during the actual hospitalization by a specialist of internal medicine. Some of them had used therapy

such as antiplatelets, anticoagulants, statins or antihypertensive drugs during the pre-hospital period.

The clinical/neurological presentation was assessed in all study patients on their admission using the Glasgow Coma Scale (GCS), the National Institutes of Health Stroke Scale (NIHSS), the Hunt-Hess scale (HHS), while the functional outcome after SAH has been assessed using modified Rankin Scale (mRS) on the hospital discharge.

In all SAH patients presented with headache, data such as prior headache history, time from onset to peak of pain intensity, accompanying symptoms, pain localization and quality, state at time of headache onset, duration of headache and accompanied clinical presentation of SAH were assessed. The pain intensity was scored using Visual Analogue Scale (VAS).

2.4. Radiological evaluation

Immediately after arrival at the hospital all study patients underwent multi slice computed tomography (MSCT) of brain (Aquilion 64 Toshiba). The obtained scans were reviewed by a neuroradiologist, blinded to the clinical findings and the other patients' features. The presence, laterality, and territory of SAH were noted. Cerebral angiography was not part of the routine investigations, but applied when it was accessible or considered as necessary. The results of cerebral angiography were described in relation of the presence or absence of arteriovenous malformations.

2.5. Lumbar puncture/biochemical evaluation

If the MSCT of brain was normal or inconclusive, a lumbar puncture was done in a close temporal relation between cerebrospinal fluid (CSF) sampling and signs and symptoms onset. The CSF was analyzed for the presence of red blood cells or xanthochromia, parallel with the other routinely performed biochemical analysis.

2.6. Diagnosis of non traumatic SAH

The diagnosis of SAH was established on the basis of the presence of subarachnoid blood on unenhanced MSCT of the brain or xanthochromia or red blood cells ($> 5 \times 10^6/l$) in the final sample of CSF, with or without an aneurysm or arteriovenous malformation evident if cerebral angiography was performed. Non-traumatic etiology was defined as the absence of direct or indirect trauma to the head in days ago previous to each sign or symptom onset. SAH was treated by the neurosurgery if it has been indicated or aggressively managed by using calcium antagonist, and triple-H therapy (hypertension, hypervolemia, hemodilution) when it was appropriate.

2.7. Statistics

All obtained data were recruited and evaluated in reference to demographics, actual and previous medical history and findings from clinical and neurological examinations as well as findings from performed diagnostic procedures, additional discharge diagnosis, etc. All data are presented as medians with range throughout the text, or, when it was appropriate, as means \pm SD.

Binary logistic regression was performed in order to measure the influence of multiple factors on the possibility of headache onset in patients with SAH. The model contains more independent variables (ages, gender, data from medical history and clinical examinations etc). It was shown that the model as a whole was statistically significant χ^2 (df = 10, N = 430) = 89.871, $p < 0.001$, and that it successfully discriminates SAH patients with and without headache. The Hosmer–Lemeshow test results ($\chi^2 = 4.212$, df = 8, $P = 0.838$) showed that the goodness of fit was satisfactory. Model explains between 18.9% (r^2 , Cox & Snell) and 26.8% (r^2 , Nagelkerke) of the variance in headache onset and successfully classifies 74% of cases.

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