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CLINICAL AND NEUROIMAGING STUDIES IN PATIENTS WITH ACUTE SPONTANEOUS INTRACEREBRAL HEMORRHAGE.

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ABSTRACT

Objective: To define the prognostic value of clinical and neuroimaging parameters on the 30-th day mortality and clinical outcome after spontaneous intracerebral hemorrhage (sICH).

Materials and methods: we examined 88 patients with sICH admitted to Neurology Clinic, UMHAT Pleven within 48 hours after clinical symptoms onset. Glasgow Coma Scale (GCS) score was used to assess the primary stroke severity; neurological deficit on admission was assessed by National Institute of Health Stroke Scale (NIHSS); clinical outcome at discharge was evaluated by modified Rankin Scale (mRS) and by Glasgow Outcome Scale (GOS) on the 30-th day after sICH onset. Hematoma volume was measured by the formula of Kothari: AxBxC/2 in ml. The statistical analysis was performed by SPSS 19.0 and Statgraphics plus 4.1 for Windows.

Results: Initial assessment of primary stroke severity and neurological deficit by GCS è NIHSS, hematoma localization and volume were found strongly correlated with the clinical outcome on the 30-th day after the sICH onset. Age and vascular risk factors did not correlate with the clinical outcome. Male patients had better survival on the 30-th day compared with the female ones.

Discussion: Neurological deficit on admission, hematoma localization and volume were found reliable predictors of the 30-th day clinical outcome that could serve for early stratification of patients and optimal choice of therapeutic approach.

Key words: CT, neurological deficit, sICH, clinical outcome.

INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) is a type of stroke usually caused by a vessel rupture followed by spontaneous leakage of blood in the brain parenchyma [4]. sICH accounts for only 15-20% of all strokes but is associated with the highest mortality and disability rate [11, 22]. Despite the achievements of advanced neuroimaging methods and new therapeutic opportunities of neurovascular intensive care the parameters of sICH morbidity and mortality remain unchanged [2, 8]. Almost 40% of the patients die before the 30-th day after sICH, 66% of the survivors are severely disabled and only 20% recover their functional independence on the 6-th month after the sICH [22].

According to the guidelines of *ÀÍÀ* [American Heart Association] modern treatment of sICH is mainly supportive and is still one of the greatest challenges in the neurologicall practice [17]. The health and social policy of some countries, providing easy access to highly qualified medical professionals, effective primary prophylaxis and control of vascular risk factors, urgent admission to stroke units with modern intensive care equipment, results in stable reduction of sICH incidence during the last years [25, 26].

Unlike ischemic stroke sICH is less investigated in Bulgaria. There is a substantial lack of population-based studies on the problems of sICH in our country. No prospective studies, based on the hematoma volume measurement and correlative clinical and neuroimaging analyses of neurological deficit and clinical outcome are also conducted [3]. An urgent necessity for performing scientific investigations on sICH arises that could facilitate identification of patients with the highest mortality and disability risk and offer new therapeutic approaches.

The aim of the present study was to define the predictive value of some clinical and radiological parameters for the clinical outcome on the 30-th day after sICH.

MATERIAL AND METHODS

Patients

Of the 337 patients with sICH, admitted to the Neurology Clinic, UMHAT "Dr. G. Stranski", Pleven from March 2005 to July 2010, only 88 (38 males, 50 females, median age 63.8±11.7 years) were selected on the grounds of strict exclusion and inclusion criteria. From the study were excluded patients with hemorrhage due to brain tumor, trauma, hemorrhagic transformation of ischemic infarction, rupture of an aneurysm or AVM. No individuals with intraventricular spread of blood or subarachnoidal hemorrhage,

acute or chronic infections, cancer, kidney and liver diseases or past surgical procedures were included. Patients with sICH admitted to the clinic after the first 48 hours of clinical symptoms onset were also excluded from the study. All experiments were conducted in accordance with the rules and regulations approved by the University Research Ethics Committee. Inform consent was obtained by all the patients or their authorized relatives.

Neurological assessment

A detailed questionnaire assessing the medical history and physical state of the patients was filled out by a neurologist. Data regarding demographic and risk factors, concomitant diseases and treatment, were collected prospectively. Initial stroke severity was assessed by GCS [27], neurological deficit on admission by NIHSS [6]. Functional outcome at discharge was evaluated by mRS [29] and by the means of GÎS [13] on the 30-th day after the sICH onset. Clinical outcome was defined as a good one for patients with mRSd"2 è GOS=from 4 to 5 points and as unfavorable one for those with mRSe"3 and GOS=from 2 to 3 points.

Neuroimaging measurement

Computer tomography scan of the brain was performed on admission with *General Electrics Âright Speed 4 - Helical MDCT* (Multi Detector Computed Tomography). Hematoma type, localization and volume were analysed. According to its localization hematomas were classified as supratentorial (lobar and basal) and subtentorial. Hemorrhage volume was measured by a simplified formula for the volume of an ellipsoid, (AxBxC)/2; where A is the maximum diameter of the hemorrhage on the CT slice with the largest area of hemorrhage, B is the maximum diameter 90° to A on the same slice, and C is the number of axial slices multiplied by the slice thickness [15] (Fig.1). According to hemorrhage volume hematomas were classified into: < 30 cm^3, from 30 to 60 cm^3 and > 60 cm^3 [7]. Presence of brain edema, ventricular compression and midline shift were also assessed.

Statistical analysis

Statistical analysis was performed with Statistical package of Social Sciences SPSS 19.0 and Statgraphics plus 4.1 for Windows. The normality of data was checked with the Shapiro–Wilk test. The significance of differences between groups was assessed by Student's t-test and one-way ANOVA analysis of variance for normally distributed data, and by the Mann–Whitney U-test and Kruskal–Wallis test for non-parametric data. Correlative analysis of Spearman or Pearson and regression analysis were used to examine the correlative ratios between the clinical and neuroimaging parameters according to the type of distribution. Logistic regression was used to assess the prognostic value of statistically significant factors on the dependant variable „outcome on the 30-th day". A value of $p < 0.05$ was considered statistically significant.

RESULTS

The basic characteristics and potential factors associated with clinical outcome on the 30-th day after the onset of sICH are given in **Table1.** Of all the 88 patients included in the study, median age 63.3±14.1 years, 38 (43.2%) were male. According to the medium GOS score - 2.9±1.4 points and mRS score - 5.1±1.5 the clinical outcome on the 30-th day after sICH was defined as comparatively unfavorable. Of 26 (29.5%) patients with lethal outcome only 7 (26.9%) were male. Arterial hypertension was found in 81 (92.0%) patients with sICH, diabetes mellitus had only 7 (8.0%) patients and 23 (26.1%) had Ischemic Heart Disease (IHD). History of alcohol abuse had 57 (64.8%) patients and smokers were 22 (25%) patients with sICH. Age, arterial hypertension, systolic blood pressure (SBP), IHD, diabetes mellitus, alcohol abuse and cigarette smoking were not statistically significant factors for the clinical outcome on the 30-th day after sICH.

Male patients showed better clinical outcome compared to female patients (r=0.21, ð=0.04). Higher diastolic blood pressure (DBP) (p=0.04) was registered in patients with poor outcome, compared with the survivors.

Initial assessment of neurological deficit by GCS and NIHSS was found significantly correlated with lethal outcome (ð=0.001). Patients with lethal outcome had less GCS score – 7.2±3.0 compared with the survivors - 11.0±1.8 points, indicating more severe clinical state and neurological deficit of the patients with lethal outcome (r=-0.26, p=0.001). Significantly higher score of NIHSS, associated with severe neurological deficit had patients with lethal outcome – 26.0±5.6 points versus those that survived – 19.0±5.8 points (r=0.31, p=0.001). The severity of neurological deficit, assessed by both scales, appeared to be a reliable predictor of the clinical outcome on the 30-th day after sICH. A statistical significance between hematoma volume and the severity of the neurological deficit assessed by GCS (Fig.2) è NIHSS (Fig.3) was also found: the increase of hematoma volume was associated with a lesser score of GCS and greater score of NIHSS, at 95% and 99% confidential interval.

Multiple logistic regression analysis demonstrated a possibility of predicting hematoma volume by initial assessment of neurologic deficit with GCS and NIHSS after the equation: **Hematoma volume** = 44.4422 + 1.20492*NIHSS - 2.91586*GCS, (ð=0.001).

Of the 78 (88.6%) patients with supratentorial localization of hematoma, 12 (13.6%) had volume > 60 ml; 30 (34.1%) < 30 ml and almost every second patient (52.3%) had hematoma volume from 30 to 60 ml. Of all the 26 patients with lethal outcome (29.5%), 23 (88%) had basal or thalamic hematoma and only 1 patient (4.0%) with lobar hematoma died. Patients with the so called large mixed hematoma had the highest mortality rate: 6 times greater was the proportion of patients with lethal outcome (54%), compared to the survivors (8%) (Fig.4).

Lethal outcome was found strongly correlated with some of the radiological variables as hematoma localization (r=0.47, p=0.001) and volume (r=0.55, p=0.001). Patients with lethal outcome had twice greater hematoma volume (1.0±28.0 ml) in comparison with the patients who survived the 30-th day after sICH (32.7±15.5ml).

According to the logistic regression analysis

hematoma volume was independent predictor of the clinical outcome on the 30-th day after sICH (OR=1.156, ð=0.005): the increase of hematoma volume with 1 ml increased the possibility of lethal outcome with 15.6%. The model had good discrimination ability (ROC area=0.972; SE=0.023) with optimal sensitivity 90% and specificity - 90%.

Of the 62 (70.5%) survivors, 35.3% were severy disabled, 25% moderately disabled and only 10.2% achieved functional independence on the 30-th day of sICH. The leading cause for lethal outcome were concomitant cerebral and somatic complications in 20.5%, followed by cerebral complications in 8% and only 1% somatic complications. Treatment at the clinic lasted 11±3 days according to the sICH therapeutic algorithm, approved by the health authorities in our country (minimum 7 days hospital treatment).

DISCUSSION

Despite the increasing stroke incidence as a result of world population ageing, sICH still remains an unresolved medical problem in modern neurology. The choice of therapeutic approach is difficult and is mainly dominated by the initial subjective decision of the consulting neurologist. Treatment is mostly symptomatic, and the clinical outcome in post-stroke patients is usually poor with severe disability. There is an urgent necessity for new experimental and clinical investigations to further clarify the early objective indicators for the clinical course and outcome of sICH aiming to optimize the diagnostic and therapeutic results [5, 9, 20].

Age is an important parameter associated with increased risk for brain hemorrhage morbidity and mortality [12, 19], but according to our results age did not prove to be a significant factor for the outcome. The hypothesis that increased arterial hypertension and SBP, in particular, predicts hematoma expansion associated with severe neurologic deficit and higher mortality [1, 10, 28], was not confirmed by our results. The statistically significant correlation between DBP and poor outcome found in our study needs further clarification with prospective studies on more sICH patients. The result that male patients had better outcome than female ones also needs further study confirmation.

Some clinical parameters indicating the severity of bleeding, early mortality and poor outcome were identified on the base of longitudinal study results [11, 14]. We established significant correlations between the neurological deficit, evaluated on admission and hematoma volume. Such data confirm the clinical significance of GCS and NIHSS in predicting clinical outcome on the 30-th day after sICH [11, 14]. Careful analysis of the study results allows promoting GCS and NIHSS feasibility for initial neurological assessment in sICH patients because of their high level of objectivity and easy performance.

Radiological variables are often used for constructing predictive models as reliable indicators of stroke severity and poor outcome [18, 21, 23, 24]. Some authors [7, 16] define hematoma volume as the key prognostic factor of sICH outcome. In the present study hematoma volume was correlated with the neurological deficit assessed by GCS and NIHSS. The complex analysis of the study results reveals that hematoma volume and localization influence significantly clinical outcome on the 30-th day after sICH. Deep basal and thalamic hemorrhages were found associated with poor outcome. The greater was the hematoma volume more severe was the neurological deficit of the patients. Thus hematoma volume was identified as independent predictor of lethal outcome on the 30-th day after sICH.

In conclusion, our study results, despite some limitations, confirm the prognostic value of clinical and neuroimaging parameters for the 30-th day clinical outcome after. Complex neurological assessment by the means of GCS and NIHSS, hematoma volume and localization provide unique opportunities to neurologists for early and exact prediction of sICH clinical course and outcome, especially important in three directions: for early stratification of patients who could improve under intensive care, from those with suggested poor outcome; in choosing the best individual therapeutic approach-surgical or conservative and for better communication with patients and their relatives.

Fig. 1. Calculating hematoma volume after the method of R. Kothari et al. - AxBxC/ 2 in ml (cm^3), where: 1 = A - the maximum diameter of the hemorrhagic lesion; 2 = B - the maximum diameter perpendicular to A; L = C - number of slices of 10 mm.

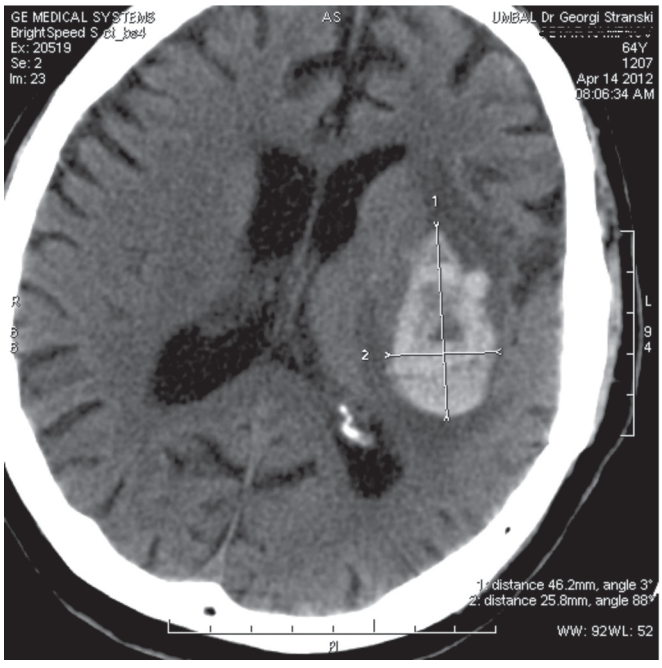

Table 1. Baseline clinical and neuroimaging characteristics associated with clinical outcome on the 30-th day after sICH.

Parameter	Patients with sICH n=88	Survivors n=62	Patients with lethalal outcome n=26	P
Age [years]	63.8 ± 11.7	64.0 ± 10.7	63.3±14.1	ns
Male sex, n (%)	38 (43.2)	31(50.0)	7 (26.9)	0.04*
Vascular risk factors				
Arterial hypertension, n (%)	81 (92.0)	57 (91.9)	24 (92.3)	ns
SBP [mm Hg]	182±31	179±32	188±28	ns
DBP [mm Hg]	102±15	99±15	107±13	0.04*
Ischemic Heart Disease, n (%)	23 (26.1)	14 (22.6)	9 (34.6)	ns
Diabetes mellitus, n (%)	7 (8.0)	5 (8.1)	2 (7.7)	ns
Alcohol abuse, n (%)	57 (64.8)	42 (67.7)	15 (57.7)	ns
Cigarette smoking, n (%)	22 (25.0)	15 (24.2)	7 (26.9)	ns
Neurological examination				
GCS on admission [points]	10.0±2.9	11.0.±1.8	7.2±3.0	0.001**
NIHSS on admission [points]	21.3±6.7	19.0±5.8	26.0±5.6	0.001**
GOS on the 30-th day [points]	2.9±1.4	3.6±0.7	1.0±0	0.001**
mRS at discharge [points]	5.1±1.5	4.3±1.0	7.0±0	0.001**
Radiological variables				
Localization, n (%)				0.001**
Medial to the capsule	26 (29.5)	20 (32.3)	6 (23.1)	
Lateral to the capsule	23 (26.1)	20 (32.3)	3 (11.5)	
Mixed hematoma	19 (21.6)	5 (8.1)	14 (53.8)	
Lobar hematoma	10 (11.4)	9 (14.5)	1 (3.8)	
Brain stem hematoma	6 (6.8)	4 (6.4)	2 (7.8)	
Cerebellar hematoma	4 (4.6)	4 (6.4)	0 (0)	
Hematoma volume [ml]	41.0±23.8 37.5 (22.5-51.5)	32.7 ±15.5 30 (20-42)	61.0±28.0 52 (42.0-72.0)	0.001**

Data are presented as median value ±SD or mediana (25 - 75 percentile)

**p<0.05, **p<0.01– statistically significant difference between the patients that survived and those with lethal outcome on the 30-th day of sICH.*

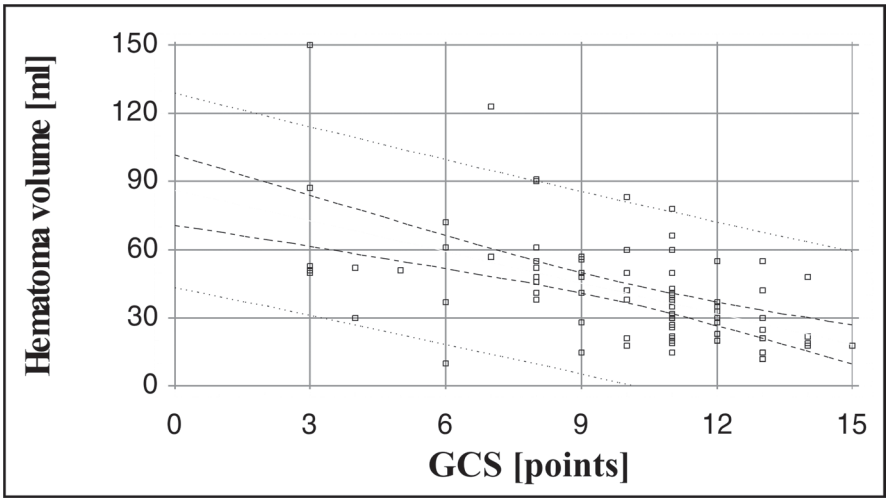

Fig. 2. Correlation between the neurological deficit assessed with GCS and hematoma volume (hematoma volume = 86.2022-4.52824* GCS; p=0.001)

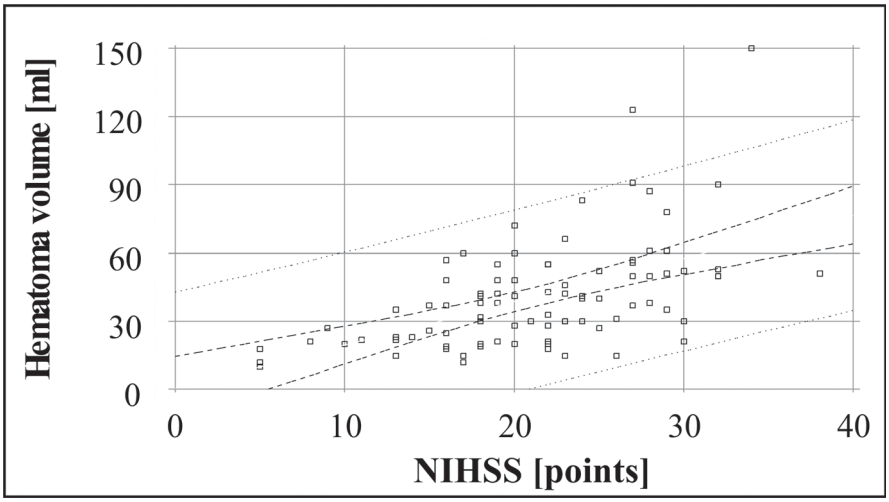

Fig. 3. Correlation between the neurological deficit by NIHSS and hematoma volume (hematoma volum (0.0658829-0.00156512* NIHSS; p=0.001)

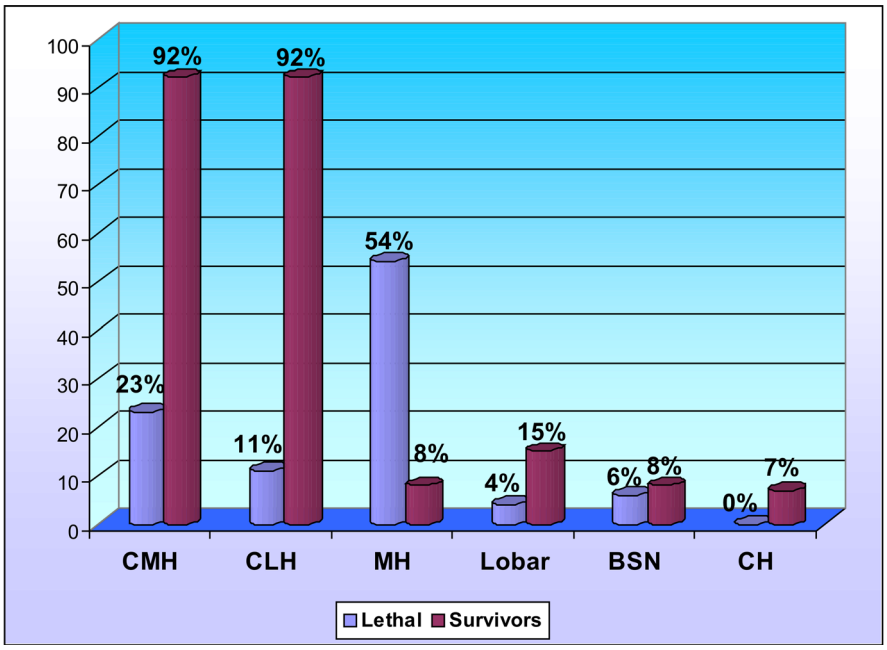

Fig. 4. Distribution of patients by hematoma localization and clinical outcome.

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