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Analysis of the diagnostic informativity of non-contrast computed tomography markers of intracerebral hemorrhage expansion in assessment of the individual risk of early neurological deterioration in patients with hemorrhagic hemispheric stroke

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The aim of the study was to evaluate the diagnostic informativity of non-contrast computed tomography (NCCT) markers of intracerebral hemorrhage (ICH) expansion in assessment of the individual risk of early neurological deterioration (END) in patients with hemorrhagic hemispheric stroke (HHS).

Materials and methods. A prospective, cohort study was conducted involving 333 patients in the acute period of hypertensive spontaneous supratentorial ICH on the background of conservative therapy. The level of neurological deficit was assessed using the Full Outline of Unresponsiveness (FOUR) coma scale and the National Institute of Health Stroke Scale (NIHSS). The computed tomography of the brain was used to verify the ICH volume, the midline shift (MS), the secondary intraventricular hemorrhage volume (IVHV) and NCCT markers of intracerebral hemorrhage expansion. As a combined clinical endpoint, END was considered (decrease of the FOUR scale score ≥2 or/and increase of the NIHSS score ≥4 or/and lethal outcome within 48 hours of hospitalization).

Results. Early neurological deterioration was registered in 112 patients. On the basis of a comparative analysis, it was established that the specific weight of END was significantly higher in subcohorts of patients with individual NCCT markers of intracerebral hemorrhage expansion, than it was in subcohorts of patients without corresponding NCCT signs ($p < 0.0001$). It was established that the following NCCT markers of ICH expansion are the most sensitive predictors of END: hypodensity, swirl sign and irregular shape (sensitivity >90.0 %). The most specific NCCT markers were island sign, black hole sign, blend sign, satellite sign and heterogeneous density (specificity >87.0 %). In accordance with the multiple logistic regression analysis, hypodensity (OR (95 % CI) = 13.56 (4.54–40.49), $p < 0.0001$) and island sign (OR (95 % CI) = 5.94 (2.05–17.16), $p = 0.0010$) are independently associated with the risk of END. A highly sensitive multi-prediction logistic regression model was elaborated in order to predict END in patients with HHS which takes into account the most informative NCCT markers of ICH expansion (hypodensity, island sign) and quantitative neuroimaging indicators (MS, IVHV) (AUC ± SE (95 % CI) = 0.92 ± 0.02 (0.89–0.95), $p < 0.0001$).

Conclusions. Non-contrast computed tomography markers of ICH expansion are associated with increased risk of END in patients with HHS. Hypodensity and island sign are independent predictors of END. The integration of NCCT markers of ICH expansion with quantitative neuroimaging indicators (MS, IVHV) in the structure of the multi-prediction logistic regression model allows to assess the individual risk of END with an accuracy of >85.0 %.

Ключові слова: внутрішньомозковий крововилив, рентгенівська томографія, прогноз.

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Аналіз діагностичної інформативності неконтрастних комп'ютерно-томографічних маркерів прогресування внутрішньомозкового крововиливу у визначенні індивідуального ризику раннього клініко-неврологічного погіршення у хворих на геморагічний півкульовий інсульт

А. А. Кузнєцов

Мета роботи – оцінити інформативність неконтрастних комп'ютерно-томографічних (НККТ) маркерів прогресування внутрішньомозкового крововиливу (ВМК) у визначенні індивідуального ризику раннього клініко-неврологічного погіршення (РКНП) у хворих на геморагічний півкульовий інсульт (ГПІ).

Матеріали та методи. Здійснили проспективне, когортне дослідження із залученням 333 пацієнтів у гострому періоді гіпертензивного спонтанного супратенторіального ВМК на тлі консервативної терапії. Рівень неврологічного дефіциту оцінювали за шкалою коми Full Outline of Unresponsiveness (FOUR) та National Institute of Health Stroke Scale (NIHSS). За даними комп'ютерної томографії головного мозку визначили об'єм ВМК, латеральну дислокацію (ЛД) серединних структур мозку, об'єм вторинного внутрішньошлуночкового крововиливу (ОВВШК) та НККТ-маркери прогресування ВМК. Як комбіновану кінцеву клінічну точку визначили РКНП (зменшення сумарного бала за шкалою коми FOUR ≥2 та/або збільшення сумарного бала за NIHSS ≥4, та/або летальний наслідок протягом 48 годин після госпіталізації).

Результати. Раннє клініко-неврологічне погіршення зареєстровано у 112 пацієнтів. У результаті порівняльного аналізу встановили: в субкогортах пацієнтів з окремими НККТ-маркерами прогресування ВМК питома вага РКНП достовірно вища, ніж у субкогортах пацієнтів без таких ($p < 0,0001$). Найчутливіші предиктори РКНП – гіподенсивність, ознака «завихрення» та неправильна форма осередку ураження (чутливість >90,0 %), а найбільш специфічні – ознаки «острівця», «чорної діри», «змішування», «супутника» та гетерогенна щільність осередку ураження (специфічність >87,0 %). За даними множинного логістичного регресійного аналізу, з ризиком РКНП незалежно асоційовані гіподенсивність (ВШ (95 % ДІ) = 13,56 (4,54–40,49), $p < 0,0001$) та ознака «острівця» (ВШ (95 % ДІ) = 5,94 (2,05–17,16), $p = 0,0010$). Побудо-

вано високочутливу мультипредикторну логістичну регресійну модель для прогнозування РКНП у хворих на ГПІ, що враховує найінформативніші НККТ-маркери ВМК (гіподенсивність, ознака «острівця») та кількісні нейровізуалізаційні показники (ЛД, ОВВШК) (AUC ± SE (95 % CI) = 0,92 ± 0,02 (0,89–0,95), p < 0,0001).

Висновки. Неконтрастні комп'ютерно-томографічні маркери прогресування ВМК асоційовані з підвищеним ризиком РКНП у хворих на ГПІ. Незалежні предиктори РКНП – гіподенсивність та ознака «острівця». Інтеграція НККТ-маркерів прогресування ВМК із кількісними нейровізуалізаційними показниками (ЛД, ВВШК) у структурі мультипредикторної логістичної регресійної моделі дає змогу визначати індивідуальний ризик РКНП із точністю >85,0 %.

Cerebral hemorrhagic stroke and, in particular, its most widespread form – spontaneous supratentorial intracerebral hemorrhage (SSICH) is the most destructive type of acute cerebrovascular disorders in the medical and social aspect [1,2,3]. The modern paradigm of the specialized care provided to the specified contingent of patients includes, first of all, the use of an individual approach to the determination of the optimal treatment strategy [4]. Moreover, the most important basis for the appropriate decisions is the earliest possible verification of the short-term prognosis. This makes it possible to timely identify patients with a high risk of unfavorable course and outcome of the acute period of the disease on the background of conservative therapy, as well as to identify those whose treatment requires more active medical and tactical actions and, in particular, neurosurgical intervention (as a part of "life-saving strategy") [5].

The combined endpoint, which integrates the adverse course types of the acute period of SSICH, is early neurological deterioration (END) [6]. Here are the possible components of END: a decrease of the Full Outline of UnResponsiveness (FOUR) scale score ≥2 and/or an increase of the National Institute of Stroke Scale (NIHSS) score ≥4 and/or death within 48 hours of the onset of the disease [7]. Depending on the progression speed, the following types of END are distinguished: fulminant (up to 60 minutes from the onset of the disease); acute (1–12 hours); subacute (24–48 hours) [8].

At the same time, it was established that the main link in the pathogenesis of END is the intracerebral hemorrhage expansion. An increase of the volume of intracerebral hemorrhage initiates a progressive combined (midline shift / transtentorial shift) of the brainstem structures in the rostro-caudal direction with the further development of secondary hemorrhages in the pons of the brain and the subsequent wedging of the bulbar structures into the cervical-dural funnel and the onset of death [9].

All of the above justifies the feasibility of further research aimed at the elaboration of informative criteria for the prognosis of END. It was proven that the density heterogeneity and shape irregularity on non-contrast computed tomography of the brain are associated with a high risk of intracerebral hemorrhage expansion [10]. The avalanche model of hematoma expansion is considered to be the most accepted: peripheral vessels are the second to be sheared after the initial vessels rupture, which results in the constant source of bleeding. Fresh blood mixes with a clot, which causes higher hemorrhage heterogeneity. The prevalence of heterogeneity when speaking about hematoma expansion, may be potentially explained by the fact that hyperattenuating regions are making more stable bleed zones and lower attenuating areas. Hemorrhages which grow usually have irregular shape and can change, expanding in various directions after the time passes. Irregular hemorrhages may occur at an intermediate stage of maturity, when the bleeding continues persisting bleeding or when the intrahemorrhage pressure is high, which is a favorable condition for the hematoma to bulge into brain structures [11,12,13].

Relevant non-contrast computed tomography (NCCT) markers of intracerebral hemorrhage expansion were identified [14,15]. In spite of established association between NCCT signs and intracerebral hemorrhage expansion, informativeness of these markers as potential end-point clinical predictors needs clarification [11]. Thus in some investigations the prognostic value of the intracerebral hemorrhage expansion NCCT markers as lethal outcome and poor functional outcome predictors was validated [16,17,18].

However, there are no studies devoted to the analysis of the diagnostic informativity of NCCT markers of intracerebral hemorrhage expansion in assessment of the individual risk of END.

Aim

The aim of the study is to evaluate the diagnostic informativity of non-contrast computed tomography markers of intracerebral hemorrhage expansion in assessment of the individual risk of early neurological deterioration in patients with hemorrhagic hemispheric stroke.

Materials and methods

The study included 333 patients (194 men and 139 women, age 65 [57–75] years) with first-onset hypertensive SSICH. The patients were hospitalized within the first 24 hours after the onset of the disease to the department of acute cerebrovascular disorders of the Municipal nonprofit enterprise "City Hospital No. 6" of the Zaporizhzhia City Council. Signed informed consent for the patient's participation in the study was mandatory.

The diagnosis was established according to the data of a neuroimaging study, which was carried out using Siemens Somatom Spirit (Germany) or Toshiba Asteion (Japan), taking into account the localization, size of the lesion, midline shift, the presence of secondary intraventricular hemorrhage.

The intracerebral hemorrhage volume (ICHV) was calculated using the ellipsoid formula:

ICHV (ml) = (a × b × c) / 2,

where a, b, and c are the linear dimensions of the lesion (cm). Midline shift (MS) was detected as average from septum pellucidum and pineal gland displacement (mm). The intraventricular hemorrhage volume (IVHV) was assessed with the help of the exponential formula, based on the value of the total score on the Intraventricular Hemorrhage scale [19].

The density of the lesion was assessed according to the 5-point Barras density scale, where gradations I and II of the specified scale correspond to the homogeneous density of intracerebral hemorrhage; gradations III, IV and V correspond to heterogeneous density. The shape of the lesion was evaluated according to the 5-point categorical Barras shape scale, where gradations I and II of the specified scale correspond to the correct shape of the lesion; gradations III, IV and V correspond to an irregular shape [20].

Non-contrast computed tomography (NCCT) markers of intracerebral hematoma expansion, which are derivatives of its density (heterogeneous density, swirl sign, hypodensity, black hole sign, blend sign, fluid level) and shape (irregular shape, island sign, satellite sign) were also recorded. The verification of the above-mentioned markers was carried out in accordance with the appropriate neuroimaging standards for their detection, interpretation and registration [11].

The level of neurological deficit was assessed during admission to the hospital and during the course of the acute period of the disease using the NIHSS and the FOUR scale. Early neurological deterioration was a cumulative endpoint, which was considered to be the occurrence of one or more of the following events within 48 hours from admission on the background of conservative therapy: a decrease of the FOUR scale score ≥2; an increase of the NIHSS score ≥4; lethal outcome.

Patients who met at least one of the following criteria were excluded from the study: a cerebral stroke in anamnesis; intracerebral hemorrhage caused by cerebral infarction, brain tumor, taking anticoagulants; presence of confirmed aneurysm or arterio-venous malformation of cerebral vessels; somatic pathology in the stage of decompensation; malignant tumors; extracerebral cause of death according to autopsy data.

All patients were examined by a neurosurgeon. In most of the cases conservative therapy was chosen as the most optimal tactic. Patients received therapy in accordance with the Unified protocol for providing medical care to patients with cerebral hemorrhagic stroke, approved by order of the Ministry of Health of Ukraine No. 275 dated 04/17/2014 [21]. 19 patients were transferred to a neurosurgical hospital for surgical treatment. The data regarding the patients was also excluded from the analysis in the event that the duration of observation on the background of conservative therapy was less than 48 hours (as a result of transfer to the neurosurgical department), and in the event that during the time of stay in the neurological hospital, none of the variants of END were recorded.

Statistical data processing was performed using Statistica 13.0 software (StatSoft Inc., USA, serial number JPZ804I382130ARCN10J) and MedCalc (version 18.2.1). The Shapiro–Wilk test was used to assess the normality of the distribution. As most of the studied indicators did not have a normal distribution, descriptive statistics are presented in the form of median and interquartile range. Mann–Whitney U test was used to identify intergroup differences in quantitative indicators. Pearson`s Chi-squared test was used to assess the relations between qualitative (discrete) indicators. Logistic regression analysis and ROC-analysis were used for prognostic tools elaboration. Odds ratio (OR), relative risk (RR), sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and forecast accuracy were assessed. A significance level of $p < 0.05$ was considered critical for rejecting null hypotheses.

Results

The clinical and paraclinical characteristics of the studied patients during their admission to hospital were presented as follows: FOUR scale score – 15.0 [12.0–16.0], NIHSS score – 15.0 [9.0–21.0], ICHV – 14.3 [5.9–44.7] ml, the presence of midline shift – in 214 (64.3 %) patients, the severity of midline shift – 2.5 [0.0–5.5] mm, the presence of SIVH – in 194 (58.3 %) patients, IVHV – 6.0 [0.0–30.0] ml.

The density of the lesion was heterogeneous in 122 (36.6 %) patients, the shape of the lesion was irregular in 200 (60.1 %) patients, the swirl sign was visualized in 156 (46.8 %) patients, hypodensity in 188 (56.5 %) people, the black hole sign occurred in 67 (20.1 %) patients, the blend sign – in 30 (9.0 %) patients, the island sign – in 50 (15.0 %) patients, the satellite sign – in 81 (24.3 %) patients. Fluid level was not detected in any of the patients.

Indicators of the specific weight of NCCT markers of the intracerebral hemorrhage expansion in groups of patients with different ICHV are shown in *Table 1*. As it can be seen, NCCT markers of intracerebral hemorrhage expansion are associated with a bigger ICHV.

Neurological deterioration within 48 hours from admission at hospital was registered in 112 (33.6 %) patients (66 men and 46 women, age 63.0 [55.0–76.0] years), while the indicated endpoint during the first 24 hours was verified in 99 patients, in the period from 24 to 48 hours it was registered in 19 cases (in 6 patients it was preceded by neurological deterioration in the form of consciousness level decreasing during the first 24 hours of hospitalization). Early neurological deterioration was not recorded in 221 patients (128 men and 93 women, age 65 [58–74] years).

Indicators of the specific weight of END in subcohorts of patients with the presence / absence of appropriate NCCT markers of intracerebral hemorrhage expansion were as follows: the presence of heterogeneous density of the lesion – 77.9 %, homogeneous density – 8.1 % (Pearson's Chi-squared = 168.3, $p < 0.0001$); with the swirl sign – 64.7 %, without the swirl sign – 6.2 % (Pearson's Chi-squared = 126.9, $p < 0.0001$); with hypodensity – 57.4 %, without hypodensity – 2.8 % (Pearson's Chi-squared = 109.4, $p < 0.0001$); with the black hole sign – 74.6 %, without black hole sign – 23.3 % (Pearson's Chi-squared = 63.0, $p < 0.0001$); with the blend sign – 53.3 %, without the blend sign – 31.7 % (Pearson's Chi-squared = 5.7, $p = 0.0168$); with an irregular shape – 52.5 %, without irregular shape – 5.3 % (Pearson's Chi-squared = 79.6, $p < 0.0001$); with the island sign – 90.0 %, without the island sign – 23.7 % (Pearson's Chi-squared = 83.5, $p < 0.0001$); with the satellite sign – 70.4 %, without the satellite sign – 21.8 % (Pearson's Chi-squared = 64.5, $p < 0.0001$). Therefore, it can be seen from the above data that all registered NCCT markers of intracerebral hematoma expansion are reliably associated with END.

Table 1. Indicators of the specific weight of NCCT markers of the intracerebral hemorrhage expansion in groups of patients with different ICHV

NCCT markers of intracerebral hemorrhage expansion	ICHV		Pearson's Chi-squared	p
	<30 mL (n = 217)	≥30 mL (n = 116)		
Heterogeneous density	18.9 %	69.8 %	84.2	<0.0001
Swirl sign	21.7 %	94.0 %	158.2	<0.0001
Hypodensity	35.5 %	95.7 %	111.1	<0.0001
Black hole sign	3.7 %	50.9 %	104.4	<0.0001
Blend sign	3.2 %	19.8 %	25.3	<0.0001
Irregular shape	38.7 %	100.0 %	118.0	<0.0001
Island sign	1.8 %	39.7 %	84.4	<0.0001
Satellite sign	7.4 %	56.0 %	96.9	<0.0001

Table 2. Indicators of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of NCCT markers of intracerebral hematoma expansion as criteria for predicting END in patients with hemorrhagic hemispheric stroke

Criteria for predicting END in patients with hemorrhagic hemispheric stroke	Se	Sp	PPV	NPV	Accuracy
Heterogeneous density	84.8 %	87.8 %	77.9 %	91.9 %	86.8 %
Swirl sign	90.2 %	75.1 %	64.7 %	93.8 %	80.2 %
Hypodensity	96.4 %	63.8 %	57.4 %	97.2 %	74.8 %
Black hole sign	44.6 %	92.3 %	74.6 %	76.7 %	76.3 %
Blend sign	14.3 %	93.7 %	53.3 %	68.3 %	67.0 %
Irregular shape	93.8 %	57.0 %	52.5 %	94.7 %	69.4 %
Island sign	40.2 %	97.7 %	90.0 %	76.3 %	78.4 %
Satellite sign	50.9 %	89.1 %	70.4 %	78.2 %	76.3 %

Se: sensitivity; **Sp:** specificity; **PPV:** positive predictive value; **NPV:** negative predictive value.

Thus, the heterogeneous density of the lesion is associated with an increase of the END risk by 9.7 times (RR (95 % CI) = 9.66 (6.07–15.40), p < 0.0001), the swirl sign – by 10.4 times (RR (95 % CI) = 10.42 (5.81–18.68), p < 0.0001), hypodensity – by 20,8 times (RR (95 % CI) = 20.82 (7.86–55.16), p < 0.0001), the black hole sign – by 3.2 times (RR (95 % CI) = 3.20 (2.47–4.15), p < 0.0001), the blend sign – by 1.7 times (RR (95 % CI) = 1.68 (1.16–2.45), p = 0.0063), the irregular shape of the lesion – by 10.0 times (RR (95 % CI) = 9.98 (4.79–20.76), p < 0.0001), the island sign – by 3.8 times (RR (95 % CI) = 3.80 (3.02–4.78), p < 0.0001), the satellite sign – by 3.2 times (RR (95 % CI) = 3.22 (2.45–4.24), p < 0.0001).

The reliable changes of all mentioned clinical and neurological parameters during hospital admission between patients with and without END were revealed: NIHSS score (22 [15–30] versus 13 [8–17], p < 0.0001), FOUR scale score (12 [5–15] versus 16 [14–16], p < 0.0001), ICHV (55 [21–85] mL versus 11 [5–24] mL, p < 0.0001), midline shift (7 [3–11] mm versus 2 [0–4] mm, p < 0.0001), IVHV (30 [14–55] mL versus 0 [0–11] mL, p < 0.0001), heterogeneous density of the lesion (84.8 % versus 12.2 %, p < 0.0001), swirl sign (90.2 % versus 24.9 %, p < 0.0001), hypodensity (96.4 % versus 36.2 %, p < 0.0001), black hole sign (44.6 % versus 7.7 %, p < 0.0001), blend sign (14.3 % versus 6.3 %, p = 0.0168), irregular shape of the lesion (93.7 % versus 43.0 %, p < 0.0001), island sign (40.2 % versus 2.3 %, p < 0.0001), satellite sign (50.9 % versus 10.9 %, p < 0.0001).

In accordance with the logistic regression analysis, the following dependent predictors of END were verified: NIHSS score (OR (95 % CI) = 1.16 (1.12–1.21), p < 0.0001), FOUR scale score (OR (95 % CI) = 0.74 (0.69–0.80), p < 0.0001), ICHV (OR (95 % CI) = 1.04 (1.03–1.05), p < 0.0001), midline shift (OR (95 % CI) = 1.40 (1.29–1.52), p < 0.0001), IVHV (OR (95 % CI) = 1.08 (1.06–1.09), p < 0.0001), heterogeneous density of the lesion (OR (95 % CI) = 40.15 (20.87–77.27), p < 0.0001), swirl sign (OR (95 % CI) = 27.70 (13.90–55.42), p < 0.0001), hypodensity (OR (95 % CI) = 47.59 (16.90–133.96), p < 0.0001), black hole sign (OR (95 % CI) = 9.68 (5.21–17.98), p < 0.0001), blend sign (OR (95 % CI) = 2.46 (1.16–5.25), p = 0.0195), irregular shape of the lesion (OR (95 % CI) = 19.89 (8.85–44.73), p < 0.0001), island sign (OR (95 % CI) = 29.01 (11.07–76.06), p < 0.0001), satellite sign (OR (95 % CI) = 8.51 (4.85–14.94), p < 0.0001).

Table 2 shows indicators of sensitivity, specificity, PPV, NPV and the accuracy of NCCT markers of intracerebral hematoma expansion as criteria for predicting END.

As shown in *Table 2*, the most sensitive predictors of END are hypodensity (Se = 96.4 %, Sp = 63.8 %, predictive accuracy = 74.8 %), swirl sign (Se = 90.2 %, Sp = 75.1 %, predictive accuracy = 80.2 %) and irregular shape (Se = 93.8 %, Sp = 57.0 %, predictive accuracy = 69.4 %), whereas the most specific are island sign (Se = 40.2 %, Sp = 97.7 %, predictive accuracy = 78.4 %), black hole sign (Se = 44.6 %, Sp = 92.3 %, predictive accuracy = 76.3 %), satellite sign (Se = 50.9 %, Sp = 89.1 %, predictive accuracy = 76.3 %), blend sign (Se = 14.3 %, Sp = 93.7 %, predictive accuracy = 67.0 %) and heterogeneous density (Se = 84.8 %, Sp = 87.6 %, predictive accuracy = 86.8 %).

In accordance with the results of multiple logistic regression analysis it was detected, that END risk was independently associated with the following NCCT markers of intracerebral hemorrhage expansion: hypodensity (OR (95 % CI) = 13.56 (4.54–40.49), p < 0.0001) and island sign (OR (95 % CI) = 5.94 (2.05–17.16), p = 0.0010).

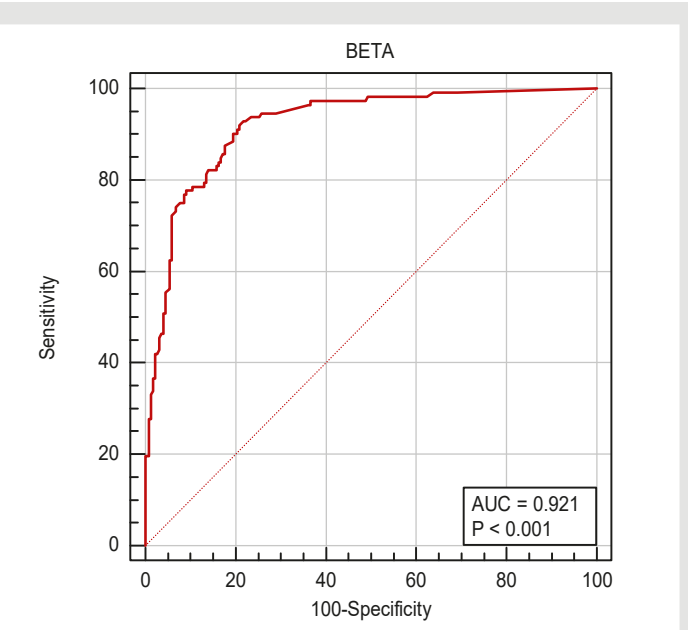

Fig. 1. ROC-curve of multipredictive logistic regression model for individual END risk verification in patients with acute SSICH.

Midline shift severity (OR (95 % CI) = 1.11 (1.01–1.21), p = 0.0227) and IVHV (OR (95 % CI) = 1.04 (1.08–1.06), p = 0.0002) were also an independent END predictors. The binary logistic regression equation was developed based upon all mentioned parameters that were integrated in this multipredictive model. This equation looks like the following:

$$B = -3.927 + 2.607 \times P1 + 1.781 \times P2 + 0.103 \times \times P3 + 0.036 \times P4,$$

where –3.927 – intercept (β0);
P1 – hypodensity (1 – present, 0 – absent);
P2 – island sign (1 – present, 0 – absent);
P3 – midline shift severity, mm;
P4 – intracerebral hemorrhage volume, mL.

The cut-off value β (>–1.011) was detected by ROC-analysis as an integrated predictor END in patients with SSICH (Se – 92.0 %, Sp – 79.2 %, PPV – 69.1 %, NPV – 95.1 %). The evaluation of informativeness and quality of predicting model was made by using: accuracy – 86.5 %; AUC ± SE (95 % CI) = 0.92 ± 0.02 (0.89–0.95), p < 0.0001 (*Fig. 1*).

Indicators of endpoints specific weight were the following: in cohort with β > –1.011 (n = 149) – 69.1 %, with β ≤ –1.011 (n = 184) – 4.9 %. Thus, β > –1.011 was associated with END risk increasing by 14.1 times (RR (95 % CI) = 14.13 (7.41–26.97), p < 0.0001).

Discussion

According to the neuroimaging study, a wide range of different NCCT markers of intracerebral hemorrhage expansion (hypodensity, swirl sign, heterogeneous density, black hole sign, blend sign, the irregular shape of the lesion, island sign and satellite sign) were registered in the general cohort of patients. The highest specific weight was registered in the following markers: irregular shape (60.1 %), hypodensity (56.5 %), swirl sign (46.8 %) and heterogeneous density (36.6 %). Satellite sign (24.3 %), black hole sign (20.1 %), island sign (15.0 %) and blend sign (9.0 %) were verified in a smaller number of patients. Fluid level was not detected in any of the patients. In accordance with the available data, fluid level is a specific marker of oral anticoagulant-associated intracerebral hemorrhage [22]. Patients with intracerebral hemorrhage which resulted from taking oral anticoagulants were not included in the study.

On the basis of a comparative analysis, it was established that the specific weight of END was significantly higher in subcohorts of patients with individual NCCT markers of intracerebral hemorrhage expansion (hypodensity, swirl sign, heterogeneous density, black hole sign, blend sign, irregular shape, island sign, satellite sign), than it was in subcohorts of patients without corresponding NCCT signs. So, it has been proven that hypodensity, swirl sign, heterogeneous density, black hole sign, blend sign, irregular shape, island sign and satellite sign are associated with an increased risk of END in patients with hemorrhagic stroke. The presence of the above-mentioned NCCT signs in the spectrum of dependent predictors of END is also confirmed by logistic regression analysis. Taking into account the high informativity of hypodensity, swirl sign, heterogeneous density, black hole sign, blend sign, irregular shape, island sign and satellite sign as NCCT markers of intracerebral hemorrhage expansion [11,14,15,16,17,18], the obtained results are consistent with modern ideas about the leading role of hematoma progression in the pathogenesis of END in the specified contingent of patients.

Indicators of sensitivity, specificity and accuracy of NCCT markers of intracerebral hematoma expansion were assessed as criteria for predicting END in patients with hemorrhagic hemispheric stroke. It was established that the following NCCT markers of intracerebral hematoma expansion are the most sensitive predictors of END: hypodensity, swirl sign and irregular shape (Se > 90.0 %, predictive accuracy 69.4–80.2 %). Therefore, the sensitivity indicators of the above-mentioned NCCT signs according to the results of our study were slightly higher than the ones described in other studies, in which their sensitivity to the assessment of the risk of intracerebral hemorrhage progression was evaluated (Se 64.0–83.0 %) [16,17].

The most specific NCCT markers were island sign, black hole sign, blend sign, satellite sign and heterogeneous density (Sp > 87.0 %, predictive accuracy 67.4–86.8 %). The obtained data are consistent with the results of other studies in which showed a high specificity of the island sign, black hole sign and blend sign in the verification of the individual risk of intracerebral hematoma expansion (Sp 90.0–98.0 %) [15,17,23]. At the same time, the specificity indicators of satellite sign and heterogeneous density according to the results of our study were slightly higher than in other studies, where the informativity of the above-mentioned NCCT signs as for the assessment of the risk of progression of intracerebral hemorrhage was evaluated (Sp 69.0–78.0 %) [10,16].

On the basis of the multiple logistic regression analysis, a multi-predictor model was built for predicting the END in patients with hemorrhagic hemispheric stroke. Independent predictors were as follows: hypodensity, island sign, MS and IVHV. The presence of certain NCCT signs in the spectrum of independent predictors also confirms the leading role of intracerebral hemorrhage expansion in the pathogenesis of END. This model integrates the informativity of individual predictors included in its composition. On the basis of the ROC analysis, the optimal cut-off value β was determined, which acts as a highly sensitive integral neuroimaging predictor of END and allows to assess the short-term prognosis on the background of conservative therapy with an accuracy of 86.5 % (AUC ± SE (95 % CI) = 0.92 ± 0.02 (0.89–0.95), p < 0.0001).

Thus, in accordance with the results of the NCCT study, markers of intracerebral hematoma expansion are informative predictors of END in patients with hemorrhagic hemispheric stroke. A non-invasive and economically available method is used in order to assess the markers, which is the gold standard of neuroimaging in the specified contingent of patients. That is the reason why a number of researchers consider NCCT as a real and widely available alternative to digital subtraction angiography for the stratification of the risk of intracerebral hematoma expansion at the initial diagnostic stage [11,24]. The above justifies the expediency of the assessment of NCCT markers of intracerebral hematoma expansion for the timely identification of patients with an increased risk of END as a component of the basis for further selection of optimal treatment tactics.

Conclusions

1. The following NCCT markers of intracerebral hemorrhage expansion are associated with an increased risk of END in patients with hemorrhagic stroke: hypodensity (RR (95 % CI) = 20.82 (7.86–55.16), p < 0.0001), swirl sign (RR (95 % CI) = 10.42 (5.81–18.68), p < 0.0001), heterogeneous density (RR (95 % CI) = 9.66 (6.07–15.40), p < 0.0001), black hole sign (RR (95 % CI) = 3.20 (2.47–4.15), p < 0.0001), blend sign (RR (95 % CI) = 1.68 (1.16–2.45), p = 0.0063), the irregular shape of the lesion (RR (95 % CI) = 9.98 (4.79–20.76), p < 0.0001), island sign (RR (95 % CI) = 3.80 (3.02–4.78), p < 0.0001) and satellite sign (RR (95 % CI) = 3.22 (2.45–4.24), p < 0.0001).

2. Hypodensity is the most informative independent predictor of END among NCCT markers of intracerebral hemorrhage expansion that take into account the density of the lesion in patients with hemorrhagic hemispheric stroke (Se = 96.4 %, Sp = 63.8 %, accuracy = 74.8 %; OR (95% CI) = 13.56 (4.54–40.49), p < 0.0001). The island sign is the most informative independent predictor of END among NCCT of intracerebral hemorrhage expansion that take into account the shape of the lesion (Se = 40.2 %, Sp = 97.7 %, accuracy = 78.4 %; OR (95 % CI) = 5.94 (2.05–17.16), p = 0.0010).

3. A highly sensitive multi-predictor logistic regression model was developed, which integrates the prognostic value of NCCT markers of intracerebral hemorrhage expansion (hypodensity, island sign) with the informativity of quantitative neuroimaging indicators (midline shift, secondary intraventricular hemorrhage volume) and allows to verify the individual risk of END with an accuracy of 86.5 % (AUC ± SE (95 % CI) = 0.92 ± 0.02 (0.89–0.95), p < 0.0001).

Prospect for further research is the development of integral neuroimaging criteria for the prediction of early clinical and neurological deterioration in patients with spontaneous supratentorial intracerebral hemorrhage as a component of the basis for the selection of an individual treatment tactic.

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