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Differentiation of density of ischaemic brain tissue in computed tomography with respect to neurological deficit in acute and subacute period of ischaemic stroke

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Summary

Background: The detecion of ischaemic brain tissue by a CT depends on degree and time of hypoperfusion. The aim of the present study was to establish interrelation between morphologic changes in CT scans and clinical classification of focal neurological deficit.

Material/Methods: We analyzed data from 139 consecutive patients enrolled in a prospective cohort study at Clinic of Neurology University Hospital in Bialystok, at which emergency CT for patients suspected of having acute (>6 h) ischaemic stroke was performed. Next follow up nonenhanced CT scans were obtained between 7 and 10 day after admission.

Resultts: In general, the presence of an ischaemic hypodensity in a patient with signs and symptoms of acute stroke signifies irreversible infarction. In hyperacute and acute stage of ischaemic stroke focal decreased attenuation was about 10–20 HU. In subacute stage focal parenchymal hypodensity further decreased to 20–30 HU. Patients with mild neurological deficit and quick recovery had smaller focal areas of infarct with slight density changes compared to larger territory of infarct extent in patients with severe neurologic symptoms.

Conclusions: In subacute stage of ischaemic stroke extent of parenchymal changes and degree of hypodensity correlates with stroke severity and may have some prognostic significance.

Key words: ischaemic stroke • computed tomography • hypodensity • neurological deficit

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Background

Brain strokes constitute the third cause of deaths, right after the myocardial infarctions and neoplasms, and they are the main cause of long-term disabilities [1]. As much as 72–86% of the brain strokes are of ischaemic type.

Computed tomography (CT) examination is a world-wide imaging technique of choice in stroke stages and the only method in the settings of an emergency room that enables a quick evaluation of the range and location of ischaemic foci, as well as differentiation between the ischaemic and haemorrhagic stroke [1,2].

It determines the presence and range of the ischaemic focus but also the evolution of pathological changes [2]. There are no contraindications for the use of this method. This is a widely available and easy to use, quick and repeatable method, which makes it an optimal diagnostic tool [3,4]. It is also relatively cheap and connected with a low rate of complications [3]. Sensitivity and specificity of the CT in detecting ischaemic lesions depends mainly on the time that elapsed from the moment of the onset of the clinical signs and symptoms to the moment of exam.

According to many authors, the early ischaemic changes in the first 24 hours of stroke are visualised with the CT

method in 5–90% of cases [3–6]. Such a wide discrepancy may result from i.a. uncertain interpretation of the early ischaemic changes shown in the head CT, and a lack of detailed information on the location and intensification of the neurological deficit [7].

Early changes in the CT scan of patients with an ischaemic stroke are a radiological sign of brain oedema [8,9]. Their presence in the CT scan reflects the severity and duration of hypoperfusion. The ischaemia results in the movement of water from the extracellular compartment to the inside of the neurons, which causes a cytotoxic swelling leading to a decreased density (hypodensity) of the ischaemic brain tissue [3,6]. Hydration of the brain tissue which increases its volume by 1%, decreases its density by 2.6 HU, which makes the more hydrated tissues hypodensive in CT examination. [10]. It is believed that the density of the brain tissue decreased by 20–30 HU, as compared to non-ischaemic regions, is an indirect indicator of a recent stroke [11–13].

The aim of the work was to evaluate the degree of hypodensity within the ischaemic brain tissue, with respect to the clinical state of the patients in an acute and subacute stage of the ischaemic stroke. The aim was followed by:

- Evaluating the clinical state and its correlation with the CT scan in acute and subacute stage of the ischaemic stroke of the brain,
- Evaluating the evolution of ischaemic changes visualized in brain CT, by comparing the results of the subsequent examinations

Material and Methods

From April 2002 to September 2004 we analysed 162 patients with clinical symptoms of acute (>6 h) ischaemic stroke of the brain, hospitalised at Neurological Department of the Hospital of the Medical University of Białystok. The evaluation excluded patients with a diagnosed transient ischaemic attack (TIA), past brain stroke with permanent clinical sequele and deaths before the repeated CT, as well as patients admitted to the hospital later than 24 hours from the onset of the ailment [14]. Final evaluation included 139 patients: 89 men and 50 women, in a mean age of 66.5 years.

Physical examinations were conducted by a specialist neurologist, with the use of the National Institutes of Health Stroke Scale. Examinations evaluated 13 signs and symptoms, with a score of 0–2 or 3 admitted for each item. The highest summative score of 30 meant the most severe clinical state. The evaluation of clinical symptoms expressed in a focal neurological deficit was performed at the day of admission to our Neurological Department and then between the seventh and tenth day of hospitalisation. The patients were divided into five groups, on the basis of results, according to the severity of clinical symptoms.

Group 0: no symptoms in the follow-up study,
Group I: from 1 to 5 points in the NIH scale – mild condition,
Group II: from 6 to 10 – moderately severe condition,
Group III: from 11 to 15 – severe condition,
Group IV: from 16 to 21 – very severe condition.

All patients had at least two CT scans of the head. The baseline one, in the settings of the ER – in the first 24 hours after the symptoms onset, and the second one – a follow-up examination in the 7^{th}–10^{th} day of hospitalisation, preceded by an evaluation of patient's neurological state. The choice of the day of the repeat examination was based on reports, according to which the strongest correlation (of 70–80%) between the clinical state and the image is obtained between the seventh and the tenth day of stroke [15].

Computed tomography was carried out with the use of Toshiba TCT-500S. We applied the sequence technique, in supine position, and the X-ray beam parallel to the eye-ear plane, with a window width of 80/40 HU and supratentorial thickness of 10 mm and the thickness used in the examination of the posterior intracranial structures: 5 mm. The CTs were unenhanced.

All images were analysed on a diagnostic monitor and subjected to processing – enlargement, choosing the right 'window', measurements of the brain tissue density (x-ray attenuation) and measurements of the size of the lesions [16].

Both the baseline, as the follow-up CT was performed with the use of the same parameters. The range of the area of decreased density (hypodensive region) and the degree of x-ray attenuation in the stroke region were compared with the results obtained within the normal hemisphere.

Regions of decreased attenuation rate (hypodensive regions), shown in CT, that are a direct indicator of ischaemic neurological defects, were divided into groups, according to the rate of hypodension:

a) Slight decrease in the degree of X-ray attenuation – difference of max. 10 HU, as compared to the normal hemisphere;
b) Medium decrease in the degree of X-ray attenuation – from10 HU to 20 HU, as compared to the normal hemisphere;
c) Considerable decrease in the degree of X-ray attenuation – from 20 HU to 30 HU, as compared to the normal hemisphere;
d) A low degree of X-ray attenuation – decrease over 30 HU, as compared to the normal hemisphere.

The results of the study were subjected to a statistical analysis. For the parameters that could be measured we found an arithmetic mean and standard deviation. Qualitative variables were shown in a percentage distribution. We calculated also the Pearson correlation coefficient for continuous variables and the Spearman coefficient for discontinuous variables (r). Normal distribution variables, evaluated with the Kolomogorov conformity test, were compared between different groups with the use of a Student's t-test. Mann-Whitney test was used for the variables inconsistent with the normal distribution. We assumed the level of significance at $p<0.05$. The calculations were made with the use of the following statistical packages: SPSS 12.0 P and STATISTICA PL.

Tabele 1. Focal hypodensity on CT image in acute stage of ischaemic sroke referring to the clinical state.

Clinical state	Number of patients	No symptoms of hypodension		Symptoms of hypodension	
		n	%	n	%
I	49	13	26.5	36	73.5
II	51	19	37.3	32	62.7
III	32	8	25.0	24	75.0
IV	7	1	14.3	6	85.7
Total I–IV	**139**	**41**	**29.5**	**98**	**70.5**

Table 2. The detailed analysis of the degree X-ray attenuation in the individual clinical conditions of the acute period of the ischaemc stroke.

Clinical state	Rate of hypodension							
	1		2		3		Total 1–3	
	n	%	n	%	n	%	n	%
I	11	30.6	20	55.6	5	13.9	36	100.0
II	11	34.3	15	46.9	6	18.8	32	100.0
III	7	29.2	12	50.0	5	20.1	24	100.0
IV	–	–	6	100.0	–	–	6	100.0
Total I–IV	**29**	**29.6**	**53**	**54.1**	**16**	**16.3**	**98**	**70.5**

1 – Decrease in X-ray attenuation by 10 HU; 2 – Decrease in X-ray attenuation by 10–20 HU; 3 – Decrease in X-ray attenuation by 20–30 HU.

Results

The evaluation of X-ray attenuation symptom in acute stage of ischaemic brain stroke, with respect to the patients' clinical state

No decreased density of the brain tissue was observed in 41 (29.5%) patients in acute stage of ischeamic brain stroke. A large proportion of the remaining 98 patients revealed decreased density of the brain tissue and this symptom was most typical for patients in severe (III – 75.0%) and very severe stage (IV – 85.7%) – (Table 1, Figure 1).

A detailed analysis of the X-ray attenuation degree in every single abovementioned case of acute stage of ischaemic brain stroke revealed that a slightly decreased density in the focus of the stroke,. i.e. up to 10 UH as compared to the other hemisphere, was present in 29.6% of all cases of hypodensity. In cases of mild, moderately severe and severe condition the percentage amounted to 30% for every group. Very severe condition was not concerned (Table 2).

A decrease in brain tissue density by 10–20 HU, as compared to the other hemisphere, was most frequently observed and concerned 53 patients, which constituted 54.1% of all cases of hypodension. It was present in half of the patients in mild, moderately severe and severe state. This rate of brain tissue hypodensity in ischaemic focus was observed in every patient in severe condition.

A considerable decrease in the rate of X-ray attenuation, from 20 to 30 HU (as compared to the opposite hemisphere), was observed in 16 patients only. i.e. 16.3% of all cases of decreased attenuation.

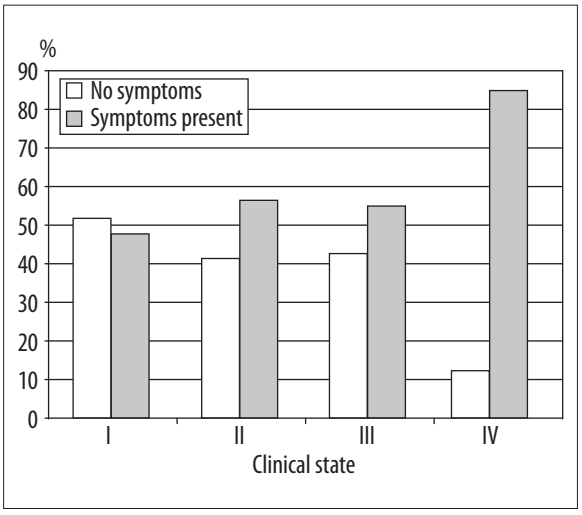

Figure 1. Occurrence of the hypodensity with respect to the degree of neurological deficit in acute period of the ischaemic stroke.

The evaluation of X-ray attenuation symptom in subacute stage of ischaemic brain stroke, with respect to the patients' clinical state

In subacute ischaemic stroke of the brain, the attenuation of X-ray was observed in 97.8% of all patients and in 6 patients (clinical state – 0, refer to Table 3) with no clinical symptoms of neurological deficit, as well as in 75 out

Table 3. Focal hypodensity on CT image in subacute stage of ischaemic stroke referring to the clinical state.

Clinical state	Number of patients	No symptoms of hypodension		Symptoms of hypodension	
		n	%	n	%
0	6	–	–	6	100.0
I	78	3	3.8	75	96.2
II	18	–	–	18	100.0
III	20	–	–	20	100.0
IV	17	–	–	17	100.0
Total 0–IV	**139**	**3**	**2.2**	**136**	**97.8**

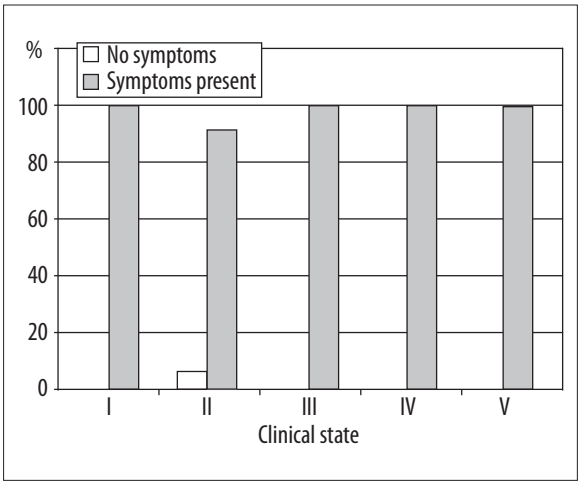

Figure 2. Occurrence of the hypodensity with respect to the degree of neurological deficit in subacute period of the ischaemic stroke.

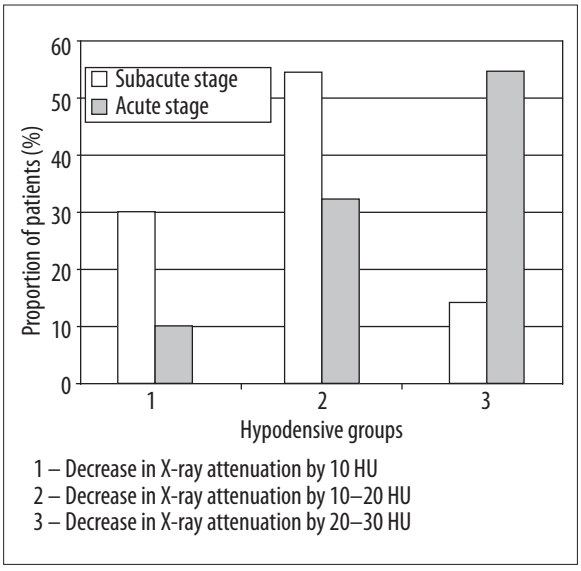

Figure 3. The comparison of the frequency of the individual groups of hypodensity in the acute and subacute period of the ischaemic stroke.

of 78 patients clinically qualified as mild condition. The above mentioned symptom was observed in all severe cases (Table 3 and Figure 2).

A detailed analysis of the rate of X-ray attenuation in every single clinical state, in subacute ischaemic brain stroke, revealed that a slight decrease, of up to 10 HU (as compared to the other hemisphere), concerned only 14 patients, without clinical symptoms or with an insignificant neurological deficit (Table 4).

The most characteristic for the subacute ischaemic brain stroke was a decrease of density in the ischaemic focus of 20 to 30 HU, as compared to the other, normal hemisphere. It was present in the largest number of patients – 74, which constituted 54.4% of all hypodensive cases and was typical for severe and very severe conditions – II – IV (Table 4).

The comparison of hypodensive changes in both stages revealed that in the acute ischaemic strokes, the most frequent symptom was the attenuation decreased by 10–20 HU (as compared to the other hemisphere). In subacute strokes it was a decrease by 20–30 HU that was observed the most frequently and it was three times more often than in the case of acute brain srokes (Figure 3).

The statistical analysis of the obtained results showed that the decrease in X-ray attenuation of 10–20 HU (as compared to the other hemisphere) is statistically significant for the course of stroke and increase in neurological deficit (P=0.0017). There were no statistically significant differences between the acute and subacute stage of the ischaemic brain stroke with the density decreased by 10 HU and by 20–30 HU.

The analysis of deaths during hospitalisation (n=20) showed that the decreased density was observed early in this group, i.e. during the first CT examination (18/20). The degree of hypodension in most of the patients from this group, evaluated in the second examination, turned out to be significantly decreased – by 20–30 HU in most of the cases (Table 5).

Radiological evaluation of the first, baseline CT exam showed no statistically significant correlation with patient's clinical state evaluated on patient's admission to the hospital (Table 6). Increased hypodension, on the other hand, evaluated in imaging follow-up studies (after 7 days and later) correlated strongly and statistically significantly with

Table 4. The detailed analysis of the degree X-ray attenuation in the individual clinical conditions of the subacute period of the ischaemc stroke.

Clinical state	Rate of hypodension							
	1		2		3		Total 1–3	
	n	%	n	%	n	%	n	%
0	1	16.7	3	50.0	2	33.3	6	100.0
I	11	14.7	29	38.6	35	46.7	75	100.0
II	2	11.1	4	22.2	12	66.7	18	100.0
III	–	–	7	35.0	13	65.0	20	100.0
IV	–	–	5	29.4	12	70.6	17	100.0
Total 0–IV	**14**	**10.3**	**48**	**35.3**	**74**	**54.4**	**136**	**9.8**

1 – Decrease in X-ray attenuation by 10 HU; 2 – Decrease in X-ray attenuation by 10–20 HU; 3 – Decrease in X-ray attenuation by 20–30 HU.

Table 5. Distribution of hypodensity groups in the first and second CT examination among the patients who died during the hospitalization.

CT study	Rate of hypodension			
	0	1	2	3
I	2	5	8	5
II	0	0	4	16

0 – No chan ges in attenuation degree; 1 – Decrease in X-ray attenuation by 10 HU; 2 – Decrease in X-ray attenuation by 10–20 HU; 3 – Decrease in X-ray attenuation by 20–30 HU.

Table 6. The correlation of the degree of ischaemia with the clinical state estimated in the neurological inspection: I – acute stage, II – subacute stage.

	Density I		Density II	
	r	P	r	P
Physical examination I	0.049	Not significant	0.360	0.0001
Physical examination II	0.277	0.001	0.621	0.001

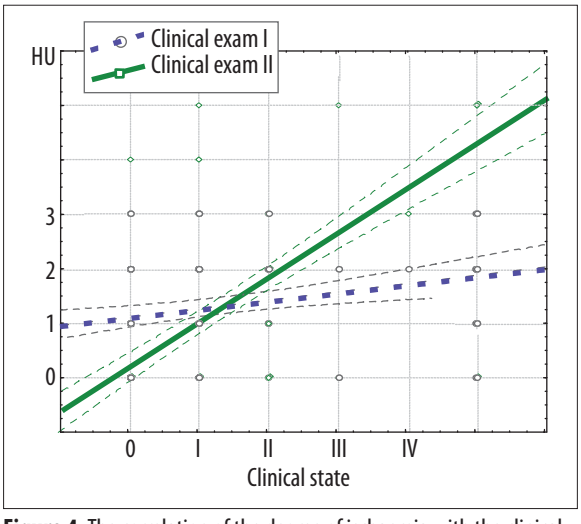

Figure 4. The correlation of the degree of ischaemia with the clinical state estimated in the neurological inspection

the patient's clinical state, evaluated at that time (Table 6 and Figure 4). We also revealed statistically significant, positive correlations between the CT scan evaluation in the first examination and the repeat neurological evaluation (physical examination number II) (r=0.227, p=0.001), as well as between the intensification of hypodension in the II CT examination, and the baseline neurological evaluation (physical examination number I) (r=0.36; p=0.0001) (Table 6).

Discussion

Decreased density of the brain tissue is a result of cytotoxic oedema connected with the movement of water from extracellular space to the inside of neurons. The baseline examination revealed a decreased density in 70.5% of the cases. The proportion surged in the second examination to 97.8%. The density of the brain tissue in the baseline CT in patients with ischaemic stroke decreased most of the time by 10–20 HU (as compared to the other hemisphere) and this degree of hypodension was also prevalent in very severe cases (IV – 100.0%).

A high rate of hypodensive areas concerned all clinical groups in an equal degree. However, important is the

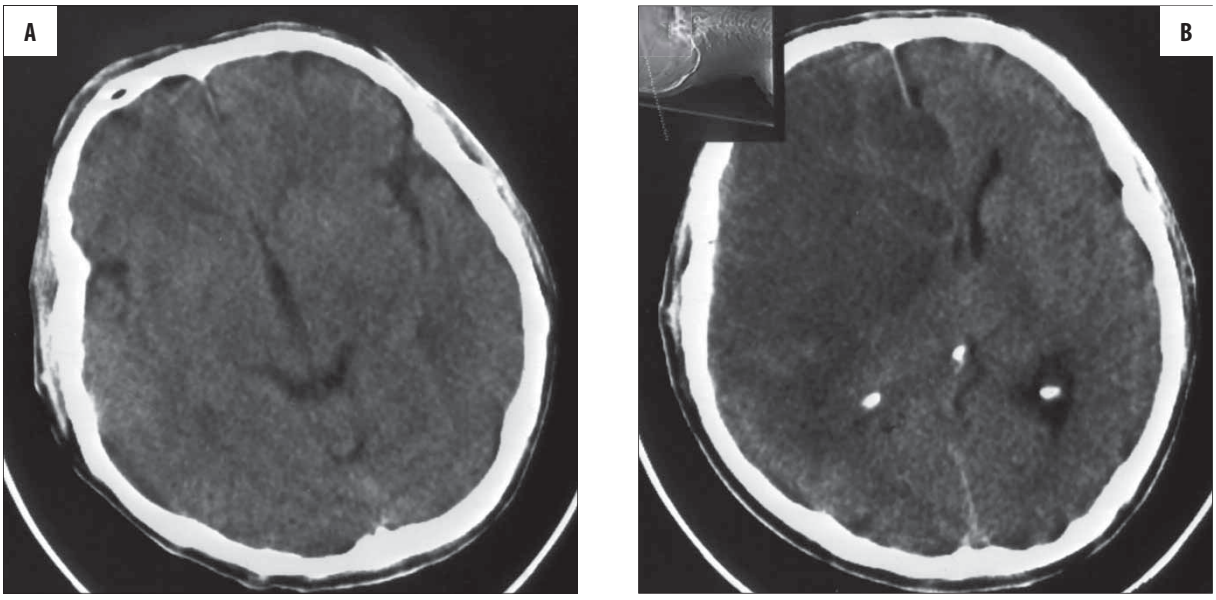

Figure 5. The patient M.O., age 72, very severe clinical state, patient unconscious with the symptoms of the left-sided hemiparesis. CT of the head made in first and sixth day from onset of symptoms, lesions situated in the right hemisphere of the brain: (**A**) acute period – poor gray matter–white matter distinction, narrowing of Sylvian fissure, loss of cortical sulci, discreet frontal and temporal decrease in parenchymal attenuation; (**B**) the extensive hypodense focus in the right hemisphere with the huge mass effect.

observation of the degree of X-ray attenuation with respect to different groups of clinical state and the evolution of this degree in the course of the stroke. A slight decrease in the degree of attenuation, i.e. up to 10 HU, observed in the baseline examination, was present in approx. 30% of all studied cases. The most frequently observed symptom was, however, the decrease in brain tissue density in the acute stage of ischaemic stroke of 10–20 HU – in over 50% of the studied patients. It concerned all patients with a severe neurological deficit.

Our observations are in conformity with the results by i.a. Dippel et al., according to whom an obvious decrease in the brain tissue density – i.e. over 10 HU – was present in 83% of the patients, while a slight decrease (up to 10 HU) in more than 60% of the study group [17]. However, there is no reference to the severity of neurological deficit.

The results of the study lead us to a conclusion that frequently observed decrease in density by 10–20 HU, observed in the baseline study, concerns first of all clinically severe cases. Similar results were presented by Ladurner et al. The decrease in density by 10–20 HU, revealed in in his material, concerned 76% of the clinical cases in mild condition and 95% cases described as severe.

The follow-up examination conducted in our study group revealed an increase in the number of cases of a decreased density of the brain tissue – the symptom observed in 98.7% of the patients. The number of cases of a slight decrease in the degree of density (up to 10 HU) decreased nearly three times – these were mostly asymptomatic cases. The number of patients with hypodension of 10–20 HU decreased 1.5 time and concerned a part of the patients with neurological recovery. At the same time, we observed a tendency of a decreasing brain tissue density in the subacute stage of the ischaemic stroke.

The density decreased by 20–30 HU, was three time more frequently observed in the follow-up CT examination than in the baseline examination (Figure 3) and it concerned severe cases mainly. It shows that the evaluation of the degree of hypodension is extremely important in the evaluation of the course of stroke. Hypodension of the ischaemic tissue by 10–20 HU (as compared to the other hemisphere) that was observed in all clinically severe cases in the baseline study, did not change in about 30% of the cases subjected to the follow-up study, and intensified (by 20–30 HU) in 70% cases from this clinical group.

Our observations showed that early hypodensive changes in the course of the ischaemic stroke of the brain are irreversible and indicate a region of a subsequent infarct. Prognostically significant are the degree and rate of density decrease within the brain tissue (Figure 4).

Some researchers believe that a slight X-ray attenuation below 10 HU may be connected with a favourable course of the stroke [15]. Further decrease in the degree of X-ray attenuation by 10–20 HU in patients with a severe neurological deficit may be a prognostic factor of an unfavourable course of the stroke. Similar conclusions are presented by other authors. According to Heiss for example, a decrease in density by 20–30 HU is connected with a severe clinical state and irreversible symptoms of the stroke [18,19]. The degree of hypodension being a prognostic symptom of the stroke course, can be confirmed by our study results. The statistically significant changes observed in the baseline CT correlate positively with the clinical state in the subacute stage ($r=0.227$, $P=0.001$). Also the degree of hypodension revealed in the second CT examination was statistically connected with the severity of the clinical state in the subacute stage (Table 6, Figure 4).

Conclusions

To sum up, after the analysis of the examinations, three statements are well-founded:

1. Retrospective analysis of the baseline CT images enables us to diagnose over 85% of early CT symptoms of the acute ischaemic brain stroke.

2. There is a strong correlation of the clinical state and the image between the acute and subacute ischaemic brain stroke. A decrease in the degree of X-ray attenuation by 10–20 HU and more, in patients with a severe neurological deficit, is a prognostic factor of an unfavourable course of the stroke.

3. A follow-up CT examination in the subacute stage of the ischaemic stroke should become a standard diagnostic and prognostic procedure.

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