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S. Kamenova[1*] A. Kondybayeva[2] , J. Krupinski[3], Zh. Dyusembaeva[4], G. Umutbaeva[4]., N. Buyrakulova[4], O. Antonyuk[4], M. Arshidinova[4], G. Karimov[4].

[1]Al-Farabi Kazakh National University, Almaty, Kazakhstan
[2]Asfendiyarov KazNMU, Department
of Nervous Diseases with the Course of Neurosurgery, Almaty, Kazakhstan
[3]Neurology Department, Mutua de Terrassa Hospital, Terrassa, Barcelona, Spain
[4]City Clinical Hospital No7, Stroke Unit No1 Almaty, Kazakhstan
*e-mail dr.kamenova@mail.ru

CLINICAL FEATURES AND REASONS FOR THE PROGRESSION OF ISCHEMIC STROKE IN THE ACUTE PERIOD

We examined 663 patients who were admitted to the clinic by ambulance, for determine the factors of clinical deterioration and progression of ischemic stroke in the acute period of the first 24-72 hours.Among the patients received in the acute period, a fatal out come occurred in 7.23% (48) patients, men - 45.8% and women - 54.2%.

At the time of admission to the hospital, almost 96.7% of patients with acute ischemic stroke had a disorder of consciousness from stunning to coma. The most significant risk factors for the development of ischemic stroke among 663 patients were arterial hypertension - 80.1%, chronic heartfailure - 57.9%, coronary heart disease - 25.5%, atrial fibrillation - 19.5%, type 2 diabetesmellitus 12.5%. In accordance with the international criteria of TOAST (1993), pathogenetic mechanisms of the development of ischemic stroke have been determined in patients. Atherothrombotic stroke developed in 303 (45.7%), cardioembolic stroke in 185 (27.9%) patients, lacunar stroke in 167 (25.2%) patients, undefined genesis stroke in 8 (1.2%) patients.

The progression of neurological deficiency in ischemic strokiie is a bad prognostic factor.

Keywords: Stroke, acute period, clinical features, risk factors, aggravating factors of progression, pathogenetic subtypes of ischemic stroke.

Introduction

Stroke ranks second among deaths [1-4], is the main cause of morbidity in old age [2,3] and persistent disability leading to disability [3,4].

Many researchers suggest that the frequency of stroke increases rapidly with age and doubles in each decade after the age of 55 [3,4].

The literature shows that the incidence increases in older age groups, amounting to 670-970 cases per 100,000 people per year among persons aged 65-74 [3.4.5]. In this case, ischemic stroke under 35 years of age is more common in men than in women, and in older age groups, higher incidence is observed in women [3].

The problem of a stroke is one of priority the direction˘ social˘ politicians in Kazakhstan. According to official statistics of the Ministry of Health of the Republic of Kazakhstan, every year more than 40 thousand cases of stroke are registered in our country, of which 5 thousand die in the acute period of 1-7 days and another 5 thousand within 30 days after discharge home [7.8].

According to Akshulakov S.K. et all. (2018) [8] The mortality rate in hospital for treated cases with ONMK (hemorrhagic ischemic strokes) in the Republic of Kazakhstan for 12 months of 2017 amounted to 13.3%, there is an increase of 0.7% compared to 2016 data. Analysis of the sex and age structure of all deaths in hospital showed that men were 54% and women were 46%. The high level of fatality is observed in the age group from 41 to 70 years of age at 60% [8].

In randomized and prospective controlled clinical studies comparing hospital treatment of stroke with alternative service, it has been proved that treatment of stroke in specialized departments improves the end result-survival [9,10]. Progression of symptoms after arrival in hospital is a serious problem for the outcome of the disease [11,12,13]. Acute stroke refers to urgent, often critical conditions requiring urgent medical care, and priority actions taken by the first hours, which are fundamental for further repair of damaged brain tissue and favorable prognosis for the patient [13]. Positive dynamics are believed to be achieved by careful monitoring and maintenance of physiological homeostasis [13,14]. Early neurological deterioration is associated with

increased mortality within 7 days of stroke onset [15,16].

It should be noted that a number of physiological functions usually involved in cerebral metabolism (control of blood pressure, heart rate, temperature, glycemia) play a key role in the development of the ischemic process, and can also exacerbate the process of brain damage during the first hours of ischemic stroke [15,16].

On the basis of the above, we focused our study on neurological deterioration during the first 24-72 hours in patients with acute ischemic stroke admitted to hospital after the onset of the first symptoms, because this time is crucial for the possible progression of brain infarction.

This work is due to the lack of research in our country related to hospital fatality and the influence of factors on the early deterioration and progression of ischemic stroke in the acute period.

Research objective is: determining clinical deterioration and progression of ischemic stroke in the acute period of the first 24-72 hours.

Our tasks included identifying possible mechanisms and causes leading to ischemic stroke, as well as studying factors associated with progression and early neurological deterioration in the acute stroke phase.

Material and Methods

This prospective study was conducted for 10 months and included 663 patients with acute ischemic stroke who were hospitalized in the city clinical hospital № 7 of Almaty.

We compared two groups of patients with ischemic stroke: group-1 (n = 615) with a favorable prognosis, and group-2 with an unfavourable fatal outcome (n = 48) in the acute stroke period. Detailed clinical, laboratory and instrumental examination were carried out according to clinical protocols of the Republican Center for Health Development of the Ministry of Health of the Republic of Kazakhstan from 2016, as well as algorithms of actions and diagnostic criteria at the stage of reception rest, intensive care unit, neuroreanimation department.

We compared demographic characteristics, risk predictors, laboratory-instrumental examination data, comorbid diseases in patients diagnosed with ischemic stroke in the acute period of both groups.

The study was approved by an ethical committee. The diagnosis of stroke was based on ICD-10, WHO 1992.

Criteria for inclusion in the study

- Age of patients more than 25 years
- For the first time the arisen ischemic stroke aterotromboticheskу, kardioembolicheskу or lacunary (the 1st day), confirmed with neurovisualization methods.
- the informed consent to a research was signed by All patients or their lawful representatives.

Criteria for exclusion from study

- the Ischemic stroke with hemorrhagic treatment;
- Subarakhnoidalny hemorrhage.
- System diseases of connecting fabric;
- Existence in the anamnesis of oncological diseases,
- Existence in the anamnesis of tuberculosis,
- Existence in the anamnesis of alcohol or drug addiction, mental diseases;
- Thromboses of deep veins.
- Hereditary trombofiliya;
- Absence with own hand signed (or other independent witness in the absence of physical capacity of signing by the patient) forms of the informed consent.

Among our patients, only 1.04% of patients received treatment with recombinant tissue plasminogen activator (rtPA), of which a positive result was observed in only 3 cases. These patients were excluded from the study to ensure homogeneity of the group.

The diagnostic process was organized as much as possible in the reception department and included the following elements: collection of complaints and history, general physical examination, neurological examination with auxiliary evaluation scales, emergency laboratory (clinical, biochemical analyses, coagulogram) examinations, electrocardiogram (ECG) and X-ray examination of the chest, if necessary, consultations of specialists. Mandatory emergency specific studies: CT or MRI, transcranial duplex Doppler study.

According to the clinical protocol, mandatory scheduled examinations were carried out during the first 24 hours of hospitalization, if necessary - in dynamics.

In the work we used the following estimated scales of neurological status of patients:

- for assessment of level of consciousness used a scale of a coma of Glasgow,
- the neurologic status with assessment of neurologic deficiency was estimated on NIHSS scale
- the standardized screening testing of function of swallowing
- the modified scale of Renkina-MRS

Early progression of symptoms was defined as increasing the NIHSS score by two or more points (or stroke-related fatality) between arrival and day 3. According to the internationally accepted definetion, we investigated the deterioration within 24-72 hours after the arrival of one of the following NIHSS points: level of consciousness, swallowing, speech, movement of eyeballs, motor function of the arm and leg. Patients with early neurological impairment were compared to patients with unchanged or improved NIHSS scores [17].

Statistical methods

Data processing was done using Microsoft ® Office 's Excel 2016 Tabular Processor Data Analysis Suite, IBM SPSS Statistics version 23 for Windows.

Results and Discussion

Results and Discussion we did not observe sexual differrences among the hospitalized 663 patients due to ischemic stroke, there were 52.9% (351) of women and 47.1% (312) of men. The average age of patients was 62, 5 ± 5.6 years for men and 71, 4 ± 5.1 for women.

The diagram clearly shows the prevalence of ischemic stroke at the age of 60-80.

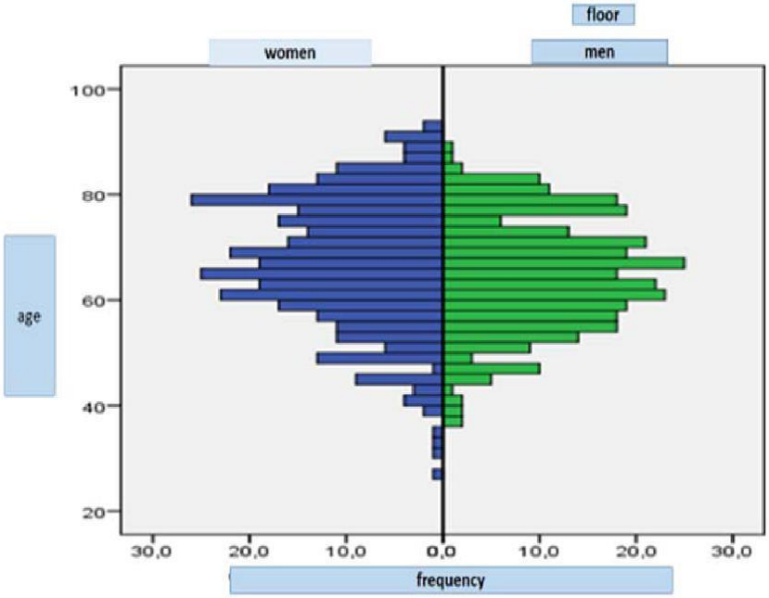

Figure 1 – Description of patients with ischemic stroke by sex and age. (Pareto's chart)

From the total number of patients with an ischemic stroke (663) almost at 7.23% (48) patients in the sharp period there came the lethal outcome, the number of men of 45.8% and women of 54.2%.

The most significant risk factors for ischemic stroke among 663 patients were arterial hypertension - 80.1%, chronic heart failure - 57.9%, ischemic heart disease - 25.5%, atrial fibrillation - 19.5%, type 2 diabetes mellitus - 12.5%. In history, 10.8% of patients had a myocardial infarction. In 8.7% of patients with stroke development was preceded by transitionally ischemic attack. Chronic obstructive pulmonary disease was detected in 1.7% of patients, chronic kidney disease in 0.5%.

In accordance with the international criteria of TOAST (1993), pathogenetic mechanisms for the development of ischemic stroke have been determined in patients. Atherotrombotic stroke developed in 303 (45.7%), cardioembolic stroke in 185 (27.9%) patients, lacunar stroke or small vascular disease in 167 (25.2%) patients, undefined genesis stroke in 8 (1.2%) patients.

In the analysis of neurological status of patients, various degrees of expression of motor and sensitive disorders, brain nerve lesions, symptoms of oral automatism, bulbar and pseudobulbar syndrome, dysphonia, dysarthria, speech disorders, gnosis and praxis disorders, depression, etc.

At the time of admission to hospital, almost 96.7% of patients in acute ischemic stroke had a disorder of consciousness from deafening to coma. The average Glasgow coma score was 10.9 ± 2.6 (Table 1).

Table 1 – Assessment of consciousness level in patients with different pathogenetic subtypes of ischemic stroke.

subtypes of an ischemic stroke	n=663	Scale of a coma of Glasgow Points + Averagedeviation	Standarderror	95% ConfidenceInterval for Average
Aterotrombotic	303	10±0,656	0,038	9-12 points
Cardioembolic	185	8 ±0,813	0,060	4-10 points
Lacunar	167	14±0,459	0,036	12-14 points
Uncertaingenesis	8	9±0,354	0,125	4-10 points
Intotal	663	11±0,827	0,032	9-13 points

The most severe patients with consciousness suppression at admission were identified with cardioembolic stroke (8 0.813) and uncertain pathogenetic subtype (9 0.354) points.

The determination of the severity of ischemic stroke conducted on the NIHSS score scale showed that the severity of neurological symptoms averaged 12.0 ± 6.8 points when admitted. Of the total number of patients with ischemic stroke, a mild degree of severity on the NIHSS scale was found in 57 (8.6%) patients, an average degree in 460 (69.4%), a severe degree in 88 (13.3%), an extremely severe degree of severity was found in 58 (8.7%) patients.

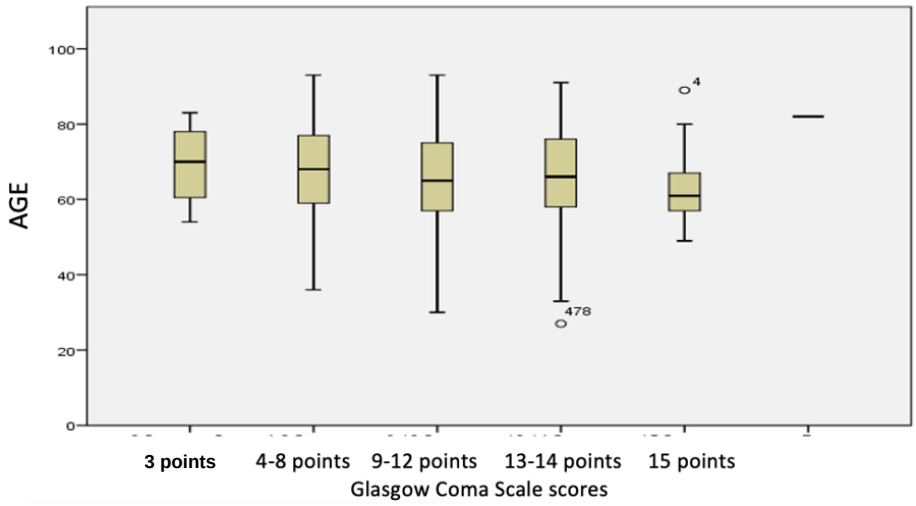

Figure 2 – Description of the level of consciousness of patients according to age (Drawer chart. IBM SPSS Statistics 23,0).

When admitted, patients with cardioembolic stroke were characterized by neurological disorders over the age of 65. Patients with lacunar stroke had less pronounced neurological disorders compared to patients in the other groups. But in lacunar stroke patients, motor aphasia was reliably more common, which exacerbated disability.

Analysis of early fatality showed that a statistically significant indicator in age characteristics among the examined group-2 patients was between 65 and 79 years of age ($p < 0.001$). Of these, 64.6% (31) died in the first day (up to 24 hours) of hospital stay. In 16.7% (8) patients mortality occurred in the following 3 days (72 hours), in 18.75% (9) during the first week. The average age of patients in group-2 with adverse mortality was 68, 3 ± 12.0, including in females 75, 6 ± 5.8 and in males 67, 6 ± 3.2.

At the time of admission, all patients in Group-2 with NIHSS mortality were rated as a severe stroke (21 to 42 points). We have obtained a statistically

significant difference in the NIHSS score when arriving in the groups being compared. It was in these patients in group-2 with an adverse outcome that the deterioration continued to increase.

Comparison of demographic and clinical data of both groups of patients shows that when comparing groups by age and sex were comparable. The median age of group-1 was 65.0 11.7 and group-2 was 68.3 12.0 years, respectively. Women in the 1-group had 53.8% in the second group 54.1%, men 46.1% and 45.8% respectively. In group 1, women under the age of 39 and over the age of 90 predominated.

Cardioembolicpathogenetic subtype of ischemic stroke occurred more frequently 56.3% (27) in group-2 with fatal outcome than in the first group - 25.7% (158), respectively ($p < 0.001$).

In group-2 with fatal outcome, atherotrombotic subtype of ischemic stroke was detected in 43.8% (21) and 45.9% (282) in the opposite group. Lacunar subtype 27.2% (167) and uncertain genesis 1.3% (8) is diagnosed in group-1 only.

Statistically significant progression of severity of neurological symptoms on Glasgow coma scale and NIHSS scale, and functional disorders on Rankin scale in the second group was revealed when comparing average values and standard deviations with the first ($p < 0.001$).

Higher scores of functional gross life disorders with a rating of 5 on the Rankin scale were mRS observed in 77.8% (35) of 2-group patients on admission, compared to 1-group where there were mild and moderate life limitations in 84.0% (517) patients. Only 15.9% (98) had a score of 4-5 ($p = 0.0001$).

An assessment of the severity of ischemic stroke on the NIHSS scale at admission, during the first hours after symptoms appeared, showed that the severity of neurological symptoms averaged 11.1 5.9 points in group-1 and 22.5 7.3 points in group-2s, respectively ($p = 0.0001$).

The progression of neurological symptoms is more evident in the group with cardioembolic stroke and atherotromboticpathogenetic subtypes of ischemic stroke (Figure 3).

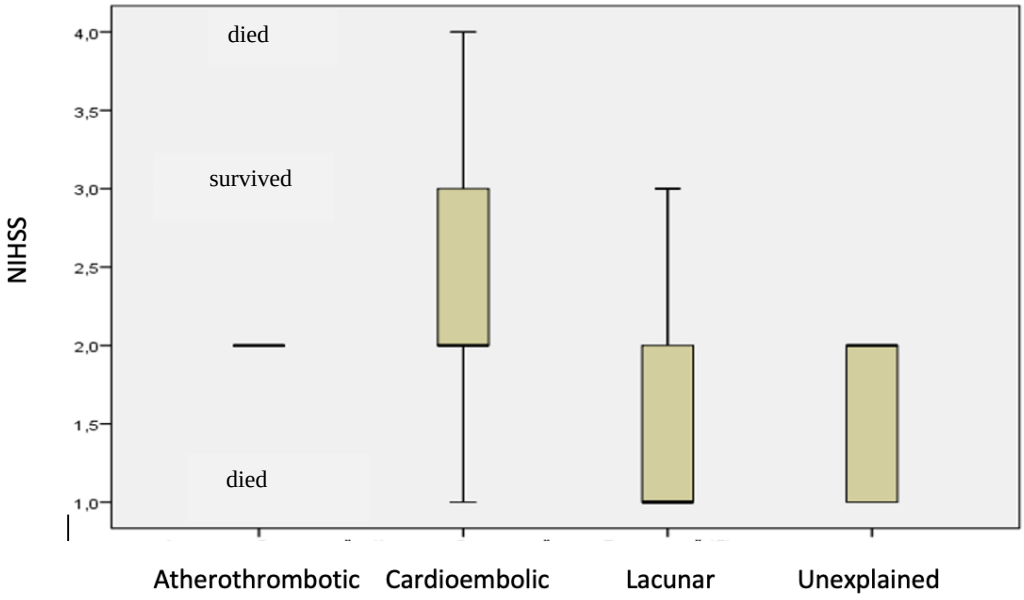

Figure 3 – Equalization of the degree of stroke severity on the NIHSS scale, in patients with different pathogenetic subtypes of ischemic stroke in both groups (Box diagram. IBM SPSS Statistics 23,0).

t seems essential to note that the results of our study confirmed the importance of assessing early neurological deterioration. After 24 hours in hospital, the NIHSS parameters increased to 11.5 5.6 and 26.5 7.0 points in the compared groups, respectively ($p < 0.001$).

The progressing course of a stroke which is followed by increase of neurologic symptomatology within 24-72 hours on NIHSS scale on ≥1 points was observed at 245 (36.8%), at 418 (63.1%) patients the neurologic status remained stabler in the same hours.

And among group-2 with a lethal outcome 42 (87.5%) patients had early neurologic deterioration (assessment of NIHSS of ≥1 point), within the first 24 hours after the beginning of a stroke, in opposite group 202 (32.8%) (p<0.001). The degree of progression on the NIHSS scale after 72 hours in hospital is significantly more often detected in the same group p < 0.001 (X^2 = -8.035).

When assessing neurological status in group-2, speech disorder, paresis 7 and 12 of a pair of cranial nerves were more often detected. It has been found that impairment of swallowing function is most common in patients of group-2 in 75% (36), in the opposite group 0.7% (4) p < 0.001 * *

When assessing neurological symptoms after 24-72 hours in hospital. In the second group, there was a significant increase in focal and global symptoms, including a change in consciousness (to deep coma level) p < 0.001, X^2 = -16.745 (equal).

Statistically significant indicators of adverse outcome were observed at delivery of patients later than 4 hours < 0.001. Late delivery of patients to hospital is associated with severe stroke, which is rated on the NIHSS scale as severe stroke (21 to 42 points).

Thus, the most important factors directly related to high mortality in acute ischemic stroke (24-72 hours) are (p < 0.001): the age of patients over 67 years. Later admission to hospital from the moment of stroke start 59.2% against 32.3% group with favorable outcome (p < 0.001).

Table 2 – Assessment of risk factors influence in acute period of ischemic stroke

RiskFactors	Group-1 (*n* = 615) *n* (%)	Group-2 (*n* =48) *n* (%)	X^2	*p-value*
Arterialhypertension	491 (79.8)	40 (83.3)	0.157	0.692
Chronicheartfailure	355 (57,7%)	29(60,4%)	0.163	0.704
Myocardialinfarction	65 (10,5)	7 (14,5)	0.192	0.685
Fibrillationofauricles	107 (17.4)	22 (45.8)	21.194 X^2	<0.001
Coronaryheartdisease	133 (21.6)	36 (75%)	64.004 X^2	<0.001
Type 2 diabetesmellitus	67 (10.9)	16 (33.3)	18.473 X^2	<0.001
Chronicobstructivepulmonarydisease	6 (1.0)	5 (10.4)		0.001**
Chronicdiseaseofkidneys	2 (0.3)	1 (2.1)		0.202**

* t-test
**Exact criterion of Fischer
Average - t-test comparison for independent groups (quantitative data), with variance inequality
Sharecomparison - X^2 test

is important to note that atrial fibrillation, ischemic heart disease, type 2 diabetes mellitus, chronic obstructive pulmonary disease were significantly more common (p < 0.001), CBP (p = 0.202 * *) causes of deterioration resulting in death (Table 2).

When comparing the incidence of risk factors, diastolic blood pressure was equally encountered in both groups without a significant difference in the group of survivors of 91.7 9.5mHg. Article and in the opposite group 93.1 16.0

Systolic blood pressure was significantly higher in the group with a fatal average of 172.7 44.27 mmHg.

We have identified a link between severe stroke (NIHSS 16-42 points) and high systolic blood pressure of more than 180 mm Hg in almost 50% of patients with death in the acute stroke period. When admitted to hospital in the same group of patients in 18.6% (9) cases, severe stroke was associated with low systolic blood pressure less than 90 mm Hg and low diastolic blood pressure less than 60 mm Hg.

In group-1, the average systolic blood pressure in the patients was 167.1 31.12 and in 57.7% of the patients, the systolic blood pressure was below 180 mm Hg.

We traced arterial hypertension in groups with different ischemic stroke subtypes to 95% confidence interval for mean value (Table 3).

Table 3 – Blood pressure at various pathogenetic subtypes of ischemic stroke

ABP	pathogenetic subtypes of ischemic stroke	n=663	BPmmHg. mean deviation ± standard error	(95%confidence interval)
CSBD	Aterotrombotic	303	158,45±26,387	155,47-161,43
	Cardioembolic	185	192,32±28,236	188,23-166,42
	Lacunar	166	201,57±17,649	198,86-204,27
	Uncertaingenesis	8	153,75±26,152	131,89-175,61
Intotal		663	167,49±31,950	165,05-169,93
DBP	Aterotrombotic	303	91,01±8,634	90,04-91,99
	Cardioembolic	185	89,43±13,056	87,54-91,33
	Lacunar	167	95,93±7,457	94,79-97,07
	Uncertaingenesis	8	92,50±8,864	85,09-99,91
Intotal		663	91,83±10,115	91,06-92,60

Patients with the highest and lowest blood pressure levels in the first 24 hours after a stroke were more likely to have early neurological impairment and lethal prognosis. Patients with systolic artery pressure at intake below 120 mm Hg had an increased risk of death compared to patients with AAD between 140-150 mm Hg.

There is also a link between high levels of systolic artel pressure at intake and mortality only in cardioembolic, and low numbers of systolic artel pressure at atherotrombotic subtypes of ischemic stroke.

According to the literature, the increase in blood pressure after ischemic stroke is assumed to be an adaptive response that helps to maintain cerebral blood flow and perfusion of the ischemic half, despite the loss of cerebral autoregulation.

Conversely, it is believed that an excessive increase in blood pressure can lead to neurological deterioration from the hemorrhagic transformation, especially in the presence of a damaged blood-brain barrier [10,13,14].

Thus, the aggravating factors of progression in the acute period of ischemic stroke-related to early mortality are concomitant diseases: uncontrolled arterial hypertension, atrial fibrillation, diabetes mellitus, chronic obstructive pulmonary disease.

All patients in the first day of the disease to verify the diagnosis were subjected to CT or MRI of the brain, at the same time the localization and size of the focus were taken into account (Table 3). It was established that the severity of ischemic stroke of the patient was in direct statistically significant relation with the size of the focus of the injury ($p < 0.001$).

Table 4 – Size of the focus in the groups being compared

Focus size	group 1 n=615	group 2 n=48	X^2	p-value
No heart attack, but clinical symptoms persist < 24 hours	34 (5.5%)	0 (0.0%)		
Infarction< 1.5 cmindiameter	209 (34.0%)	2 (4.2%)		<0.001
Infarction up to 1/3 of the territory of the middle cerebral artery or 1.5-5 cm in diameter	313 (50.9%)	3 (6.3%)		<0.001
Infarction 1/3-2/3 middle cerebral artery or > 5 cm, without the effect of occupied area	44 (7.2%)	20 (41.7%)	212.7 (X^2)	<0.001
Infarction 2/3 of middle cerebral artery territory or > 5 cm in diameter plus area effect	15 (2.4%)	23 (47.9%)		<0.001

Intracranial hypertension syndrome, expression of brain edema and stroke were objectified for MRI or CT at admission (within 24 hours) or during admission to hospital in 102 patients. Intracranial hypertension was observed at extensive strokes (the diameter of the focus was more than 5 cm). The large centers with a diameter more than 5 cm are revealed in the first group in 9.6% (59) cases from them 2.4% (15) with perifocal hypostasis, in group-2 with a lethal outcome of 89.6% (43), and with perifocal hypostasis was 23 (47.9%) patients (p <0.001). The centers of the average sizes also prevailed in the first group of 50.9% (313) against the second group of 6.3% (3). The lacunary centers <1.5 cm in the diameter are revealed in the first group in 34.0% (209). In the second group lacunar foci were found in 4.2% (2) both foci were dissected in the brain stem (p < 0.001).

Swelling of the brain, accompanied by compression of the brain stem, led to death.

Arterial hypertension and hemorrhagic transformation on MRI (in patients with cardioembolic stroke) contributed to the severity of the prognosis.

In the course of the study, we considered it important to carry out an analysis of the distribution of patients on the localization of the heart of infarction (MRI) and the localization of the affected arteries according to the UZDG, with the possibility to determine the dependence of the progression of neurological symptoms in the acute period of ischemic stroke. There were no significant differences in the degree of progression of neurological symptoms and localisation of the focus and basin of the affected arteries.

Cardioembolic stroke is a severe condition due to the large size of the heart attack, with a high level of intra-hospital fatality (56.3%) and significant neurological dysfunction with more severe life disorders with a rating of 5 on the Rankin mRS scale.

Brain swelling is the leading cause of early deterioration and death in patients with large heart attacks.

Our study found that dangerous for hospital mortality in acute period of ischemic stroke, brain swelling usually develops for the first seven days after hospitalization, but 37.5% (18) of patients died in the first 24 hours after symptoms appear.

As a result of the single-factor analysis, it was found that the most significant predictors of deterioration with an increased risk factor of hospital mortality in the acute period of ischemic stroke at admission are: impaired swallowing function, impaired breathing function (32 patients were on the spark ventilation of the lungs), depressed consciousness on the Glasgow coma scale up to 4-10 points. Patients with cardioembolic subtype under 67 years of age, with high systolic arderial pressure (above 160 mmHg), and patients with atherotrombotic ischemic stroke subtype over 65 years of age (p < 0.000) with low systolic blood pressure (below 118 mmHg).

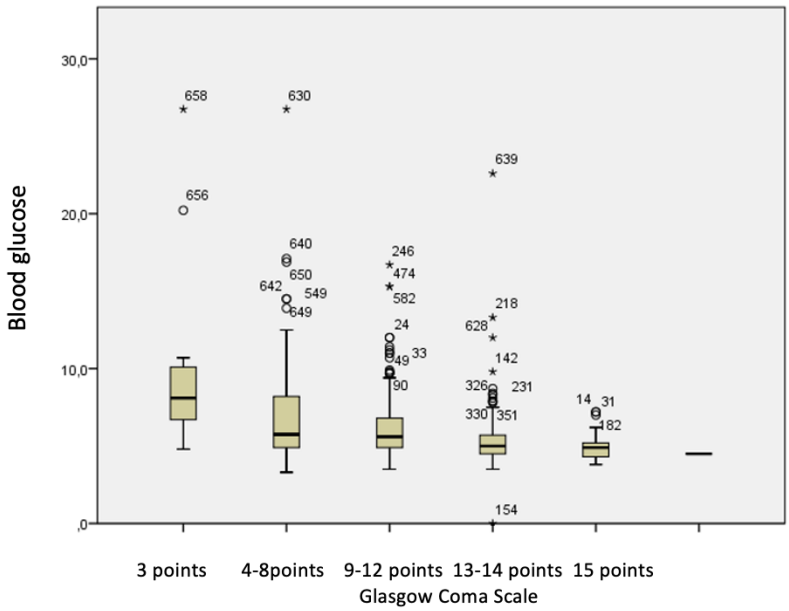

Figure 4 – Glucose levels in patients with different levels of consciousness (Drawer chart. IBM SPSS Statistics 23,0).

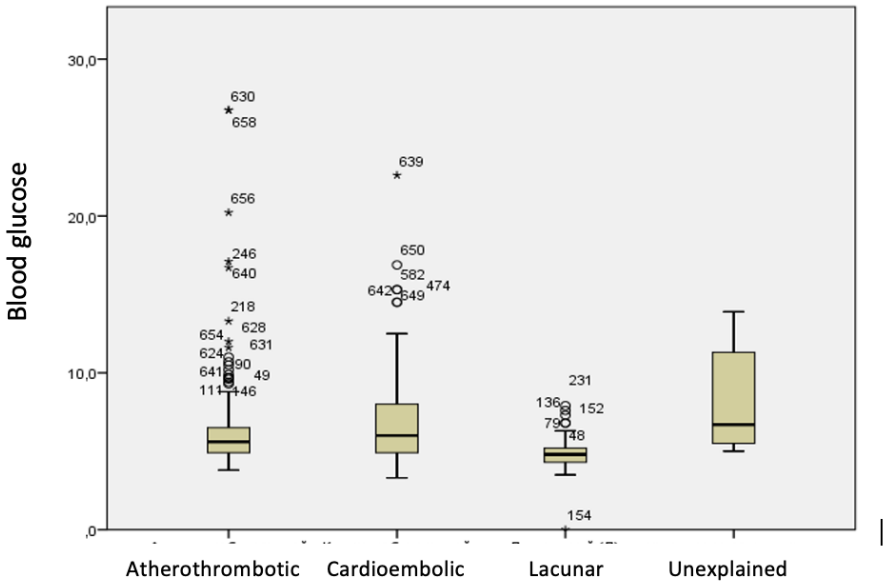

Figure 5 – Glucose levels in patients with different pathogenetic subtype of AI (Box diagram. IBM SPSS Statistics 23,0).

Data from laboratory indicators (general blood test, blood glucose and coagulogram) of patients of two observation groups showed that hyperglycemia was significantly more common in the second group than in the first group $p < 0.001$. Hyperglycemia is detected in acute period in patients with depressed consciousness by Glasgow coma scale up to 4-10 points, and reliably more often in patients with cardioembolic and atherothrombotic subtypes of ischemic stroke (Fig.4.5)

Conclusion

Thus, aggravating factors of progression in the acute period are: late delivery of patients to hospital, age over 65 years, swallowing disorders, concomitant diseases of atrial fibrylation, ischemic heart disease, chronic heart failure, chronic obstructive pulmonary disease, diabetes mellitus of the second type, chronic kidney disease, as well as hyperglycemia, size of infarction focus more than 5 cm in diameter with the effect of occupied area.

The progression of neurological deficiency in ischemic stroke is a poor prognostic factor. Worsening acute stroke in the early stages of its development 24-72 hours is common and has potentially serious consequences for the patient. Progression increases fatality and disability. Our study suggests that it is particularly important in the acute stroke period to draw the attention of medical staff to these factors in order to stabilize the progression of neurological symptoms.

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