

UDC 616.831-005.4-036.11

DOI: 10.22141/2224-0713.8.110.2019.187888

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Thalamic stroke outcomes: a prospective hospital-based cohort study

Abstract. Background. Stroke is the second-leading global cause of death behind heart disease, accounting for 11.8 % of total deaths worldwide. However, currently, there are not enough published prospective hospital-based cohort studies that report and analyze outcomes of thalamic stroke. The purpose of this study is to determine the features of acute thalamic stroke outcomes in a prospective hospital-based cohort study, providing a comprehensive clinical and neuroimaging analysis of the treatment results and assessing the outcomes of acute thalamic stroke. **Materials and methods.** We prospectively recruited 319 acute stroke patients, admitted within 24 hours from the onset of the stroke symptoms to the Neurological Center at an academic hospital (Oleksandrivska Clinical Hospital) in Kyiv, Ukraine. Comprehensive neurological, clinical, laboratory, ultrasound, and neuroimaging examination was performed in all patients. **Results.** MRI/CT-proven thalamic stroke was diagnosed in 34 (10.6 %) out of 319 persons, forming a study group: 22 patients (average age 61.9 ± 10.2 years) were diagnosed with an acute isolated ischemic thalamus infarction; 12 (average age 59.0 ± 9.6 years) — with an acute thalamic hemorrhage. Specific neurological outcomes of infarctions and hemorrhages in different thalamic territories were analyzed, compared, and described. **Keywords:** thalamus; stroke; thalamic stroke; ischemic stroke; hemorrhage; stroke outcomes

Introduction

Worldwide, stroke is one of the leading causes of death and long-term disability, being also a leading cause of dementia and depression [1–16]. Globally, one in four people over age of 25 will have a stroke in their lifetime [10, 17]. Over 116 million years of healthy life is lost each year due to stroke-related death and disabilities [10, 18]. There are over 13.7 million new strokes each year [10, 19]. On average, stroke occurs 15 years earlier in — and causes more deaths of — people living in low- and middle-income countries, when compared to those in high-income countries [8, 20–22].

Thalamic strokes are not rare, accounting for approximately 11 to 23–25 % of cases of all posterior circulation strokes, especially in combination with damage to other structures [23–25]. However, currently, there are not

enough published prospective hospital-based cohort studies that report and analyze acute thalamic stroke outcomes [23, 25–31].

The outcomes of thalamic strokes depend on a variety of often interacting factors. The most important factors are the type of stroke, its severity, length of stay in a hospital, and a time to the first aid treatment from the moment the disease developed, the volume and intensity of provided treatment, patient's age, and the underlying somatic background that causes a stroke [30]. Inevitably, the legitimate question arises — what is the role of each of these factors in the complex process of patient recovery? Given all this, we performed a comprehensive clinical and neuroimaging analysis of the treatment results and assessed the outcome of the disease in 34 patients with thalamic stroke: 22 persons with isolated thalamus infarction and 12 — with thalamic hemorrhage.

The purpose: to determine the features of acute thalamic stroke outcomes in a prospective hospital-based cohort study, providing a comprehensive clinical and neuroimaging analysis of the treatment results and assessing the outcome of the acute thalamic stroke.

Materials and methods

The materials and methods of this prospective hospital-based cohort study of acute ischemic stroke patients were reported previously [29–31]. Briefly, all study participants were admitted to the Neurological Center of Oleksandrivska Clinical Hospital (Kyiv, Ukraine). The Neurological Center consists of an admission department, clinical department of neurology, department of cerebrovascular pathology with intensive care/stroke unit, and a research department of neurology. Patients were admitted to the hospital within the first 24 h since the first stroke symptoms occurred. All stroke cases were reviewed by at least two board-certified neurologists with training in cerebrovascular diseases. Clinical history, 12-lead electrocardiogram, blood testing, carotid ultrasound, head computed tomography and/or brain magnetic resonance imaging (MRI) were obtained for all study participants. Stroke was defined according to criteria of the World Health Organization, American Heart Association/American Stroke Association guidelines for adult stroke, and was confirmed by neuroimaging [32, 33]. The etiology of stroke was classified according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria [34]. The National Institutes of Health Stroke Scale (NIHSS), the Modified Rankin Scale (mRS), the Barthel index (BI), and the Charlson Comorbidity Index (CCI) were determined for all participants. Secondary stroke prevention was prescribed according to the American Heart Association/American Stroke Association and the European Stroke Organisation Guidelines, immediately after the stroke diagnosis was made [35–41]. Stroke education programs were provided to all study participants [11, 16, 30, 42–45].

Parametric and non-parametric statistic methods were applied. The log-rank test was used for univariate comparisons of event-free survival between groups. A two-sided $p < 0.05$ was considered significant for all analyses. All statistical analyses were performed using IBM SPSS Statistics Version 22.

Results and discussion

In total, 319 adult patients with acute MRI/CT-proven stroke were screened: 204 (63.9 %) persons were diagnosed with an acute posterior circulation ischemic stroke, and 115 (36.1 %) had an intracerebral hemorrhage. Thalamic stroke was detected in 34 (10.6 %) out of 319 patients, forming a study group:

— 22 persons (12 men, 10 women aged 50 to 84 years, average age 61.9 ± 10.2 years) were diagnosed with an acute isolated thalamus infarction;

— 12 individuals (5 men, 7 women aged 57–75 years, average age 59.0 ± 9.6 years) had thalamic hemorrhage.

The outcomes of isolated ischemic thalamic stroke

The analysis of neurological deficit, according to the NIHSS, in patients with isolated thalamic stroke showed that in lacunar infarction it corresponded to a mild stroke

(2 to 8 points; mean \pm standard deviation was 4.14 ± 0.24 points), and in non-lacunar infarction — to a moderate stroke (9 to 12 points; mean \pm standard deviation of 10.7 ± 0.24 points). Only one patient with bilateral thalamic stroke had a very severe neurological deficit (17 points).

Taking into account the indicator of disability, according to the Modified Rankin Scale, the distribution was as follows:

— 10 patients showed mild disability, maintaining the ability to walk without assistance (mRS score of 3 points);

— 8 persons had moderately severe disability, being unable to walk and cope without assistance (mRS score of 4 points);

— in 4 individuals, the degree of disability was severe (mRS of 5 points).

Paramedian and central localization of thalamic stroke caused the most severe disability.

The outcomes of lacunar and non-lacunar isolated thalamic stroke

The outcomes of lacunar and non-lacunar isolated thalamic stroke were not the same.

In 4 patients with lacunar infarction, a complete regression of neurological symptoms (neurological recovery) occurred on the 7th day, and in 3 more patients — on the 14th day of treatment (on average 10.30 ± 0.98 days), being considered as a type of minor ischemic stroke. The speed of neurological recovery in patients with non-lacunar strokes depended on the location and the volume of thalamic infarction, the level of patient's consciousness at admission, the severity of the stroke, and associated diseases. The best short-term prognosis was revealed in patients with isolated infarction of the lower lateral and posterolateral thalamic territory, the worst — in patients with infarction in the paramedian and central vascular territory, especially in cases with persistent cognitive and neuropsychological manifestations.

The prognosis for isolated *non-lacunar* thalamic infarctions on the 21st day of treatment was favorable (mRS score ≤ 2 points) in 12 (80.0 %) patients, unfavorable (mRS score of 3 to 4 points) — in 3 (20.0 %). Complete restoration of neurological functions (mRS score ≤ 2 points, BI ≥ 95 points) occurred in 5 (33.3 %) patients (a type of minor ischemic stroke); moderate recovery (mRS score of ≤ 2 points, BI ≥ 80 points) — in 7 (46.7 %) persons; moderately severe degree of disability (mRS score > 2 points, BI < 80 points) persisted in 3 (20.0 %) cases. The severe outcomes in these 3 patients were determined not only by the localization of the stroke foci, but also by the Charlson Comorbidity Index (score ≥ 3 points) that reflects the number and severity of concomitant diseases (cardiovascular, endocrine, lung, and kidney) [46].

Very good results were achieved on the 90th day after thalamic stroke: a favorable functional outcome was observed in 14 (93.3 %) patients. Among them, complete neurological recovery occurred in 8 (53.3 %) patients, moderate — in 6 (40.0 %) patients, and only 1 patient with bilateral thalamic infarction had moderately severe disability (mRS score of 4 points). There were no cases of early death (in the first 2 weeks) and death in the remote period (after 2 weeks). How-

ever, one patient with bilateral infarction in the paramedian territories with thalamic dementia died in the long-term period after a stroke (2 years later).

Hemorrhagic thalamic stroke outcomes

Underlying neurological deficit, according to the NIHSS, in patients with thalamic hemorrhage corresponded to a moderate stroke (10–12 points) in 3 cases, to severe stroke (13–15 points) — in 6, to very severe (16–17 points) — in 3. The distribution of patients according to the indicator of disability by the Modified Rankin Scale was as follows:

— in 9 persons, moderately severe disability was revealed; they were unable to walk and self-care without assistance (mRS score of 4 points);

— in 3 cases, the degree of disability was severe (mRS score of 5 points).

The most severe disability was noted in patients with compression of the following anatomical formations of the brain that are adjacent to the thalamus by the hemorrhagic masses and perifocal edema: the internal capsule, the dorsal midbrain, and with the expansion of hemorrhage in the medial direction.

Due to intensive therapy and early rehabilitation measures, on the 21st day of observation, high treatment efficiency was registered in 3 (25.0 %) patients (2 points) with a hematoma volume of 10 to 15 cm³. Moderate efficacy was observed in 4 (33.3 %) cases (mRS score ≤ 3 points) with volumes of thalamic hemorrhage of 15–30 cm³. In 3 (25.0%) persons with a hematoma volume of more than 30 cm³ and severe stroke course, the severe disability (mRS score of 4 points) persisted. Cases of early death (in the first 2 weeks) were noted in 2 (16.7 %) patients admitted in a coma, with a hematoma volume of more than 30 cm³ located medially, with a bleeding into the ventricles of the brain.

Positive results were achieved on the 90th day of observation — a favorable outcome was observed in 7 (70.0 %) patients: complete neurological recovery was observed in 4 (40.0 %) of them, moderate — in 3 (30.0 %). In 2 (20.0 %) persons, moderate disability (mRS score of > 2 points) persisted, and only 1 patient had moderately severe disability (mRS score of 4 points).

Summarizing outcomes of thalamic strokes, the following points can be made:

1. The outcome and the speed of neurological recovery in patients with acute thalamic stroke depend on the type of stroke, length of stay in the hospital, and the time from the stroke manifestation to the treatment.

2. The severe degree of impaired consciousness (e.g., stupor, coma) at the time of hospitalization is a prognostically unfavorable factor for thalamic strokes and significantly worsens the outcome of disease.

3. The severity of neurological deficit at the beginning of treatment, the clinical course, and the outcome of a thalamic stroke depend on the topographic location and the size of the infarction. The best short-term (on the 21st day) and long-term (on the 90th day) outcomes were observed in patients with isolated infarction of the lower lateral and posterior lateral vascular territory, the worst — in patients with infarction of the paramedian and central vascular territory.

4. The volume of stroke hematoma and its early increase negatively affect functional recovery: more favorable clinical course during the therapy and better outcomes were noted with hematoma volumes of 10–15 cm³; the volume of more than 15–30 cm³ complicates the clinical course of the stroke, increases the severity of cerebral, neuropsychological, and focal neurological symptoms, worsens the functional outcome of the disease; 2 patients admitted in a coma and with a hematoma volume of more than 30 cm³ located medially in the thalamus had a fatal outcome in the first week after a stroke as a result of bleeding into the ventricles of the brain.

Conclusions

The results of our observations on treatment effectiveness in patients with thalamic stroke in the specialized neurological center undoubtedly confirm statements regarding the unconditional hospitalization of all patients with acute stroke directly to the stroke department. In many European countries, stroke units are formed mainly in the neurological departments [47]. Neurologists should play a key role in the treatment of cerebral stroke without diminishing the importance of collaborative experience in this field (consultation of a neurosurgeon, cardiologist).

Conflicts of interests. Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

Author contributions: *S.M. Vynychuk* — study concept and design, statistical analysis, interpretation of data, literature review, critical revision of the manuscript for important intellectual content; *M.M. Prokopiv* — study concept and design, data acquisition, statistical analysis, interpretation of data, literature review, critical revision of the manuscript for important intellectual content; *L.M. Trepet* — study design, data acquisition, statistical analysis, interpretation of data; *O.Ye. Fartushna* — study concept and design, literature review, statistical analysis, interpretation of data, article concept and design, drafting the article, critical revision of the manuscript for important intellectual content.

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Received 27.09.2019

Revised 10.10.2019

Accepted 23.10.2019 ■

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Наслідки таламічних інсультів: проспективне клінічне когортне дослідження

Резюме. Актуальність. Інсульт є другою за частотою причиною смертності у світі, поступаючись лише смертності від серцево-судинних захворювань. Проте на сьогодні опубліковано недостатньо проспективних клінічних досліджень, у яких описані й проаналізовані клінічні характеристики та наслідки таламічних інсультів. **Мета дослідження:** визначити особливості наслідків гострого таламічного інсульту в проспективному клінічному когортному дослідженні, забезпечивши всебічний клінічний і нейровізуалізаційний аналіз результатів лікування та наслідків гострого таламічного інсульту. **Матеріали та методи.** Ми провели проспективне клінічне когортне дослідження 319 пацієнтів із гострим ішемічним інсультом, які надійшли до неврологічного центру Олександрів-

ської клінічної лікарні (м. Київ, Україна) протягом перших 24 годин з моменту розвитку хвороби. Усі пацієнти пройшли комплексне клініко-неврологічне, лабораторне, ультразвукове та нейровізуалізаційне обстеження. **Результати.** Серед 319 хворих із гострим ішемічним інсультом нейровізуалізаційно підтверджений таламічний інсульт діагностовано в 34 (10,6 %) осіб: у 22 (середній вік $61,9 \pm 10,2$ року) виявлено гострий ізолюваний інфаркт таламусу, а в 12 пацієнтів (середній вік $59,0 \pm 9,6$ року) — гострий таламічний крововилив. Описані, проаналізовані та порівняні клінічні наслідки інфарктів різних таламічних територій.

Ключові слова: таламус; інсульт; таламічний інсульт; ішемічний інсульт; крововилив; наслідки інсульту

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Исходы таламических инсультов: проспективное клиническое когортное исследование

Резюме. Актуальность. Инсульт является второй по частоте причиной смертности в мире, уступая лишь смертности от сердечно-сосудистых заболеваний. Тем не менее в настоящее время опубликовано недостаточно проспективных клинических когортных исследований, в которых описаны и проанализированы клинические характеристики и последствия таламических инсультов. **Цель исследования:** определить особенности исходов острого таламического инсульта в проспективном клиническом когортном исследовании, обеспечить всесторонний клинический и нейровизуализационный анализ результатов лечения и исходов острого таламического инсульта. **Материалы и методы.** Мы провели проспективное клиническое когортное исследование 319 пациентов с острым ишемическим инсультом, поступивших в неврологический центр Александровской кли-

нической больницы (г. Киев, Украина) в течение первых 24 часов с момента развития болезни. Все пациенты прошли комплексное клинико-неврологическое, лабораторное, ультразвуковое и нейровизуализационное обследование. **Результаты.** Среди 319 больных с острым ишемическим инсультом нейровизуализационно подтвержденный таламический инсульт диагностирован у 34 (10,6 %) пациентов: у 22 (средний возраст $61,9 \pm 10,2$ года) выявлен острый изолированный инфаркт таламуса, а у 12 пациентов (средний возраст $59,0 \pm 9,6$ года) — острое таламическое кровоизлияние. Описаны, проанализированы и сравнены клинические последствия инфарктов различных таламических территорий.

Ключевые слова: таламус; инсульт; таламический инсульт; ишемический инсульт; кровоизлияние; последствия инсульта