

Analysis of thrombolytic therapy in ischemic stroke treatment

Analiza przebiegu leczenia udaru niedokrwiennego mózgu z wykorzystaniem trombolizy

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ABSTRACT

INTRODUCTION: Stroke is a widespread disease in the community. For this reason, its treatment is a major challenge for medical staff. Currently one of the most effective methods of treatment of ischemic stroke is thrombolysis.

MATERIALS AND METHODS: The medical records of 91 patients diagnosed with acute ischemic stroke treated with thrombolysis and hospitalized in the Lower Silesian Specialist Hospital in Wrocław in the years 2007–2013 have been analyzed for the study. Statistical analysis of the material was performed.

RESULTS: The analysis of the studied material showed that:

- only a small number of patients with ischemic stroke are treated with thrombolysis
- the largest group of patients were individuals who at the stage of qualification for the treatment scored 6 points in The National Institutes of Health Stroke Scale, or NIH Stroke Scale (NIHSS)
- neurological deficits were resolved in 46% of patients within 24 hours after thrombolytic therapy
- an average point value according to the modified Rankin scale assessing the patients' level of disability was 1.08 after completion of hospitalization.

CONCLUSIONS:

1. The neurological condition of most patients during thrombolytic treatment improved significantly during the administration of rt-PA.
2. After the hospitalization process, 6 out of 10 patients demonstrated full self-reliance.
3. Active involvement of the patient and the family in the therapeutic process enhances patient autonomy.
4. There was no record of a worse health condition following the treatment.
5. Thrombolytic therapy is an effective treatment for ischemic stroke.

KEY WORDS

treatment, ischemic stroke, thrombolysis

STRESZCZENIE

WSTĘP: Udar mózgu jest szeroko rozpowszechnionym schorzeniem w społeczeństwie, dlatego jego leczenie stanowi poważne wyzwanie dla personelu medycznego. Obecnie jedną z najskuteczniejszych metod leczenia ostrej fazy udaru niedokrwiennego jest tromboliza.

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MATERIAŁ I METODY: Analizie poddano dokumentację medyczną 91 pacjentów ze zdiagnozowanym udarem niedokrwiennym mózgu, leczonych z wykorzystaniem trombolizy, hospitalizowanych w Dolnośląskim Szpitalu Specjalistycznym we Wrocławiu w latach 2007–2013. Materiał poddano analizie statystycznej.

WYNIKI: Analiza materiału badawczego wykazała, iż:

- tylko niewielki odsetek chorych z udarem niedokrwiennym jest leczony za pomocą trombolizy,
- wśród badanych najliczniejszą grupę stanowiły osoby, które na etapie kwalifikacji do leczenia uzyskały 6 pkt w skali NIHSS,
- w pierwszej dobie po leczeniu trombolitycznym stwierdzono u 46% pacjentów całkowite wycofanie się deficytów neurologicznych,
- po zakończonej hospitalizacji średnia liczba punktów według zmodyfikowanej skali Rankina, oceniająca stopień niesprawność pacjentów, wyniosła 1.08.

WNIOSKI:

1. Stan neurologiczny większości pacjentów leczonych trombolitycznie uległ znacznej poprawie w trakcie podawania leku Actylise.
2. Po zakończonej hospitalizacji pełny zakres samodzielności odzyskało 6 na 10 pacjentów.
3. Aktywny udział chorego i rodziny w procesie terapeutycznym zwiększa samodzielność pacjenta.
4. Nie stwierdzono przypadków pogorszenia stanu zdrowia w wyniku leczenia.
5. Leczenie trombolityczne jest skuteczną metodą leczenia udaru niedokrwiennego mózgu.

SŁOWA KLUCZOWE

leczenie, udar mózgu, tromboliza

INTRODUCTION

Stroke is a life threatening condition, which is one of the major causes of death and disability worldwide. It is a huge medical, social and economic issue [1]. Currently, one of the treatment methods in patients with ischemic stroke is systemic thrombolysis (intravenous) using recombinant tissue-type plasminogen activator (rt-PA) (in Poland used officially since 2003, although the first successful thrombolysis procedure was already introduced in 2000). Fibrinolytic therapy on a large scale has been implemented within the framework of the National Programme for the Prevention and Treatment of Cardiovascular Diseases (POLKARD), and since 2010 rt-PA has been used in the extended time window – up to 4.5 hours (270 minutes after the onset of symptoms) [2].

Due to the narrow therapeutic window, the following are crucial: pre-hospital actions involving rapid diagnosis of disease symptoms by people from the immediate surroundings of the patient, first aid and calling a qualified medical rescue team, and then rapid transport of the patient to a center with a stroke unit performing thrombolysis [3]. Only if the above series of actions from the so-called chain of survival occur, it will raise the percentage of patients with stroke successfully treated with thrombolysis, with future chances of achieving the greatest efficiency and independence.

The aim of the study is a retrospective analysis of thrombolytic treatment of ischemic stroke, with particular emphasis on how the treatment affected the general condition and neurological condition of patients.

MATERIAL AND METHODS

A retrospective analysis of the medical records included 91 patients diagnosed with ischemic stroke and treated with the use of thrombolysis in the Department of Neurology with a stroke unit in the T. Marciniak Lower Silesian Specialist Hospital between 2007–2013. The analysis included:

- medical documentation of patients: medical history, special care forms, temperature forms, doctor's orders, medical consultations;
- documentation of nursing care: nursing procedures history, current nursing care health assessment forms, nursing care forms;
- digital documents: statistical data of patients with confirmed ischemic stroke under hospital treatment in 2007–2013, including patients scheduled for treatment with the use of thrombolysis.

Scheduling patients for thrombolytic therapy, drug dosage and monitoring patient condition during treatment was conducted according to the guidelines from the POLKARD programme. The analysis included patient age, sex, time from the onset of symptoms to start of treatment, the dynamics of the neurological condition during treatment and after its completion. The level of patient disability at discharge was assessed using the modified Rankin scale. The material was processed using Microsoft Office 2007. Statistical analysis was performed using the statistical software package STATISTICA v. 8 GB and MedCalc program. The normality of the variables distribution was assessed using the Shapiro-Wilk test. Analysis of the studied material included the following tests:

T-student, chi-square, Mann-Whitney U and Fisher at the significance level $p < 0.05$.

RESULTS

In 2007–2013, 3267 patients were hospitalized in the T. Marciniak Lower Silesian Specialist Hospital for ischemic stroke, most of them in 2013 – 595 patients. However, thrombolytic therapy was performed only in 91 cases – 48 women and 43 men. Detailed data are presented in Table I.

Table I. Number of patients hospitalized for ischemic stroke, including those treated with thrombolysis

Tabela I. Liczba pacjentów hospitalizowanych z powodu udaru niedokrwinnego mózgu, w tym leczonych trombolitycznie

Year	Patients hospitalized for ischemic stroke		Patients treated with thrombolysis	
	N	%	n	%
2007	348	10	3	3
2008	360	11	3	3
2009	432	13	2	2
2010	510	16	8	9
2011	495	15	17	19
2012	527	17	25	28
2013	595	18	33	36
Total	3267	100	91	100

The largest group of patients eligible for thrombolytic treatment included patients from the age group 52–59 years of age – 30%. Detailed data are presented in Table II.

Table II. Age of patients treated with thrombolysis

Tabela II. Wiek pacjentów leczonych trombolitycznie

Age	n	%
30–36	10	11
46–50	15	16
52–59	27	30
60–66	20	22
74–78	11	12
85–90	8	9
Total	91	100

The majority of patients treated with thrombolysis were professionally active people (65%), while every fifth respondent was retired, and every sixth a pensioner. The stroke incident occurred mostly during some activity (69%), only in 31% of cases did the incident take place during resting.

The vast majority of patients (79%) experienced symptoms that might indicate a potential vascular incident, prior to the onset of stroke. The most common symptoms were severe headache (33%), hypertensive crisis (30%) and numbness in the upper limbs (11%). The analysis showed that gender does not determine the type of symptoms that may forerun a stroke (there is no statistically significant relation-

ship between the variables – Fisher's exact test: $p = 0.3447$). The largest group of analyzed cases consisted of patients whose time from the onset of stroke symptoms to treatment was up to 3 hours (42%). Only 30% of the patients had treatment started within 2.5 hours of symptom onset, 16% underwent treatment up to 3.5 hours from the onset of symptoms, and in the case of 12% of patients, treatment was administered up to 4 hours.

The analyzed group of patients at the time of admission to the hospital presented numerous neurological deficits of varying degrees of severity. Detailed data are presented in Fig. 1. All the patients were diagnosed with paresis in different places and of different intensity. However, more than half of the patients did not experience any problems with consciousness, and contact was logical. Statistical analysis showed that men more often than women at the time of qualification for treatment were conscious and in logical contact (chi-square test was performed with Yates correction: $X^2 = 4.6321$, $df = 1$, $p = 0.03138$). It was also tested whether gender has an impact on the occurrence of certain neurological deficits in patients scheduled for thrombolytic therapy. Statistical analysis showed that only eyeball movement in one direction was more frequent in women (chi-square test performed with Yates correction: $X^2 = 4.859$, $df = 1$, $p = 0.0275$). Gender does not have any significant impact on other types of deficits.

The CT scan of the head made before administering thrombolytic therapy showed recent ischemic lesions in 54% of patients, 11% displayed no vasogenic changes, and a history of vasogenic changes was observed in 35% of patients. Among the patients, the largest group comprise people that at the stage of qualification for the treatment received 6 points on NIHSS (minimum value). The highest scores of 17 and 20 points (20 – maximum value) on NIHSS was received by 20% of patients. The average number of points was 10.03. The standard deviation was 4.47. Detailed data are presented in Table III.

The non-parametric Kruskal-Wallis test was used (as the condition of the variable distribution normality in the studied groups was not fulfilled) to examine whether there is a dependence between the time passed since the onset of symptoms to thrombolytic therapy and neurological condition of patients, according to NIHSS at the stage of qualification for thrombolytic treatment. Statistical analysis showed that there is a statistically significant dependence between the time passed from the onset of symptoms to thrombolytic therapy and neurological condition of patients on NIHSS at the stage of qualification for thrombolytic treatment – patients with a shorter time gap from the onset of symptoms until the initiation of treatment, have a smaller neurological deficit ($\chi^2 = 9.2928$, $df = 3$, $p = 0.02564$).

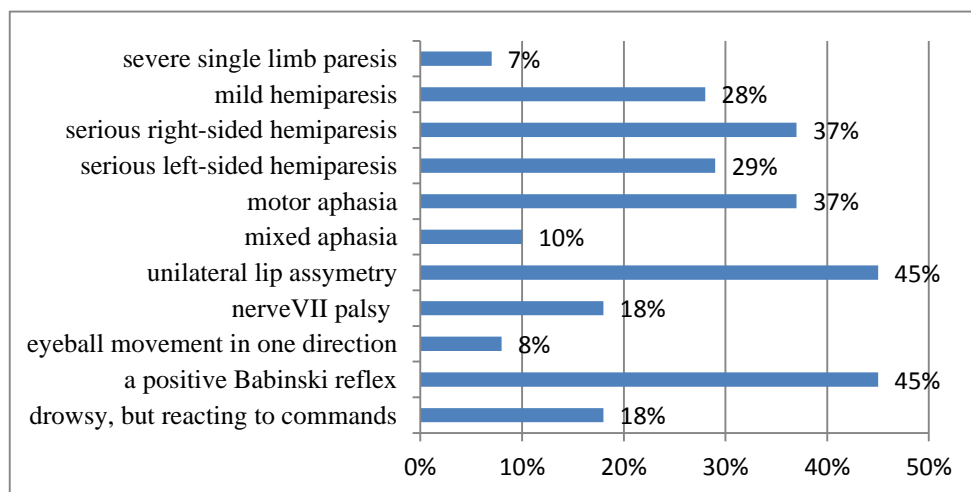


Fig. 1. Neurological deficits in patients scheduled for thrombolytic therapy.

Ryc. 1. Deficyty neurologiczne u pacjentów zakwalifikowanych do leczenia trombolitycznego.

Table III. Number of points obtained by patients on NIHSS at stage of qualifying for thrombolysis and time from onset of stroke symptoms
Tabela III. Liczba punktów uzyskanych przez chorych w skali NIHSS na etapie kwalifikowania do trombolizy a czas od wystąpienia objawów udaru

Number of points on NIHSS	Up to 2.5 hours	Up to 3 hours	Up to 3.5 hours	Up to 4 hours
6	40.74	56.76	13.33	25
10	25.93	16.22	33.33	41.67
11	7.41	21.62	20	16.67
17	18.52	2.7	13.33	0
20	7.41	2.7	20	16.67
Total	100	100	100	100

At the stage of qualifying for thrombolytic therapy, the largest group consisted of patients with a blood pressure remaining at 150/90 mmHg level, while one in five patients was diagnosed with high blood pressure (about 220/110 mmHg), which required administering proper medications to lower blood pressure. During administration of the drug, the largest group of patients were those whose blood pressure remained at 150/90 mmHg. In contrast, only 10% of patients had a blood pressure of 220/110 mmHg. In subsequent days of hospitalization, blood pressure increased incidentally to 170/100 mmHg in 35% of patients. However, in 12% of patients blood pressure went up to 220/110 mmHg. Statistical analysis showed that gender had no significant impact on blood pressure levels either at the qualification stage or during treatment.

In the course of administering rt-PA, 27% of patients experienced a reversal of speech disorders. Moreover, in 27% of patients paresis diminished, while in 11% of other patients other symptoms reversed. However, 24% of patients had a temporary reversal of symptoms. No improvement was observed in 11% of pa-

tients. However, on the first day after thrombolytic therapy 46% of patients observed complete reversal of neurological deficits. No improvement was observed in one out of four patients, while in 30% of patients partial improvement of paresis was noticed. Statistical analysis showed that the neurological deficit in patients with ischemic stroke on the first day after treatment with thrombolysis reversed faster in the case of women (Fisher's exact test: $p = 0.04246$). Patients who underwent thrombolysis were mainly hospitalized from 11 to 15 days (60%). Unfortunately, in 13% of patients the hospital stay was extended up to 30 days. Statistical analysis showed that the gender of the patient had no significant impact on the duration of hospitalization (chi-square test: $X^2 = 3.2714$, $df = 2$, $p = 0.1948$).

After hospitalization, patient disability was assessed according to the modified Rankin scale (Table IV) [4] taking into account gender, duration of hospitalization and the involvement of the patient and family in the process of health education which aimed at changing their lifestyle.

Table IV. Rankin Scale [4]

Tabela IV. Skala Rankina

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms, able to carry out all usual duties and activities
2	Slight disability, unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability, requiring some help, but able to walk without assistance
4	Moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability, bedridden, incontinent and requiring constant nursing care and attention
6	Dead

The analysis of the study material shows that the percentage of patients:

- fully able-bodied or with a small disability (0–1 pts. Rankin scale) was 62%,
- with moderate disability (2–3 pts. on Rankin scale) was 13%,
- with a significant disability (4 pts. on Rankin scale) was 15%.

The average point value on the Rankin scale for all the patients at discharge was 1.08 (standard deviation 1.42, min 0, max 4). Statistical analysis showed that gender has no significant effect on the extent of patient disability ($\chi^2 = 0.2981$, $df = 2$, $p = 0.8615$)

Table V. Degree of patient disability on Rankin scale and vs. time of hospitalization

Tabela V. Zakres niesprawności pacjenta według skali Rankina a czas hospitalizacji

Degree of disability on Rankin scale	Hospitalization time		
	from 7 to 10 days (%)	from 11 to 15 days (%)	from 16 to 30 days (%)
0	92	40.74	0
1	8	42.59	0
3	0	12.96	25
4	0	3.7	75

In order to examine whether there is a relationship between the time of hospitalization and the extent of disability after treatment (Table V), the possibility of using the parametric test was checked. Since the condition of normal distribution of the variables in the study groups was not fulfilled (the Shapiro-Wilk test was used) the non-parametric Kruskal-Wallis test was done. It has been shown that there is a statistically significant relationship between the duration of hospitalization and the extent of disability according to the Rankin scale after the completion of treatment ($\chi^2 = 45.2833$, $df = 2$, $p = 1.468 \cdot 10^{-10}$) – i.e., patients who are more self-reliant go through shorter hospitalization.

Table VI. Degree of disability on Rankin scale and level of engagement of patient and family in educational process

Tabela VI. Zakres niesprawności pacjenta według skali Rankina a stopień zaangażowania pacjenta i jego rodziny w proces edukacji

Degree of disability on Rankin scale	Degree of family and patient engagement in educational process		
	no interest on family side (%)	no interest on patient side (%)	engagement and cooperation (%)
0	16.67	0	68.85
1	61.11	66.67	9.84
3	16.67	16.67	8.2
4	5.56	16.67	13.11

How participation and involvement of the patient and his family in health education aimed at changing their lifestyle (promoting a healthy lifestyle) affected the degree of patient disability assessed on the Rankin scale (Table VI) was also studied. For this purpose, the non-parametric Kruskal-Wallis test was used

(since the condition of normal distribution of the variables in the studied groups was not fulfilled). Statistical analysis showed that the more patient and his family are active in the therapeutic team, the smaller the degree of disability after treatment on the Rankin scale ($\chi^2 = 16.1231$, $df = 2$, $p = 0.0003154$).

DISCUSSION

Analysis of the study material showed both a systematic increase in hospitalizations related to diagnosed ischemic stroke, as well as an increase in the percentage of patients treated with thrombolysis. Unfortunately, the total number of patients treated with rt-PA is still quite small – only 2.8%. Research carried out in one of the centers in Wrocław [5] covering data for the years 2004 to 2007 confirm the low percentage of thrombolytic therapy in the treatment of ischemic stroke. In contrast, a retrospective study conducted in Warsaw [6] and Sandomierz [7] shows that the percentage was higher and amounted to 8.1% and 12.45%.

One of the factors responsible for this situation is the narrow therapeutic window and too late arrival of patients to centers specializing in stroke treatment.

A meta-analysis showed that the factor determining the effectiveness of thrombolytic therapy is the time from the onset of stroke symptoms to administration of the drug [8]. The highest efficiency of therapy is in the patients whose treatment started within 90 minutes of symptom onset [9,10]. The studies show that the mean time from the onset of symptoms to administration of rt-PA was 3 hours. The ECASS III study [11] and SITS – ISTR [12] published in 2008 compared the effectiveness of rt-PA and a placebo administered within 3 to 4.5 hours after stroke and proved the efficacy also in the extended time window.

Unfortunately, the research by Owe et al. [13] in 2006 showed that only 23% of patients arrive at the hospital within 3 hours of incident onset, and the vast majority after 6 hours. This is confirmed by the research carried out in Ostrowiec [14], where only 18% of patients with symptoms of stroke went to hospital within 3 hours after the onset of symptoms, and another 11% within 4.5 hours. The solution to this problem could be education aimed at teaching society how to quickly recognise the symptoms of stroke and raising awareness of the need for immediate medical attention. Educational activities should be focused on the people at risk of stroke (diagnosed with risk factors), their families, care-givers and colleagues.

Our study shows that thrombolytic treatment is most common in patients aged 52–59 (30%) – average age 53 years. Similar results were also obtained by Gurański et al. [5]. However, the studies of other authors show that thrombolytic therapy is performed mainly in elderly patients – average age > 65 years [7,11,13,15,16,17].

Among those receiving treatment in our study, women were the majority. However, the conclusions from the studies of other authors indicate that men are more often treated with rt-PA [5,7,13,15,17].

The research carried out by Rosińczuk-Tonderys J. [18] shows that headaches as well as tingling and numbness of the limbs often precede the occurrence of stroke. Among the surveyed patients, stroke was preceded by headache in 33% of them, every third patient experienced a hypertensive crisis, and in every tenth, transient numbness of an upper limb appeared. In contrast, 21% of patients did not report any alarming symptoms. The extent of neurological deficit has a significant impact on the course of thrombolytic therapy. In the studied group of patients, the average score on NIHSS was 10 points.

In the study group, the average score on NIHSS was 10 points and was comparable with the severity of neurological deficits in a study carried out Hacke et al. [11]. Studies by other authors [5,7,15,17] show that at the stage of qualification for thrombolytic therapy the average score on NIHSS was slightly higher (about 12–13 pts.), while in the population of Warsaw [6], and Bergen [13] it was 8 points.

In 24 hours after thrombolytic therapy, resolution of the neurological deficits was observed in 46% of patients. A study by Gurański et al. [5] shows that half of the patients during administration of rt-PA noticed significant improvement in clinical status whereas Sobolewski et al. [7] report that 38% of patients experience late improvement, i.e. improvement of at least 4 points on NIHSS within 2–24 hours. The studies by Wawrzyńczyk et al. [15] and Roje-Bedeković et al. [17] show that in the majority of patients, their neurological condition assessed on NIHSS 24 hours after thrombolysis was better than on arrival on NIHSS.

According to the guidelines from the Expert Group of the Section of Cerebrovascular Diseases of the Polish Neurological Society from 2012, in patients qualified for thrombolytic therapy, blood pressure should be less than 185 mmHg for systolic blood pressure (SBP – systolic blood pressure) and 110 mmHg for diastolic blood pressure (DBP – diastolic blood pressure) [19]. Unfortunately, most patients in the acute phase of ischemic stroke have high blood pressure, which may be connected with both pre-existing hypertension, as well as with an acute reaction associated with the stroke itself.

The studies show that at the qualification stage for treatment, every third patient had blood pressure remaining at the level of 150/90 mmHg, and one in five patients were diagnosed with high blood pressure (approximately 220/110 mmHg). The studies by Hacke [11] and Roje-Bedeković [17] carried out in Croatia show that the average level of blood pressure in patients treated with thrombolytic therapy at the

time of qualification amounted to 152/84 mmHg and 154/88 mmHg respectively.

In our study, the degree of patient disability was assessed according to the Rankin scale at discharge from hospital. More than 60% of patients demonstrated no disability or the remaining symptoms did not affect daily functioning in a negative way (Rankin scale 0 or 1). Similar results were obtained by Alderazi [16] in patients at discharge treated with thrombolysis, with no previous neurological disorders, at the age up to 80 and not suffering from diabetes. The studies by Gurański et al. [5] and Sobolewski et al. [7], who evaluated patients one month after the onset of stroke, show that 35% and 37% received 0 or 1 point on the Rankin scale respectively. According to studies by other authors [7,11,17], who checked patients after 90 days after stroke onset, 20 to 50% of patients had no symptoms or just a slight degree of disability. Unfortunately, in our study 15% of patients at discharge from hospital displayed a severe neurological deficit (4–5 pts. Rankin scale). Similar results were obtained by Sobolewski et al. [7] and Gurański et al. [5], who evaluated the studied patients a month after the stroke, and Hacke et al. [11] who conducted an assessment 90 days after an episode of stroke. However, the study conducted in Croatia [17] three months after the onset of symptoms shows that the number of patients with a severe neurological deficit was even higher (25%). Patients after ischemic stroke treated with thrombolysis should be educated how to take care of themselves to live a healthy life. Healthcare workers are responsible for:

- providing the patient and his family with knowledge of stroke risk factors;
- promoting a healthy lifestyle that eliminates or reduces the occurrence of modifiable risk factors;
- encouraging regular visits and active participation in therapy conducted by a GP and specialists;
- assisting and supervising the rehabilitation process at home [20].

CONCLUSIONS

1. The neurological condition of the majority of patients treated with thrombolysis improved significantly during the administration of rt-PA.
2. After hospitalization, 6 out of 10 patients demonstrated self-reliance.
3. Active participation of the patient and the family in the therapeutic process enhances patient autonomy.
4. No cases of condition deterioration were observed during treatment.
5. Thrombolytic therapy is an effective treatment for ischemic stroke.

Author's contribution

Study design – J. Rosińczuk

Data collection – K. Bonk

Data interpretation – K. Bonk

Statistical analysis – J. Rosińczuk, K. Bonk, A. Kołtuniuk

Manuscript preparation – J. Rosińczuk, A. Kołtuniuk

Literature research – A. Kołtuniuk

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