Endovascular treatment of acute ischemic stroke with aid of mechanical thrombectomy and intra-arterial thrombolysis

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Aims and objectives

Stroke is the third leading cause of death and a major cause of disability in adults. Annually in our country due to stroke hospitalized is about 60,000 of people. The incidence of stroke in Poland is 177 cases per 100,000 men and 125 cases per 100,000 women [1]. In subsequent years, the number of patients hospitalized with acute stroke may increase considerably, that is why it is crucial to develop new treatments for this disease.

Recanalization of occluded artery is strongly associated with improved functional outcomes and reduced mortality [2]. Treatment of the acute ischemic stroke include two possible methods of therapy: medication, mainly intravenous thrombolysis and endovascular treatment - intraarterial thrombolysis and mechanical thrombectomy. Intravenous thrombolytics (recombinant tissue plasminogen activator (rt-PA)) administered within 4.5 hours after the onset of symptoms is standard procedure of treatment acute ischemic stroke [3,4]. The method of intravenous thrombolysis has a low percentage restoration of cerebral arteries patency [5,6]. Using endovascular methods such as: intraarterial thrombolysis and mechanical thrombectomy, extends the therapeutic window and allows to achieve larger number of successful recanalization [2,7,8].

The aim of this study (research) was to establishment the efficacy and safety of the endovascular management of stroke using endovascular techniques: intraarterial thrombolysis and mechanical thrombectomy.

Methods and materials

Patients:

The retrospective study involved a group of 18 patients hospitalized in 2005-2012 who were treated with intraarterial thrombolysis and mechanical thrombectomy. In all cases assessed risk factors of stroke, the results indicate that the most common cause occurring in 66.67% of cases (n=12), is hypertension. On further places there were found coronary artery disease, hyperlipidemia and diabetes [Fig. 1].

Overall 24 procedures were performed. Intraarterial trombolysis was performed in 54.17% (n=13) and mechanical thrombectomy was carried out in 45.83% (n=11) interventions. The investigated group consisted of 7 (38.89%) women and 11 (61.11%)
The average age of the patients was 60 years (SD ±17; median 60 years; range 26-84 years).

Arterial occlusion refers to various of cerebral arteries. Most frequently (22.22%) obliteration involved middle right cerebral artery. Subsequently, occlusion occurred in the basilar artery and the left middle cerebral artery [Table 1].

**Conditions for being qualified to the procedure:**

To evaluate neurological deficit in patients with ischemic stroke National Institutes of Health Stroke Scale (NIHSS) has been used. The assessment of the neurological status before the surgery was performed in the Emergency Room. Afterwards, depending on the availability of diagnostic methods, the patients were mainly examined by using TK (n=14), angio-CT (n=13) and DSA (n=8) [Fig. 2]. First of all, CT was performed to patients with suspected stroke, to exclude intracerebral hemorrhage, subdural and epidural hematoma, and to confirm ischemia and determine the extent of ischemic damage. Angio-CT conducted for the identification and location of the occlusion. One patient underwent MR-DWI. All inclusion / exclusion criteria that were used to qualify for the endovascular treatment are shown in table [Table 2, Table 3].

**Devices and description of the procedure:**

**# Intraarterial thrombolysis:**

- Invasive technique of the treatment of acute ischemic stroke,
- The time window for this technique is up to 6 hours from the onset of symptoms,
- It involves the direct introduction of fibrinolytics to the clot within the obstructed vessel,
- This causes a local increase of the fibrinolytics concentration which is high enough to dissolve the clot, while maintaining low systemic concentrations. This is effective in preventing side effects,
- Medications : rt-PA dose < 0.9 mg/kg (approximately 50 mg).

Course of treatment : surgery was performed under general anesthesia. At the begining of the procedure there was a venipuncture of the femoral artery on the right side and the catheter was introduced by the Seldinger method. Then, the contrast media administered to show the obstructed cerebral vessel. Subsequently the diagnostic catheter was replaced by microguidewire and microcatheter was introduced whose end was placed in the proximal part of the thrombus. Rt-PA was administered at a right dose and the thrombus was penetrated by the microguidewire. Continuous observation during thrombus dissolution treatment was carried out using the DSA. During the
intervention, Heparin solution in saline is used for permanent washing of the catheter and microcatheters.

# Mechanical thrombectomy:

# Solitaire FR:

- Mechanical thromboectomy stent used for the treatment of ischemic stroke,
- This allows immediate restoration of flow through the occluded vessel and by expansion of it above the thrombus there is possibility to remove the clot,
- Therapeutic time window is up to eight hours for the front part and up to 15 hours for the back part of the circulation from the first symptoms.

Course of treatment: The procedure was performed under general anesthesia. The procedure was performed with the venipuncture of the right femoral artery, catheter was introduced using the Seldinger method. Then, the contrast media was administered to visualize the location of obstruction. Stent Solitaire FR was depressurized above the thrombus without complete releasing. Stent was extended for 1-2 minutes, then was gently pulled out of the body through a guiding catheter and thrombus was removed. The aim of the angiography control was to assess recanalization and confirmation of the reperfusion. During the intervention, heparin solution in saline is used for permanent washing of the catheter and microcatheters.

# Penumbra Device:

- Device, specially designed to remove mechanically the clot,
- It works in two ways: first way is based on the fragmentation of thrombus, which fragments are aspirated, what protects the catheter from plugging or circumferential displacement of these fragments and the second way relies on the direct removal of the embolus with balloon stopping flow in the vessel for a while,
- It consists of three main parts: the catheter reperfusion, separator and thrombus removal ring,
- All elements can be used with a catheter-6-Fr,
- The aspiration pump generates underpressure -20 in/Hg.

Course of treatment: The procedure was performed under general anesthesia. The procedure was performed with the venipuncture of the right femoral artery, catheter was introduced using the Seldinger method. Reperfusion catheter was placed under the proximal end of the thrombus using a catheter guiding. After removal the guiding catheter the separator was introduced, which crushed the thrombus and its fragments aspirated by the underpressure generated by the aspiration pump. During the intervention, heparin solution in saline is used for permanent washing of the catheter and microcatheters.
Evaluation of the efficiency and safety of treatment:

After surgery, angiography DSA was performed [Fig. 3, Fig. 4]. Angiograms were analyzed by a radiologist. The effectiveness of cerebrovascular recanalization was assessed by the TICI scale (thrombolysis in cerebral infarction) [Table 4]. The aim of treatment was to achieve the level of #2b [9].

After treatment imaging was performed: CT/MR (24-36 hrs.), which aimed to detect potential complications of endovascular procedures, such as: perforation of the vessel; dissection of the vessel wall; embolization of another vessel, that was mentioned in the procedure; symptomatic intracranial hemorrhage (#4 points NIHSS or later death); complications at the injection site (groin) requiring surgical intervention or transfusion of blood products [10].

Neurological deficits in patients with ischemic stroke was determined on the basis of the National Institutes of Health Stroke Scale (NIHSS). The neurological examination was conducted immediately after the treatment and then 24 hours, 7 days, and 30 days after the treatment. An NIHSS score of 0 point or 1 point or an improvement of #10 points was defined as the successful outcome of the therapy and reduction of neurological symptoms. The degree of disability of patients was determined 3 months after the surgery with the modified Rankin Scale (mRS). mRS at 3 months of #2 was defined as the absence of disability.

Images for this section:
Fig. 1: Risk factors of stroke.

Table 1: The most common location of obstruction.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right middle cerebral artery (MCA R)</td>
<td>6</td>
<td>22,22</td>
</tr>
<tr>
<td>Basilar artery (BA)</td>
<td>5</td>
<td>18,52</td>
</tr>
<tr>
<td>Left middle cerebral artery (MCA L)</td>
<td>5</td>
<td>18,52</td>
</tr>
<tr>
<td>Right internal carotid artery (ICA R)</td>
<td>3</td>
<td>11,11</td>
</tr>
<tr>
<td>Left vertebral artery (VA L)</td>
<td>3</td>
<td>11,11</td>
</tr>
<tr>
<td>Right anterior cerebral artery (ACA R)</td>
<td>2</td>
<td>7,41</td>
</tr>
<tr>
<td>Superior cerebellar artery (SCA R)</td>
<td>1</td>
<td>3,70</td>
</tr>
<tr>
<td>Left internal carotid artery (ICA L)</td>
<td>1</td>
<td>3,70</td>
</tr>
<tr>
<td>Right posterior cerebral artery (PCA R)</td>
<td>1</td>
<td>3,70</td>
</tr>
</tbody>
</table>
Fig. 2: Diagnostic methods before the treatment. (A) CT scan: hyperdense change in the course of the M2 segment of the right middle cerebral artery, (B) CT scan: occlusion in the course of the M2 segment of the right middle cerebral artery, (C) CT angiography: occlusion in the course of the M2 segment of the right middle cerebral artery, (D) MR T2 sequence: ischemic stroke of the brain stem.
# MECHANICAL THROMBECTOMY

## I. Inclusion criteria:

1. The clinical diagnosis of acute ischemic stroke (exclusion of cerebral hemorrhage on CT).
2. The precise time of onset of symptoms of the current stroke and the opportunity to start thrombectomy, time frame: up to 8 hours for the stroke from the frontal circle (vertebra) and up to 15 hours for the stroke from posterior circle (vertebra - kreg) of vascularity.
3. Age over 18 years.
4. Confirmed by Angio-CT, and then subtraction angiography (DSA) obstruction of the large arterial trunk (ICA, MCA-M2 segment, VA, BA, PCA).
5. Ineffectiveness of the intravenous thrombolysis or the failure to accomplish the inclusion criteria.
6. Ruled out the existence of other causes of the neurological deficit or causes which may mask the stroke (e.g.: hypoglycemia, state after seizure, metabolic encephalopathy, conversion ...).

## II. Exclusion criteria:

1. Inability to clarify the time of onset of the symptoms.
2. Rapid resolution of the neurological symptoms before the treatment.
3. Minor neurological symptoms (NIHSS <5 pts.).
4. Allergy to radiographic contrast agents in a history.
5. Reported earlier haemorrhagic diathesis.
6. Reported earlier coagulation factors deficit.
7. Confirmation of the intracranial hemorrhage on CT scan or MRI.
8. A significant mass effect on CT scan with the shifting brain structures to the opposite side or area hypodensity covering > 1/3 of the area of the middle cerebral artery vascularization.
10. Suspected presence of the vascular malformation or aneurism MRI or CT.
11. A history of intracranial haemorrhage or suspected intracranial haemorrhage.
12. Previous stroke or serious head injury within the last 3 months.
13. Damage to the CNS in a history (cancer or a history of surgery within the skull or spine).
14. INR > 3.0, also oral anticoagulant therapy.
15. The use of heparin within 48 hours before the stroke and APTT two times longer than the upper normal limit.
16. Thrombocytopenia < 30 000 / mm3.
17. Hypo- or hyperglycemia (<50mg/dl or >400mg/dl).
18. Systolic blood pressure > 185 and diastolic blood pressure > 110 mmHg, despite of intensive lowering it.
19. Puncture an artery or a large vein in a place impossible to press in the last 7 days.
20. Recent history of external heart massage or childbirth (within the last 10 days).
21. Myocardial infarction within the last 3 months.
22. Major surgery, a large injury or bleeding from the gastrointestinal tract or urinary tract during the last three months.
23. Existing or recently severe and life-threatening bleeding.
24. Severe liver diseases (e.g.: liver failure, cirrhosis, portal hypertension, active inflammation) or acute pancreatitis.
25. Pregnant or lactating women.
26. Expected life time less than three months for the reasons other than the current stroke.

The patient should not be treated if the points 1-6 of part I are marked NO, or in part II are marked YES.
**Table 2:** Inclusion and exclusion criteria of endovascular treatment: mechanical thrombectomy.
**INTRAARTERIAL THROMBOLYSIS**

### I. Inclusion criteria:

1. The diagnosis of acute ischemic stroke.
2. The precise time of onset of symptoms and the ability to start an intravenous infusion of rt-PA up to 6 hours of symptom onset (3 hours intravenous treatment and 6 hours - treatment with intra-arterial).
3. Age 18 - 75 years.
4. Ruled out the existence of the other causes of the neurological deficit, i.e. intracerebral hemorrhage, or other reasons that may mask the stroke (CT and / or MRI).

### II. Exclusion criteria

1. Rapid resolution of the neurological symptoms.
2. Minor neurological symptoms, such as: small sensory deficit.
3. Inability to clarify the time of onset of symptoms.
4. Occurrence of the seizures.
5. Suspicion of the subarachnoid hemorrhage.
6. Recent myocardial infarction.
7. Current treatment with oral anticoagulants or heparin intravenously with abnormal values of INR and APTT (in terms of standards as for untreated, eg INR> 1.7, PT> 15s;).
8. Thrombocytopenia < 100 000 / mm3
9. Hypo- or hyperglycemia with the values that the neurological symptoms may occur (<50mg/dl or> 400mg/dl).
10. Systolic blood pressure > 185 mmHg and diastolic blood pressure > 110 mmHg at the beginning of the treatment, in spite of the administration of 1-2 doses of 10 mg i.v. labetalol.
11. Disorders of blood coagulation or platelet function (excluding patients receiving antiplatelet drugs).
12. Arterial puncture in a place impossible to press in the last 7 days.
13. Recent history of external heart massage within the last 10 days.
14. Major surgery, a large injury or bleeding from the gastrointestinal tract or urinary tract during the last 3 months.
15. Gastric ulcer disease in the past 3 months, esophageal varices.
16. Previous stroke or serious head injury within the last 3 months.
17. A history of intracranial haemorrhage.
19. Hemorrhagic diathesis, existing or previous severe haemorrhage.
20. Hemorrhagic retinopathy (e.g. in diabetes)
21. Dissecting aneurysm of the aorta or suspecting it, abnormalities of the arteries or veins development.
22. Severe liver disease (including: liver failure, cirrhosis, portal hypertension, active hepatitis).
23. Women of childbearing period (excluding the states where there is certainty of the impossibility of getting pregnant, such as sterilization).
24. Lactating women.
25. Other life-threatening disease of the patient (e.g. malignant cancer), which can lead to death of a patient within a few months.
26. Occurrence of the intracranial hemorrhage on CT scan or MRI.
27. Hypodense lesions involving > 33% of the territory of vascularization MCA (hyperdense changes in MRI-DWI).
28. The suspected presence of vascular malformation, or aneurysm in MRI or CT.
Table 3: Inclusion and exclusion criteria of endovascular treatment: intraarterial thrombolysis.
Fig. 3: (A) Digital subtraction angiography before treatment: occlusion of the right middle cerebral artery. (B) Digital subtraction angiography after intraarterial thrombolysis: flow through the right medial cerebral artery, visible microcatheter in the right internal carotid artery. (C) Digital subtraction angiography before mechanical thrombectomy: occlusion of the right middle cerebral artery. (D) Digital subtraction angiography after mechanical thrombectomy: flow through the right medial cerebral artery, visible microcatheter in through the right medial cerebral artery. (E) Digital subtraction angiography before mechanical thrombectomy: occlusion of the right medial cerebral artery. (F) Digital subtraction angiography after mechanical thrombectomy: flow through the right medial cerebral artery.
Fig. 4: (A) CT angiography: occlusion of the basilar artery. (B) CT angiography control after surgery: flow through the basilar artery. (C) Digital subtraction angiography before mechanical thrombectomy: occlusion of the basilar artery. (D) Digital subtraction angiography after mechanical thrombectomy: flow through the basilar artery. (E) CT angiography control after surgery: flow through the basilar artery. (F) Embolic cloth obtained after mechanical thrombectomy.

<table>
<thead>
<tr>
<th>TICI Scale</th>
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<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2a</td>
</tr>
<tr>
<td>2b</td>
</tr>
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<td>3</td>
</tr>
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Table 4: TICI Scale.
Results

In the study group, consisting of 18 patients, have been performed 24 interventions of targeted thrombolysis and mechanical thrombectomy. Four patients (22.22%) required two stages of the treatment process and one patient (5.56%) underwent three interventions. In 12 cases the duration of the surgery has been measured and the time of onset of stroke symptoms by the end of the surgery. The average duration of procedure is 157 minutes (SD ±57; median 158 minutes). The longest surgery lasted 250 minutes, and the shortest 55 minutes.

The time between the first symptoms of stroke and the end of the procedure was from 265 to 1170 minutes with the average time 491 minutes (SD ±240; median 415 minutes).

In 62.50% of cases (n=15) the effect of entire revascularization has been achieved and in another 12.50% of cases (n=3) only partial recanalization has been achieved. Only in 25% of procedures (n=6) recanalization of the artery has been failed (TICI #1). The highest percentage of recanalized arteries were obtained by following the procedure of intraarterial thrombolysis - 69.24% (TICI #2b). In the case of mechanical thrombectomy total patency (TICI #2b) was restored in 54.55%. The effect of partial revascularization (TICI =2a) gained in 15.38% of cases of intraarterial thrombolysis and mechanical thrombectomy in 36.36%. Artery patency failed (TICI #1) in 15.38% of cases of intraarterial thrombolysis and 9.10% of mechanical thrombectomy. The differences in results are statistically significant (p <0.001) [Fig. 5].

Neurological examinations were performed with 17 patients. Neurological deficit was determined by using the scale of the National Institutes of Health Stroke Scale (NIHSS) and compared with the results obtained before the treatment. During the patients’ hospitalization there were two deaths. First death occurred 6 days after, and the second one 8 days after the surgery. Additionally, in one case, we do not have the results of the patient's neurological examination, which was carried out 30 days after the surgery. For this reason, the frequency of the improvement of the neurologic status for NIHSS scale was based on the results of carried out neurological examination. This examination has been referred to group of 16 patients - 7 days after the surgery, and to group of only 14 patients - 30 days after the surgery.

Immediately after the surgery none of the patients presented reduction in neurological symptoms. In examination performed two hours after the procedure, neurological changes allow for a successful evaluation of the outcome of the therapy was found in 17.65% (n=3) cases. The next assessment of the neurological status was made on the first day after the surgery. In this case, a successful result was obtained with 11.76% (n=2)
patients. On the seventh day successful result of the neurological status was achieved with 31.25% (n=5) patients, and on the thirtieth day with 57.14% (n=8) patients [Fig. 6].

Comparing the results of evaluation patients' neurological status thirty days after the surgery, with the results of recanalization artery, appears that revascularization brings improvement in the neurological status in 66.67% of the cases. However in the patients' group with no or only a partial restoring patency of the artery, that improvement is only in 40% of the cases.

In addition, before the surgery 17 patients had the evaluation of the functioning state, using the Rankin scale, and 14 patients were able to make a further assessment after ninety days of the treatment. Before performing cerebral artery recanalization with 23.53% of patients (n=4), the result indicated the entire functionality (mRS #2). However, three months after the surgery mRS #2 reached 57.14% of patients (n=8).

Images for this section:

![Image](image-url)

**Fig. 5:** The effectiveness of cerebral artery recanalization.
**Fig. 6:** Assessment of improvement of neurological status by NIHSS scale.
Conclusion

DISCUSSION

The aim of treatment of acute ischemic stroke is the rapid restoration of flow in a occluded vessel. Rapid recanalization associated with the improved clinical status of the patient and a reduction in mortality [2]. Ischemic stroke can be treated in two ways: Pharmacological - intravenous thrombolysis and endovascular treatment - mechanical thrombectomy and intraarterial thrombolysis. The standard method of treatment is intravenous thrombolysis, the therapeutic window of this method is up to 4.5 hours. Intravenous thrombolysis method is characterized by low efficiency [5]. The use of endovascular methods extends the therapeutic window up to 6 hours for targeted thrombolysis and up to 15 hours for mechanical thrombectomy [11,12].

Our work shows that there is an alternative for patients in whom intravenous thrombolysis was ineffective or for those who do not fulfill the eligibility criteria for it.

Patients with acute ischemic stroke subjected with endovascular treatment (intra-arterial thrombolysis and mechanical thrombectomy) a high percentage of recanalization at the level of 62.50% without a concomitant increase in bleeding complications was observed. The clinical condition of the patients according to the scale NIHHS was improved up to 66.67% of total revascularization and in 40% of cases with partial patency vessel or the lack of recanalization.

Patients, who were embraced by target thrombolysis treatment achieved complete (TICI #2b) or partial (TICI =2a) restoration of flow in 84.62% of cases. In this study the MELT gives a partial or total vascular patency with 73.7% of patients [13]. However, in this case, except for using guidewire mechanical techniques were not used to restore the flow. In 69.24% of cases complete patency (TICI #2b) vessels using targeted thrombolysis has been achieved. This result is similar to what was obtained PROACT II study [14,15].

In our thesis, of effective flowing, we used both techniques of mechanical thrombectomy achieved complete or partial patency vessels in 63.65% of patients. High efficiency of Penumbra Set has been confirmed in a study Penumbra Pivotal Stroke Trial [16]. The study SWIFT found a better long-term effects of patients' treatment, faster, more effective and safer recanalization with Solitaire FR stent comparing with MERCI Set [17].

In numerous reports to assess the obtained flow in patient's vessels with targeted thrombolysis an adapted classification of the TIMI (Thrombolysis in Myocardial Infarction)
was used. In 2003 a specific intracranial cerebral circulation classification TICI (Thrombolysis in Cerebral Infarction) was suggested, which was used to assess recanalization in our publication [9,18].

Evaluation of the degree of disability was based on the modified Rankinscale. Before endovascular treatment 23.53% of the patients scored indicated a state of able-bodied (mRS #2). However, after 90 days of the treatment mRS #2 reached 57.14% of the patients, which proves almost 2.5-fold reductions in disability. These results are similar to results reported by several centres for various endovascular stroke therapy [19, 20, 21, 22, 23]. Before the endovascular treatment 76.47% of the patients scored indicated a state of disability (mRS >2).

There are reports of more post-surgery complications and increased mortality after application of invasive methods as compared to intravenous rt-PA [10]. However, our results show that through appropriate inclusion criteria and combination therapy it's possible to reduce the risk of life-threatening complications at a satisfactory therapeutic level.

The main restriction in our study is the lack of a control group and the small size of the study group. Therefore, our conclusions concerning safety and effectiveness of the procedure are limited.

**FINAL CONCLUSIONS**

The study showed that endovascular techniques are effective and safe in the treatment of ischemic stroke. The greater effectiveness is more characteristic for intraarterial thrombolysis than mechanical thrombectomy. Patients' condition, who were treated by endovascular technique was significantly improved. The main limitation of the results was the small patients' number, that's why our conclusions regarding the safety and efficacy of these methods do not reflect this condition in the population.

Currently, there is no doubt that a certain group of patients with ischemic stroke can certainly benefit from the use of endovascular procedures. We should always remember to take into account of such treatments when we deal with patients who suffer from stroke.

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References