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Study of Ischemic Stroke Treatment Results Using Mechanical Thrombechtomy and of Factors Affecting Them

SUMMARY OF DOCTORAL DISSERTATION

Medicine and Health Sciences,
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The doctoral dissertation was written at Vilnius University during 2015–2019.

Academic supervisor:
Prof. Dr. Dalius Jatužis (Vilnius University, medicine and health sciences, medicine – M 001).

Scientific consultant:
Prof. Dr. Algirdas Edvardas Tamošiūnas (Vilnius University, medicine and health sciences, medicine – M 001).

Dissertation will be defended in a public meeting of the Dissertation Defence Panel:

Chairman - Prof. Habil. Dr. Algirdas Utkus (Vilnius University, medicine and health sciences, medicine – M 001).

Members:
Prof. Dr. Giedrius Davidavičius (Vilnius University, medicine and health sciences, medicine – M 001);
Prof. Dr. Vytautas Kasiulevičius (Vilnius University, medicine and health sciences, medicine – M 001);
Prof. Dr. Grzegorz Kozera (Gdansk Medical University, medicine and health sciences, medicine – M 001);
Prof. Dr. Rūta Mameniškienė (Vilnius University, medicine and health sciences, medicine – M 001).

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VILNIAUS UNIVERSITETAS

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Išeminio insulto gydymo mechanine trombektomija rezultatų ir jiems poveikį darančių veiksnių tyrimas

DAKTARO DISERTACIJOS SANTRAUKA

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Mokslinis vadovas - prof. dr. Dalius Jatužis (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001).

Mokslinis konsultantas - prof. dr. Algirdas Edvardas Tamošiūnas (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001.

Disertacija ginama viešame disertacijos Gynimo tarybos posėdyje:

Pirmininkas – prof. habil. dr. Algirdas Utkus (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001).

Nariai:
prof. dr. Giedrius Davidavičius (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Vytautas Kasiulevičius (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Grzegorz Kozera (Gdansko medicinos universitetas, Medicinos ir sveikatos mokslai, medicina – M 001);
prof. dr. Rūta Mameniškienė (Vilniaus universitetas, Medicinos ir sveikatos mokslai, medicina – M 001).

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ABBREVIATIONS

ASPECTS	Alberta Stroke Program Early CT Score
ICH	Intracerebral Haemorrhage
IVT	Intravenous Thrombolysis
CT	Computed Tomography
CTA	Computed Tomography Angiography mode
CTP	Computed Tomography Perfusion mode
mRS	modified Rankin Scale
MRI	Magnetic Resonance Imaging
MRI PWI/DWI	Perfusion/Diffusion Weighted Magnetic Resonance Imaging
MTE	Mechanical Thrombectomy
NIH	*National Institute of Health*
NIHSS	National Institute of Health *Stroke Scale*
PH	Parenchymal Haemorrhage
AF	Atrial Fibrillation
TICI	Thrombolysis in Cerebral infarction
ICA	Internal Carotid Artery
MCA	Middle Cerebral Artery
VUHSK	Vilnius University Hospital Santaros Klinikos

1. INTRODUCTION

1.1. Research problem

Ischemic stroke is an acute cerebrovascular disease, which can often cause permanent neurological deficit or death. It is also one of the most common and economically damaging diseases, especially among older people. Globally, it ranks as the second most frequent cause of death among those over sixty years of age. In Lithuania, there were 21,110 known cases of strokes (ICD-10 I60-I64) in 2018, with 16,546 (or 78%) of them being ischemic strokes. The Institute of Hygiene notes that acute ischemic stroke has been one of the most common causes of death in recent years. In 2017, there were 3,267 deaths caused by stroke (61.25% of cases were women), with 2,528 of them being by ischemic stroke (which amounts to 77% of all deaths from this disease). By comparison, myocardial infarction caused 1,145 deaths in 2017 (50.92% of cases being women), which means that infarction causes only over a third as many deaths.

Despite substantial investment into primary prevention over the last few decades, the age-standardized incidence of stroke in Europe has risen from 95 to 290 of 100,000 per year. It is only in recent years that the curve flattened and even took a downward slope [1]. Approximately 1.1 million Europeans suffer a stroke each year, and the number is expected to rise to 1.5 million by 2025 due to population ageing. Epidemiological studies continue to show the increasing incidence of ischemic strokes among younger people (under 50 years of age), with about 10% of diagnosed cases currently falling within this age group [2]. It is estimated that this number has risen by up to 40% world-wide over the recent decades [3]. This may be attributed to the progress in neuro-visual check-ups and MRI diffusion sequences in particular, as well as an increase in modifiable risk factors (e.g. hypertension, smoking, etc.) and substance abuse [4]. The increasingly growing socio-economical burden on society of this still fatal disease prompts us to strive to improve neuro-visual examination algorithms and analyse the most effective and instantly applicable treatment methods, which would significantly improve clinical outcomes in patients who suffered ischemic stroke.

Ischemic stroke comprises some 85% of all strokes, with most of it occurring due to large vessel occlusion. Quick, safe, and effective recanalization of a suddenly damaged cerebral circulation artery remains the key issue to address in present-day treatment of stroke patients. Up until the end of 2014, the only officially recommended treatment available for ischemic stroke was medication-based treatment, namely the intravenous injection of recombinant tissue plasminogen activator (IV r-tPA) within 4.5 hours from the onset of symptoms [5]. However, the utility of a systemic intravenous treatment in patients with moderate or acute ischemic stroke is limited, with early recanalization being available to less than 30% of patients with occlusion of the internal carotid, middle cerebral, or basilar artery [6]. It is by now established that the effectiveness of intravenous thrombolysis (IVT) depends on thrombus length and localization: the larger the occluded artery and the longer the thrombus, the less likely one is to succeed in dissolving it. Selective injection of a thrombolytic agent into an occluded artery may result in a good outcome, as first shown in a clinical trial by the PROACT II study. It compared clinical outcomes in 180 patients with acute ischemic stroke due to middle cerebral artery occlusion after selective intraarterial injections of a thrombolytic agent or heparin injection. With as many as 40% good clinical outcomes, it prompted an even more active search for a more aggressive intraarterial therapy tactic [7].

Mechanical thrombectomy (MTE) is a relatively recent reperfusion therapy method that seeks to restore impaired cerebral circulation by removing thrombi – i.e. the emboli that caused cerebral ischemia – from blocked arteries using special extractors or aspiration catheters. Given the overwhelming effectiveness of this method compared with the conservative treatment or even IVT, it can already be described as revolutionary, calling for further scientific research to address challenges related to patient selection and improvement of safety and effectiveness, as well as availability for everyone who needs it. Since 2015, nine randomized clinical studies have demonstrated the clinical utility of MTE in patients with ischemia exactly due to large-artery occlusion. This was an especially significant breakthrough, as the previously conducted SYNTHESIS Expansion Trial, IMS-III, and MR RESCUE trials had failed to show clinical benefit of MTE in treating ischemic strokes after intravenous thrombolysis (or as its substitute) [8]–[10].

The first clinical trial to demonstrate the clinical utility of MTE was MR CLEAN (*Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands*), which showed that in patients with ischemia occurring due to occlusion in anterior cerebral circulation endovascular treatment is effective and safe when conducted within 6 hours from the onset of symptoms [11]. Quite recently, clinical trial results published by DAWN (*DWI or CTP Assessment With ClinicalMismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo*) [12] have prompted the American Heart Association (AHA) and the American Stroke Association (ASA) to revise their guidelines and expand the therapeutic window of MTE for selected patients to 24 hours. So patient selection by time alone is not a rational option, as ischemic core development is closely linked to individual patient’s hemodynamic parameters (i.e. the condition of extracranial carotid arteries and intracerebral collaterals, perfusion pressure, and size of the affected territory). It is only by using neuro-visual examination that one can more accurately determine the volume of the core and penumbra (the potentially salvageable brain tissue) and decide about the prospect of recanalization.

Most of the prospective randomized studies seeking to identify ischemic changes in the middle cerebral artery (MCA) territory were conducted using *Alberta Stroke Program Early CT Score (ASPECTS*) so as to be able to determine the volume of the salvageable tissue even without the aid of perfusion imaging and by relying on CTA-assisted localization of the thrombus. ASPECTS 6–10 is a widely used clinical standard, indicating that 5 or 0 segments out of 10 in the MCA territory have been damaged. The problem, however, is that the scale varies significantly between one observer and the next due to very intricate early CT changes, while also varying due to the localization of the affected segment, with the scores (and regions themselves) not being clinically equivalent even within the MCA territory. So, a score of 7 with, on the one hand, the presence of lesions in the basal ganglia and, for example, the right temporal lobe, and the same score with, on the other hand, occlusions in MCA M1 or, say, M2, are completely different prognostic values, and this is why those clinical studies that applied very strict neuro-visual examination (CT, CTA, CTP, or MRI PWI/DWI) selection criteria have manged to reach a very high percentage of good clinical outcomes. In the Australian clinical study EXTEND IA (*Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection)*, the ischemic core in MTE patients could not exceed 70 ml, and the penumbra could not be below 20%, all of which resulted in good clinical outcomes in 71% of cases [13].

One can only be pleased on behalf of those in luck, yet the scientific community is becoming increasingly aware it is facing the following question: which patients or even which groups of patients do not deserve a treatment as effective as this? Could these be older patients? The frequency of good clinical outcomes (mRS 0-2) tends to decrease along with patient’s age after they’re 75 [14]. Clinical studies have so far been unable to demonstrate the damage or increased frequency of complications from MTE in patients over 80, quite the opposite: MR CLEAN has shown that the frequency of good clinical outcomes in this age group is higher than among younger patients [11]. MTE is not officially contraindicated in older patients, but it is specified that one must take note of their comorbidity and carefully consider the suitability for the procedure of older patients whose day-to-day functioning is impaired (mRS > 1), as the prognosis depends on not only on the person’s chronological age but also their functional condition prior to the onset of symptoms. In many trials, selection criteria pay special attention to this group and the standards applied to it remain stricter.

MTE is indicated in all patients with acute anterior circulation large artery occlusion regardless of the severity of symptoms. To note, patients with NIHSS score ≤5 were not included in most of these trials (with the exception of MR CLEAN, which had 15 such patients); however, other studies confirm a correlation between mild initial ischemic stroke symptoms and their leptomeningeal collateral scores [15]. So a mild neurological deficit (NIHSS ≤5) and frequent clinical lability in cases of large-artery occlusion are attributable only to factors related to well-developed collaterals and systemic perfusion, and to this day no one can say for sure (or, at least, visualise accurately) what the extent of their compensatory capacities is in cases of, say, a sudden drop in arterial blood pressure during an acute ischemic stroke.

Another unknown in the context of patient x's selection algorithm and possible clinical outcomes is the effect of intravenous thrombolysis (IVT) in cases of large-artery occlusion. In certain groups of patients, clinical trials (MR CLEAN and EXTEND IA) managed to achieve complete artery recanalization by performing IVT prior to MTE, yet only in a small fraction (2.9% and 3% of patients respectively). There has been no evidence to date suggesting a greater probability of intracranial haemorrhage if IVT therapy is performed prior to an invasive procedure, but the extent to which an injection of r-tPA improves the perfusion of small branches in the damaged territory remains to be seen. It is believed that in cases of large-artery occlusion IVT becomes a preventive measure against the spread of the thrombus or occlusion of new branches prior to MTE. Current guidelines state that IVT must be performed as soon as possible within 4.5 hours from the onset of symptoms, and that this should not delay an MTE procedure; MTE, too, should not contraindicate an initiation of IVT [16]. We are still awaiting the results of randomized clinical trials (SWIFT DIRECT and MR CLEAN-NO IV) that compared direct- and bridging MTE treatment approaches. According to the recently published results of a randomized clinical trial that compared clinical outcomes only in patients suitable for IVT, direct-MTE results are just as good as those of bridging treatment [17]. There is a growing discussion on this topic among respected scientists. Retrospective studies and meta-analyses show that there is no proven advantage of hypothetical bridging MTE treatment[18]. It is only one of them that suggests better clinical outcomes, lower death rate, and greater frequency of successful recanalization in IVT+MTE patients, with their symptomatic intracerebral haemorrhage (SICH), however, staying the same as that of direct-MTE patients[19]. There has been no regulation to date regarding bridging treatment, with every medical centre interpreting it in their own way. This means that not every patient even within the same group is actually administered the same dose of a thrombolytic agent. A good number of medical centres do not stop r-tPA infusion even during an MTE procedure, while some continue it even after a successful large-artery recanalization. It is surmised that this could aid in the dissolution of micro-embodies and perfusion of the small cortical arteries. Like some other medical centres in Europe, we stop the infusion of a thrombolytic agent immediately prior to the arterial puncture[20]. So, the issue of r-tPA dosage in combined reperfusion treatment has so far been a largely untouched and not specifically researched topic.

Ischemic stroke is a multi-etiological, rapidly- progressing disease that calls for multi-disciplinary treatment solutions and whose clinical outcomes depend on a multitude of factors. MTE is a new and very effective method of treatment, whose effect on patient’s condition varies due to both individual and systemic factors, with many of them still at the stage of scientific analysis – let alone the effect of different combinations of reperfusion methods (IVT and MTE). The added value of IVT in large-artery occlusion patients undergoing MTE treatment remains one of the most controversial topics to this day in the area of ischemic stroke treatment.

1.2. Research hypothesis

Mechanical thrombectomy is an effective and safe treatment method in ischemic stroke patients with anterior circulation artery occlusion. Its clinical outcomes depend on many factors and combinations thereof, as well as the use of intravenous thrombolysis: even a small (bolus) dose of an intravenous thrombolytic agent improves both the dynamics of a neurological condition and the clinical outcomes following mechanical thrombectomy without a significant increase in the frequency of intracerebral haemorrhage.

1.3. Research objective

To assess mechanical thrombectomy treatment results and factors affecting them in ischemic stroke patients.

1.4. Research tasks

(1) To assess the influence of patients' risk factors, demographic indicators, and functional status on mechanical thrombectomy treatment results.

(2) To assess the effect of bridging therapy on clinical outcomes in patients with acute anterior circulation ischemia who were treated using mechanical thrombectomy.

(3) To assess factors that may affect the effectiveness of MTE treatment:

a) the time elapsed between the onset of symptoms and the arrival to a medical institution and performance of neuro-visual examination as well as its assessment, and until the start of MTE and recanalization;

b) morphological radiological changes in the cerebrum (the size of the territory with cerebral ischemia, i.e. the early ischemic changes quantified by the ASPECTS, and the location of arterial occlusion) identified using neuro-visual radiological examination methods (i.e. native computed tomography (CT), and CT angiography (CTA) and perfusion (CTP) modes);

c) clinical characteristics of ischemic stroke (neurologic deficit severity measured using the NIH (National Institute of Health) Stroke Scale);

d) periprocedural factors: the anaesthesia applied, the dose of the intravenous thrombolytic agent, the devices used for the mechanical thrombectomy (namely, the balloon occlusion catheter), the number of thrombectomy sessions, the success of the first session, and the recanalization score using the TICI (*Thrombolysis in cerebral infarction)* perfusion scale.

(4) To assess both early and late results of this type of treatment and any complications that may arise:

a) functional outcome quantified using the modified Rankin Scale (mRS) 90 days after the procedure;

b) recanalization rate in the occlusion territory using the TICI scale;

c) dynamics of the neurological condition using the NIH Stroke Scale after 2 hours and 24 hours from MTE;

d) complications.

1.5. Statements to be defended

1. The clinical outcomes of mechanical thrombectomy depend on not only periprocedural factors but also patients' demographic indicators and comorbidities.
2. In cases of successful mechanical thrombectomy (TICI 2b-3), patients' neurological condition improves far more rapidly, irrespectively of IVT application.
3. Mechanical thrombectomy application without intravenous thrombolysis is a safe and effective treatment method in

ischemic stroke patients with anterior circulation artery occlusions.

4. Bridging therapy (IVT+MTE) is safe with respect to intracerebral haemorrhage development irrespectively of the intravenous thrombolytic agent dose in all participating patients.

1.6. Novelity of the Study

MTE is a relatively new and burgeoning specialised reperfusion method of treating acute ischemic stroke with, however, constantly changing guidelines in view of newly published research results. It was only in 2015 (the year in which our study was initiated) that it became an officially recommended treatment method of large-artery occlusion. A lot of additional factors that might affect the clinical outcomes in ischemic stroke patients treated with MTE remain unresearched. Each of the medical centres specialising in ischemic stroke treatment applies its own methodology due to its regional specifics, financial situation, and technical capabilities for both diagnostic analysis and MTE procedures themselves in ischemic stroke patients. In Lithuania, there has been no in-depth study of and no published research to date on the effect of different factors on the clinical outcomes in patients with anterior cerebral circulation ischemia treated with MTE.

The originality and distinctiveness of this piece of research on the application of bridging MTE in ischemic stroke patients with anterior circulation artery occlusion is summarised as follows:

1. At the time this research started, there was no single prospective study published on the potential added value of IVT in patients treated with MTE. It was only the prospective study published at the end of 2018 that showed a statistically insignificant relationship between good clinical outcomes (mRS 0-2) favouring the bridging therapy (IVT+MTE: n=523,

53.6%; direct MTE: n=222, 41.8%; adjusted odds ratio (AOR): 1.61; 95% confidence interval (CI) 1.29 – 2.01) [21].

2. The only recently- published randomized clinical study of bridging MTE available did not demonstrate an advantage of bridging therapy over the methodology of direct MTE [17]. Currently, other multi-centre clinical trials (SWIFT DIRECT and MR CLEAN-NO IV) are still at the randomization phase.
3. Global literature contains no published research on the influence of different r-tPA dosages on the clinical outcomes and the frequency of complications in patients treated with MTE. Japan is the only country recommending a smaller total IVT r-tPA dose (0.6mg/kg) in ischemic stroke patients due to racial differences in the fibrinolytic system [22]. The latest review of Asia-based studies concludes that the group of patients who were administered a smaller total dose of IVT contained far more patients who never managed to achieve functional independence (though the frequency of sICH was smaller) [23].

2. METHODOLOGY

This research was conducted the prospective methodology by including all anterior cerebral ischemia patients in Vilnius University Hospital Santaros Klinikos (VUHSK) treated with MTE provided they meet the inclusion criteria described below. A permit to carry out biomedical research was obtained from the Vilnius Regional Biomedical Research Ethics Committee (No.158200-17-884-407). Prior to being included in the study, all participants or their relatives signed a personal information and consent form.

After being included, patients were surveyed and their anonymized medical records were gathered in the database created specifically for this study. Demographic data was gathered using the VUHSK database (electronic medical records): patients' age, sex, history of smoking, data on atrial fibrillation, diabetes, PAH, coronary heart disease and dyslipidemia. Data on neurological assessments (NIH Stroke Scale; performed by certified medical neurologists) and instrumental research as well as data on complications that occurred and the dynamics of functional condition (mRS scale) during a 90-day period were collected during the observation period itself following the protocol for ischemic stroke treatment with MTE.

The primary endpoint is functional independence in a 90-day period (mRS scale). The secondary endpoints are successful reperfusion (TICI scale) and neurological changes in 2 and 24 hours after MTE procedure (NIH Stroke Scale). Safety outcomes were mortality within the 90-day period and intracerebral haemorrhage.

Criteria for inclusion in the study and the observation protocol was prepared by the dissertation supervisor Prof. Dalius Jatužis and the supervisee Marius Kurminas.

2.1. Criteria for inclusion in the study

The study included all ischemic stroke patients over 18 years of age treated with MTE. Patients were not included in the study if they declined to participate in it.

2.1.1. Indications for an MTE procedure:

1. The time between the onset of symptoms and arterial puncture is known not to exceed 6 hours.
2. In cases when the disease onset time is not known (e.g. wake-up stroke) and in special circumstances, the decision is made case by case according to neuro-visual examination data (provided that criteria in (4) below is met).
3. The functional condition of the patient prior to stroke is at ≤ 2 mRS.
4. Cerebral CTA scan or digital subtraction angiography (DSA) procedure indicate ICA occlusion and/or MCA M1/M2 segment

occlusion. ASPECTS of ≥ 6 and CTP representing the penumbra zone.

5. In patients aged 80 or above, ASPECTS of ≥ 10.

2.1.2. Contraindications:

1. Blood glucose level at < 2.8 mmol/l or > 22 mmol/l.
2. Uncontrolled arterial hypertension: systolic ABP > 185 mmHg or diastolic ABP > 110 mmHg.
3. Cerebral CT/MRI scan shows signs of intracerebral or subarachnoid haemorrhage and/or a pronounced mass effect with a midline shift, changes in the brainstem or cerebral hemispheres.
4. CNS injury with a high risk of bleeding (tumour, abscess, vascular malformation).
5. History of intracerebral haemorrhage.
6. Subacute bacterial endocarditis.
7. Severe comorbidities with poor prognosis.

A clinical diagnosis of acute cerebral ischemic stroke had to be issued after determining the severity of neurological deficit using the NIH Stroke Scale and verifying it by CT scan data.

Treatment tactics were decided in accordance with the MTE protocol approved by VUHSK. In suitable patients, IVT, following current indications, was initiated as quickly as possible, while also preparing the patient for an MTE procedure. IVT was performed by administering r-tPA (alteplase): the total dose was 0.9mg/kg body weight, up to a maximum amount of 90mg; 10% of the total dose was administered by rapid intravenous injection (bolus), with the rest being infused over 60 minutes by syringe infusion pump. IVT would have to be stopped in the X-ray operating room before arterial puncture, and so not all patients received a full IVT dose. In some cases, by the joint decision of the medical neurologist and the interventional radiologist or cardiologist, patients would undergo MTE treatment without IVT – at times, even in the absence of direct contraindications of IVT (large-artery occlusion, a long thrombus, or IVT application would delay the initiation of MTE). Contraindications of IVT would mean the start of MTE treatment.

2.1.3. Observation protocol

Clinical outcomes were assessed 90 days after MTE procedure: the functional condition on the mRS scale of participating patients was assessed over the phone by the present author. The following clinical events were also assessed in all participating patients during the observation period:

1. Neurological condition dynamics on the NIH Stroke Scale 2 and 24 hours after MTE.
2. Ischemic lesion volume 24 hours after MTE.
3. Manifestation of intracerebral haemorrhage 24 hours after MTE or in cases of patients' sudden deterioration.
4. Death caused by cerebral ischemia.
5. Functional condition and clinical outcomes in participating patients 90 days after MTE.

2.2. Participating patients

The study included 191 patients in total: 85 men (44.5%) and 106 women (55.5%). Their average age was 68.06±11.24 years, with the youngest patient being 24 and the oldest 95 years old.

Male patients were on average younger than female patients ($p < 0.001$), with men's mean age being at 64.84±11.35 years, and women's at 70.64±10.28 years.

Analysis of patients' anamnesis indicated that a majority of them (87.43%) were diagnosed with primary arterial hypertension. About half of patients were diagnosed with dyslipidemia (54.45%) and atrial fibrillation (50.26%). As shown in Table 1, about 1 patient in 3 was a smoker (31.41%).

Table 1. Anamnesis record of participating patients

Anamnesis record	n (%)
Primary arterial hypertension (PAH)	167 (87.43%)
Congestive heart failure (CHF)	71 (37.17%)
Coronary heart disease	85 (44.5%)
Atrial fibrillation	96 (50.26%)
Type 2 diabetes mellitus	37 (19.37%)
Dyslipidemia	104 (54.45%)
Smoking	60 (31.41%)
Previous stroke	37 (19.37%)

CT characteristics prior to treatment

Native CT images of the ischemic zone showed ASPECTS values ranging from 6 to 10, because this was part of the MTE selection criteria. In most cases (90), native CT scans showed no early ischemic changes, with an ASPECTS score of 10 (see Fig. 1.).

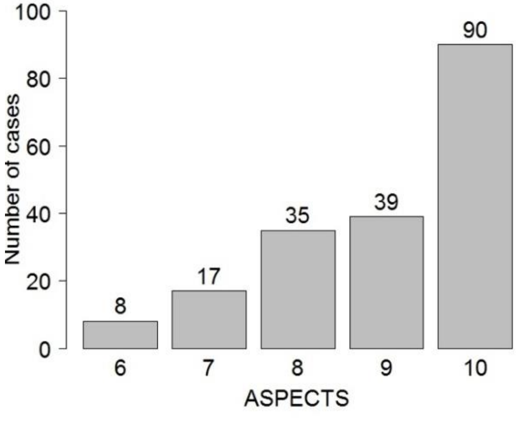


Fig. 1. Distribution of ASPECTS scores

Patients were split into two groups by IVT application: the group treated with direct MTE and the bridging therapy (IVT+MTE) group.

The latter was further divided into sub-groups according to the intravenous thrombolytic agent dose administered to them: the bolus-IVT group (administered less than 30% of full IVT dose), the partial-IVT group (administered between 30% and 50% inclusive), the up-to-75%-IVT group (administered more than 50% and up to 75%), and the full-IVT-dose group. Participating patients were divided into two groups by age (18 to 70 and over 70 years old); into two groups according to the ASPECTS score for early ischemic changes (6–7 and 8–10); and into three groups according to the degree of ICA stenosis (0–50%; 51–99%; and 100%).

2.3. MTE procedure

All participating patients underwent cerebral angiography in order to make CTA data (the location of occlusion) more precise as well as being treated with MTE.

The common femoral artery (arteria femoralis communis) – usually, the right common femoral artery – served as the first choice for procedural access. Using a modified Seldinger technique, an 8F hydrophilic tube with a haemostasis valve (introducer) was inserted into the lumen of the artery. In cases when transfemoral access was technically impossible (due to leg-artery or abdominal aorta occlusion, atypical branching of the carotid arteries, or type III aortic arch), the procedure was performed via the forearm (arteria brachialis) or directly via the common carotid artery (CCA; arteria carotis communis); CCA puncture, however, was performed only once.

Over a 0.035-inch wire, a 4–5 F diagnostic catheter was inserted via the hydrophilic tube into the common or the internal carotid artery of the side of the lesion and cerebral angiography was performed. A 0.035-inch, 260cm-long Emerald replacement guidewire (*Cordis, Santa Clara, CA*) was fed through the diagnostic catheter into the ICA (in case of its occlusion, into the CCA), then replacing the diagnostic catheter with an 8F Cello *(Medtronic, Irvine, CA*) or FlowGate (*Stryker Neurovascular, Fremont, CA*) balloon occlusion catheter.

Over a 0.014 wire, a Rebar (*Medtronic*) or Trevo (*Stryker*) microcatheter was guided via the ballon guide catheter to the site of the occlusion, where the wire was slightly withdrawn into the lumen of the catheter so that the site of the occlusion could be passed atraumatically, simply with a soft tip of the microcatheter. Having successfully passed the site of the occlusion and positioned the microcatheter tip distally from it (by at least two centimetres), the wire is pulled back and superselective angiography performed by injecting a very small amount of contrast medium so as to ensure that the microcatheter sits in the central lumen of the artery rather than being its small branch or extravasated. A Solitaire (Medtronic) or Trevo ProVue (Stryker) stent retriever is navigated into the microcatheter up to its distal tip. The selection of the stent retriever's diameter and length is based on the site of the occlusion. The microcatheter is withdrawn and the stent retriever expands (at the site of the occlusion – only partially, due to the thrombus). Depending on the specifics of the situation, the stent is maintained in place for 3 to 5 minutes (if, after expanding the stent, the blood flow in the damaged territory has been partially restored due to compression of the thrombus, a longer waiting time is possible) so that its metal strands capture the thrombus. Then, having proximally suspended the blood flow in the ICA or CCA using the balloon occlusion catheter and proximal aspiration with a 50ml syringe, the microcatheter and the stent retriever are smoothly pulled back from the system. The lumen of the balloon occlusion catheter is cleared and an angiographic control performed. In case occlusion is still indicated, the microcatheter and the stent retriever are washed with a physiological solution and the procedure is repeated until the procedure is effective or becomes impossible for technical reasons (e.g. the fractionation of the thrombus and distal embolization into smaller branches unreachable with these devices or angiographic control showing no effect whatsoever after 5 sessions).

In cases of tandem occlusion, ICA occlusion was passed through with a 0.014-inch wired and expanded using a Maveric balloon guide catheter (Medtronic). The balloon occlusion catheter is pushed through the already-expanded area somewhat distally and the usual MTE procedure is continued in order to extract the distal thrombus. After ICA recanalization, the balloon occlusion catheter is navigated more proximally to the CCA and an angiographic control is performed to determine the degree of ICA stenosis. In case of no satisfactory result of angiographic control, a Wallstent self-expanding stent (Boston Scientific Corporation) is navigated and implanted into the ICA stenosis site. The catheters are pulled back, and the puncture site bleeding is stopped using an 8F Angio-Seal vascular closure device.

Assessment of MTE results and calculation of the degree of ICA stenosis

This study considered artery recanalization (the MTE result) an angiographic success when the blood flow in the territory of the revascularized artery after the procedure reached a TICI (*Thrombolysis in Cerebral infarction*, Table 2) grade of 2b or 3:

Table 2. TICI grading scale for quantifying the degree of perfusion

Grade	Definition
0	No perfusion
1	Minimal contrast media penetration without clear signs of target-territory perfusion.
2a	Partial perfusion of distal branches, with 2/3 of the target-territory being filled.
2b	Partial perfusion of distal branches, with the entire target-territory being filled, albeit more slowly.
3	Complete perfusion.

The degree of ICA stenosis was quantified on the basis of pre-MTE angiographic imaging using the NASCET (*North American Symptomatic Carotid Endarterectomy Trial*) [24] methodology for determining the degree of the angiographic narrowing of the ICA. The degree of narrowing, in per cent, is calculated by subtracting the narrowest ICA stenosis diameter (a) from the diameter of normal distal ICA (b), and dividing by the post-stenotic ICA diameter (b).

$$\text{NASCET degree of stenosis (\%)} = [(b-a)/b] \times 100\%$$

24-hour post-thrombolysis CT scan and ischemic stroke volume measurement

All patients, 24 hours after the procedure, underwent a cerebral CT scan so as to assess the volume and localization of ischemic changes and rule out the occurrence of intracerebral haemorrhage. CT scans were performed in the urgent examination sub-section of the radiology section I of the VUHSK department of radiology and nuclear medicine using a GE Discovery 64-slice computed tomography scanner (General Electric Healthcare, Milwaukee, WI, USA). CT scan parameters: duration of a single revolution of the X-ray tube is 1 second, slice thickness – 5mm, X-ray tube voltage – 120kV, X-ray tube current – 210mA, scope of the scan – from base of the skull to top.

All images obtained from the scan were forwarded to the dedicated radiology workstation, and their processing and assessment was done using 3D Slicer (version 4.9.0). All non-contrast CT images were assessed by a single researcher: the present author. The final ischemic volume was estimated by delineating the lesion territory in a semi-automated way using a specialised marker (a yellow circle in the image below) in the axial plane of each 5-mm slice and adjusting it in other planes. The software automatically fills the gaps between slices and calculates the total volume of the marked territory in millilitres (Fig. 2 and 3).

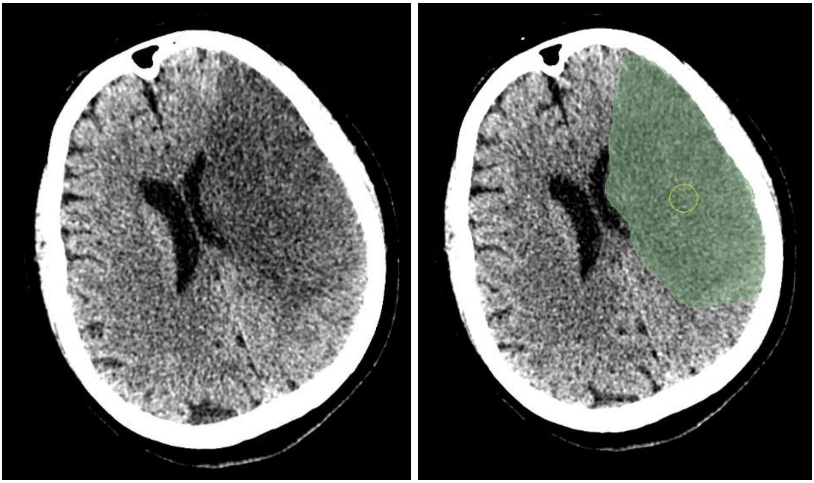
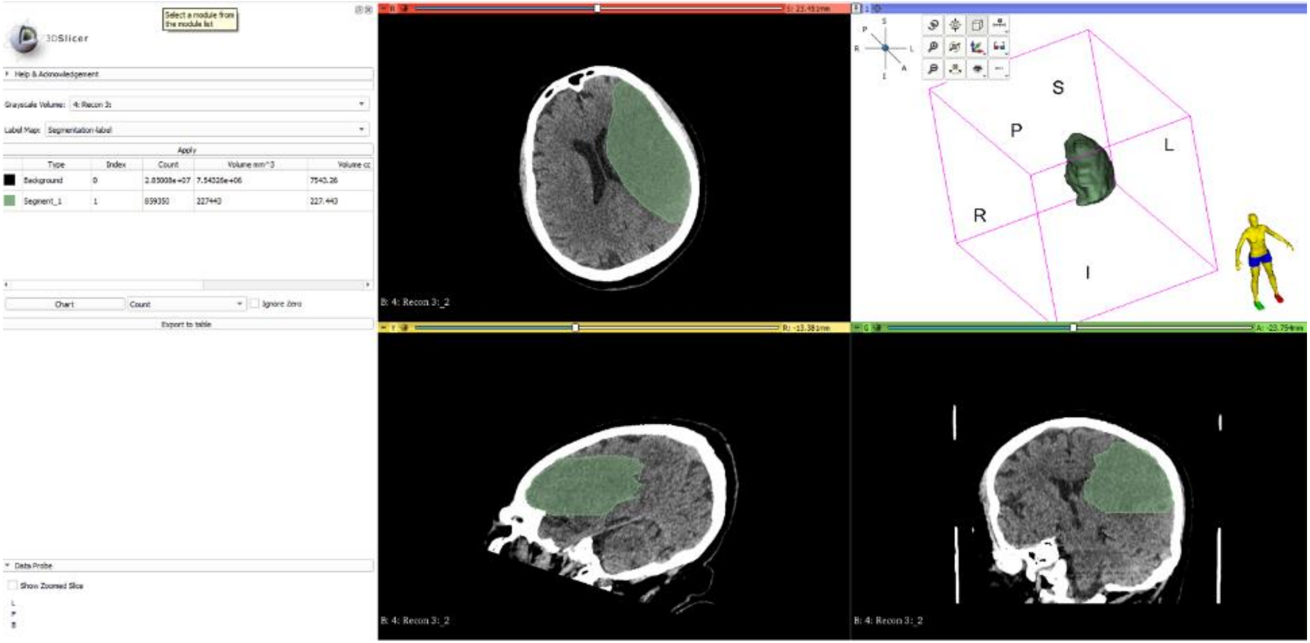


Fig. 2 Ischemic segment (CT scan of the hypodense zone, on the left) and its marking (on the right).



Grayscale Volume: 4: Recon 3:

Label Map: Segmentation-label

	Type	Index	Count	Volume mm^3	Volume cc
■	Background	0	2.85008e+07	7.54326e+06	7543.26
🟩	Segment_1	1	859350	227443	227.443

Count

☐ Ignore zero

Fig. 3. Ischemic volume marked (across various planes and its 3D reconstruction) and calculated (Segment_1).

Intracerebral haemorrhages were classified by their anatomic-radiological characteristics, in accordance with the ECASS I and II (European Cooperative Acute Stroke Study) [25] classification (see Table 3).

Table 3. Intracerebral haemorrhage classification

Type of ICH	Anatomic-radiological appearance
Haemorrhage infarction type 1 (HI1)	Small hyperdense petechiae in the ischemic territory without mass effect
Haemorrhage infarction type 2 (HI2)	More confluent hyperdense petechiae in the ischemic territory without mass effect
Parenchymal hematoma type 1 (PH1)	Intracerebral haemorrhage occupying up to 30% of the ischemic territory with mild mass effect
Parenchymal hematoma type 2 (PH2)	Intracerebral haemorrhage occupying more than 30% of the ischemic territory with significant mass effect

Based on their clinical manifestation, intracerebral haemorrhages were split into symptomatic and asymptomatic ones according to PROACT II (Prolyse in Acute Cerebral Thromboembolism) criteria. [7] Symptomatic haemorrhage, according to the ECASS II (Second European Cooperative Acute Stroke Study) classification is any symptomatic intracranial haemorrhage that was not indicated by a cranial CT scan prior to thrombolysis or MTE and worsens the patient’s neurological condition by 4 points or more on the NIH Stroke Scale [26].

3. RESULTS

3.1. General characteristics

3.1.1.Characteristics of time intervals

The average period of time between the onset of symptoms and a consultation with a medical neurologist in the emergency room (doors) or the department in which the stroke occurred (in case of VUHSK inpatients) is 128 minutes (there were 9 wake-up stroke patients with unknown time of the onset of symptoms). The majority of patients, i.e. about 60% reached a medical institution within 2 hours (120 mins), while some 20% did so in 4 hours.

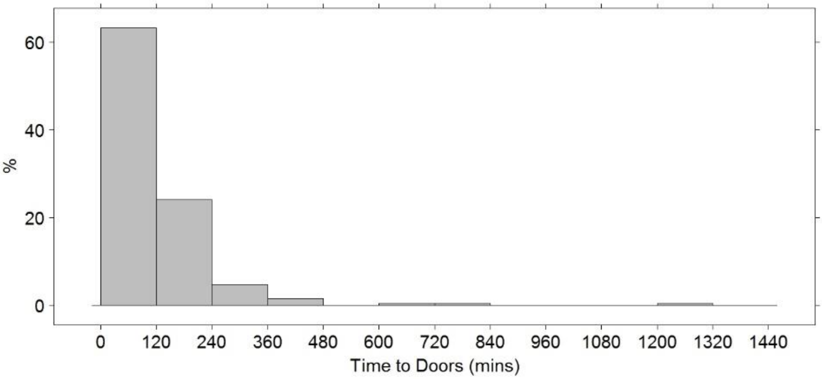


Fig. 4 Histogram of time distribution prior to arrival

A cerebral CT of patients was performed and assessed in, on average, half an hour (33 mins) after the arrival (see Fig. 5 below, left-hand side). The quickest time was 7 minutes and almost all patients underwent a CT scan within 1 hour, with the exception of a few isolated cases taking more than one hour.

The average time between a CT scan and MTE is roughly one hour (54 mins). In over 60% of cases, this interval of time was up to one hour, with about 30% of cases taking between one and two hours (see Fig. 5 below, right-hand side).

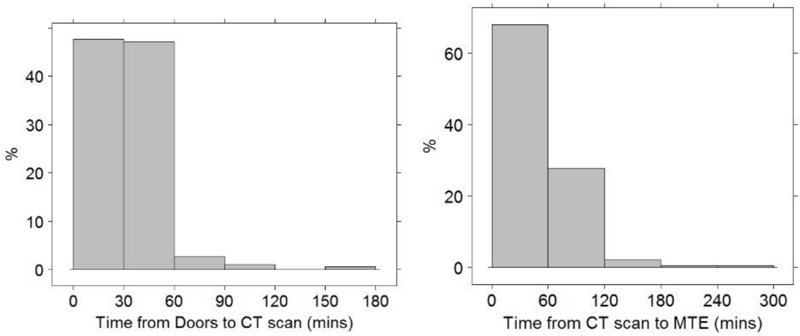


Fig. 5. Histograms of time distribution until a CT scan (on the left) and between a CT scan and MTE (on the right)

Table 4. Numerical characteristics of time elapsed until a specific procedure

Time interval / mins	**min**	**Q1**	**Me-dian**	**Mean**	**Q3**	**Max**	**NA**
Symptoms to Doors	1.0	66.5	98.0	128.0	150.0	1320.0	9
Doors to CT scan	7.00	22.00	31.00	33.88	40.00	151.00	2
CT scan to MTE	10.00	35.00	50.00	54.66	69.00	246.00	2
MTE duration (puncture to recanalization)	10.00	25.00	40.00	47.11	60.00	185.00	–
Symptoms to recanalization	85.0	191.2	240.0	261.8	297.0	1480.0	9
Doors to IVT	7.0	27.0	37.0	39.21	49.0	120.0	120

The duration of the quickest MTE was 10 minutes and the longest artery recanalization took 185 minutes. On average, the duration of MTE is less than one hour (47 minutes). The most common (about 40%) were MTE procedures taking between 30 and 60 minutes (see Fig. 6 below, left-hand side).

The average time between the onset of symptoms and recanalization was 261 minutes. Almost all cases fall within the interval of up to 445 minutes (see Fig. 6 below, right-hand side), with only a few taking more than 445 minutes or 7.42 hours.

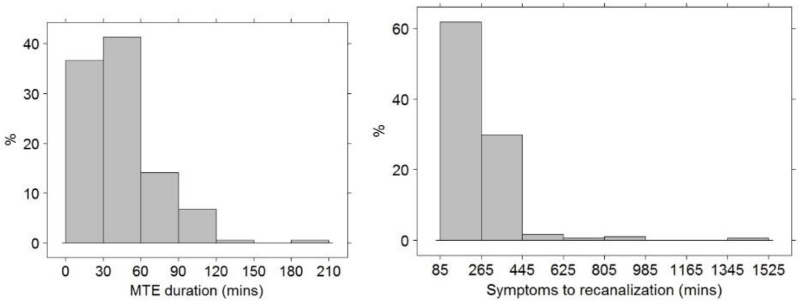


Figure 6. Histograms of time distribution of MTE duration (on the left) the time from the onset of symptoms to recanalization (on the right)

3.1.2.Bridging MTE

IVT treatment prior to MTE was given to a smaller proportion of all participating patients, namely 71 (37.17%): the largest proportion of them – 34 patients – were injected with a full IVT dose (100%), with 14 getting the up-to-75% IVT dose, 16 getting less than half (<50%), and 7 only managing to get injected with only slightly more than a bolus dose (<30%) of IVT prior to MTE.

The average time between the arrival and an IVT procedure was 38 minutes. The longest time elapsed until an IVT procedure was 120 minutes, yet there was only one such case. Most cases fall within the 30 to 60 minutes interval (see Fig. 7 below).

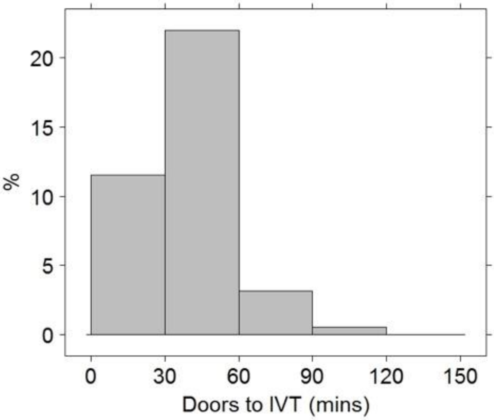


Fig. 7. Histogram of time distribution between arrival and IVT

3.1.3.Characteristics of MTE procedure

The majority of occlusions – 112 (58.6%) – were observed in the M1 segment of the middle cerebral artery (MCA). As show in Table 5, the rarest were tandem occlusions (ICA and more distal occlusions) – 23 (12%) – and T-type occlusions (ICA bifurcation) – 29 (15.2%). Somewhat more frequent (99 occlusions (51.8%)) were lesions in the left-side ICA.

Table 5. Occlusion frequency by localization

Occlusions	M1	M2	T-type	ICA	Tandem	Left ICA
Number of cases (%)	112 (58.64%)	41 (21.47%)	29 (15.18%)	35 (18.32%)	23 (12.04%)	99 (51.83%)

Successful recanalization of the artery (TICI 2b-3) during MTE was achieved in 164 patients (85.9%).

The largest proportion of revascularizations were completed in one thrombectomy session (85, 44.5%), with 41 (21.5%) taking two sessions and 4 participating patients failing to receive even a single thrombectomy session. The average number of thrombectomy sessions was 2.2.

Less than half of MTE procedures – 84 cases (44.7%) – qualified as first-pass success.

In most patients (90.1% or 172 cases), application of the balloon occlusion catheter was successful. The study has also shown that in most patients – 141 cases (73.8%) – there was no hemodynamically significant narrowing of the internal carotid artery on the side of the lesion (ICA stenosis from 0 to 50%). Hemodynamically significant stenosis (ICA stenosis from 51 to 99%) was observed in 37 patients (19.4%), while in 11 (6.8%) it was the occlusion that had been diagnosed in the first place. ICA stent placement procedure had to be performed in 29 patients (15.2%) during MTE.

3.1.4. Characteristics of neurological condition dynamics (NIH Stroke Scale)

Neurological condition in patients treated with MTE rapidly improves as is evidenced by falling NIH Stroke Scale average scores over the course of treatment: the average NIHSS score upon arrival was 12.8±5, 2 hours after procedure it was 8.3±5.9, and 24 hours after MTE it was cut almost in half, being at 6.7±6. The second diagram (Fig. 8), illustrating patient-by-patient NIHSS dynamics, indicates that despite the fall in the NHISS score over time across patients on average, there were some patients whose NHISS score rose over time. Mostly, these are the cases of unsuccessful MTE.

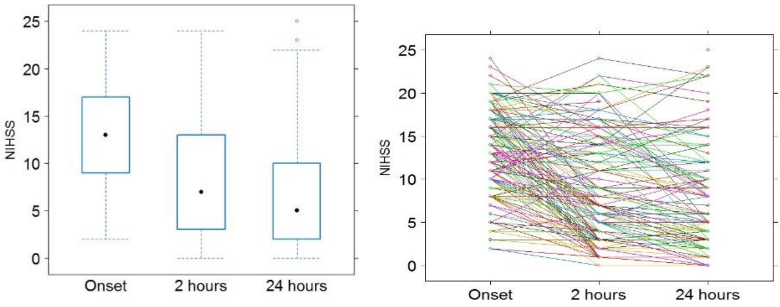


Fig. 8. Rectangular diagram of NIHSS scores (on the left) and each patient's dynamics (on the right)

3.1.5.First-day (24 hrs) CT characteristics

Final ischemic volume, measured 24 hours after MTE in CT imagery, usually did not exceed 50ml (see Fig. 9 below). There were some patients with no post-MTE ischemic changes indicated, yet there were also cases of ischemic lesions in nearly all of the hemisphere. On average, final ischemic volume was at 41.5±77.5.

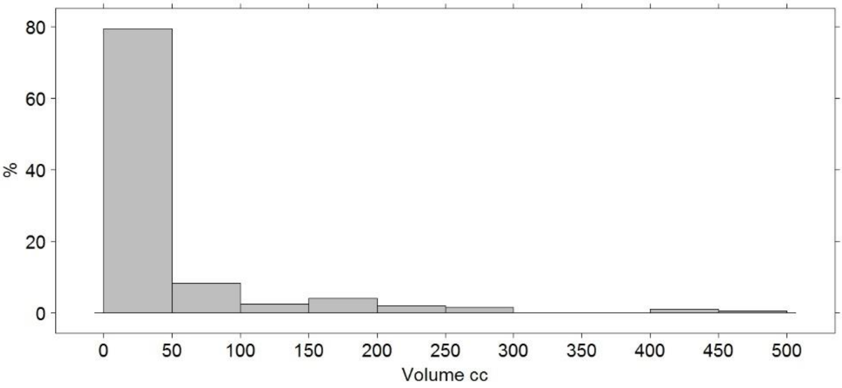


Fig. 9. Histogram of final ischemic volume distribution

3.1.6.Functional condition dynamics (MRS scale)

MRS average prior to the onset of symptoms was at 0.6±0.6, while 90 days later it was already at 2.3±2.

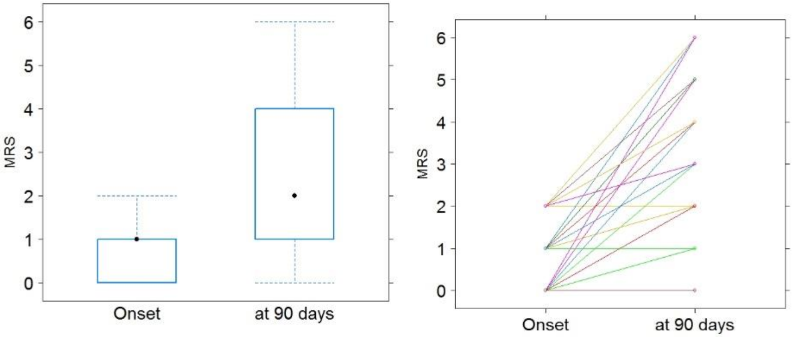


Fig. 10. Boxplot of MRS measurements (on the left) and MRS measurement dynamic in each patient (on the right)

3.1.7. Frequency of adverse periprocedural and late clinical events

Table 12 lists case numbers of specific complications. Mostly, those were asymptomatic intracerebral haemorrhage cases (26 patients), with periprocedural fractionation of the thrombus and distal embolization (in previously non-occluded branches, e.g. of the anterior cerebral artery) observed in 24 patients (12.6%). To note, most of these embolizations were cleared during repeated MTE sessions. Symptomatic intracerebral haemorrhage (sICH) occurred in 12 patients (6.3%), with 13 patients (6.8%) dying of stroke.

Table 12. Numerical characteristics of complications

Complication	0 (unobserved)	1 (observed)
aICH	165 (86.39%)	26 (13.61%)
sICH	179 (93.72%)	12 (6.28%)
Distal embolization	167 (87.43%)	24 (12.57%)
Death by stroke	178 (93.19%)	13 (6.81%)

If one divides ICH and SAH (subarachnoid haemorrhage) cases by their anatomic-radiological characteristics, it can be seen that they occurred almost in one patient out of five (19.9%). It should be noted, however, that those also included cases of mixed ICH (e.g. SAH together with hemorrhagic stroke (HS) or parenchymal haemorrhage (PH)). There were 5 such cases.

Table 13. Numerical characteristics ICH types and SAH

Type of ICH	0	HI1	HI1/SAH	HI2	HI2/SAH	PH1	PH2	PH2/SAH	SAH
no. of (%)	153 (80.10%)	8 (4.19%)	1 (0.52%)	9 (4.71%)	2 (1.04%)	2 (1.04%)	8 (4.19%)	2 (1.04%)	6 (3.14%)

3.2. Determining relationships between patient characteristics

3.2.1. MTE success factors

The average age of patients with successful MTE is a little lower than that of patients whose MTE was unsuccessful, but these differences in age are not statistically significant (p = 0.1702).

Table 14. Numerical characteristics of the relationship between successful MTE and patients' age

Successful MTE (TICI scale)	min	Q1	Median	Mean	Q3	Max	SD	t-test
No	37	66	71	70.81	76.5	90	10.98	p = 0.1702
Yes	24	62	69	67.61	75	95	11.247	

3.2.2.MTE success and concomitant pathology

The success of MTE (TICI 2b and TICI 3) bears no statistically significant relationship to any particular comorbidity in patients.

The table below shows that from all intervals of time included in the study only MTE duration is related to the success of MTE ($p < 0.0001$): successful MTEs take about half the time of unsuccessful ones: 42.65 and 74.22 minutes respectively.

Table 15. Characteristics of successful MTEs and MTE time intervals

Time interval / mins	**Successful MTE**	**min**	**Q1**	**Median**	**Mean**	**Q3**	**Max**	**SD**	t-test, WT
Symptoms to Arrival	No	30.00	65.25	93.00	115.04	126.75	408.00	87.96	p = 0.4647, p = 0.5886
	Yes	1.00	70.00	99.00	130.21	155.00	1320.00	140.19	
	All	1.0	66.5	98.0	128.0	150.0	1320.0	133.89	
Doors to CT scan	No	13.00	20.00	36.00	38.56	42.00	151.00	29.789	p = 0.3593, p=0.9636
	Yes	7.00	24.00	31.00	33.10	40.00	110.00	14.75	
	All	7.00	22.00	31.00	33.88	40.00	151.00	17.684	
CT to MTE	No	10.00	36.00	53.00	54.96	65.50	194.00	34.05	p = 0.9592, p = 0.9364
	Yes	10.00	35.00	49.50	54.60	69.00	246.00	29.05	
	All	10.00	35.00	50.00	54.66	69.00	246.00	29.716	
MTE duration (puncture to recanalization)	No	15.00	59.50	70.00	74.22	88.50	185.00	32.911	$p < 0.0001$, $p < 0.0001$
	Yes	10.00	25.00	37.50	42.65	55.00	140.00	23.393	
	All	10.00	25.00	40.00	47.11	60.00	185.00	27.19	
Symptoms to recanalization	No	125.00	240.00	260,00	284.35	315.00	635.00	106.76	p = 0.279, p = 0.0530
	Yes	85.00	188.75	233.00	258.06	290.00	1480.00	145.72	
	All	85.0	191.2	240.0	261.8	297.0	1480.0	140.86	
Doors to IVT	No	20.00	23.25	32.50	40.50	44.00	120.00	28.29	p = 0.8568, p = 0.4657
	Yes	7.00	29.50	38.00	38.95	50.00	87.00	15.61	
	All	7.0	27.0	37.0	39.21	49.0	120.0	18.11	

(WT) means Mann-Whitney-Wilcoxon test

IVT was applied to a smaller proportion of all participating patients, namely 71 (37.2%).

IVT application and the success of MTE are independent features (p = 0.52), i.e. the percentage of successful MTEs in patients treated with IVT is similar to that of patients not treated with IVT: 83.1% and 87.2% respectively.

Table 16. Numerical characteristics of the relationship between IVT and the success of MTE

Successful MTE	IVT = 0	IVT = 1	Total	Chi-squared test
No	15 (12.82%; 55.56%)	12 (16.9%; 44.44%)	27 (14.36%; 100%)	p=0.5294
Yes	102 (87.18%; 63.35%)	59 (83.1%; 36.65%)	161 (85.64%; 100%)	
Total	117 (100%; 62.23%)	71 (100%; 37.77%)	188 (100%; 100%)	

(IVT = 0) means IVT was not applied; (IVT = 1) means IVT was applied.

3.2.3. Effect of bridging therapy on MTE parameters

We checked whether important periprocedural factors (number of thrombectomy sessions, MTE duration, and first-pass success of recanalization) bear a relationship to IVT application. Neither the average number of thrombectomy sessions, nor the average MTE duration are related to IVT application (p = 0.78 and p = 0.77 respectively). The first-pass success of recanalization also bears no relationship to IVT application (p = 0.99): the first-pass success of MTE was at about 45% in both groups, i.e. those that were injected with IVT and those that were not.

3.2.4. Effect of bridging therapy on participants' neurological condition dynamics

Table 17 lists numerical characteristics of NIHSS scores for each point in time (on arrival, 2 hours after MTE and 24 hours after MTE) for the group of patients injected with IVT and the group not injected with IVT. We can see that the mean NIHSS score is slightly lower in patients treated with IVT, yet we had to assess whether this difference is statistically significant and used the linear mixed model for this purpose.

Table 17. Numerical characteristics of IVT application and NHISS score dynamics

IVT application	Point in time	mins	Q1	Median	Mean	Q3	Max	SD
IVT = 0	On arrival	2.00	10.00	13.00	13.24	17.00	24.00	5.064
	After 2 hours	0.00	3.25	7.00	8.51	13.00	24.00	6.184
	After 24 hours	0.00	2.00	5.00	6.66	10.00	25.00	6.109
IVT = 1	On arrival	4.00	8.00	12.00	12.18	16.00	23.00	4.847
	After 2 hours	0.00	3.00	6.00	7.87	12.25	21.00	5.634
	After 24 hours	0.00	2.00	5.00	6.80	10.00	23.00	5.991

(IVT = 0) means IVT was not applied; (IVT = 1) means IVT was applied.

We first compared the NIHSS score on arrival with the score 2 hours after IVT. It tends to decrease by 4.64 points on average ($p < 0.0001$), but there is no statistically significant difference in the size of this decrease between patients treated with IVT and those that were not (p = 0.82).

A comparison between the 2-hour and the 24-hour points showed that the average change between them was −2.13 (p<0.0001), yet there was no statistically significant difference in the dynamic of these two points in time between patients treated with IVT and those that were not (p = 0.087).

Compared with the NIHSS score on arrival, the score 24 hours after IVT tends to decrease by 6.39 points (p < 0.0001), and there is also no statistically significant difference here between the two IVT groups (p = 0.28).

Figures 11 and 12 illustrate the above dynamic across IVT group.

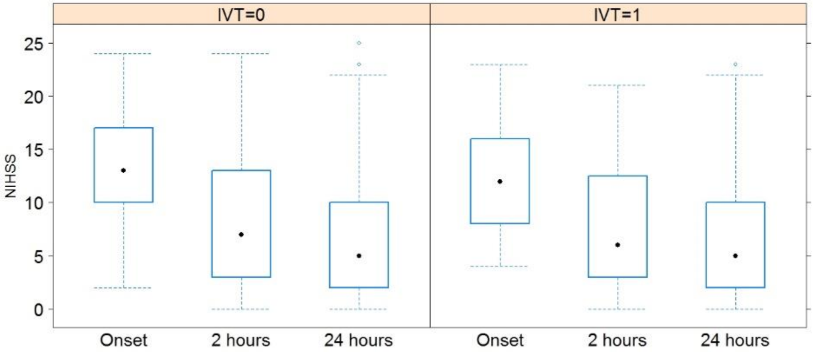


Fig. 11. Boxplot of neurological condition change (in NIHSS score): no IVT (IVT = 0) on the left and with IVT (IVT = 1) on the right.

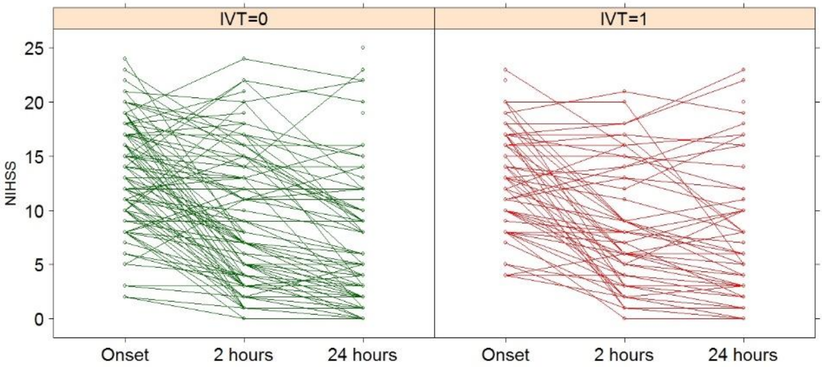


Fig. 12. Neurological condition change (in NIHSS score) patient by patient: no IVT (IVT = 0) on the left and with IVT (IVT = 1) on the right.

3.2.5. Effect of MTE success on neurological condition change

Table 18 lists numerical NIHSS characteristics at each point in time of patients successfully treated with MTE (TICI 2b and TICI 3) and those whose MTE treatment was unsuccessful (there 27 unsuccessful procedures in total). The table 18 shows (as do Fig. 13 and 14) a greater change indeed in the average NIHSS score after a successful MTE.

Table 18. Effect of successful recanalization on neurological condition change

MTE successful	Point in time (of NIHSS score)	mins	Q1	Median	Mean	Q3	Max	SD	N
No	On arrival	5.00	10.00	14.00	13.44	17.00	23.00	5.09	27
	After 2 hours	6.00	11.00	16.00	14.55	18.00	22.00	4.90	20
	After 24 hours	2.00	8.00	12.00	12.48	16.00	25.00	5.89	21

Yes	On arrival	2.00	9.00	13.00	12.73	17.00	24.00	4.99	158
	After 2 hours	0.00	3.00	6.00	7.39	11.00	24.00	5.58	142
	After 24 hours	0.00	2.00	5.00	5.93	8.00	23.00	5.65	154

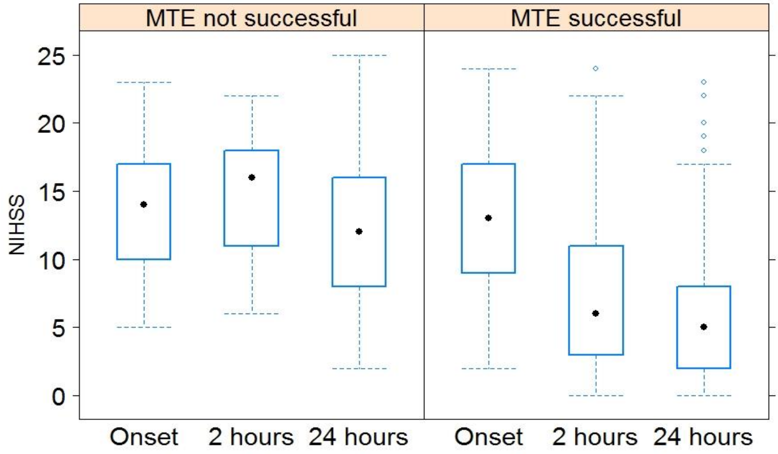


Fig.13. Boxplot of neurological condition change (NIHSS score) and MTE results

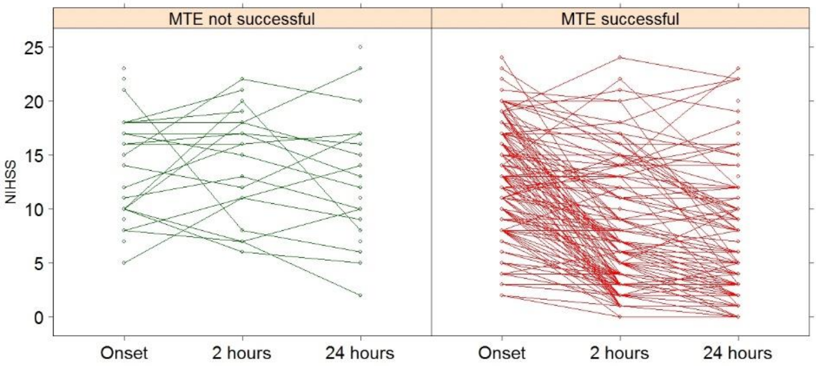


Fig.14. Neurological condition change (NIHSS score) by MTE results

In cases of successful MTEs, patients' NIHSS score 2 hours after the procedure was, on average, 6.38 points lower than in cases of unsuccessful MTEs ($p < 0.0001$). There is no statistically significant difference in the NIHSS score change between 2 and 24 hours after the procedure in patients with successful MTE and those with unsuccessful MTE ($p = 0.710$). Compared with NIHSS score on arrival, however, the score 24 hours after the procedure was, on average, 6.173 points lower in patients with successful MTE vis-à-vis patients with unsuccessful MTE ($p < 0.0001$). See Table 19.

Table 19. The results of estimated Linear mixed model where hypotheses about NIHSS differences at different time points and relationship with MTE results are estimated

Points of comparison	Effect included in the Linear mixed model	Estimated parameter values (standard error), p value
NIHSS after 2 hours vs. NIHSS on arrival	Intercept	13.44 (0.96), p = 0.000
	Time point: After 2 hours	1.04 (1.12), p = 0.353
	MTE successful	−0.75 (1.04), p = 0.475
	Time point: After 2 hours *MTE successful	−6.38 (1.20), p = 0.000
NIHSS after 24 hours vs. NIHSS after 2 hours	Intercept	14.54 (1.19), p = 0.000
	Time point: After 24 hours	−1.48 (0.80), p = 0.067
	MTE successful	−6.79 (1.28), p = 0.000
	Time point: After 24 hours *MTE successful	−0.32 (0.85), p = 0.710
NIHSS after 24 hours vs. NIHSS on arrival	Intercept	13.44 (0.963), p = 0.000
	Time point: After 24 hours	−0.564 (1.162), p = 0.628
	MTE successful	−0.746 (1.041), p = 0.475
	Time point: After 24 hours *MTE successful	−6.173 (1.242), p = 0.000

3.2.6. Effect of MTE success on final ischemic volume

In cases of successful MTEs, final ischemic volume is, on average, significantly lower (p = 0.0002): it is equal to 26.6±54.9ml; the distribution of means also appears to be considerable (see Fig. 15). In cases of unsuccessful MTEs, final ischemic volume, on average, increases by 100ml, reaching 129.5±124.8ml.

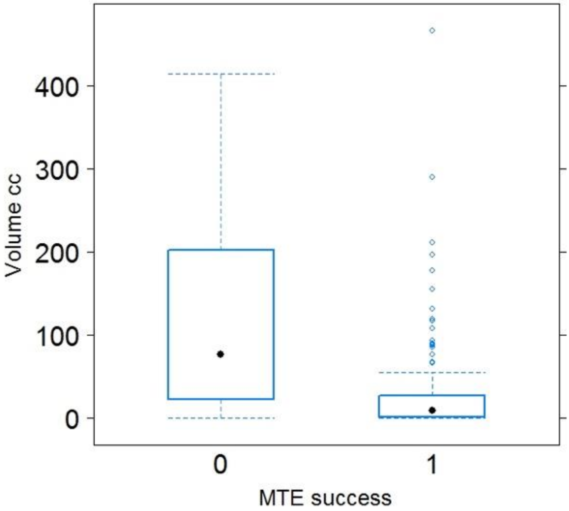


Fig. 15. Boxplot of MTE success and final ischemic volume

3.2.7.Effect of bridging therapy on functional condition (mRS scale)

Table 20 lists numerical characteristics of mRS prior to the onset of symptoms and 90 days after MTE in patients treated with IVT and those not treated with MTE. We can see that the average mRS score in bridging therapy patients (IVT = 1) is somewhat lower both prior to the onset of symptoms and 90 days after treatment.

The mRS score in patients treated with IVT is, on average, 0.30 points lower (p = 0.0016). If we compare two points in time (prior to MTE and 90 days after it), we see that the average mRS score change after 90 days is 1.69 points ($p < 0.0001$) and that this mRS score change difference between patients treated with IVT and those that were not is not statistically significant ($p = 0.8790$). These results are illustrated in the diagrams below. The first of them is a boxplot displaying numerical characteristics of mRS scores, and the second provides patient-by-patient mRS dynamics.

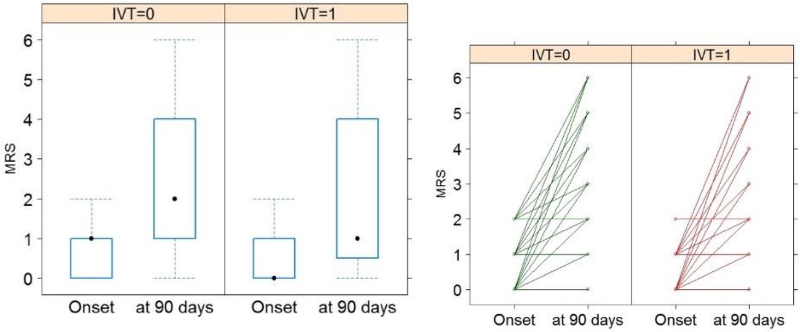


Fig. 16. Boxplot of numerical characteristics of mRS scores (on the left) and patient-by-patient mRS dynamics (on the right).

3.2.8. Effect of bridging therapy on functional condition (mRS scale) by thrombolytic dosage

Functional condition change measured in mRS points was significant in all groups of different IVT dosage yet slightly different across some of them: the largest average mRS score change was observed in the full-IVT dose group of patients (2.15±0.34, $p < 0.0001$), yet the difference between this dosage and any other dosage is not statistically significant (see Table 20, which shows $p = 0.60$ between <30%-IVT and 100%-IVT; $p = 0.08$ between <50%-IVT and 100%-IVT; and $p = 0.11$ between <75%-IVT and 100%-IVT).

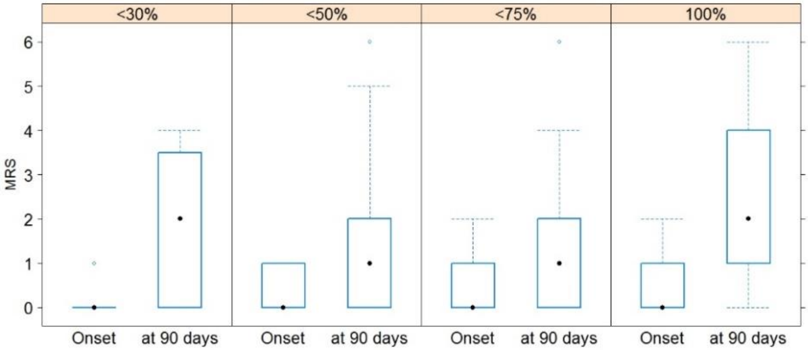


Fig. 17. Boxplot of IVT dosage and mRS score changes

3.2.9. Effect of bridging therapy on frequency of complications

Asymptomatic ICH (excluding SAH) was somewhat more frequent in patients not treated with IVT (p = 0.054): 14.17% in those treated with IVT and 4.23% in those not treated with IVT. However, there were very few cases of aICH in the study, i.e. only in 20 patients out of 191, which means that further data is needed to assess the accuracy of this conclusion.

IVT application bears no relationship to either HI or PH values: respectively, p = 0.138 and p = 0.415.

The number of symptomatic intracerebral haemorrhages (sICH) and IVT application have no statistically significant relationship (p = 0.2083), yet sICH was somewhat more frequent in bridging-therapy patients (9.8% compared with 4.17%). Given the low number of sICH cases, however, this conclusion might not be fully reliable.

The number of SAH was larger when IVT was not applied compared to when it was (7.5% and 2.8% respectively), yet these differences are not statistically significant (p = 0.307). However, there were only 2 instances of SAH in bridging therapy patients, which means that further data is needed to assess the accuracy of this conclusion.

The number of deaths of stroke and IVT application have no statistically significant relationship either ($p = 0.843$).

The number of distal embolization cases was larger when IVT was not applied compared to when it was (15.9% and 7.04% respectively), yet these differences are not statistically significant ($p = 0.117$).

ICA stenting and IVT application also have no statistically significant relationship ($p = 0.7639$).

3.3. Relationship between good clinical outcomes and various characteristics included in the study

Each characteristic against which we wanted to check mRS scores 90 days after the procedure received its own logistic regression analysis; their results are listed in Table 20. Marked in red are cases in which the characteristic in question had a relationship to good or bad 90-day mRS clinical outcome. As we can see, good/bad clinical outcomes are related to: age ($p = 0.05$), the age-group of patients over 70 ($p = 0.05$) and much more so with the age-group of patients over 60 ($p = 0.005$); ASPECTS score of >=8 ($p = 0.0001$); coronary heart disease diagnosis ($p = 0.0113$); and atrial fibrillation ($p = 0.016$); also observed is a relationship to type 2 diabetes ($p = 0.06$). Of all time intervals included in the study, 90-day mRS bears a statistically significant relationship only to the duration of MTE itself ($p < 0.0001$) and the time elapsed between the onset of symptoms and recanalization (>= 270 mins).

With a 1-year increase in patients' age, the odds of a bad 90-day mRS clinical outcome increases by 1.03 times; CI = (1.001; 1.058).

With a 5-year increase in patients' age, the odds of a bad 90-day mRS clinical outcome increases by 1.15 times; CI = (1.004; 1.329).

With a 10-year increase in patients' age, the odds of a bad 90-day mRS clinical outcome increases by 1.3 times; CI = (1.008; 1.765).

If we compare the <70 and >=70 age-groups, we see that the odds of a bad clinical outcome in patients over 70 years of age increases by 1.78 times; CI = (0.999; 3.274).

If we compare the <60 and >=60 age-groups, we see that the odds of a bad clinical outcome in patients over 60 years of age increases by 3.5 times; CI = (1.534; 9.104).

ASPECTS score of <8 increases the odds of a bad clinical outcome by as many as 6.8 times (2.708; 19.649)

Coronary heart disease diagnosis increases the odds of a bad clinical outcome by 2.15 times; CI = (1.194; 3.928).

Atrial fibrillation increases the odds of a bad clinical outcome by 2.1 times; CI = (1.151; 3.807).

Type 2 diabetes increases the odds of a bad clinical outcome by 1.99 times; CI = (0.963; 4.142).

With a 5-minute increase in MTE duration, the odds of a bad clinical outcome increases by 1.15 times; CI = (1.082; 1.231).

With a 10-minute increase in MTE duration, the odds of a bad clinical outcome increases by 1.3 times; CI = (1.171; 1.515).

With a 30-minute increase in MTE duration, the odds of a bad clinical outcome increases by 2.3 times; CI = (1.607; 3.475).

If the time elapsed between the onset of symptoms and recanalization exceeds 270 minutes, the probability of a bad clinical outcome increases by 2.28 times; CI = (1.219; 4.289).

Table 20. Logistic regression analyses of the relationship between 90-day mRS and the characteristic specified (characteristics that bear a statistically significant relationship to 90-day mRS are marked in red). In addition to the characteristic in question, each model also includes an intercept. The intercept is no of importance in interpreting results, however.

Effects included in the logistic regression model	Parameter value	Standard error	p value
Intercept	−0.5819	0.2025	0.00406
Sex	0.2252	0.2993	0.45174
Intercept	−2.39064	0.99287	0.016
Age	0.02788	0.01422	0.050
Intercept	−0.7916	0.2238	0.0004
Aged >=70	0.5868	0.3022	0.0522
Intercept	−1.5198	0.4173	0.00027
Aged >=60	1.2551	0.4482	0.0051
Intercept	−0.3709	0.1857	0.0458
IVT	−0.3012	0.3121	0.3345
Intercept	−0.37086	0.18572	0.0458
IVT dose of < 30% (compared with no IVT)	0.08318	0.78602	0.9157
IVT dose of < 50% (compared with no IVT)	−0.72775	0.60649	0.2302
IVT dose of < 75% (compared with no IVT)	−0.92842	0.67730	0.1704

IVT dose of 100% (compared with no IVT)	0.01418	0.39487	0.9713
Intercept	−0.7673	0.1678	4.83e-06
ASPECTS <8	1.9199	0.4975	0.0001
Intercept	−1.0986	0.4714	0.0198
PAH	0.6981	0.4971	0.1602
Intercept	−0.6559	0.1925	0.000656
Chronic heart failure	0.4581	0.3065	0.135051
Intercept	−0.8383	0.2116	7.42e-05
Coronary heart disease	0.7677	0.3031	0.0113
Intercept	−0.8575	0.2255	0.000144
Atrial fibrillation	0.7323	0.3045	0.016164
Intercept	−0.6349	0.1699	0.000186
Type 2 diabetes mellitus	0.6889	0.3702	0.062750
Intercept	−0.3765	0.2195	0.0863
Dyslipidemia	−0.2173	0.3002	0.4692
Intercept	−0.3277	0.1874	0.0803
Smoking	−0.5196	0.3383	0.1246
Intercept	−0.4763	0.1658	0.00406
Previous stroke	−0.0201	0.3773	0.95752

Intercept	−0.45676	0.29320	0.119
ICA stenosis of 0–50%	−0.05029	0.34088	0.883
Intercept	−0.4658	0.1661	0.00504
ICA stenosis of 51–99%	−0.1473	0.3823	0.69995
Intercept	−0.5377	0.1549	0.000519
ICA stenosis of 100%	0.7201	0.6250	0.249311
Intercept	−0.5274865	0.2118907	0.0128
Duration of time: symptoms to doors	0.0000842	0.0011398	0.9411
Intercept	−0.655607	0.323801	0.0429
Duration of time: Doors to CT scan	0.004996	0.008397	0.5518
Intercept	−1.833304	0.353766	< 0.0001
Duration of time: MTE procedure	0.028095	0.006541	< 0.0001
Intercept	−0.604500	0.409789	0.140
Duration of time: Doors to MTE	0.001411	0.004327	0.744
Intercept	−0.572391	0.313136	0.0676
Duration of time: CT scan to MTE	0.001585	0.005004	0.7514
Intercept	−0.857570	0.334167	0.0103
Duration of time: symptoms to recanalization	0.001294	0.001127	0.2508
Intercept	−0.8232	0.1999	3.83e-05

Duration of time: symptoms to recanalization >=270 mins	0.8232	0.3201	0.0101
Intercept	−0.07428	0.62357	0.905
Duration of time: Doors to IVT	−0.01392	0.01514	0.358

Having combined all significant characteristics within a multilevel logistic regression model, we can observe that patient's age becomes not statistically significant (perhaps its significance in the model expresses itself via certain previous diseases, which themselves remained significant; after all, the older the patient, the more comorbidities there are). The reduction in the significance of diabetes, too, could perhaps be attributable to its correlation with other diseases included in the model (such as coronary heart disease and atrial fibrillation). The interval of time between the onset of symptoms and recanalization that is longer than 4.5 hours (>270 minutes) is also insignificant, and perhaps this is because it carries the same information as MTE duration, which itself remained a significant factor in the model.

Table 21. Parameters of the estimated multilevel logistic regression model

Effects included in the model	Parameter value	Standard error	p value
Intercept	−4.163219	1.388065	0.00271
Age	0.006038	0.019668	0.75885
ASPECTS <8	2.348373	0.566016	< 0.0001
Coronary heart disease	0.762439	0.380265	0.04496
Atrial fibrillation	0.956832	0.400808	0.01697
Type 2 diabetes mellitus	0.712291	0.458569	0.12035
Duration of time: MTE procedure	0.034723	0.008053	< 0.0001
Duration of time: symptoms to recanalization >=270 mins	0.481649	0.388215	0.21473

Table 22. Adjusted odds ratios after an assessment of the overall logistic regression model that only includes significant characteristics

Effects included in the model	Odds ratio	Confidence interval of the estimated odds ratio
ASPECTS <8	10.408	CI = (3.732; 33.114)
Coronary heart disease	2.146	CI = (1.065; 4.400)
Atrial fibrillation	2.577	CI = (1.264; 5.425)
MTE duration (with a 10-minute increase)	1.474	CI = (1.277; 1.730)

By way of summarising the results of the logistic regression analysis, we can say that MTE results (in terms of good clinical outcomes) bear a significant relationship to: the ischemic core volume (ASPECTS score of <8); two comorbidities (coronary heart disease and atrial fibrillation); and the duration of MTE itself. All of these factors significantly increase the possibility of a bad (mRS >2) 90-day clinical outcome.

Graphs and numerical characteristics of these significant relationships (number of cases and their percentage values) are provided below.

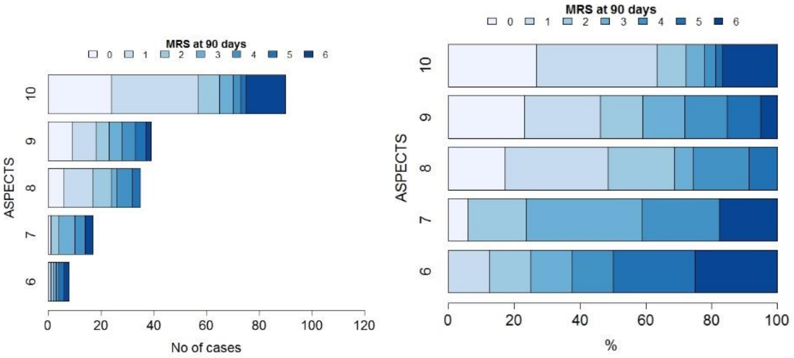


Fig. 18. Graphical representation of ASPECTS and mRS scores in absolute values (on the left) and percentage points (on the right)

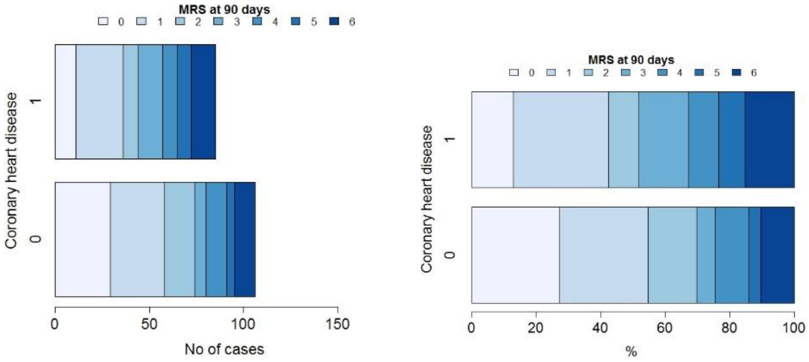


Fig. 19. Graphical representation of coronary heart disease and mRS scores in absolute values (on the left) and percentage points (on the right)

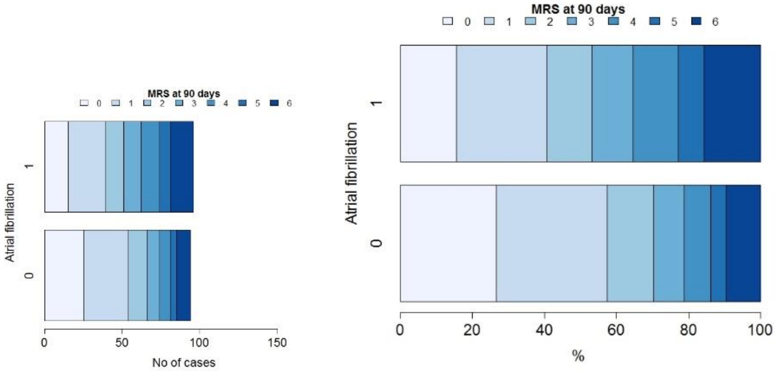


Fig. 20. Graphical representation of atrial fibrillation and mRS scores in absolute values (on the left) and percentage points (on the right)

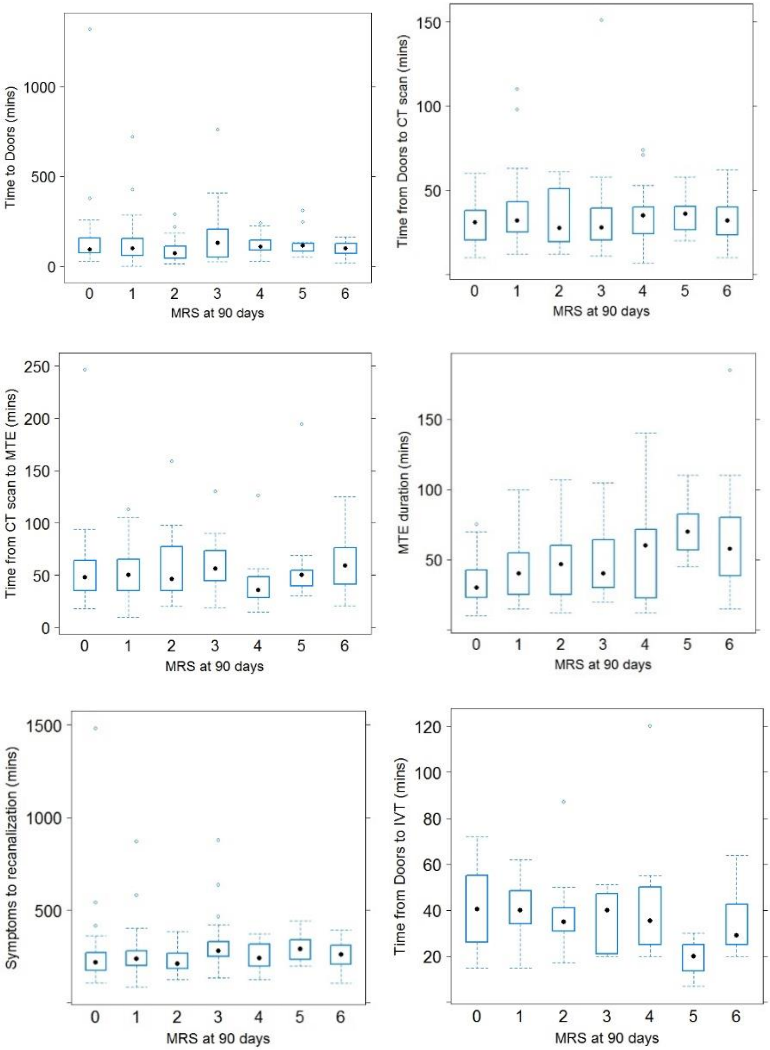


Fig. 21. Boxplot of time intervals and 90-day mRS

We additionally assessed not only the effect of IVT application but also its interplay with other characteristics included in the study. We tested hypotheses such as whether there is a significant relationship between IVT and patient's sex or between IVT and patient's age. We have determined that IVT application in patients with 51–99% ICA stenosis increases the odds of a good 90-day clinical outcome by 4.667 times (CI = 1.103; 25.053).

Table 23. Parameter values of logistic regression analysis of significant characteristics after also including the relationship of IVT application to ICA stenosis of 51 to 99%

Effects included in the logistic regression model	Parameter value	Standard error	p value
Intercept	−3.47	0.59	0.000
ASPECTS <8	2.38	0.55	0.000
Coronary heart disease	0.75	0.37	0.044
Atrial fibrillation	0.79	0.38	0.039
MTE procedure	0.04	0.01	0.000
ICA stenosis of 51-99% (−)*IVT	−0.05	0.41	0.896
ICA stenosis of 51-99% (+)*IVT	−1.35	0.85	0.111

Table 24. Adjusted odds ratios after a re-assessment of the logistic regression model that now includes the relationship between IVT application and ICA stenosis

Effects included in the model	Odds ration	Confidence interval of the estimated odds ratio
ASPECTS <8	10.843	CI = (3.905; 34.295)
Coronary heart disease	2.108	CI = (1.026; 4.405)
Atrial fibrillation	2.213	CI = (1.053; 4.784)
MTE duration (with a 10-minute increase)	1.495	CI = (1.291; 1.762)
ICA stenosis of 51-99% (+)*IVT	3.873	CI = (0.845; 25.025)

4. DISCUSSION OF FINDINGS

To the best of our knowledge, this is the first study to consider the effect of different IVT dosage in bridging therapy patients who suffered ischemic stroke due to anterior circulation artery occlusion. It is important to note the trend we observed of IVT dose of 100% having the strongest effect on clinical outcomes, with the average mRS score change of 2.15±0.34 points ($p < 0.0001$); however, differences between this dosage and others were not significant. This, relatively strongest negative effect on clinical outcomes in participating patients results from, in our view, the study design itself, with IVT being terminated on entering the X-ray operating room right before arterial puncture. It is likely that the interval of time between arrival and the start of mechanical thrombectomy was longer among patients treated with a full dose of r-tPA. Also, no single IVT-dosage group exhibited a statistically significant effect on 90-day clinical outcomes compared with the direct-MTE group.

Another crucial aspect of this study was the juxtaposition of bridging- and direct MTE treatment methods. Unlike with other recently published studies [27], our groups of participating patients were not strictly divided by their suitability for IVT, because, by the decision of the medical neurologist and the specialist performing the intervention, IVT was not initiated in all patients suitable for it. This allows us to improve, to an extent, on the often-criticised design of such studies (admittedly, however, most of them are retrospective studies), because patients unsuitable for IVT tend to have more comorbidities that result in IVT simply being contraindicated in them or they arrive at a medical institution more than 4.5 hours later. Probably the most important issue currently discussed in the area of bridging therapy is the safety of intra-arterial mechanical manipulations after IVT or even during it. According to our study, there was no significant difference between bridging- and direct-MTE groups in terms of either aICH or sICH; however, aICH was more frequent in the direct-MTE group (14.17% vs. 4.23%), and conversely with sICH: it was more frequent in the bridging-therapy group (9.86% vs. 4.17%). Data on this from studies published in this area has been inconclusive, with the frequency of complications ranging between 1.9% to 15.8% [28], but according to latest meta-analysis [29], the frequency of sICH – as shown by 16 similar studies with 3,903 patients in total – tends to rise in bridging therapy patients (OR 0,86; 95% CI 0,63 to 1,17), albeit not in a statistically significant manner – just like in our study. According to 15 studies (with 3,635 patients in total) with little heterogeneity, the frequency of aICH is similar in both groups (OR 0.93; 95% CI 0.72 to 1.19); whereas studies comparing its frequency only in patients suitable for IVT indicate a lower risk of aICH in direct-MTE patients (OR 0.49; 95% CI 0.3 to 0.81). The added value of thrombolysis in IVT-suitable patients treated with MTE has not received comprehensive research because IVT has so far been officially recommended in all patients in this group even if MTE is anticipated. It remains unclear whether meta-analysis results indicating a greater frequency aICH in IVT patients is a sufficient cause for concern, yet our study results, too, indicate that direct MTE is both sufficiently safe and effective. Due to an absolutely small number of ICH cases in bridging therapy patients, we did not divide these complications into groups by IVT dosage.

In a separate analysis of periprocedural SAH, which is in many cases treated as an iatrogenic complication (due to vascular micro-wire perforation, dissection, or ruptures of arterioles or venules in the subarachnoid space during MTE), we observed them to be somewhat more frequent in direct MTE patients (7.5% vs. 2.82%). There were only 11 such cases in our study (including 5 mixed cases with either HI or PH), and so no statistical significance between the groups was found to exist (p = 0.3071). According to published studies, this complication arises in 1% to 6.5% of cases [28]. The study by Perry P. Ng et al, it was more frequent in MTE patients receiving more than one or two thrombectomy sessions (62.5% vs. 18.2%, p = 0.01) [30]. We did not observe any differences when comparing these two groups: the bridging therapy group had a first-pass success rate of 44.12% and direct-MTE group that of 45%, with the average number of MTE sessions being at 2.23 and 2.16 respectively. So a somewhat larger frequency of SAH in direct MTE patients could perhaps be attributable, if anything, to differences in the average age and functional condition of patients within the group.

As with most studies published to date, we did not find a reliable relationship between the added value of IVT application and good clinical outcomes in MTE patients. Both bridging-therapy and direct-MTE patient groups exhibited a similar frequency of good clinical outcomes (p = 0.8790) and death from stroke (p = 0.8433) in a 90-day period despite the fact that the functional condition in bridging therapy patients prior to the onset of symptoms was better by 0.30 points (0.41 vs. 0.71). It is only in the meta-analysis published in 2017 by Mistry E.A. et all that one can find data suggesting that IVT application prior to MTE has a relationship to somewhat better 90-day clinical outcomes (OR 1.28; 95% CI 0.93–1.75; p = 0.12) and significantly lower mortality (OR 0.56; 95% CI 0.36–0.86; p = 0.007) [27]. It should be noted, however, that many of these clinical trials were the first to prove the benefits of MTE, with their group of endovascular therapy patients not being randomized for IVT application, while, for example, the average time in the criteria for endovascular therapy selection in the MR CLEAN study was more than 2 hours from the initiation of IVT. Yet a meta-analysis published in 2019 showed that bridging therapy has no advantage in IVT-suitable patients over direct MTE in terms of good (mRS 0-2) clinical outcomes (OR = 0.93, 95% CI 0.57–1.49), nor did it indicate higher mortality (OR = 0.84, 95% CI 0.40–1.75) [29]. Very similar results were also obtained by the first multi-centre randomized clinical study that focused only on patients suitable for IVT [17]. The study conducted by over 40 stroke treatment centres in China has shown that MTE is safe and effective with regard to clinical outcomes (in mRS; OR = 1.09, 95% CI 0.81–1.40; p = 0.04). Although there were more of successful recanalizations (numerically speaking) in the bridging-therapy group (84.5% vs. 79.4%), the observed trend of a rising aICH (36.2% vs. 33.3%; p =

0.45) as well as of a rising sICH (6.1% vs. 4.3% respectively; p = 0.30) in the bridging-therapy group resulted in similar 90-day mortality rates (18.8% vs. 17.7% respectively; p = 0.71). Should these trends be confirmed by the results awaited in other randomized trials, the global guidelines for acute ischemic stroke treatment with MTE are likely to be revised. Upon arrival to a stroke treatment centre with a capability to immediately perform MTE, patients could be treated with MTE without the initiation of IVT even in the absence of contraindications to the thrombolytic agent in them.

In assessing the factors affecting the success of the procedure, we did not observe its relationship to demographic factors, comorbidities (p = 0.1366), or IVT application (p = 0.5294). However, we did observe a statistically insignificant (p = 0.1702) trend of patients successfully treated with MTE being, on average, of a somewhat lower age (67.6 vs. 70.8 years respectively). Similar conclusion is shared by other authors, too [31], but there are also some published results that tend to place more emphasis on the influence of age-related vascular anatomic changes (more pronounce tortuosity, intima-media thickness, and atherosclerosis) on the prospects of revascularization. The study by Kim D. et al analysed the prospects of revascularization in patients across different age-groups (divided into those aged 60 to 79 and those aged 80 or older) and determined that reperfusion is more likely to succeed in the younger age-group of the two (TICI 2b–3 75.3% vs 40% respectively, p = 0.002) [32]. The most frequent cause of a failed procedure in the younger age-group, according to the authors, is multiple unsuccessful thrombectomy sessions (92.3%); with respect to the older age-group, they note that the location of occlusion was technically unreachable in 50% of patients due to age-related changes mentioned above. Our study showed that successful MTE procedures, in our case, were much shorter (37.50 minutes on average) compared with cases of unsuccessful recanalization (70 minutes on average; p < 0.0001). This factor (namely, MTE duration) was also shown to be significant in a regression analysis, where we assessed its relationship to good clinical outcomes (p < 0.0001). We found that a 10-minute increase in MTE duration increases the probability of a bad clinical outcome (OR 1.474; 95% CI 1.277–1.730). Analogous results are reached in a recently published American study by Hassan A. et al, which considers the relationship between good clinical outcomes and intervals of time [33]. According to them, the duration of MTE in patients with good clinical outcomes was 44±25 minutes, compared with 51±33 minutes in patients with bad clinical outcomes (p = 0.040). In their study, the difference between these groups in terms of the interval of time between the onset of symptoms and recanalization was also significant – 273±86 minutes and 33 ±96 minutes respectively (p<0.001). While this factor – namely, the time between the onset of symptoms and recanalization being longer than 270 minutes or 4.5 hours and related to a bad clinical outcome – was also found to be significant in our study's initial logistic regression model, it subsequently lost its significance (p = 0.2147) in the adjusted model that comprised all significant factors, as did age and type 2 diabetes. It is likely that both of those factors are related, and yet a stronger influence on clinical outcomes was had by the rate of recanalization success, which was unequivocally larger in MTE procedures shorter in duration.

Aside from the success of MTE already discussed, the main factors leading to bad 90-day clinical outcomes in our participating patients were: relatively larger volume of initial ischemic lesions with ASPECTS score of <8 (OR 10.408; 95% PI 3.732–33.111, p < 0.0001); coronary heart disease (OR 2.146; 95% PI 1.065–4.400, p = 0.0341) and atrial fibrillation (OR 2.577; 95% PI 1.264–5.425, p = 0.0105). As many as one half of patients participating in our study were diagnosed with atrial fibrillation (50.26%), with coronary heart disease found in 44.5% of patients. According to published studies, patients with atrial fibrillation are also older and have more comorbidities, with IVT contraindicated in them due to anticoagulants they are taking, and this is why they are the main candidates for direct MTE (class IA recommendation) with a worse prognosis of good clinical outcomes compared with patients without this disorder [34].

The situation is similar with the diagnosis of coronary heart disease (CHD): it correlates with age and comorbidities, while also being described as a prognostic factor of a bad clinical outcome in case of ischemic stroke of non-cardioembolic origin. According to the AHA and ASA data from 2018 [35], CHD was the leading cause of death in patients with cardiovascular disease in the US (43.8%), with stroke ranking second (16.8%). So, the dependence of bad clinical outcomes on CHD indicated by our study was only to be expected. Both pathologies share the same modifiable risk factors, such as dyslipidemia, hypertension, smoking, diabetes, lack of physical activity, and obesity. By modifying them, one could significantly reduce the risk of ischemic stroke, which, according to published studies, is increased two-fold by CHD. In our study, we assessed the area of early ischemic stroke on the ASPECTS scale, dividing the patients into groups of small (8 to 10 points) and moderate (6 to 7 points) ischemic changes. Results from clinical studies suggest that patients with smaller ischemic changes prior to MTE stand a greater chance of being functionally independent, with a lower risk of hemorrhagic transformation and death, too [36]. Our study confirms this conclusion: patients with small ischemic changes are at a 10 times lower risk of a bad clinical outcome compared with patients with larger ischemic changes. As with many other researchers, we did not includes patients with ischemic changes of 5 points or fewer, even though, according to some authors, patients in the 5–7 point group also show a positive trend in terms of good clinical outcomes [37].

Our study divided patients into 3 groups based on the degree of ICA stenosis (<50%, 51–99%, and occlusion), observing the trend of better clinical outcomes in the group of patients with hemodynamically significant stenosis (51–99%) when IVT was applied to them. It appeared to be significant in the initial logistic regression analysis (OR 1.54; p = 0.048), yet this changed in the adjusted model comprising all significant factors (p = 0.111). One may hypothesize that IVT improves the functioning of intracerebral collaterals that develop due to slowly progressing yet serious stenosis in cases of sudden arterial occlusion, thus ensuring a more moderate progression of ischemic lesions and a better clinical outcome following revascularization. According to research published to date, the level of development of leptomeningeal collaterals in ischemic stroke patients tends to vary a lot, and no clear clinical or demographic factors affecting the degree of their development have so far been identified [38]. Recently, the Dutch scientist Jan W. Dankbaar et al studied 188 patients treated for ischemic stroke due to M1 occlusion and was unable to find a relationship between extracranial ICA stenosis and the collaterals' degree of development [39]. It should be noted, however, that ICA stenosis of >70% was observed in only 18 patients (4 with weak and 14 with robust leptomeningeal collaterals), and while the trend is clear here, this hypothesis, which was also proposed by studies discussed above [40];[41] will probably need a larger sample of participants to be sustained. Perhaps IVT is exactly the factor that determines the rheological properties of blood and improves the already-formed collateral arterial supply or opens small branches near the thrombus. This year's study by P. Senners et al shows that lVT application is an independent factor that significantly improves the prospect of early recanalization (prior to MTE) in patients with strongly expressed collaterals ($p = 0.029$) [42]. Cases of early revascularization were not included in our study.

5. CONCLUSIONS

1. Coronary heart disease and atrial fibrillation are the key comorbidities affecting clinical outcomes in anterior circulation ischemic stroke patients treated with mechanical thrombectomy. Patients' age and sex had no effect on their treatment results.
2. Different intravenous thrombolytic agent dosage in bridging therapy patients treated with mechanical thrombectomy due to anterior circulation occlusion had no effect on their clinical outcomes.

3. Small early ischemic changes in the cerebrum (8 points or more on the ASPECTS scale) and successfully arterial recanalization (TICI 2b or TICI 3) are the key factors affecting the effectiveness of mechanical thrombectomy in seeking good clinical outcomes in ischemic stroke patients with anterior circulation artery occlusion.
4. In terms of the development of complications and the success of recanalization and in view of both early and late ischemic stroke treatment results, mechanical thrombectomy without intravenous thrombolysis is a safe and effective method of treatment in patients with anterior circulation artery occlusion.

6. PRACTICAL RECOMMENDATIONS

1. Strengthening the prevention of coronary heart disease and atrial fibrillation, improving professional qualifications of specialists performing interventional procedures are the main tasks in seeking better clinical outcomes in ischemic stroke patients with anterior circulation artery occlusion.
2. It is instructive continuously to analyse mechanical thrombectomy treatment results in order to make the chain from diagnosis to therapy ever more effective in all stroke treatment centres. Opening up large-artery occlusions requires an individually chosen and, given the centre’s capabilities, the most rapidly applicable treatment tactic, which, in our case, was mechanical thrombectomy irrespective of whether intravenous thrombolysis had started or not.
3. Mechanical thrombectomy can be used as first-line treatment in ischemic stroke patients with anterior circulation artery occlusion.
4. Intravenous infusion of a thrombolytic agent in bridging therapy patients can be stopped immediately prior to mechanical thrombectomy.

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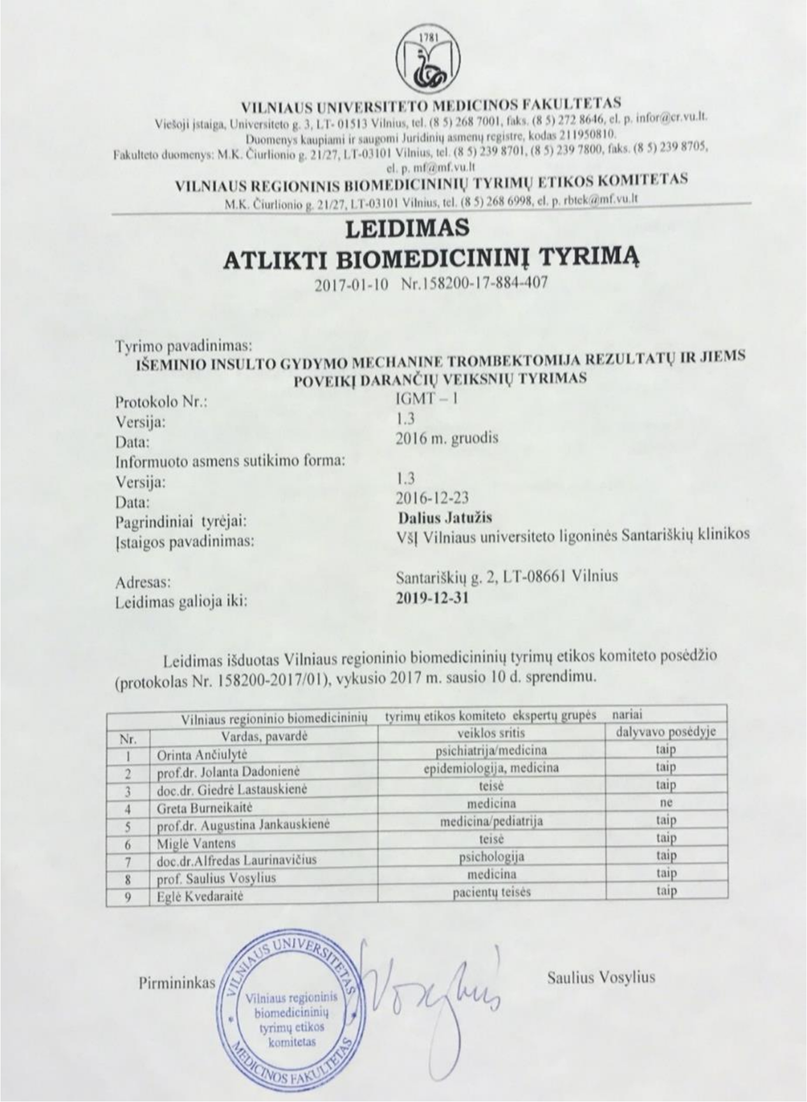
ANNEXES

Authorization Provided by the Vilnius Regional Biomedical Research Ethics Committee



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VILNIAUS UNIVERSITETO MEDICINOS FAKULTETAS
Viešoji įstaiga, Universiteto g. 3, LT- 01513 Vilnius, tel. (8 5) 268 7001, faks. (8 5) 272 8646, el. p. infor@cr.vu.lt.
Duomenys kaupiami ir saugomi Juridinių asmenų registre, kodas 211950810.
Fakulteto duomenys: M.K. Čiurlionio g. 21/27, LT-03101 Vilnius, tel. (8 5) 239 8701, (8 5) 239 7800, faks. (8 5) 239 8705,
el. p. mf@mf.vu.lt
VILNIAUS REGIONINIS BIOMEDICININIŲ TYRIMŲ ETIKOS KOMITETAS
M.K. Čiurlionio g. 21/27, LT-03101 Vilnius, tel. (8 5) 268 6998, el. p. rbtek@mf.vu.lt

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2017-01-10 Nr.158200-17-884-407

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Versija:	1.3
Data:	2016 m. gruodis
Informuoto asmens sutikimo forma:	
Versija:	1.3
Data:	2016-12-23
Pagrindiniai tyrėjai:	**Dalius Jatužis**
Įstaigos pavadinimas:	VšĮ Vilniaus universiteto ligoninės Santariškių klinikos
Adresas:	Santariškių g. 2, LT-08661 Vilnius
Leidimas galioja iki:	**2019-12-31**

Leidimas išduotas Vilniaus regioninio biomedicininių tyrimų etikos komiteto posėdžio (protokolas Nr. 158200-2017/01), vykusio 2017 m. sausio 10 d. sprendimu.

Vilniaus regioninio biomedicininių tyrimų etikos komiteto ekspertų grupės nariai			
Nr.	Vardas, pavardė	veiklos sritis	dalyvavo posėdyje
1	Orinta Ančiulytė	psichiatrija/medicina	taip
2	prof.dr. Jolanta Dadonienė	epidemiologija, medicina	taip
3	doc.dr. Giedrė Lastauskienė	teisė	taip
4	Greta Burneikaitė	medicina	ne
5	prof.dr. Augustina Jankauskienė	medicina/pediatrija	taip
6	Miglė Vantens	teisė	taip
7	doc.dr.Alfredas Laurinavičius	psichologija	taip
8	prof. Saulius Vosylius	medicina	taip
9	Eglė Kvedaraitė	pacientų teisės	taip

Pirmininkas Saulius Vosylius

Curriculum Vitae

Name: Marius KURMINAS
Date of borth: 1983-06-30

Workplace: Vilnius University Hospital Santaros Klinikos,
Center of Radiology and Nuclear medicine.
Position: Radiologist, Interventional radiologist.
Address: Santariškių Str. 2, 08661 Vilnius, Lithuania
Email: Marius.kurminas@santa.lt

Qualifications: 2011 Vilnius University – Radiologist (MPL-16913)
2007 Vilnius University – Medical doctor (MPL-10473)

PUBLICATIONS

Kurminas M., Berūkštis A., Misonis N., Tamošiūnas A. E., Jatužis D. Periprocedūriniai mechaninės trombektomijos veiksniai, lemiantys sėkmingą rekanalizaciją ir geras klinikines išeitis ligoniams su priekinės cirkuliacijos baseino arterijos okliuzija. Neurologijos seminarai 2019; 23(81): 140-148. DOI: 10.29014/ns.2019.19. http://www.neuroseminarai.lt/2019-2381-140-148/

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Posters

1. **M.Kurminas** „Basilar artery thrombectomy“ ICCA (Acute Stroke Interventions & Carotid Stenting) conference 2018 April 17-18, Warsaw, Poland.

Oral presentations

2. **M. Kurminas** “Interventional stroke treatment” 6th International meeting on acute cardiac care and emergency medicine, 2018 September 14-15, Vilnius, Lithuania.
3. **M. Kurminas** „Optimalus išeminio insulto vaizdinimas ir intervencijos". Mokslinė – praktinė konferencija Embolinio insulto diagnostikos ir gydymo naujovės, 2018 Lapkričio 29, Vilnius, Lietuva.
4. **M. Kurminas** “Mechaninė trombektomija už protokolo ribos – kaip? kada?“ mokslinė – praktinė konferencija Ankstyva insulto diagnostika ir gydymas, 2016 Gruodžio 15, Vilnius, Lietuva.
5. **M. Kurminas**, N. Misonis “Interventional stroke treatment” 5th International Meeting on Acute Cardiac Care and Emergency Medicine, 2016 May 6-7, Vilnius, Lithuania.
6. **M. Kurminas** ‘‘Endovaskulinė trombektomija: išmoktos pamokos ir klinikinė patirtis’’ Lietuvos insulto asociacijos konferencija, 2016 Balandžio 1-2, Trakai, Lietuva.
7. **M. Kurminas** ‘‘Ūmaus insulto endovaskulinio gydymo galimybės’’ mokslinė – praktinė konferencija Radiologija 2015, 2015 10 16-17, Vilnius, Lietuva.
8. **M. Kurminas** ‘‘Mechaninės trombektomijos praktinis taikymas’’ Lietuvos insulto asociacijos konferencija, 2015 Gegužės 15-16, Bačkonys, Lietuva.

NOTES

Vilnius University Press
9 Saulėtekio Ave., Building III, LT-10222 Vilnius
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