

Analysis of mechanical thrombectomy outcomes at University Hospital Split in a two-year period

Levesque, Christian Benedict Joseph

Master's thesis / Diplomski rad

2024

Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj: **University of Split, School of Medicine / Sveučilište u Splitu, Medicinski fakultet**

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:171:839160>

Rights / Prava: [In copyright](#)/[Zaštićeno autorskim pravom.](#)

Download date / Datum preuzimanja: **2024-09-18**



Repository / Repozitorij:

[MEFST Repository](#)



UNIVERSITY OF SPLIT



**UNIVERSITY OF SPLIT
SCHOOL OF MEDICINE**

Christian Levesque

**ANALYSIS OF MECHANICAL THROMBECTOMY OUTCOMES AT UNIVERSITY
HOSPITAL SPLIT IN A TWO-YEAR PERIOD**

Diploma thesis

**Academic year:
2023/2024**

**Mentor:
Prof. Ivica Bilić, MD, PhD**

SPLIT, SEPTEMBER 2024

TABLE OF CONTENTS

1. INTRODUCTION	1
1.1. CLASSIFICATION AND ETIOLOGY OF STROKE.....	3
1.2. RISK FACTORS & PREVENTION OF ISCHEMIC STROKE	6
1.3. CLINICAL PRESENTATION & DIAGNOSIS OF ACUTE ISCHEMIC STROKE	7
1.4. IMAGING AND ISCHEMIC CORE & PENUMBRA.....	8
1.5. TREATMENT	10
1.5.1. TISSUE PLASMINOGEN ACTIVATOR	10
1.5.2. MECHANICAL THROMBECTOMY	11
2. OBJECTIVES	14
3. PATIENTS AND METHODS	16
3.1. STUDY DESIGN.....	17
3.2. STUDY POPULATION	17
3.3. STROKE & MECHANICAL THROMBECTOMY PROTOCOL	17
3.4. METHODS OF COLLECTING AND ANALYZING DATA.....	19
3.5. STATISTICAL ANALYSIS	23
4. RESULTS	24
4.1. BASELINE ANALYSES	25
4.2. ORDINAL LOGISTIC REGRESSION.....	28
4.3. TICI & mRS COMPARISON	31
5. DISCUSSION	34
6. CONCLUSION	39
7. REFERENCES	41
8. SUMMARY	48
9. SUMMARY IN CROATIAN	50

ACKNOWLEDGEMENT

Thank you, Dr. Bilić and Dr. Jelavić, for your combined support and guidance

Thank you, Helge and Solveig, for your encouragement and respect

Thank you, Kristin, for believing in me

LIST OF ABBREVIATIONS

ACA – Anterior cerebral artery

AIS – Acute ischemic stroke

BA – Basilar artery

CTA – Computed tomography angiography

CTP – Computed tomography perfusion

DWI – Diffusion weighted imaging

ESO – European stroke organization

IV – Intravenous

LVO – Large vessel occlusion

MCA – Middle cerebral artery

MRA – Magnetic resonance angiography

MRI – Magnetic resonance imaging

MRP – Magnetic resonance perfusion

mRS – Modified Rankin Scale

MT – Mechanical thrombectomy

NCCT – Non-contrast computed tomography

NIHSS – National Institutes of health stroke scale

PCA – Posterior cerebral artery

SVD – Small vessel disease

TICI – Thrombolysis in cerebral infarction

TPA – Tissue plasminogen activator

1. INTRODUCTION

Stroke is the leading cause of permanent disability, and the third leading cause of death world-wide, following ischemic heart disease and SARS-CoV-2 (1, 2). Globally, more than 12.2 million new strokes occur each year, and 6.5 million patients die each year from stroke (3). In the United States, approximately 795,000 new strokes occur each year (4). In Europe, the annual incidence rate is approximately 1.1 million strokes (5), and in Croatia, approximately 10,000 new stroke patients annually (6). Of the 12.2 million new strokes occurring annually, approximately 87% are classified as an acute ischemic stroke (AIS), and the only two successful clinical treatments for AIS, tissue plasminogen activator (TPA) and mechanical thrombectomy (MT), have only been applied globally in the past few decades (7).

The earliest documentation and description of stroke was by Hippocrates, the father of medicine, around 400 BCE (8). The term stroke originated from the Greek word, “apoplexia”, which meant, “to be struck down” (8). Believed to be caused by a supernatural force, apoplexia was the sudden loss of consciousness and paralysis (8). And in 1599, the first recorded use of the term stroke was used, which also referred to a supernatural force (8). “The stroke of God’s hand”, according to the sudden onset of symptoms (8). Therefore, the ancient and historical classification of stroke was based more upon the sudden onset and severe impact of the disease. While the modern classification of stroke is based on the etiology and pathophysiology of the disease. The current American Heart Association definition of stroke is, “a sudden loss of neurological function caused by a disturbance in the blood supply to the brain”, with further subclassification based upon etiology and imaging findings (9).

1.1. CLASSIFICATION AND ETIOLOGY OF STROKE

Strokes are roughly organized into two primary categories based on how they disrupt the blood supply to the brain, both resulting in an abrupt loss of neurological function. Hemorrhagic stroke, the less common of the two types of strokes, accounts for 13% of all stroke cases, and refers to a sudden rupture of the intracranial blood vessels, as seen in Figure 1 (7, 10). The site and etiology of the cerebral vascular rupture determines further subclassification.

The most common causes are due to head trauma, high blood pressure, arteriovenous malformations, or aneurysms (10). Although the mortality rate from hemorrhagic stroke is high, current treatment options do not include MT, therefore we will no longer be discussing hemorrhagic stroke in this paper (3).

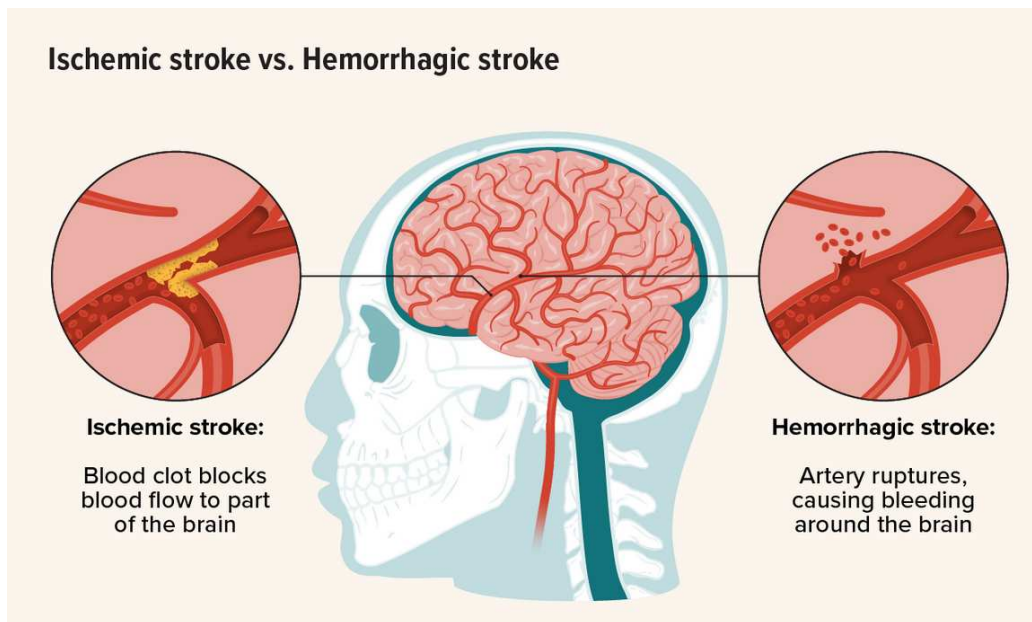


Figure 1. Illustration of the two most common types of strokes, ischemic stroke and hemorrhagic stroke. Source: Healthline [Internet]. San Francisco: Daniel Yetman; 2023 May 19. What's the difference between an ischemic and hemorrhagic stroke?; [cited 2024 Aug 9]. Available from: <https://www.healthline.com/health/stroke/ischemic-vs-hemorrhagic-stroke>

An ischemic stroke, the most commonly occurring type of stroke, is caused by a blockage of one or more blood vessels supplying the brain, resulting in reduced blood flow and subsequent damage to brain, spinal or retinal cells, as seen in Figure 1 (9).

Given the variety of ischemic stroke subtypes, two classification systems were developed for clinicians to use in order to choose the most effective treatment and to best predict patient outcomes. The TOAST system, introduced in 1993, was an easier system for classifying AIS based upon underlying cause while the more recent Causative Classification of Stroke system, developed in 2007, provided a more detailed and precise classification of AIS by incorporating more diagnostics and clinical features (12, 13). These classifications were based upon the location, source, and the type of vessel blockage. A thrombotic stroke, the most common cause of an ischemic stroke is caused by a clot formed within a large vessel in the brain, primarily due to atherosclerosis (15, 16). The process of atherosclerosis frequently occurs in regions of turbulent blood flow like arterial bifurcations, where lipids are deposited into arterial walls, leading to plaque formation and vessel stenosis, thus increasing the risk of stroke (16). As a result, the symptoms of a thrombotic stroke develop more gradually over time as the clot grows and progressively obstructs greater amounts of blood flow to the brain, spine or retina (15). A blood vessel narrowed by atherosclerosis is more likely to be occluded by further clot formation or by a travelling embolus from a near or distant site of the body.

An embolic stroke, the second most common type of ischemic stroke often presents with a sudden clinical onset of symptoms, typically caused by a ruptured plaque originating from a non-occlusive atherosclerosis of the aortic arch, cervical, or cerebral arteries, or from the venous system, referred to as a paradoxical embolism (17). However, emboli causing an AIS most frequently develop in the heart, often referred to as a cardioembolism (18). In developed countries, atrial fibrillation is believed to be the primary cause of cardioembolism and up to 25% of all ischemic strokes (18). It was previously believed that ischemic strokes due to unknown cause, referred to as cryptogenic ischemic strokes, contributed to the majority of all non-thromboembolic ischemic strokes (17). Although advancements in imaging techniques suggest that the majority of cryptogenic ischemic strokes are actually thromboembolic in origin (17). Therefore, approximately 75% of all ischemic strokes are thromboembolic and potentially treatable by MT if the occlusion occurs in a large cerebral vessel (7, 17, 19).

The pathogenesis of an ischemic stroke primarily involves the occlusion of larger cerebral blood vessels that can be visualized with a computed tomography angiography (CTA) scan shortly after the stroke occurs (20). In order of frequency, the most common large vessel occlusions (LVO) caused by thromboembolic strokes are the middle cerebral artery (MCA); the internal carotid artery (ICA); the basilar artery (BA); the vertebral arteries; and the anterior cerebral artery (ACA) (21). The size and more crucially, the part of the brain that the blocked cerebral vessel is serving determines the clinical presentation of the LVO, as seen in Figure 2.

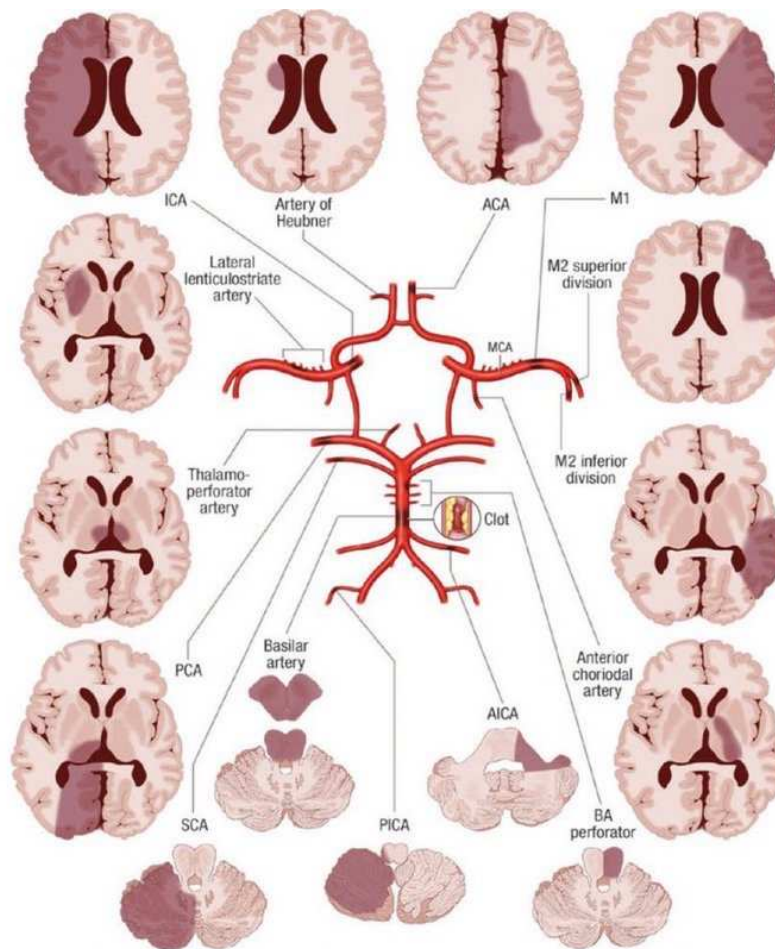


Figure 2. The Circle of Willis, large vessel occlusions and associated brain vascular territories affected by ischemic stroke. Source: Wijdicks EFM. *Examining Neurocritical Patients*. New York: Springer; 2021. p. 40

In contrast to LVO, small vessel disease (SVD) is characterized by the occlusion of small perforating arteries, which frequently result in lacunar strokes that occur deep inside the brain (16, 23). Lacunar strokes usually result in small, deep infarcts in the thalamus, basal ganglia, internal capsule, and subcortical white matter (16). They are mostly the result of hypertension, diabetes and aging (14). Despite being the most often affected vessels in a lacunar stroke, the lenticulostriate arteries of the MCA are harder to detect with CTA and magnetic resonance imaging (MRI) because of their small diameter (14, 16, 23). Furthermore, the pathogenesis of SVD differs from thromboembolic LVO because they are often the result of microatheromas or lipohyalinosis (23). For these reasons, MT was not designed to treat lacunar strokes and SVD and therefore we will no longer be discussing these types of strokes in this paper.

1.2. RISK FACTORS & PREVENTION OF ISCHEMIC STROKE

In order to reduce the prevalence of ischemic strokes, particularly in developed nations, ischemic stroke prevention is crucial (18). The implementation of primary and secondary prevention measures effectively depends upon identifying the modifiable and non-modifiable risk factors. The most significant modifiable risk factors for stroke are obesity, coronary heart disease, excessive alcohol consumption, hypertension, diabetes mellitus, and current smoking status (18). The non-modifiable risk factors include genetic predisposition, age, gender and ethnicity (18). Age has been demonstrated to be the most potent non-modifiable risk factor as the incidence of ischemic stroke doubles every 10 years after the age of 55 (24). Although women have a larger lifetime risk of stroke compared to men since they are more likely to outlive males, the prevalence of stroke in males is greater than that of younger women (25). Lastly, most likely due to social, cultural and genetic factors, South Asians experience strokes more frequently compared to Caucasians (26).

By targeting modifiable risk factors, primary prevention measures have a significant role in lowering the initial risk of an ischemic stroke (18). Raising awareness of these risk factors among the general population, with a focus on hypertension in particular, has been found to be the most significant modifiable risk factor, accounting for approximately half of all ischemic strokes (27).

These risk factors can be reduced by limiting or stopping alcohol consumption, smoking cessation, controlling dyslipidemia with statin medication, and controlling hypertension by antihypertensive medications if needed, and maintaining a healthy body weight through dietary changes and frequent, moderately to intense physical activity (28-30). The goal of secondary prevention is to prevent subsequent strokes from happening after a cerebrovascular incident. More vigorous control of diabetes, hyperlipidemia, and hypertension using the same lifestyle modifications and medications as in primary prevention, along with antiplatelet or anticoagulant treatments depending on the etiology of the stroke (30). To avoid a cardioembolic stroke, individuals with atrial fibrillation must receive anticoagulation therapy such as warfarin or direct oral anticoagulants (30).

1.3. CLINICAL PRESENTATION & DIAGNOSIS OF ACUTE ISCHEMIC STROKE

Depending on the location and size of the occluded vessel, thromboembolic ischemic strokes usually appear with an acute clinical presentation. Patients with AIS often present with a sudden onset of neurological deficits (31). Common focal neurological symptoms include hemiparesis, defined as unilateral weakness or numbness of the face, arm or leg, as well as hemisensory deficits, such as a loss of sensation or altered sensory perception on one side of the body (31). Speech abnormalities, known as aphasia, are defined by a difficulty in comprehending or generating speech, usually the result of AIS in the dominant hemisphere of the patient (31). Diplopia (double vision), altered consciousness, ataxia (loss of coordination or balance), dysarthria (slurred or unclear speech), visual field deficits, loss of vision in one or both eyes, nystagmus (involuntary eye movements), vertigo, cognitive changes, and in severe cases, an abrupt and intense headache are additional common focal neurological symptoms of AIS (31). It is critical to identify these symptoms because there is a brief window of opportunity for successful intervention with thrombolysis or MT to restore cerebral blood flow (20). Minimizing and avoiding treatment delays is crucial, as such delays can lead to higher rates of morbidity and death, additionally, ruling out other conditions, such as seizures, conversion disorder, migraines, and metabolic disturbances like hypoglycemia, that could mimic the symptoms of AIS, is equally important (20, 31).

The diagnosis of AIS is typically confirmed through imaging studies. The most commonly used studies are non-contrast computed tomography (NCCT) and CTA (31). There are several useful non-radiological methods available in the pre-hospital and emergency settings that can help with the initial identification of AIS and those patients who may benefit from MT. Given that the focal neurological symptoms of AIS can manifest rapidly, “FAST” (face, arms, speech, and time) is a useful acronym that is simple to learn and use for a prompt diagnosis (32). The National Institutes of Health Stroke Scale (NIHSS), a 15-item scale, has become a more useful method for estimating the severity of stroke and neurological impairment (33). A NIHSS score >4, combined with a clinical suspicion of AIS calls for immediate diagnostic imaging (20). Ensuring the best approach for ruling out stroke mimics and establishing eligibility for TPA therapy involves a comprehensive patient history, including the first neurologic symptoms time of onset and medical history (31). Vital signs should also be taken, as well as routine laboratory blood tests such as complete blood counts, coagulation studies, metabolic panels and a 12-lead electrocardiogram should be performed (31). After excluding stroke mimics, a NCCT scan or MRI should be performed to determine the cause of the focal neurological symptoms, if intravenous (IV)-TPA therapy is necessary, and if the patient is eligible for a CTA and MT treatment (20, 31).

1.4. IMAGING AND ISCHEMIC CORE & PENUMBRA

In order to diagnose AIS, assess the severity and provide informed treatment decisions, accurate and timely imaging is essential. An NCCT scan is usually the first imaging modality used in the examination of suspected AIS because of its widespread availability, speed, and effectiveness in excluding hemorrhagic stroke and other stroke mimics (31). Although the inability of NCCT to identify early ischemic changes within the initial hours following first stroke symptoms is a drawback (34). Alternatively, MRI, more precisely, diffusion weighted imaging (DWI) is safer for pregnant patients and more sensitive than NCCT when identifying acute ischemic changes within minutes of stroke onset (20). DWI can reliably reveal the precise location and extent of infarcted brain tissue, an important imaging method for assessing MT effectiveness for late onset AIS patients (35). Due to the limited availability and lengthier acquisition time, MRI is less frequently utilized in hyperacute situations (35).

Patients who exhibit clinical suspicion of AIS, NIHSS score >4 , and a negative NCCT scan for stroke mimics and hemorrhagic stroke, should promptly undergo a CTA scan to visualize the cerebral vasculature and determine the location of the occlusion, as seen in Figure 3 (20). As an alternative, patients with renal impairment or contrast allergies may benefit from magnetic resonance angiography (MRA), which can also visualize the cerebral vessels but without the need for contrast agents (36). In regard to distal vessel occlusions, MRA cannot provide the same level of detail as CTA (37). According to ESO guidelines, MT is the preferred treatment option with best medical management for AIS patients with LVO found with CTA or MRA, even if the patient presents within 6 hours of the onset of first symptoms (20). The challenges that arise after 6 hours are due to the extent of the infarcted brain tissue, referred to as the ischemic core and penumbra, where there is a larger chance of complications with MT, which could lead to higher rates of morbidity and mortality (38). Advanced imaging with computed tomography perfusion (CTP) or magnetic resonance perfusion (MRP) is crucial for determining whether a viable penumbra is present and whether there is a notable mismatch between the ischemic core and the penumbra in those AIS patients presenting after the 6-hour MT window (20, 39).

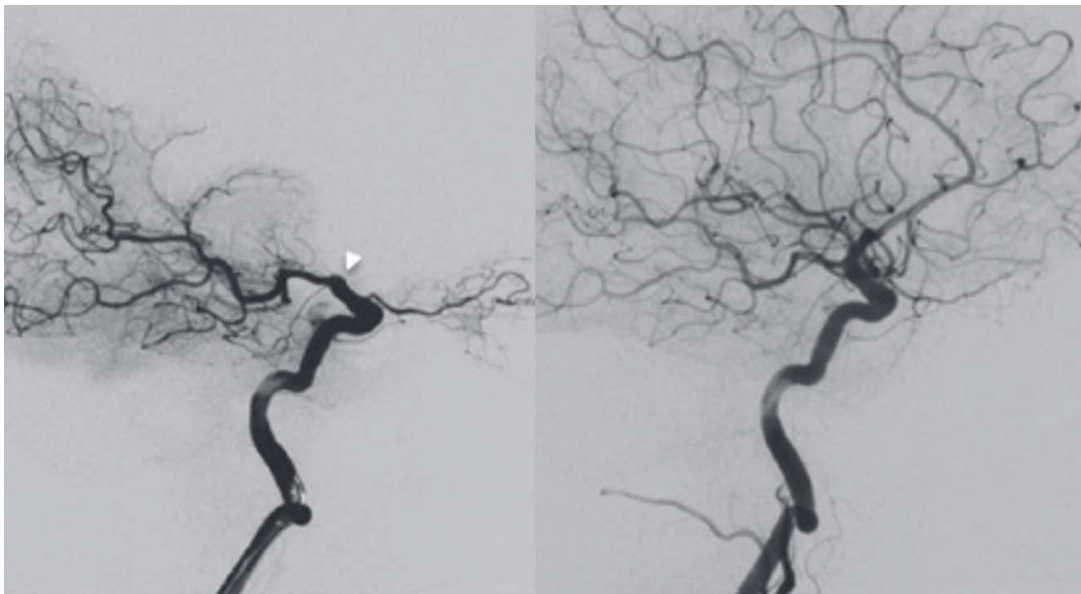


Figure 3. CT angiography of the right middle cerebral artery: Pre- and post-mechanical thrombectomy. Source: Volný O, Haršány M, Mikulík R. Homonymous visual field defects. New York: Springer Cham, 2017. p. 31-41

An AIS occurs when there is a blockage in the blood supply to the brain, resulting in tissue destruction. The affected region of the brain is separated into the penumbra and the ischemic core (35). The brain region that suffers the greatest drop in blood flow, known as the ischemic core, sustains irreversible damage soon after a stroke occurs as a result of rapid cell death due to oxygen and glucose deprivation (41). Even though the brain cells of the affected region are under stress, the ischemic penumbra, which envelops the core, continues to receive moderate amounts of oxygenated blood (35). However, collateral circulation can only sustain the deprived brain cells for a brief period of time (35). Hence, the penumbra is the main target of thrombolysis and MT treatment and thus, represents possibly salvageable brain tissue if blood flow is rapidly restored (35). DWI, CTP, or MRP can determine the size and mismatch between the ischemic core and penumbra in AIS patients even within the first few hours after symptom onset (39).

1.5. TREATMENT

1.5.1. TISSUE PLASMINOGEN ACTIVATOR

For patients who present with AIS, the only approved systemic reperfusion treatment at this time is IV-TPA with alteplase (42). TPA was first authorized by the US FDA in June 1996, and to ensure maximal safety and effectiveness, alteplase is still governed by stringent inclusion and exclusion criteria. Since systemic thrombolysis with TPA activates plasminogen to improve the rate of clot disintegration, and thus improves blood flow where clots occur (42). The exclusion criteria were designed to exclude those individuals who are more likely to experience internal bleeding when treated with TPA.

Since thrombolysis therapy has been shown to be more successful when given as soon as possible after a stroke, there is still a need for broad access and quick decision-making among medical professionals to guarantee IV-TPA is given to AIS patients as soon as possible (7, 15, 20). The greatest benefit has been observed when treatment is started during the first 3 hours of stroke symptoms (15). Regardless, ESO recommendations have found IV-TPA to still be effective within 4.5 hours of stroke onset (20). This discrepancy is due to the possibility that time exacerbates the ischemic mismatch (35).

More recently, Bai *et al.* has used DWI and MRI T2-weighted imaging on AIS patients presenting after 4.5 hours to monitor and better select individuals who could still benefit from TPA treatment (43). Since each stroke patient has a unique ischemic core and penumbra size, according to the dogma of personalized medicine, it is impractical to establish treatment time restrictions if clinicians do not know the degree of mismatch for each AIS patient.

Despite being a major medical advancement, thrombolysis therapy is not regarded as a stand-alone treatment for AIS (20). TPA works well for small to moderate-sized clots, but in cases of LVO, TPA alone may not be enough to restore blood flow, as recanalization rates have been shown to be as low as 13% to 50% (44). Regardless of time sensitivity, TPA will always carry a risk of symptomatic intracerebral hemorrhage (35). Additionally, not all patients will experience complete vessel recanalization, as some studies have shown that up to 70% of patients treated with TPA still retain a residual thrombus, requiring further intra-arterial therapy, such as MT (44).

1.5.2. MECHANICAL THROMBECTOMY

For AIS patients with LVO, MT has revolutionized how ischemic strokes are treated. MT is a minimally invasive surgical procedure that begins with a small groin incision (45). Following insertion of a specialized catheter into the femoral artery, real-time fluoroscopy is used to guide the catheter to the location of the blood clot in the brain where an aspiration device or stent retriever is deployed, as seen in Figure 4 (45). The aspiration device can generate suction to remove the clot directly, while the stent retriever extends to capture the clot (45). After the removal of the clot and blood flow to the afflicted brain region is restored, the interventional radiologist evaluates the level of reperfusion and provides a Thrombolysis in Cerebral Infarction (TICI) score (20). According to McCarthy *et al.* there is a correlation between improved long-term outcomes and higher rates of reperfusion, TICI 2b-3 (20, 46).

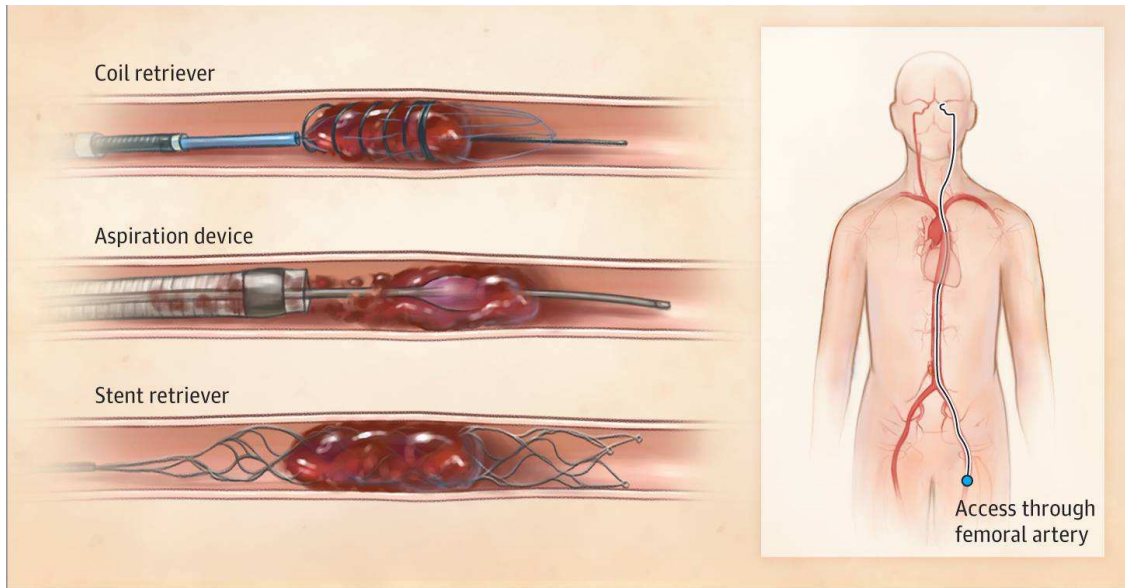


Figure 4. Mechanical thrombectomy devices and catheter navigation to cerebral vessels. Source: Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review. *Jama*. 2015;14:1451-62

The development and subsequent improvement of MT after its initial FDA approval in 2004 is evidence of the progress made in clinical research and medical technology (48). The Merci retriever, an ensnaring and extracting wire shaped like a corkscrew was the first device approved (48). However, there was a significant rate of problems related to hemorrhage or damage to the vessels, and the success rate was not high (48). Significant progress in MT did not occur until the early 2010s, when the stent retrievers Solitaire and Trevo were introduced and provided better clinical outcomes and recanalization, 61% versus Merci 24% and 86% versus Merci 60%, respectively (44). Results such as these were discovered in 2015 and 2016 from randomized control trials such as MR CLEAN, ESCAPE, SWIFT, PRIME, and EXTEND-IA (44). These trials showed that MT followed by IV-TPA was the superior treatment strategy for AIS patients presenting with LVO (20, 44). Further enhancements in recanalization therapy are currently carried out with aspiration catheters and sophisticated stent retrievers, frequently used in combination.

The modified Rankin Scale (mRS) is the most crucial primary outcome measure for assessing the efficacy of MT on a stroke patient’s functional recovery and quality of life (20, 49).

In addition to helping clinicians make decisions about the rehabilitation, discharge, and continuing care of stroke patients, the mRS is an essential tool for evaluating the outcomes of stroke therapy in randomized control trials (49). The ideal result following MT is to achieve a mRS ≤ 2 , because this score is associated with significantly improved outcomes (20, 46). When comparing the outcomes of MT in clinical studies, the mRS score on day 90 following MT therapy has become the accepted benchmark in the field of stroke research since the patient's recovery has typically stabilized at this point and is less likely to fluctuate significantly afterwards (49). A disparity has been noted in clinical studies of MT, the patient may still suffer from a poor prognosis or die even in the event that full recanalization and ideal reperfusion (TICI 3 score) are achieved (35, 50). A number of factors can lead to this, including patients with severe comorbidities such as congestive heart failure; the extent of irreversible brain damage prior to reperfusion; reperfusion injury causing secondary changes such as calcium overload, inflammation, oxidative stress, and disruption of the blood-brain barrier; and hemorrhagic transformation, the rupture of previously damaged blood vessels (35, 50). By decreasing these consequences with prompt AIS therapy and identifying patients who are most likely to benefit from reperfusion using appropriate imaging modalities, healthcare practitioners hope to prevent the discrepancy of TICI and mRS (35). The size and mismatch between the ischemic core and penumbra in AIS patients can be assessed with DWI, CTP, or MRP (20, 35, 39). When there is a larger mismatch, smaller ischemic core relative to penumbra, MT with TPA has been demonstrated to be the most successful, according to mRS on day 90 (20, 34, 44).

Retrospective case-control studies using the DAWN or DIFUSE-3 extended time window criteria (6-24 hours) have revealed a phenomenon known as the "late-window paradox", which states that positive outcomes with MT are still achievable despite the conventional wisdom that delaying treatment worsens patient outcomes because it increases brain damage (20, 51). After 24 hours of symptom onset, AIS patients with collateral circulation and slower infarct progression can still benefit from MT, even with a significant ischemic penumbra after prolonged ischemia (35, 51). This contradiction adds to the mounting evidence that clinicians can continue to further reduce the morbidity and mortality of ischemic stroke through the use of more sophisticated imaging modalities, better MT procedures, and a greater understanding of the pathology of ischemic brain tissue.

2. OBJECTIVES

To analyze and compare the outcomes of stroke patients treated with mechanical thrombectomy after hospital discharge during the years 2021 and 2022. Additionally, to investigate how patient demographic and clinical variables may influence or predict stroke outcomes, as measured by the modified Rankin Scale.

We predict that patients treated for stroke in 2022 with mechanical thrombectomy will have better outcomes compared to those treated in 2021. Furthermore, specific demographic and clinical variables, such as lower NIHSS scores, higher TICI scores, absence of diagnosed diabetes and atrial fibrillation, and absence of SARS-CoV-2 infection, will be associated with more favourable stroke outcomes.

3. PATIENTS AND METHODS

3.1. STUDY DESIGN

This study is a retrospective, observational cohort study. We examined the data collected of all stroke patients admitted to the University Hospital of Split that underwent MT treatment during the years 2021 and 2022. The inclusion, exclusion criteria and treatment plan for MT and/or TPA treatments were based upon the European Stroke Organization (ESO) guidelines (20, 52). The patient demographic and clinical variables that were included in this study are: age, gender, NIHSS score, systolic and diastolic blood pressure, diagnosed hypertension, diagnosed atrial fibrillation, blood glucose level, diagnosed diabetes, diagnosed SARS-CoV-2, CTA evidence of cerebral vessel occlusion, TICI score and mRS. Due to the retrospective nature of this study and the reliance on patient data entered into each patient's individual medical record, it was deemed unnecessary to notify the patients of their inclusion in this study. All work was conducted in compliance with the ethical standards and tenets of the Declaration of Helsinki, as approved by the University Hospital of Split Ethical Committee on January 29, 2024, under registration number: 2181-147/01-06/LJ.Z.-24-02.

3.2. STUDY POPULATION

In the intensive care unit of Neurology, University Hospital of Split between the dates of January 1, 2021, to December 31, 2022, a total of 160 stroke patients received MT treatment, as seen in Table 1. Seventy patients in the year 2021 with an average age of 75.5 ± 11 years, comprised of 32 males and 38 females. Ninety patients in the year 2022, with an average age of 72.5 ± 13.5 years, comprised of 37 males and 53 females.

3.3. STROKE & MECHANICAL THROMBECTOMY PROTOCOL

All persons admitted to University Hospital of Split in 2021 or 2022 with clinical suspicion of an acute ischemic stroke (NIHSS >4) or a confirmed stroke diagnosis underwent a prompt NCCT scan to rule out intracerebral hemorrhage. Once intracerebral hemorrhage was ruled out, patients underwent an immediate a CTA to assess for LVO. If a large infarction was identified on the CTA, the patient was prepared for MT treatment by an interventional radiologist in hospital.

If necessary, the patient would be anesthetized, and a 6F Sophia guide catheter was inserted through a right sided percutaneous femoral access and navigated to the clot with fluoroscopic imaging. Once the guide catheter was in place, a NeuronMax device was used to retrieve or aspirate the clot based upon the attending radiologist's recommendations. After the effectiveness of the MT treatment was evaluated with fluoroscopy and a TICI score was assigned, the NeuronMax and 6F Sophia guide catheter were removed, and hemostasis of the femoral access site was achieved. Based upon the guidelines of the ESO, the mRS should be performed 90 days after MT (20, 49), however some patients died or were transferred to their closest residential hospital for recovery and rehabilitation, therefore the mRS for the majority of the participants in this study was performed earlier than 90 days.

The number of patients in this study who received concurrent TPA treatment with MT was not available due to updates in the patient health record system in Firule hospital in 2021. However, the use of IV-TPA before MT was administered in accordance with the inclusion criteria and acute stroke treatment guidelines established by the ESO (52).

3.3.1. Mechanical Thrombectomy Inclusion Criteria

- Evidence of acute ischemic stroke within twenty-four hours of proposed MT treatment
- Diagnosed neurological deficit on hospital admission, NIHSS >4
- Negative result on NCCT for intracranial hemorrhage
- CTA confirmed LVO

3.3.2. Mechanical Thrombectomy Exclusion Criteria

- Extensive early infarct signs on CT, core infarct larger than 70mL
- Significant Pre-stroke disability (mRS \geq 3)
- Severe comorbid conditions
- Intra-cranial hemorrhage or coagulopathy
- Greater than twenty-four hours since first symptom of acute ischemic stroke

3.3.3. *CT/CTA Exclusion Criteria*

- Known allergy to contrast
- Renal impairment, potential for contrast-induced nephropathy
- Pregnancy (relative contraindication)

3.3.4. *TPA Inclusion Criteria*

- Clinical diagnosis of acute ischemic stroke with neurological deficit, NIHSS >4
- Onset of first stroke symptoms within 4.5 hours of proposed TPA treatment
- Negative result on NCCT for intracranial hemorrhage
- Adults, 18 years or older

3.3.5. *TPA Exclusion Criteria*

- Evidence of intra-cranial hemorrhage on NCCT
- Recent major surgery or trauma, within past fourteen days
- Recent stroke or head trauma, within past three months
- Coagulopathy, and platelet count less than 100 000/mm³
- Severe hypertension, systolic pressure >185 mmHg or diastolic pressure >110 mmHg
- Active internal bleeding, gastrointestinal or urinary tract, within past twenty-one days
- Anticoagulant use with INR > 1.7

3.4. **METHODS OF COLLECTING AND ANALYZING DATA**

Patient demographics, baseline clinical variables including an NIHSS stroke severity scale and a SARS-CoV-2 nasopharyngeal swab test were taken on hospital admission for all acute ischemic stroke patients admitted to the University Hospital of Split during the years 2021 and 2022. The TIC1 score was evaluated by the attending radiologist upon clot removal and the mRS was performed by the attending neurologist at an appropriate time to ensure the score accurately reflected the patient's outcome, post-MT. The authors of this study used Jamovi, a statistical software program, version 2.5.3.0, to examine all aforementioned clinical data that was entered into the University Hospital of Split, IBIS health information system.

3.4.1. *NIHSS*

A 15-item stroke severity scale developed in 1989 to assess stroke severity in emergency departments that includes the following categories (33):

- Level of consciousness
 - 0 – Alert
 - 1 – Drowsy but arousable
 - 2 – Obtunded
 - 3 – Stupor
 - 4 – Coma
- Level of consciousness questions:
 - 0 – Both correct
 - 1 – One correct
 - 2 – Both incorrect
- Level of consciousness commands
 - 0 – Correctly perform both commands
 - 1 – Correctly performs one command
 - 2 – Both commands performed incorrectly
- Best gaze;
 - 0 – Normal
 - 1 – Partial gaze palsy
 - 2 – Forced deviation
- Visual field;
 - 0 – No visual loss
 - 1 – Partial loss in one or both eyes
 - 2 – Complete loss in one or both eyes
- Facial weakness;
 - 0 – Normal
 - 1 – Minor weakness
 - 2 – Moderate weakness
 - 3 – Severe weakness

- Arm motor function;
 - 0 – Normal
 - 1 – Minor weakness
 - 2 – Moderate weakness
 - 3 – Severe weakness
 - 4 – No movement
- Leg motor function;
 - 0 – Normal
 - 1 – Minor weakness
 - 2 – Moderate weakness
 - 3 – Severe weakness
 - 4 – No movement
- Limb ataxia;
 - 0 – No ataxia
 - 1 – Slight ataxia
 - 2 – Moderate ataxia
 - 3 – Severe ataxia
- Sensory;
 - 0 – Normal
 - 1 – Mild sensory loss
 - 2 – Moderate sensory loss
 - 3 – Severe sensory loss
- Language;
 - 0 – No aphasia
 - 1 – Mild aphasia
 - 2 – Moderate aphasia
 - 3 – Severe aphasia
 - 4 – Mute

- Dysarthria;
 - 0 – Normal
 - 1 – Mild dysarthria
 - 2 – Moderate dysarthria
 - 3 – Severe dysarthria
- Neglect;
 - 0 – No neglect
 - 1 – Mild neglect
 - 2 – Moderate neglect
 - 3 – Severe neglect

3.4.2. *TICI scale*

A scale developed in 2003 by Higashida *et al.* was used to evaluate the degree of cerebral reperfusion following endovascular treatment for acute ischemic stroke (53, 54):

- TICI 0. No reperfusion
- TICI 2a. Minimal reperfusion <50%
- TICI 2b. Minimal reperfusion >50%
- TICI 2c. Minimal reperfusion >90%
- TICI 3. Complete reperfusion

3.4.3. *Modified Rankin Scale*

A standardized disability outcome measure performed 90 days post-acute ischemic stroke treatment to assess patient recovery from stroke (20):

- 0. No symptoms
- 1. No significant disability; able to perform usual activities of daily living
- 2. Slight disability; unable to carry out all previous activities
- 3. Moderate disability; requires help but can still walk unassisted
- 4. Moderately severe disability; unable to walk and perform own bodily needs without assistance
- 5. Severe disability; bedridden, incontinent and requires constant care
- 6. Death

3.5. STATISTICAL ANALYSIS

The figures and tables used in this study were created with Microsoft Excel, version 16.85, manufactured by Microsoft in Redmond, Washington, USA. The statistical analyses were performed with Jamovi, a statistical software package, version 2.5.3.0, manufactured by Jamovi Project in Sydney Australia. An ordinal logistic regression was used to analyze the mRS with the patient predictor variables in their respective year of hospital admission. The predictor variables included the clinical variables and demographics collected for each patient, such as: age; sex; NIHSS; systolic and diastolic pressure; atrial fibrillation status; hypertension status; covid status; diabetes status; blood glucose level; CTA vessel occlusion; and TICI score. A Mann Whitney U test was performed to compare the respective TICI scores and mRS outcomes between the year 2021 and 2022. This statistical test was chosen due to the non-normal distribution of the data and the ordinal structure of the TICI and mRS scales. The statistical significance of this study was defined as $p < 0.05$.

4. RESULTS

4.1. BASELINE ANALYSES

Baseline demographics and clinical variables were attained from 160 patients during hospital admission for acute ischemic stroke and MT treatment. The difference in mean, median and mode of patient demographic and clinical variables between year 2021 and 2022 were not substantially different, as seen in Table 1.

A greater number of patients were previously diagnosed with atrial fibrillation and hypertension before hospital admission for stroke, while the majority of patients recorded in 2021 were not previously diagnosed with diabetes, as shown in Figure 5. A considerable minority of patients in the year 2021 and 2022, tested positive for SARS-CoV-2 when they were admitted to the University Hospital of Split for stroke.

Figure 6, illustrates the most common sites of LVO identified by a CTA for acute stroke. The results showed that the most frequently observed site of occlusion in 2021 and 2022 was the right and left MCA M1, while a larger proportion of these strokes occurred in year 2022. The data revealed an increase in stroke frequency in 2022 for LVO of the right and left MCA M2, as well as the right and left MCA and ACI, however a greater number of basilar strokes were seen in 2021.

Table 1. Demographics and clinical variables of mechanical thrombectomy patients in years 2021 and 2022.

Parameter	Year 2021 (N=70)					Year 2022 (N=90)				
	N	Mean ± SD	Median	Mode	Min- Max	N	Mean ± SD	Median	Mode	Min- Max
Age (years)	70	75.5±11	78.0	83.0	37-91	90	72.5±13.5	75	82	28–92
SYS (mmHg)	68	149±31	150	130	90-250	87	148±33	140	140	80–230
DIA (mmHg)	68	85±17	80	80	55-150	87	85±20	80	70	50-180
BGL (mmol/L)	69	7.8±2.7	7.1	5.70	4.6-18	83	8.0±3.1	7.0	6.40	3.7-22.4
NIHSS (0-42)	33	15±4.0	16	18	3.0-21	50	14±3.6	14	14	4.0-22
TICI Score (0-3)	69	1.97±1.3	3.0	3.0	0.0–3.0	88	2.16±1.2	3.0	3.0	0.0–3.0
mRS (0-6)	70	4.0±1.75	4.0	6.0	0.0-6.0	90	3.7±2.2	4.0	6.0	0.0–6.0

Abbreviations: SD – Standard Deviation; NIHSS - National Institutes of Health Stroke Scale; SYS – Systolic Pressure; DIA – Diastolic Pressure; BGL – Blood Glucose Level; TICI – Thrombolysis in Cerebral Infarction; mRS - Modified Rankin Scale

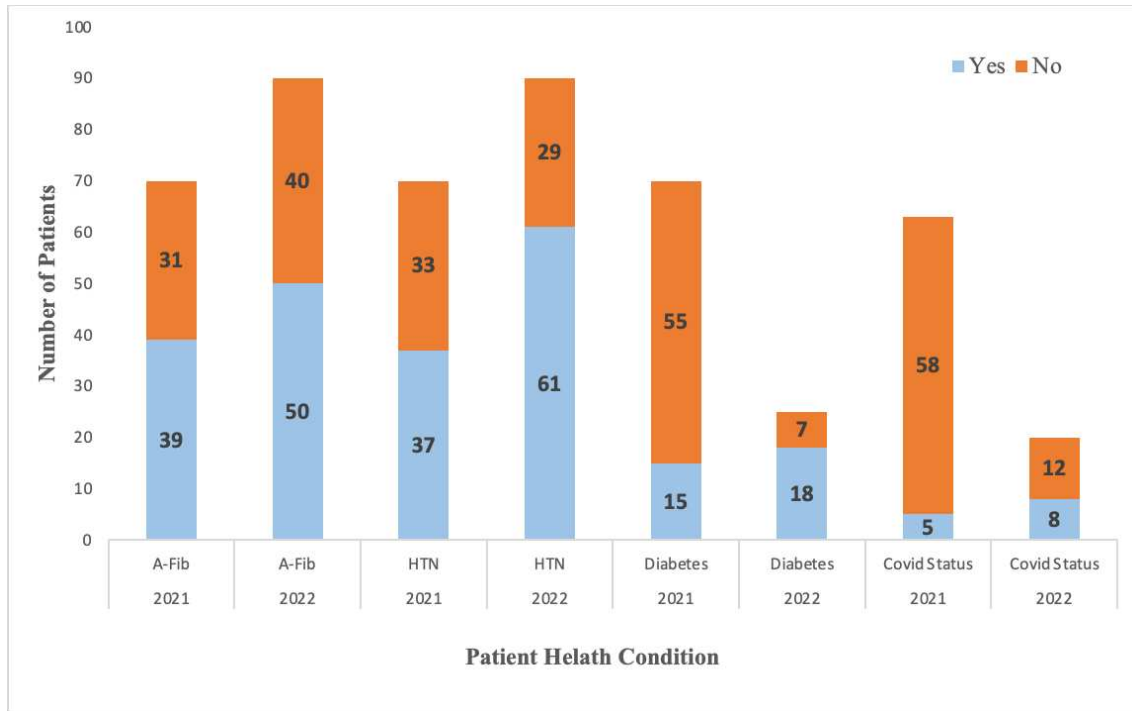


Figure 5. Stacked bar plot representing the frequency of patients with atrial fibrillation (y/n); hypertension (y/n); diabetes (y/n); and covid status (y/n) in year 2021 and 2022

Abbreviations: A-Fib – Atrial Fibrillation; HTN – Hypertension

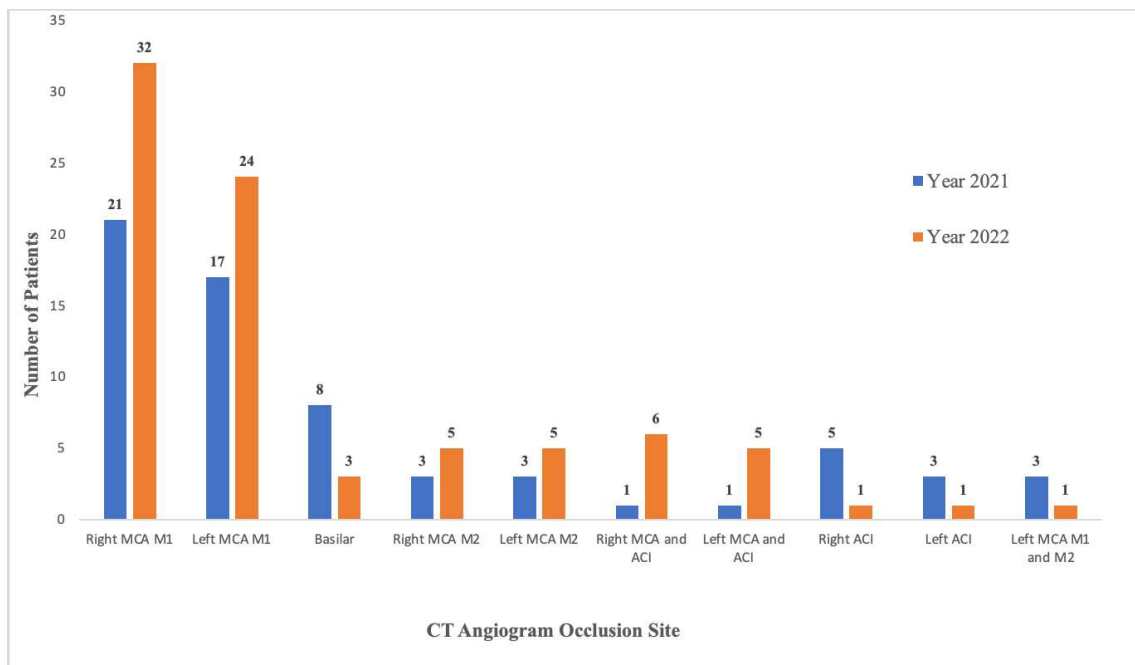


Figure 6. Distribution of the most common stroke occlusion sites confirmed by CT angiogram in year 2021 and 2022

Abbreviations: MCA – Middle Cerebral Artery; ACI - Internal Carotid Artery; M1 – First segment of Middle Cerebral Artery; M2 – Second segment of Middle Cerebral Artery

4.2. ORDINAL LOGISTIC REGRESSION

An ordinal logistic regression analysis was performed to assess the impact of different predictor clinical variables of admitted acute ischemic stroke patients and the immediate result of MT treatment, as indicated by a TICI score, on a standardized disability outcome measure, mRS.

For stroke patients in 2021, the ordinal logistic regression analyses indicated that each one-year increase in age, and each one mmol/L increase in blood glucose level, was associated with an increased odds of attaining a greater mRS by a factor of 1.04 (OR = 1.04, 95% CI [1.00, 1.08], $p = 0.042$) and 1.17 (OR = 1.17, 95% CI [1.00, 1.38], $p = 0.048$), respectively. However, for each one-unit increase in TICI score, the odds of achieving a lower mRS increased by a factor of 0.64 (OR = 0.64, 95% CI [0.45, 0.89], $p = 0.009$), as shown in Table 2.

For stroke patients in 2022, the results revealed that for each one-year increase in age and for each one mmol/L increase in blood glucose level, was associated with an increased odds of attaining a greater mRS by a factor of 1.04 (OR = 1.04, 95% CI [1.01, 1.07], $p = 0.012$), and 1.14 (OR = 1.14, 95% CI [1.01, 1.30], $p = 0.046$), respectively. Additionally, each one-unit increase in NIHSS score and being male, was associated with an increased odds of attaining a greater mRS increased by a factor 1.22 (OR = 1.22, 95% CI [1.06, 1.42], $p = 0.007$), and a lower mRS increased by a factor 0.45 (OR = 0.45, 95% CI [0.209, 0.965], $p = 0.042$), respectively, as seen in Table 3.

Table 2. Ordinal Logistic Regression of mRS in year 2021.

Parameter	Estimate	SE	Odds Ratio	95% CI	P*
Age (years)	0.040	0.020	1.04	(1.00, 1.08)	0.042
Sex (M/F)	-0.095	0.424	0.91	(0.395, 2.09)	0.823
NIHSS (0-42)	0.0729	0.073	1.08	(0.932, 1.25)	0.319
SYS (mmHg)	0.0124	0.007	1.01	(0.999, 1.03)	0.074
DIA (mmHg)	0.008	0.013	1.01	(0.984, 1.03)	0.537
BGL (mmol/L)	0.159	0.080	1.17	(1.00, 1.38)	0.048
Diabetes (Y/N)	1.03	0.529	2.80	(1.01, 8.15)	0.052
A-Fib (Y/N)	0.361	0.426	1.43	(0.624, 3.33)	0.397
HTN (Y/N)	0.602	0.429	1.82	(0.790, 4.28)	0.161
Covid Status (Y/N)	0.029	0.776	1.03	(0.225, 5.02)	0.971
CTA VO (1-32)	0.018	0.025	1.02	(0.968, 1.07)	0.488
TICI (0-3)	-0.445	0.172	0.64	(0.454, 0.892)	0.009

Abbreviations: SE – Standard Error; NIHSS - National Institutes of Health Stroke Scale; SYS – Systolic Pressure; DIA – Diastolic Pressure; BGL – Blood Glucose Level; A-Fib – Atrial Fibrillation; HTN – Hypertension; CTA VO – Computed Tomography Angiography Vessel Occlusion; TICI – Thrombolysis in Cerebral Infarction

*Ordinal Logistic Regression

Table 3. Ordinal Logistic Regression of mRS in year 2022.

Parameter	Estimate	SE	Odds Ratio	95% CI	P*
Age (years)	0.037	0.015	1.04	(1.01, 1.07)	0.012
Sex (M/F)	-0.792	0.389	0.45	(0.209, 0.965)	0.042
NIHSS (0-42)	0.198	0.074	1.22	(1.06, 1.42)	0.007
SYS (mmHg)	0.011	0.006	1.01	(1.00, 1.02)	0.061
DIA (mmHg)	0.019	0.011	1.02	(0.99,1.04)	0.067
BGL (mmol/L)	0.129	0.064	1.14	(1.01, 1.30)	0.046
Diabetes (Y/N)	0.583	0.795	1.79	(0.37, 8.75)	0.463
A-Fib (Y/N)	-0.003	0.377	0.997	(0.475, 2.09)	0.993
HTN (Y/N)	-0.348	0.403	0.706	(0.318, 1.55)	0.388
Covid Status (Y/N)	1.67	0.909	5.32	(0.962, 36.2)	0.066
CTA VO (1-32)	0.037	0.024	1.04	(0.990, 1.09)	0.126
TICI (0-3)	-0.286	0.160	0.751	(0.546, 1.02)	0.073

Abbreviations: SE – Standard Error; NIHSS - National Institutes of Health Stroke Scale; SYS – Systolic Pressure; DIA – Diastolic Pressure; BGL – Blood Glucose Level; A-Fib – Atrial Fibrillation; HTN – Hypertension; CTA VO – Computed Tomography Angiography Vessel Occlusion; TICI – Thrombolysis in Cerebral Infarction

*Ordinal Logistic Regression

4.3. TICI & mRS COMPARISON

A Mann-Whitney U test was used to compare the TICI and mRS scores between patients who underwent MT treatment in year 2021 and 2022. As seen in Table 1, the median TICI and mRS scores in year 2021 were the same in year 2022, 3.0 and 4.0, respectively. The results of the Mann-Whitney U test revealed no statistical differences in the TICI or mRS scores of years 2021 and 2022, ($U = 2783$, $p = 0.310$), and ($U = 2955$, $p = 0.495$), respectively, as seen in Table 4.

Figure 7 and 8, represent the frequency of TICI and mRS score outcomes post-MT treatment in 2021 and 2022, respectively. The most commonly occurring TICI score in both years was TICI 3. The second most commonly occurring was TICI 0. In 2021, the least common TICI score was 1, whereas in 2022, it was TICI 2C, as seen in Figure 7. Regarding mRS, the most frequently observed score in both years was mRS 6, followed by mRS 5. In 2021, the least common mRS was mRS 0, and in 2022, it was mRS 3, as shown in Figure 8.

Table 4. Mann-Whitney U test comparing the results of mechanical thrombectomy in years 2021 with 2022

Parameter	U Statistic	Mean Difference	95% CI	P*
TICI Scores (0-3)	2783	-2.24e-5	(-2.79e-6, 3.15e-6)	0.310
mRS (0-6)	2955	5.06e-6	(-6.64e-5, 1.00)	0.495

Abbreviations: TICI – Thrombolysis in Cerebral Infarction; mRS – Modified Rankin Scale

*Mann Whitney U test

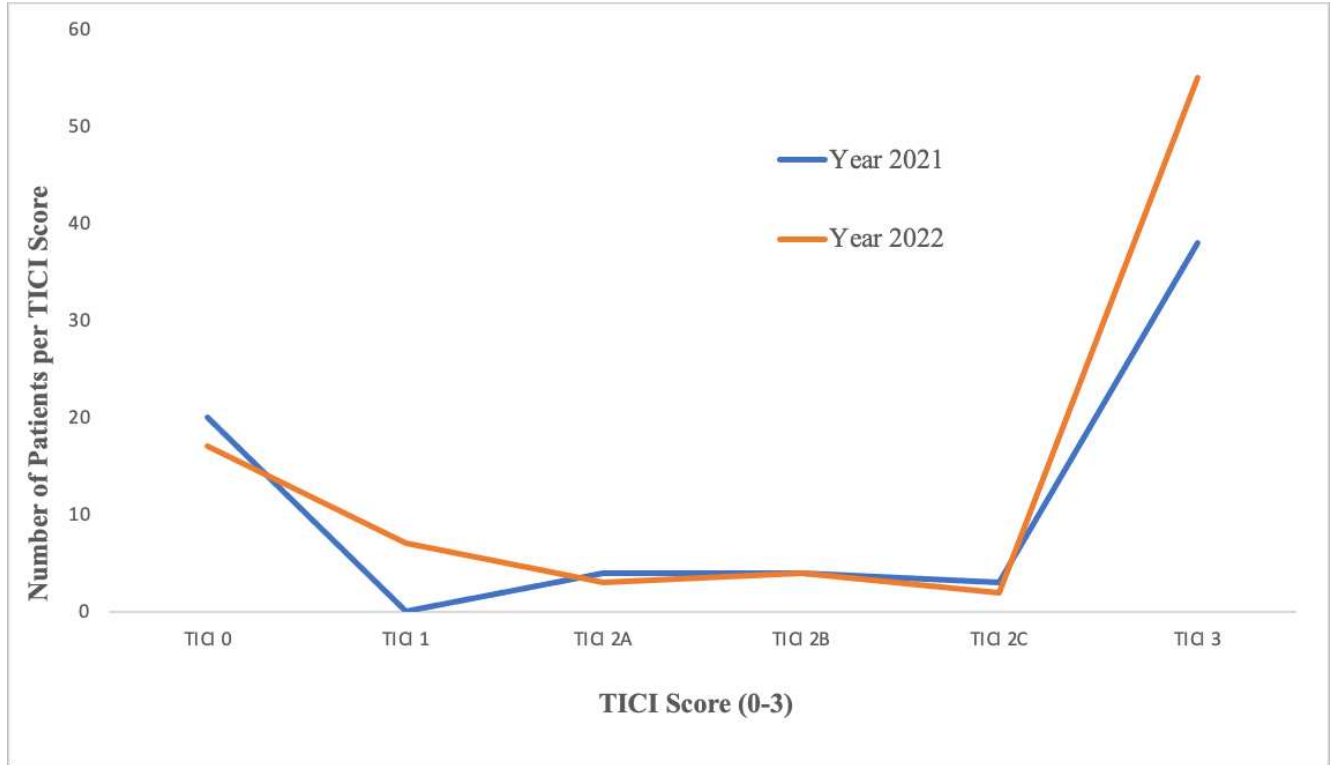


Figure 7. Comparison of TICI scores between year 2021 and 2022

Abbreviations: TICI 0 – No Reperfusion; TICI 1 – Minimal Reperfusion; TICI 2a – Partial Reperfusion <50%; TICI 2B – Partial Reperfusion >50%; TICI 2C – Partial Reperfusion >90%; TICI 3 – Complete Reperfusion



Figure 8. Comparison of modified Rankin Scale scores between year 2021 and 2022

Abbreviations: mRS 0 – No Symptoms; mRS 1 – No Significant Disability; mRS 2 – Slight Disability; mRS 3 – Moderate Disability; mRS 4 – Moderately Severe Disability; mRS 5 – Severe Disability; mRS 6 – Dead

5. DISCUSSION

The purpose of this retrospective study was to compare the clinical and radiological outcomes of AIS patients treated with MT in the University Hospital of Split in the years 2021 and 2022, based upon their resulting mRS. Furthermore, the mRS was used to identify which patient demographic and clinical variables could influence or predict stroke outcomes. A mRS ≤ 2 following MT is considered a positive stroke outcome, according to ESO recommendations (20, 46). Since the peak of SARS-CoV-2 cases in Croatia occurred in late 2021, we included recent COVID-19 diagnosis with the patient demographic and clinical variables that have been well-documented in the literature for their impact on MT outcomes (20, 55).

Age has been determined in previous research to be a substantial non-modifiable risk factor for AIS, especially in those 65 years of age and older (24). Due to the prevalence of comorbidities that impair AIS management and recovery, older age has been associated with greater mortality and morbidity following a stroke, with the largest effect seen in individuals over 80 years (24, 56). Our results are consistent with these findings, as seen in Tables 1-3, the median age of AIS patients in both years was above 65, and an increase in age was significantly associated with a modestly negative effect on stroke outcomes post-MT. Another significant non-modifiable risk factor is gender (25). Although women under 85 have a lower prevalence of stroke than males, women have higher rates of mortality and morbidity post-MT, potentially as a result of biological differences in their responses to stroke and stroke treatment, or comorbidities such as depression which may prolong recovery (25, 57). Perhaps as the result of variations in sample size and gender distribution between the two years of AIS patients, a statistically significant strong effect for male gender and better stroke outcomes was detected in 2022 and not 2021.

The most significant modifiable risk factor for AIS is hypertension, a highly prevalent chronic disorder that can go unnoticed in the population regardless of increasing blood pressure with age (58). For these reasons we chose to include the blood pressure values of patients included in this study along with their clinical hypertension status to determine if these clinical variables effect the outcome of AIS patients treated with MT. Given the link to aging and hypertension, atrial fibrillation, an important risk factor for stroke and stroke outcome, was also examined in relation to mRS post-MT (18, 30).

Our study demonstrated no statistically significant predictive influence of hypertension diagnosis on MT results, which is contrary to the findings that point to a relationship between hypertension and high blood pressure with poor mRS outcomes at 3 months post-MT, as seen in Tables 1 and 2 (57). However, the systolic blood pressure values in both 2021 and 2022, and the diastolic blood pressure values in year 2022 were close to statistical significance. We concluded that with a larger sample size like the 6650 patients evaluated in Yuan *et al.* we could have potentially saw a significant predictive effect of blood pressure values on mRS outcomes (59). The timing of mRS evaluations in our study and the potentially variability in the mRS assessment may have contributed to the lack of predictive significance for hypertension status. Although atrial fibrillation was highly prevalent in our study population, there was no discernible impact of atrial fibrillation on the outcomes of stroke post-MT.

Diabetes and elevated blood glucose levels are both associated with an increased stroke risk and poor outcomes post-MT, therefore both clinical variables were included in our study (18, 30). The detrimental effects of diabetes and hyperglycemia are attributed to persistent microvascular damage to vessels and accelerated atherosclerosis (18, 30). Our results supported these findings, increased blood glucose levels were significantly associated with worse outcomes in both 2021 and 2022, although the impact of diabetes, while moderate to strong, was not statistically significant, as seen in Tables 2 and 3. We concluded that the lack of information on diagnosed diabetes in 2022 and the reduced sample size in 2021 were the most likely causes for these inconsistent results with current literature.

Since the onset of the COVID-19 pandemic, emerging evidence suggests that SARS-CoV-2 infection raises the risk of ischemic stroke by processes involving pro-inflammatory and pro-coagulation events that are comparable to those of hyperglycemia and hypertension (60). According to a retrospective analysis of COVID-19 MT patients in America, these patients had longer hospital stays and a higher rate of inpatient mortality (61). These findings were most likely caused by non-neurological symptoms of the virus, such as sepsis and respiratory failure (61). As shown in Table 3 and Figure 5, we discovered that, despite the fact that there was limited data on patients tested for SARS-CoV-2 in 2022 than in 2021, there was a very strong predictive effect between this diagnosis and a worsening of stroke outcomes in 2022.

This correlation was determined to be near, but not statistically significant. We concluded that if more data was available, the outcome would have been statistically significant.

Regarding the location of LVO, the distribution was consistent with current literature, where the majority of LVOs occur in the M1 and M2 segments of the MCA, as seen in Figure 6 (62). A higher frequency of right-sided LVOs were revealed in our study. Anatomical differences in the branching patterns of the brachiocephalic trunk provided one explanation for this discrepancy (63). Another reason could be that clinicians at the University Hospital of Split are more adept at identifying right-sided strokes than those serving in other European stroke centers, since Portegies *et al.* discovered that left-sided strokes are disproportionately easier to recognize than right-sided strokes because LVO of the left side commonly causes language and speech difficulties (64). In addition, as Figure 6 illustrates, there was an atypically increased incidence of basilar strokes in 2021. Since basilar strokes are typically rare and fatal occurrences, accounting for only 1-4% of all ischemic strokes, we assumed that the higher incidence in 2021 was most likely caused by COVID-19 infections, either concurrently or previously, given that the SARS-CoV-2 pandemic peaked in Croatia in late 2021 (55, 65). Our conclusion was supported by a retrospective cohort study by Kojundžić *et al.* where a greater percentage of basilar LVO was discovered in AIS patients in Croatia who underwent MT with concurrent COVID-19 infection (66). We could only speculate that this was the most likely reason for the unexpectedly high percentage of basilar strokes in 2021 because there was little information regarding their SARS-CoV-2 status in their medical history.

According to the ESO, AIS patients who present with a lower NIHSS score, less than 15, typically have better post-MT results than patients with higher scores, while patients with NIHSS scores of more than 20 experience significantly worse outcomes (20). These results are consistent with our findings in 2022, as seen in Table 3, there was a statistically significant moderate influence on negative stroke outcomes post-MT for every increase in NIHSS score. The results would most likely also be statistically significant in 2021 if there was additional data available on the NIHSS scores of those patients admitted in 2021.

Lastly, a TICI score of 3 indicates an optimal MT result due to complete blood flow restoration with the lowest chance of intracranial hemorrhage and other post-MT sequelae (42, 35, 50). As shown in Table 2 and Figure 7, only the AIS patients in 2021 benefited from a statistically significant inverse association between TICI score and MT outcome, even though the majority of MT treatments performed at the University Hospital of Split resulted in a TICI score of 3. The results shown in Table 4 and Figure 7, demonstrate that the performance of the Interventional Radiologists was deemed stable, as there was no statistical difference seen in the results of the Mann-Whitney U test comparing the TICI scores between 2021 and 2022. Similarly, as seen in Table 4, a statistically insignificant Mann-Whitney U test comparing the post-MT outcomes of mRS scores between the two years was essentially the same for MTs performed in 2021 and 2022. As Figure 8 illustrates, while the majority of MT treatments performed at the University Hospital of Split produced the highest TICI score, the overall outcome as determined by mRS was also high, which corresponded to greater mortality and morbidity. This discrepancy has prompted a significant number of ongoing research to determine blood biomarkers, ways to increase recanalization rates, and improve on the examination of clinical and neuroradiological aspects that could be utilized to lessen post-MT complications that worsen mRS in individuals with AIS (42, 35, 50).

This study emphasizes the complexity of predicting the prognosis of AIS following MT, and thus highlighting the need for further research on patient variables such as age, gender, diabetes, hypertension and COVID-19 infection. Although our results are consistent with the current body of literature in some aspects, they also reveal gaps in our understanding of MT efficacy that may be better understood with significantly larger sample sizes and more systematic data gathering. Furthermore, we acknowledge that the retrospective nature and single-center design of this observational cohort study presents inherent limitations. Improving prediction models should be the main goal of future research in order to maximize patient outcomes.

6. CONCLUSION

This analysis of AIS patients who underwent MT at the University Hospital of Split in 2021 and 2022 has illustrated several important clinical variables that could affect the prognosis of stroke patients. Our results support previous studies, especially when it comes to identifying the effects of age, gender and blood glucose levels on post-MT recovery. However, they also draw attention to the complications related to hypertension and atrial fibrillation as prognostic factors.

The results of this study show that although atrial fibrillation and hypertension were highly prevalent in the AIS patients analyzed, they had no statistically significant effect on the outcomes of mRS post-MT. This contrasts previous research, which implies that differences in sample size, data collection, and mRS assessments and scheduling may have an impact on post-MT outcomes. Further investigation into the long-term consequences of SARS-CoV-2 on stroke patients should be performed as evidenced by the strong but borderline statistically significant predictive effect of concurrent infection on post-MT outcomes.

The overall poor mRS results suggest a disconnect between procedural success and patient recovery, even though TICI scores show effective recanalization in most patients. This discrepancy necessitates ongoing attempts to improve MT methods, find novel biomarkers and prevent the underlying causes that influence post-MT complications.

In order to improve the effectiveness of MT, future research should build on these findings with more diverse patient populations and to further reduce the burden of stroke, primary prevention is essential as many stroke survivors require long-term rehabilitation and chronic care.

7. REFERENCES

1. Grefkes C, Fink GR. Recovery from stroke: current concepts and future perspectives. *Neurol Res and Pract.* 2020;1:17.
2. World Health Organization [Internet]. Geneva: World Health Organization. Global health estimates: life expectancy and leading causes of death and disability; 2020 [cited 2024 Aug 9]. Available from: <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates>.
3. World Stroke Organization [Internet]. Geneva: World Health Organization. Global Stroke Fact Sheet 2022; 2022 [cited 2024 Aug 9]. Available from: https://www.world-stroke.org/assets/downloads/WSO_Global_Stroke_Fact_Sheet.pdf.
4. Tsao CW, Aday AW, Almarzooq ZI, Anderson CA, Arora P, Avery CL et al. Heart disease and stroke statistics—2023 update: a report from the american heart association. *Circulation.* 2023;8:93-621.
5. Béjot Y, Bailly H, Durier J, Giroud M. Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med.* 2016;12:391-8.
6. Kadojić D, Demarin V, Dikanović M, Lušić I, Tuškan-Mohar L, Trkanjec Z et al. Incidence of stroke and transient ischemic attack in croatia: a population based study. *Coll Antropol.* 2015;3:723-7.
7. Saini V, Guada L, Yavagal DR. Global epidemiology of stroke and access to acute ischemic stroke interventions. *Neurology.* 2021;97:6-16.
8. Coupland AP, Thapar A, Qureshi MI, Jenkins H, Davies AH. The definition of stroke. *J R Soc Med.* 2017;1:9-12.
9. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the american heart association/american stroke association. *Stroke.* 2013;7:2064-89.
10. Lee SH. *Stroke revisited: hemorrhagic stroke.* 1st ed. New York: Springer; 2018. p. 3-6.
11. Healthline [Internet]. San Francisco: Daniel Yetman; 2023 May 19. What's the difference between an ischemic and hemorrhagic stroke?; [cited 2024 Aug 9]. Available from: <https://www.healthline.com/health/stroke/ischemic-vs-hemorrhagic-stroke>.

12. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. *Stroke*. 2001;12:2735-40.
13. Ay H, Benner T, Murat Arsava E, Furie KL, Singhal AB, Jensen MB et al. A computerized algorithm for etiologic classification of ischemic stroke: the causative classification of stroke system. *Stroke*. 2007;11:2979-84.
14. Adams Jr HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of org 10172 in acute stroke treatment. *Stroke*. 1993;1:35-41.
15. Catanese L, Tarsia J, Fisher M. Acute ischemic stroke therapy overview. *Circ Res*. 2017;3:541-58.
16. Kim JS, Pathophysiology of transient ischaemic attack and ischaemic stroke. In: Norrving B, editor. *Oxford textbook of stroke and cerebrovascular disease*. Oxford: Oxford University Press; 2014. p. 35 – 50.
17. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol*. 2014;4:429-38.
18. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. *Circ Res*. 2016;9:1340-7.
19. Petty GW, Brown Jr RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke*. 1999;12:2513-6.
20. Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M et al. European stroke organisation (ESO)-european society for minimally invasive neurological therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke. *J Neurointerv Surg*. 2023;8:1-30.
21. Rai AT, Link PS, Domico JR. Updated estimates of large and medium vessel strokes, mechanical thrombectomy trends, and future projections indicate a relative flattening of the growth curve but highlight opportunities for expanding endovascular stroke care. *J Neurointerv Surg*. 2023;3:349-55.
22. Wijndicks EFM. *Examining Neurocritical Patients*. New York: Springer; 2021. p. 40.

23. Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. *Lancet Neurol.* 2010;7:689-701.
24. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ et al. Heart disease and stroke statistics—2014 update: a report from the american heart association. *Circulation.* 2014;3:28-292.
25. Persky RW, Turtzo LC, McCullough LD. Stroke in women: disparities and outcomes. *Curr Cardiol Rep.* 2010;12:6-13.
26. Cainzos-Achirica M, Fedeli U, Sattar N, Agyemang C, Jenum AK, McEvoy JW et al. Epidemiology, risk factors, and opportunities for prevention of cardiovascular disease in individuals of south asian ethnicity living in europe. *Atherosclerosis.* 2019;286:105-13.
27. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP et al. Heart disease and stroke statistics—2019 update: a report from the american heart association. *Circulation.* 2019;10:56-528.
28. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F et al. Primary prevention of cardiovascular disease with a mediterranean diet supplemented with extra-virgin olive oil or nuts. *N Engl J Med.* 2018;25:34-48.
29. Owolabi MO, Thrift AG, Mahal A, Ishida M, Martins S, Johnson WD et al. Primary stroke prevention worldwide: translating evidence into action. *Lancet Public Health.* 2022;1:74-85.
30. Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SC et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. *Stroke.* 2011;1:227-76.
31. Yew KS, Cheng EM. Diagnosis of acute stroke. *Am Fam Physician.* 2015;8:528-36.
32. Toral L. Be FAST to recognize stroke. *Nursing 2023.* 2021;2:51-4.
33. Kwah LK, Diong J. National institutes of health stroke scale (NIHSS). *J Physiother.* 2014;1:61.
34. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the american heart association/american stroke association. *Stroke.* 2019;12:344-418.

35. Kim BJ, Kang HG, Kim HJ, Ahn SH, Kim NY, Warach S et al. Magnetic resonance imaging in acute ischemic stroke treatment. *J Stroke*. 2014;3:131-45.
36. Attenberger UI, Morelli JN, Schoenberg SO, Michaely HJ. Assessment of the kidneys: magnetic resonance angiography, perfusion and diffusion. *J Cardiovasc Magn Reson*. 2011;1:13-70.
37. Legrand L, Naggara O, Turc G, Mellerio C, Roca P, Calvet D et al. Clot burden score on admission T2*-MRI predicts recanalization in acute stroke. *Stroke*. 2013;7:1878-84.
38. Mehta AM, Desai SM, Jadhav AP. Mechanical thrombectomy for acute ischemic stroke: current state and future directions. *Curr Treat Options Neurol*. 2024;1:297-318.
39. Konstas AA, Goldmakher GV, Lee TY, Lev MH. Theoretic basis and technical implementations of CT perfusion in acute ischemic stroke, part 2: technical implementations. *AJNR Am J Neuroradiol*. 2009;5:885-92.
40. Volný O, Haršány M, Mikulík R. Homonymous visual field defects. New York: Springer Cham, 2017. p. 31-41.
41. Astrup J, Siesjö BK, Symon L. Thresholds in cerebral ischemia-the ischemic penumbra. *Stroke*. 1981;6:723-5.
42. Maïer B, Desilles JP, Mazighi M. Intracranial hemorrhage after reperfusion therapies in acute ischemic stroke patients. *Front Neurol*. 2020;11:599908.
43. Bai QK, Zhao ZG, Lu LJ, Shen J, Zhang JY, Sui HJ et al. Treating ischaemic stroke with intravenous tpa beyond 4.5 hours under the guidance of a MRI DWI/T2WI mismatch was safe and effective. *Stroke and Vasc Neurol*. 2019;4:8-13.
44. Bhaskar S, Stanwell P, Cordato D, Attia J, Levi C. Reperfusion therapy in acute ischemic stroke: dawn of a new era?. *BMC Neurol*. 2018;18:8.
45. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009-18.
46. McCarthy DJ, Diaz A, Sheinberg DL, Snelling B, Luther EM, Chen SH et al. Long-term outcomes of mechanical thrombectomy for stroke: a meta-analysis. *Sci World J*. 2019;7403104.
47. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review. *JAMA*. 2015;313:1451-62.

48. Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS et al. Mechanical thrombectomy for acute ischemic stroke: final results of the multi MERCI trial. *Stroke*. 2008;39:1205-12.
49. ElHabr AK, Katz JM, Wang J, Bastani M, Martinez G, Gribko M, Hughes DR, Sanelli P. Predicting 90-day modified Rankin Scale score with discharge information in acute ischaemic stroke patients following treatment. *BMJ Neurol Open*. 2021;1:e000177.
50. Farghaly WM, Ahmed MA, El-Bassiouny A, Hamed AA, Shehata GA. Predictors of three months mortality after endovascular mechanical thrombectomy for acute ischemic stroke. *The Egypt JNeurol Psychiatry Neurosurg*. 2022;58:96.
51. Legio C. Endovascular treatment beyond the 24-hour mark [Internet]. *Stroke Research: European Stroke Organization*; 2023 [cited 2024 Aug 9]. Available from: <https://eso-stroke.org/endovascular-treatment-beyond-the-24-hour-mark/>.
52. Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C et al. European stroke organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Euro Stroke J*. 2021;6:I-LXII.
53. Fugate JE, Klunder AM, Kallmes DF. What is meant by “TICI”? *AJNR Am J Neuroradiol*. 2013;34:1792-7.
54. Almekhlafi MA, Mishra S, Desai JA, Nambiar V, Volny O, Goel A et al. Not all “successful” angiographic reperfusion patients are an equal validation of a modified TICI scoring system. *Interv Neuroradiol*. 2014;20:21-7.
55. Vilibic-Cavlek T, Stevanovic V, Brlek-Gorski D, Ferencak I, Ferenc T, Ujevic-Bosnjak M et al. Emerging trends in the epidemiology of COVID-19: the croatian ‘one health’ perspective. *Viruses*. 2021;13:2354.
56. Beuker C, Köppe J, Feld J, Meyer CL, Dröge P, Ruhnke T et al. Association of age with 1-year outcome in patients with acute ischaemic stroke treated with thrombectomy: real-world analysis in 18 506 patients. *J Neurol Neurosurg Psychiatry*. 2023;94:631-7.
57. Kobeissi H, Ghozy S, Turfe B, Amoukhteh M, Bilgin C, Kadirvel R et al. Differences between males and females following endovascular therapy for stroke: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis*. 2023;32:107124.
58. Boehme AK, Esenwa C, Elkind MS. Stroke risk factors, genetics, and prevention. *Circ Res*. 2017;120:472-95.

59. Yuan Z, Chen N, Zhou M, Guo J, Zhang Y, Li Y et al. Effects of hypertension in patients receiving mechanical thrombectomy: a meta-analysis. *Medicine (Baltimore)*. 2020;99:e19803.
60. Mbonde AA, O'Carroll CB, Grill MF, Zhang N, Butterfield R, Demaerschalk BM. Stroke features, risk factors, and pathophysiology in SARS-CoV-2–infected patients. *Mayo Clin Proc Innov Qual Outcomes*. 2022;6:156-65.
61. Ramsay IA, Fountain H, Elarjani T, Govindarajan V, Silva M, Abdelsalam A et al. Outcomes in patients with large vessel occlusion strokes undergoing mechanical thrombectomy with concurrent COVID-19: a nationwide retrospective analysis. *J Neurointerv Surg*. 2024;16:342-6.
62. Waqas M, Mokin M, Primiani CT, Gong AD, Rai HH, Chin F et al. Large vessel occlusion in acute ischemic stroke patients: a dual-center estimate based on a broad definition of occlusion site. *J Stroke Cerebrovasc Dis*. 2020;29:104504.
63. Sidiq M, Scheidecker E, Potreck A, Neuberger U, Weyland CS, Mundiyanapurath S et al. Aortic arch variations and supra-aortic arterial tortuosity in stroke patients undergoing thrombectomy: retrospective analysis of 1705 cases. *Clin Neuroradiol*. 2023;33:49-56.
64. Portegies ML, Selwaness M, Hofman A, Koudstaal PJ, Vernooij MW, Ikram MA. Left-sided strokes are more often recognized than right-sided strokes: the rotterdam study. *Stroke*. 2015;46:252-4.
65. Francalanza I, Ciacciarelli A, Caragliano AA, Casella C, Cotroneo M, Dell'Aera C et al. Acute stroke treatment in patients with basilar artery occlusion: a single-center observational study. *Cerebrovasc Dis Extra*. 2019;9:90-7.
66. Kojundžić SL, Sablić S, Budimir Mršić D, Marinović Guić M, Kraljević I, Benzon B et al. Mechanical thrombectomy in acute ischemic stroke COVID-19 and non-COVID-19 patients: a single comprehensive stroke center study. *Life*. 2023;13:186.

8. SUMMARY

Background: Stroke is a leading cause of disability and death globally. Ischemic stroke, the most common type, arises from blocked cerebral vessels. Mechanical thrombectomy is a groundbreaking treatment for certain strokes, significantly improving outcomes when administered swiftly to eligible patients.

Methods: This retrospective cohort study investigated the outcomes of mechanical thrombectomy in stroke patients at the University Hospital of Split during 2021 and 2022. The study included 160 patients (70 in 2021, 90 in 2022) who underwent MT following European Stroke Organization guidelines. Patients with suspected acute ischemic stroke (NIHSS >4) underwent NCCT and CTA to identify large vessel occlusion. The MT procedure, guided by interventional radiologists, utilized a NeuronMax device for clot retrieval. Researchers analyzed clinical data, including NIHSS scores, COVID-19 status, and other baseline variables, to assess patient outcomes. Recovery was evaluated using the modified Rankin Scale post-treatment.

Results: No significant differences in baseline demographics or clinical variables were found between 2021 and 2022. The most common pre-existing conditions were atrial fibrillation and hypertension, with a notable minority of patients testing positive for COVID-19 upon admission. The most frequent site of large vessel occlusion was the middle cerebral artery M1 segment. Older age and higher blood glucose levels were associated with poorer functional outcomes (higher mRS scores). Achieving successful reperfusion (higher TICI score) was associated with better outcomes in 2021. While no statistical difference was found in overall TICI or mRS scores between the two years, TICI 3 was the most common reperfusion outcome, while mRS 6 (death) was the most frequent functional outcome.

Conclusion: This study identified age, gender, and blood glucose as significant predictors of post-treatment outcomes in acute ischemic stroke patients treated with mechanical thrombectomy. While hypertension and atrial fibrillation were highly prevalent, they did not significantly impact outcomes. This discrepancy highlights the influence of methodological variations on study findings. Despite high rates of successful recanalization, overall functional outcomes (mRS) were poor, emphasizing the need for continued refinement of MT techniques, identification of novel prognostic biomarkers, and a strong emphasis on primary stroke prevention.

9. SUMMARY IN CROATIAN

Cili istraživanja: Moždani udar je vodeći uzrok invaliditeta i smrti u svijetu. Ishemijski moždani udar, najčešći tip, nastaje zbog blokade moždanih krvnih žila. Mehanička trombektomija je revolucionarna terapija za određene moždane udare, koja značajno poboljšava ishode kada se brzo primijeni kod odgovarajućih pacijenata.

Ispitanici I Metode: Ova retrospektivna kohortna studija istraživala je ishode MT u bolesnika s moždanim udarom u KBC-u Split tijekom 2021. i 2022. godine. Studija je obuhvatila 160 bolesnika (70 u 2021., 90 u 2022.) podvrgnutih MT-u prema smjernicama Europske organizacije za moždani udar. Bolesnici sa sumnjom na akutni ishemijski moždani udar (NIHSS > 4) podvrgnuti su NCCT-u i CTA-i radi identifikacije okluzije velikih krvnih žila. MT postupak, vođen intervencijskim radiolozima, koristio je NeuronMax uređaj za uklanjanje ugruška. Analizirani su klinički podaci, uključujući NIHSS skorove, COVID-19 status i druge početne varijable, kako bi se procijenili ishodi bolesnika. Oporavak je procijenjen pomoću modificirane Rankinove skale (mRS) nakon liječenja.

Rezultati: Nisu pronađene značajne razlike u početnim demografskim ili kliničkim varijablama između 2021. i 2022. godine. Najčešća prethodna stanja bila su fibrilacija atriya i hipertenzija, s značajnom manjinom pacijenata pozitivnih na COVID-19 prilikom prijema. Najčešće mjesto okluzije velikih krvnih žila bio je M1 segment srednje moždane arterije. Starija dob i viša razina glukoze u krvi bili su povezani s lošijim funkcionalnim ishodima (viši mRS). Postizanje uspješne reperfzije (viši TICI skor) bilo je povezano s boljim ishodima u 2021. godini. Iako nije pronađena statistička razlika u ukupnim TICI ili mRS rezultatima između dvije godine, TICI 3 bio je najčešći ishod reperfzije, dok je mRS 6 (smrt) bio najčešći funkcionalni ishod.

Zaključci: Ova studija identificirala je dob, spol i glukozu u krvi kao značajne prediktore ishoda nakon liječenja u bolesnika s akutnim ishemijskim moždanim udarom liječenih MT-om. Iako su hipertenzija i fibrilacija atriya bili vrlo česti, nisu značajno utjecali na ishode. Ova neusklađenost naglašava utjecaj metodoloških varijacija na nalaze studije. Unatoč visokim stopama uspješne rekanalizacije, ukupni funkcionalni ishodi (mRS) bili su loši, što naglašava potrebu za kontinuiranim usavršavanjem MT tehnika, identifikacijom novih prognostičkih biomarkera i snažnim naglaskom na primarnoj prevenciji moždanog udara.