# The early outcome of thrombectomy in patients with basilar artery stroke

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### UNIVERSITY OF SPLIT SCHOOL OF MEDICINE

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# THE EARLY OUTCOME OF THROMBECTOMY IN PATIENTS WITH BASILAR ARTERY STROKE

### **DIPLOMA THESIS**

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### LIST OF ABBREVIATIONS:

BAO	Basilar artery occlusion
BA	Basilar artery
TIA	Transient ischemic attack
AIS	Acute ischemic attack
BP	Blood pressure
AF	Atrial fibrillation
CCA	Common carotid artery
ICA	Internal carotid artery
ECA	External carotid artery
ACA	Anterior cerebral arteries
MCA	Middle cerebral arteries
TF	Transverse foramen
FM	Foramen Magnum
РС	Posterior circulation
PICA	Posterior inferior cerebellar arteries
ASA	Anterior spinal artery
AICA	Anterior inferior cerebellar arteries
SCA	Superior cerebellar arteries
РСА	Posterior cerebral arteries
ASA/AHA	American stroke association/ American heart association
INR	International normalized ratio
APTT	Activated prothrombin time
NIHSS	National institute of health stroke scale
SAH	Subarachnoid hemorrhage
ICH	Intracerebral hemorrhage

BP	Blood pressure
MSCT	Multi-slice computed tomography
СТА	Computed tomography angiography
TICI	Thrombolysis in cerebral infarction scale
DM	Diabetes mellitus
AH	Arterial hypertension
TBW	Total body weight
PC - CS	Posterior circulation collateral score

**1. INTRODUCTION** 

Stroke is the major cause of long-term disability in adults and the second leading cause of death worldwide. In 2019 the total number of 5180 persons died from stroke incidents in Croatia, being responsible for 10% of all deaths at that respective year (1). In Croatia, Europe and worldwide the incidence of cerebral stroke is increasing with age and dramatically increase after the age of 65.

There are many known stroke risk factors that can be recognized and treated and even prevented. Many of these risk factors that are related to lifestyle such as alcohol, smoking, inactivity, and unhealthy diet could be modified. All of them can also lead to other comorbidities that can additionally increase risk for cerebral ischemic stroke. Examples of these conditions are hypertension, diabetes mellitus, hyperlipidemia, obesity, and various heart diseases. All these risk factors and comorbidities if treated and followed well under the lead of healthcare providers can drastically decrease the numbers of the cerebral ischemic assaults.

The currently used therapy modalities for the cerebral ischemic stroke are IV thrombolysis and mechanical thrombectomy. The time of onset until procedure and procedure duration have the greatest impact on the outcome of the patients. The patients' health status prior to the ischemic stroke and the status upon admission to the hospital are also of great importance. These parameters will also help clinician to decide what is the best treatment option for each individual patient.

Most studies are concerned in the anterior cerebral circulation strokes while posterior circulatory occlusion and basilar artery occlusion (BAO) are significantly less evaluated. The posterior cerebral strokes are accountable for 1/5 of all cerebral ischemic strokes and because of that the success and outcome of their therapy options are less reliable.

#### 1.1. Stroke

Stroke is defined as acute neurological deficit with duration longer than 24 hours that have the cerebrovascular etiology. Strokes are today the main leading cause of chronic disability and currently one of the most common causes of death worldwide. In the United States (U.S.) it is the 4th leading cause of death among elderly population (age over 55) (2). There are two main types of stroke: ischemic and hemorrhagic. Acute ischemic stroke (AIS) is caused by an occlusion of the cerebral artery and hemorrhagic stroke is caused by rupture of artery. Transient ischemic attack (TIA) is characterized as neurological symptoms lasting less than 24 hours (1). It should be noted with greatest caution and seriousness because TIAs are very often a warning sign for a severe or devastating stroke. Acute ischemic stroke (AIS) is today responsible for 87 - 90% of all strokes(2). This occurs when blood flow through one or more of the cerebral arteries is blocked and impairs blood flow to specific part of brain. This could be caused by typical two differentials, an embolic or thrombotic clot (3). Embolic stroke comes from a clot or small plaque, most commonly from blood clot origin from the heart or other site in the body (aortic arch, carotid artery etc.) from where it breaks off, travel and occlude the smaller/narrow vessel in the brain. This stroke is usually rapid, happening without any warning signs. Thrombotic stroke, which is more common of the two types, occurs when the clot forms directly within an artery in the brain (2). This type of stroke is seen more commonly in the older population, typically with already known atherosclerosis, high cholesterol, and diabetes. It usually occurs suddenly, during sleep or early mornings but can also develop gradually over time (hours-days) and often has uniform TIAs that are preceding. On the other side, hemorrhagic strokes are caused with cerebral blood vessel ruptures (2). There are two types of hemorrhagic stroke: intracerebral (10%) - bleeding within brain vessel and subarachnoid hemorrhage (3% of all strokes) - bleeding in subarachnoid space between membranes (2).

#### 1.1.1. Incidence and prevalence

Stroke is the second leading cause of death in the adult population worldwide, as for Europe and Croatia as well (1). The incidence and prevalence of general stroke increases with the raising age of the patient. In adults 35 - 45 years of age have incidence of 30 - 120/100.000 strokes per year and raising to 670 - 970/100.000 per year at age of 65 - 75 years (2). The risk for stroke is doubling after age of 55. In persons under the age of 35 the incidence is dramatically lowered with 2.5/100.000 per year (2). In Croatia 12.000 - 13.000 people are treated for ischemic strokes annually and over 5000 patient death were caused by this cerebral insult in 2019. (1) Unlike in adult population where ischemic stroke is most frequent, in younger population most prevalent is hemorrhagic stroke (2).

For basilar artery stroke specifically the incidence, frequency and prevalence are much rarer; approximately 1/5 strokes in the adult population are caused by occlusion in the posterior circulation (4). Further the Basilar artery occlusion (BAO) accounts for 27% of all posterior

circulation strokes. Luckily this makes BAO only 1% of all cerebral ischemic strokes (4). There is an increased frequency in male population, with a ratio 2:1 (4). Also leasion in the basilar artery supply have a very grave prognosis, with 85% of mortality rate and with severe disability in survivors (5).

#### 1.1.2. Risk factors

General risk factors for stroke are hypertension, cigarette smoking, heavy alcohol consumption, high cholesterol, diabetes, obesity, inactivity, heart disease (AF) and older age. These factors can further be divided into nonmodifiable and modifiable, where the last mentioned can be regulated and lower risk for stroke. The modifiable ones being the level of physical activity, smoking and alcohol consumption (2).

Hypertension is considered as the most significant risk factor for stroke, also seen in a BAO. In as many as 70% of cases they have hypertension as underlaying disease (4). Blood pressure above 140/110 mmHg causes a significant risk (3). Over time this will stress and weaken the arterial wall and increase the risk especially for hemorrhagic stroke. On the other hand, it can also thicken and narrow the wall of the cerebral arteries and in atherosclerosis the pressure can trigger a debris cut off (emboli) and travel to block an artery (3). High cholesterol levels and atherosclerosis as isolated case of an inflammatory disease of the arterial wall that will make it hard, stiff, and narrow with buildup of lipid debris. Like for hypertension it can in time cutoff and block or also weaken artery predisposing for rupture (3). Considerations regrading weight, diet, lifestyle and checking your blood pressure regularly and eventually treat hypertension therapeutically may help to reduce the risk of stroke. Smoking and its chemical components like carbon monoxide and nicotine will accelerate the propagation of atherosclerosis. Also, it will increase the fibrinogen levels in the blood and enhance blood thickening and by this predispose blood for clotting. Diabetes is severely increasing the risk of having a stroke because of its direct impact on atherosclerosis development, which will further narrow and tighten the arteries and contribute to the stroke risk. The insulin resistant type of diabetes is having greater risk than the insulin dependent type (6).

Carotid artery stenosis logically increases the risk and prevalence of stroke. Most patients are not aware of the condition, it increases with age and is found in 50% of asymptomatic patients in the age over 65 (7). Typically, they will experience one or more TIAs that should alarm us that

within days, weeks, or months the stroke would follow. Lifestyle modifications to decrease atherosclerosis and hypertension etc. can help to prevent this condition as well as surgery - carotid endarterectomy (8).

Atrial fibrillation (AF) is also one of the risk factors that increases with age. In patients over 65 years of age the prevalence is 6% (2). The percentage of stroke caused by AF in age above 80 years is approximately 25%. Naturally based on this the risk is severely increased in patients with additional valvular disease (9). AF classified as disturbed or irregular heartbeats is causing an irregular, ineffective and disturbed pumping of the atria that is having a blood stagnation. Therefore, this will have a predisposition for blood clots to form. One or more emboli are then at risk to easily break off, enter the circulation and block the smaller diameter arteries, most often those supplying the brain (10). Patient themselves are not always aware of the condition but may experience light headedness, may faint, feel palpitations and breathing difficulties for shorter periods of time and sometimes even experience several smaller TIAs (11). Because of this high risk of embolization, the patients that are detected and registered with AF should be started on anticoagulants. Vitamin-K antagonist oral type warfarin or newer direct oral anticoagulants (DOAC) - direct thrombin inhibitor such as Dabigatran, factor Xa inhibitor such as Rivaroxaban and Apixaban are anticoagulants used in AF for prophylactically stroke treatment.

For other stroke or TIA etiologies antiplatelets are administered. Anticoagulants and antiplatelets can potentially reduce the stroke risk by 60 and 20 % respectively (12).

To conclude, in the prevention of cerebrovascular disorders beside medical therapy (antiplatelets, anticoagulants, statins, antihypertensives, antidiabetics etc.) lifestyle changes are also especially important. Mediterranean diet, regular physical exercise, reduction of body weight, smoking cessation and moderate alcohol intake are highly recommended.

#### 1.2. Anatomy of the anterior and posterior arterial cerebral circulation

Brain is the main energy-requiring organ of the human body and is unique compromising 2% of total body weight (TBW) but still it requires as much as 50% of blood glucose (13). By this we understand that it is also one of the highest blood- perfused organs to maintain these standards. The cerebral circulation contains the anterior and posterior circulation (PC) pathways; both with

origin in the aorta. Measured by contrast MRI even 72% of the total cerebral blood flow is formed by anterior circulation (14).

#### **1.2.1.** Anterior cerebral circulation

On right side the brachiocephalic trunk gives branches to the right common carotid artery and right subclavian artery. On the left side the left carotid artery branch directly from aortic arch and branch into internal and external carotid arteries from the carotid bifurcation (16). Internal carotid artery (ICA) is responsible for the anterior cerebral circulation, while external supplies face, thyroid gland etc. Internal carotid artery enters the circle of Wills on both sides and forms the anterior circulation of the brain that consists of two middle cerebral arteries (MCA) and two anterior cerebral artery (ACA) that are connected through the anterior communicating artery. ACA is supplying the medial and superior parts of the frontal lobes and superior parietal lobes (17). Lesion/occlusion in this part of circulation will present as weakness or paralysis and sensory loss of lower extremity on opposite side of lesion. MCA is the largest of three major cerebral arteries and it supplies the lateral areas of the frontal, temporal and parietal lobes. Symptoms from lesion of this artery will be recognized as weakness or paralysis of the contralateral face and extremities; more pronounced weakness of arm, and depending on dominant side of brain aphasia or dysarthria/anarthria (15).

#### 1.2.2. Posterior cerebral circulation

The posterior circulation (PC) provides the brain with 1/3 of total blood flow that perfuses the brain, but it provides the supply for the part of nervous systems that has most delicate and life demanding functions. This circulation origins from the vertebral arteries (18). These specific arteries follow the proximal ascending branch of the subclavian arteries. The brachiocephalic trunk on the right side gives a branch for right subclavian artery while on the left side it is originated directly form the aortic arch. On both sides of the neck, vertebral arteries enter the cervical vertebral transverse process, most commonly at the level of C6, and then continue superiorly through transverse foramens (TF) until they reach the posterior part at level of C1 where they penetrate the dura mater and start their intracranial course after entering the foramen magnum (FM) at base of skull (15). Then two vertebral arteries fuse into one basilar artery (BA) and along its length it gives of several branches that supply the posterior portions of the brain. This posterior part of brain consist of the cerebellum, anterior and posterior part of the brainstem and the occipital lobes (18). Prior to this anastomosis vertebral artery gives of two branches; the posterior inferior cerebellar artery (PICA) (18) and the branch for descending anterior spinal artery (ASA) that will supply the anterior part of the spinal cord(19).

The PICA supplies the dorsolateral parts of medulla and ventral parts of cerebellum(15). The symptomatology of an occlusion or lesion in this part of the posterior circulation will result in ataxia, dizziness, nausea and vomiting, nystagmus, hoarseness, dysphagia, dysarthria, ipsilateral Horner syndrome, ipsilateral loss of temperature and pain sensation in the face and contralateral sensory loss in trunk and limbs. This is known as Wallenberg syndrome (20).

The lesions in ASA supplying territory will produce neurological symptoms known as anterior cord syndrome consisting of extremities weakness below the level of lesion as well as loss of pain and temperature and autonomic dysfunction below the lesion with preservation of vibratory sense and proprioception (21).

Further the BA will give off several, mostly bilaterally divisions along its course: the anterior inferior cerebellar arteries (AICA), pontine arteries, superior cerebellar arteries (SCA) and posterior cerebral arteries (PCA) (15). The PCA will form the posterior parts of Wills circle through posterior communicating arteries (15). The PCA origins in the pontomesencephalic junction and it gives the main vascular supply to the occipital lobe and some inferior parts of temporal and parietal lobes. A lesion in this areas will cause symptomatology corresponding to visual field problems and prosopagnosia (22). In general, the area supplied by BA is the brainstem, cerebellum and posterior cerebrum/cortex; the areas of the brain that are in charged for movements coordination, balance, vision, speech and some specific "control-centers" for sleep, consciousness, swallowing, breathing, digestion and heart rate (23).

#### 1.3. Initial treatment of stroke

In the acute setting of stroke, the goal is to stabilize the patient and do a quick complete initial assessment and evaluation followed by laboratory diagnostics and imaging studies. This is desirable to be performed as quick as possible maximally within 60 min of the patients arrival to the hospital (24). Initially after the patients are evaluated it should be determined if they are

candidates for active treatment and follow protocol for management with thrombolysis and/or thrombectomy.

There are some easily detectable measurements that should be done to exclude stroke mimics. For example, hypo or hyperglycemia can be identified upon admission to the ER. Both can in severe cases provoke neurologic symptoms and mimic an acute ischemic stroke. A solution as easy as administering glucose or insulin IV for those patients that can provide improvement and sometimes be even lifesaving and should not be missed (25).

Hyperthermia in case of stroke suspicion should be assessed by antipyretics because the increased temperature can worsen the neurological outcome and also increase the morbidity in the patient (26). The blood pressure (BP) of the patient at emergency admission should be assessed, as many patients can be severely hypertensive. From the ASA guidelines there is a caution of acute lowering the BP medically. On the other hand, if the patient is hypotensive at admission there should immediately be initiated an attempt to increase the BP pharmacologically, as this will increase the likelihood of improving the blood flow in the critically stenosed areas (26). Other measure that is also important in emergency setting is SpO<sub>2</sub> monitoring and oxygen therapy if saturation falls below 94%.

In the case of TIAs it is important to start the primary as well as secondary management, to prevent stroke. TIAs makes the risk of stroke extremely high. Within 48 hours 50% of strokes occurs after suffering a TIA and further leave the patient with 10% risk of a nearby stroke within the next 30 days after a TIA. So as one can understand the recognition in an acute setting at the admission is highly important to prevent further risk of stroke.(24)

#### 1.3.1. Thrombolysis

Thrombolysis also called thrombolytic therapy, is medically induced clot dissolving within the blood vessels. Thrombolysis in general is used for ischemic strokes, and some other thromboembolic events such as pulmonary embolisms, deep vein thrombosis and ischemic heart attacks with ST-elevations (27).

#### **1.3.2.** Indications, administration, and specific agent(s) used.

Thrombolysis is done in an emergency setting to improve the blood flow and thereby decrease the potential tissue and organ damage. In the life-threatening situation the thrombolysis

may be a good option after general stabilization of the patient and it is beneficial to reduce the major disability and even prevent death of a patient if initiated ideally within 1-3 hours from the onset of symptoms of ischemic stroke (28). The optimal use of thrombolytic therapy is within 3 hours of symptom start but there are recently lot of reports suggesting that prolonging time window for 6 hours can still be successful and improve neurological outcomes (29). The absolute indications for thrombolysis therapy are when onset of symptoms is less than 4.5 hours ago, the NIHSS score is > 4, if the blood pressure is below 185/110 mmHg and serum glucose is over 2.8 mmol/L. Additionally the MSCT (Multi-slice computed tomography) should ideally show normal or early signs of cerebral ischemia, even though the moderate ischemic changes are not a contraindication for thrombolysis (30).

There are different types of thrombolytic agents used: Streptokinase (Kabikinase), Anistreplase (Eminase) and the rtPA/Alteplase (recombinant tissue plasminogen activator). So far, the only agent approved to use in AIS is currently Alteplase. This is a serine protease that works as an enzyme that converts the plasminogen to plasmin, and causes the clot-destruction (31). The way of administration is usually intravenously (IV) in the dosage of 0.9 mg per kg of body weight; 10% of dosage is given initially as IV bolus through one minute and the rest through the one-hour infusion with maximal total dosage of 90 mg. There have been 12 large-scale high-quality trials, with 7012 patients with AIS treated with rtPA within 6 hours of onset symptoms, showing the significant benefit of treatment. The greatest outcome was among patients treated within three hours of onset. The benefits were similar in those patients above as under 80 years of age.(32)

#### 1.3.3. Side effects, absolute and relative contraindications for thrombolysis.

Thrombolysis as all other types of medical therapy can have risks and side effects. One of the most dangerous potential side effects is bleeding. The two different types of bleedings are possible, the intra- and extracranial types of bleeding. The intracranial bleeding is the term used to describe bleeding inside the skull that could be in the brain, in ventricular system, subarachnoid or subdural space. As many as 7% of patients who are treated with thrombolysis develop this specific complication (33). The review of some meta-analysis showed that an intracranial hemorrhage was the most frequent cause of early death (within 7 days) among these patients (34). Also, allergy to

the thrombolytic agents can develop. The orolingual angioedema is the most common and dangerous consequence of the allergy related to the thrombolysis.

There are some absolute contraindications, where the patient is not candidate for thrombolytic treatment and will have severe risk over benefit. The finding on image modalities characteristic for intracranial hemorrhage as well as any previous history of intracerebral hemorrhage are among these absolute contraindications. As well as an uncontrollable high blood pressure exceeding 185/110 mmHg, severe head trauma in the last seven days or previous stroke within the last 90 days upon admission. Hypoglycemia (< 2.7 mmol/L) and hyperglycemia (>22.2 mmol/L) are also contraindicated so measuring serum glucose level is important in all patients with suspected ischemic cerebral events, because especially hypoglycemia can mimic stroke as previously mentioned. Also known thrombocytopenia with platelet count lower than 100.000/mm<sup>3</sup> or coagulopathy of any source are factors that are included in absolute contraindication of thrombolysis in cerebral ischemic stroke patients. Any therapeutic dosage of heparin in last 48 hours, INR > 1.7 from warfarin therapy, any known hereditary/acquired hemorrhagic diseases, any advanced liver, kidney or heart disease are also indicators of absolute contraindications. (35).

When it comes to another group, the relative contraindications the clinician must consider it in the overall picture with the clinical situation. This division of patients based on general health conditions and so on, can be facilitated and easier determined by using these recommended guidelines. Among relative contraindications are severe neurological impairment (NIHSS >22), severe head trauma in the last 3 months, MI within last 30 days, major surgery within last 14 days or patients that have a history of SAH or ICH. Also pregnancy can be seen as relative contraindications for this therapy (36) as well as advanced age are in this group, showing that patients over 85 years of age receiving thrombolytic therapy had a double the mortality rate compared to younger population (35).

#### 1.4. Thrombectomy

Thrombectomy is an endovascular treatment (EVT) or more specifically interventional neuroradiological procedure that is performed for treatment of patients with acute stroke caused by large vessel occlusion (LVO) - most commonly M1 segment of MCA or less often by occlusion of ACI or BA. The main aim is to unblock the affected artery to avoid the permanent obstruction and further tissue damage to specific part of the brain supplied by occluded artery. The IV

thrombolytic therapy should also be initiated, if there are no contraindications in the patients that are suitable for the thrombectomy preferably within 4.5 hours of symptom start. The thrombectomy is recommended within 6 hours of the beginning of symptoms, but for the BAO satisfactory results could be achieved even if the procedure is performed within 24 hours after symptom appearance, if there are good collaterals that can provide supply for the deprived area (37).

During the procedure, a specially - designed clot removal device is inserted through a catheter – usually at the groin through the femoral artery and is guided toward the ACI or VA from where it is inserted towards to blocked artery to remove the clot either by aspiration or by specific technic of clot removal with stent retriever. The procedure is done under the radiological imaging, usually CTA to confirm the placement of stent and clot location as well as to evaluate the success of treatment.

Indications for thrombectomy following the emergency CT should be without any signs of hemorrhages or visible larger areas of stroke. This to exclude the patients that ideally would not benefit from the procedure or be even harmful for the patient. On the CTA there should be a clear visible occlusion of BAO, also location of vessel occlusion can have an impact on the inclusion criteria for thrombectomy (38).

Level of the function of patients before stroke is also an important factor. The indications for thrombectomy in the posterior circulation, preferably for this an BAO, is modified Rankin scale (mRS.)-score of 0 - 1 before the symptom onset. On the contrary the relative contraindication will be a mRS-score higher than 1, meaning that the patient before the BAO already had some physical disability.

Anyhow, the neurologist and the interventional radiologist should overweight the risk vs the benefit of thrombectomy for every specific patient. The possible periprocedural complications are bruising of the area where the catheter is inserted, vasospasm of the vessel of access, hematoma or intracerebral hemorrhage, forming of pseudoaneurysm at puncture site, distal clot embolization or arterial tearing (39).

#### 1.5. Stroke by BAO and its outcomes

BAO counts roughly for1 - 4% of all types of ischemic strokes and is still considered as a dangerous and often fatal diagnosis. This is based on the fact that it is difficult to diagnose and manage properly in the given time - frame for optimal results (40). The delayed or prodromal symptoms of BAO can be as nonspecific as headache and neck pain or vertigo and nausea (41). A more abrupt type of symptomatology in BAO is rapid onset of both bulbar and motor symptoms and decreased consciousness. The focal motor deficit can be seen as hemi or quadriplegia, speech difficulties and facial palsy(42). Generally, if the BAO is untreated, it will usually lead to a rapid deterioration seen as the reduced level of consciousness and may even lead to coma and/or death. The most typical symptoms of BAO are sudden death or loss of consciousness. Followed by somnolence, visual and oculomotor defects, speech problems, behavioral problems, and if affecting the mid or proximal portion of the BA supplying the pons specifically can result in locked in symptoms or coma. Typically motor dysfunction is absent in BA occlusions (40).

The outcomes of BAO thrombectomies are strongly corelated to the collaterals. So a good baseline collateral status or a posterior circulation collateral score (PC - CS) over 6, stroke severity prior to procedure as a NIHSS lower than 15 and proved distal BAO as well as a recanalization time maximum 6 hours after onset of symptoms have the most favorable outcome after BAO thrombectomy (43).

#### 1.6. NIHSS and mRS

The NIHSS is the national institute of health stroke scale that is used to quantify the neurological impairment. This stroke scale functions as a tool to easier asses the severity and localization of the stroke. The scale is composed of 11 items; each item is graded as a specific score of 0-4, 0-3 or 0-2, where the low score is normal function, and higher score is sign of significant functional disturbance. The items that are evaluated are level of consciousness, answering to questions and the execution of commands, horizontal eye movements, visual field tests, tests for possible facial palsy, motor function in arms and legs, sensorium, language, speech, limb ataxia and finally extinction and inattention (44). All scores are gathered to a total score, maximum score of 42 presents severe stroke symptoms while minimum of 0 means that there are no stroke symptoms.

Modified Rankin Scale - mRS is used for detecting the degree of dependence in patients daily activities (45). It is widely used in neurologic assessment and in neurologic clinical trials. Originally this scale was established in 1957, with a scale graded from 1 - 5. In the late 1980s it was modified to contain a score of 0 for the patients with no impairment in daily activity. Later in 2000s the score 6 was added to the scale system to denote death of the patient. So today in the neurological assessment scale in from of 0-6 is most used. Zero meaning no symptoms, 1 no significant symptom; the patient can carry out daily activities without any help but has some slight symptoms. 2 meaning slight disability; can assess his own affairs but some of the previous daily activities can not be done without assistance. 3 meaning moderate disability; the patients are depending on some help but can walk without any assistance. 4 means moderate disability; cannot attend his own needs and require help to walk. 5 severe disability; requires constant care and attention, usually bedridden, incontinent and disoriented and 6 meaning that the patient is dead. (45).

#### 1.7. TICI score

Treatment in cerebral ischemia score (TICI score) is used to evaluate the grade of reperfusion after endovascular procedures like thrombectomy. This score is used to assess the immediate effect of treatment and can have a strong impact on the outcome (46). The degree of reperfusion is evaluated by CTA right after thrombectomy procedure. The degree of 0 applies for no reperfusion. Degree of I mean that it has some small amount of antegrade reperfusion. In IIa reperfusion has been achieved but in less than half of the supplying territory of occluded artery and in IIb reperfusion is achieved in more than half of the initially occluded artery. In TICI score of III total reperfusion has been achieved. The grades IIb and III are categorized as successful reperfusion after a thrombectomy (47).

### **2. OBJECTIVES**

#### 2.1. Aim of study:

The main purpose of this study was the evaluation of the early outcome of patients with stroke caused by basilar artery occlusion after endovascular treatment – thrombectomy. The aim was also to determine whether there are some predictors of good outcome and to compare our results with already published data.

#### 2.2. Hypotheses:

- Thrombectomy for patients with basilar artery occlusion is safe and effective treatment.
- The earlier that procedure is performed the outcome is better.
- Previous comorbidities (cardiovascular diseases, hypertension, diabetes etc.) as well as previous medical treatment (antiplatelets, anticoagulants and statins) will have an impact on the success of thrombectomy and on the early functional improvement.

### **3. MATERIALS AND METHODS**

#### 3.1. Study design

Patients included in this study were patients with basilar artery stroke confirmed with CTA. Additionally, every patient was treated with thrombectomy. Among 253 patients with acute ischemic stroke treated with thrombectomy in the specific time-period, only 19 of them had proven BAO. Patients that had insufficient data in their medical journals were excluded. The number of excluded patients was three. Total number of patients included in study was 16.

#### **3.2.** Measurements of the outcomes of the procedure

To measure the outcome of thrombectomy success and early functional outcome of patients we used TICI-score, mRS and NIHSS. Good outcome was defined as TICI 2b and or 3, mRS  $\leq$  2 and NIHSS  $\leq$  5.

#### **3.3. Research structure**

The method used was a retrograde cohort study analysis. We revised medical records of patients treated at the neurology department of the University hospital of Split in the timeframe from January 2018 until December of 2020.

#### **3.4.** Ethical approval

The Ethical committee of the University Hospital Split approved this research (Klasa: 500-03/21-01/41; Urbroj: 2181-147/01/06/M.S.-20-02). All data and rights of patients were protected in accordance with ethical standards of Croatian laws and WMA Helsinki declaration 1964-2013.

#### 3.5. Statistical analysis

Collected data were analysed using statistical software MedCalc (MedCalc Software, Ostend, Belgium, version 17.4.1). Qualitative data were expressed as whole numbers and percentage while quantitative data were expressed as mean  $\pm$  standard deviation or mean and interquartile range. The normality of distribution was estimated using Kolmogorov-Smirnov test. Fisher's exact test was used for comparison of qualitative variables. Wilcoxon test used for paired samples The level of statistical significance was set at P < 0.05.

### 4. RESULTS

The total number of thrombectomy procedures in the Neurology department at the University hospital Split in the time window of our study, from January 2018 until December 2020, was 253 patients. Out of this specific group of patients the total number of patients with BAO was 19. Three of patients had to be excluded because of insufficient medical data. Our patients were predominantly male, by the number of 11 (68.7%) with mean age of 72.3 years (72.3  $\pm$  11.9). Regarding the comorbidities prior to cerebral ischemic event atrial fibrillation was found in only one patient, as well as cardiomyopathy and ischemic coronary event. We collected these comorbidities into one group of cardiovascular disorders. Diabetes mellitus type 2 was found in three (18.7%) and arterial hypertension in 9 patients (56.2 %).

For the prior therapy with antiplatelet, anticoagulant and statins the results were rather surprisingly low corresponding to three, zero and zero patients, respectively. So, only three (7%) of our patients was treated with antiplatelets prior to the BAO.

Blood pressure in first 24 hours were also evaluated and the mean/standard deviation was for systolic blood pressure 155.9 mmHg and for diastolic 85.6 mmHg. All these results are further described in Table 1.

Parameter	Study population
Male gender N (%)	11 (68.7)
Age (years)	$72.3 \pm 11.9$
Diabetes mellitus N (%)	3 (18.7)
Arterial hypertension N (%)	9 (56.2)
Cardiovascular diseases N (%)	3 (18.7)
Dyslipidaemia N (%)	1 (6.2)
Prior antiplatelet treatment N (%)	3 (18.7)
Prior anticoagulant treatment N (%)	0(0)
Prior statins treatments N (%)	0 (0)
Systolic blood pressure (mmHg) <sup>†</sup>	$155.9 \pm 27.3$
Diastolic blood pressure (mmHg) <sup>†</sup>	$85.6 \pm 14.1$
Mean NIHSS score at admission	11.0
Mean mRS score at admission	5.0

**Table 1.** Basic characteristics of study population

Data are presented as whole number (percentage) or mean  $\pm$  standard deviation.

† During the first 24 hours of hospital admission

The mean time from the onset of symptoms until the arrival to the hospital was 176 minutes with the minimum of 25 and maximum of 900 min (data for six patients were missing). The mean time from the hospital arrival till the beginning of thrombectomy was 136 minutes, the shortest time was 35 and the longest 280 min (data for one patient was missing). We joined this two times in one called stroke duration and its mean duration was  $128.5 \pm 17.6$  min. The mean time of thrombectomy duration was  $52.7 \pm 29.0$  min (data for six patients were missing).

In all our patients thrombectomy was performed by aspiration and in only one (6.25%) with the combination with stent retriever, the remaining 15 procedures (93.75%) was with mechanical aspiration only.

The number of successful thrombectomies measured in TICI scale (for TICI IIb - III) was 12 out of 16 procedures (75%). The number of complete reperfusion (TICI III) was achieved in ten patients (62.5%), and the number of patients with TICI score over IIb was two (12.5%) while unsuccessful reperfusion with a TICI lower than 2a was in four of our patients (6.25%) of these, three patients (18.75%) with TICI 0.

There was no significant impact of concomitant thrombolysis treatment on better early outcome of thrombectomy evaluated by the NIHSS and mRS. The NIHSS was evaluated as greater or smaller than five (NIHSS of 5 determining small neurological deficit and good outcome), P = 0.242 (Fishers exact test). The mRS was evaluated as greater or smaller than two P = 1.000 (Fishers exact test).

In our group no previous comorbidity could be determined as a predictor of a bad outcome, measured as mRS  $\geq$  5 at the discharge (Table 2).

	mRS<5	mRS <u>&gt;</u> 5	<b>P</b> *
Cardiovascular disease	2	1	
No cardiovascular disease	5	8	0.550
Diabetes mellitus	1	2	
No diabetes mellitus	6	7	1.000
Hypertension	4	5	
No hypertension	3	4	1.000

**Table 2:** Comorbidities as predictor of bad outcome.

\* Fisher exact test

With the remark of exceedingly small sample (only three patients) previous antiplatelet treatment did not have any impact on the thrombectomy success (TICI scale) measured with P=1.000 (Fisher exact test). Previous antiplatelets did not have any effect on the early functional outcome measured by the NIHSS, P=0.454, (Fishers exact test) as well as by mRS at the discharge P=0.489 (Fishers exact test).

The infarction size measured on control CT (categorized as none, small, medium, or large) did not show any statistical significance regarding the success of thrombectomy measured by TICI score (shown in Table 3).

Table 3: Connection of good the	rombectomy outcome	(TICI 2b+3) at	nd infarct size on CT

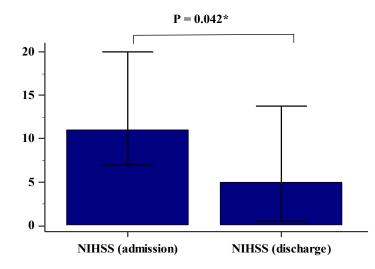
	TICI 0-IIa	TICI IIb-III	<b>P</b> *
None	0	3	
Small size	1	4	
Medium size	2	2	
Large size	1	3	0.340

\* Fisher exact test

On the control CT-scan there was no signs of complications in form of bleeding after thrombectomy procedure in any of our patients.

Median NIHSS score at admission was 11.0 (7.0 - 20.0) and the mean mRS score at admission was 5.0 (4.0 - 5.0). while median NIHSS and mRS on discharge were 5.0 (0.5 - 13.75) and 5.0 (3.5 - 6.0) respectively. For the impact of thrombectomy on early outcome we used the difference of the NIHSS and or mRS at admission and discharge. There was a statistically significant difference in NIHSS change, the NIHSS at discharge was significantly lower compared P=0.042 with NIHSS the arrival (Wilcoxon the at test) (Figure 1). There was no statistically significant difference in mRS between admission and discharge P=1.000 (Wilcoxon test).

The total number of patients that died during the hospitalization after thrombectomy procedure was 5 (31.25%). These patients were not included in analysis for the outcome of thrombectomy measured by NIHSS while they were included in those measured by the mRS.



**Figure 1:** Comparison between NIHSS at admission and at discharge (N=11<sup>†</sup>)

Data are presented as median (IQR).

\* Wilcoxon test for paired samples

† The five dead patients were not included in the analysis

### **5. DISCUSSION**

Even though the posterior circulation accounts for only 20% of the cerebral blood supply the mortality and morbidity of occlusions in this area and in BA is extremely high corresponding to approximately 85% and lowers to 40% with successful and early recanalization (4). We can logically understand, based on the significantly important structures of its supply as mentioned previously, that the mortality and morbidity can be this high (4). There are numerous multicentric studies published about the cerebral ischemic strokes in the anterior cerebral circulation considering their treatment modalities and options and their outcomes. Examples of this are studies like: "REVASCAT" Jovin *et al.* (48), "ESCAPE" Goyal *et al.*(49) and "EXTEND" Campbell *et al.*(50)

For the posterior circulation and ischemic strokes caused by BAO the number of multicentric studies is extremely low and most of the data and the recommendations for treatment are collected from single centre study.

The purpose of our study was to evaluate the early outcome of the thrombectomy treatment in patients with BAO. We also wanted to determine whether there are some predictors of good and results with published bad outcomes and compare already data. to our Out of the total number of 253 thrombectomy procedures in the timeframe analysed only the small number of patients (19 of them) underwent the thrombectomy because of a BAO. Because of a missing data we could include only 16 of them in our study. This low sample size affected our results, so that any statistical analysis had extremely low power and some analysis included only few patients so that they were pointless.

The predominant gender in our study was male (68.7%), with mean age of 72.3. Our data are in concordance with the study of Kang *et al.* (51).in which the majority was also male gender (56.6%) with the mean age of 71 years. As for the Gory *et al.* (52) the majority of patients was also males (61%) and the mean age was 65. The median NIHSS score at admission in our study was 11.0 that is comparable with the study of Kang *et al* (51) where the NIHSS was 17 and as well as in the study of Gory *et al.*(52) where the median score at admission was 16.

Among our patients. for 75% of them we achieved successful reperfusion (TICI IIb-III) after the thrombectomy. In comparison to the other studies the successful reperfusion after thrombectomy was 91.3 % in study of Dong-Hun Kang *et al.* (51) and 79% in the study of Gory

*et al.* (52). We can say that though the rate of successful reperfusion in our study is very high in the comparison with some other studies we still have the room for improvement.

The reason for little lower percentage of thrombectomy success could be in the long time of stroke duration (time from the start of symptoms till the beginning of the thrombectomy). Stroke duration time in our study was  $128.5 \pm 17.6$  min. Though when compared to Kang *et al.* study (51) where the mean duration was  $165.5\pm357$  min or to the study of Gory *et al.* (52) where the stroke duration was  $225\pm382$  min our stroke time is not so long. Regarding the thrombectomy duration itself our results are a bit worse than those previously published – our mean duration was  $52.7 \pm 29.0$  min while in the study of Kang *et al.* (51)it was  $25\pm69.75$  min.

The early outcome for our patients was quite well; the NIHSS was significantly lowered at discharge than it was at the admission. At admission it was 11.0 and was lowered to 5.0 at discharge. In the study of Kang *et al.* (51) and Gory *et al.* (52) the mean NIHSS at admission was 17 and 16 respectively, and they did not evaluate the NIHSS at discharge because they were focused on the mRS status 90 days after the procedure, compared with the immediate reperfusion status after thrombectomy.

The mRS scale is more used to evaluate the handicap or functional independence of the patient with BAO (45) In our study we did not find any statistical difference between mRS scores at the admission and discharge. Possible explanation is the short time that we used for the evaluation, and it is expected for our patient to get better according the mRS after the neurorehabilitation especially because their early neurological recovery according to the NIHSS was already significantly better.

A weakness of this study is that it was a retrospective one, the number of patients is very low, and it was done in only one centre. Despite that, the value of this study that it is pointing out the importance of recognizing patients with BAO as well as the importance of performing the thrombectomy for these patients. Also, it is exposing the weaknesses in our daily work (long stroke time duration before the beginning of the procedure and need for medical records with more detailed information and data) that could be done better to provide even more successful care for our patients.

## 6. CONCLUSIONS

From our study we can conclude:

- Endovascular thrombectomy is effective and safe for treating patients with acute BAO.
- Thrombectomy for BAO can be performed with high reperfusion rate.
- Previous comorbidities and medical treatment did not affect the thrombectomy outcome.

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### 8. SUMMARY

#### **Objective:**

The main purpose of this study was to evaluate the early outcome of patients with stroke caused by basilar artery occlusion after endovascular treatment – thrombectomy. The aim was also to determine whether there are some predictors of good outcome and to compare our results with already published data.

#### Materials and methods:

We included 16 patients with proven BAO treated with thrombectomy from the Department of Neurology in University Hospital Split in the timeframe from January 2018 until December 2020. To measure the outcome of thrombectomy success and early functional outcome of patients we used TICI-score, mRS and NIHSS. This was retrospective cohort study. We revised medical records of included patients. Collected data were analyzed using statistical software MedCalc (MedCalc Software, Ostend, Belgium, version 17.4.1)

#### **Results:**

Most of our patients were male (68.7 %) with the mean age of 72.3 years. The rate of successful reperfusions (TICI IIb-III) was 75%. We did not notice any serious side effects of treatment. No comorbidities or previous medical treatment did affect the thrombectomy outcome. The early outcome – reduction of NIHSS on the discharge was significantly lower than on the admission 5.0 (0.5 - 13.75) vs 11.0 (7.0 - 20.0) respectively, P = 0.042 (Wilcoxon test).

#### **Conclusion:**

The thrombectomy is a safe and effective treatment modality for BAO. The neurological status of patients on the discharge is significantly better than on the admission.

# 9. CROATIAN SUMMARY

#### Naslov:

Rani ishod trombektomije kod bolesnika s moždanim udarom uzrokovanim okluzijom bazilarne arterije.

#### Ciljevi:

Glavni cilj studije bio je procijeniti rani ishod endovaskularnog liječenja – trombektomije kod bolesnika s okluzijom bazilarne arterije. Cilj je bio i pronaći prediktore dobrog ishoda te usporediti naše rezultate s rezultatima u već objavljenim studijama.

#### Materijali i metode:

U studiju je uključeno 16 bolesnika s dokazanom okluzijom bazilarne arterije koji su liječeni trombektomijom u Klinici za neurologiju KBC Split u razdoblju od siječnja 2018.g. do prosinca 2020.g. Za procjenu uspješnosti trombektomije korištena je TICI ljestvica a za procjenu ranog funkcionalnog oporavka mRS i NIHSS. Studija je bila retrospektivna kohortna. Podaci su prikupljeni iz medicinske dokumentacije i obrađeni uz pomoć statističkog softvera MedCalc (MedCalc Software, Ostend, Belgium, verzija 17.4.1).

#### **Rezultati:**

Većina naših pacijenta su bili muškarci (68.7 %), prosječne dobi od 72.3 godine. Trombektomija je bila uspješna (TICI IIb-III) kod 75% pacijenata. Nismo zabilježili nikakve ozbiljnije nuspojave vezane uz zahvat. Nikakvi komorbiditeti niti prethodna medikamentozna terapija nisu utjecali na ishod zahvata. Rani ishod – NIHSS pri otpustu u odnosu na prijem bio je značajno niži (5.0 (0.5 - 13.75) naspram 11.0 (7.0 - 20.0), P = 0.042 (Wilcoxon test).

#### Zaključci:

Trombektomija je sigurna i učinkovita terapijska metoda za liječenje moždanog udara uzrokovanog okluzijom bazilarne arterije. Neurološki status bolesnika pri otpustu je značajno bolji nego pri prijemu.

# **10. CURRICULUM VITAE**

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