**UNIVERSITY OF SPLIT**

**SCHOOL OF MEDICINE**

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# IMPACT OF THE COVID-19 PANDEMIC ON THE TIME-TO-PICTURE AND THE PICTURE-TO-PUNCTURE TIME IN ACUTE STROKE PATIENTS IN A RURAL REGION: A RESTROPSECTIVE COHORT STUDY

**Diploma Thesis**

**Academic year:**
**2023/2024**

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**Split, July 2024**

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***ACKNOWLEDGEMENT***

Firstly, I would like to extend my gratitude to my mentor Dr. Zühlke, for granting me the opportunity to work on my thesis under his guidance. Our collaboration has been a pleasure, and I have appreciated his support throughout. Secondly, I want to give special thanks to Shadi, whose support was essential in completing this work. Lastly, I also want to acknowledge the help of AI technology, which greatly assisted in writing and formatting this thesis.

Furthermore, I want to thank the University of Split School of Medicine and Medical School REGIOMED for paving the way for me to pursue my academic aspirations and realize my dream of becoming a doctor. A special thanks to Prof. Dr. Brachman, who always had an open ear for his students.

Lastly, I want to express my gratitude to my friends and family who supported me throughout my entire medical studies. During times of stress, anger, and resignation, they continually motivated me. A special thanks goes to my parents, aunt, and uncle, who made the entire study journey possible, and to my twin sister Emily, without whom I could not have accomplished all of this.

## List of Abbreviations

| | | |
|---|---|---|
| AIS | - | Acute ischemic stroke |
| TIA | - | Transient ischemic attack |
| ACA | - | Anterior cerebral artery |
| PCA | - | posterior cerebral artery |
| IV t-PA | - | Intravenous thrombolysis |
| MT | - | Mechanical Thrombectomy |
| SARS CoV-2 | - | Severe Acute Respiratory Syndrome Coronavirus Type 2 |
| COVID-19 | - | Coronavirus Disease 2019 |
| LVO | - | Large vessel occlusion |
| LoE1 | - | Level of Evidence, grade 1 |
| LoE2 | - | Level of Evidence, grade 2 |
| PSC | - | Primary stroke centers |
| CSC | - | Comprehensive stroke centers |
| STENO | - | Stroke Network with Telemedicine in Northers Bavaria |
| FSH | - | Framingham Heart Study |
| ER | - | Emergency Room |
| HCP | - | Healthcare professionals |
| CT | - | Computed tomography |
| CTA | - | CT Angiography |
| MRI | - | Magnetic Resonance Imaging |
| ESMIN | - | European Society of Minimal Invasive Neurology |
| AF | - | Atrial fibrillation |
| LDL | - | Low density lipoprotein |
| DM | - | Diabetes Mellitus |
| NIH | - | National Institute of Health |
| RKI | - | Robert Koch Institut |
| PPE | - | Personal protective equipment |
| FFP | - | Filtering Facepieces |
| Q-Q-Plot | - | Quantile - Quantile Plot |
| PreCP | - | Pre COVID-19 group |

| | | |
|---|---|---|
| DurCP | - | During COVID-19 group |
| PTP | - | picture-to-puncture |
| DTP | - | door-to-picture |
| SE | - | Standard error |
| IQR | - | Interquartile range |
| min | - | minutes |
| e.g. | - | example |

# 1. INTRODUCTION

## 1.1. Acute Ischemic Stroke (AIS)

### 1.1.1. Definition of AIS

A stroke, also known as a cerebrovascular incident, is a medical emergency that occurs when blood flow to the brain is interrupted or severely reduced causing neuronal damage. Despite the World Health Organization (WHO) defining an acute stroke as "rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin" (1), advancements in science, neuroimaging, and comprehension have outdated classic definitions. Consequently, a consistent definition in clinical practice remains elusive. A stroke can be classified into hemorrhagic, subarachnoid, and ischemic, with ischemic strokes being the most prevalent type (2,3). This thesis will focus on ischemic stroke. The International Classification of Disease (ICD) defines cerebral ischemic strokes as “an acute focal neurological dysfunction caused by focal infarction at single or multiple sites of the brain or retina. Evidence of acute infarction may come either from a) symptom duration lasting more than 24 hours, b) neuroimaging or other technique in the clinically relevant area of the brain” (4). When blood flow is obstructed, the affected region of the brain (or retina) is deprived of oxygen and nutrients, leading to sudden damage and dysfunction in that area. It is crucial to highlight that this damage persists for more than 24 hours, distinguishing an AIS from a transient ischemic attack (TIA), which normally does not result in long-term brain damage (5).

### 1.1.2. Brain vascular anatomy

The vascular supply of the brain (Figure 1) is essential in maintaining its metabolic needs and overall function. It is therefore not surprising that brain receives its blood supply from a complex network of blood vessels, giving rise to both the anterior and posterior circulation systems that supply it with blood. From the paired internal carotid artery arising from the common carotid artery, the main blood vessels of the anterior circulation arise: the anterior cerebral artery (ACA) and the larger middle cerebral artery (MCA), with the ACA consisting of five segments (A1-A5) and the MCA consisting of five main segments (M1M5) (6). The anterior circulation is vital for supplying blood to the frontal, parietal, temporal lobes, and anterior part of the deep cerebral hemispheres. Of particular importance is the MCA, which supplies blood to crucial deep brain structures such as the basal ganglia and internal capsule, where voluntary movement is regulated, and motor and sensory fibers are located (6,7).

The posterior circulation of the brain is established through the formation of the basilar artery, which originates from the merging of the right and left vertebral arteries. The basilar artery further subdivides into branches, notably the posterior cerebral arteries (PCA). These arteries play a crucial role in supplying blood to the posterior regions of the brain, including the occipital lobes, brainstem, cerebellum, and posterior part of the deep cerebral hemisphere (6,7). The anterior and posterior circulation are interconnected by the circle of Willis, a cerebral arterial circle. This structure plays a vital role in maintaining continuous blood flow to the brain, even in situations where blood flow through the internal carotid artery, vertebral arteries, or basilar artery is compromised (6).

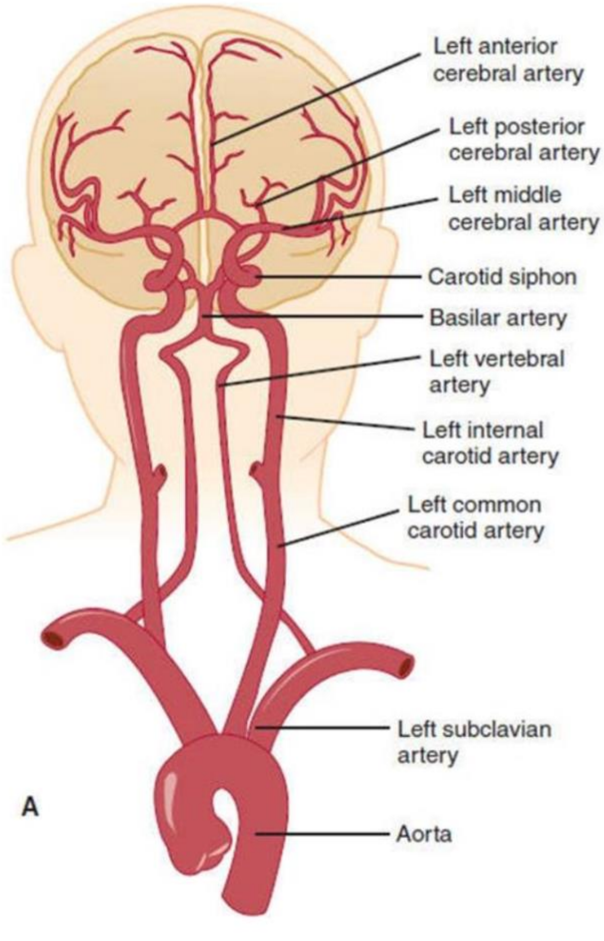



**Figure 1.** Major cerebral arteries

Source: Shakkotai V, Lomen-Hoerth C. Nervous system disorders. In: Hammer G, McPhee S, editors. Pathophysiology of disease: An introduction to clinical medicine. 8th ed. China: McGraw-Hill Education;2019.p.207

Depending on which arteries are affected in an AIS, specific symptoms manifest. Figure 2 illustrates the regions prone to arteriosclerosis (dark read) within intracranial vessels, highlighting the sites most frequently impacted by occlusion. Among the most affected vessels is the MCA (7), along with its lenticulostriate branches, which provide blood to the basal ganglia and internal capsule. In cases where stroke occurs due to blockage in these arteries, hallmark symptoms such as paralysis and sensory loss in the contralateral leg or foot may manifest (7).

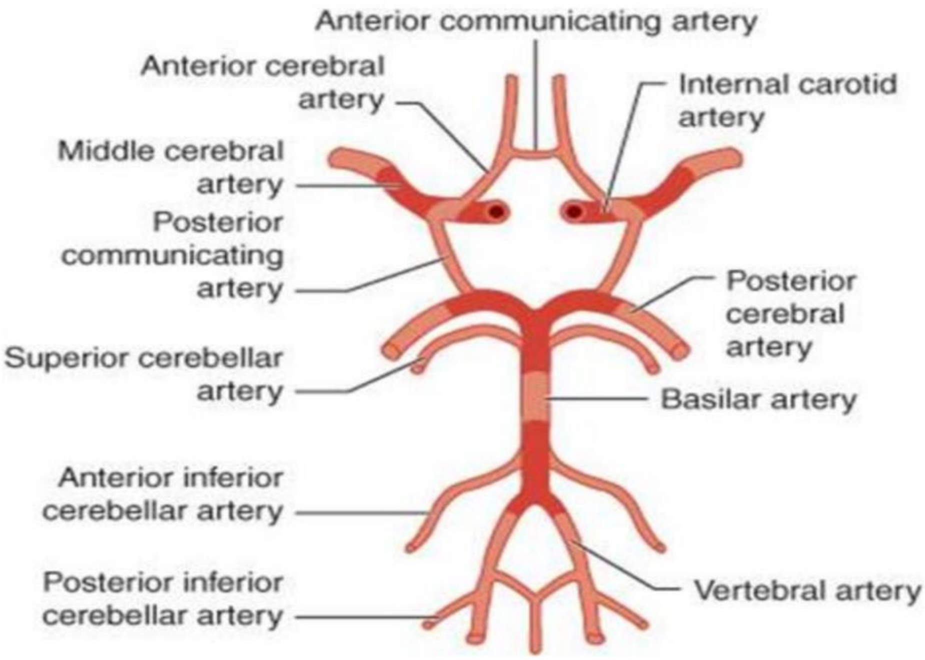



**Figure 2**. Sites of predilection for arteriosclerosis in the intracranial anterior circulation
Source: Shakkotai V, Lomen-Hoerth C. Nervous system disorders. In: Hammer G, McPhee S, editors. Pathophysiology of disease: An introduction to clinical medicine. 8th ed. China: McGraw-Hill Education;2019. p.209

### 1.1.3. Pathophysiology

In an acute ischemic stroke, a blood vessel that supplies the brain region becomes obstructed. This blockage can occur due to either a thrombus, which is a blood clot formed directly within the blood vessel, or an embolus, which is a clot that originates elsewhere in the circulatory system, often from the heart, aortic arch, or carotid arteries. Thrombosis typically affects arteries such as the internal carotid, middle cerebral or basilar arteries, while emboli commonly block MCA (7). Several vascular disorders are associated with a thrombotic or embolic occlusion of cerebral vessels (Figure 3), with the most common and most studied being arteriosclerosis. It all starts with damage to the inner lining of an artery (endothelium) that can occur from multiple sources, including mechanical stress, inflammation, or biochemical factors.

This injury triggers a response where monocytes and lymphocytes attach to the damaged area and move into the artery wall. This process stimulates the growth of smooth muscle cells and fibroblasts, leading to the formation of fibrous plaques. Over time, these plaques can narrow and harden the artery, potentially leading to complete blockage (thrombus) or rupture of the plaque (embolus) (7-9).

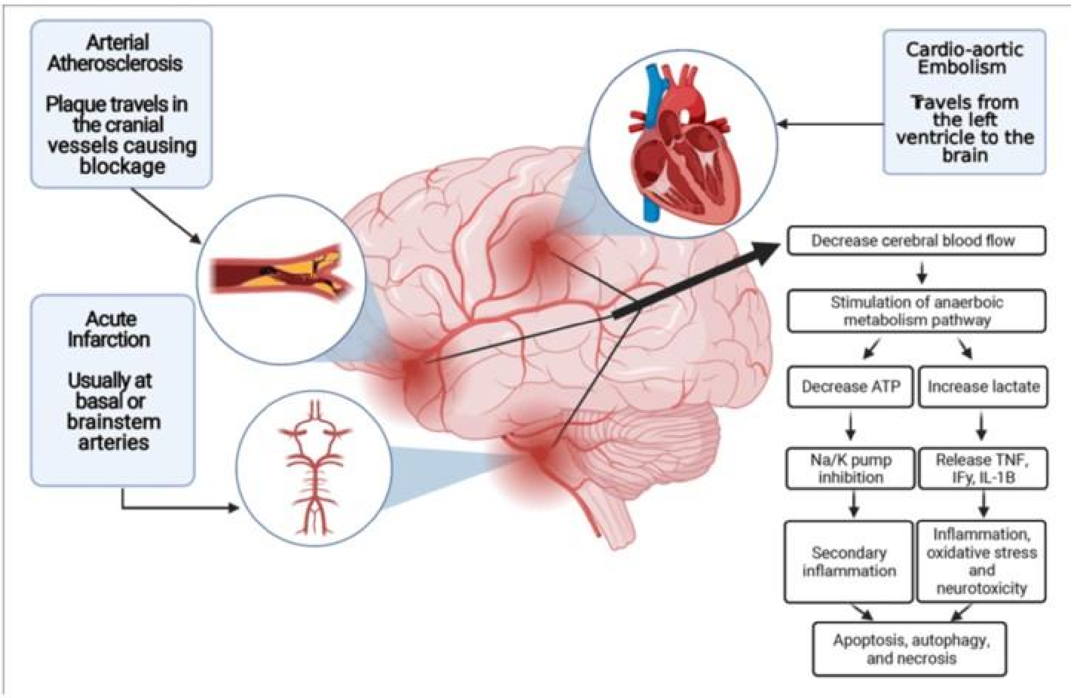
| **Vascular Disorders** |
|---|
| Atheriosclerosis |
| Fibromuscular dysplasia |
| Vasculitis |
| Systemic (polyarteritis nodosa, lupus, giant cell arteritis, granulomatosis with polyangiitis (formerly Wegner granulomatosis), Takayasu arteritis) |
| Primary CNS |
| Meningitis (syphilis, tuberculosis, fungal, bacterial, herpes zoster) |
| Drug induced (cocaine, amphetamine) |
| Carotid or vertebral artery dissection |
| Lacunar infarction |
| Migraine |
| Multiple progressive intracranial occlusion (moyamoya syndrome) |
| Venous sinus thrombosis |
| **Cardiac Disorders** |
| Mural thrombus |
| Rheumatic heart disease |
| Arrhythmias Endocarditis |
| Mitral valve prolapse |
| Paradoxical embolus |
| Atrial myoma |
| Prosthetic heart valves |
| **Hematologic Disorders** |
| Thrombocytosis |
| Polycythemia |
| Sickle cell disease |
| Leukocytosis |
| Hypercoagulable states (homocysteinemia, protein S deficiency, antiphospholipid syndrome, sickle cell disease) |

**Figure 3**. Conditions associated with focal cerebral ischemia

Source: Shakkotai V, Lomen-Hoerth C. Nervous system disorders. In: Hammer G, McPhee S, editors. Pathophysiology of disease: An introduction to clinical medicine. 8th ed. China: McGraw-Hill Education;2019. p.209

Regardless of the etiology of the embolic or thrombotic event causing the obstruction of the blood vessel, various pathologic mechanisms occur, leading to neuronal and thus brain damage. The most extensively studied pathological mechanism involves the activation of anaerobic metabolism, resulting from insufficient blood flow (Figure 4). Normally, brain tissue receives 60-70ml of blood flow per 100g of brain tissue per minute; in case of a decrease in blood flow of only 25ml per 100g per minute, it cannot sustain aerobic metabolism(10), leading to diminished oxygen and glucose supply. With the diminished oxygen supply cells resort to anaerobic metabolism, a less efficient pathway resulting in decreased adenosine triphosphate (ATP) synthesis and accumulation of lactate as a byproduct of anaerobic metabolism. Lactate provokes the release of inflammatory cytokines, such as Tumor Necrosis Factor (TNF) and Interleukin-1 (IL-1), exacerbating the cellular stress response. Cytokines such as TNF-α, IL-1, and IL-6 play crucial roles in amplifying and intensifying inflammatory responses. They achieve this by activating immune cells, facilitating the recruitment of leukocytes to inflammatory sites, and fostering the production of additional proinflammatory cytokines and chemokines. Furthermore, the proinflammatory cytokines, especially TNF-α (11), stimulate different cell death mechanisms by activating different signaling pathways leading to necrosis, apoptosis, or autophagy (12-14). This cascade of events contributes to neuronal damage and worsens ischemic injury. The depletion of ATP disrupts the function of crucial cellular mechanisms, notably the sodium- potassium pump, which is essential for cellular homeostasis. Consequently, cellular dysfunction ensues (13,15).

The depletion of energy further amplifies neuronal excitotoxicity (9,13,15). The disruption of cellular homeostasis triggers an excessive release of glutamate, which, via its NMDA receptors, induces an influx of calcium ions. This heightened intracellular calcium concentration initiates a cascade of diverse mechanisms ultimately culminating in neuronal demise. Elevated calcium levels activate various enzymes, resulting in the breakdown of cellular structures (15), while also inducing mitochondrial dysfunction, exacerbating ATP depletion, and the release of reactive oxygen species (ROS). This cascade of events amplifies oxidative stress, worsening cellular injury and ultimately leading to neuronal death (9,13,15,16).




| Blood supply disruption and ischemic stroke pathogenesis. ATP indicates adenosine triphosphatase; IFγ, Interferon gamma; IL-1B, interleukin 1B; K, potassium; Na, sodium; TNFα, tumor necrosis factor α.

**Figure 4**. Blood supply disruption and ischemic stroke pathogenesis https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2022.870141/full

### 1.1.4. Epidemiology

Stroke is a significant global health concern, being the second leading cause of death in the world and the third leading cause of death and disability combined (17,18). According to the 2022 Global Stoke Factsheet, there are over 12.2 million new strokes each year globally, and 6 ½ million people die from stroke annually. The likelihood of experiencing a stroke in one's lifetime has increased by 50% in the past 17 years, estimating that one out of every four individuals may face a stroke at some point in their lifetime. Although stroke predominantly affects the elderly, it is noteworthy that 62% of all strokes occur in people under the age of 70, with 16% occurring in young adults aged between 15 and 49 years old (18). According to German studies, stroke also continues to rank as the second most common cause of mortality following coronary heart disease (19). The Burden of Stroke in Europe Report states 88,922 new strokes per year in Germany, with a lifetime prevalence among individuals aged 40-79 years of 2.9% (19,20).

### 1.1.5. Risk factors

Although the causes of suffering from an acute ischemic stroke are variable there are studied non-modifiable and modifiable risk factors, contributing to the development of strokes. Non-modifiable risk, marking the higher risk for the occurrence of stroke factors (21), includes higher age, male sex, and African ancestry as well as genetic factors. With advancing age, the likelihood of experiencing a stroke becomes more prominent, with incidence increasing significantly. More specifically, the risk doubles for each decade after reaching the age of 55 (3,21). With higher age, various physiological and vascular changes appear. Conditions like hypertension, diabetes mellitus (DM), hyperlipidemia occur more frequently in the elderly. This emphasizes the importance of modifiable risk factors, which account for 90% of all stroke burden (2). An international, multicenter case control study (INTERSTROKE) in 32 countries identified potential modifiable risk factors, which represent 90% of the stroke risk (91.5% of ischemic stroke, 87.1% of intracerebral hemorrhage) (22). The risk factors include hypertension, current smoking, waist-to-hip ratio, diet, physical inactivity, hyperlipidemia, diabetes, alcohol consumption, cardiac causes, psychosocial stress, and depression. (2, 4). Hypertension marks the most important modifiable risk factor in the physiology of stroke occurrence. The continuous damage to the endothelium and the accumulation of fat and cholesterol at these damaged sites lead to the formation of atherosclerotic plaques. This process, along with turbulent blood flow, elevates the likelihood of blood clot formation and damage to small blood vessels in the brain. These events result in reduced blood flow and oxygen levels - crucial in increasing the occurrence of ischemic strokes (8,23).

When examining DM, it is of no surprise that individuals with this condition carry an elevated risk of experiencing an ischemic stroke. The Framingham Heart Study (FHS), a cohort study examining DM type II patients over 20 years, revealed that diabetic patients had a 2.5–3.5 times higher incidence of ischemic stroke compared to the control group (24). Distinct metabolic pathways (Figure 5) are activated because of prolonged elevation in glucose levels, heightened presence of free fatty acids in the bloodstream, and increased resistance to insulin. These pathways culminate in significant dysfunction and damage to the endothelial cells, resulting in vascular impairment and a heightened likelihood of ischemic stroke (25).

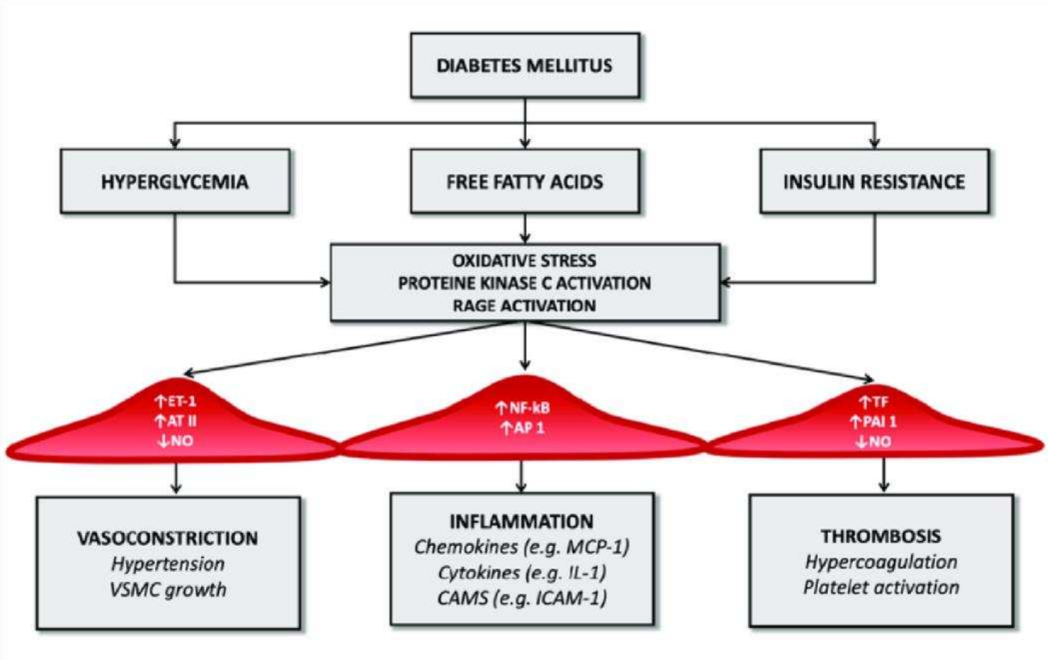



**Figure 5**. Diabetes mechanism of vascular damage

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8877605/figure/ijms-23-02397-f001/

Various cardiac conditions are linked to an increased risk of ischemic stroke. The FHS, analyzing 5,070 participants after 34 years follow-up, showed that there is a twofold increase in the occurrence of stroke with coronary heart disease, more than a threefold increase with hypertension, a fourfold increase with chronic heart failure, and almost a fivefold increase in the presence of atrial fibrillation (AF) (26). AF poses a heightened risk of stroke, especially among the elderly, making them particularly susceptible to such cerebrovascular events.

Although studies on abnormalities in serum lipid levels associated with ischemic stroke are limited and controversial (27), there is a linkage between higher total cholesterol and triglyceride levels in the blood and ischemic stroke occurrence (28,29). Specifically, oxidized cholesterol, Low-Density Lipoprotein (LDL) in particular, initiates inflammation and gives rise to the formation of plaque on the walls of blood vessels, that, just as hypertension and diabetes mellitus, predisposes to impeding blood flow and atherothrombotic events. (29,30)

Engaging in lifestyle factors such as a diet rich in saturated fats and cholesterol, regular alcohol consumption, smoking, lack of physical activity, and obesity raise the likelihood of experiencing an ischemic stroke (31). These behaviors collectively contribute to the emergence of risk factors like hypertension, atherosclerosis, and diabetes, substantially elevating the overall risk of AIS.

As stated above, many risk factors increase the danger of experiencing a stroke. According to the WHO high blood pressure and tobacco smoking are the most significant modifiable risk factors. Intervention in these risk factors can substantially lower the incidence of stroke (32).

### 1.1.6. Diagnosis

A fast and accurate diagnosis of AIS significantly influences patient outcome. Even before reaching the emergency room (ER), ideally within an acute stroke center, individuals experiencing specific symptoms indicative of AIS are in urgent need of intervention. It is therefore imperative that not only healthcare professionals (HCP) but also the public are prepared to recognize stroke symptoms promptly. The "FAST" acronym, a widely employed neurological screening tool, underscores the importance of recognizing **F**acial drooping, **A**rm weakness, **S**peech difficulty, and **T**ime urgency (4, 33, 34). The cornerstone of the diagnostic process is immediately recognizing the hallmark symptoms. In addition to a detailed medical history and physical examination, HCP employ stroke scales such as the National Institutes of Health (NIH) Stroke Scale to assess symptom severity and to initiate appropriate treatment. Also, guidelines emphasize immediate brain imaging with computed tomography (CT), CT angiography (CTA) or magnetic resonance imaging (MRI) to be conducted in all suspected stroke cases (34). This ensures timely intervention and improves the chances of positive outcomes for stroke patients, while also enabling a differentiation between hemorrhagic and ischemic strokes.

### 1.1.7. Treatment options

"Time is brain" is a critical concept in the treatment of ischemic stroke. For every minute the brain is deprived of oxygen and nutrients in an acute ischemic stroke, 1.9 million neurons are lost (35) causing permanent brain damage. This makes a rapid reperfusion treatment inevitable. Various reperfusion treatment options have been established, allowing the removal of the clot and hence a restoration of blood flow. The most common treatment for AIS is intravenous thrombolysis (IV t-PA) and Mechanical thrombectomy (MT) (36). Intravenous thrombolysis involves the introduction of a tissue plasminogen activator (t-PA), typically alteplase, directly into the bloodstream, usually within 4.5h of symptom onset. The plasminogen activator activates the natural enzyme plasmin, which in turn breaks down the fibrin that constitutes the blood clot, leading to dissolution. Another method is the MT, an endovascular treatment involving a specialized catheter removing the blood clot mechanically.

Frequently, “bridging therapy” is employed, where a combination of MT and IV t-PA is used. The administration of IV t-PA initiates clot dissolution, and the MT physically removes the clot (35,36). For both strategies an organized and efficient acute stroke care is essential, with key elements comprising education of patients on stroke symptoms, ensuring prompt access to ambulance services, transportation to specialized stroke centers, and conducting brain imaging to rule out hemorrhage prior to treatment. Stroke units in hospitals provide a multidisciplinary team of specialized HCP’s and advanced medical equipment to provide immediate and intensive care for individuals who have suffered a stroke.

## 1.2. Mechanical thrombectomy

### 1.2.1. Technique

For years intravenous thrombolysis was standard and the approved treatment for AIS patients. Nevertheless, the disadvantages of this intervention, like its risk of bleeding, its narrow time window, and the inefficacy in large or extensive blood clots, allowed endovascular therapy with MT to emerge. In 2015, five randomized trials (MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND IA) showed efficacy of endovascular thrombectomy with MT (37). Consequently, the latest guidelines for HCPs from the American Heart Association (AHA) and American Stroke Association (ASA) states endovascular treatment of an AIS as standard (38). As mentioned above, MT is a type of endovascular intervention in stroke patients that, under angiographical control, removes a blood clot occluding a cerebral artery. Over time, various techniques and procedures have been developed to facilitate reperfusion: aspiration devices, suction thrombectomy devices, that remove the occlusive clot via vacuum aspiration, coil retrievers (first generation MT devices), removing the clot by deploying a flexible coil through a catheter, which expands to create a mesh-like structure entangling and trapping the clot and allowing its removal. Lastly, stent retrievers (second generation MT devices) that also work by being inserted into the blood clot through a catheter, where it self-expands and engaged the clot, allowing for its retrieval and restoration of blood flow (39). In all methods, the primary objective is to clear the obstructed artery, enabling the restoration of blood flow to the vessel and thereby preserving the ischemic penumbra.

### 1.2.2. Indication

In general, endovascular intervention is recommended for individuals with AIS resulting from a large vessel occlusion (LVO), indicating a blockage in the internal carotid artery, middle cerebral artery, vertebral, or basilar artery. The national guidelines of the German Society of Neurology (DGN) 2022 provided a clear recommendation for conducting an MT in stroke patients (34): it is indicated for "patients with acute ischemic stroke, clinically relevant neurological deficit and occlusion of a large artery in the anterior circulation, if possible, within 6 hours (time between symptom onset and groin puncture)" (LoE1), especially in patients with an occlusion in the artery carotis interna and/or in the middle cerebral artery trunk (M1 segment). An MT is also indicated if one or more M2 Segments are occluded (LoE2), as well as in patients with an occlusion in a vertebrobasilar artery (LoE2). The guidelines stress the importance of a time window of 6h after symptom onset to perform an MT, emphasizing the earlier the attempt of revascularization, the better the clinical outcome (LoE1). If patients with an occlusion in the anterior circulation are beyond the 6h time window, an MT should be considered and performed if, through advanced imaging (e.g. visualization of small infarct core, mismatch, collateral assessment) and compatible clinical symptoms, salvageable tissue is seen (LoE1) (34).

### 1.2.3. Procedure

As previously emphasized, prompt intervention is imperative for patients with LVO. Consequently, stroke patients must rapidly be admitted to qualified stroke centers equipped to perform MT. While Germany has enhanced the care of stroke patients through the establishment of primary stroke centers (PSC), advanced therapeutic interventions like IV t-PA or mechanical thrombectomy cannot be conducted in the PSC (40). Comprehensive stroke centers (CSC), which provide for the technical infrastructure and interventional neuroradiologists, are needed, yet rare in Germanies' rural regions. Strategies had to be developed to facilitate access to interventions like IV t-PA and MT. Telemedical stroke networks were established, that ensure uniform stroke treatment for all patients (41). The REGIOMED hospitals in Coburg, Lichtenfels and Sonneberg are all part of the Stroke Network with Telemedicine in Northern Bavaria (STENO) (42) allowing for the best medical stroke treatment in their area. Regional clinics connected through this network can consult with specialized neurologists, assessing the patient online and determining the appropriate therapy for this patient. Depending on the therapy needed and on the patient's condition a decision of a continued treatment in the local clinic or of a transfer to one of the specialized stroke clinics can be taken (42).

In the context of conducting MT for stroke patients three approaches are utilized to ensure timely care: “mothership”, where the patient is directly transported to the CSC, “Drip and ship”, relocating the patient to a CSC after initial assessment, and “Drip and Drive”, bringing an interventional neuroradiologist to the PSC to conduct the MT procedure (41, 43). In the hospitals of REGIOMED at Lichtenfels, Coburg and Sonneberg, all three locations serve as regional stroke units equipped for performing an MT, utilizing the “drip and drive approach”: after the patient is admitted to the ER, urgent vascular imaging is done with a CT and CTA, so as to confirm the indication for the conduction of an IV t -PA and/or MT. The patient then typically remains at the admitting hospital where initial preparations for the endovascular treatment is conducted. This involves positioning the patient preparing for angiography, establishing catheter access most commonly through the artery femoralis puncture, and, if feasible, advancing the catheter into the aorta or carotid artery. Meanwhile, the interventional neuroradiologists travels to the admitting hospital, on-sight ideally focusing exclusively on the aspiration or retriever thrombectomy procedure (44,45).

### 1.2.4. Complications

As MT being an invasive therapeutic procedure, it is associated with numerous complications occurring before, during or after the intervention. The interventional neuroradiologist may encounter challenges in accessing the clot, leading to a prolonged procedure and to an elevated risk of complications, resulting in poorer clinical outcomes. Additional periprocedural complications include bruising at the puncture site and the potential occurrence of vasospasm in the accessed vessel, making it more challenging to reach distal lesions or increasing the likelihood of early reocclusion (46,47). Moreover, severe complications such as iatrogenic arterial dissections, intracerebral hemorrhage due to vessel perforation, intracerebral hematoma, or the initiation of new emboli in previously unaffected territories or further downstream in the affected vessel, may also arise (47). These complications should not be neglected, and both the neurologist and interventional neuroradiologist need to thoroughly evaluate the risk-to-benefit ratio of thrombectomy for each patient.

### 1.2.5. Outcome

Despite being a more invasive procedure compared to other stroke management techniques, endovascular thrombectomy has become indispensable in stroke care. Numerous trials indicate that this method, especially in patients with LVO, outperform conventional stroke management or intravenous thrombolysis. The European Society of Minimally Invasive Neurology Therapy (ESMINT) unequivocally illustrates the advantage of employing endovascular thrombectomy in patients with LVO within 6h of symptom onset, as opposed to relying solely on medical therapy (45, 48). Additionally, with the emerging of advanced stent retrievers such as Solitaire, TREVO and Revive, which exhibit significantly improved recanalization rates compared to earlier versions, endovascular thrombectomy has evolved into a standard procedure in the treatment of stroke (38,45). In fact, next generation retrievers Embotrap III or Tiger triver might show a better performance, indicating a recanalization rate of more than 60% of the affected territory is raised by more than 80%.

## 1.3. Covid pandemic

### 1.3.1. Influence on health care system

1n December 2019, the world encountered one of its most serious challenges to date. Originating in Wuhan, China, the respiratory, highly contagious SARS CoV-2 virus began its gradual spread around the world, with the first case recorded in Germany on January 27, 2020 (49). The situation rapidly evolved into a global COVID-19 pandemic, precipitating an unparalleled and unimaginable global health crisis. The need for care caught nations off guard, presenting challenges of an unprecedented nature. It did not take long for the situation to escalate into a global pandemic, developing into a word-wide health crisis never seen before (50,51).

The healthcare sector faced substantial challenges and underwent significant changes that demanded adaptation. In response to the nationwide crisis, Germany's Robert Koch Institute (RKI), the national Public Health Institute, introduced guidelines to ensure the proper implementation of safety measures in hospitals. This included the incorporation of personal protective equipment (PPE) such as the use of Filtering Facepieces (FFP2 or FFP3), protective aprons, and disposable gloves, alongside the introduction of numerous new protocols for disinfection. Beyond the critical emphasis on hand disinfection, there was an increased focus on the more time-consuming task of disinfecting contaminated patient surfaces, appliances, and equipment (52).

Health care services were constrained, demanding only individuals with acute, life-threatening conditions to seek the ER. Given the highly contagious nature via airborne particles and droplets of the SARS-COV-2 Coronavirus numerous hospitals faced a high number of patients needing ICU bed, ventilators, and medical staff (51). Like many other nations, Germany was grappling with a shortage of medical staff, particularly qualified nurses, even before the onset of the pandemic (53). The increase of patient numbers, coupled with heightened medical care needs and additional organizational responsibilities such as testing and isolation protocols, exacerbated the preexisting issue of staff shortage in German hospitals, challenging an adequate patient care even more.

Despite the surge in COVID-19 cases requiring intensive medical care, the hospital admission rate in German hospitals notably declined throughout the pandemic (54,55). This decline encompassed not only elective procedures, e.g. hip replacement surgeries, but also emergency admissions for critical conditions such as myocardial infarction (54). Several factors contributed to this trend, including the implementation of preventive measures that curbed the spread of illnesses, concerns over COVID-19 exposure dissuading non-urgent medical visits, hospitals prioritizing resources for COVID-19 patients, reduced incidence of accidents and injuries during lockdowns, and public awareness campaigns advocating for responsible healthcare utilization (54).

### 1.3.2. Influence on stroke care

An experienced, skilled interdisciplinary team is crucial for rapid and sufficient treatment of acute stroke patients. Patients arriving in the ED with suspicion of an AIS must be evaluated immediately, analyzing if a thrombolysis or endovascular intervention is needed. But during the COVID-19 pandemic additional measures needed to be reinforced to limit a spread of the disease (56, 57). Patients had to be screened for a COVID infection before further assessment by the stroke team, and appropriate PPE had to be used. Following the examination, thorough disinfection of the entire room and equipment had to be carried out to prevent further contamination (58-60). It appears that these extra measures could have altered the workflow in acute stroke management, potentially impacting the timely assessment, promptness treatment and hence outcome.

During the COVID-19 pandemic, a noticeable decline in hospital admissions for stroke correlated with the prevalence of SARS-CoV-2 infections (56,61). This reduction in admissions likely alleviated strain on healthcare staff and equipment, enabling providers to concentrate more on urgent treatments for conditions like AIS. Additionally, with fewer admissions, healthcare providers may have experienced reduced pressure to quickly triage and treat patients, potentially resulting in a more streamlined workflow and allowing for greater attention to each patient's needs.

# 2. OBJECTIVES

## 2.1. Aim of the study

The aim of this study is to investigate whether the COVID-19 pandemic led to a significant increase of time in the workflow of MT treatment.

## 2.2. Hypothesis

Given the additional measures taken during the COVID-19 pandemic, there is an observed extension in the workflow for acute stroke management, assessed through "door-to-picture" (DTP) and "picture-to-puncture" (PTP) prolongation time. The duration of these diagnostic and treatment processes is now longer than pre-pandemic. This could result in a less favorable outcome for acute stroke patients undergoing MT treatment.

# 3. SUBJECTS AND METHODS

### 3.1. Study design

For this retrospective cohort study 218 subjects undergoing MT in REGIOMED hospitals in Coburg, Sonneberg and Lichtenfels were analyzed before and during the COVID19 pandemic by comparing DTP and PTP value. The study utilized anonymous, saved data from the ORBIS (DEADALUS Healthcare group) system, a hospital information system used by hospitals of REGIOMED. Data were filtered from the ORBIS system of patients in the REGIOMED hospitals in Coburg, Sonnenberg and Lichtenfels between January 1st 2017 to March 31st 2022.

### 3.2. Participants

The analyzed sample, obtained from OPS-836, comprised 218 patients, with 110 individuals from Lichtenfels, 83 from Coburg, and 25 from Sonneberg, 96 patients among them belonging to the pre-COVID group, 122 patients to the during-COVID group. Included were subjects in whom, between January 1st 2017 and March 31st 2022, an occlusion in the Aa. carotis communis et interna, vertebralis, cerebri media in M1 to M3, cerebri anterior in A1 to A3, basillaris and cerebri posterior in P1 was detected and resolved via thrombectomy. This study was limited to subjects treated in one of the REGIOMED hospitals at Lichtenfels, Coburg or Sonneberg. Subjects in whom the intervention had to be aborted or the vascular occlusion could not be achieved were excluded, as were patients with insufficient documented medical data. For the aforementioned hypothesis the control group consists of subjects with thrombectomy procedure before the pandemic (PreCP) (January 1st 2017 to January 31st 2020), and the experimental group with subjects undergoing a thrombectomy during the pandemic (DurCP) (March 1st 2020 to March 31st 2022).

### 3.3. Data sources/Measurement

All data required for this study were collected from the ORBIS system containing all relevant healthcare data about the patients. The exact timing of the CT scans was collected through the DeepUnity PACS software (DEADALUS Healthcare Group).

### 3.4. Variables

Multiple variables of interest were extracted from ORBIS. Demographic information of the participants at baseline included gender and age. DTP and PTP variables were assessed for the experimental group and the control group.  DPT was calculated as the difference in minutes between the registered time of patient's arrival at the hospital and the timing of the CT scan. PTP was calculated as the difference in minutes between timing of the patient's CT scan and commencement of Mechanical Thrombectomy (time of the groin puncture).

### 3.5. Potential bias

Data for this study were acquired through ORBIS, a well-structured electronic database integral to healthcare documentation.  However, the potential for bias exists if the documentation is incomplete, inaccurate, or flawed. To mitigate this risk, we exclusively relied on data directly extracted from the CT scan performed by the CT program, and the surgery protocol completed during the thrombectomy procedure.

The study did not account for the workload of the ER and the number of staff on duty on a given day, crucial aspects of the workflow and patient care during MT. To mitigate this influence, we addressed the issue by including a sizable and diverse participant pool, encompassing individuals from various hospitals.

### 3.6. Statistical analyses

Normality of the DTP and PTP distributions per group was determined visually via QQ plots and using the Shapiro-Wilk test. As results indicated non-normal distributions, the Wilcoxon Rank Sum Test was used to test for group differences. The alpha level, meaning level of significance, was set to $\alpha = 0.05$ ($P<0.05$).

Statistical analyses were performed using R version 4.1.1 (R Core Team, 2021). Data visualization was conducted using the "ggplot2" package (Wickham, 2016), grouped summary statistics were calculated using the "car" package (Fox & Weisberg, 2019). Statistical tests were performed using functions from base R's "stats" package.

### 3.7. Ethical approval

The research project received approval from the Institutional Review Board (IRB) of the Medical School REGIOMED Coburg on February 19$^{th}$, 2024, in accordance with §2 of its Statutes. Given the retrospective nature of this project, additional study registration was not deemed necessary.

# 4. RESULTS

We analyzed a total number of 218 patients. Four patients were excluded due to incomplete data. In both groups there were cases of missing data, resulting in unequal sample sizes between groups and measures. Before the onset of the COVID-19 pandemic, the median duration of DPT time in the cohort was 12 minutes (IQR = 10.80). During the pandemic, the median duration showed a slight increase to 15 minutes (IQR = 11.50), resulting in a difference of 3 minutes before vs. during the pandemic. A further increase in time was observed when examining the duration for PTP time: prior to the pandemic, the median duration was 75 minutes (IQR = 57.50), while during the pandemic the median duration rose to 82 minutes (IQR = 54.50). This results in a difference of 7 minutes. Table 1 displays the descriptive statistic of the data.

**Table 1**. Descriptive statistic of the data

| **Group** | **Mean** | **SD *** | **Median** | **IQR†** |
|---|---|---|---|---|
| PreCP Door-to-Picture (N =74) | 16.92 | 18.37 | 12 | 10.80 |
| DurCP Door-to-Picture (N = 95) | 19.69 | 18.88 | 15 | 11.50 |
| PreCP Picture-to-Puncture (N = 96) | 79.10 | 46.22 | 75 | 57.5 |
| DurCP Picture-to-Puncture (N=118) | 97.466 | 62.85 | 82 | 54.5 |

Data are presented as numbers in minutes

**Abbreviations**: **PreCP**: Pre COVID-19 group; **DurCP**: During COVID-19 group

*Standard Deviation

†Interquartile Range

To visualize the distribution of our data set, we used quantile-quantile plots (Q-Q plots) for each group (Figures 6-9). Figures 6 and 7 show non-normal distributions, as evidenced by points that clearly deviate from the reference line.

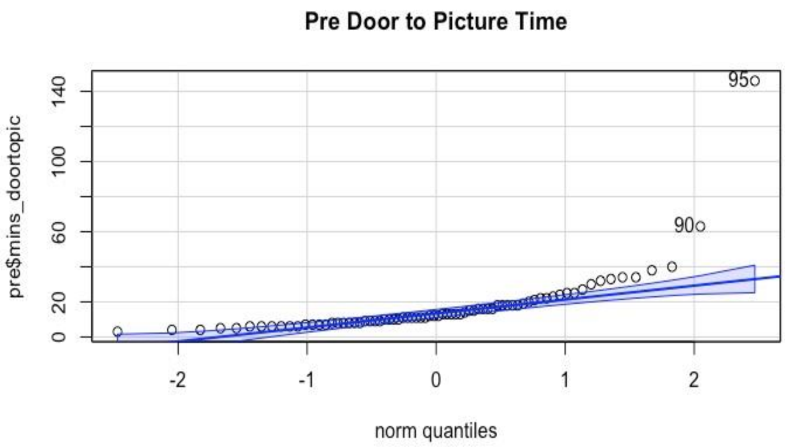



**Figure 6.** Q-Q Plot “door-to-picture” in the PreCP group

*Shapiro-Wilk test

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: https://www.R-project.org/ Accessed February 2024

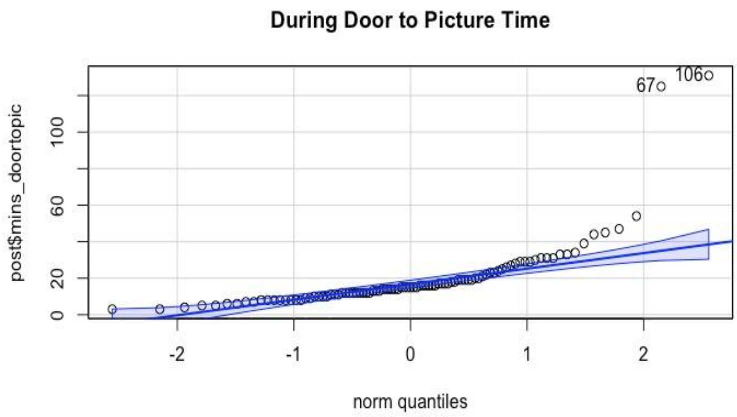



**Figure 7.** Q-Q Plot “time-to-picture in the DurPD group

*Shapiro-Wilk Test

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: .https://www.R-project.org/ Accessed February 2024

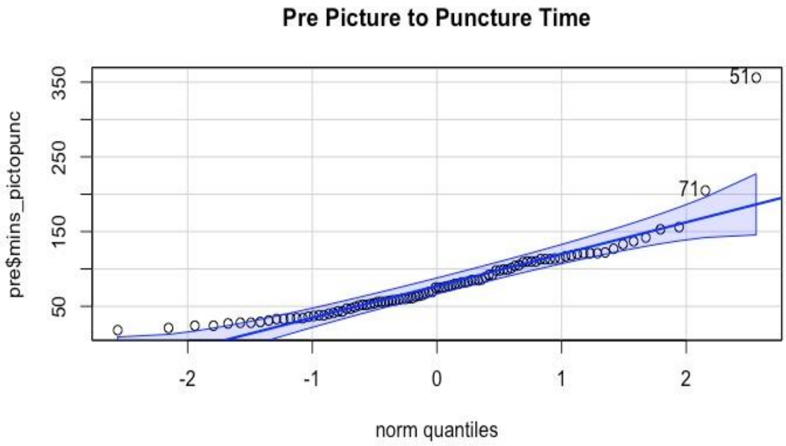



**Figure 8**. Q-Q Plot "picture-to-puncture" in the PrePD group

*Shapiro-Wilk Test

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: . https://www.R-project.org/ Accessed February 2024

Only Figure 8, the Q-Q plot for the PreCP group for the PTP time, display a Q-Q plot indicative of a normal distribution (Figure 8). However, when comparing this plot with the corresponding histogram (Figure 11) and boxplot (Figure 13), outliers are still evident, reinforcing our theory of a non-normal distribution in this group. Although the PrePC group with the PTP time variable shows fewer outliers and a narrower distribution than the other groups, it still does not follow a normal distribution, as confirmed by the Shapiro-Wilk test. Figure 9 again clearly depicts a non-normal distribution in the DurPD group for the PTP time, as the points significantly diverge from the reference line.

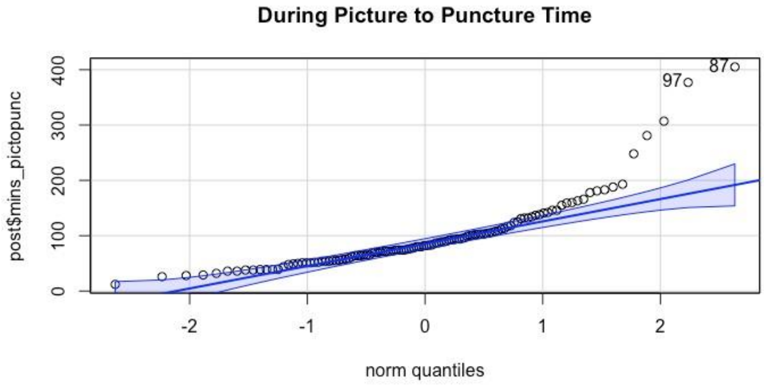



**Figure 9.** Q-Q Plot "picture-to-puncture" in the DurPD group

*Shapiro-Wilk Test

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: .https://www.R-project.org/ Accessed February 2024

To enhance understanding of the asymmetrical distribution in our dataset, we further examined both the histograms (Figure 10 and Figure 11) and the boxplots (Figure 12 and Figure 13). The histograms for the DTP variable in both the PrePD and DurPD groups (Figure 10), as well as for the PTP variable (Figure 11), indicate a right-skewed distribution. This skewness strongly suggests a non-normal distribution. Additionally, both groups exhibit outliers, which are uncommon in normally distributed data.

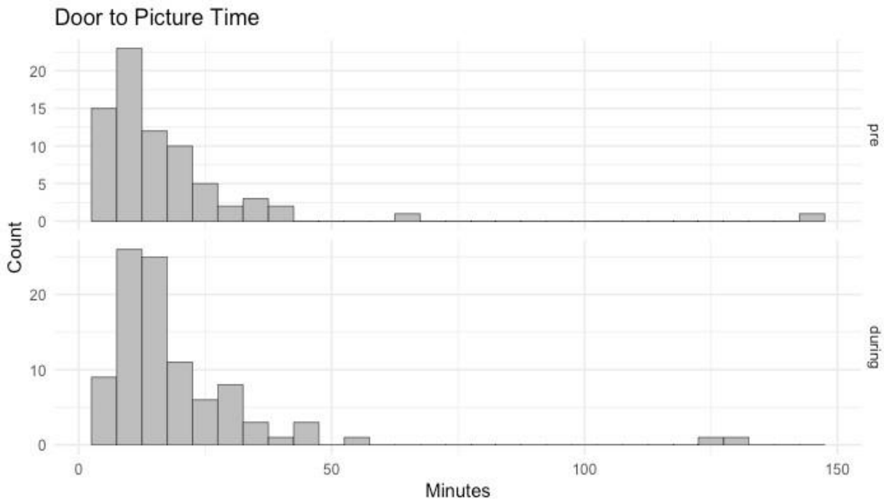



**Figure 10**. Histogram in the "door-to-picture"

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: .https://www.R-project.org/ Accessed February 2024

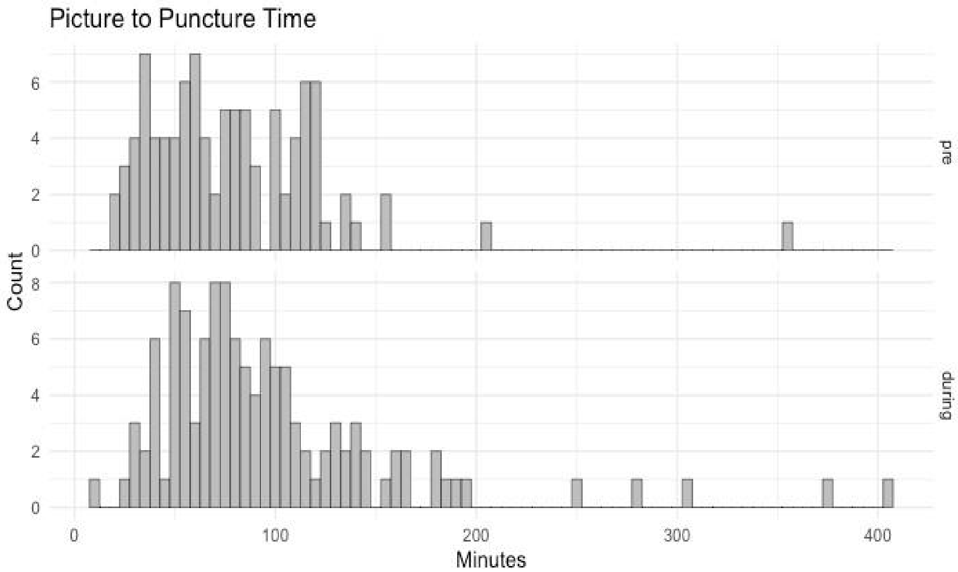



**Figure 11**. Histogram in the "picture-to-puncture"

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: . https://www.R-project.org/ Accessed February 2024

The boxplots for the DTP variable in both the PrePD and DurPD groups (Figure 12), as well as for the PTP variable (Figure 13), indicate a non-normal distribution, as evidenced by a rightward skew. This skewness is reflected in the longer right-side whiskers and a greater number of outliers on the right. Unlike a normal distribution where whiskers are typically of similar length and fewer outliers are present, here the data significantly deviates from this pattern. Additionally, the positioning of the boxes, particularly noticeable in Figure 13, is not symmetrical around the median, further confirming the asymmetrical nature of the distribution.

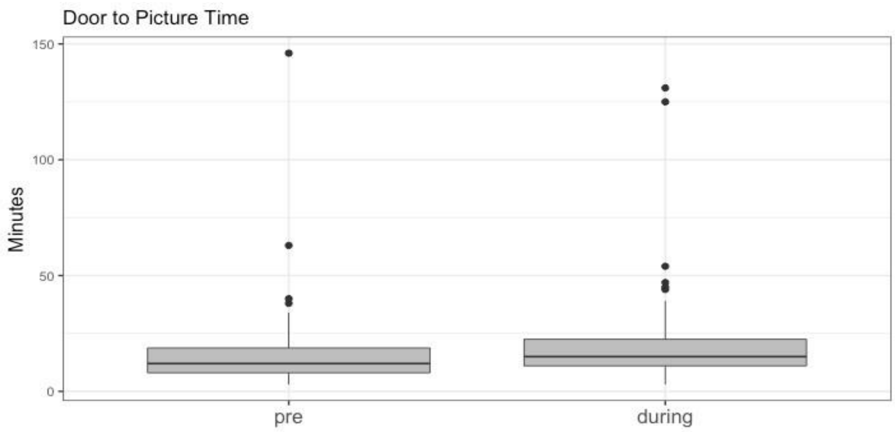



**Figure 12**. Boxplot “door-to-picture” time

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: .https://www.R-project.org/ Accessed February 2024

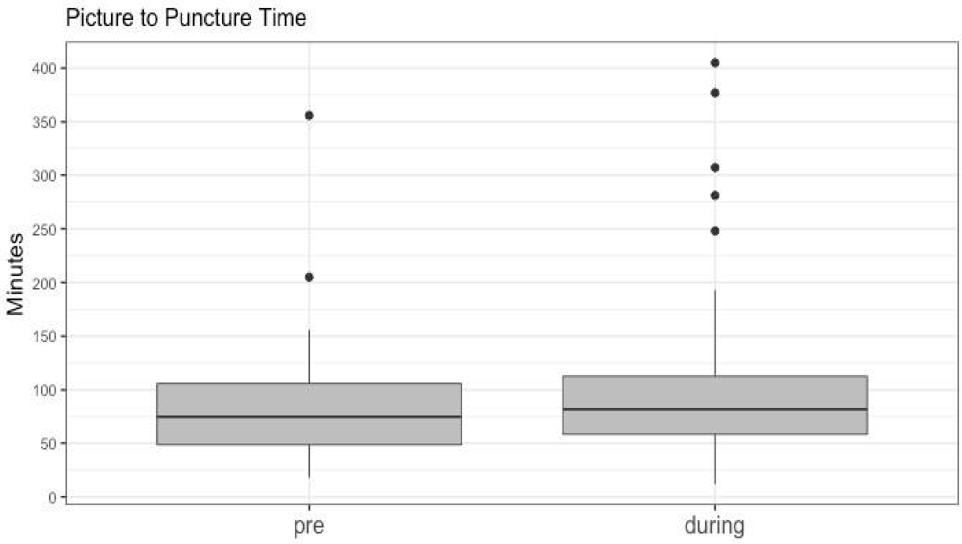



**Figure 13.** Boxplot “picture-to-puncture” time

† R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. [Internet]. 2021. Available from: .https://www.R-project.org/ Accessed February 2024

The visual inspection with Q-Q plot, boxplot and histograms clearly indicate a nonnormal distribution in all four groups. This was confirmed using the Shapiro-Wilk Test of normality for each measure and each group (Table 2). The test results indicated a statistically significant deviation from the normal distribution in each group, indicated by p-values smaller than 0.05. Due to the violation of the normality assumption necessary for parametric tests, we chose a non-parametric statistical test for our subsequent analyses.

**Table 2**. Shapiro-Wilk Test

| **Group** | **Variable** | ***W*†** | ***P**** |
|---|---|---|---|
| PreCP | Door-to-Picture | 0.820 | <0.001 |
| DurCP | Picture-to-Puncture | 0.784 | <0.001 |
| PreCP | Door-to-Picture | 0.530 | <0.001 |
| DurCP | Picture-to-Puncture | 0.581 | <0.001 |

Data are presented as numbers

* Shapiro-Wilk test for normality

† Test statistic for Shapiro Wilk Test

**Abbreviations**: **PreCP**: Pre COVID-19 group; **DurCP**: During COVID-19 group

To test for statistically significant differences in DTP and PTP times before vs. during the pandemic, we utilized the Wilcoxon Rank Sum Test (Table 3). The results of the Wilcoxon Rank Sum Test indicate that MT times increased both for DTP (W = 2895.5, P = 0.003, r = 0.17) and PTP times (W = 4669.5, P = 0.01, r = 0.17). Nevertheless, according to Cohen's classification of effect size the effect size (r) of 0.17 is small.

**Table 3.** Wilcoxon Rank Sum Test

| **Group** | **W†** | ***P*** | r‡ |
|---|---|---|---|
| Door-to-Picture | 2895.5 | 0.03 | 0.17 |
| Picture-to-Puncture | 4669.5 | 0.01 | 0.17 |

Data are presented as numbers

* Wilcoxon Rank Sum Test

† Test statistic for Wilicoxon Rank Sum test

‡ Effect Size

The findings from this study indicate a potential impact of the COVID-19 pandemic on the workflow of MT implementation. Longer DTP and PTP times were observed during the pandemic period versus the pre-pandemic period. As a result, our hypothesis regarding an extension in the workflow for acute stroke management evaluated through DTP and PTP prolongation, appears to be supported by the data. These observed delays in DTP and PTP times during the pandemic underline the potential influence of the pandemic on the workflow of acute stroke management.

# 5. DISCUSSION

The aim of this retrospective study was to investigate whether there is a difference in workflow of MT implantation during the COVID-19 pandemic, by specifically analyzing DTP and PTP times. Our initial hypothesis stated that we expected to observe an increase in this workflow of MT during the covid- 19 pandemic. The data presented have shown that the statistical analysis confirmed our hypothesis. Both the DTP and PTP values showed increased during the COVID 19-pandemic, justifying the assumption that the MT procedures could not be conducted as fast as before the pandemic outbreak.

Overall, both DTP and PTP times showed an increase during the COVID-19 pandemic, with PTP times showing a significant increase of approximately 18 minutes. Regarding the median, which is more suitable for analyzing non-normally distributed data compared to mean, we observed that for both DTP and PTP time median values were markedly higher during the COVID-19 period compared to pre-pandemic levels. This suggests a longer duration in both DTP and PTP time during the pandemic, which could be indicative of shifts in the workflow and external influences during the pandemic. The IQR values for the DTP and PTP variables in both the PreCP and DurCP groups show that there is a reasonable amount of variation within each group and variable. Due to similar IQR values across the different groups, the amount of variation is consistent. This suggests that our estimates of the population median are not due to random chance but reflect real differences in the data.

Considering these aspects, while there was some variability in individual data points, our estimates of the overall median remain fairly accurate. Consequently, we can conclude that there was indeed an increase in the MT workflow during the COVID-19 pandemic based on the provided data. Although the effect size of 0.17 suggest a small effect according to conventional guidelines (Cohen's classification), there is a small but observable effect, especially, with the p-value in both DTP and PTP being less than the significance level of 0.05. Nevertheless, it is crucial to approach these findings with caution and account for other potential factors that might have influenced the observed changes in workflow. The variability in both DTP and PTP times underscores the need for further investigation into factors contributing to these variations and potential interventions to improve workflow efficiency.

One can speculate about the reasons that lead to the increase in workflow we observed. The implementation of supplementary measures to enhance safety for healthcare workers could be one reason (62):

- The introduction of additional triage screening processes to assess patients upon arrival,
- the provision of adequate personal protective equipment (PPE) and
- maintaining high standards of hygiene and infection control, particularly through rigorous cleaning and disinfection procedures implemented between consecutive computed tomography (CT) scans.

On the other hand, the increase in DTP and PTP time was lower than we expected. One could argue that the German healthcare system and ED promptly adapted to the challenges posed by the pandemic. Through fast adjustments to acute stroke care protocols, efforts were made to enhance efficiency, diminish treatment delays, and prioritize the safety of both patients and healthcare workers by mitigating potential exposure risks (60). Additionally, with fewer patients in the ER resources could be more efficiently allocated to the needs of the most critically ill individuals. Undoubtedly, further investigations are needed, particularly to explore the disparities in workflow between the REGIOMED hospitals during and prior to the pandemic, the adherence to pandemic protocols outlined in guidelines, and the accuracy of the data collection process. As a result, these findings must be interpreted with caution.

Upon reviewing similar studies, which more commonly analyzed workflow time intervals with “door-to-puncture” not “picture-to-puncture” intervals, it becomes evident that there is a diversity of findings regarding changes in workflow time intervals. For instance, a Germany-wide study conducted by the Ludwig-Maximilians-Universität Munich (63) revealed minimal variance in pre- and intrahospital workflow time intervals for MT patients admitted in 2020 compared to 2019. However, it did note a slight increase in “door-to-puncture” time (47min vs 38 min, $p = 0.005$) for patients admitted through interhospital care in 2020, coinciding with the COVID-19 pandemic. In a New York study, a trend toward longer median DTP (16min vs 12 min; $p=0.05$) was observed, possibly due to additional precautionary measures aimed at preventing further contamination (62). Similarly, a study from France (64), conducted at the Lyon Comprehensive Stroke Center, found small differences in DTP and “door-to-puncture” times between the two periods. However, it did report a notable increase in “door-to-puncture” time among patients transferred for MT. A stroke center in Malaysia (65) even reported a better an improvement in intrahospital workflow, observing shorter “door-topicture” and “door-to-puncture” times during the COVID-19 pandemic compared to the period before. These findings show the complex and multifaceted nature of the impact of the COVID19 pandemic on stroke care workflows, highlighting variations across different healthcare settings and regions.

A potential limitation of this study, as outlined in the study bias section (see point 3.5 above) pertains to data quality. There may be errors in the recording of data, particularly regarding the precise timing of patient arrival in the emergency room or the exact timing of mechanical thrombectomy procedures. Additionally, there is uncertainty regarding whether protocols were consistently followed, and if additional safety measures were effectively implemented. Also, we were unable to report which specific components of stroke workflow may have contributed to the delay from imaging to treatment. Our study primarily relies on observation and not on active intervention on the events studied. Consequently, there may be factors influencing our results that could not be fully accounted form, known as residual confounding. Furthermore, our analysis utilized data sourced from rural hospitals, characterized by lower patient volumes and perhaps fewer resources. These hospitals serve populations with distinct demographic profiles, compared to larger urban facilities and stroke centers with highly standardized protocols. As a result, it is important to recognize that our findings may not fully represent the broader landscape of thrombectomy and stroke care in Germany.

# 6. CONCLUSION

Our retrospective study has examined the impact of the COVID-19 pandemic on the workflow of mechanical thrombectomy implantation, hereby focusing on DTP and PTP intervals. Our initial hypothesis was validated by statistical analysis, demonstrating an increase in workflow during the pandemic period. Both DTP and PTP times experienced increases, indicating a shift in workflow dynamics. However, our study has limitations, including potential errors in data recording and in the observational nature of the study. Further investigation is warranted to explore disparities in workflow, adherence to pandemic protocols, and the accuracy of data collection processes. Nevertheless, despite these limitations, our study contributes valuable insights into the impact of the COVID-19 pandemic on mechanical thrombectomy workflow. Understanding these factors is essential for refining stroke care protocols, minimizing treatment delays, and enhancing overall patient care both during and beyond the COVID-19 crisis.

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# 8. SUMMARY

**Objectives**: Acute ischemic stroke (AIS) is a frequently encountered and severe medical emergency needing rapid intervention. This thesis aimed to investigate whether the COVID-19 pandemic has resulted in an increase in the duration of the workflow associated with Mechanical Thrombectomy (MT) treatment for patients with acute ischemic stroke.

**Material and methods:** This retrospective cohort study analyzed 218 subjects who MT at REGIOMED hospitals in Coburg, Sonneberg, and Lichtenfels, both before and during the COVID-19 pandemic. Data were extracted from the ORBIS system covering patients with occlusions in various cerebral arteries who underwent thrombectomy from January 1$^{st}$ 2017, to March 31st, 2022. We compared door-to-picture (DTP) and picture-to-puncture (PTP) values between two groups: a control group, the Pre COVID-19 group (PreCP) comprising subjects who underwent thrombectomy before the pandemic (January 1st, 2017, to January 31st, 2020), and an experimental group, the During COVID-19 group (DurCP) comprising subjects treated during the pandemic (March 1st, 2020, to March 31st, 2022). Statistical analyses were performed using the Wilcoxon Rank Sum Test due to non-normal distributions, with a significance level value set at $\alpha = 0.05$. Data visualization and summary statistics were conducted using R software and specific packages, including ggplot2 and car.

**Results:** Prior to the COVID-19 pandemic, median DTP time was 12 minutes (interquartile range (IQR) = 10.80), increasing slightly to 15 minutes (IQR = 11.50) during the pandemic. Similarly, PTP time increased from a median of 75 minutes (IQR = 57.50) pre-pandemic to 82 minutes (IQR = 54.50) during the pandemic, reflecting a difference of 3 and 7 minutes.
We found a non-normal distribution of data in all four groups, confirmed through visual inspection and the Shapiro-Wilk test. With significant deviations from normality, nonparametric tests were chosen for subsequent analyses. Utilizing the Wilcoxon Rank Sum Test, significant increases in DTP and PTP times during the pandemic were observed (DTP: W = 2895.5, P = 0.003, r = 0.17; PTP: W = 4669.5, P = 0.01, r = 0.17), although effect sizes were small according to Cohen's classification.

**Conclusion:** Both DTP and PTP times showed increases during the pandemic period compared to pre-pandemic levels, with PTP times notably rising by approximately 18 minutes. Median values for both DTP and PTP times were notably higher during the pandemic, indicating longer durations, possibly influenced by workflow shifts, external factors during the pandemic, or measurement errors. While the effect size was small according to conventional guidelines,

statistical significance was found in both DTP and PTP times. However, caution is warranted in interpreting these findings, considering potential confounding factors. Further investigation is needed to understand factors contributing to workflow variations and to identify interventions to enhance efficiency.

# 9. CROATIAN SUMMARY

**Ciljevi**: Akutni ishemijski moždani udar (AIM) je često susretana i ozbiljna medicinska hitnost koja zahtijeva brzu intervenciju. Ovaj rad je imao za cilj istražiti je li pandemija COVID-19 rezultirala povećanjem trajanja radnog tijeka povezanog s liječenjem mehaničkom trombektomijom (MT) kod pacijenata s akutnim ishemijskim moždanim udarom.

**Materijal i metode**: Ova retrospektivna kohortna studija analizirala je 218 ispitanika koji su podvrgnuti MT u bolnicama REGIOMED u Coburgu, Sonnebergu i Lichtenfelsu, kako prije, tako i tijekom pandemije COVID-19. Podaci su izvučeni iz ORBIS sustava, pokrivajući pacijente s okluzijama u različitim cerebralnim arterijama koji su podvrgnuti trombektomiji od 1. siječnja 2017. do 31. ožujka 2022. godine. Uspoređivali smo vrijednosti od ulaska do snimanja (DTP) i od snimanja do punkcije (PTP) između dvije skupine: kontrolne skupine, Pre COVID-19 skupine (PreCP) koja obuhvaća ispitanike koji su podvrgnuti trombektomiji prije pandemije (1. siječnja 2017. do 31. siječnja 2020.) i eksperimentalne skupine, Tijekom COVID-19 skupine (DurCP) koja obuhvaća ispitanike liječene tijekom pandemije (1. ožujka 2020. do 31. ožujka 2022.). Statističke analize provedene su korištenjem Wilcoxonovog testa zbroja rangova zbog nenormalnih raspodjela, s razinom značajnosti postavljenom na $\alpha$ = 0,05. Vizualizacija podataka i sažetak statistika provedeni su korištenjem R softvera i specifičnih paketa, uključujući ggplot2 i car.

**Rezultati**: Prije pandemije COVID-19, medijan DTP vremena bio je 12 minuta (interkvartilni raspon (IQR) = 10,80), blago se povećavajući na 15 minuta (IQR = 11,50) tijekom pandemije. Slično tome, PTP vrijeme povećalo se s medijana od 75 minuta (IQR = 57,50) prije pandemije na 82 minute (IQR = 54,50) tijekom pandemije, što odražava razliku od 3 i 7 minuta. Utvrdili smo nenormalnu distribuciju podataka u sve četiri skupine, potvrđenu vizualnom inspekcijom i Shapiro-Wilkovim testom. Zbog značajnih odstupanja od normalnosti, za daljnje analize odabrani su neparametrijski testovi. Korištenjem Wilcoxonovog testa zbroja rangova, tijekom pandemije zabilježena su značajna povećanja DTP i PTP vremena (DTP: W = 2895,5, P = 0,003, r = 0,17; PTP: W = 4669,5, P = 0,01, r = 0,17), iako su veličine učinka bile male prema Cohenovoj klasifikaciji.

**Zaključak**: I DTP i PTP vremena pokazala su povećanje tijekom pandemijskog razdoblja u usporedbi s razdobljem prije pandemije, pri čemu su PTP vremena značajno porasla za približno 18 minuta. Medijan vrijednosti za oba DTP i PTP vremena bio je značajno veći tijekom pandemije, ukazujući na dulje trajanje, moguće pod utjecajem promjena u radnom tijeku,

vanjskih čimbenika tijekom pandemije ili pogrešaka u mjerenju. Iako je veličina učinka bila mala prema konvencionalnim smjernicama, statistička značajnost pronađena je u oba DTP i PTP vremena. Međutim, potreban je oprez u tumačenju ovih nalaza, s obzirom na moguće zbunjujuće čimbenike. Daljnje istraživanje je potrebno kako bi se razumjeli čimbenici koji pridonose varijacijama u radnom tijeku i identificirale intervencije za poboljšanje učinkovitosti.