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INTEGRATED STUDY MASTER’S THESIS

Mechanical Thrombectomy for Basilar Artery Thrombosis: Endless Controversy

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Annotation

Basilar artery thrombosis can be defined as a rare but highly severe form of stroke within the posterior circulation. It often presents with very high mortality and morbidity rates. Although accounting for only 1% of all ischemic stroke cases, BAO is a serious clinical challenge due to its nonspecific symptoms and the need for rapid diagnosis and intervention [1]. BAO is primarily caused by mechanisms that are also the cause of other types of ischemic strokes, mainly atherosclerosis and embolism [7]. This review aimed to critically analyze the existing evidence for mechanical thrombectomy for BAO, the criteria for patient selection, and the resulting treatment outcomes.

Tasks:

1. Examine existing research on the pathogenesis, epidemiology, and clinical outcomes of BAO.
2. Assess the literature on mechanical thrombectomy, including its mechanisms, efficacy, and safety.
3. Analyze previous studies on the implementation of endovascular treatment (EVT) for BAO, providing insights into decision-making processes and patient outcomes.
4. Identify emerging trends and future directions in the treatment of BAO.

The Research Literature Search Strategy involved a manual search in the PubMed and Google Scholar databases with the keywords “Basilar Artery,” “Occlusion,” “Thrombectomy,” “Endovascular Treatment,” and “Controversy.” A total of 58 articles were included in this literature review, and each article was screened according to its importance for the review, especially various studies that evaluate the efficacy of Endovascular Treatment (EVT) as opposed to Standard Medical Therapy (SMT) and resulting outcomes of the treatment. To include the most recent literature and evaluate completed trials, only English studies published in the last 15 years were allowed. This review concludes that BAO management still reflects a need for further research to refine treatment strategies, optimize patient selection, and determine the most effective use of EVT and adjunct therapies while also providing a possibility of EVT becoming a more standardized approach for BAO if ongoing research continues to support its efficacy.

Key Words: Basilar Artery Thrombosis, Thrombectomy, Thrombolysis, clinical examination and diagnosis, Comparative Effectiveness.

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Used Abbreviations

ACS	Anterior Circulation Stroke
AFib	Atrial Fibrillation
AICA	Anterior Inferior Cerebellar Artery
ASA	Anterior Spinal Artery
ATTENTION	*Endovascular Treatment for Acute Basilar Artery Occlusion*
BAO	Basilar Artery Occlusion
BAOCHE	*Basilar Artery Occlusion Chinese Endovascular*
BASICS	*Basilar Artery International Cooperation Study*
BEST	*Basilar Artery Occlusion Endovascular Intervention Versus Standard Medical Treatment*
BGC	Balloon Guide Catheter
COVID-19	Coronavirus Disease 2019
CTA	Computed Tomography Angiography
DAC	Distal Access Catheter
DWI	Diffusion Weighted Imaging
EVT	Endovascular Therapy (or *Endovascular Treatment*)
IAT	Intra-Arterial Thrombolysis
IVT	Intravenous Thrombolysis
LKN	Last Known Normal
LVO	Large Vessel Occlusion
MeSH	Medical Subject Headings
mRS	modified Rankin Scale
MRI	Magnetic Resonance Imaging
MRA	Magnetic Resonance Angiography
MT	Mechanical Thrombectomy
NIHSS	National Institutes of Health Stroke Scale
pc-ASPECTS	Posterior Circulation Acute Stroke Prognosis Early Computed Tomography Score
PCA	Posterior Cerebral Artery
PCS	Posterior Circulation Stroke
PICA	Posteroinferior Cerebellar Artery
RCT	Randomized Controlled Trial

RESCUE-RE	*Registration Study for Critical Care of Acute Ischemic Stroke after Recanalization*
SCA	Superior Cerebellar Artery
SMT	Standard Medical Therapy
sICH	Symptomatic Intracranial Hemorrhage
TICI	Thrombolysis in Cerebral Infarction
VA	Vertebral Artery

1. Introduction

Basilar artery occlusion (BAO) is a rare but highly severe form of stroke within the posterior circulation. It often presents with very high mortality and morbidity rates. Although accounting for only 1% of all ischemic stroke cases, BAO represents a serious clinical challenge due to its unspecific symptoms and the need for rapid diagnosis and intervention. The complexity of BAO underlines the importance of stroke research that will surely require timely and effective treatment to prevent severe complications or death [1]. The treatment of BAO is still a matter of debate, and there is no right evidence as to which option is superior [2]. Classic treatments, like intravenous thrombolysis (IVT), also known as standard medical therapy (SMT), are being challenged by more recent approaches, such as mechanical thrombectomy, also referred to as endovascular treatment (EVT). While quite effective in cases of anterior circulation stroke (ACS), extending EVT into BAO is less likely, and additional studies will be required [3]. It remains a challenging task to investigate whether EVT provides a significant benefit over SMT in patients with BAO. It has emerged that mechanical thrombectomy is a safe and promising treatment modality for ischemic stroke, in which the blood clots can be directly taken out from the arteries and restore the blood flow. Its potential benefits for BAO have gained increasing interest, but its role is still debated. The effectiveness, safety, and overall impact of EVT on BAO can only be evaluated by further prospective trials [4].

This literature review critically analyses the existing evidence for mechanical thrombectomy for basilar artery thrombosis over the last decade. It considers various studies that evaluate the efficacy of EVT as opposed to SMT, the criteria for selecting patients, and the resulting outcomes of the treatment to analyze the controversies surrounding its application.

Tasks:

1. Examine existing research on the pathogenesis, epidemiology, and clinical outcomes of basilar artery occlusion.
2. Assess the literature on mechanical thrombectomy, including its mechanisms, efficacy, and safety.
3. Analyze previous studies on the implementation of EVT for BAO, providing insights into decision-making processes and patient outcomes.
4. Identify emerging trends and future directions in the treatment of BAO.

2. Methodology

2.1 Literature Search Strategy:

The research literature search strategy for this review on mechanical thrombectomy in treating basilar artery thrombosis was mainly conducted in the PubMed and Google Scholar databases. These databases were selected due to their wide selection of peer-reviewed articles and their relevance to this topic. The search strategy was developed by using a combination of the PICO Table and the Medical Subject Headings, MeSH terms. The key search terms included "Basilar Artery," "Occlusion," "Thrombectomy," "Endovascular Treatment," and "Controversy." The Boolean Operator "AND" was applied to combine the terms and expand the search to include various variants. The search was filtered by applying different filters. Only English studies published in the last 15 years were included to ensure that the most applicable and current data was reviewed. Also, the studies were limited to human studies to maintain clinical relevance. The searches were conducted between October 2023 and November 2023. All search results were documented using the Zotero reference management system. The initial search yielded over 500 articles, which were then screened based on the following inclusion and exclusion criteria (Figure 1).

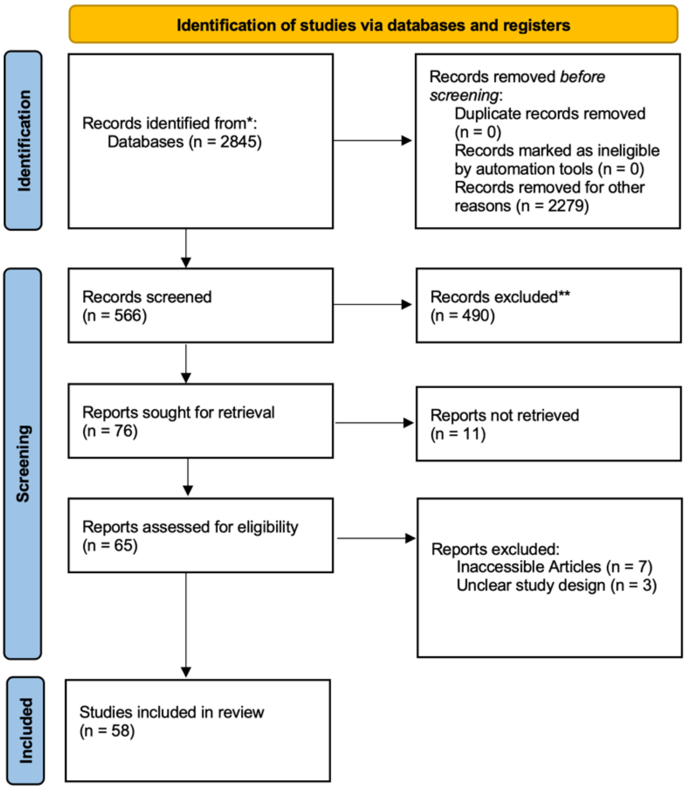

Figure 1: PRISMA 2020 flow diagram for new systematic reviews. Own illustration based on PRISMA guidelines.

2.2 Selection Criteria:

The Selection Criteria for this review were carefully evaluated and applied to ensure the relevance to the clinical question. These Criteria include:

2.2.1 Inclusion Criteria

Study Types: Peer-reviewed research articles, systematic reviews, meta-analyses, and clinical trials were included. These study types were chosen due to their ability to provide qualitative evidence on the topic.

Patient Population: The search focused mainly on the adult population diagnosed with different types of ischemic stroke. Pediatric cases were excluded to ensure the best possible comparison between different outcomes and procedures.

Interventions: The review focused on studies where endovascular treatment was used. Other interventions, such as intravenous thrombolysis or conservative management were also included to conclude different outcomes.

Outcomes: The outcomes of interest in this review were neurological recovery, survival rates, revascularization process, and complications associated with the procedures.

2.2.2 Exclusion Criteria

Study Types: Studies with unclear study designs, animal studies, and non-peer-reviewed articles were excluded due to their lower level of evidence.
Language: Articles published in languages other than English were not included to avoid potential misinterpretation of study findings.
Publication Date: Articles published before 2009 were excluded to ensure that only current findings were used.
Outcomes: Non-relevant outcome measures that were not useful for interpretation or did not provide any value were not included.
In total, 58 articles have been included in this research literature review, and each article was screened according to its importance for the thesis, especially regarding the implementation of mechanical thrombectomy and the comparison between different interventions.

3. Basilar Artery Thrombosis: Clinical Overview

3.1 Definition

Basilar Artery Thrombosis is defined as a serious and life-threatening condition characterized by the formation of a blood clot within the basilar artery. This artery is one of the main arteries that supplies blood to the brainstem and posterior circulation. Acute occlusion of the basilar artery results in ischemia in the brainstem and poor collateral compensation of perforating branches of the basilar artery and part of the cerebellum or thalami [5].

3.2 Anatomy

The Basilar Artery—in Latin, arteria basilaris —is a midline vessel that originates from the medullo-pontine junction by the confluence of the two vertebral arteries and bifurcates into the right and left posterior cerebral arteries [6]. The Basilar Artery is further subdivided into three main segments, with the first proximal segment beginning at the vertebral artery (VA) and ending at the anterior inferior cerebellar arteries (AICA), the middle segment from the AICA to the origin of the superior cerebellar arteries (SCA), and the distal segment from SCA to the terminal posterior cerebral arteries (PCA) (Figure 2) [7]. Throughout its course, the basilar artery gives off several important branches. The pontine arteries are perforating vessels supplying the pons—a crucial section of motor control and sensory analysis. Arising off the basilar artery inferiorly, anterior inferior cerebellar arteries (AICAs) supply the lower part of the cerebellum, including structures such as the inferior and middle cerebellar peduncles. Most commonly, this vessel originates from the labyrinthine or internal auditory artery, supplying the inner ear, which is vital for hearing and balance. Further distally, the basilar artery also gives off the superior cerebellar arteries before its bifurcation. These paired vessels supply the superior part of the cerebellum, a region significant for the coordination of voluntary movements. This strategic placement and branching of the basilar artery ensure that crucial sections of the brain and brainstem are constantly provided with oxygenated blood, which is vital for maintaining neurological functions. Any pathology of the basilar artery in a clinical sense may cause severe consequences [6].

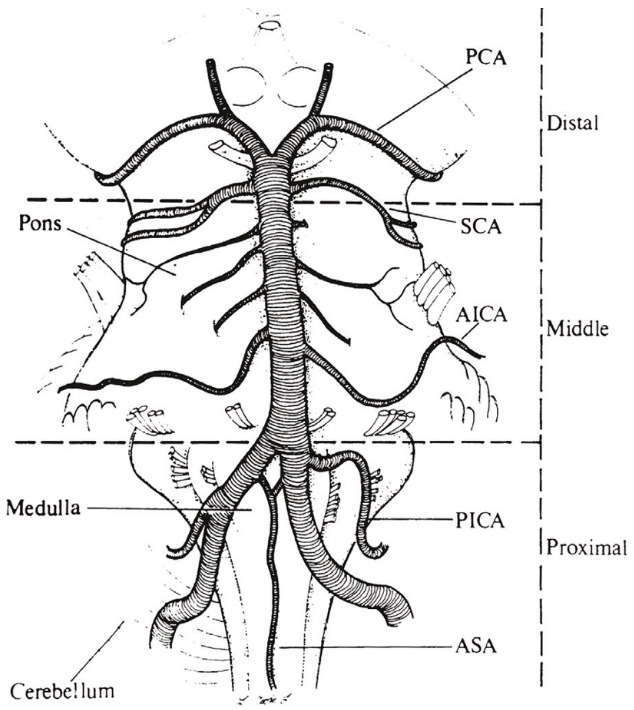

Figure 2: Schematic representation of the vertebral and basilar arteries with major branches (ASA, PICA, AICA, SCA, PCA). Adapted from Caplan et al., 2005.

3.3 Epidemiology

Basilar artery occlusion is considered a rare condition. The exact numbers are difficult to report due to the challenges in diagnosing and reporting. Various autopsy studies estimated the occurrence of basilar artery occlusion at a very low rate of about 2 in every 1000. Despite being rare, stroke registries in the United States reported that BAO may account for up to 27% of ischemic strokes in the posterior circulation [8]. Ikram and Zafar [7] reported that it is estimated that around 1% of all ischemic strokes are accounted for BAO, which shows that despite being a rare pathology, it presents with a high significance.

3.3.1 Demographic Factors

Basilar artery stenosis occurs in different racial and ethnic groups. Atherosclerotic basilar artery stenosis is more common in African American and Asian populations than it is in white populations. There is a gender difference with a male-to-female ratio of 2:1 for basilar artery thrombosis [9].

3.3.2 Age-Related Prevalence

There is a relation between the age and etiology of BAO. Atherosclerotic basilar artery occlusion occurs most commonly during the sixth and seventh decades, whereas occlusion of the distal basilar artery, usually due to embolism, is most common during the fourth decade. In addition, basilar artery occlusion is seen more often in women of older age than in men [9].

3.4 Etiology and Pathogenesis

Basilar artery occlusion is primarily caused by mechanisms that are also the cause of other types of ischemic strokes, mainly atherosclerosis and embolism. It causes an interruption of the blood flow through the basilar artery, which results in infarction of the brainstem, pons, and regions supplied by the basilar artery and its branches. These occlusive events most often occur in the proximal and middle segments of the basilar artery [7]. Causes of BAO include thromboembolism, atherosclerotic disease, and vascular dissection. The mechanism of occlusion varies depending on which segment is involved. The midportion of the basilar artery, along with the vertebrobasilar junction, is commonly associated with atherosclerotic disease. Embolic sources tend to lodge more frequently in the distal third of the basilar artery, particularly at its top and the vertebrobasilar junction. Arterial dissection is also more common in the extracranial vertebral artery and is often related to neck injuries and cervical chiropractic adjustments, although intracranial dissections are extremely rare [9].

3.4.1 Causes

Atherosclerosis

The leading cause of BAO is atherosclerosis, which is defined as the process of plaque buildup within the arterial walls due to endothelial injury. Common risk factors include dyslipidemia, diabetes mellitus, hypertension, and cigarette smoking. Those factors result in damage to the tunica intima of blood vessels, which then expose subendothelial collagen, which leads to platelet adhesion and activation and later infiltration of low-density lipoproteins (LDL), which damage the endothelium and undergo oxidation. As the process continues, macrophages arrive and ingest these oxidized lipids, transform them into lipid-laden foam cells, and form fatty streaks, the earliest visible lesions of atherosclerosis. These fatty streaks then develop into fibrous plaques, which can narrow the arterial lumen and lead to stenosis. If those plaques rupture, they can occlude the proximal vessel or create distal emboli, obstructing smaller cerebral arteries within the posterior circulation [7].

Embolism

Another important etiological factor in BAO is embolism. It is caused when thrombotic material travels and occludes the basilar artery or its branches. One of the main causes is cardiac conditions, which cause thrombus formation, such as atrial fibrillation, recent myocardial infarction, valvular heart diseases, and heart failure with wall abnormalities. Artery-to-Artery embolism can also occur when atherosclerotic plaques, which are located within the vertebral arteries or proximal segments of the basilar artery, rupture and cause distal occlusions [7].

Mechanical and rare causes

Mechanical causes and other rare causes of BAO include conditions like Bow Hunter’s syndrome or vertebrobasilar insufficiency, which is caused by external compression of the vertebral artery by rotational movements of the head. This condition requires endovascular reconstruction, surgical decompression, or other bypass interventions. Also, in recent emerging studies, new evidence implicates the possibility of COVID-19 infection and a prothrombotic state, which can increase the risk of BAO, especially in risk groups like pregnant women. Other conditions like congenital vascular abnormalities like "8-shaped" basilar artery fenestration malformations, hematological disorders such as acute myelogenous leukemia, and inflammatory diseases like Crohn's disease have been associated with BAO due to their increased predisposition to thrombotic events [7].

3.5 History and Physical Examination

Patients with BAO often present with symptoms showing significant impairment in the function of the brainstem and posterior circulation. The most common clinical signs are motor deficits, such as hemiparesis, quadriparesis, and cranial nerve abnormalities, especially around the facial nerve area. These motor symptoms are frequently accompanied by dizziness, headache, and speech difficulties, with dysarthria and challenges in word articulation being particularly prominent. Nausea, vomiting, and visual disturbances, including changes in vision and binocular diplopia, are also frequently reported by patients. An altered level of consciousness is a critical and common finding in cases of BAO. There are three general patterns in which basilar artery thrombosis can present:

1) In the rapid onset pattern, patients may experience the sudden onset of severe motor and bulbar symptoms, together with a decreased level of consciousness. 2) The insidious or stuttering symptoms manifest gradually over a few days and present initially as a combination of mild symptoms that worsen over time and result in the development of disabling motor deficits, significant bulbar symptoms, and impaired consciousness. 3) The prodromal pattern presents with symptoms including headache, neck pain, transient visual disturbances, binocular diplopia, dysarthria, dizziness, hemiparesis, paresthesia, ataxia, and tonic-clonic movements, which are symptoms prior to the complete occlusion and are important warning signs. “Herald hemiparesis” is a term that describes transient and unilateral weakness that can lead to more permanent neurological deficits [7].

3.6 Evaluation

When a patient arrives with symptoms that suggest a BAO, the first initial step in the emergency department (ED) is a non-contrast CT scan of the head, which is a crucial imaging tool for ruling out hemorrhagic stroke. In the meantime, critical clinical information that should be collected are blood pressure, blood glucose levels, the time of symptom onset or last known normal (LKN), National Institute of Health Stroke Scale (NIHSS) score, anticoagulant or antiplatelet use, medical and surgical history, and renal function. If bleeding can be ruled out by the CT scan and BAO is suspected, a CT angiogram of the head and neck should be performed to identify a large vessel occlusion (LVO). If no CT angiography is available, the second line option would be an MR angiogram of the brain to evaluate cerebral vessels. For further characterization of the stroke, an MRI of the brain without contrast can be conducted later, but it should not delay the initial revascularization treatments such as intra-arterial thrombolysis (IAT) and mechanical thrombectomy (MT). In diffusion-weighted imaging (DWI) sequences, the "smoggy" or "hazy" appearance of the pons due to diffusion restriction can be a predictor of favorable neurologic outcomes following mechanical thrombectomy [7]. Also, the mid-basilar artery angle is a potential factor that increases the likelihood of pontine infarction (Figure 3). Additionally, the mid-basilar artery angle may exacerbate plaque burden and increase the likelihood of pontine infarction. The target mismatch, which is defined as an initial infarct size of less than 70 ml with a ratio of ischemic tissue to infarct volume of 1.8 or greater, has shown to be a potential criterion for selecting candidates for endovascular therapy. Thrombolysis in cerebral infarction (TICI) grade of 2c/3 is often used as a target for successful reperfusion in patients who undergo endovascular treatment [7].

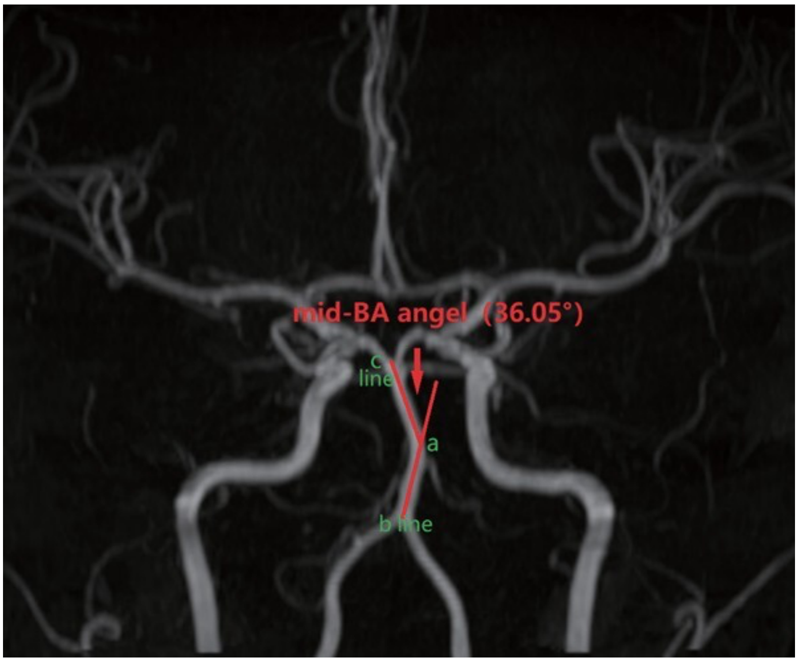

Figure 3: Illustration of the mid-basilar artery angle. Adapted from Li et al., 2022

3.7 Prognosis and Complications

Basilar artery occlusion is associated with a particularly severe prognosis. The overall mortality rate for BAO is estimated to be as high as 80% [5]. However, this statistic depends on outcomes, such as successful recanalization, which can significantly reduce it. Patients who undergo successful recanalization, either through intravenous or intra-arterial thrombolysis, exhibit a lower mortality rate, which can range between 33% and 50%, compared to 74% to 100% in comparison to those patients who do not receive thrombectomy or have failed reperfusion. If patients receive timely thrombolysis, positive functional outcomes in approximately 24% to 35% of patients can be achieved, but still, a significant proportion of these patients may experience significant deficits [9]. Key prognostic factors include the extent and duration of thrombosis, time to LKN, and the effectiveness of the initial treatment because an early intervention successful recanalization is important for improving the chance of a better outcome, and delayed treatment and failed revascularization typically lead to poor outcomes, including severe neurological deficits and high mortality rates [7]. Complications, which can be associated with basilar artery thrombosis, are significant and can severely impact immediate and long-term outcomes despite the advances in pharmacologic and mechanical thrombosis treatments, including endovascular therapy. Common complications include intracranial or extracranial bleeding, aspiration pneumonia, and thromboembolic events such as deep vein thrombosis and pulmonary embolism [9]. Other complications are myocardial infarction, recurrent stroke, and infections such as urinary tract infections and pneumonia [7].

Patients who survive the acute phase of BAO are at risk of additional complications, such as pressure ulcers, contractures, and dysphagia, which can further complicate recovery and rehabilitation. Many survivors require extensive physical and occupational therapy to regain and maintain functionality [9].

4. Treatment Options for Basilar Artery Thrombosis

BAO is considered a life-threatening condition that requires urgent treatment. The patients should be admitted to the stroke unit as fast as possible. Early recanalization to preserve the ischemic penumbra is key to successful treatment and a positive prognosis [5]. Möhlenbruch et. al [4] concluded that recanalization presents the best predictor of good outcomes in BAO and only a 13% chance of good outcomes in non-recanalized patients. Recanalization can be accomplished by either systemic thrombolysis (IVT), intra-arterial thrombolysis (IAT), or mechanical thrombectomy [9].

4.1 Mechanical Thrombectomy

There are four primary endovascular techniques that are commonly used in the context of basilar artery occlusion: contact aspiration thrombectomy, stent retriever thrombectomy, combined stent retriever and aspiration thrombectomy, and angioplasty, with or without stenting. The first three methods are most often considered as first-line approaches for EVT, whereas angioplasty is more commonly used for large-vessel occlusions (LVO) associated with intracranial atherosclerosis or in cases where initial techniques fail. If stenting is required, antiplatelet therapy is initiated acutely and maintained during the follow-up phase [10].

4.1.1 Contact Aspiration Thrombectomy

During an endovascular procedure, a guiding catheter—either a long introducer sheath or a balloon guide catheter for proximal flow arrest—is advanced to the target proximal cervical vessel, such as the carotid or vertebral artery (Figure 4). Over a microcatheter and microwire, a large-bore aspiration catheter is then advanced intracranially to the proximal segment of the thrombus. Once positioned, the aspiration catheter is connected to an aspiration system, either a pump or a negative-pressure syringe. After a brief period of dwell time, the catheter is slowly retracted to aspirate the thrombus [11].

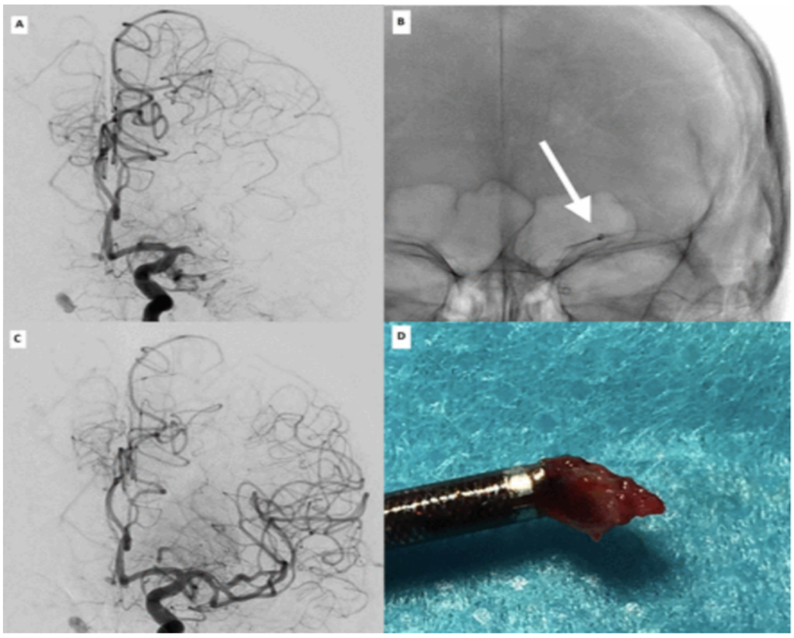

Figure 4: Illustration of the direct aspiration technique in mechanical thrombectomy. Adapted from Boisseau et al., 2020.

4.1.2 Stent Retriever Thrombectomy

To provide access to the occlusion site, a guiding catheter is positioned in the dominant or the most accessible vertebral artery. Devices such as the Solitaire FR or Revive SE are commonly used. The stent retriever is left in place for a few minutes after being deployed distal to the thrombus. In some cases, it remains deployed longer if additional intra-arterial thrombolysis with recombinant tissue plasminogen activator (rtPA) is anticipated. If additional intra-arterial thrombolysis with recombinant tissue plasminogen activator (rtPA) is required, the stent retriever can be left deployed for a longer period. To complete the thrombectomy, the microcatheter and stent retriever are withdrawn, and aspiration is applied through the guide catheter to remove the clot and restore blood flow (Figure 5). To ensure correct device placement and evaluate the success of recanalization, angiographic imaging is used throughout the procedure [4].

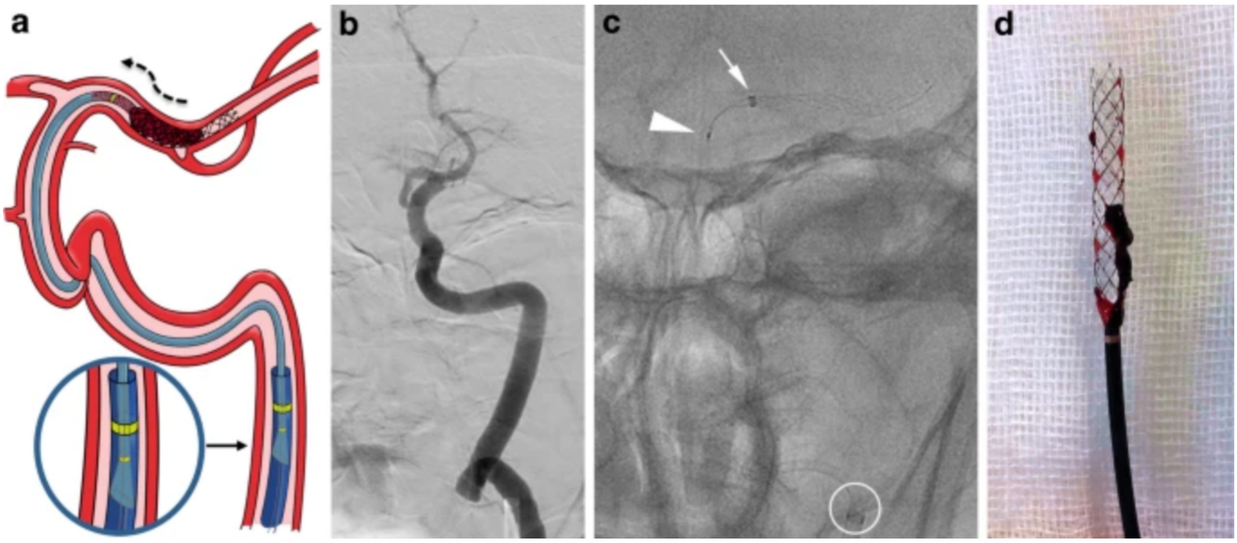

Figure 5: Illustration of the QTM and stent retriever technique. Adapted from Remollo et al., 2021.

4.1.3 Combined stent retriever and aspiration thrombectomy

Stent retrievers, microcatheters, guide catheters, and distal access catheters (DAC) are used as a combination for this procedure. Once the guidewire establishes access, the microcatheter delivers the stent retriever to the thrombus to deploy and capture it. The DAC is advanced to the clot, and under continuous aspiration, the stent retriever and DAC are withdrawn together, or the stent is partially retracted into the DAC while aspirating [12]. The balloon guide catheter (BGC) often plays a critical role by inflating to temporarily block blood flow, thereby preventing embolic events and speeding up the procedure [13]. The combined use of stent retrievers with aspiration catheters, including BGCs and DACs, has been demonstrated to improve procedural success and minimize complications. Prominent approaches include Solumbra (combined stent retriever and suction thrombectomy) [14],[15],[16], ARTS (aspiration-retriever technique for stroke) [17], CAPTIVE (continuous aspiration prior to intracranial vascular embolectomy) [18], SAVE (stent retriever-assisted vacuum-locked extraction) [19] , and BADDASS (balloon guide with large-bore distal access catheter and dual aspiration with stent retriever) (Figure 6) [20].

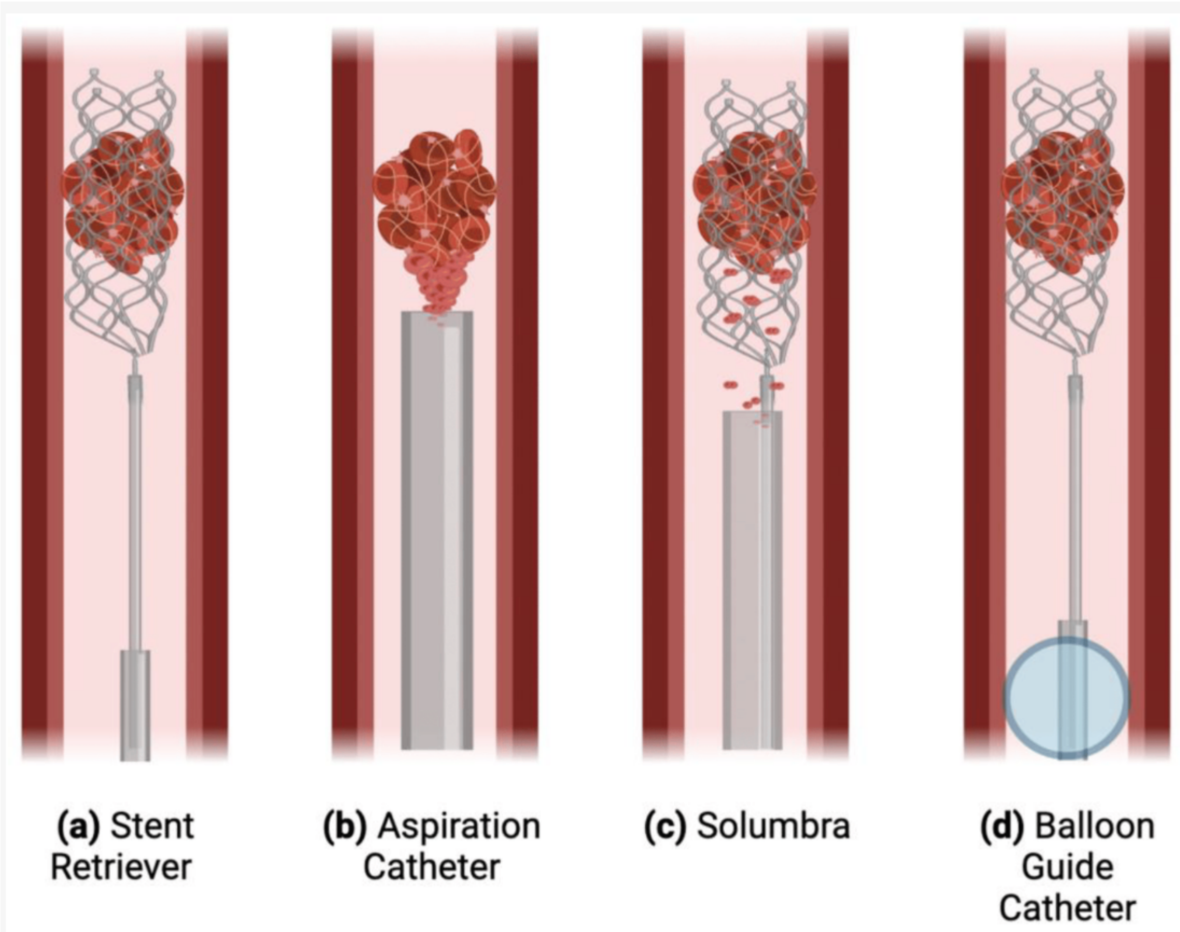

Figure 6: Overview of different endovascular thrombectomy techniques. Adapted from Huang et al., 2022.

4.1.4 Angioplasty

Angioplasty is more often used for large vessel occlusions LVO [10]. The direct angioplasty (DA) technique differs from traditional endovascular methods. After navigating a microcatheter past the occlusion using a microwire, angiography is performed to assess the length of the blockage. An exchange microwire is then used to advance a balloon into the occlusion site, which is inflated multiple times (1–3 times for 30 seconds each). If the occlusion persists or reoccludes due to severe stenosis, rescue stenting is performed (Figure 7). Depending on vessel and lesion characteristics, either a balloon-expandable or self-expanding stent is selected. Before the stent is deployed, the patients receive intravenous heparin. Additionally, tirofiban or dual antiplatelet therapy with aspirin and clopidogrel is administered before and after the stenting to prevent re-thrombosis. Post-procedure, patients continue with aspirin and clopidogrel for three months [21].

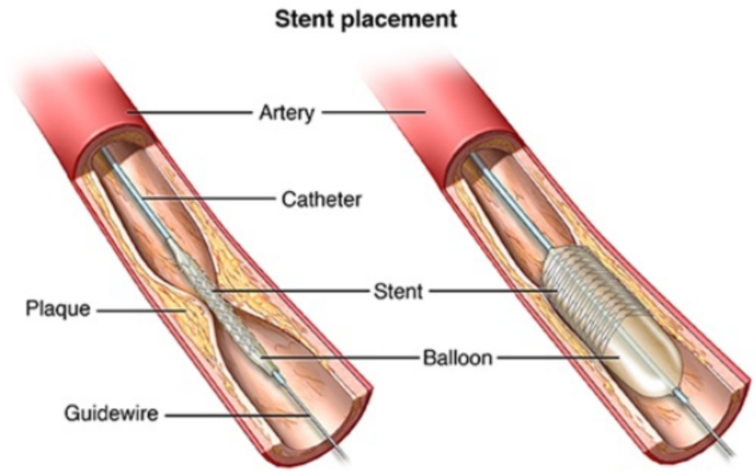

Figure 7: "Schematic illustration of stent placement in neurovascular interventions. Source: Johns Hopkins Medicine, available at https://www.hopkinsmedicine.org, accessed on 5 December 2024."

4.2 Intravenous Thrombolysis

Intravenous thrombolysis (IVT) is a systemic procedure used to treat acute ischemic stroke by dissolving the blood clots via the intravenous administration of thrombolytic agents. The primary medication used in this procedure is a recombinant tissue plasminogen activator (tPA), such as alteplase [22]. IVT works by converting plasminogen to plasmin, which then breaks down fibrin, a key component of blood clots [23]. IVT is most effective when administered within a narrow time window from symptom onset, generally within 0 to 4.5 hours. The thrombolytic agent is delivered intravenously, with a standard dosage of alteplase 0.9 mg/kg—10% administered as an initial bolus over 2 minutes and the remaining 90% infused over 60 minutes [24]. The advantages of IVT include non-invasiveness and the ability to access clots in the entire vascular system. Its efficacy is limited by the risk of bleeding complications and the time window for administration. Therefore, careful patient selection and monitoring must be considered to minimize the risk and optimize the outcomes [25]. In addition, for patients with acute ischemic stroke of 4.5-9 hours duration and known onset time, the European Stroke Organisation (ESO) strongly recommends intravenous thrombolysis with alteplase, if adavanced imaging – such as perfusion imaging or MRI – demonstrates a core/perfusion mismatch indicative of salvageable brain tissue, and mechanical thrombectomy is either not indicated or not planned. This recommendation is based on low quality evidence [26], but supported by randomized controlled trials such as EXTEND [27], ECASS 4 [28] and EPITHET [29]. In context the ESO guidelines emphasize that intravenous thrombolysis beyond 4.5 hours up to 9 hours is conditional on advanced imaging selection to identify patients with viable brain tissue who may benefit. Without advanced imaging, thrombolysis is not recommended in this late window due to lack of demonstrated benefit and safety concerns. The recently published ESO/ESMINT 2024 guideline extends these considerations specifically to the management of BAO. Although no randomized trials have directly compared IVT with no IVT in BAO, the guidelines draws upon observational data such as the BASICS registry, which reported a higher rate of favorable outcomes (modified Rankin Scale [mRS] 0–2) following IVT, with an unadjusted odds ratio of 1.83 (95% CI, 1.10–3.06). Consequently, the expert panel reached consensus suggesting IVT for patients within 4.5 hours of last known well, assuming no contradictions and absence of extensive ischemic changes in the posterior circulation. Moreover, IVT was supported by the majority of experts for patients presenting with 4.5 and 12 hours and even up to 24 hours, under the same conditions [30]. These recommendations are underpinned by single-arm studies reporting that nearly half of BAO patients treated with IVT alone, including those beyond six hours, achieved functional independence (mRS 0–3), with symptomatic intracranial hemorrhage rates (7-11%) comparable to those in the anterior circulation trials. In summary, the ESO/ESMINT guidelines reflect a shift away from the rigid time-based thresholds towards individualized, imaging-guided treatment strategies in the posterior circulation stroke

4.3 Intra-arterial Thrombolysis

Intra-arterial thrombolysis (IAT) is a more localized approach designed to dissolve clots directly at the occlusion site within major brain arteries. This technique is beneficial for large vessel occlusions where intravenous thrombolysis alone may be insufficient. The procedure begins with the insertion of a guiding catheter through the femoral artery, which is then navigated to the occlusion site using fluoroscopic guidance. A microcatheter is advanced through the guiding catheter to the clot location, allowing for direct delivery of thrombolytic agents, such as rtPA, into the clot. (Figure 8). The dosage and infusion rate can be tailored to the clot's characteristics and the patient's response. Continuous monitoring and imaging are employed to assess clot dissolution and blood flow restoration. IAT offers several advantages, including targeted thrombolytic delivery and the potential to extend the treatment window beyond the 4.5-hour limit of intravenous thrombolysis. However, it is more invasive than IVT, involving catheterization and associated risks such as vessel injury and bleeding. The procedure also requires specialized equipment and expertise, limiting its availability compared to intravenous methods [31].

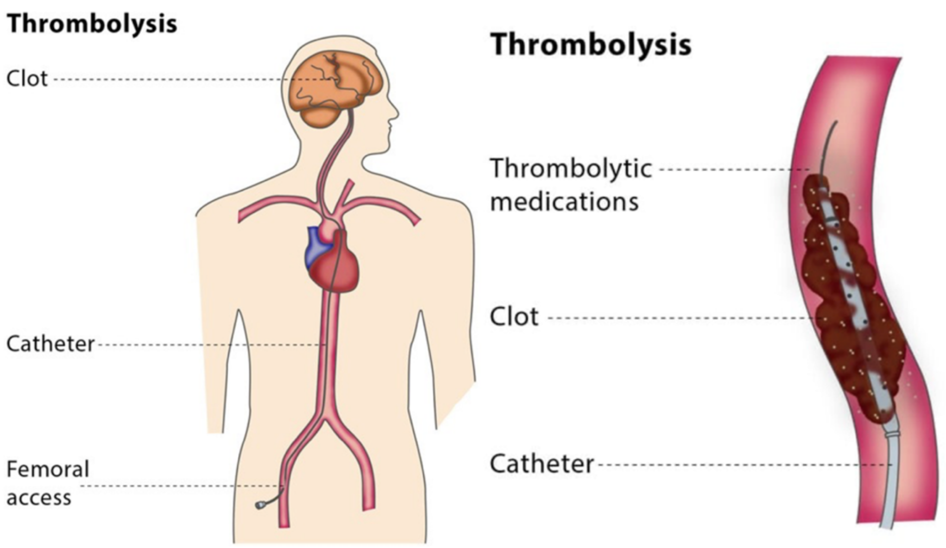

Figure 8: Illustration of thrombolysis technique in acute ischemic stroke. Source: Cardiovascular and Interventional Radiological Society of Europe, available at https://www.cirse.org, accessed on 5 December 2024.

4.4 Eliminating the Etiology

One of the primary reasons for BAO is atherosclerosis. In controlling risk factors like dyslipoproteinemia, diabetes, cigarette smoking, and hypertension, the risk of stroke can be reduced enormously [32]. Atrial fibrillation (AFib) is another key factor in stroke risk. The EMBRACE trial [33] highlights the importance of 30-day cardiac monitoring to enhance the detection of AFib and facilitate goal-directed anticoagulation therapy, which is essential in preventing recurrent strokes by addressing modifiable risk factors. Similarly, the CRYSTAL AF trial [34] demonstrated that prolonged cardiac monitoring using insertable cardiac monitors for 6 to 12 months is superior in detecting AFib in patients who have experienced a stroke. In cases of cryptogenic stroke, where the underlying cause remains unclear, the ARCADIA trial [35] explores the role of atrial cardiopathy identified through echocardiogram, NT-proBNP, and EKG findings in determining the most effective antithrombotic treatment. Recent studies have also focused on patent foramen ovale (PFO). The RESPECT trial [36] found that combining PFO closure with antiplatelet therapy provides superior protection against recurrent ischemic strokes compared to medical management alone. Similarly, the CLOSE trial [37] confirmed that large PFO closure combined with antiplatelet therapy outperforms medical management alone, although it is associated with a higher risk of developing atrial fibrillation post-procedure.

Management of hyperlipidemia and hypertriglyceridemia has been shown to influence stroke risk as well. The REDUCE-IT trial [38] reported that high-dose icosapent ethyl, a purified form of eicosapentaenoic acid, effectively reduces stroke risk in patients with hypertriglyceridemia who are already on high-dose statin therapy.

5. Key Studies and Findings

The management of BAO remains an area of active investigation, with ongoing debate about the most effective treatment strategies. In recent years, several key trials have been conducted to evaluate and compare different therapeutic approaches, including endovascular treatments and medical management. Endovascular treatments, which involve techniques such as mechanical thrombectomy (MT), have shown promise in anterior circulation LVO but are also still a topic of debate about their relative efficacy compared to conventional medical management in PCO [39]. These trials have addressed critical questions regarding the success rates, safety profiles, and overall impact of various endovascular techniques on patient outcomes.

This section will provide an overview of the key studies that have contributed to the understanding of BAO treatment. By examining these trials, we aim to clarify the effectiveness of different approaches, identify areas of consensus and controversy, and guide future research directions on managing this challenging condition.

5.1 BEST Trial

5.1.1 Background

The BEST Trial (Basilar Artery Occlusion: Endovascular vs. Standard Therapy) [40],[2],[41],[42] was a randomized clinical trial aimed at evaluating the efficacy of EVT compared to conventional medical management in patients with BAO. The study was conducted between 2015 and 2017 to address the gaps in BAO treatment options by comparing EVT with standard medical care. The study focused on patients presenting within 8 hours of symptom onset and had a primary endpoint like the BASICS trial [40],[43],[2],[41] , assessing the proportion of patients achieving a favorable primary outcome, defined as a modified Rankin Scale score of 3 or less at 90 days. The trial faced early termination due to high crossover rates and a significant drop in participant enrollment.

5.1.2 Design and Methods

The BEST Trial was designed as a randomized controlled trial comparing EVT with medical management. Originally planned to enroll 288 participants, the trial was terminated early after enrolling only 131 patients. This early termination was partly due to a high crossover rate, where 22% of patients initially assigned to the control group (medical management) switched to receive EVT. The trial employed an intention-to-treat analysis to evaluate outcomes, though per-protocol and as-treated analyses were also conducted to assess the effects of EVT more specifically.

Intravenous thrombolysis (IVT) was administered to 27% of the control group and 32% of the EVT group. The etiology of BAO in half of the patient cohort was attributed to atherosclerosis.

5.1.3 Results

The intention-to-treat analysis of the BEST Trial revealed no significant difference in the primary outcome between the EVT and medical management groups. Specifically, 42% of patients in the EVT group and 32% in the medical management group achieved a favorable outcome (modified Rankin Scale score ≤3), with an adjusted odds ratio of 1.74 (95% CI, 0.81–3.74). However, per-protocol and as-treated analyses demonstrated better outcomes for those receiving EVT, suggesting that patients who received endovascular therapy had improved results compared to those who only received medical management. Despite these findings, there were similar mortality rates, 33% in EVT vs 38% in the medical management group. Between the two groups, though, the EVT group had a higher rate of symptomatic intracranial hemorrhage (sICH). The trial's high crossover rate and early termination highlight the challenges and complexities in assessing the efficacy of different treatment approaches for BAO.

5.2 BASIC Trial

5.2.1 Background

The BASICS (Basilar Artery International Cooperation Study) Trial [40],[43],[2],[41],[44]was an international randomized clinical trial designed to evaluate the efficacy of endovascular therapy (EVT) compared to best medical management for patients with basilar artery occlusion (BAO). The trial was conducted from 2011 to 2019 to determine whether EVT could offer superior functional outcomes and survival benefits over conventional treatment methods. The study enrolled patients presenting within 6 hours of symptom onset and initially focused on those with a National Institutes of Health Stroke Scale (NIHSS) score of 10 or higher. Due to slow enrollment, the trial protocol was adjusted to include patients with a wider range of NIHSS scores. The primary outcome measure was the proportion of patients achieving a favorable functional outcome, defined as a modified Rankin Scale score of 0-3 at 90 days.

5.2.2 Design and Methods

The BASICS Trial was a multi-center, randomized controlled trial comparing EVT with best medical management for BAO patients. A total of 300 patients were enrolled, with 154 assigned to the EVT group and 146 to the medical management group. Intravenous thrombolysis (IVT) was administered to 78.6% of patients in the EVT group and 79.5% in the medical management group. The trial faced challenges, including slow recruitment and high treatment rates outside the trial protocol, with 29.2% of patients receiving endovascular therapy despite being assigned to the medical management group. Methodological adjustments during the trial led to the inclusion of patients with milder strokes (NIHSS < 10), potentially affecting the assessment of EVT efficacy. The trial also noted an imbalance in the presence of atrial fibrillation, with 29% in the EVT group compared to 15% in the medical management group. A notable feature of the trial was its low crossover rate of 3.33%.

5.2.3 Results

The BASICS Trial found no significant difference in the primary outcome between the EVT and medical management groups. Specifically, 44% of patients in the EVT group and 38% in the medical management group achieved a favorable functional outcome (modified Rankin Scale score 0-3), with a relative risk of 1.2 (95% CI 0.92–1.50). Despite the numerical improvement in functional outcomes (6.5% absolute risk reduction) and lower mortality (4.9% absolute risk reduction) in the EVT group, these differences did not reach statistical significance. Symptomatic intracranial hemorrhage (sICH) occurred in 4.5% of the EVT group compared to 0.7% in the medical management group. Mortality rates at 90 days were 38.3% in the EVT group and 43.2% in the medical management group, with a relative risk of 0.87 (95% CI 0.68–1.12). Subgroup analysis revealed a potential benefit in the higher severity cohort (NIHSS ≥10), with 38.7% achieving a good clinical outcome in the EVT group versus 26.5% in the medical management group, although this analysis lacked statistical power. Changes in patient criteria, treatment imbalances, and methodological issues complicated the trial's interpretation.

5.3 BAOCHE Trial

5.3.1 Background

The BAOCHE (Basilar Artery Occlusion Chinese Endovascular) Trial [45], [41], [46], [3] was designed to evaluate the efficacy of endovascular therapy (EVT) for basilar artery occlusion (BAO) in patients who presented late, specifically between 6 to 24 hours after symptom onset. Conducted between 2016 and 2022, this trial targeted a patient population typically ineligible for intravenous thrombolysis or had not achieved successful recanalization with initial treatments. The trial's objective was to determine whether EVT could improve outcomes in this challenging cohort. Due to promising early results, the trial was terminated early following a planned interim analysis.

5.3.2 Design and Methods

The BAOCHE Trial was an international randomized controlled trial focusing on late presenters with BAO. Initially, the trial aimed to enroll 318 patients, but it was stopped early after 217 participants were enrolled due to significant differences in primary outcomes observed in the interim analysis. Patients were randomized to receive EVT or best medical management. The trial included individuals with an NIHSS score of 6 or higher, reflecting moderate to severe strokes. EVT was compared to standard medical management, which typically included supportive care and anticoagulation therapy. The primary endpoint was the rate of favorable functional outcomes, measured by the modified Rankin Scale (mRS) score of 0–3 at 90 days.

5.3.3 Results

The BAOCHE Trial demonstrated that patients receiving EVT had a higher rate of favorable functional outcomes, with 46.4% of EVT patients achieving an mRS score of 0–3 compared to 24.3% in the medical management group. Additionally, EVT was associated with a lower 90-day mortality rate. However, this benefit came with a trade-off, as the EVT group experienced a higher incidence of symptomatic intracranial hemorrhage (sICH), with rates of 5.9% compared to 1.1% in the medical management group. These findings suggest that EVT may be an effective treatment option for acute BAO, potentially shifting management practices. Nevertheless, the higher rate of sICH warrants caution, and further research is needed to understand the treatment's efficacy and safety fully.

5.4 ATTENTION Trial

5.4.1 Background

The ATTENTION Trial [2], [42], [46], [3] was designed to address the ongoing debate regarding the efficacy of endovascular thrombectomy (EVT) in the management of acute basilar artery occlusion (BAO). Previous studies, including the BEST and BASICS trials, had provided mixed results, with some suggesting potential benefits of EVT while others showed inconclusive or neutral outcomes. The ATTENTION Trial aimed to clarify these uncertainties by comparing EVT combined with best medical care against best medical care alone in a well-defined patient population.

5.4.2 Design and Methods

The ATTENTION Trial was a multicenter, prospective, randomized, open-label study conducted across 36 centers in China and conducted between 2021 and 2022. It enrolled patients who presented with moderate-to-severe strokes resulting from BAO within a 12-hour window from symptom onset. The trial aimed to evaluate the effectiveness of EVT in addition to best medical care compared to best medical care alone. Eligibility criteria included patients with a National Institutes of Health Stroke Scale (NIHSS) score of at least 10 and confirmed basilar-artery occlusion via neuroimaging. Exclusion criteria included pre-stroke disability scores, intracranial hemorrhage on imaging, or insufficiently high PC-ASPECTS scores. Patients were randomly assigned in a 2:1 ratio to receive either EVT alongside best medical care or best medical care alone. The EVT group underwent various interventional treatments based on the treating team's discretion, including stent retrievers, thromboaspiration, balloon angioplasty, and stent deployment. General anesthesia was used in approximately 56% of these procedures, with adjunct procedures performed as needed. The primary outcome was a modified Rankin Scale (mRS) score of 0 to 3 at 90 days, indicating a favorable functional outcome. Secondary outcomes included detailed assessments of functional status, quality of life measures, and safety evaluations, with all outcomes assessed via structured telephone interviews by blinded neurologists or nurses and reviewed by a central imaging laboratory.

5.4.3 Results

The ATTENTION Trial demonstrated that patients receiving EVT, in addition to best medical care, had significantly better functional outcomes at 90 days compared to those receiving only best medical care. Specifically, 46.0% of patients in the EVT group achieved a favorable mRS score of 0 to 3, compared to 22.8% in the medical management group. The proportion of patients achieving an mRS score of 0 to 2 was also higher in the EVT group (33.2% vs. 10.5%). In terms of mortality, the EVT group experienced a lower rate at 36.7% compared to 55.2% in the medical management group. However, the EVT group had a higher incidence of symptomatic intracranial hemorrhage (5.3% vs. 0%). These findings suggest that EVT can significantly improve functional outcomes and reduce mortality in patients with acute BAO, although it is associated with a higher risk of symptomatic intracranial hemorrhage. The results underscore the need for further research to fully understand the balance between the benefits and risks of EVT in this patient population.

Characteristics of included trial.

	BASICS [4]	BEST [3]	ATTENTION [5]	BAOCHE [6]
Countries	Europe and Brazil	China	China	China
Study duration	2011–2019	2015–2017	2021–2022	2016–2021
Inclusion criteria	Onset < 6 h, Basilar artery occlusion confirmed by CTA/MRA, NIHSS ≥ 10, (age >85y, NIHSS<10 allowed after 2015)	Onset < 8h, BA and V4 occlusion by CTA/MRA/DSA, premorbid mRS 0–2, age>18y	Onset ⟨12 h, BA occlusion confirmed by CTA/MRA/DSA, NIHSS ≥ 10, pc-ASPECT ⟩ 8 (age > 80y), pc-ASPECT > 6 (age <80y) Premorbid mRS:0–2 if age <80y, 0 if age > 80y	6–24 h, CTA/MRA/DSA confirm BA, bilateral V4 occlusion, age 18~80y, NIHSS ≥ 6, pc-ASPECT ≥6, mid-pons index ≤ 2, premorbid mRS ≤ 1
Comparison	EVT vs BMM	EVT vs BMM	EVT vs BMM	EVT vs BMM
Age, years	67	65	67	64
Sample size (men)	300 (65%)	131 (76%)	340 (68%)	217 (73%)
Baseline NIHSS	22	32	24	20
Baseline pc-ASPECTS	10	8	9	8
IVT	121 (79%)	18(27%)	69 (30%)	15 (14%)
Medical history				
Hypertension	93 (60%)	45(68%)	162 (72%)	90(82%)
AF	44 (29%)	18(27%)	45(20%)	14(13%)
smoking	64 (61%)	22(33%)	62 (27%)	34 (32%)
Dyslipidemia	43 (32%)	3 (5%)	61 (27%)	4 (4%)
DM	32 (22%)	10 (15%)	48 (21%)	30 (27%)
Etiology				
Embolic	51 (35%)	14 (21%)	46 (20%)	11 (10%)
ICAD	53 (36%)	37 (56%)	90 (40%)	75 (68%)
Onset to reperfusion, minutes	N/A	400 (269–526)	414 (288–528)	790 (626–1000)
Crossover rates				
EVT to BMM	2%	5%	1%	1%
BMM to EVT	5%	22%	3%	4%
Device used in EVT group				
2nd generation Stent retriever	53/118 (45%)	64/77 (83%)	Only stent retriever:11/226 (5%)	103/110 (94%)
Suction	58/118 (49%)	N/A	Only aspiration:77/226 (34%) Combined technique:110/226 (49%)	3/110 (3%)
PTA	30/138 (22%)	3/77 (4%)	PTA with or without stenting in intracranial:88/226 (39%)	40 (36%)
stenting	23/137(17%)	20/77 (26%)	PTA with or without stenting in extracranial:18/226 (8%)	41 (37%)
TICI 2b or 3 in EVT arm	63/88 (72%)	45/63 (71%)	208/223 (93%)	89/101 (88%)
sICH definition	Heidelberg bleeding classification	ECASS-II criteria	SIT-MOST criteria	SIT-MOST criteria

Table 1: Comparison of major trials on basilar artery occlusion treatment. Acronyms: BASICS = Basilar Artery International Cooperation Study, BEST = Basilar Artery Occlusion Endovascular Intervention versus Standard Medical Treatment, ATTENTION = Endovascular Treatment for Acute Basilar Artery Occlusion, BAOCHE = Basilar Artery Occlusion Chinese Endovascular. Data from Lin et al., 2023."

5.5 RESCUE-RE Trial

5.5.1 Background

The RESCUE-RE (Registration Study for Critical Care of Acute Ischemic Stroke after Recanalization) Trial [47] is an ongoing, nationwide, prospective, observational cohort study conducted in China. The trial focuses on patients who have experienced acute ischemic stroke (AIS) with large vessel occlusion (LVO) and have undergone endovascular treatment (EVT) at comprehensive stroke centers. Initiated in July 2018 and running through October 2020, the RESCUE-RE Trial aims to evaluate the efficacy and safety of EVT specifically for acute ischemic stroke due to basilar artery occlusion (BAO). It compares direct EVT (DEVT) with a combination of intravenous thrombolysis followed by EVT (IVT+EVT).

5.5.2 Design and Methods

This study is a prospective cohort trial conducted at 18 comprehensive stroke centers across China. Patients included in the study were those over 18 years old who experienced AIS and had documented LVO in the basilar artery, with treatment administered within a 4.5-hour window for intravenous thrombolysis where applicable. The trial adhered to observational study epidemiology reporting guidelines. Patients were required to have a prestroke modified Rankin Scale (mRS) score of ≤2 and were followed for three months. Data collection involved comprehensive assessments of demographics, clinical variables, and outcomes, with imaging reviewed by blinded radiologists. EVT procedures included thrombectomy, aspiration, angioplasty, stent implantation, and their combinations. The primary outcome was functional independence, defined as an mRS score of 0–2 at 90 days. Secondary outcomes included mortality, successful reperfusion, reocclusion, and the incidence of symptomatic intracranial hemorrhage (sICH).

5.5.3 Results

Out of the 310 patients analyzed, 241 (78%) underwent DEVT, while 69 (22%) received IVT+EVT. The primary outcome analysis indicated that fewer patients in the DEVT group achieved an mRS score of 0–2 at 90 days compared to those in the IVT+EVT group after adjusting for potential confounders. Despite this, the difference in mortality rates between the groups was not statistically significant. Subgroup analyses revealed that patients with a baseline NIHSS score of 10-21 had better 90-day functional outcomes in the IVT+EVT group. Other demographic and clinical subgroup analyses showed trends but no statistically significant differences. The study's findings were further contextualized through a meta-analysis, confirming a significant positive correlation between receiving IVT before EVT and achieving functional independence. However, there was substantial heterogeneity across the studies included in the meta-analysis. The RESCUE-RE Trial underscores the potential benefits of bridging therapy with IVT followed by EVT over direct EVT alone, suggesting that such an approach may enhance functional outcomes for patients with AIS due to BAO. It also highlights the need for personalized treatment strategies based on individual patient characteristics and stroke severity.

5.6 BASILAR Trial

5.6.1 Background

The BASILAR (Endovascular Therapy for Acute Basilar Artery Occlusion) study [48] is a nonrandomized prospective registry that examined the efficacy of endovascular treatment (EVT) in patients with acute basilar artery occlusion (BAO). Conducted across 47 comprehensive stroke centers in China, the trial enrolled patients between January 2014 and May 2019. The primary aim was to compare the outcomes of patients treated with EVT in addition to standard medical therapy versus those treated with standard medical therapy alone for acute BAO within 24 hours of symptom onset.

5.6.2 Design and Methods

The BASILAR study included a cohort of 829 patients, of whom 647 received EVT plus standard medical therapy and 182 received standard medical treatment alone. All patients had an acute BAO within 24 hours of their last known well time. Importantly, there was no significant difference in the median National Institutes of Health Stroke Scale (NIHSS) scores between the two groups (27 vs. 26.5). The primary outcome measured was functional independence, defined as a modified Rankin Scale (mRS) score of 0–2 at 90 days. Secondary outcomes included 90-day mortality rates and the incidence of symptomatic intracranial hemorrhage (sICH). Additionally, a subgroup analysis was conducted to assess the effect of the baseline posterior circulation Acute Stroke Prognosis Early Computed Tomography Score (pc-ASPECTS) on the efficacy of EVT.

5.6.3 Results

The BASILAR trial found that patients in the EVT group had significantly better outcomes compared to those receiving standard medical therapy alone. The rate of favorable outcomes (mRS 0–2 at 90 days) was 27.4% in the EVT group compared to 7.1% in the medical therapy group ($p < 0.001$). The EVT group also had a significantly lower 90-day mortality rate (adjusted odds ratio [OR] 2.93; 95% confidence interval [CI] 1.95–4.40; $p < 0.001$), although they experienced a higher rate of sICH (7.1% vs. 0.5%; $p < 0.001$). The number needed to treat (NNT) was 4.4, indicating that 4.4 patients needed to be treated with EVT for one additional patient to achieve the ability to walk unassisted. Subgroup analysis further revealed that patients with a baseline pc-ASPECTS score of ≥8 benefitted significantly more from EVT than those with lower scores.

5.7 ENDSTROKE Trial

5.7.1 Background

The ENDOSTROKE trial [49] is an investigator-initiated, multicenter registry focused on evaluating the clinical and procedural factors associated with outcomes äand recanalization in patients undergoing endovascular treatment (EVT) for basilar artery (BA) occlusion. Given the variability in stroke severity and response to treatment, this study aimed to better understand the predictors of successful outcomes and recanalization in this specific patient population.

5.7.2 Design and Methods

The ENDOSTROKE registry included 148 consecutive patients with confirmed BA occlusion, with 59% of the participants receiving intravenous thrombolysis prior to EVT. Recanalization was defined using the Thrombolysis in Cerebral Infarction (TICI) score, with successful recanalization indicated by a TICI score of 2b–3. The collateral status was assessed using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology grading system, with imaging data reviewed by a blinded core laboratory. Clinical outcomes were measured using the modified Rankin Scale (mRS), with good outcomes defined as an mRS score of 0–2, and moderate outcomes as mRS 0–3. Follow-up assessments were conducted at a median of 120 days post-procedure. Key variables such as age, hypertension, initial stroke severity, collateral status, and pretreatment imaging were analyzed to identify predictors of both recanalization and clinical outcomes.

5.7.3 Results

The trial demonstrated that 34% of patients achieved good clinical outcomes (mRS 0–2), while 42% had moderate outcomes (mRS 0–3). Mortality was reported at 35%. Successful recanalization (TICI 2b–3) was achieved in 79% of cases. Independent predictors of favorable clinical outcomes included stroke severity (as measured by NIHSS), collateral status, and the use of magnetic resonance imaging (MRI) prior to EVT. In multivariate analysis, collateral status and the use of stent retrievers were identified as independent predictors of successful recanalization. However, the study found that successful recanalization alone did not directly predict clinical outcomes, highlighting the importance of other factors, such as stroke severity and collateral circulation, in determining patient prognosis.

6. Controversies and Debates

6.1 Efficacy and Effectiveness

One of the primary controversies regarding BAO treatment is the efficacy of different interventions, especially EVT. Acute BAO leads to severe disability or death in approximately 70% of patients, which makes effective treatment strategies critical [2]. Several trials have investigated the effectiveness of EVT compared to standard medical treatment (SMT), but results have been mixed. Earlier trials, such as the BEST and BASICS trials, failed to show a statistically significant advantage for EVT over SMT despite trends toward more favorable outcomes with EVT. These studies faced poor enrollment and high crossover rates, which introduced bias into the population. More recent trials, such as the ATTENTION and BAOCHE trials, have shown that EVT can significantly improve outcomes for patients with BAO. The ATTENTION trial demonstrated that EVT was associated with better functional outcomes at 90 days, with a higher percentage of patients achieving a modified Rankin Scale (mRS) score of ≤3 (46.0% vs. 22.8%) and a significantly lower risk of mortality (36.7% vs. 55.3%). The BAOCHE trial found that patients treated with EVT had better functional outcomes (mRS 0–3: 46.4% vs. 24.3%) and trends towards lower mortality. In addition to these, the RESCUE-RE trial, an ongoing prospective cohort study in China, adds new evidence. The study compared direct EVT (DEVT) with a combination of intravenous thrombolysis followed by EVT (IVT+EVT). While the trial found that fewer patients in the DEVT group achieved functional independence (mRS 0–2) at 90 days, there was no statistically significant difference in mortality rates. These findings support the possible benefits of a bridging therapy approach, with IVT preceding EVT. The BASILAR trial showed that outcomes in the EVT group were considerably better than in the SMT-only group, with a higher rate of functional independence (27.4% vs. 7.1%) and lower 90-day mortality (adjusted OR 2.93). Importantly, patients with higher posterior circulation Acute Stroke Prognosis Early Computed Tomography Score (pc-ASPECTS) scores (≥8) derived more benefit from EVT. However, sICH was significantly higher in the EVT group (7.1% vs 0.5%), which is essential to consider. The ENDOSTROKE trial added further insights by highlighting that successful recanalization (TICI 2b–3) does not necessarily predict clinical outcomes. Independent predictors of favorable outcomes included stroke severity and collateral status rather than recanalization alone. This trial emphasizes the importance of individualized treatment approaches, where factors beyond recanalization determine patient prognosis. This suggests that EVT may be an effective treatment option for BAO, but the risks and benefits must be carefully weighed, particularly in patients with varying stroke severity and collateral status.

6.2 Patient Selection Criteria

Patient selection remains a crucial factor in the success of EVT for BAO, with ongoing debates about which patients are most likely to benefit from the intervention. Earlier trials like BASICS and BEST struggled with high crossover rates and protocol changes that affected their patient populations. Together with the inclusion of patients with mild strokes, these issues may have contributed to the lack of statistically significant benefits for EVT in these studies. If we compare those findings with the ATTENTION and BAOCHE trials, which excluded patients with milder strokes and strictly adhered to their protocols, it shows more convincing benefits for EVT.
Both trials focused on patients with more severe symptoms (baseline National Institutes of Health Stroke Scale [NIHSS] score ≥10), which may explain their more favorable outcomes. Subgroup analyses of BASICS and BAOCHE also found that patients with NIHSS scores between 10 and 20 benefited more from EVT, while those with scores below or above this range showed less improvement. The RESCUE-RE highlighted the relevance of stroke severity in patient selection, as it showed that patients with a baseline NIHSS score between 10-21 benefited more from bridging therapy (IVT+EVT) compared to direct EVT (DEVT) [2]. This further highlights the importance of assessing the stroke severity as a criterion to decide whether to perform EVT. However, it is important to mention that BEST, ATTENTION, BAOCHE, and BASILAR trials are all conducted in China, so caution is advised when generalizing these findings to non-Chinese populations. Additionally, the BASILAR trial introduced the role of imaging in patient selection, showing that patients with a pc-ASPECTS score of ≥8 had significantly better outcomes with EVT. Similarly, the ENDSTROKE trial demonstrated that collateral circulation and MRI-based assessments could predict better recanalization outcomes, highlighting the need for robust imaging and collateral assessment in selecting EVT candidates. Overall, these findings highlight the importance of comprehensive patient evaluation by combining stroke severity (NIHSS 10-21), imaging characteristics (pc-ASPECTS ≥8), and collateral circulation to identify the patient population that benefits most from EVT. While patients with moderate to severe symptoms seem to benefit most, the role of EVT in patients with milder or more severe strokes remains uncertain. Future studies are needed to refine selection criteria and ensure that EVT is used in the patients who are most likely to benefit.

6.3 Comparative Effectiveness of Mechanical Thrombectomy vs. Other Treatments

The comparative effectiveness of mechanical thrombectomy (MT) versus other treatments, such as intravenous thrombolysis (IVT) or best medical management (SMT), remains a point of debate. Both the BASICS and BEST trials did not demonstrate a significant advantage for endovascular treatment (EVT) over SMT. However, both trials faced limitations, including high crossover rates and protocol changes, which likely influenced their outcomes. In contrast, the ATTENTION and BAOCHE trials highlighted the benefits of EVT, particularly in reducing mortality and improving functional outcomes. A recent meta-analysis of the BASICS, BEST, ATTENTION, and BAOCHE trials [46] confirmed that EVT is associated with improved functional outcomes and reduced mortality compared to SMT. However, the increased risk of symptomatic intracranial hemorrhage (sICH) with EVT remains a critical concern, with a pooled relative risk (RR) for sICH of 7.77 (95% CI, 2.36 to 25.59). The RESCUE-RE trial added further complexity to the debate by comparing direct EVT (DEVT) to IVT, followed by EVT (IVT+EVT). Results showed that patients receiving IVT prior to EVT achieved better functional outcomes (mRS 0–2 at 90 days), particularly in the subgroup with NIHSS scores of 10–21. However, mortality rates did not differ significantly between the DEVT and IVT+EVT groups. These findings suggest that a bridging therapy approach may be advantageous for patients with moderate to severe strokes, though additional randomized controlled trials are necessary to validate this. The BASILAR trial, a nonrandomized prospective registry, provided further support for EVT, showing that patients treated with EVT plus standard medical therapy had significantly better functional outcomes (mRS 0–2 at 90 days) than those treated with medical therapy alone. It also found a lower 90-day mortality rate in the EVT group despite a higher incidence of sICH. Subgroup analysis indicated that patients with a posterior circulation Acute Stroke Prognosis Early Computed Tomography Score (pc-ASPECTS) of ≥8 benefited more from EVT. The ENDOSTROKE trial examined procedural factors influencing EVT outcomes, such as collateral circulation and imaging techniques. While successful recanalization (TICI 2b–3) was achieved in 79% of cases, recanalization alone did not directly predict clinical outcomes. Instead, stroke severity, collateral status, and MRI-based assessments emerged as more critical predictors of prognosis. As thrombectomy techniques continue to evolve, incorporating devices like stent retrievers, aspiration devices, and their combinations, further research is needed to refine treatment strategies. Each device may exhibit varying efficacy in different patient populations, and future studies should aim to identify the most effective approaches tailored to individual patient characteristics, stroke severity, and imaging findings.

7. Emerging Trends and Future Directions

7.1 Ongoing Research

In recent years, significant advances have been made in stroke management, particularly in mechanical thrombectomy and pharmacological interventions. Several ongoing clinical trials are exploring innovative approaches to further improve outcomes in patients with large vessel occlusion (LVO) and basilar artery occlusion (BAO). One of the notable ongoing studies is the CHOICE Trial [50] [51], which investigates the use of adjunct intra-arterial alteplase. The results suggest that this approach may enhance functional outcomes without increasing the risk of symptomatic intracranial hemorrhage (sICH), particularly in patients who have undergone successful reperfusion in anterior LVO strokes. Due to the COVID-19 pandemic, the trial had to be terminated early. Therefore, these findings should be interpreted as preliminary. Similarly, the application of Tenecteplase (TNK) has garnered attention. Intravenous administration of TNK has shown promising results, with higher reperfusion rates and improved functional outcomes compared to alteplase in patients treated with endovascular thrombectomy (EVT) for both anterior and posterior circulation LVOs [50].

Furthermore, intra-arterial TNK administration during EVT appears to be safe and effective, as suggested by the BRETIS-TNK Trial [50],[52] which indicates that TNK may enhance first-pass reperfusion and overall outcomes. A critical trial directly relevant to BAO is the INSIST-IT Trial [50], which focuses on using intra-arterial TNK following successful reperfusion in acute BAO patients treated with EVT. The study aims to determine whether this pharmacological adjunct can further improve outcomes, hypothesizing that TNK could enhance post-reperfusion recovery in this challenging subgroup. The DAWN Trial (Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) [53] demonstrated significant benefits of thrombectomy in patients presenting with acute ischemic stroke between 6 and 24 hours after symptom onset, provided there was a clinical-radiographic mismatch. Similarly, the DEFUSE-3 Trial (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3) [54] showed improved functional outcomes in patients treated with MT within 6 to 16 hours, particularly in those with middle cerebral artery (MCA) or internal carotid artery (ICA) LVOs. Carotid endarterectomy (CEA) remains a key intervention for preventing ischemic strokes due to atherosclerotic disease. The landmark NASCET Trial (North American Symptomatic Carotid Endarterectomy Trial) [55], published in 1991, demonstrated the benefit of CEA in reducing stroke risk in patients with over 70% stenosis following a transient ischemic attack (TIA) or minor stroke. More recently, the CREST Trial [56] (Carotid Revascularization Endarterectomy Versus Stenting Trial) has provided valuable long-term data, suggesting that both CEA and carotid artery stenting

(CAS) are effective in preventing stroke, though CAS may carry higher procedural risks in patients over 70 years of age. The role of dual antiplatelet therapy has also been explored extensively, particularly in high-risk patients with TIA or small ischemic strokes. The CHANCE Trial [57] (Clopidogrel in High-risk Patients With Acute Non-disabling Cerebrovascular Events), conducted in China, demonstrated a reduction in stroke risk at 90 days with the combination of aspirin and clopidogrel compared to aspirin alone, though at a slightly increased risk of bleeding. The POINT Trial [58] (Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke), a multi-center trial conducted across North America, Europe, and other regions, similarly showed the benefit of dual antiplatelet therapy. However, the risk of bleeding was notably higher with a longer treatment duration and higher clopidogrel dose. Pooled analyses of these trials suggest that the benefit of dual antiplatelet therapy is most pronounced within the first 21 days after an ischemic stroke, after which the bleeding risk may outweigh the benefits.

Together, these emerging trends underscore the continuous evolution of stroke management, with ongoing trials offering hope for further advances in patient outcomes. Future research, particularly in the use of pharmacological adjuncts to mechanical thrombectomy and the identification of optimal treatment windows, will likely shape the next generation of stroke care.

8. Conclusion

8.1 Summary of Controversies

The management of basilar artery occlusion (BAO) has been a subject of ongoing debate, reflecting significant controversies in the field. One central issue is the efficacy of endovascular treatment (EVT) compared to standard medical treatment (SMT). Although EVT has demonstrated benefits for anterior circulation strokes, its role in treating BAO remains controversial. Earlier studies, such as the BEST and BASICS trials, failed to show a statistically significant advantage for EVT over SMT. These trials encountered limitations such as high crossover rates and suboptimal patient enrollment, which may have skewed their results.

In contrast, more recent research, including the ATTENTION and BAOCHE trials, suggests that EVT can substantially improve outcomes for BAO patients. The ATTENTION trial highlighted a significant increase in favorable functional outcomes and a reduction in mortality with EVT. At the same time, the BAOCHE trial also reported better functional results and trends toward lower mortality. These studies indicate that EVT may offer substantial benefits, yet the variability in trial results underscores the complexity of its application in BAO.

The debate extends to the timing of interventions as well. The optimal time window for EVT or adjunct therapies, such as intra-arterial thrombolytics, remains debated. Some studies advocate for extended treatment windows, up to 24 hours, while others caution against diminishing returns over time. The RESCUE-RE trial's exploration of direct EVT versus a combination of intravenous thrombolysis followed by EVT adds another layer of complexity. While bridging therapy showed some advantages, the lack of significant differences in mortality rates between the two approaches complicates the decision-making process. Pharmacological adjuncts, such as alteplase and tenecteplase, further contribute to the controversy. Despite their potential to improve outcomes post-thrombectomy, concerns about increased risks of hemorrhage persist. This controversy emphasizes the need for careful assessment of the risks and benefits of these agents in the context of EVT. Patient selection criteria for EVT in BAO also remain under scrutiny. Trials have employed varied selection criteria with differing impacts on outcomes. For instance, the BASILAR trial found that EVT was particularly beneficial for patients with higher posterior circulation Acute Stroke Prognosis Early Computed Tomography Score (pc-ASPECTS) scores. The RESCUE-RE trial highlighted the importance of stroke severity in predicting benefits from EVT, yet generalizing these findings to diverse populations remains challenging.

Overall, the controversies in BAO management reflect a need for further research to refine treatment strategies, optimize patient selection, and determine the most effective use of EVT and adjunct therapies. These debates underscore the complexity of treating BAO and the necessity for continued investigation to improve clinical outcomes.

8.2 Implications for Clinical Practice

The evolving evidence on treating basilar artery occlusion (BAO) has significant implications for clinical practice. Although some trials, such as BEST and BASICS, have not shown definitive benefits of mechanical thrombectomy (EVT) over standard medical treatment (SMT), recent studies like BAOCHE pave the way for broader adoption of EVT in posterior circulation strokes. If ongoing research continues to support its efficacy, EVT could become a more standardized approach for BAO, especially with the possibility of extending treatment windows based on evolving evidence. Considering extended treatment windows for interventions, as evidenced by trials like DAWN and DEFUSE-3 for anterior circulation strokes, may soon influence practices for BAO cases. Advanced imaging techniques, such as perfusion imaging, could play a crucial role in tailoring treatment decisions and identifying patients who could benefit from delayed interventions. This shift towards personalized treatment protocols may improve outcomes for patients with BAO by allowing for a more nuanced approach based on individual clinical and imaging characteristics. Integrating pharmacological adjuncts, including intra-arterial alteplase and tenecteplase (TNK), is another area poised for change. Trials such as CHOICE and INSIST-IT provide valuable insights into these agents' role in enhancing outcomes post-thrombectomy. Clinicians may need to re-evaluate the use of adjunct therapies, potentially incorporating them more widely into treatment regimens while remaining vigilant for potential complications. Moreover, the management of stroke patients, particularly those with BAO, is increasingly becoming a multidisciplinary effort. Effective treatment requires close collaboration among neurologists, interventional radiologists, and intensivists. As treatment protocols evolve and new evidence emerges, a coordinated approach will be essential to optimize patient care and improve outcomes in this complex field.

8.3 Research Gaps and Recommendations

Despite significant advances in the management of basilar artery occlusion (BAO), several important research gaps remain that require further investigation. Current trials predominantly focus on short-term outcomes, such as 90-day modified Rankin Scale (mRS) scores, leaving a critical gap in understanding the long-term quality of life and functional recovery for BAO patients. Research exploring the extended impacts of thrombectomy and adjunct therapies on patients' overall well-being and recovery trajectory is needed to provide a more comprehensive picture of treatment efficacy. Additionally, the optimal use of pharmacological adjuncts in conjunction with mechanical thrombectomy remains unclear. Although trials like CHOICE and INSIST-IT suggest potential benefits of agents such as tenecteplase or alteplase, more data are required to establish these treatments as standard practice. Future studies should focus on determining the best pharmacological strategies tailored to individual patient profiles and specific clinical scenarios. Another area that needs refinement is patient selection criteria for thrombectomy in posterior circulation strokes. Research should aim to enhance the accuracy of advanced imaging techniques to better identify patients who are likely to benefit from interventions, regardless of the time elapsed since symptom onset. This will help create more precise and effective treatment protocols. Equitable access to advanced stroke interventions is also a pressing concern. Studies should investigate how socio-economic factors and geographical disparities impact access to and outcomes from these treatments. Understanding and addressing these disparities will ensure that all patients benefit from the latest advancements in stroke care. Finally, future research should aim to include diverse populations to ensure that treatment protocols are applicable and effective across different demographic and regional contexts. This broader focus will help tailor interventions to meet the needs of a global patient population and may bring more clarity to this endless controversy.

9. References

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