Endovascular thrombectomy for acute ischemic stroke - The evolution of consensus and the absence of agreed-upon definitions

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Emma Hall

LUND
UNIVERSITY

DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD) at the Faculty of Medicine at Lund University to be publicly defended on 24 of April 2026 at 09.00 in Torsten Landberg föreläsningssal, Strålbehandlingshuset, Klinikgatan 5, Lund

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Abstract

Background and aims: This PhD thesis aimed to improve understanding of complications and outcomes after endovascular thrombectomy (EVT) for ischemic stroke by integrating clinical and radiological factors.
Methods: Using nationwide Swedish registry data (EVAS, Riksstroke, and linked health registries), four prospective registry-based observational studies examined (I) hemorrhagic complications in relation to occlusion site, (II) temporal trends in comorbidity burden and associated outcomes, (III) EVT results in medium vessel occlusions (MeVO) across comorbidity strata, and (IV) differences between intracranial subterminal Internal Carotid Artery (ICA-I) and ICA terminus (ICA-T) occlusions.
Results: Between 2015–2022, EVT volume increased substantially. Paper I (n=3153) showed that severe hemorrhagic complications after EVT were uncommon but differed by occlusion location: symptomatic intracranial hemorrhages were most frequent in intracranial ICA occlusions, whereas isolated subarachnoid hemorrhage occurred more often after EVT in M2 and more distal occlusions and was predominantly non-symptomatic. This supports occlusion-specific risk stratification and tailored post-procedural monitoring. In Paper II (n=4735), comorbidity burden increased over time and was strongly associated with worse functional outcome and higher mortality. Nevertheless, successful recanalization rates were similar across comorbidity groups and consistently associated with improved outcomes. These findings underscore the need to prevent post-procedural complications and indicate that multimorbidity should not be considered an absolute contraindication to EVT. Paper III (n=983) found that, among patients with medium vessel occlusions, successful EVT was associated with early neurological improvement and favorable 90-day functional outcomes even in patients with very severe comorbidity burden, without higher rate of symptomatic intracranial hemorrhage. Paper IV (n=1013) demonstrated that ICA-I occlusions were charatarized by greater heterogeneity in clinical severity and infarct patterns and were more often misclassified on initial imaging, contributing to treatment delays.
Conclusion: In routine clinical practice, EVT was associated with favorable outcomes across a broad patient spectrum. The findings support individualized patient selection and highlight the importance of optimizing peri- and post-procedural management to maximize benefit and minimize complications.

Key words: Endovascular thrombectomy, ischemic stroke, outcome, comorbidity, occlusion site, hemorrhage

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Do you ever look at someone and wonder,
'What is going on inside their head? '

Joy from Inside out

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List of papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals. The four papers are appended in the end of the thesis.

Paper I

Hall E., Ullberg T., Andsberg G., Wassélius J. Incidence of intracranial hemorrhagic complications after anterior circulation endovascular thrombectomy in relation to occlusion site: a nationwide register study. *J. Neurointerv Surg.* 2024;16:1088-1093.

Paper II

Hall E., Hansen B.M., Pihlsgård M., Esbjörnsson M., Norrving B., Ullberg T., Wassélius J. The impact of comorbidity burden on outcomes following endovascular thrombectomy for acute ischemic stroke - a nationwide prospective observational study. *Eur. Stroke J.* Published online. 2026;11(1).

Paper III

Hall E., Wassélius J., Pihlsgård M., Ullberg T., Hansen B.M. Influence of comorbidity on endovascular thrombectomy outcomes for medium-vessel occlusion stroke: a nationwide prospective observational study. *Stroke: Vascular and Interventional Neurology.* 2025:5:e001607.

Paper IV

Hall E., Hansen B.M., Szolics A., Ullberg T., Wassélius J. Endovascular thrombectomy for subterminus internal carotid artery (ICA-I) occlusions: clinical and radiological heterogeneity in a nationwide registry. Manuscript.

Additional original publications not included in this dissertation

Wassélius J., **Hall E.**, Ramgren B., Andersson T., Ullberg T. Procedural factors associated with successful recanalization in patients with acute ischemic stroke treated with endovascular thrombectomy - a nationwide register-based observational study. *Interv. Neuroradiol.* Published online April 22, 2024. DOI:10.1177/15910199241248268

Hansen B.M, **Hall E.**, Ramgren B., Ullberg T., Wassélius J. Outcomes After Thrombectomy for Primary and Secondary Medium Vessel MCA Occlusions: a Nationwide Registry Study. *Clin. Neuroradiol.* 2025;35(1):541-549.

Hansen B.M, **Hall E.**, Szolics A., Andersson T., Wassélius J. Balloon Guide Catheter Use and Outcomes After Endovascular Thrombectomy for Ischemic Stroke Due to Large Vessel Occlusions. *Clin. Neuroradiol.* Published online September 22, 2025. DOI:10.1007/s00062-025-01570-z

Landström L., **Hall E.**, Hansen B.M., Wassélius J. Fusion imaging in endovascular thrombectomy for acute ischemic stroke. *Stroke: Vascular and Interventional Neurology.* 2025:5(4): e001636. DOI:10.1161/SVIN.124.001636

Wassélius J., **Hall E.**, Szolics A., Arnberg F., Radhi H., von Euler M., Wester P., Ullberg T., Cronberg T., Ennab Vogel N., Esbjörnsson M., Jonsson F., Andersson T., Norrving B., Hansen B.M. Large regional variation in endovascular thrombectomy rates for acute ischemic stroke in Sweden. *Eur. Stroke J.* Published online June 16, 2025. DOI:10.1177/23969873251347098

Drake M., **Hall E.**, Ramgren B., Hansen B.M., Wassélius J. Volume and attenuation patterns of chronic subdural hematoma: an annotated patient cohort of 257 patients with interrater reliability. *Tomography*. 2025;11(12):141. Published online: https://doi.org/10.3390/tomography11120141.

Hall E., Hansen BM. *"Cerebrovascular Tetraptyc*h". *Stroke: Vascular and Interventional Neurology.* 2026;6:e002124. DOI: 10.1161/SVIN.125.002124

Abbreviations

ACA = Anterior Cerebral Artery
ASPECTS = Alberta Stroke Program Early CT Score
CCI = Charlson Comorbidity Index
CTA = Computed Tomography Angiography
CTP = Computed Tomography Perfusion
DMVO = Distal Medium Vessel Occlusion
DWI = Diffusion-Weighted MRI
EVAS = the registry of EndoVAscular treatment of Stroke
EVT = Endovascular Thrombectomy
FLAIR = Fluid-Attenuated Inversion Recovery
HI = Hemorrhagic Infarct
HR = Hazard Ratio
ICA = Internal Carotid Artery
ICH = Intracranial Hemorrhage
LVO = Large Vessel Occlusion
MCA = Middle Cerebral Artery
MeVO = Medium Vessel Occlusion
MRI = Magnetic Resonance Imaging
mRS = modified Rankin Scale
NCCT = Non-Contrast Computed Tomography
NIHSS = National Institutes of Health Stroke Scale
OR = Odds Ratio
PCA = Posterior Cerebral Artery
PH = Parenchymal Hemorrhage
RCT = Randomized Controlled Trial
SAH = Subarachnoid Hemorrhage
sICH = symptomatic Intracranial Hemorrhage
TICI = Thrombolysis in Cerebral Infarction

Definitions

Global age-standardized ratio: A rate adjusted to a standard age distribution so populations with different age structures can be compared fairly.

Hazard regression: A statistical method (e.g., Cox regression) used to analyze how different factors affect the risk of an event happening over time.

Hazard ratio (HR): A measure comparing event risk over time between two groups. HR = 1 means no difference.

HERMES Collaboration: A pooled, patient-level meta-analysis with combined data from several landmark randomized trials of endovascular thrombectomy for acute ischemic stroke caused by large-vessel occlusion.

Incidence: The number of new cases of an event in a population during a specific time.

Incidence rate: The speed at which new cases occur.

Kappa: A measure of agreement between two raters beyond what would be expected by chance.

Observational study: A study where researchers do not assign treatments/exposures but instead observe what happens naturally.

Odds: The chance of an event happening divided by the chance of it not happening: $p/(1-p)$.

Odds ratio (OR): comparison of odds between two groups where OR = 1 means no difference.

Penumbra: brain tissue that is damaged due to reduced blood flow but still potentially salvageable if treated quickly.

Prospective study: A study that follows participants forward in time to observe outcomes.

Randomized controlled study: A study where participants are randomly assigned to treatment versus control to test effects with minimal bias.

Introduction

Acute ischemic stroke definition

The historical understanding of stroke and the discovery of human brain vessels is a narrative shaped by the contributions of many individuals over the centuries. Throughout history, numerous theories have emerged regarding the nature of strokes. For instance, the ancient Greeks attributed strokes to imbalances in bodily fluids (blood, phlegm, black bile and yellow bile) leading to a blockage of vital spirits (1). Other explanations included demonic influence, divine punishment, as well as interpretations based on faith and astrology.

Early knowledge about human neuroanatomy was limited. Nevertheless, individuals like Hippocrates made significant clinical observations, and described the correlation between damage to specific brain areas and various neurological symptoms. Later, Galen of Pergamon deepened the anatomical understanding by categorizing brain structures and was one of the first to describe the ventricular system (1). The Renaissance marked a turning point in the understanding of human neuroanatomy. In the 17th and 18th centuries, scientists such as Johann Jakob Wepfer and Thomas Willis provided physiological explanations for stroke, emphasizing the role of the blood flow (1, 2).

Today, we understand that strokes are caused by diseases affecting the blood vessels in the brain, and the World Health Organization defines stroke as:

> "Rapidly developed clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin" (3).

Ischemic stroke occurs when an obstruction in an intracranial blood vessel leads to restricted blood flow and consequently a lack of oxygen and glucose in specific areas of the brain. If the obstruction persists, the resulting hypoxia will lead to irreversible brain damage, with varying degrees of severity depending on the location of the occlusion and the area of affected tissue.

Stroke epidemiology and risk factors

Stroke is one of the leading causes of mortality and long-term disability worldwide (4), and its global burden has continued to grow steadily over the past three decades (4, 5). Ischemic stroke is the most common stroke subtype (6) and is usually caused by atherosclerosis, small-vessel disease, or cardioembolic events such as atrial fibrillation (7). Up to 90% of the overall stroke risk can be attributed to factors such as hypertension, physical inactivity, unhealthy diet, obesity, smoking, diabetes, dyslipidemia, psychosocial stress, and excessive alcohol consumption (8). Among these, elevated blood pressure is the single most important risk factor, followed by lifestyle-related factors including smoking, poor diet, and physical inactivity (8). Consequently, effective stroke prevention relies on optimal management of hypertension and atrial fibrillation, alongside lifestyle modification and appropriate treatment of metabolic risk factors, strategies that also reduce the risk of other cardiovascular diseases.

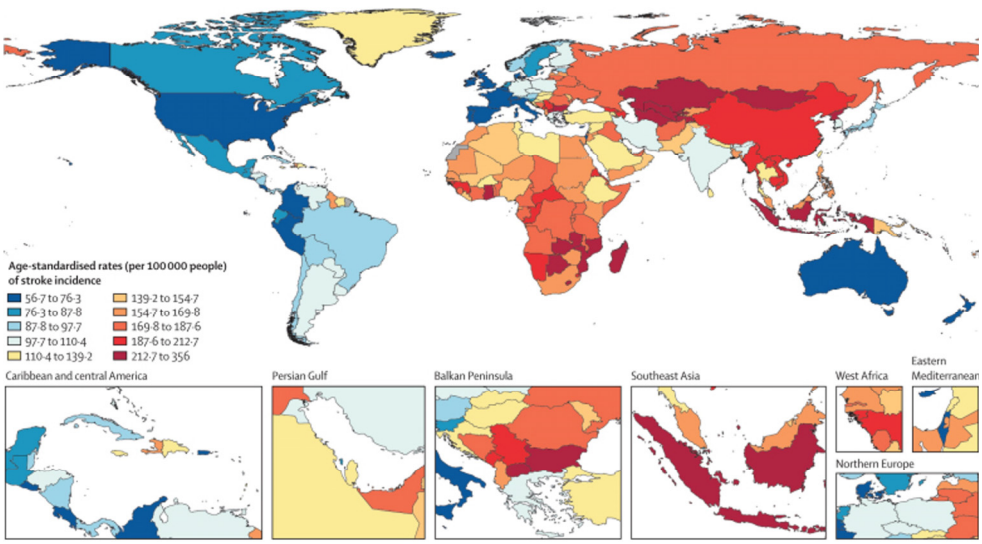

Figure 1. Global age-standardised rates (per 100 000 people) of stroke incidence (2021). Figure from GBD 2021 Stroke Risk Factor Collaborators 2024 (4), an open access article distributed under the terms of CC BY 4.0 License.

As shown in Figure 1, the global incidence of stroke exhibits substantial regional variation, with the highest age-standardized rates observed in East and Central Asia and sub-Saharan Africa, and the lowest in high-income regions such as North America and Europe (4). Between 1990 and 2019, annual deaths from ischemic stroke increased from 2.04 to 3.29 million and are projected to reach 4.90 million by 2030 (9). Despite progress in reducing some risk factors, such as smoking and

unhealthy diets, the global burden of stroke continues to rise (10), driven by population ageing (4), inadequate prevention strategies (4, 5, 11), and persistent disparities in access to stroke care, with a notable increase in incidence among individuals younger than 70 years (4).

In contrast to global trends, Sweden has experienced a decline in the incidence of acute ischemic stroke over the past decade (Figure 2) (12, 13). This reduction has been partly attributed to increased use of secondary preventive therapies, including anticoagulant treatment for atrial fibrillation and improved population-level management of hypertension (14).

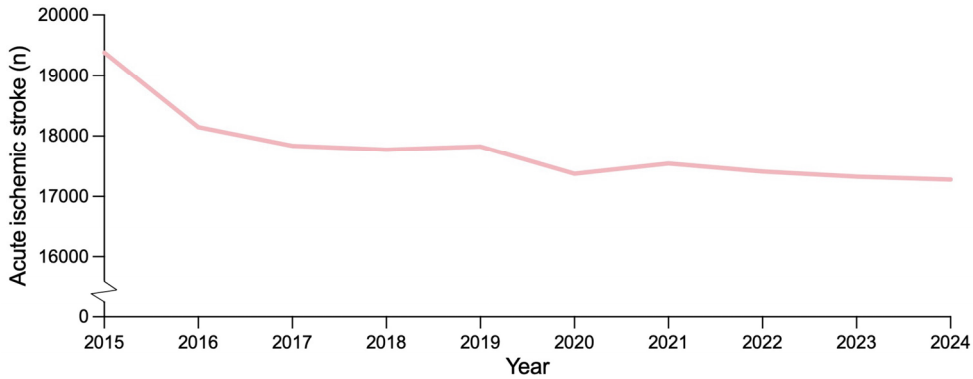

Figure 2. The annual number of acute ischemic strokes in Sweden during 2015 to 2024. Data from the Swedish National Board of Health and Welfare (12).

Anatomy

The Circle of Willis and classification of arteries

The Circle of Willis (Figure 3) is a circular network of arteries located at the base of the brain, serving as a collateral connection between the cerebral hemispheres as well as between the anterior and posterior circulation. The interconnections provide a redundancy in cerebral perfusion by allowing other vessels to compensate if one artery becomes occluded.

The major cerebral arteries include the Internal Carotid Artery (ICA), the Middle Cerebral Artery (MCA), the Anterior Cerebral Artery (ACA), the Basilar Artery, and the Posterior Cerebral Artery (PCA) (Figure 3).

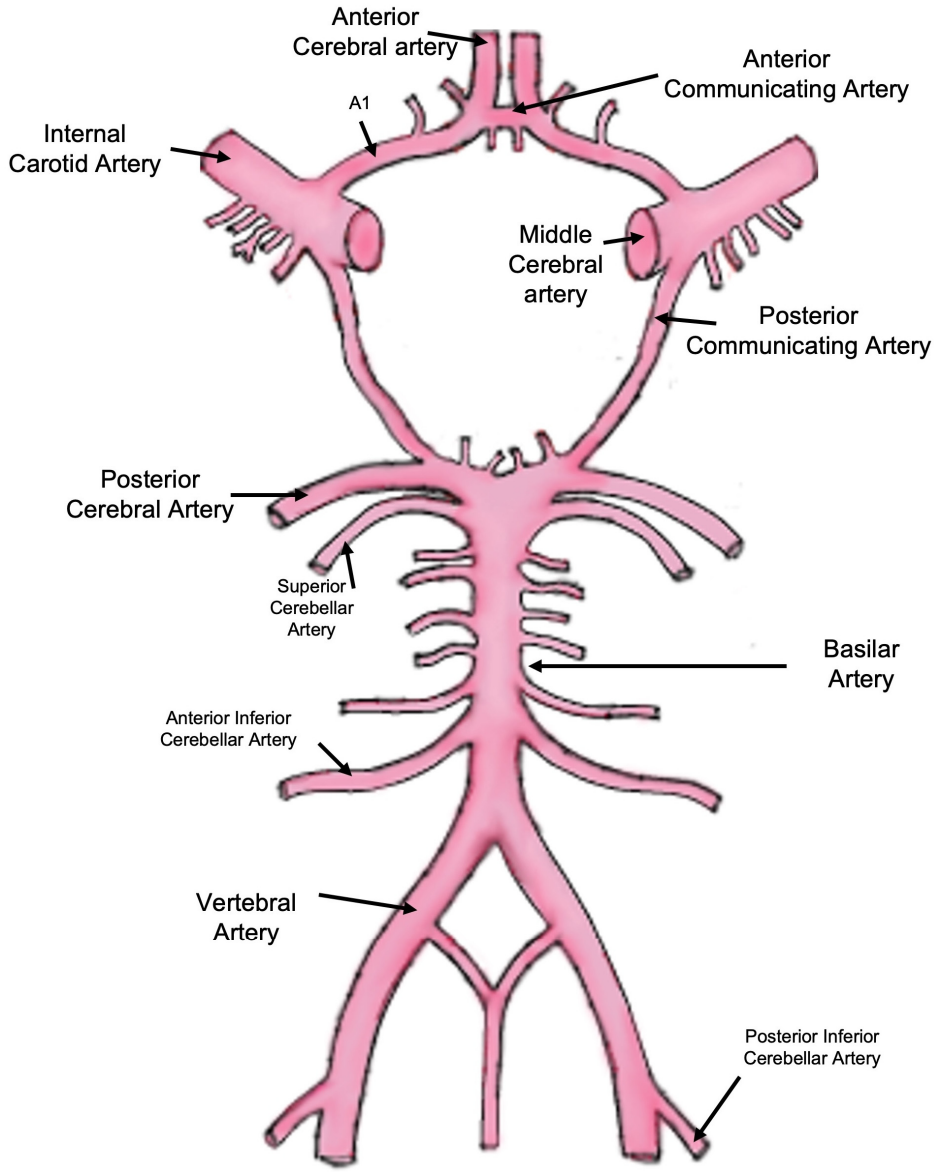

Figure 3. The Circle of Willis. Original illustration by E. Hall.

The MCA segments can be anatomically divided into four main segments: M1 (sphenoidal), M2 (insular), M3 (opercular), and M4 (cortical) (15). They can also be classified based on angulations of the vessel within the Sylvian triangle (16), which can be visualized on sagittal imaging. It is delineated by a straight line drawn parallel to the superior margins of the insular loops, which forms the roof of the

triangle (17). As an alternative to the curvature-based definition, MCA segments may be distinguished by their branching pattern (Figure 4) where the first major bifurcation of the MCA marks the origin of the M2 segments, and the subsequent divisions give rise to the M3 segments and later M4 segments.

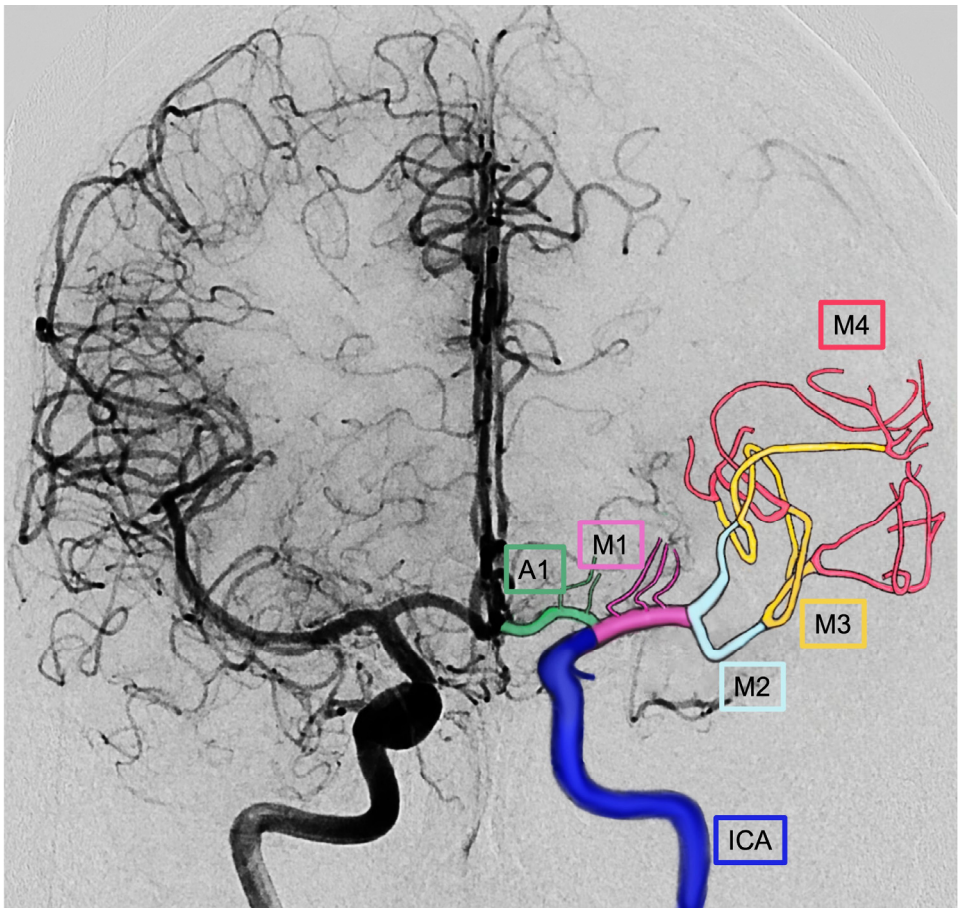

Figure 4. The MCA segments distinguished by their branching pattern. Original illustration by E. Hall.

Anatomical variations

During the complex arteriogenesis, the Circle of Willis can develop a range of anatomical variations that may impair the efficacy of collateral blood flow (18, 19). Examples are illustrated in Figure 5 and include absence or hypoplasia of the A1 segment (1%) or the Anterior Communicating Artery (5%), as well as carotid-vertebrobasilar anastomosis, such as a fetal type PCA (4-29%) where the PCA originates from the anterior circulation (18).

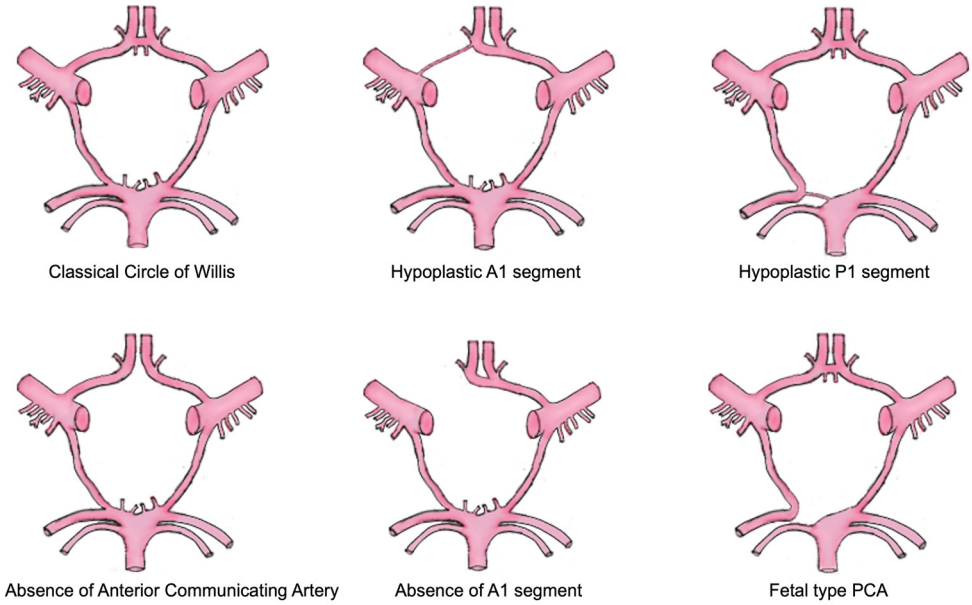

Figure 5. Variations in the Circle of Willis. Original illustration by E. Hall.

Large, Medium and Distal Medium Vessel Occlusions

Vessel occlusions are commonly classified based on the size of the affected vessels. Large Vessel Occlusions (LVOs) refer to occlusions in major intracranial arteries, including the intracranial ICA, the M1 segment of the MCA, the intracranial vertebral arteries, and the Basilar Artery. Medium Vessel Occlusions (MeVOs) can be defined as occlusions in arteries with lumen diameters ranging from 0.8 to 2.0 mm (16) and typically include the M3, A2-A3, and P2-P3. However, the classification of the intermediate segments, particularly the M2, A1, and P1, remains inconsistent due to anatomical variability in vessel diameter and branching patterns (20). For instance, the M2 segment can exhibit bifurcation, trifurcation, tetrafurcation, or even more complex branching patterns, which complicates categorization. The vessel diameters of M2 branches vary considerably, typically from 1.0 mm to 2.1 mm (21). As such, M2 occlusions could sometimes occur in dominant branches with diameters approaching those of M1, and other times in non-dominant branches more closely resembling M3 in size and distribution area.

The term MeVO is often used interchangeably with Distal Medium Vessel Occlusions (DMVOs), though DMVOs typically refers to occlusions in more distal branches within the spectrum of MeVOs (22, 23).

Table 1. Overview of the overlapping size-based classifications of intracranial vessel occlusions

	LVOs	MeVOs	DMVOs
ICA/MCA	ICA, M1, M2	M2, M3, (M4)	M3, M4
ACA	A1	A1-A3	A3
Posterior circulation	Basilar artery, P1, vertebral arteries	P1-P3	P2-P3, PICA, AICA, SCA

LVOs = Large Vessel Occlusions, MeVO = Medium Vessel Occlusions, DMVOs = Distal Medium Vessel Occlusions, ICA = Internal Carotid Artery, MCA = Middle Cerebral Artery, M1, M2, M3, and M4 = M1, M2, M3, and M4 segment of the Middle Cerebral Artery, ACA = Anterior Cerebral Artery, A1, A2, and A3 = A1, A2, and A3 segment of the Anterior Cerebral Artery, P1, P2, and P3 = P1, P2, and P3 segment of the Posterior Cerebral Artery, PICA = Posterior Inferior Cerebellar Artery, AICA = Anterior Inferior Cerebellar Artery, SCA = Superior Cerebellar Artery

Intracranial ICA occlusions

Intracranial ICA occlusions are commonly classified as either ICA-I or ICA-T occlusions (24, 25, 26). ICA-T occlusions (Figure 6A) involve the distal ICA and occludes the origin of the A1 and M1 segments. In contrast, ICA-I occlusions (Figure 6B) involve the intracranial portion of the ICA but terminate proximal to the carotid terminus. Although ICA-I occlusions may obstruct the Posterior Communicating Artery, the Ophthalmic Artery and the Anterior Choroidal Artery, the carotid terminus remains open, allowing collateral flow via the Anterior Communicating Artery and the A1 segments of the ACAs.

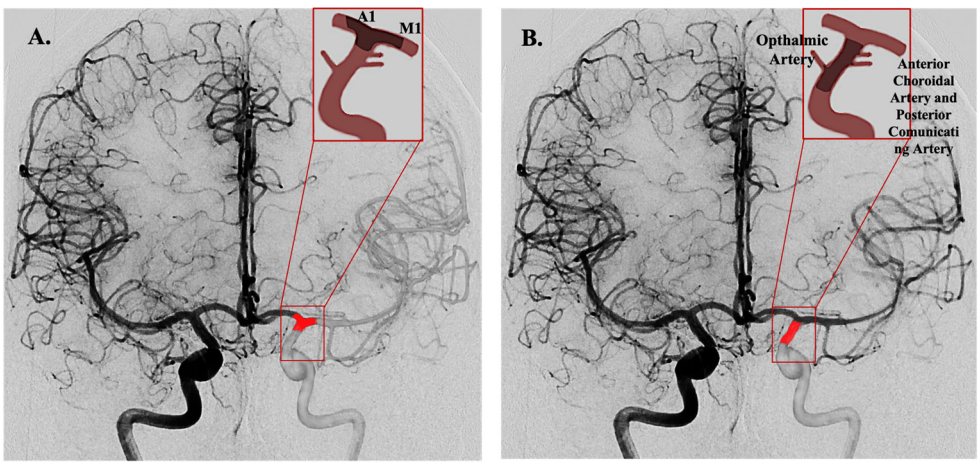

Figure 6. A) T-occlusion with thrombus in the carotid terminus involving the origin of the A1 and M1 segments, B) I-occlusion in distal ICA involving the origin of the Ophthalmic Artery, the Anterior Choroidal Artery and the Posterior Communicating Artery but not the A1 or the M1 segments. Original illustration by E. Hall.

Although both being classified as intracranial ICA occlusions, ICA-I and ICA-T occlusions differ substantially in their collateral flow capacity. Despite these

pathophysiological differences, the two occlusion subtypes are frequently pooled and analyzed as a single entity in clinical studies and together account for approximately 20% of patients undergoing endovascular thrombectomy (EVT) (27, 28). This aggregation may obscure clinically meaningful subtype-specific differences and limits the granularity of current evidence. Consequently, knowledge regarding potential differences in baseline stroke severity, symptom profiles, and radiological presentation between ICA-I and ICA-T occlusions remains limited.

Pathophysiology, collaterals and baseline imaging

Atherosclerosis

Atherosclerosis is a systemic arterial disease and one of the major causes of ischemic stroke. It is initiated by the accumulation of cholesterol and lipoproteins within the arterial intima, which triggers local oxidative stress and inflammatory pathways, promoting recruitment and adhesion of immune cells (29). This process often affects the proximal cervical ICA, and with disease progression, the plaques develop a lipid-rich necrotic core and may evolve into fibroatheromas (29). These unstable lesions are prone to rupture and intraplaque hemorrhage, causing platelet activation and thrombus formation. Subsequent plaque expansion may result in luminal obstruction or distal embolization, ultimately resulting in ischemic stroke.

Intracranial atherosclerotic disease develops through progressive concentric intimal thickening accompanied by lipid accumulation and fibrous tissue formation (30). Intracranial atherosclerotic plaques may cause ischemic stroke through several mechanisms, including in-situ thrombosis, artery-to-artery embolization, critical stenosis resulting in hemodynamic compromise, and occlusion of small penetrating arteries at their origin, a process referred to as branch occlusive disease (30).

Non-atherosclerotic mechanisms of ischemic stroke

Cardioembolic event is the other major cause of ischemic stroke, dominated by atrial fibrillation which is the most common sustained arrhythmia and associated with a fivefold increased risk of ischemic stroke (31). Oral anticoagulation represents the primary strategy for stroke prevention in this population and markedly reduces thromboembolic risk. In addition to cardioembolic sources, other examples of non-atherosclerotic mechanisms of ischemic stroke include small-vessel disease, and structural vascular abnormalities such as carotid-web (32), artery dissection (33), and systemic hypercoagulable conditions due to malignancy (33).

Penumbra and collaterals

Complete interruption of blood flow to a vascular territory leads to deprivation of oxygen and glucose, leading to failure of oxidative metabolism and a shift toward anaerobic metabolism. The ensuing depletion of adenosine triphosphate causes dysfunction of energy-dependent ion pumps characterized by intracellular sodium and water influx, and extracellular potassium efflux (34). The process is highly time-dependent (35), and the ionic imbalance results in cytotoxic edema and disruption of cellular homeostasis, ultimately causing irreversible neuronal injury within minutes.

The pial collaterals are small, thin vessels located along or just beneath the cortical surface. Through anastomotic networks, they interconnect the territories of the major cerebral arteries – the MCA, the PCA, and the ACA. Under normal, non-occluded conditions, pial collaterals are usually neither used nor easily visualized (Figure 7A), since antegrade flows in each territory remain balanced. However, when one of the primary intracranial vessels becomes occluded (Figure 7B-C), these pial collaterals serve as alternative conduits, redirecting blood flow toward the endangered region.

The term *penumbra* refers to ischemic brain tissue with metabolic and ionic imbalances, yet with preserved structural integrity and potential for functional recovery (36). Well-developed pial collateral circulation (Figure 7B) can sustain large parts of the affected territory as a potentially salvageable penumbra for many hours. In contrast, poor pial collaterals (Figure 7C) result in insufficient collateral supply, leading to rapid infarction of the ischemic region.

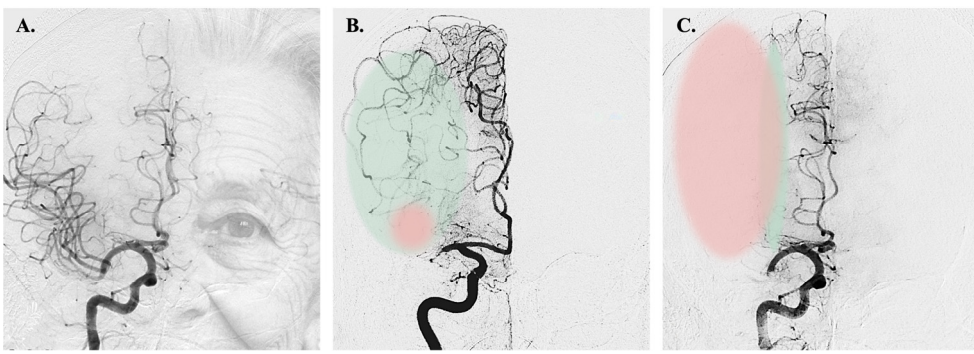

Figure 7. Digital subtraction angiographies illustrating: A) normal physiological conditions, in which the pial collaterals are typically not visible; B) M1 occlusion with well-developed pial collateral circulation, resulting in a substantial region of salvageable penumbra (green filled ellipse); and C) M1 occlusion with insufficient pial collateralization, leading to rapid infarction of a large part of the MCA territory (red filled ellipse).

Non-contrast computed tomography

Although magnetic resonance imaging (MRI) is more sensitive for detecting acute ischemic changes in brain tissue during the first 24 hours after stroke onset (37), non-contrast computed tomography (NCCT) remains the standard initial imaging modality in the acute setting in Sweden. Early ischemic changes are often subtle on NCCT. However, in the later phase of acute cerebral infarction, the extracellular water content increases (ionic edema), which may manifest as areas of hypoattenuation on NCCT (38). Additional early signs include loss of gray-white matter differentiation, and cortical swelling. The primary advantage of NCCT is its rapid acquisition and wide availability, particularly for excluding important differential diagnoses such as intracranial hemorrhage or space-occupying lesions.

Infarct size

Radiologically, infarct size can be estimated by quantifying the volume of ischemic brain tissue identified on NCCT or MRI. Infarct extent correlates closely with the location of the vascular occlusion and the adequacy of collateral circulation (39). Although not universally implemented in routine clinical decision-making, a commonly used method to quantify early ischemic changes is the Alberta Stroke Program Early CT Score (ASPECTS; Table 2, Figure 8), a 10-point scoring system designed to evaluate ischemic regions in the MCA territory (40). Since early ischemic changes can be subtle on NCCT, particularly in the hyperacute phase, ASPECTS may underestimate the true extent of the ischemic core. Nevertheless, ASPECTS has demonstrated strong prognostic value, with lower scores consistently associated with larger infarct volumes and poorer clinical outcomes (41).

Table 2. The Alberta Stroke Program Early CT Score (ASPECTS).

Points*	Description
1	M1: Anterior MCA Cortex
1	M2: MCA cortex lateral to the insular ribbon
1	M3: Posterior MCA cortex
1	M4: Anterior MCA superior territory
1	M5: Lateral MCA superior territory
1	M6: Posterior MCA superior territory
1	I: Insular ribbon
1	IC: Internal capsule
1	L: Lentiform nucleus
1	C: Caudate nucleus

MCA = Middle Cerebral Artery

***The scoring system starts at 10 and deducts one point for each affected region, meaning that a greater extent of early ischemic changes corresponds to a lower ASPECTS.

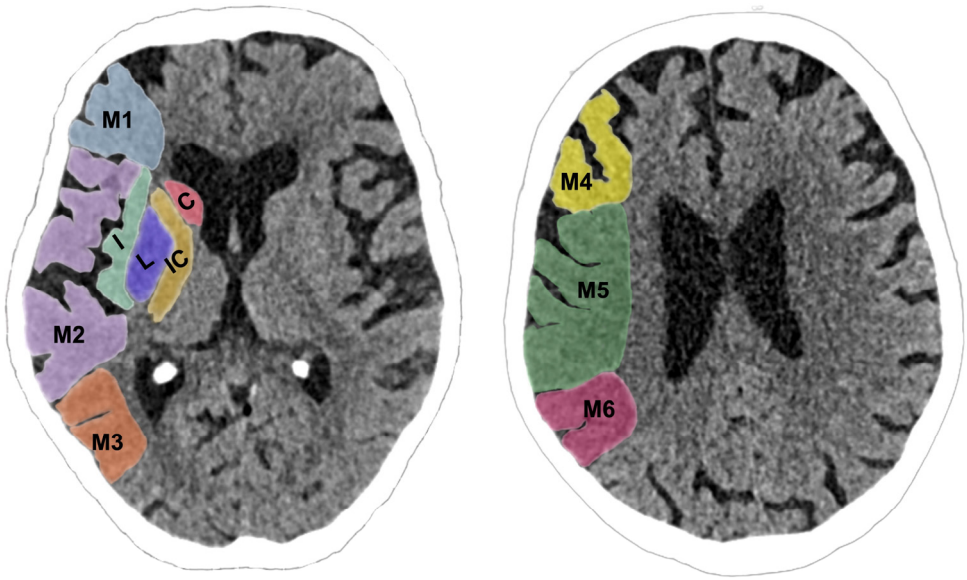

Figure 8. Illustration of the regions included in the ASPECT.

ASPECTS is restricted to the MCA territory and does not capture ischemic changes in other vascular territories. Although an ASPECTS variant for the posterior circulation has been proposed (42), it less widely used in routine clinical and research settings. As a result, the infarct burden of non-MCA strokes is often radiologically underestimated. Moreover, inter-rater agreement for ASPECTS is only moderate, even among experienced readers, and particularly for intermediate scores (41, 43). Variations in image quality, timing of imaging, and reader expertise further contribute to this limitation. These factors should be considered when interpreting ASPECTS in both clinical practice and research, especially when it is used for patient selection or outcome prediction.

Computed tomography angiography

Computed tomography angiography (CTA) is a rapid, contrast-enhanced imaging technique used to visualize the cervical and intracranial vessels. It enables direct identification and localization of arterial occlusions, evaluation of collateral blood flow, and detection of clinically relevant vascular pathology, such as carotid stenosis, arterial dissection, and tandem lesions.

Computed tomography perfusion

Computed tomography perfusion (CTP) is a dynamic imaging technique that capture the wash-in and wash-out of contrast in the brain. By acquiring rapid sequential images during contrast passage, CTP enables quantitative assessment of cerebral hemodynamics and generates parametric maps that describe different aspects of the cerebral blood flow (44):

- Cerebral blood volume: The total volume of blood within the brain tissue, expressed in milliliters/100 grams (mL/100g).
- Mean transit time: The average transit time for contrast to pass through the capillary network, expressed in seconds.
- Time to maximum (Tmax): The delay to peak tissue contrast enhancement. Prolonged Tmax is commonly used to define hypoperfused tissue.
- Cerebral blood flow (CBF): The volume of blood flowing in a unit of brain mass during a unit of time.

Perfusion imaging is sensitive to several factors that can affect image quality and reliability, including patient head motion artifacts, timing of contrast bolus and cardiac output (44). In addition, perfusion estimates may vary substantially between different post-processing software packages due to differences in imaging protocols, and threshold values (45).

Difficulties in defining the ischemic core

Early perfusion imaging studies in the 1950s demonstrated that neurological function becomes impaired when cerebral blood flow falls below 31 mL/100 g/min (46). Subsequent clinical studies in patients undergoing carotid surgery showed that hemiparesis consistently occurred when relative cortical cerebral blood flow dropped below 30% of baseline (CBF<30%) (47). This threshold has since been widely used in acute ischemic stroke imaging to define critically hypoperfused tissue, commonly referred to as ischemic core.

The ischemic penumbra is generally defined as the volume of hypoperfused but potentially salvageable tissue surrounding the ischemic core and is most commonly quantified as the mismatch between tissue volumes with a Tmax >6 seconds and tissue volumes with CBF <30% (44) (Figure 9).

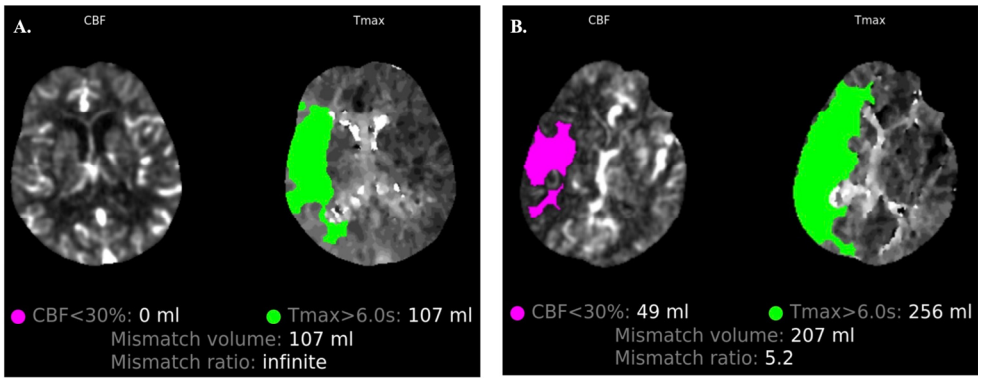

Figure 9. CT perfusion mismatch examples. A: Patient with a large volume of hypoperfused tissue (107 mL) but no critically hypoperfused tissue (CBF<30% is 0), resulting in a mismatch (penumbra) volume of 107 mL. B: A patient with extensive volume of hypoperfused tissue (256 mL), including 49 mL critically hypoperfused tissue (CBF<30%), resulting in a mismatch (penumbra) volume of 207 mL.

However, the ischemic core is often overestimated on perfusion imaging (48) and experimental as well as clinical studies have demonstrated that brain tissue with CBF as low as 5 to 15 mL/100 g/min may recover function if reperfusion is achieved within approximately 30 minutes (49, 50). Moreover, early diffusion changes on MRI can be partially reversible in the early time window (51, 52). Consequently, tissue classified as ischemic core on early imaging does not necessarily represent established infarction, but rather a probabilistic estimate of tissue at exceptionally high risk of progressing to infarction in the absence of rapid reperfusion.

The development of ischemic core is influenced not only by the severity and duration of blood flow reduction but also by tissue characteristics and anatomical location. Animal models and clinical studies have demonstrated that tissue tolerance to ischemia varies, with gray matter being more vulnerable than white matter (53, 54, 55). Furthermore, patient-related factors such as advanced age (56), diabetes mellitus (57), and preexisting brain injury including leukoaraiosis (58), further reduce ischemic tolerance.

Taken together, ischemic injury is a multifactorial dynamic process influenced by the severity and duration of perfusion deficit, tissue-specific vulnerability, and individual patient factors. Consequently, precise delineation between infarcted and non-infarcted tissue is not possible in the early stage of acute ischemic stroke.

Magnetic resonance imaging

In Sweden, MRI is seldom used in the acute settings of ischemic stroke. The technique can be used for perfusion imaging as well as for detecting early cytotoxic

edema, which appears as increased signal intensity in diffusion-weighted magnetic resonance imaging in combination with low values on the apparent diffusion coefficient maps. Cytotoxic edema can be detected on diffusion-weighted MRI (DWI) within minutes after the cerebral blood flow falls to 20-30 mL/100 g/min (55). In later stages of the ischemic process, the ionic edema progresses to vasogenic edema which is visible as increased signal on Fluid-Attenuated Inversion Recovery (FLAIR) MRI and typically indicate established infarction. The DWI–FLAIR mismatch describes the discrepancy between regions showing cytotoxic edema and those showing vasogenic edema and is therefore used as an MRI-based definition of penumbra (59).

Endovascular thrombectomy for acute ischemic stroke

Historically, stroke has been considered a condition without therapeutic options. It was not until the late 20th century that significant advances in stroke management began to emerge, initially through risk factor modification and secondary prevention. This progress was followed by critical trials in 1994–1995 demonstrating that intravenous thrombolysis could significantly improve clinical outcomes in patients with acute ischemic stroke (60, 61), mirroring earlier therapeutic advances in the treatment of myocardial infarction.

The early development of interventional endovascular treatment was characterized by experimental approaches. Initial strategies included delivery of intra-arterial thrombolysis directly at the occlusion site (62), or mechanical clot manipulation using repeated pushes with guidewires or catheters (63, 64). Early mechanical thrombus retrieval attempts were made with tools originally designed for different purposes, such as the gooseneck snare used to retract dislodged coils or catheters (65, 66). The first endovascular thrombectomy was performed in Sweden at Sahlgrenska University Hospital in 1994, using an intravascular retrieval snare (67). Encouraged by these early experiences, researchers developed the first dedicated tools for EVT during 2001–2002 (68), marking the beginning of modern endovascular stroke therapy.

While initial studies of EVT showed promising results regarding rates of successful vessel recanalization, early randomized controlled trials (RCTs) failed to show superiority of EVT compared to best standard care in terms of clinical outcome (69, 70, 71). However, in 2015, five RCTs were published demonstrating an overwhelmingly positive treatment effect of thrombectomy for LVOs in the anterior circulation when performed within 6, 8, or 12 hours of stroke onset (72, 73, 74, 75, 76). Ever since, EVT has gradually been implemented in high-income countries,

and subsequent studies have focused on broadening its indications as well as optimizing the timing and procedural techniques for optimal use.

The EVT procedure

The EVT procedure begins with arterial puncture, most commonly via the femoral or radial artery. A catheter system is then navigated into a cervical vessel, either the Internal Carotid Artery for anterior circulation strokes, or the Vertebral Artery for posterior circulation strokes. The procedure is performed in an angiography suite using digital subtraction angiography (Figure 7), where contrast injections enable real-time visualization of the cerebral vasculature. Digital subtraction angiography allows precise localization of the occlusion site, assessment of collateral circulation, and evaluation of vessel anatomy before, during, and after the intervention.

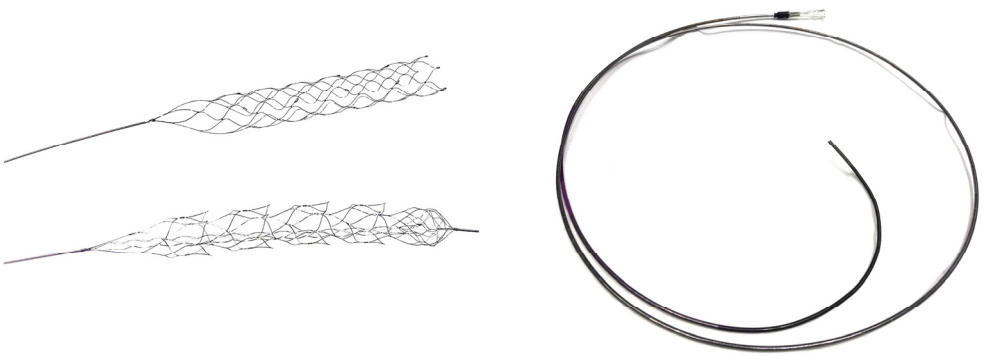

Figure 10. Two stent-retrievers (left) and one distal access catheter (right). Picture by E. Hall.

Once intracranial access is established, thrombectomy can be performed using direct aspiration with a distal access catheter advanced to face the clot. Alternatively, or additionally, a microwire and a microcatheter are navigated through or alongside the clot. The microwire is subsequently replaced by a stent-retriever device which is deployed through the microcatheter across the thrombus. During retrieval of the expanded stent-retriever, temporary proximal flow arrest in the ICA is often achieved by inflating a balloon-guide catheter extracranially, thereby reducing the risk of distal embolization.

After the procedure, radiographic follow-up with cone-beam CT may be performed directly in the angiography suite. This allows for early identification of procedure-related complications, particularly intracranial hemorrhage, as well as detection of large infarctions or significant cerebral edema. In addition, a follow-up NCCT is routinely performed within 4-24 hours, either as standard post-procedural imaging or earlier if clinical deterioration occurs, to assess infarct evolution and exclude

delayed hemorrhagic transformation. Ideally, this follow-up NCCT should be acquired using a dual-energy protocol, which allows differentiation between true hemorrhage and residual contrast enhancement.

Acute ischemic stroke severity and outcome

Stroke severity

Clinically, stroke severity is often measured by the National Institutes of Health Stroke Scale (NIHSS) that was developed in the early 1980s (77). It is a standardized tool that quantifies neurological impairment through a structured bedside examination. These evaluations encompass tests of level of consciousness, eye movements, visual fields, facial weakness, motor function in arms and legs, coordination, sensory loss, speech, and language skills. The total score on the NIHSS ranges from 0 to 42, with higher scores indicating more severe neurological deficits.

The NIHSS is a widely used tool for assessing stroke severity in the anterior circulation. It does not, however, evaluate key clinical features of posterior circulation stroke, such as ataxia, diplopia, nystagmus, and bulbar dysfunction, which may result in an underestimation of stroke severity in these patients (78).

The modified Rankin Scale

As ischemic stroke is a long-term disabling condition, measures of function and disability are well suited as outcome assessments. The modified Rankin Scale (mRS) is a commonly used clinical tool that measures the degree of disability or independence in daily activities, with scores ranging from 0 to 6 (Table 3) (79). An mRS of 0-2 indicates functional independence with the ability to carry out daily activities with no or minimal assistance. mRS of 3-5 indicate increasing level of functional dependency.

Table 3. The Modified Rankin scale (mRS).

mRS	Disability
0	No symptoms.
1	No significant disability. Able to carry out all usual activities despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead.

Factors with influence on EVT outcome

Age and sex

Advancing age is a non-modifiable strong stroke risk factor. Approximately every third to fourth stroke occurs in patients aged 80-84 years, and every fifth occurs in those aged 85 and over (80). Advanced age is generally regarded a negative prognostic factor in acute ischemic stroke and following EVT. Post-hoc analyses of RCTs have demonstrated increased mortality and functional dependency in older patients compared to younger ones, with the most pronounced difference observed in those over 80 years of age (27). Nevertheless, there is observational data supporting beneficial treatment effect of EVT even in elderly patients (81).

While there are small differences in the rate of technical success and complications between sexes, males tend to have lower NIHSS at baseline and better clinical outcome after EVT compared to females (82, 83). Females also tend to be older (83) with a higher prevalence of functional dependence before stroke compared to men (84). Furthermore, due to longer life expectancy for women, they are more likely to live alone which may delay time from symptom onset to first medical contact and arrival at a stroke unit (85).

Comorbidities

Although many RCTs allow for participants with common comorbidities such as hypertension, diabetes mellitus, and atrial fibrillation, they often have strict inclusion and exclusion criteria which limit the participation of patients with substantial medical complexity and exclude patients with severe comorbidities. These restrictions are implemented to reduce confounding, and ensure patient safety, but they also result in study populations that may not fully reflect real-world clinical practice. Consequently, registry-based studies play an important complementary role by capturing broader patient populations with multiple or more severe comorbidities.

Previous observational EVT studies have reported poorer outcomes in patients with conditions such as cancer (86), metabolic syndrome (87), and frailty (88). However, in routine clinical practice, patients with ischemic stroke often present not with a single comorbidity, but with multiple coexisting conditions. This clustering of comorbidities is becoming increasingly common globally due to prolonged life expectancy and increased survival rates from acute and chronic conditions (89). Multimorbidity has therefore emerged as a major determinant of prognosis, treatment decisions, and outcomes in modern stroke care. Importantly, due to the underrepresentation of these patients in RCTs, there remains a knowledge gap regarding the effectiveness and safety of EVT, and optimal peri-procedural

management, in patients with severe comorbidity burden and high medical complexity.

The Charlson Comorbidity Index (CCI) was developed to predict 1-year mortality in patients with multiple comorbidities (90). It summarizes overall comorbidity burden by combining 19 medical diagnoses, each given an individual weight based on its impact on mortality risk (Table 4). Individual weights are summed into a total score, with higher scores reflecting greater comorbidity burden and increased risk of death within 1 year.

Table 4. Diagnoses included in the original Charlson Comorbidity Index and the weight of the individual diagnoses in the index.

Diagnoses and ICD-10 code	Weight in the index
Solid tumor, non-metastatic (C00-76)	2
Solid tumor, metastatic (C77-79)	6
Leukemia/myeloma (C88-96)	2
Chronic liver disease, mild (B18, K70, K72)	1
Chronic liver disease, moderate/severe (K73-74)	3
Chronic kidney failure (N18)	2
Chronic obstructive pulmonary disease (J44)	1
Rheumatoid arthritis (M04-05)	1
Peripheral vascular disease (I70, I73)	1
Congestive heart failure (I25, I50)	1
Myocardial infarction (I21-22)	1
Diabetes (E10-E11)	2
Dementia (F00-03)	1
HIV/AIDS (B20-24)	6
Ulcer disease (K25-26)	1
Cerebrovascular disease (I67.9)	1
Hemiplegia (G83.1-3)	1
Lymphoma (C81-86)	2

HIV = Human Immunodeficiency Virus, AIDS = Acquired Immunodeficiency Syndrome

There are numerous comorbidity indices, including several variations of the CCI. For example, there is one stroke-adapted CCI which includes fewer diagnoses compared to the original version but the differences in prediction of outcomes between this index and the original CCI is minimal (91). Furthermore, a large Danish study including more than 200.000 stroke patients over an 18-year period could, using the original CCI, successfully predict the mortality and functional outcome of the patient group (92). Given the demographic and healthcare similarities in the Scandinavian countries, the original CCI can be considered well-validated for use in Swedish stroke population as well.

Pre-stroke disability

Like multimorbid patients, individuals with pre-stroke functional dependency (mRS 3-5) are frequently excluded from RCTs. Consequently, the treatment effect of EVT in this population is not fully established. Existing observational analyses have typically compared successful versus unsuccessful EVT rather than EVT versus no EVT. These studies indicate a favorable effect of successful reperfusion (93, 94) and show that approximately one-fifth of patients with pre-stroke mRS 3 and about one-third of those with pre-stroke mRS 4–5 return to their baseline functional level three months after EVT (95).

Procedural factors

Technical success

Angiographic scales quantifying the technical success as degree of revascularization or reperfusion within the occluded vascular territory are essential outcome measures in EVT research. Early EVT studies adopted the Thrombolysis in Myocardial Infarction (TIMI) scale, originally developed for coronary reperfusion (96). However, because TIMI was designed for the coronary circulation, it inadequately reflected the complexity of cerebral hemodynamics, collateral flow, and distal tissue reperfusion. This limitation prompted the development of the Thrombolysis in Cerebral Infarction (TICI) scale as a measurement of downstream territory reperfusion (97). Subsequently, the modified TICI (mTICI) scale further refined the reperfusion grading by subdividing partial reperfusion in the vascular territory into 2a (<50%) and 2b (≥50%) (98). The TICI 2c grade was later introduced to distinguish near-complete reperfusion (TICI 2c) from complete reperfusion (TICI 3). More recently, the expanded TICI (eTICI) scale has been proposed, providing a more granular stratification of reperfusion outcomes (98, 99, 100).

Achieving a favorable TICI grade is an important quality metric in EVT, and the association between successful recanalization or reperfusion and obtaining good functional outcome has been well demonstrated (101). Initially, TICI 2a or better was regarded successful recanalization (102). Expectations have, however, risen as technologies and operator performance have improved, and TICI 2b has become the more widely accepted threshold.

This shift is further supported by the pooled analysis of major EVT RCTs (HERMES), which showed that functional outcomes improved progressively with higher degrees of reperfusion, while identifying TICI 2b as the optimal dichotomous threshold for predicting good functional outcome (101). Although some studies suggest additional benefit with higher reperfusion grades, others have not demonstrated a clear difference in long-term functional outcomes between eTICI 2b

and 2c, despite reports of early clinical advantages among patients achieving eTICI 2c reperfusion (103).

Table 5. Overview of the TICI scales.

Grade	Original TICI	mTICI	mTICI with 2c	eTICI
0:	No reperfusion	No reperfusion	No reperfusion	No reperfusion
1:	Penetration with minimal perfusion	Penetration with minimal perfusion	Penetration with minimal perfusion	Penetration with minimal perfusion
2a:	Partial perfusion <2/3 of the territory	Partial perfusion <50% of the territory	Partial perfusion <50% of the territory	Partial perfusion <50% of the territory
2b:	Complete perfusion of the territory but slower than normal	Partial perfusion ≥50% of the territory	Partial perfusion ≥50% of the territory	Partial perfusion, 50-66% of the territory
2b:	-	-	-	Partial perfusion 67-89% of the territory
2c:	-	-	Near complete perfusion except slow flow or few distal cortical emboli	Near-complete perfusion, 90-99% of the territory
3:	Complete perfusion	Complete perfusion	Complete perfusion	Complete perfusion (100%)

TICI = Thrombolysis in Cerebral Infarction, mTICI = modified Thrombolysis in Cerebral Infarction, eTICI = expanded Thrombolysis in Cerebral Infarction.
*In EVAS, TICI 2c was first introduced in 2017.

The TICI scales were primarily developed for LVOs, which makes them difficult to apply to MeVOs and DMVOs. Distal arteries supply smaller vascular territories, meaning that estimates of the "percentage reperfusion" become more uncertain and less clinically meaningful. In addition, the concept of reperfusion percentage may be interpreted either as reperfusion within the treated distal branch and its downstream vascular tree (e.g., M3 and beyond) or as reperfusion within the main trunk territory (i.e., the entire territory of the MCA), which further complicates the use of TICI grading in distal occlusions.

Technical aspects

The use of stent-retriever is a safe and well-established EVT-technique (27), and can favorably be used together with balloon-guide catheter that features an inflatable balloon near its distal tip. When inflated, it provides mechanical support and temporary occlusion of antegrade flow, which reduces the risk of downstream embolization during clot retrieval (104).

The use of balloon-guide catheters has been associated with higher rates of successful recanalization and early neurological improvement in systematic reviews and meta-analyses (105, 106), observational studies (107, 108), and a post hoc RCT

(109). In addition, balloon-guide catheter use has been linked to lower complication rates (110). Evidence suggests that these benefits are most pronounced when balloon-guide catheters are used in combination with stent retrievers (106, 108, 111) whereas their advantage may be diminished when combined with distal aspiration catheters, which can interfere with effective flow reversal (112). However, the benefit of balloon-guide catheters has been questioned after the publication of the multicenter RCTs, one of which failed to demonstrate improved recanalization rates with balloon-guide catheter use (113) while another was terminated prematurely due to safety concerns in the balloon-guide catheter group (114).

Direct aspiration thrombectomy can be used either as a stand-alone technique or as a part of a combined approach with stent-retriever. Direct aspiration as a stand-alone technique is associated with shorter arterial puncture to recanalization times (115). However, a combined approach integrating direct aspiration and stent-retriever can enhance clot removal, further reduce embolic risk, and has been associated with superior first-pass effect (116). Despite this, findings across studies are conflicting, and the overall differences in clinical outcome between technical approaches appear to be minor (116, 117, 118, 119). No single method is universally superior; rather, the choice of technique depends on operator preference, device availability and reimbursement, the patient´s vascular anatomy, and clot location.

Time is brain

There is a strong association between shorter time from stroke onset to recanalization and better clinical outcomes. Based on the influential 2015 trials, EVT was restricted to a narrow therapeutic time window of 0–6 hours, and patients presenting later were generally considered unsuitable for treatment. This paradigm shifted fundamentally following the publication of the DAWN and DEFUSE 3 trials in 2017–2018, which showed that patients with LVOs in the anterior circulation and favorable perfusion imaging profiles can benefit from EVT far beyond the traditional time limits, up to 24 hours after stroke onset (120, 121).

However, rapid and successful reperfusion remains a critical determinant of outcome, and achieving complete revascularization on the first attempt (often referred to as the first-pass effect) without the need for rescue therapy is associated with superior clinical results (122).

Anesthetic approach

The debate regarding the optimal anesthetic approach for EVT – general anesthesia versus conscious sedation – has been ongoing for years. Early meta-analyses pooling data from RCTs reported heterogenous results, but suggested a potential advantage of non-general anesthesia approaches while emphasizing that the requirement for general anesthesia should not preclude EVT (123). Concerns related to general anesthesia have primarily focused on delays to arterial puncture, anesthesia-associated pneumonia, and peri-procedural hypotension.

Anesthesia-induced hypotension, mediated by systemic vasodilation, may reduce cerebral perfusion pressure and compromise collateral blood flow to penumbral tissue (124), potentially resulting in larger infarct volumes and worse functional outcomes (125). However, these potential disadvantages may be compensated by procedural benefits associated with general anesthesia, including shorter times from arterial puncture to reperfusion and higher rates of successful recanalization (107, 126).

Rapid induction of general anesthesia while maintaining adequate intracranial perfusion pressure is therefore essential in patients undergoing EVT. More recent RCTs and meta-analyses generally favor general anesthesia and show either improved or comparable functional outcomes relative to non-general anesthesia approaches (126, 127, 128, 129). These findings may reflect advances in anesthetic management and growing expertise among anesthesiology teams.

Core infarct size and site of occlusion

Large ischemic core

For many years, patients with large ischemic cores (volume ≥50 mL or ASPECTS <6 on baseline imaging) were not considered eligible for EVT. The early EVT trials (72, 73, 74, 75, 76) primarily enrolled patients with small to moderate infarct cores (ASPECTS ≥6), based on the assumption that large cores represented predominantly irreversible tissue damage, limited salvageable penumbra, and an overall poor prognosis.

This perspective changed with the publication of the six large core RCTs, RESCUE-Japan LIMIT (130), SELECT2 (131), TENSION (132), TESLA (133), LASTE (134), and ANGEL-ASPECT (135). Collectively, these studies demonstrated that EVT is safe and effective in selected patients with anterior circulation LVOs with large ischemic cores, despite a higher risk of complications, including intracranial hemorrhage (ICH) (136, 137, 138).

These studies highlighted that infarct size alone should not preclude EVT treatment (139). However, several limitations should be acknowledged. Except for TENSION, all trials only included patients with a pre-stroke mRS of 0–1, and many excluded patients older than 80 or 85 years. Furthermore, while EVT was associated with reduced mortality and higher rates of functional independence, it also led to an increase in the proportion of patients surviving with moderate disability (mRS 3–4).

The 2026 American Heart Association/American Stroke Association Guidelines for acute ischemic stroke now recommend EVT in selected patients with large ischemic core LVO in the anterior circulation presenting up to 24 hours after symptom onset, to improve functional outcomes and reduce mortality (140). This applies to patients

younger than 80 years with a NIHSS ≥6, a pre-stroke mRS of 0–1, an ASPECTS of 3–5, and no significant mass effect on imaging. For similar patients presenting within 6 hours of symptom onset but with very low ASPECTS (0–2), EVT may still be considered reasonable to improve functional outcomes and reduce mortality, provided they are younger than 80 years, have an NIHSS score ≥6, a pre-stroke mRS score of 0–1, and no significant mass effect on imaging (140).

Vessel occlusion site

The five groundbreaking RCTs in 2015 demonstrated overwhelmingly positive treatment effect of EVT for anterior circulation LVOs, which in MR CLEAN included the intracranial ICA, M1, M2, A1 and A2 (72). These trials excluded posterior circulation LVOs, which, although relatively rare, are associated with high mortality and poor outcomes despite administration of intravenous thrombolysis (141, 142). Early RCTs investigating EVT for posterior circulation LVOs initially failed to demonstrate a clear treatment benefit, mirroring the early experience of EVT in anterior circulation stroke (143, 144). However, subsequent studies have shown positive treatment effect of EVT for basilar artery occlusions up to 24 hours after stroke onset, despite a higher incidence of symptomatic intracranial hemorrhage (sICH) (145).

Patients with MeVOs/DMVOs account for approximately 25-40% of all acute ischemic strokes (22). Although clinical outcomes are generally more favorable than those observed in LVOs, MeVOs remain associated with substantial morbidity, even among patients treated with intravenous thrombolysis (146, 147). Encouraged by the post hoc analyses suggesting a potential benefit of EVT also in MeVOs (148), three RCTs — DISTAL, ESCAPE-MeVO, and DISCOUNT — were conducted to evaluate the efficacy and safety of EVT in this population. These trials did not demonstrate a significant clinical benefit of EVT for MeVO/DMVO patients. Moreover, EVT was associated with a higher incidence of severe adverse events, including sICH and pneumonia (147, 149, 150, 151). Notably, the trials differed in their inclusion criteria, underscoring the challenges in defining and classifying MeVOs and DMVOs. Additionally, approximately 20% of patients enrolled in the DISTAL trial had a pre-stroke mRS of ≥3, and rates of successful recanalization (defined as TICI 2b–3) were low across all three studies.

Table 6. Overview of inclusion criteria and demographics in the MeVO/DMVO trials.

	DISTAL	ESCAPE-MeVO	DISCOUNT
Inclusion			
M2	Non-dominant or co-dominant	All	Distal
M3	All	All	All
M4	All	-	-
A1	All	-	All
A2-A3	All	All	All
P1	All	-	All
P2-P3	All	All	All
Minimum NIHSS score	4, or disabling symptoms	5, or minimum 3 with disabling symptoms	5, or significant aphasia
Stroke onset to randomization	0-24 h	0-12 h	0-8 h
Demographics			
Median age	77	75	74
Median NIHSS	6	8	8
Prestroke mRS ≥2	20.0%	-	-
Median time from last seen well to randomization, hours	3.9 h	4.5 h	-
TICI 2b-3	71.7%	75.1%	77.0%

M1, M2, M3, and M4 = M1, M2, M3, and M4 segment of the Middle Cerebral Artery, A1, A2, and A3 = A1, A2, and A3 segment of the Anterior Cerebral Artery, P1, P2, and P3 = P1, P2, and P3 segment of the Posterior Cerebral Artery, NIHSS = National Institutes of Health Stroke Scale, mRS = modified Rankin Scale, h = hours, TICI = Thrombolysis in Cerebral Infarction

Complications

Complications related to EVT can affect both the immediate procedural success as well as the patient's subsequent recovery. Perioperative complications may delay or prevent successful recanalization or hinder the initiation of secondary preventive therapies, thereby increasing the risk of long-term disability or recurrent stroke. EVT-related complications may also lead to neurological deterioration, for example through distal embolization (152, 153) or procedural vessel injury (153, 154), reperfusion hemorrhages (152, 153), and severe infections, which may further impair neurological outcomes or even result in death. Understanding the nature and clinical consequences of EVT-related complications is essential for improving procedural safety and treatment results.

Definition of intracranial hemorrhages and symptomatic intracranial hemorrhages

ICH represents a potentially severe and life-threatening complication following EVT. It may occur because of vascular injury during the endovascular procedure,

or as a reperfusion-related bleeding when cerebral blood flow is restored to infarcted tissue with a disrupted blood-brain barrier (155), typically occurring within the first 24 hours after EVT.

Despite its beneficial effects on reperfusion and functional outcomes, intravenous thrombolysis is a recognized risk factor for ICH following EVT (156). Other known ICH risk factors include advanced age (157), hypertension, diabetes, increased time from stroke onset to EVT initiation, and low ASPECTS (158, 159). Also, hyperglycemia worsens ischemic brain injury by amplifying metabolic failure, contributing to blood-brain barrier breakdown, risk of edema and hemorrhagic transformations (160).

The post-EVT ICHs range from small petechial hemorrhagic infarcts (HI1 and HI2), parenchymal hematomas (PH1 and PH2), parenchymal hematomas remote to the infarct (PHr), intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), and subdural hemorrhage (SDH) (Figure 11).

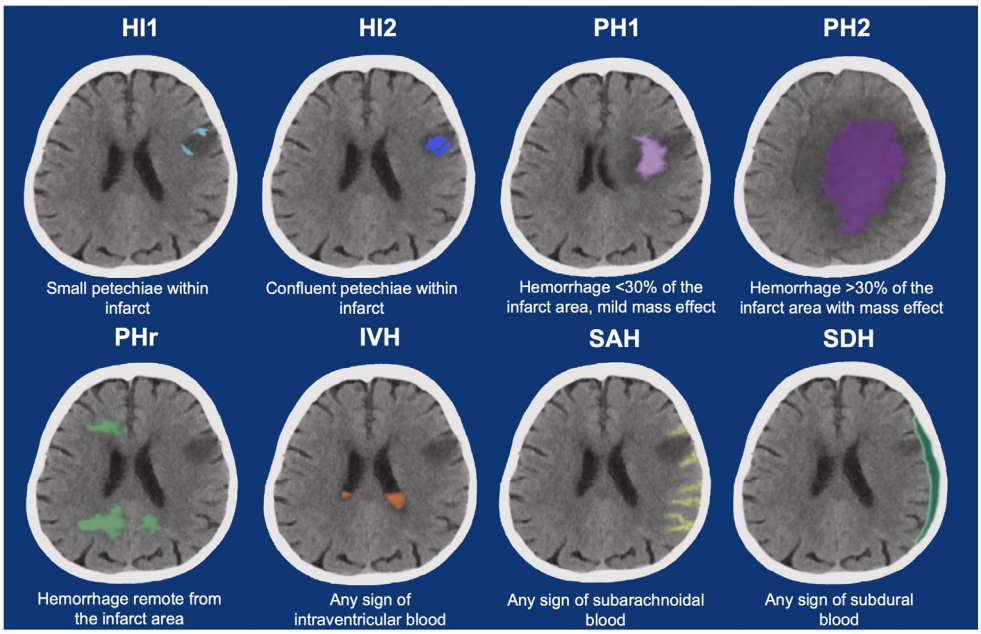

Figure 11. Illustrations and anatomical descriptions of intracranial hemorrhagic complications after EVT.

The hemorrhages are divided into symptomatic ICH (sICH) and non-symptomatic ICH (non-sICH), based primarily on the degree of neurological deterioration. The distinction between sICH and non-sICH is of great importance. sICH is strongly associated with poor functional outcome and increased mortality, and typically necessitates urgent supportive care, potential reversal of anticoagulation, and close monitoring in intensive care settings. In contrast, non-sICH is generally regarded as

a primarily radiological finding. While it may influence the timing and choice of secondary prevention strategies, such as initiation of antiplatelet or anticoagulant therapy, non-sICH has limited clinical consequences and does not adversely affect long-term functional outcome (161, 162). Known sICH risk factors include diabetes, high blood-glucose (163, 164), low ASPECTS (130, 165), and failed recanalization (166).

The definition of sICH has evolved over the years, which complicates direct comparisons between studies. In the early intravenous thrombolysis trials, such as ECASS II, sICH was defined as the presence of any ICH combined with an increase of ≥4 points in NIHSS or adverse event indicating clinical decline, including loss of consciousness and death (167). In the ECASS III, the criteria became stricter, requiring a causal relationship between the ICH and the clinical deterioration or death (168). Other definitions have evolved after the ECASS studies, including the Heidelberg Bleeding Classification where they also included ICHs associated with an increase of ≥2 points in a single NIHSS item, or major intervention such as intubation or hemicraniectomy (169).

Numerous attempts have been made to develop prediction models aimed at the early identification of patients at increased risk of sICH. These models typically incorporate multiple variables including age, ASPECTS, NIHSS, treatment time delays, blood pressure, and blood glucose levels. However, in routine clinical practice, the ability to accurately discriminate between patients who will develop hemorrhagic complications and those who will not remain limited. Reliable identification of patients at particularly high risk represents a key clinical challenge as risk stratification is essential for early and targeted interventions.

Aim of the thesis

The overall aim of this PhD thesis was to enhance the understanding of EVT-related complications and outcomes, with a focus on both clinical and radiological factors, in order to support treatment decision-making and improve patient outcomes.

The specific aims were as follows:

Paper I: To investigate the severity and subtypes of hemorrhagic complications after EVT in relation to occlusion location in the anterior circulation.

Paper II: To describe the distribution and temporal trends of high comorbidity burden among Swedish stroke patients treated with EVT, and to evaluate functional outcomes, including mortality, procedural success rates, complication rates, and the clinical impact of successful EVT in patients with and without multiple comorbidities.

Paper III: To assess early neurological improvement, 90-day functional outcomes, and post-procedural intracerebral hemorrhage following EVT for medium vessel occlusions in patients with and without a high comorbidity burden.

Paper IV: To examine differences in clinical outcomes and radiological phenotypes between patients with intracranial subterminal ICA occlusions (ICA-I) and those with an ICA terminus (ICA-T) occlusions.

Methods

Data sources

Riksstroke

Founded in 1994, Riksstroke is the Swedish national quality registry for stroke care (170). It includes all hospitalized patients with acute stroke in Sweden and collects data on clinical factors and subsequent follow-up. Riksstroke was established by the Swedish National Board of Health and Welfare. In collaboration with national health care authorities, it utilizes its data to inform and update revised stroke guidelines. Together with the Swedish board of health and welfare, Riksstroke has defined key performance indicators against which the performance of all Swedish hospitals is measured. Riksstroke reports the key performance indicators to the European Stroke Organization and to World Stroke Organization for international comparisons (170). Riksstroke serves as a foundation for registry-based stroke research and is a tool for hospitals to continuously improve the quality of stroke care.

Data quality checks are conducted automatically during web form registration and through statistical process control. Individual hospital coverage rates and automated registration procedures are regularly reviewed and updated. Several studies have validated the data in Riksstroke, estimating that it covers at least 90% of acute stroke patients (171, 172).

EVAS – The Registry of EndoVAscular treatment of Stroke

The EVAS registry is the Swedish national quality registry for endovascular treatment of ischemic stroke (173). Established in 2012, EVAS has systematically collected clinical and procedural data since 2013 (173), with the aims to improve the quality of endovascular procedures and to facilitate research. The registry produces annual summaries, and its national coverage has increased over time, reaching more than 98% during the study periods (174, 175).

All EVTs performed in Sweden, at the currently seven thrombectomy centers, are registered in EVAS. The clinical and technical EVT variables included in this thesis are collected from EVAS. These include, for example, TICI, occlusion location, and NIHSS. Furthermore, EVAS registers post-procedural information, including peri- and postoperative complications.

The Swedish National Patient Registry

Data on comorbidities used in Paper II and III were obtained from the National Patient Registry, managed by the National Board of Health and Welfare. It includes comprehensive data on all completed inpatient stays and specialized outpatient care, including diagnoses classified according to the International Classification of Diseases-10 (176). However, it does not contain information on primary care. The coverage of the registry is high, ≥96%, and has improved over time (177).

The Swedish Prescribed Drugs Registry

The National Prescribed Drug Registry is regulated by the Swedish government and was established in 2005. It contains information on all prescribed drugs in Sweden dispensed in pharmacies according to the Anatomical Therapeutic Chemical (ATC) classification system, as well as age, sex and personal identification number (178). Missing data are less than 0.3% (179). Data were collected for filled prescriptions for dementia medications (ATC N06DA02, N06DA03, N06DA04, and N06DX01), to increase the completeness of dementia diagnoses in Paper II and III.

PACS

The Picture Archiving and Communication System (PACS) is a digital system used to store, retrieve, manage, and display medical images such as NCCTs and digital subtraction angiographies.

Definition of variables

Modified ASPECT

ASPECT is not routinely used in the clinical practice in Sweden, and the EVAS infarct classification does not fully correspond to the original ASPECTS system. To account for radiological stroke size, a modified ASPECTS (mASPECTS) was therefore applied in Papers I-IV. The categories were defined as follows:

- mASPECTS 10: no visible ischemic injury.
- mASPECTS 7–9: infarct involving <1/3 of the MCA territory *or* isolated basal ganglia involvement.
- mASPECTS 5–6: infarct involving <1/3 of the MCA territory *and* basal ganglia involvement.
- mASPECTS 0–4: infarct involving >1/3 of the MCA territory.

In Paper II, posterior-circulation strokes were also included and early ischemic changes in the cerebellum, pons, or medulla oblongata were classified as mASPECTS 0–4.

Modified Rankin Scale

The post-EVT 90-day mRS outcome in Paper II, III, and IV are derived from follow-up questionnaires with self-reported responses registered in Riksstroke. Data are collected via postal questionnaires or telephone interviews. The questionnaire encompasses current living-status and general dependency on next-of-kin/family member, as well as three questions: 1) How is your mobility now? 2) Do you need help from somebody else to visit the toilet? and 3) Do you need help getting dressed and undressed? In this thesis, mRS 0-2 after 90 days is considered a favorable outcome. Mortality data in Riksstroke are complete, and the translation of self-reported outcome to nurse-adjudicated mRS grades has been validated with high agreement (172, 180).

Perioperative complications

In the EVAS registry, severe perioperative complications are systematically recorded. These complications encompass vessel perforation, hypoperfusion, perforating artery injury, arterial dissection, severe cardiac arrhythmia, thromboembolic event in the lower extremities, material malfunction, severe iatrogenic puncture site complication, injury to a new vascular territory, and stent thrombosis.

Postoperative complications

Although malignant infarction primarily represents a consequence of the ischemic stroke itself rather than a complication directly attributable to EVT (181), it is nevertheless registered as a postoperative complication in the EVAS registry. Other postoperative adverse events documented in the EVAS include severe infections such as pneumonia, major cardiovascular events (including heart failure, cardiac arrest, pulmonary embolism, pulmonary edema, and arrhythmia), as well as ICH.

sICH

Hemorrhages occurring 4–36 hours following EVT were classified as sICH if they were either registered as sICH in Riksstroke or resulted in a minimum 4-point increase in NIHSS or death within 7 days. The sICH definition in paper I-III aimed to follow the Heidelberg Bleeding Classification framework. However, since itemized NIHSS were first introduced in Riksstroke in 2020, the applied definition most closely resembles the ECASS III criteria (page 38).

Study subjects and outcome assessments

Table 7. Overview of methodological aspects of the four papers included in the thesis.

	Paper I	Paper II	Paper III	Paper IV
Study period	2015-2020	2015-2021	2015-2021	2016-2022
Study materials	EVAS, Riksstroke	EVAS, Riksstroke, the Swedish Patient Registry, the Prescribed Drugs Registry	EVAS, Riksstroke, the Swedish Patient Registry, the Prescribed Drugs Registry	EVAS, Riksstroke, PACS
Study design	Prospective registry-based observational study	Prospective registry-based observational study	Prospective registry-based observational study	Prospective registry-based observational study
Inclusion criteria(s)	Anterior circulation ischemic stroke treated with EVT	Ischemic stroke treated with EVT	MeVO in anterior circulation treated with EVT	ICA-I and ICA-T occlusions
Exclusion criteria(s)	ACA occlusion, no EVT performed	No EVT performed, history of previous stroke, functional dependency or unknown functional level pre-stroke	No EVT performed, history of previous stroke, functional dependency or unknown functional level pre-stroke	Tandem or multiple occlusions, for secondary outcome also dissections
Included in the study (n)	3153, 3077 in the main analysis	4735	983	1013
Exposure	Occlusion in intracranial ICA, M1 or M2 and beyond	CCI 0, CCI 1, CCI 2 and CCI ⩾3	CCI 0, CCI 1-2, and CCI ⩾3	ICA-I and ICA-T occlusions
Primary outcome measures	sICH	Temporal changes in comorbidity burden, mRS 0-2 at 90 days	Successful recanalization and mRS 0-2 at 90 days, within each CCI group	Median and variance in NIHSS before and after EVT, successful recanalization, early neurological deterioration, mRS 0-2 after 90 days
Secondary outcome measures	Subtype of ICH	Successful recanalization, peri- and postoperative complications, in relation to CCI	mRS 0-1 at 90 days, sICH and changes in NIHSS	Accuracy of initial radiology reports
Sub-analysis	-	Successful recanalization and mRS 0-2 within each CCI group	-	NIHSS before EVT and CT perfusion data, for patients with variants in the Circle of Willis
Variables used for multiple imputation	-	CCI, age, sex, pre- and postoperative NIHSS scores, mTICI score, mASPECTS, use of general anesthesia	CCI, age, sex, pre- and postoperative NIHSS scores, mTICI score, mASPECTS	mRS before stroke onset, age, sex, pre- and postoperative NIHSS scores, diabetes, mTICI score, mASPECTS

EVAS = The Registry of EndoVAscular treatment of Stroke, PACS = The Picture Archiving and Communication System, EVT = EndoVascular Thrombecomy, MeVO = Medium Vessel Occlusion, ICA = Internal Carotid Artery, ACA = Anterior Cerebral Artery, n = number, CCI = Charlson Comorbidity Index, sICH = symptomatic IntraCranial Hemorrhage, mRS = modified Rankin Scale, ICH = IntraCranial Hemorrhage, NIHSS = National Institutes of Health Stroke Scale, CT = Computed Tomography, mASPECTS = modified Alberta Stroke Program Early CT Score, mTICI = modified Thrombolysis in Cerebral Infarction

Paper I

Population

Paper 1 included all patients registered in both EVAS and Riksstroke that were treated with EVT due to occlusion in the anterior circulation between 2015 and 2020. Since isolated ACA occlusions were rare, they were excluded from the study along with patients in whom no EVT was performed.

Exposure

Occlusion types were categorized into ICA (which included both I- and T-type), M1, and M2 and beyond, and were defined by their proximal end.

Outcome

- Primary outcome: Symptomatic intracranial hemorrhage.

The outcome was sICH within 4–36 hours after EVT. ICHs were defined as sICH if they were registered as sICH in Riksstroke or caused at least a 4-point increase in NIHSS or death within 7 days. Cases with malignant MCA infarction, other severe adverse event or unrelated death were labeled "uncategorized ICH" due to uncertain attribution. Hemorrhagic complications with a maximum NIHSS increase of 3 points, were classified as non-sICH.

- Secondary outcome: Subtype of intracranial hemorrhage.

The ICHs were further divided into ICH subtypes as presented in Figure 11. Cases with >1 hemorrhagic subtype were classified by the most severe type, except for IVHs which were analyzed separately. Isolated subarachnoid bleedings were classified as SAH, whereas SAH in combination with parenchymal bleedings were classified by the most severe parenchymal type.

Statistics

Univariable logistic regression was used to assess the association between occlusion type and sICH. Multivariable logistic regression was then performed to adjust for potential confounders. These included sex, age, hypertension, diabetes, anticoagulant or antiplatelet use, NIHSS before EVT, mASPECTS, and intravenous thrombolysis. Cases classified as uncategorized ICH were excluded from the primary analysis.

Two sensitivity analyses were conducted to test the stability of the results: in one, the uncategorized ICHs cases were included in the sICH group, and in the other, they were included in the non-sICH group.

Paper II

Population

In Paper II, we included all patients treated with first-ever EVT treatment for acute ischemic stroke in Sweden during 2015-2021. Data were obtained from EVAS and Riksstroke, as well as the Swedish Patient Registry, and the Swedish Prescribed Drugs Registry. Patients with spontaneous reperfusion, pre-stroke mRS 3-5 or unknown pre-stroke mRS, were excluded from the study.

Exposures

Comorbidity burden was assessed according to the original CCI, if diagnosed within 5 years prior to stroke onset in the Swedish Patient Registry. The CCI was divided into four groups: no comorbidity (CCI 0); moderate comorbidity burden (CCI 1); severe comorbidity burden (CCI 2); and very severe comorbidity burden (CCI≥3).

Outcome

- Primary outcomes: The distribution and temporal changes of comorbidity burden within the Swedish EVT population, as well as the association between comorbidity burden and a favorable outcome, defined as mRS 0-2 after 90 days.
- Secondary outcomes: The association between comorbidity burden and successful recanalization (mTICI 2b-3), perioperative complications, postoperative complications, and 90-day survival rate.
- Sub-analysis: The association between successful recanalization and a favorable outcome within each CCI group. Non-recanalization was defined as mTICI 0-2a or failure to access occlusion site.

Statistics

Univariable logistic regression assessed the relationship between comorbidity burden and a favorable outcome as well as successful recanalization, perioperative complications, and postoperative complications. A multivariable logistic regression analysis was then performed to analyze the association between CCI and a favorable outcome, adjusting for sex, age, pre-EVT NIHSS, successful recanalization, time from stroke onset to arterial puncture, and mASPECTS.

In the sub-analysis, the association between successful recanalization and favorable 90-day functional outcome, stratified by CCI group, was examined with multivariable logistic regression analyses, adjusting for age, sex, NIHSS score prior to EVT, time from stroke onset to arterial puncture, and mASPECTS. Patients with perioperative complications were excluded from the sensitivity analysis.

Cox regression was used to analyze probability of survival, which was illustrated with Kaplan-Meier curves. The analyses were stratified by CCI group and successful recanalization, perioperative complications and postoperative complications.

Missing mRS data were handled using multiple imputation by chained equations. Twenty datasets were generated, and estimates were combined using Rubin's rules. Imputed data were included in both mRS illustrations and in the logistic regression analyses for mRS.

Paper III

Population

The population in Paper III was the same as in Paper II, however only patients with anterior circulation MeVO were included. Comorbidity burden was weighted according to the original CCI and stratified into no comorbidity (CCI 0); moderate to severe comorbidity (CCI 1–2); and very severe comorbidity (CCI ≥3). MeVO was defined as occlusion in the M2 or M3 segment of the MCA, based on the reporting neurointerventionist's description of the occlusion.

Exposure

Outcomes for successfully recanalized patients (mTICI 2b-3) were compared to non-recanalized patients (mTICI 0-2a or failure to access occlusion site).

Outcome

- Primary outcomes: The association between successful recanalization and a favorable outcome (mRS 0-2 after 90 days), stratified by CCI group.
- Secondary outcomes: Excellent outcome (mRS 0–1) and changes in NIHSS postoperatively versus preoperatively. sICH was analyzed as a safety outcome.

Statistics

Univariable and multivariable logistic regression models were applied to assess the association between successful recanalization and favorable as well as excellent outcome. In the multivariable regression analyses, we adjusted for age, sex, and preoperative NIHSS.

Differences in the incidence of ICH and sICH between recanalized and unsuccessfully recanalized patients within each CCI group were analyzed with χ^2 test. Changes in median NIHSS before versus after EVT were expressed as ΔNIHSS.

Missing follow-up mRS values were addressed as in Paper II.

A sensitivity analysis for favorable outcome was performed excluding patients with perioperative vessel perforation, as this complication may result in early termination of the EVT procedure before recanalization is achieved.

Paper IV

Population

All patients treated with EVT for intracranial ICA occlusion between 2016-2022 were included in the main analysis.

For sub-analysis and secondary outcome, all patients treated with EVT for ICA-I occlusion in Lund were included. In the secondary analysis, the next consecutive EVT-treated ICA-T case was also included as controls.

Exposure

For primary and secondary outcomes, patients were grouped into ICA-I and ICA-T occlusion.

In the sub-analysis, exposure was anterior axis and posterior axis variants in the Circle of Willis, in patients with ICA-I occlusions. Anterior axis variants were divided into 1) unbroken anterior axis and 2) broken anterior axis defined as hypoplastic or absent A1 segment or Anterior Communicating Artery. Posterior circulation variants were divided into 3) unbroken anterior axis with fetal PCA and 4) unbroken anterior axis with non-fetal PCA.

Outcome

- Primary outcomes: Clinical outcomes included median and variance in NIHSS before and after EVT, and successful recanalization, early neurological deterioration, and mRS 0-2 after 90 days. Differences in NIHSS before EVT and CT perfusion imaging was analyzed for patients with anatomical variations in the sub-analysis.
- Secondary outcomes: Accuracy and common pitfalls of the initial radiology reports of ICA-I occlusions compared to ICA-T occlusions.

Statistics

The differences in median NIHSS before and after EVT, age, and time from stroke onset to arterial puncture were analyzed with Mann-Whitney U-test. Levene's test was used for exploring the variance in NIHSS. The association between occlusion location and favorable outcome (mRS 0-2) was evaluated with univariable logistic regression.

In the sub-analysis, differences in median pre-EVT NIHSS were presented with median with interquartile range (IQR) analyzed with Mann-Whitney U-test. CT perfusion data were presented with means.

The results of the validation of initial radiology reports (secondary outcome) were presented as simple proportions.

General statistics

Errors

In statistical testing, errors can occur when the conclusion does not match the true situation.

- Type 1 errors: concluding an effect or a difference, when there is none. This can happen for example by chance, by multiple testing without correction, or by setting too high significance level.
- Type 2 errors: failing to detect a true effect. This can happen because of lack of statistical power (small sample size and/or small effect size), inappropriate statistical test, or a large variability in data.
- Type 3 errors: correct conclusion, but with a misunderstanding of the underlying effect. These errors happen because of measurement errors, misclassifications or poorly designed studies.

Logistic regression

Logistic regression is a statistical method used to examine the association between one or more independent variables and a binary outcome. Univariable logistic regression estimates the relationship between a single independent variable and an outcome, while multivariable logistic regression models include more than one independent variable, allowing for adjustment of confounders in order to reduce statistical errors (182). The primary effect measure derived from logistic regression is the odds ratio (OR). The OR describes how the odds of the outcome differ between groups for categorical exposures, or how the odds change with each unit increase in a continuous exposure.

Hazard regression

Hazard regression refers to statistical methods used to examine time-to-event data (183). These methods are applied when the outcome of interest is not only whether

an event occurs, but also when it occurs, assuming sufficient follow-up time, as in survival analysis. The effect measure is typically the hazard ratio (HR), which reflects the relative rate at which an event occurs, that is, the change in event rate associated with a one-unit increase in the exposure. Cox proportional hazards regression is the most commonly used hazard regression model in medical research.

Multiple imputation by chained equation

Multiple imputation by chained equation is a commonly used method for handling missing data in observational studies. It is a structured approach that accounts for uncertainty in the imputation process by generating multiple imputed datasets rather than a single completed dataset. Compared with excluding incomplete cases or using single imputation, multiple imputation by chained equation generally results in less biased estimates and more accurate measures of variability. The method is performed in several steps (184):

First, missing values are replaced with plausible values generated from a statistical model that uses available variables as predictors.

The imputation cycle runs through all variables multiple times, updating the imputed values in each iteration until the values stabilize.

This process is repeated several times (typically 5-20) to create multiple complete datasets, each of which is analyzed separately using the same statistical approach.

Finally, the results from these analyses are combined using Rubin's rules, which account for variability both within and between the imputed datasets, resulting in pooled estimates with corresponding confidence intervals and p-values.

Parametric and non-parametric tests

Parametric and non-parametric statistical tests are commonly used for group comparisons but differ in their underlying assumptions and performance characteristics. Standard parametric tests are typically based on means and standard deviations, and require normally distributed data and equal group variance (182). Non-parametric tests are used when data do not follow a normal distribution and are useful for small samples and skewed data (182). They generally compare medians or ranked values rather than means. Common examples are the Mann–Whitney U test for comparing two independent groups, the Wilcoxon signed-rank test for paired samples, and the Kruskal–Wallis test for more than two independent groups (183). These tests are more flexible than parametric tests but may be slightly less sensitive in detecting true differences between groups.

Ethics

All studies included in this thesis were approved by the Swedish Ethical Review Authority (Dnr 2019-00678 and 2022-00890-02). In Sweden, stroke patients (or when necessary, their next of kin) are informed about registration in EVAS and Riksstroke and that the data may be used for research and quality improvement. The 90-day follow-up is based on opt-in consent, obtained when patients return the questionnaire. No separate consent is collected for individual research projects. Participation in Riksstroke and EVAS involves no direct risk, and patients may decline or withdraw at any time.

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) is an initiative developed by epidemiological researchers with the aim of improving the quality and transparency of reporting in observational studies (185). It is supported and made available through the EQUATOR Network (Enhancing the QUAlity and Transparency Of health Research) (186), which provides reporting standards for a wide range of study designs. The STROBE Statement emphasizes clear reporting of what was planned, what was done, what was found, and how conclusions were drawn. It consists of a checklist of 22 items that should be addressed in reports of analytical observational studies, including cohort, case-control, and cross-sectional designs. All four papers in this thesis were reported in accordance with the STROBE checklist for cohort studies.

Results

The annual number of EVTs increased steadily during the study periods, from 380 in 2015 to 1825 in 2024 (Figure 12). This, in combination with decreased incidence of acute ischemic stroke, have resulted in a steady increase in EVT rate (EVT/acute ischemic stroke).

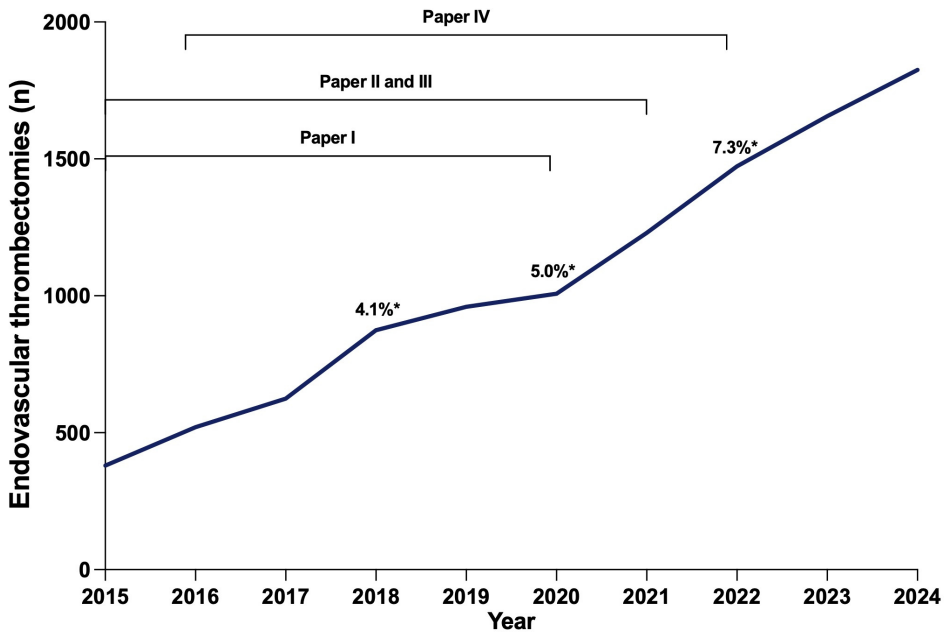

Figure 12. The annual number of EVTs performed in Sweden during 2015 to 2024, and * = annual EVT-rate (EVT/acute ischemic stroke). Data from EVAS annual report 2024 (175) and Wasselius et al 2025 (13).

Paper I - Occlusion location and intracranial hemorrhagic complications

Paper I included 3153 patients treated with EVT during 2015-2020. 76 patients with ICH were labelled uncategorized due to concomitant other severe complications and excluded from the main analyses. Out of the 3077 patients included in the main analyses, 1710 (55.6%) presented with an M1 occlusion, 609 (19.8%) with an ICA occlusion and 758 (24.6%) with an occlusion in M2 or beyond. Baseline characteristics for these patients are shown in table 1, Paper I.

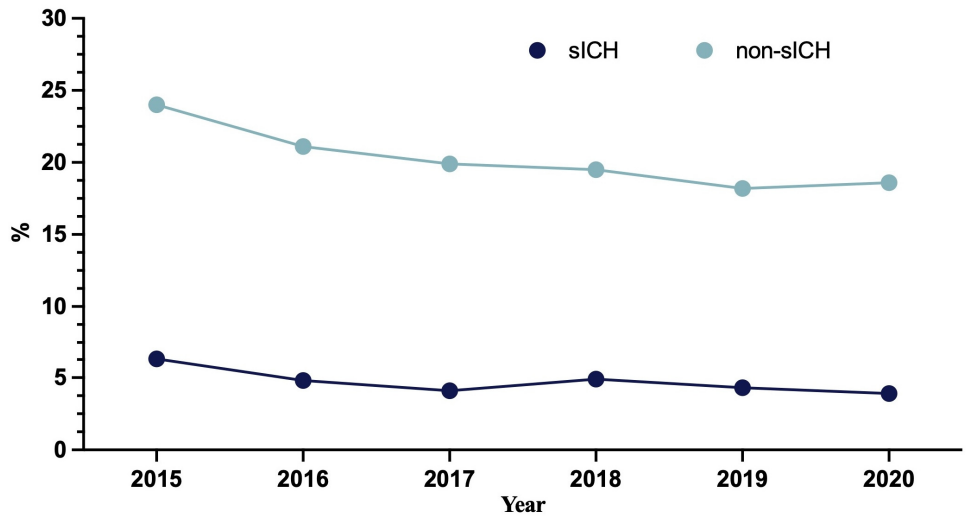

Figure 13. Incidence of sICH and non-sICH during 2015–2020

Symptomatic intracranial hemorrhage

Of 3153 patients, 26.0% developed any ICH within 4-26 hours. Among the 3077 patients included in the main analysis, 140 developed sICH and 605 non-ICH, corresponding to a sICH incidence of 4.5% (140/3077).

Table 8. The association between occlusion site and any ICH analyzed with univariable logistic regression analysis with M1 as reference.

Occlusion site	Any ICH, n (%)	OR (95% CI)	p-value
M1	402 (23.5)	reference	reference
M2 & beyond	192 (25.3)	1.10 (0.91-1.35)	0.329
ICA	151 (24.8)	1.07 (0.87-1.33)	0.523

ICH = IntraCranial Hemmorhage, OR = Odds Ratio, CI = Confidence Interval, M1 = M1-segment of middle cerebral artery, M2 = M2-segment of middle cerebral artery, ICA = Internal Carotid Artery

Any post-EVT ICH was most common for occlusions in and beyond the M2 (25.3%), and least common after EVT in the M1 (23.5%), the difference was however not significant (table 8).

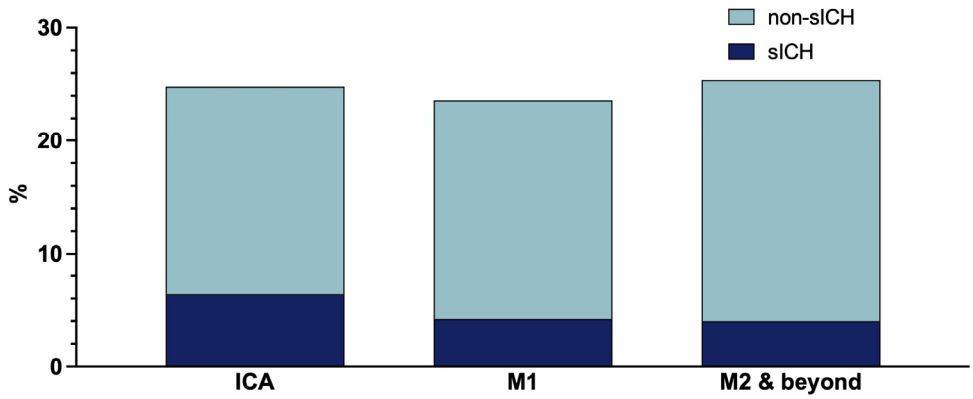

Figure 14. Incidence of sICH and non-sICH after EVT in ICA, M1 and M2 & beyond.

Non-sICH was the predominant hemorrhagic complication across all occlusion sites (Figure 14). sICH was most common after EVT for ICA occlusions (6.4%), compared with M1 (4.2%) and M2 & beyond occlusions (4.0%). This association was significant (Table 9) and remained so after adjustment for confounders. No significant difference in sICH incidence was found between M1 occlusions and occlusions in M2 & beyond.

Table 9. The association between occlusion site and sICH analyzed with univariable logistic regression analysis with M1 as reference.

Occlusion site	sICH, n (%)	Univariable logistic regression		Multivariable logistic regression*	
		OR (95% CI)	p-value	OR (95% CI)	p-value
M1	71 (4.2)	reference	reference	reference	reference
M2 & beyond	30 (4.0)	0.95 (0.62-1.47)	0.822	1.02 (0.63-1.64)	0.952
ICA	39 (6.4)	1.58 (1.06-2.35)	0.026	1.58 (1.01-2.46)	0.044

sICH = symptomatic IntraCranial Hemmorhage, OR = Odds Ratio, CI = Confidence Interval, M1 = M1-segment of middle cerebral artery, M2 = M2-segment of middle cerebral artery, ICA = Internal Carotid Artery

*Adjusted for sex, age, hypertension, diabetes, oral anticoagulant or antiplatelet treatment at admission, National Institute of Health Stroke Score at baseline, modified Alberta Stroke Program Early CT Score and intravenous thrombolysis

Subtype of intracranial hemorrhage

The most common hemorrhagic subtype after EVT for ICA occlusions was HI2 (7.9%), followed by PH2 (4.4%). For M1 and M2 & beyond occlusions, isolated SAH was the most frequent subtype (7.8% and 12.4%, respectively), followed by HI2 (7.3% and 4.1%). These hemorrhages were predominantly classified as non-sICH. In contrast, IVH and PH2 were most often categorized as sICH (63.6% and 58.5%, respectively) and occurred most frequently in the ICA group (Figure 15).

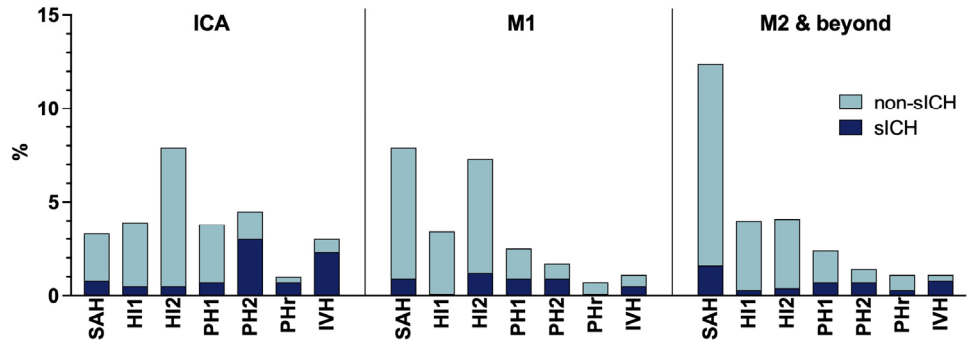

Figure 15. Incidence of subtype of ICH and the distribution of sICH and non-sICH within the ICH types, statified by occlusion location.

Sensitivity analyses

Among 821 patients with ICH, 76 could not be definitively classified as sICH or non-ICH due to the presence of severe concomitant conditions, such as malignant infarction, sepsis, or liver failure, which contributed to death. These patients were excluded from the primary analyses. To evaluate the stability of our findings, we conducted two sensitivity analyses: in both, the association between ICA occlusions and sICH remained consistent, regardless of whether the uncategorized ICHs were included in the overall population (but not classified as sICH) or incorporated into the sICH group.

Paper II - Comorbidity burden and outcomes after endovascular thrombectomy

The distribution and temporal changes of comorbidity burden

Out of 4735 patients, 1914 (40.0%) had a CCI of 0 (no comorbidity), 699 (14.8%) had a CCI of 1, 975 (20.6%) had a CCI of 2, and 1147 (24.1%) had a CCI ≥3. Baseline characteristics for these patients are shown in table 1, Paper II.

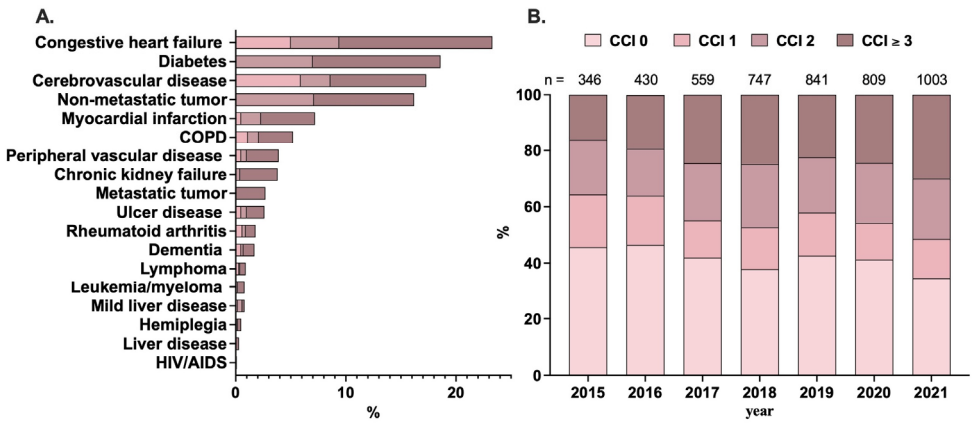

Figure 16. A) comorbidities included in the original CCI and their frequency in the EVT population, B) the annual number of EVTs and the annual frequency of each CCI group during the study period.

Favorable outcome

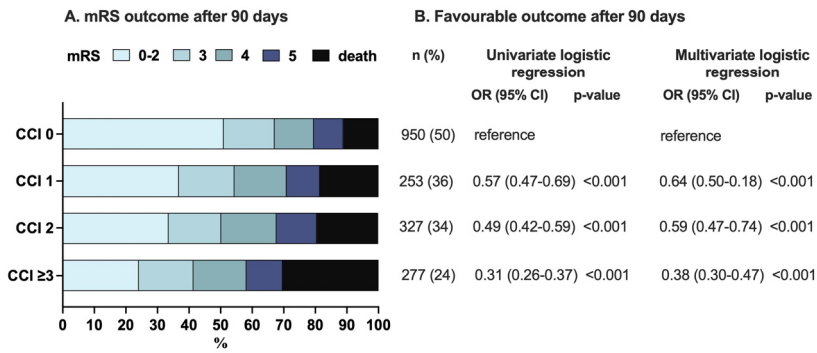

Figure 17. A) mRS outcome 90 days after EVT; and B) favorable outcome (mRS 0-2) 90 days after EVT analyzed with univariable logistic regression and multivariable logistic regression adjusted for age, sex, NIHSS score before EVT, successful recanalization, time from stroke onset to arterial puncture, and mASPECTS.

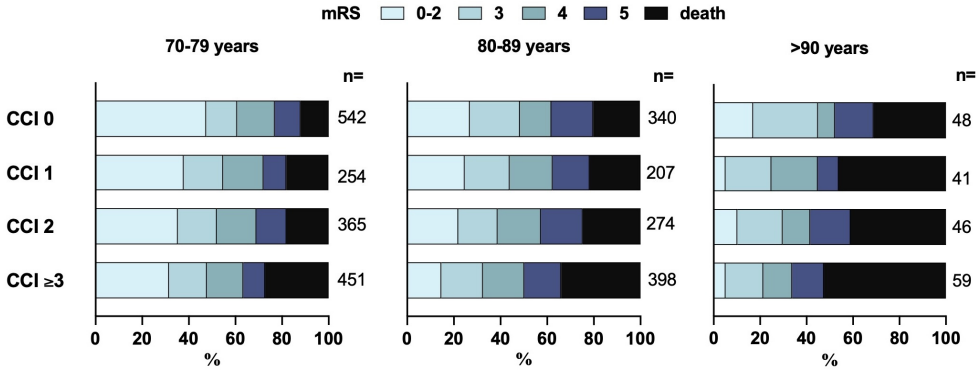

Figure 18. mRS outcome after 90 days, stratified by age group.

Successful recanalization, peri- and postoperative complications, and 90-day survival rate

The rate of successful recanalization was lowest for patients with CCI ≥3, however no significant difference was observed between CCI groups (Table 10). Perioperative complications were most common for patients with CCI 2, and there was a significant association between increased comorbidity burden (CCI 2 and CCI ≥3) and perioperative complications.

Table 10. The association between occlusion site and successful recanalization, perioperative complications and postoperative complications analyzed with univariable logistic regression analysis.

	n (%)	OR (95% CI)	p-value
Successful recanalization			
CCI 0	967 (83.5)	reference	reference
CCI 1	599 (85.7)	1.11 (0.92-1.35)	0.25
CCI 2	819 (84.0)	0.97 (0.78-1.19)	0.77
CCI ≥3	941 (82.0)	0.85 (0.66-1.08)	0.17
Perioperative complications			
CCI 0	136 (7.1)	reference	reference
CCI 1	62 (8.9)	1.37 (0.93-1.74)	0.11
CCI 2	96 (9.8)	1.43 (1.09-1.88)	0.011
CCI ≥3	84 (7.3)	1.03 (0.78-1.37)	0.83
Postoperative complications			
CCI 0	300 (15.7)	reference	reference
CCI 1	122 (17.5)	1.14 (0.90-1.43)	0.28
CCI 2	210 (20.6)	1.41 (1.15-1.71)	<0.001
CCI ≥3	232 (20.2)	1.38 (1.14-1.67)	<0.001

OR = Odds Ratio, CI = Confidence Interval, CCI = Charlson Comorbidity Index

For all CCI-groups, both peri- and postoperative complications were increased in non-recanalized patients compared to successfully recanalized patients (Paper II, Figure 2C).

As mortality data were complete, all 4735 patients were included in the Kaplan-Meier survival analyses assessing 90-day mortality (Figure 19). The Kaplan-Meier curves demonstrate reduced survival rates for patients with perioperative complications, irrespective of recanalization status, and an even lower survival rate in patients with postoperative complications, across all CCI groups. In the CCI ≥3 group, postoperative complications had an especially negative impact on the probability of survival.

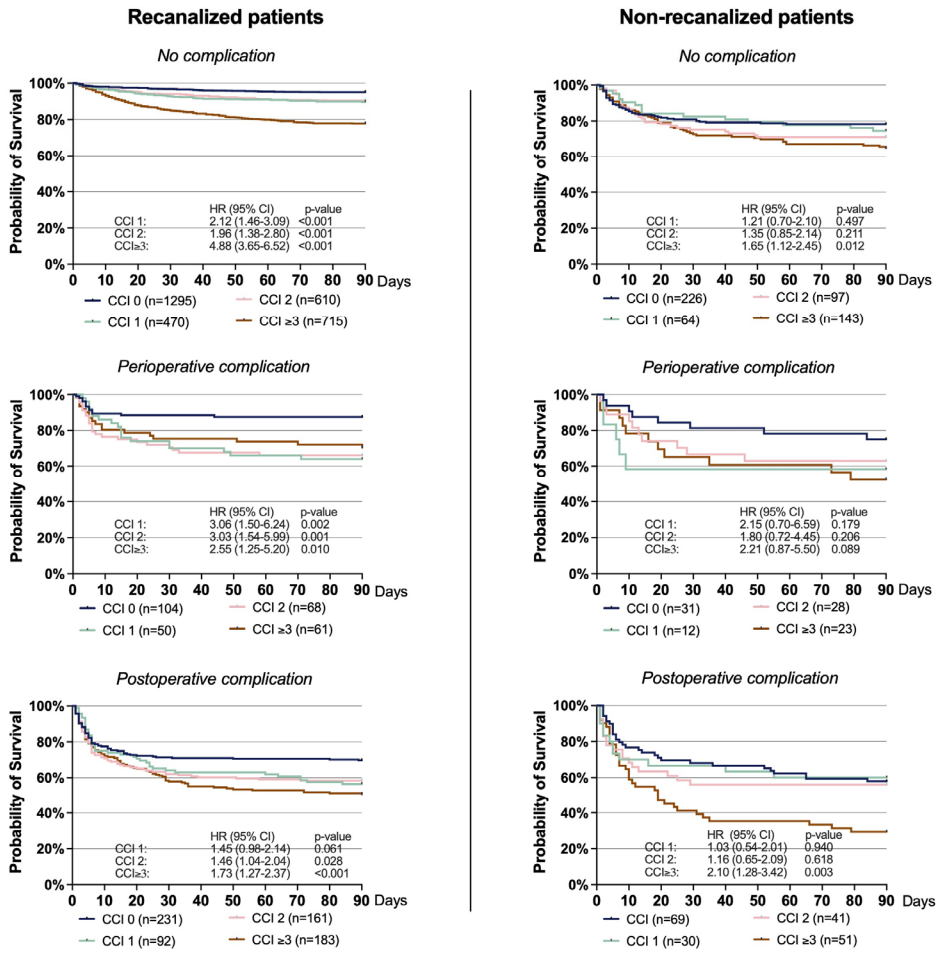

Figure 19. Kaplan-Meier curves illustrating the survival rate for patients with and without successful recanalization, perioperative complications, and postoperative complications, stratified by comorbidity burden groups. HR = Hazard ratio, CI = Confidence interval.

Successful recanalization and a favorable outcome

The baseline characteristics of successfully recanalized and non-recanalized patients stratified into groups based on comorbidity burden are shown in table 2 in Paper II.

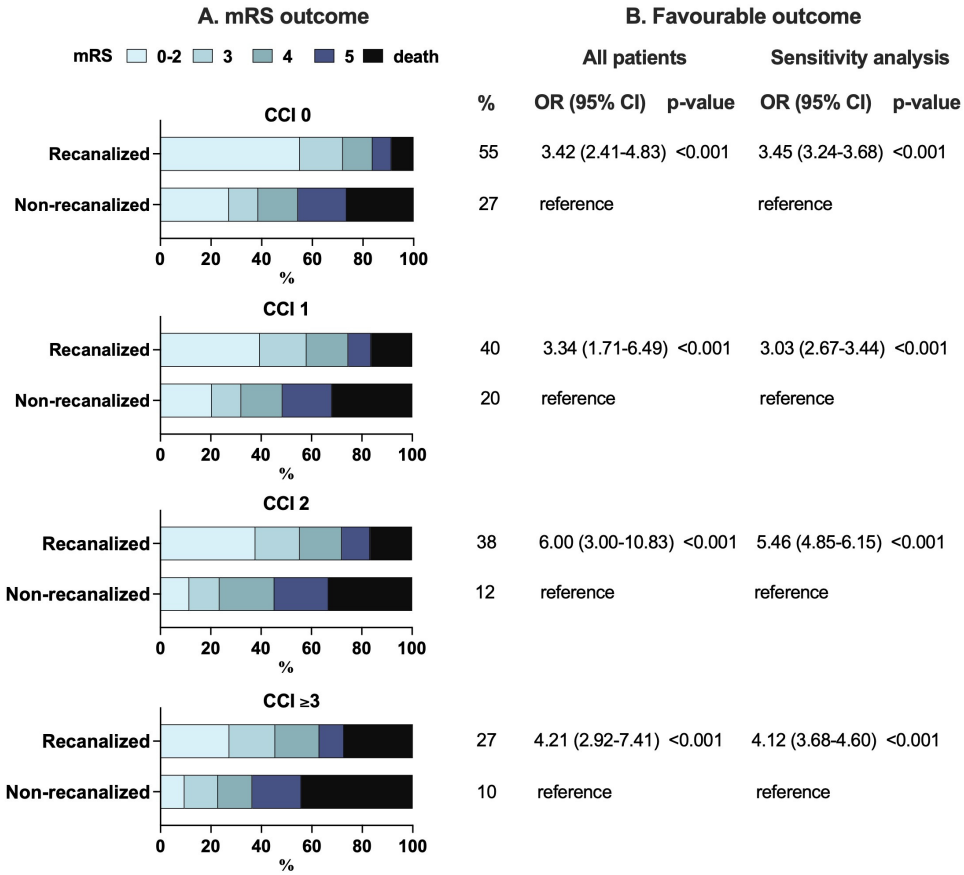

Figure 20. A) mRS outcome 90 days after EVT for recanalized and non-recanalized patients; and B) favorable outcome (mRS 0-2) 90 days after EVT analyzed with multivariable logistic regression adjusted for age, sex, NIHSS score before EVT, time from stroke onset to arterial puncture, and mASPECTS. In the sensitivity analysis, patients with perioperative complications (n=378) were excluded from the multivariable regression analysis.

Paper III - Comorbidity burden and MeVOs

Among 983 pre-stroke functionally independent patients with anterior circulation MeVO treated with EVT 2015-2021 in Sweden, 368 (37.4%) had no comorbidity (CCI 0), 348 (35.4%) had moderate to severe comorbidity burden (CCI 1–2), and 267 (27.2%) had a very severe comorbidity burden (CCI ≥3). Demographics for successfully recanalized and non-recanalized patients, stratified by CCI group, are presented in Paper III, Table 2.

Successful recanalization and functional outcomes

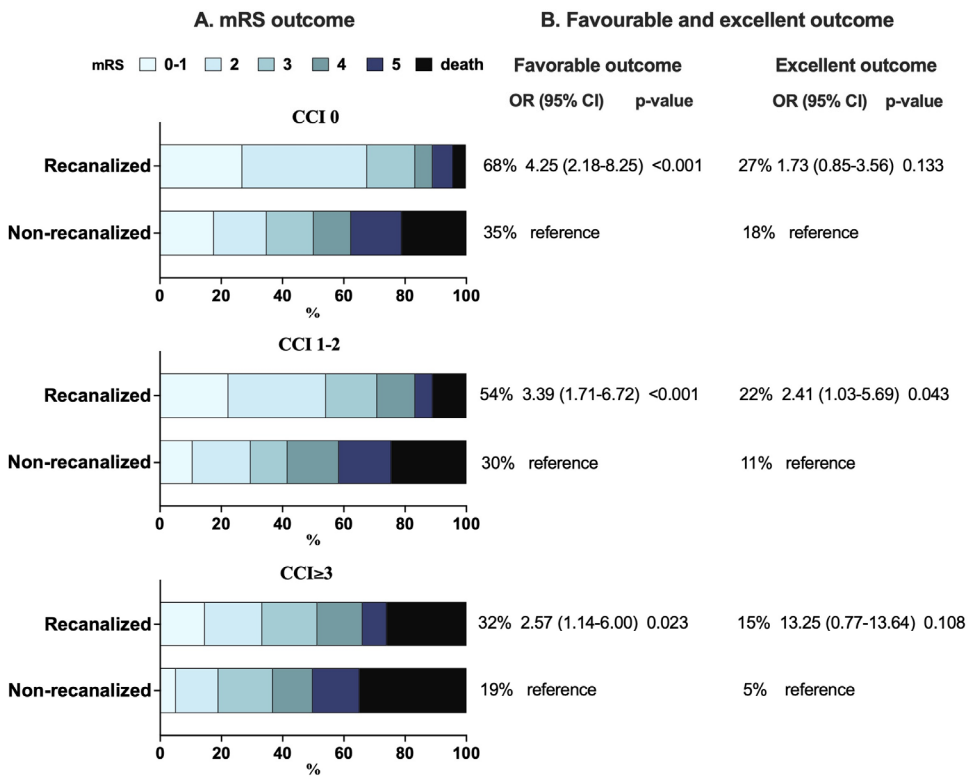

Figure 21. A) mRS outcome after 90 days; and B) the association between recanalization status and favorable as well as excellent outcome analyzed with multivariable logistic regression analysis adjusted for age, sex, and preoperative NIHSS.

Sensitivity analysis

Patients who were not successfully recanalized had a higher rate of vessel perforation (5.6%) compared to those who were successfully recanalized (1.4%; p<0.001). After excluding patients with vessel perforation from the multivariable logistic regression analyses, the association between successful recanalization and favorable outcome remained significant across all CCI groups, even when adjusting for age, sex and preoperative NIHSS.

Hemorrhagic complications and ΔNIHSS

The incidence of sICH in the entire study population was 4.6% for successfully recanalized patients, compared with 11.7% for non-recanalized patients.

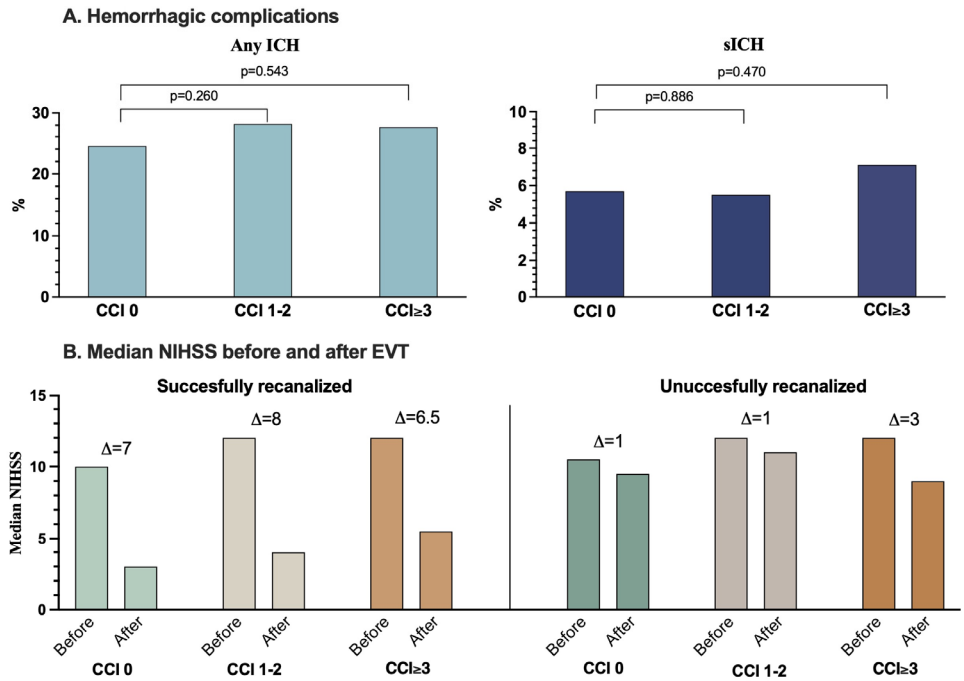

Figure 22. A) Incidence of any ICH as well as sICH for each CCI group, and B) median NIHSS before and after EVT.

Paper IV - Clinical and radiological outcomes in ICA-I and ICA-T occlusions

Out of 6163 patients treated with EVT during 2016-2022, 356 (9.5%) patients with ICA-I occlusion and 657 (17.6%) patients with ICA-T occlusions were identified. Baseline data and stroke characteristics for these patients are presented in Table 1, Paper IV.

Clinical and radiological outcomes

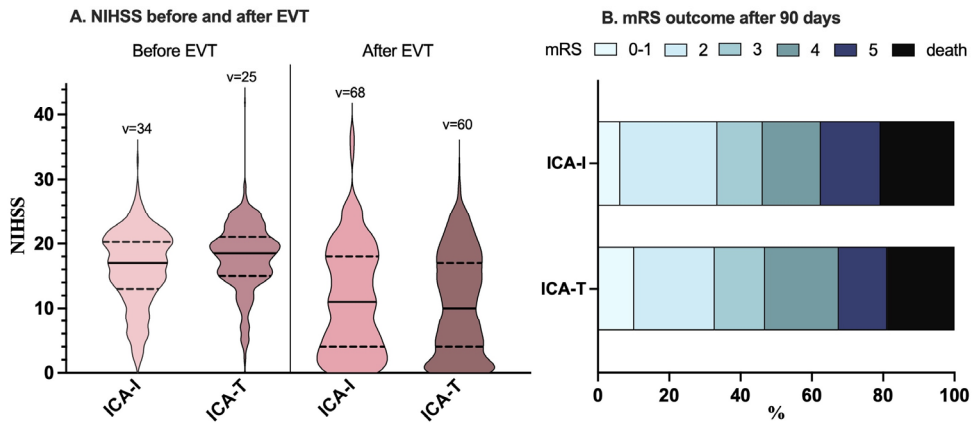

Figure 23. A) NIHSS with median, IQR and variance (v) before and after EVT; B) mRS outcome after 90 days (pre-stroke mRS 0-2).

Median NIHSS before EVT was lower in ICA-I than ICA-T occlusions (17 vs 19; p<0.001), with greater baseline variability in ICA-I (variance 34 vs 25; p<0.001). At 24 hours after EVT, median NIHSS was similar between groups. Time from stroke onset to arterial puncture was significantly longer in ICA-I occlusions (median 4:21 h) compared with ICA-T (median 3:31 h) (p=0.001). Rates of successful recanalization (mTICI 2b–3) were similar across groups. Early neurological deterioration was slightly more common in patients with ICA-I occlusions (11%) compared with ICA-T (8.2%), but the difference was not statistically significant (p=0.150). mASPECTS differed between groups (p=0.019). ICA-I more often had mASPECTS 10, but also slightly more severe infarcts (0–4). Posterior circulation involvement was more common in ICA-I (8.7% vs 5.3%; p=0.037).

Anatomical variants, NIHSS and perfusion imaging

During the study period, there were 45 ICA-I occlusions treated with EVT at Lund University Hospital. 37 (82.2%) had an unbroken anterior axis and 8 (17.8%) a broken anterior axis. Among those with an unbroken anterior axis, 14 (37.8%) had a fetal type PCA and 23 (62.2%) had a non-fetal type PCA.

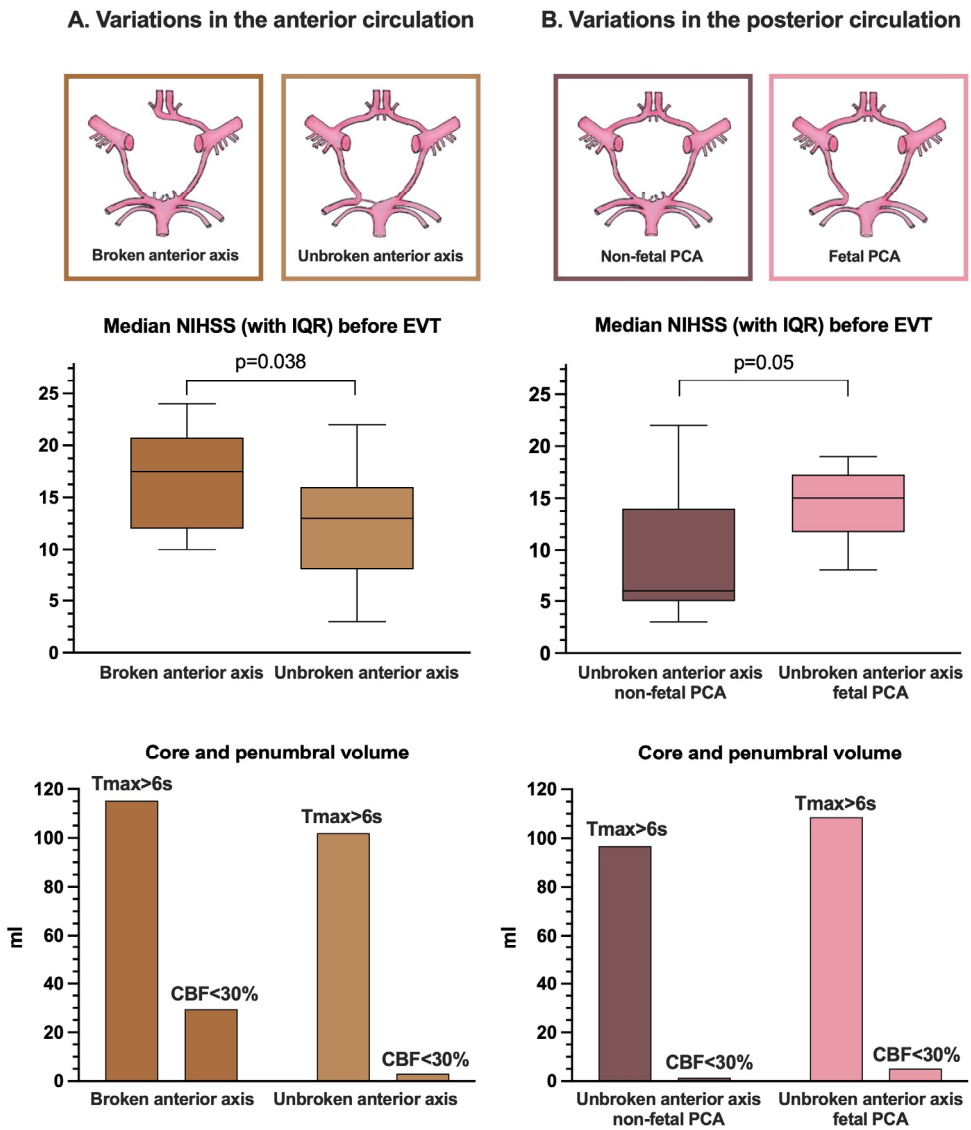

Figure 24. Median pre-EVT NIHSS and mean perfusion deficits for patients with ICA-I occlusions and anatomical variants in the anterior versus the posterior circulation.

Figure 25 illustrates four examples demonstrating how anatomical variants influence perfusion across all three major vascular territories in patients with ICA-I occlusions.

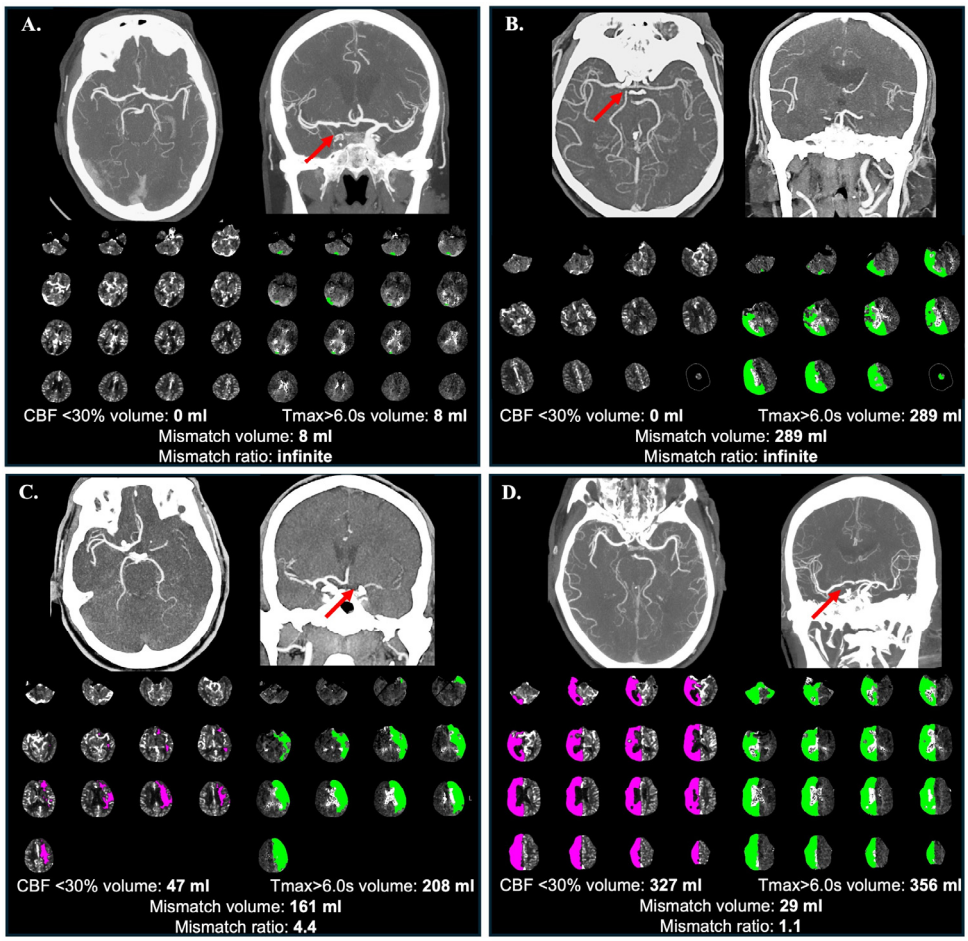

Figure 25. Perfusion imaging for patients with ICA-I occlusions.

Case A: A patient with ICA-I occlusion with an unbroken anterior axis, ipsilateral non-fetal PCA, and NIHSS 8. The perfusion imaging shows a small volume of hypoperfused tissue (8 mL) but none critically hypoperfused tissue (CBF<30% is 0).

Case B: A patient with ICA-I occlusion with an unbroken anterior axis, ipsilateral fetal-type PCA, and NIHSS 13. The perfusion imaging shows 289 ml hypoperfused tissue in the MCA and PCA territories but none critically hypoperfused tissue (CBF<30% is 0).

Case C: A patient with ICA-I occlusion with a broken anterior axis (hypoplastic A1 segment), and NIHSS 19. The perfusion imaging shows 208 ml hypoperfused tissue and 47 ml critically hypoperfused tissue (CBF<30%), with involvement of the MCA and ACA territories.

Case D: A patient with ICA-I occlusion with broken anterior axis (hypoplastic Anterior Communicating Artery), ipsilateral fetal-type PCA, NIHSS 24, and rapid loss of consciousness. The perfusion imaging shows 356 ml hypoperfused tissue and 327 ml critically hypoperfused tissue (CBF<30%), with involvement of all three major territories.

Validation of initial radiology reports

The analysis included 45 patients with ICA-I occlusions and 45 with ICA-T occlusions. Baseline CTA reports were unavailable for three ICA-I and two ICA-T patients. In the ICA-T group, all incorrect intracranial assessments were reported as M1 occlusions. In contrast, errors in the ICA-I group more frequently reflected misinterpretation of both intra- and extracranial findings, most often described as extracranial ICA occlusion or dissection without recognition of the intracranial occlusion.

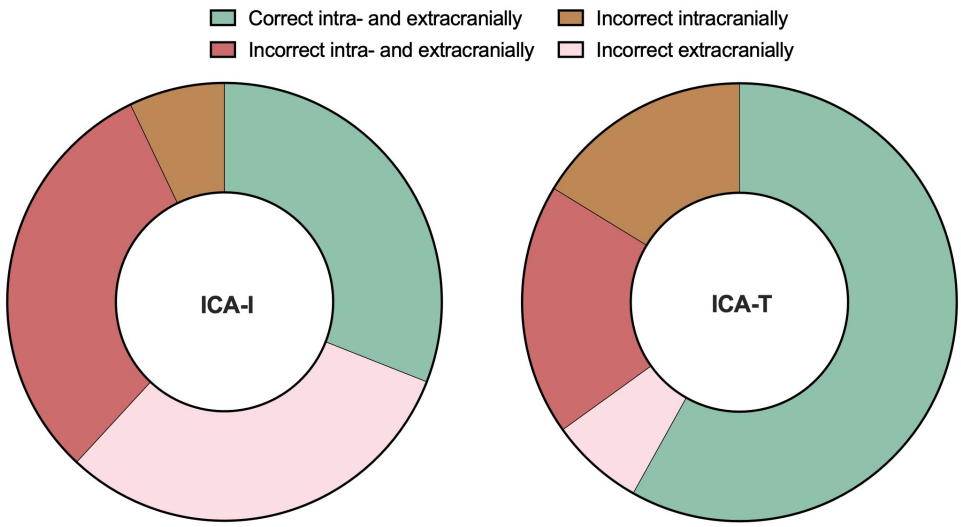

Figure 26. Initial CTA radiology report assessment of ICA-I and ICA-T occlusions.

Discussion

General discussion

EVT has fundamentally transformed the management of acute ischemic stroke, with one of the strongest treatment effects observed in modern medicine. Despite these advances, ischemic stroke remains a leading cause of long-term disability worldwide (4). In Sweden, the proportion of patients receiving EVT has increased over time to approximately 7-8% of all acute ischemic strokes, yet substantial regional differences persist (13).

A conservative treatment strategy that focuses on highly selected patients may appear favorable at first glance, yielding overall better procedural outcomes and fewer complications. However, when viewed at the population level, this approach may risk undertreatment. With an aging population there is a growing need to expand the reach of EVT to more complex patients, improve success rates, and reduce complications.

This thesis provides a comprehensive, real-world assessment of EVT outcomes in Sweden, integrating clinical, radiological, and procedural perspectives. With nationwide, high-quality registry data with near-complete coverage of EVT-treated patients, the studies capture the full spectrum of patients treated in routine clinical practice. The findings indicate an increasing willingness within the Swedish healthcare system to offer EVT to more complex patient groups and that EVT is safe across a broad patient spectrum. Importantly, the results also underscore the critical role of both the preprocedural and the postprocedural care in determining clinical outcomes. Rapid and correct identification of EVT-eligible patients, and optimization of the postoperative care, particularly regarding blood pressure control and infection prevention, emerges as a key opportunity to further improve patient outcomes and maximize the therapeutic benefit of thrombectomy.

The result supports an individualized approach to patient selection and post-procedural care, particularly for patients with complex comorbidities or challenging occlusion patterns.

Principal findings

First, the severity and type of post-EVT ICH varied by occlusion location. Severe postoperative ICHs were uncommon overall, but patients with ICA occlusions were more likely to develop IVH and space-occupying ICH, leading to a higher sICH rate. Isolated SAH was more frequent after EVT of M2 and more distal occlusions, these hemorrhages were most often defined as non-sICH.

Second, comorbidity burden among EVT-treated patients increased over time and was strongly associated with worse functional outcomes and higher mortality rates, despite similar rates of successful recanalization between the CCI groups. However, many highly multimorbid patients achieved favorable outcomes, and successful recanalization was consistently associated with improved outcomes across all levels of comorbidity burden, including patients with very severe multimorbidity.

Third, in patients with MeVOs, successful EVT was associated with clinical benefit, even in those with high comorbidity burden. Successful recanalization was linked to early neurological improvement and favorable 90-day functional outcome, without a corresponding increase in sICH risk.

Finally, baseline clinical and radiological characteristics differed in patients with ICA-I compared to those with ICA-T occlusions, despite similar functional outcomes. ICA-I occlusions were associated with greater heterogeneity in stroke severity and infarct patterns, likely reflecting differences in collateral circulation and anatomical variants of the Circle of Willis. ICA-I occlusions were frequently underrecognized on initial imaging, which may have contributed to delays in the initiation of EVT.

Occlusion location and intracranial hemorrhagic complications

In Paper I, the overall incidence of post-EVT ICH was approximately one quarter, consistent with previous studies (137). Importantly, most of these hemorrhages were classified as non-symptomatic. sICH occurred in 4.5% of patients, aligning with rates reported in major EVT trials and systematic reviews (166, 187).

A key finding was the significantly higher incidence of sICH in patients with intracranial ICA occlusions compared with M1 and M2 or more distal occlusions. This finding is consistent with previous meta-analyses (166) and likely reflects both anatomical and hemodynamic factors. Proximal occlusions often involve

lenticulostriate perforators with limited collateral capacity, predisposing to deep and large infarctions. Reperfusion of large infarcted areas (188) and elevated post-procedural blood pressure (189) have both been associated with increased risk of sICH. However, aggressive blood pressure lowering may be harmful and has been associated with worse functional outcomes, as demonstrated in the ENCHANTED2/MT and OPTIMAL-BP trials, which showed that reducing systolic blood pressure below 120 mmHg (ENCHANTED2/MT) and 140 mmHg (OPTIMAL-BP) should be avoided in post-EVT settings (190, 191).

Although recent trials have shown benefit of EVT in patients with large infarct core at baseline (138, 192), the risk of sICH after EVT for proximal occlusions remains an important concern. Post-procedural blood pressure management therefore requires a careful balance between preserving adequate cerebral reperfusion and minimizing the risk of hemorrhagic complications. Baseline blood pressure was incompletely reported in the registries and was consequently excluded from the analyses to reduce the risk of confounding, which limits our ability to assess its role in the development of sICH. Nevertheless, the results in paper I support an individualized management strategy in which occlusion location and infarct size are actively considered when assessing hemorrhagic risk and guiding post-procedural blood pressure targets. Further studies are warranted to define optimal, location-specific blood pressure strategies following EVT.

In contrast to proximal occlusions, patients with M2 and more distal occlusions exhibited a higher incidence of subarachnoid hemorrhages. This is likely related to mechanical factors, such as stretching and manipulation of smaller and more fragile distal vessels during EVT. Interest in EVT for MeVOs has increased in recent years; however, three multicentre RCTs with PROBE[1] design failed to demonstrate a clear EVT-treatment benefit and instead reported an increased incidence of sICH in this patient population (147, 151, 193).

Paper I demonstrated lower rates of successful recanalization in M2 and more distal occlusions, compared with proximal vessels, highlighting the technical challenges associated with EVT in these vascular territories. Importantly, in our real-world cohort, the rate of sICH among patients with M2 or more distal occlusions was low (4%), suggesting that clinically overt hemorrhagic complications are relatively uncommon following EVT in MeVOs. This observation has important clinical implications, as it suggests that hemorrhagic risk alone may not fully account for the lack of treatment benefit observed in the RCTs. Alternatively, non-sICH has a greater clinical impact than traditionally assumed, potentially affecting neurological recovery despite not meeting formal sICH criteria. In patients with MeVOs, who

[1] Prospective Randomized Open-label Blinded Endpoint

presented with a median baseline NIHSS score of 6-8 in the RCTs, an increase of four points represents a substantial neurological deterioration. This highlights a potential limitation of current sICH definition when applied to MeVOs and suggests that alternative or more granular hemorrhage classifications may be required to better capture clinically relevant complications in this population.

Taken together, these findings provide clinically relevant reassurance regarding the procedural safety of EVT in distal occlusions, while simultaneously emphasizing the need for improved patient selection, refined outcome measures, and further research to identify subgroups of MeVO patients most likely to benefit from EVT. Future optimization of endovascular techniques may improve recanalization rates in MeVOs and reduce the incidence of sICH. Such advances may ultimately allow a clearer treatment effect of EVT to be demonstrated in subgroups of this patient population.

Comorbidity burden and outcomes after endovascular thrombectomy

Paper II demonstrated a clear temporal increase in comorbidity burden among pre-stroke functionally independent patients treated with EVT in Sweden, rising from 16% to 30% of the total EVT population. This trend likely reflects both an aging population and an increased willingness to offer EVT to patients with more complex medical profiles.

Despite an overall poorer prognosis with increasing comorbidity burden, approximately one fifth of patients with a very severe comorbidity burden achieved functional independence (mRS 0-2) at 90 days, and more than 40% attained an mRS score of 3 or better. These outcomes were strongly influenced by age: only 5% of patients aged over 89 years with a very severe comorbidity burden achieved functional independence at 90 days, and 10% of those aged 80-89 years. This suggests that age substantially modifies the association between comorbidity burden and functional outcome and highlights the importance of considering age-comorbidity interactions when estimating prognosis and treatment benefit.

The association between higher comorbidity burden and poorer outcome was primarily driven by increased mortality, whereas differences in functional dependency among survivors were less pronounced. Importantly, comorbidity burden had minimal impact on technical success rates and periprocedural complications, indicating that procedural feasibility and safety are largely preserved even in patients with substantial multimorbidity. This distinction is clinically

important, as it suggests that poorer outcomes in multimorbid patients are mainly attributable to limited physiological reserves, competing risks, and reduced recovery potential rather than EVT failure or procedural complications.

Postoperative complications were associated with a marked reduction in survival, independent of both recanalization status and baseline comorbidity burden, with the adverse effect being most pronounced in patients with the highest comorbidity burden. The most frequent postoperative complications were ICH and severe infections, including pneumonia and urosepsis (Paper II, Supplementary Table 2). Although Paper I demonstrates a declining incidence of ICH over time (Figure 13), these findings nonetheless suggest that further optimization of postoperative care remains warranted, particularly with respect to strategies aimed at minimizing hemorrhagic complications and preventing infections, and especially for multimorbid patients.

Successful recanalization was associated with improved functional outcomes and survival across all CCI groups. This benefit was largely driven by reduced mortality and a lower proportion of patients with severe functional disability (mRS 5) for recanalized patients, a clinically meaningful outcome given the substantial impact of severe disability on quality of life (194). Collectively, these results indicate that multimorbidity should not be regarded as an absolute contraindication to EVT. This finding is clinically important, as multimorbid patients, due to higher prevalence of atrial fibrillation and consequent anticoagulant use (195), are less often eligible for intravenous thrombolysis, making EVT their primary treatment option.

In Paper III, similar patterns were observed in patients with anterior circulation MeVOs. Successful recanalization was associated with favorable outcomes across all comorbidity groups, including patients with CCI ≥3. These real-world findings differ from those reported in the RCTs which did not demonstrate a clear clinical benefit of EVT for MeVOs (196, 197). However, several factors should be considered when interpreting this discrepancy.

First, the exposure of interest in Paper III was successful versus unsuccessful EVT, rather than EVT versus best medical therapy. This distinction is critical, as comparisons based on technical success cannot be interpreted as direct estimates of causal treatment effect.

Second, baseline stroke severity differed between our cohort and the RCT populations. The median NIHSS score in our cohort was 11, compared with 6–8 in the RCTs, indicating that our population generally had more severe neurological deficits and may therefore have had greater potential to benefit from EVT. This difference could reflect selective recruitment in the RCT setting, where patients with

more severe deficits who were perceived to have a strong indication for EVT, may have been treated outside trial protocols, while patients with milder symptoms were more likely to be enrolled. This interpretation is indirectly supported by the HERMES post-hoc meta-analysis of M2 occlusions, where the median NIHSS was 14 (148). Thus, stroke severity in our cohort falls between that reported in the MeVO RCTs and the post-hoc meta-analyses. If RCT enrollment favored patients with lower NIHSS, this could partly explain the lack of treatment effects, as fewer patients would have substantial tissue at risk and potential for clinical improvement. However, this theory remains speculative, and the potential selection bias has not been confirmed.

Taken together, Paper III supports the hypothesis that successful reperfusion remains clinically meaningful in selected MeVO patients, even among those with substantial comorbidity. However, the findings should be interpreted as evidence of the prognostic importance of recanalization rather than as definitive proof of EVT efficacy.

Clinical and radiological outcomes in ICA-I and ICA-T occlusions

Paper IV revealed important differences between ICA-I and ICA-T occlusions that extend beyond traditional occlusion classification. Despite similar rates of successful recanalization and comparable functional outcomes between ICA-I and ICA-T occlusions, ICA-I occlusions were associated with greater variability in stroke severity, including both very mild and very severe presentations. This heterogeneity might be explained by differences in collateral capacity, which in ICA-I occlusions depends heavily on anatomical variants of the Circle of Willis. Complete anterior collateral pathways may result in minimal deficits, whereas absent or hypoplastic A1 segments, anterior communicating artery variants, or fetal-type posterior cerebral arteries can lead to extensive ischemia involving multiple vascular territories.

The secondary analysis showed that ICA-I occlusions are frequently underdiagnosed and misunderstood on initial imaging. The diminishing contrast density observed in the proximal ICA during an intracranial ICA occlusion (Figure 27) is easy to misinterpret as extracranial ICA pathology, such as dissection or occlusion, explaining the high misclassification of the extracranial segment in both groups.

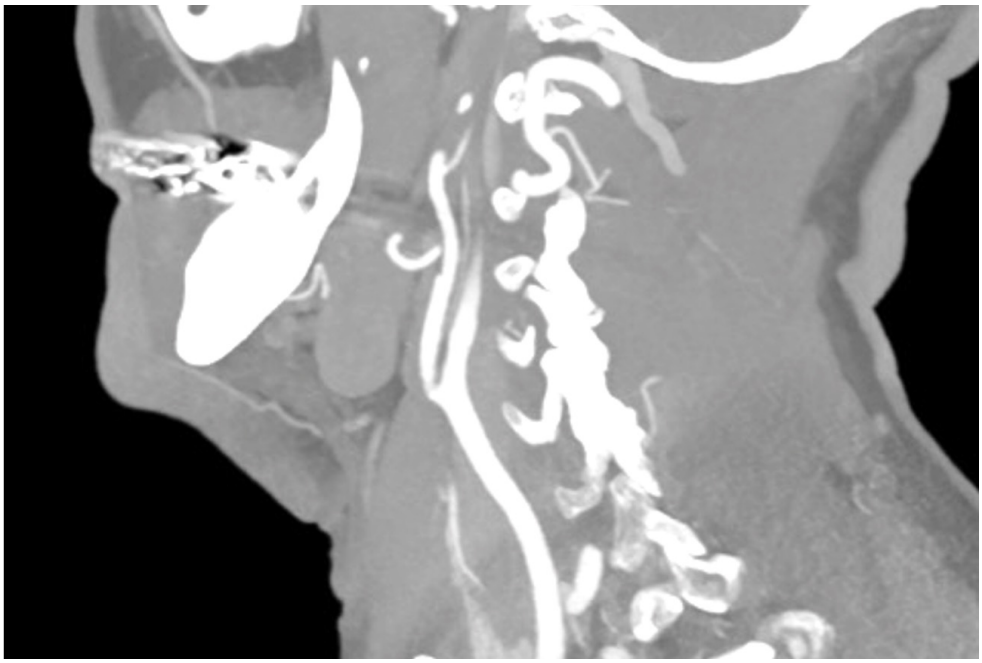

Figure 27. Sagital view of the dimishing contrast density observed on CTA in the extracranial ICA during an ICA-I occlusion.

Intracranial misclassification occurred in both ICA-I and ICA-T occlusions; however, the nature and clinical implications of these errors differed between groups. In ICA-T occlusions, misclassifications most commonly involved description of an M1 occlusion, a distinction that is unlikely to substantially influence stroke pathways or treatment timelines. In contrast, for ICA-I occlusions, the intracranial segment was frequently not reported at all. This can be one of the causes for the delayed EVT initiation seen in patients with ICA-I occlusion both in this and in earlier studies (26).

Improved awareness of ICA-I imaging patterns and routine use of perfusion imaging may facilitate earlier diagnosis and initiation of EVT, potentially improving outcomes in this challenging patient group.

Methodological considerations and strengths

The principal strength of this dissertation lies in the use of nationwide, high-quality registry data with near-complete coverage of EVT-treated patients in Sweden. This

design allows for evaluation of real-world practice across a broad and clinically relevant patient spectrum, including elderly individuals, patients with multiple comorbidities, and patients with less common or complex clinical characteristics. By linking multiple databases, we have access to comprehensive clinical and demographic information within large cohorts, enabling high statistical power and the possibility to examine rare outcomes and specific subgroups.

RCTs remain the gold standard for evaluating the efficacy and safety of medical interventions. Their primary strength lies in the use of randomization for patient allocation, which reduces confounding, and allows for strong causal inference. However, the strict inclusion and exclusion criteria in RCTs often lead to highly selected study populations, frequently excluding elderly and multimorbid patients (198), which limits the generalizability of findings to real-world clinical practice.

In contrast, registry-based studies typically include patients who are underrepresented or excluded from RCTs and therefore provide valuable insights into treatment characteristics and prognosis in broader populations. These advantages must, however, be weighed against important limitations. Variations in data quality, variable definitions, and reporting practices across centers can complicate interpretation. Observational registry-based studies are therefore vulnerable to confounding and bias, and causality cannot be established.

Bias and confounding

Bias refers to systematic errors in the design of an analysis that distort the result in a consistent direction and therefore leads to incorrect estimation of the association between an exposure and an outcome (type I-III errors).

Confounding is a systematic error that arises when an external factor is associated with both the exposure and the outcome, creating a false or distorted relationship between them. This occurs when the confounder is unevenly distributed between comparison groups. Confounders must be distinguished from mediators, which lie on the causal pathway and explain *how* an exposure affects an outcome. A third type of variable is a collider, which is influenced by both the exposure and the outcome. Colliders should not be controlled for in analyses, as doing so can introduce bias and distort causal relationships. In all four papers, potential confounders were carefully identified and included in the analyses to minimize the risk of statistical bias.

Selection bias and attrition bias in Riksstroke

Selection bias arises when the individuals included in the study do not represent the population the study intends to describe. It occurs due to systematic errors in how participants are selected or excluded, or in the factors that influence study

participation. Attrition bias is a type of selection bias which occurs when participants drop out of a study in a way that is not random.

One of the major limitations of the mRS is the potential of interobserver variability which can compromise reliability. The initial validation studies of the mRS reported moderate inter-rater agreement, with a kappa coefficient of 0.56 for pairwise observations (199). However, agreement was substantially lower across raters from different stroke centers, where the kappa decreased to 0.25 (200). More recent studies suggest that overall inter-rater reliability in multicenter settings ranges from moderate to good, although significant heterogenicity was observed across countries (201). Notably, agreement tends to improve at the higher end of the mRS, while lower scores are associated with greater inter-reader variability (201).

Even though the translation of self-reported outcome to nurse-adjudicated mRS grades has been validated with high agreement (172, 180), the system relies on patients returning the follow-up questionnaires which is an issue especially in older individuals and those with high dependency level (202). As a result, the proportion of missing mRS data in Riksstroke is substantial, approximately 20%. To address this, multiple imputation was applied to handle missing mRS values, as excluding these cases would introduce considerable attrition bias by underestimating the proportion of patients with mRS 3-5.

Information bias

Information bias arises when the data collected are inaccurate or measured inconsistently. It occurs due to errors in how information is obtained, recorded, or interpreted - such as misclassification, and faulty measurement tools.

The variables in EVAS, such as occlusion site, mTICI, and complications are reported by the performing medical center without external validation. This could lead to biased reporting and an overestimation (or underestimation) of the medical center's own results.

Paper I

To avoid overfitting in multivariable logistic regression analysis, a commonly applied rule of thumb is to include at least 10 outcome events per predictor variable, although this requirement can be somewhat relaxed, especially in sensitivity analyses (203). Based on the number of sICH events, the multivariable logistic regression model in paper I allowed for 14 confounders. However, since missing blood glucose values are substantial in EVAS, this variable could not be included, which represents a limitation. Diabetes was included instead and showed a strong association with sICH. Periprocedural intra-arterial thrombolysis was not included, as it was considered a mediator rather than a confounder.

Paper II and III

The original CCI does not include common conditions strongly associated with ischemic stroke, such as hypertension and atrial fibrillation. In addition, the index was developed in 1987, and advances in medical care have since improved the prognosis of several conditions included in the CCI. For example, HIV/AIDS which translate to the highest CCI score despite markedly improved outcomes in the modern treatment era (204). In paper II, only four patients had HIV/AIDS, making a meaningful impact on the results unlikely.

Another limitation of the CCI is that age is not included, despite age being a well-established determinant of stroke outcome (27). We were unable to identify a comorbidity index that incorporates age validated for an EVT-treated stroke population.

In addition, Swedish quality registries do not capture patients who were eligible for but not treated with EVT, introducing potential selection bias and limiting the generalizability of the findings to more medically complex patients who were considered too medically unstable to undergo EVT treatment. Inclusion of untreated eligible patients would have been necessary to assess the true treatment effectiveness of EVT in this population.

Finally, the association between successful recanalization and favorable outcomes observed in Papers II and III should be interpreted with caution. Patients without successful recanalization are more likely to have undergone prolonged, technically difficult, or prematurely terminated procedures and may therefore be disproportionately exposed to periprocedural complications, including vessel perforation. This introduces a potential form of procedural harm bias and may contribute to confounding when interpreting recanalization status as a causal determinant of outcome. However, prior studies have reported no significant outcome differences between unsuccessful EVT and best medical management, even among patients with low ASPECTS (205, 206). Moreover, in Paper III, the association between successful recanalization and favorable outcomes remained consistent across all CCI groups after exclusion of patients with perioperative vessel perforations, thereby reducing the influence of severe procedural complications on the observed estimates. In addition, the absence of neurological deterioration following EVT among unsuccessfully recanalized patients supports the interpretation that the observed outcome differences are unlikely to be primarily driven by failed EVT.

Paper IV

ICA-I occlusions are underreported by radiologists and may go undetected due to mild or subtle clinical symptoms. This under-recognition can lead to sampling bias, as the study population may disproportionately represent more clinically apparent or severe cases. Consequently, the true clinical and radiological variability of ICA-I occlusions may be greater than observed in this study. In addition, the relatively

small sample size further limits the precision of the estimates and reduces statistical power, increasing the risk that important differences may have gone undetected. The small number of cases also restricts generalizability, and the findings should therefore be interpreted with caution and validated in larger cohorts.

Future perspectives

Recovery after ischemic stroke is a multidimensional and dynamic process, and no single outcome measure can fully capture the spectrum of post-stroke disability and functional recovery. Despite its limitations, the mRS remains a clinically meaningful and widely accepted outcome measure after ischemic stroke, due to its simplicity and strong clinical relevance. However, this thesis lacks the patient perspective on health-related quality of life. Riksstroke contains a variable reflecting patients' self-perceived health-related quality of life. Complementary instruments such as the Barthel Index, which is useful for evaluating independence in activities of daily living and guiding rehabilitation planning, and the Stroke Impact Scale, which captures patient-reported physical, cognitive, and psychosocial domains of recovery, would provide important additional insights. Incorporating such measures in future studies would improve understanding of whether early clinical outcomes translate into meaningful and sustained benefits for patients.

The findings of this thesis highlight the need for future research on long-term prognosis and cost-effectiveness, particularly in patients with multiple or severe comorbidities, where the balance between benefit and risk may differ from that in healthier populations. In parallel, continued efforts to optimize the implementation of EVT are essential. This includes reduction of workflow delays, and expansion of thrombectomy centers at both national and global levels.

Furthermore, our results support studies exploring individualized blood pressure targets after EVT based on occlusion location, as well as studies about the clinical implications of small subarachnoid hemorrhages following EVT for MeVOs. Finally, the data underscore the importance of identifying effect-modifying factors such as occlusion subtype, stroke severity, and imaging-based tissue at risk, to better define which MeVO patients are most likely to benefit from EVT and to optimize future patient selection.

Beyond reperfusion, complementary treatments should continue to be studied. Neuroprotective therapies, aimed at preserving penumbral tissue and minimizing reperfusion injury, may complement EVT, particularly in patients with delayed presentation or in regions with long distances to the nearest thrombectomy center. Furthermore, implementation of mobile CT scanners in ambulances may shorten the time to diagnosis and treatment decisions, especially in geographically distant areas.

At a global level, the increasing incidence of ischemic stroke must be addressed, particularly among younger populations, where the upward trend has been notably pronounced. Future progress in EVT will also depend on a deeper understanding of biological factors. Advances in stroke genetics and molecular profiling may help identify individuals at increased risk of stroke, as well as those with vulnerability to ischemic injury, hemorrhagic complications, or reduced responsiveness to preventive therapies, thereby enabling more personalized treatment strategies. Furthermore, the management of intracranial atherosclerotic disease remains an important unresolved issue, and further studies are needed to assess the role of stenting in selected patients with significant intracranial stenosis or recurrent ischemia.

In summary, future progress in acute ischemic stroke care and EVT-outcome will rely on optimized preventive strategies, improved patient selection, complementary medical therapies, improved post-operative care and rehabilitative strategies, together with expanded access to EVT-centers.

Conclusions

This thesis offers new insights into EVT-related complications and outcomes, integrating clinical and radiological perspectives, with the primary aim of supporting informed treatment decisions and enhancing patient care.

In Paper I, we showed that serious hemorrhagic complications were relatively uncommon, but their type and severity varied according to occlusion location. This suggests that anatomical and hemodynamic factors may influence both the mechanisms and consequences of post-procedural bleeding, highlighting their importance in risk assessment and post-EVT management. However, our ability to predict which individual patients will develop hemorrhagic complications remains limited. Further studies are needed to guide location-specific preventive strategies, including individualized blood pressure management, antithrombotic treatment, and imaging-based risk stratification.

Paper II revealed a clear temporal increase in comorbidity burden among EVT-treated patients in Sweden, reflecting a broadening of EVT indications. Although more severe comorbidity was associated with poorer overall prognosis, successful recanalization and complication rates were largely unaffected, and successful recanalization was consistently associated with functional independence and reduced mortality across all comorbidity levels. These findings underscore the importance of reducing postoperative complications and shows that multimorbidity should not be regarded as an absolute contraindication to EVT.

In Paper III, successful EVT for MeVOs was shown to provide meaningful clinical benefit, including early neurological improvement and favorable 90-day functional outcomes, even in patients with high comorbidity burden, without a corresponding increase in sICH. While these findings do not replace evidence from RCTs, they provide important real-world data suggesting that selected patients with MeVOs may derive meaningful benefit from EVT. The results highlight the need for new and refined RCTs with careful patient selection and procedural optimization to analyze the benefits of EVT in distal occlusions.

Finally, in Paper IV, the detailed comparison of ICA-I and ICA-T occlusions reveals substantial clinical and radiological heterogeneity within what is often treated as a

single entity. ICA-I occlusions exhibited greater heterogeneity in baseline stroke severity, and infarct patterns. The results emphasize the need for improved understanding among radiologists and stroke physicians to optimize treatment timing and outcomes in this challenging patient group.

Collectively, these studies demonstrate that EVT is safe and associated with clinical benefits and outcomes across a broad spectrum of patients treated in routine clinical practice, including highly multimorbid individuals. They also emphasize the importance of individualized treatment decisions regarding occlusion characteristics, comorbidity profile, and procedural risk. Continued optimization of patient selection, procedural techniques, and peri- and post-procedural management has the potential to further improve outcomes and ensure that the benefits of EVT are achieved across the full spectrum of patients with acute ischemic stroke.

Popular science summary

Stroke is one of the leading causes of death and long-term disability worldwide (4). The most common form, ischemic stroke, occurs when a blood clot obstructs a cerebral artery, depriving brain tissue of oxygen and nutrients. Without rapid treatment, brain cells begin to die within minutes, often leading to permanent disability or death.

Over the past decade, stroke care has undergone a major transformation with the implementation of endovascular thrombectomy – a minimally invasive procedure in which thin catheters are navigated through the blood vessels to mechanically remove the clot from the brain. Thrombectomy has improved outcomes for countless patients and is now regarded as one of the most effective treatments in modern medicine. However, not all patients benefit equally, and the procedure carries a risk of serious complications.

Treatment outcomes are influenced by several factors. Experience (107) and the sensitivity of individual fingers (207) differ between operators, but patient-related factors are often more decisive, including vascular anatomy, stroke severity, and overall health status. To further improve stroke care, it is therefore essential to identify which patients benefit most from thrombectomy, which are at increased risk of complications, and which factors contribute to variation in treatment outcomes.

The overall aim of this thesis was to improve the understanding of clinical and radiological outcomes after thrombectomy, with a particular focus on complications, comorbidity, and differences related to the location of the vessel occlusion. The studies are based on national Swedish health registries, enabling analysis of all stroke patients treated with thrombectomy across the country.

One of the most serious complications following thrombectomy is intracranial hemorrhage. One key finding in this thesis is that serious bleeding in the brain after thrombectomy is uncommon, but the risk varies with occlusion location. Occlusions in larger and more proximal arteries were associated with more severe bleeding complications, while patients with more distal clots often had small bleedings that rarely caused major symptoms. This highlights the need for individualized monitoring after treatment.

Another central focus of the thesis was comorbidity, defined as the presence of other chronic conditions such as cardiovascular disease, diabetes, cancer, or kidney disease. Most stroke patients have multiple coexisting conditions, and the results show that the number of thrombectomy-treated patients with high or very high comorbidity burden has increased markedly in recent years. Despite an overall worse prognosis, successful clot removal was strongly associated with improved survival and functional independence even in patients with severe comorbidity. This shows that having multiple illnesses should not automatically exclude patients from receiving thrombectomy.

The thesis also examined thrombectomy in patients with occlusions in medium-sized, more distal cerebral vessels. Although these strokes often present with less severe initial symptoms, they may still lead to substantial long-term disability (146). While the benefit of thrombectomy in this patient group has not yet been established at the population level, our results indicate that successful clot removal in medium-sized vessels improves outcomes in patients both with and without significant comorbidity. However, the overall benefit was smaller and the risk of complications higher among patients with extensive comorbidity.

Finally, differences between two types of occlusions in the Internal Carotid Artery were examined. The studies revealed variations in stroke severity and imaging findings, depending on the exact occlusion site and the brain's ability to redirect blood flow through collateral vessels. Importantly, intracranial internal carotid artery occlusions were frequently misinterpreted on initial imaging, leading to treatment delays.

In summary, this thesis provides new insights into how occlusion location, comorbidity burden, and complications influence outcomes after endovascular thrombectomy. The findings support a more individualized approach to stroke treatment, in which clinical decisions are guided not only by time and imaging but also by patient health status, vascular anatomy, and risk of complications.

Populärvetenskaplig sammanfattning på svenska

Stroke är en av de vanligaste orsakerna till långvarig funktionsnedsättning och död världen över. Den vanligaste typen, ischemisk stroke, uppstår när en blodpropp blockerar ett blodkärl som försörjer hjärnan, vilket leder till syre- och näringsbrist i hjärnvävnaden. Utan snabb behandling börjar hjärnceller att dö redan inom några minuter, vilket ofta resulterar i permanent funktionsnedsättning eller död.

Under det senaste decenniet har strokevården genomgått en omfattande förändring genom införandet av endovaskulär trombektomi, en minimalt invasiv behandling där tunna katetrar förs genom blodkärlen för att mekaniskt avlägsna blodproppen från hjärnan. Trombektomi har förbättrat prognosen för otaliga patienter och betraktas idag som en av de mest effektiva behandlingarna inom modern medicin. Alla patienter har tyvärr inte lika stor nytta av behandlingen, och ingreppet är förenat med risk för allvarliga komplikationer.

Behandlingsutfallet påverkas av flera faktorer. Erfarenhet (107) och känsligheten i vissa fingrar (207) varierar mellan behandlare men patientrelaterade faktorer ofta mer avgörande för utfallet. Dessa inkluderar kärlanatomiska förutsättningar, strokens svårighetsgrad och patientens allmäntillstånd. För att ytterligare förbättra strokevården är det avgörande att förstå vilka patienter som har störst nytta av trombektomi, vilka som löper ökad risk för komplikationer och vilka faktorer som bidrar till variationer i behandlingsresultatet.

Det övergripande syftet med denna avhandling var att öka förståelsen för kliniska och radiologiska utfall efter trombektomi, med särskilt fokus på komplikationer, samsjuklighet och skillnader relaterade till kärlocklusionens lokalisation. Studierna bygger på nationella svenska hälsoregister, vilket möjliggör inkludering av samtliga strokepatienter som trombektomerats runt om i landet.

En av de allvarligaste komplikationerna efter trombektomi är hjärnblödningar. Ett centralt fynd i denna avhandling är att allvarlig hjärnblödning efter trombektomi är ovanlig, men att risken varierar beroende på ocklusionens lokalisation. Ocklusioner i större och mer centrala artärer är associerade med allvarligare

blödningskomplikationer, medan ocklusioner längre ut i kärlträdet oftare ger upphov till mindre allvarliga blödningar.

Ett annat viktigt fokusområde i avhandlingen var samsjuklighet, det vill säga förekomst av andra kroniska sjukdomar såsom hjärt-kärlsjukdom, diabetes, cancer eller njursjukdom. Många strokepatienter har oftast flera samtidiga sjukdomar, och resultatet i avhandlingen visar att antalet trombektomibehandlade patienter med hög eller mycket hög sjukdomsbörda har ökat kraftigt de senaste åren. Trots en generellt sämre prognos visar resultaten att framgångsrik trombektomibehandling är starkt kopplad till förbättrad överlevnad och funktionell självständighet även hos patienter med svår samsjuklighet. Detta visar att multipla sjukdomar i sig inte bör utgöra ett automatiskt hinder för trombektomi.

Avhandlingen undersökte även trombektomi hos patienter med ocklusioner i medelstora kärl, belägna närmare hjärnans yta. Denna typ av stroke ger inte lika allvarliga symtom som mer centrala proppar, men leder trots det ofta till betydande funktionsnedsättning. Även om nyttan av trombektomi i denna patientgrupp ännu inte är fastställd på populationsnivå, visar våra resultat att framgångsrikt avlägsnande av blodproppar i medelstora kärl förbättrar utfallet hos patienter både med och utan uttalad samsjuklighet. Den sammantagna nyttan var dock mindre och komplikationsrisken högre hos patienter med omfattande samsjuklighet.

Slutligen studerades skillnader mellan två typer av ocklusioner i arteria carotis interna, vilka ofta analyseras tillsammans trots viktiga anatomiska skillnader. Studien visar på variation i bilddiagnostiska fynd och neurologiska utfall beroende på den exakta lokalisationen av ocklusionen samt hjärnans förmåga att omdirigera blodflödet via kollaterala kärl. Det framkom även att intrakraniella ocklusioner i arteria carotis interna ofta misstolkades vid den initiala bilddiagnostiken, vilket leder till fördröjd behandling.

Sammanfattningsvis bidrar denna avhandling med ny kunskap om hur ocklusionslokalisation, samsjuklighetsbörda och komplikationer påverkar utfallet efter endovaskulär trombektomi. Resultaten stödjer ett mer individualiserat förhållningssätt till strokebehandling, där kliniska beslut inte enbart baseras på tid, bilddiagnostik och riktlinjer, utan även på patientens hälsotillstånd, kärlanatomi och risk för komplikationer.

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References

1. Gijn Jv. Stroke: a history of ideas: Cambridge University Press; 2023.
2. Willis T. Cerebri anatome: cui accessit nervorum descripto et usus: Londini: Typis Ja. Flesher, impensis Jo. Martyn & Ja. Allestry; 1664.
3. Hatano S. Experience from a multicentre stroke register: a preliminary report. Bull World Health Organ. 1976;54(5):541-53.
4. Global, regional, and national burden of stroke and its risk factors, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Neurol. 2024;23(10):973-1003.
5. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2021;20(10):795-820.
6. Feigin VL, Abate MD, Abate YH, Abd ElHafeez S, Abd-Allah F, Abdelalim A, et al. Global, regional, and national burden of stroke and its risk factors, 1990-2013;2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Neurol. 2024;23(10):973-1003.
7. Arsava EM, Helenius J, Avery R, Sorgun MH, Kim GM, Pontes-Neto OM, et al. Assessment of the Predictive Validity of Etiologic Stroke Classification. JAMA Neurol. 2017;74(4):419-26.
8. Diener HC, Hankey GJ. Primary and Secondary Prevention of Ischemic Stroke and Cerebral Hemorrhage: JACC Focus Seminar. J Am Coll Cardiol. 2020;75(15):1804-18.
9. Fan J, Li X, Yu X, Liu Z, Jiang Y, Fang Y, et al. Global Burden, Risk Factor Analysis, and Prediction Study of Ischemic Stroke, 1990-2030. Neurology. 2023;101(2):e137-e50.
10. Pu L, Wang L, Zhang R, Zhao T, Jiang Y, Han L. Projected Global Trends in Ischemic Stroke Incidence, Deaths and Disability-Adjusted Life Years From 2020 to 2030. Stroke. 2023;54(5):1330-9.
11. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10(1):14790.

12. The Swedish National Board of Health and Welfare. Statistical Database for In-Patient Care Diagnoses. Access date: 2025-11-25. [Available from: https://sdb.socialstyrelsen.se/if_stroke/val.aspx].
13. Wassélius J, Hall E, Szolics A, Arnberg F, Radhi H, von Euler M, et al. Large regional variation in endovascular thrombectomy rates for acute ischemic stroke in Sweden. Eur Stroke J. 2025:23969873251347098.
14. Drescher C, Buchwald F, Ullberg T, Pihlsgård M, Norrving B, Petersson J. Epidemiology of First and Recurrent Ischemic Stroke in Sweden 2010-2019: A Riksstroke Study. Neuroepidemiology. 2022;56(6):433-42.
15. Margetis K, Sánchez-Manso JC. Neuroanatomy, Middle Cerebral Artery. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2025, StatPearls Publishing LLC.; 2025.
16. Saver JL, Chapot R, Agid R, Hassan AE, Jadhav AP, Liebeskind DS, et al. Thrombectomy for Distal, Medium Vessel Occlusions. Stroke. 2020;51(9):2872-84.
17. Kricheff II, Taveras JM. The Angiographic Localization of Suprasylvian Space-Occupying Lesions. Radiology. 1964;82(4):602-14.
18. Hakim A, Gralla J, Rozeik C, Mordasini P, Leidolt L, Piechowiak E, et al. Anomalies and Normal Variants of the Cerebral Arterial Supply: A Comprehensive Pictorial Review with a Proposed Workflow for Classification and Significance. Journal of Neuroimaging. 2018;28(1):14-35.
19. Coulier B. Duplication of the Posterior Cerebral Artery (PCA) or "True Fetal PCA": An Extremely Rare Variant. J Belg Soc Radiol. 2018;102(1):29.
20. Ospel JM, Nguyen TN, Jadhav AP, Psychogios MN, Clarençon F, Yan B, et al. Endovascular Treatment of Medium Vessel Occlusion Stroke. Stroke. 2024;55(3):769-78.
21. Halama D, Merkel H, Werdehausen R, Gaber K, Schob S, Quäschling U, et al. Reference Values of Cerebral Artery Diameters of the Anterior Circulation by Digital Subtraction Angiography: A Retrospective Study. Diagnostics (Basel). 2022;12(10).
22. Saver JL, Chapot R, Agid R, Hassan A, Jadhav AP, Liebeskind DS, et al. Thrombectomy for Distal, Medium Vessel Occlusions: A Consensus Statement on Present Knowledge and Promising Directions. Stroke. 2020;51(9):2872-84.
23. Diprose WK, Pensato U, Almekhlafi M, Psychogios MN, Fischer U, Clarençon F, et al. Acute Management of Medium Vessel Occlusion Stroke: New Evidence and a Path Forward. Stroke. 2025.
24. Liebeskind DS, Flint AC, Budzik RF, Xiang B, Smith WS, Duckwiler GR, et al. Carotid I's, L's and T's: collaterals shape the outcome of intracranial carotid occlusion in acute ischemic stroke. J Neurointerv Surg. 2015;7(6):402-7.

25. Riegler C, von Rennenberg R, Bollweg K, Siebert E, de Marchis GM, Kägi G, et al. Endovascular therapy in patients with acute intracranial non-terminal internal carotid artery occlusion (ICA-I). Eur Stroke J. 2024:23969873241278948.
26. Riegler C, von Rennenberg R, Bollweg K, Nguyen TN, Kleine JF, Tiedt S, et al. Endovascular therapy in patients with internal carotid artery occlusion and patent circle of Willis. Journal of NeuroInterventional Surgery. 2024;16(7):644.
27. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387(10029):1723-31.
28. Ullberg T, von Euler M, Wassélius J, Wester P, Arnberg F. Survival and functional outcome following endovascular thrombectomy for anterior circulation acute ischemic stroke caused by large vessel occlusion in Sweden 2017-2019-a nationwide, prospective, observational study. Interv Neuroradiol. 2023;29(1):94-101.
29. Saba L, Cau R, Vergallo R, Kooi ME, Staub D, Faa G, et al. Carotid artery atherosclerosis: mechanisms of instability and clinical implications. European Heart Journal. 2025;46(10):904-21.
30. Gutierrez J, Turan TN, Hoh BL, Chimowitz MI. Intracranial atherosclerotic stenosis: risk factors, diagnosis, and treatment. The Lancet Neurology. 2022;21(4):355-68.
31. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22(8):983-8.
32. Chen H, Colasurdo M, Costa M, Nossek E, Kan P. Carotid webs: a review of pathophysiology, diagnostic findings, and treatment options. J Neurointerv Surg. 2024;16(12):1294-8.
33. Ekker MS, Verhoeven JI, Schellekens MMI, Boot EM, van Alebeek ME, Brouwers P, et al. Risk Factors and Causes of Ischemic Stroke in 1322 Young Adults. Stroke. 2023;54(2):439-47.
34. Song M, Yu SP. Ionic regulation of cell volume changes and cell death after ischemic stroke. Transl Stroke Res. 2014;5(1):17-27.
35. Todd NV, Picozzi P, Crockard A, Russell RW. Duration of ischemia influences the development and resolution of ischemic brain edema. Stroke. 1986;17(3):466-71.
36. Astrup J, Siesjö BK, Symon L. Thresholds in cerebral ischemia - the ischemic penumbra. Stroke. 1981;12(6):723-5.

37. Chalela JA, Kidwell CS, Nentwich LM, Luby M, Butman JA, Demchuk AM, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. Lancet. 2007;369(9558):293-8.
38. Dippel DWJ, Du Ry van Beest Holle M, van Kooten F, Koudstaal PJ. The validity and reliability of signs of early infarction on CT in acute ischaemic stroke. Neuroradiology. 2000;42(9):629-33.
39. Jung S, Gilgen M, Slotboom J, El-Koussy M, Zubler C, Kiefer C, et al. Factors that determine penumbral tissue loss in acute ischaemic stroke. Brain. 2013;136(12):3554-60.
40. Pexman JH, Barber PA, Hill MD, Sevick RJ, Demchuk AM, Hudon ME, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. AJNR Am J Neuroradiol. 2001;22(8):1534-42.
41. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet. 2000;355(9216):1670-4.
42. Altiparmak T, Nazliel B, Batur Caglayan H, Tokgoz N, Akyol Gurses A, Ucar M. Posterior Circulation Alberta Stroke Program Early Computed Tomography Score (pc-ASPECT) for the Evaluation of Cerebellar Infarcts. Neurologist. 2022;27(6):304-8.
43. Gupta AC, Schaefer PW, Chaudhry ZA, Leslie-Mazwi TM, Chandra RV, González RG, et al. Interobserver reliability of baseline noncontrast CT Alberta Stroke Program Early CT Score for intra-arterial stroke treatment selection. AJNR Am J Neuroradiol. 2012;33(6):1046-9.
44. Nicolas-Jilwan M, Wintermark M. Automated Brain Perfusion Imaging in Acute Ischemic Stroke: Interpretation Pearls and Pitfalls. Stroke. 2021;52(11):3728-38.
45. Austein F, Riedel C, Kerby T, Meyne J, Binder A, Lindner T, et al. Comparison of Perfusion CT Software to Predict the Final Infarct Volume After Thrombectomy. Stroke. 2016;47(9):2311-7.
46. Finnerty FA, Jr., Witkin L, Fazekas JF. Cerebral hemodynamics during cerebral ischemia induced by acute hypotension. J Clin Invest. 1954;33(9):1227-32.
47. Jennett WB, Harper AM, Gillespie FC. Measurement of regional cerebral blood-flow during carotid ligation. Lancet. 1966;2(7474):1162-3.

48. Broocks G, Meyer L, Winkelmeier L, Kniep H, Heitkamp C, Christensen S, et al. Overestimation of the Ischemic Core Is Associated With Higher Core Lesion Volume and Degree of Reperfusion After Thrombectomy. Radiology. 2024;312(1):e231750.
49. Jones TH, Morawetz RB, Crowell RM, Marcoux FW, FitzGibbon SJ, DeGirolami U, et al. Thresholds of focal cerebral ischemia in awake monkeys. J Neurosurg. 1981;54(6):773-82.
50. Heiss WD, Rosner G. Functional recovery of cortical neurons as related to degree and duration of ischemia. Ann Neurol. 1983;14(3):294-301.
51. Labeyrie MA, Turc G, Hess A, Hervo P, Mas JL, Meder JF, et al. Diffusion lesion reversal after thrombolysis: a MR correlate of early neurological improvement. Stroke. 2012;43(11):2986-91.
52. Kidwell CS, Saver JL, Mattiello J, Starkman S, Vinuela F, Duckwiler G, et al. Thrombolytic reversal of acute human cerebral ischemic injury shown by diffusion/perfusion magnetic resonance imaging. Ann Neurol. 2000;47(4):462-9.
53. Marcoux FW, Morawetz RB, Crowell RM, DeGirolami U, Halsey JH, Jr. Differential regional vulnerability in transient focal cerebral ischemia. Stroke. 1982;13(3):339-46.
54. Nagakane Y, Yamada K, Ohara T, Yoshikawa K, Kuriyama N, Takayasu N, et al. Preferred involvement of the basal ganglia after lenticulostriate infarction as a possible indicator of different gray and white matter vulnerability. Stroke. 2008;39(2):494-6.
55. Arakawa S, Wright PM, Koga M, Phan TG, Reutens DC, Lim I, et al. Ischemic thresholds for gray and white matter: a diffusion and perfusion magnetic resonance study. Stroke. 2006;37(5):1211-6.
56. Ay H, Koroshetz WJ, Vangel M, Benner T, Melinosky C, Zhu M, et al. Conversion of ischemic brain tissue into infarction increases with age. Stroke. 2005;36(12):2632-6.
57. Shukla V, Shakya AK, Perez-Pinzon MA, Dave KR. Cerebral ischemic damage in diabetes: an inflammatory perspective. J Neuroinflammation. 2017;14(1):21.
58. Ay H, Arsava EM, Rosand J, Furie KL, Singhal AB, Schaefer PW, et al. Severity of leukoaraiosis and susceptibility to infarct growth in acute stroke. Stroke. 2008;39(5):1409-13.
59. Thomalla G, Cheng B, Ebinger M, Hao Q, Tourdias T, Wu O, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4·5 h of symptom onset (PRE-FLAIR): a multicentre observational study. Lancet Neurol. 2011;10(11):978-86.

60. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333(24):1581-7.
61. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014;384(9958):1929-35.
62. del Zoppo GJ, Higashida RT, Furlan AJ, Pessin MS, Rowley HA, Gent M. PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. PROACT Investigators. Prolyse in Acute Cerebral Thromboembolism. Stroke. 1998;29(1):4-11.
63. Sorimachi T, Fujii Y, Tsuchiya N, Nashimoto T, Harada A, Ito Y, et al. Recanalization by mechanical embolus disruption during intra-arterial thrombolysis in the carotid territory. AJNR Am J Neuroradiol. 2004;25(8):1391-402.
64. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial Prourokinase for Acute Ischemic StrokeThe PROACT II Study: A Randomized Controlled Trial. JAMA. 1999;282(21):2003-11.
65. Wassélius J, Arnberg F, von Euler M, Wester P, Ullberg T. Endovascular thrombectomy for acute ischemic stroke. J Intern Med. 2022;291(3):303-16.
66. Kerber CW, Barr JD, Berger RM, Chopko BW. Snare retrieval of intracranial thrombus in patients with acute stroke. J Vasc Interv Radiol. 2002;13(12):1269-74.
67. Wikholm G. Mechanical intracranial embolectomy. A report of two cases. Interv Neuroradiol. 1998;4(2):159-64.
68. Gobin YP, Starkman S, Duckwiler GR, Grobelny T, Kidwell CS, Jahan R, et al. MERCI 1: a phase 1 study of Mechanical Embolus Removal in Cerebral Ischemia. Stroke. 2004;35(12):2848-54.
69. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, et al. A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke. N Engl J Med. 2013;368(10):914-23.
70. Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. N Engl J Med. 2013;368(10):904-13.
71. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke. N Engl J Med. 2013;368(10):893-903.
72. Berkhemer OA, Fransen PSS, Beumer D, Berg LAvd, Lingsma HF, Yoo AJ, et al. A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. N Engl J Med. 2015;372(1):11-20.

73. Jovin TG, Chamorro A, Cobo E, Miquel MAd, Molina CA, Rovira A, et al. Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke. New England Journal of Medicine. 2015;372(24):2296-306.
74. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. N Engl J Med. 2015;372(11):1019-30.
75. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, et al. Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke. N Engl J Med. 2015;372(24):2285-95.
76. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372(11):1009-18.
77. Brott T, Adams HP, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke. 1989;20(7):864-70.
78. Alemseged F, Rocco A, Arba F, Schwabova JP, Wu T, Cavicchia L, et al. Posterior National Institutes of Health Stroke Scale Improves Prognostic Accuracy in Posterior Circulation Stroke. Stroke. 2022;53(4):1247-55.
79. Broderick JP, Adeoye O, Elm J. Evolution of the Modified Rankin Scale and Its Use in Future Stroke Trials. Stroke. 2017;48(7):2007-12.
80. Russo T, Felzani G, Marini C. Stroke in the Very Old: A Systematic Review of Studies on Incidence, Outcome, and Resource Use. Journal of Aging Research. 2011;2011(1):108785.
81. Finitsis S, Epstein J, Richard S, Bourcier R, Sibon I, Dargazanli C, et al. Age and Outcome after Endovascular Treatment in Anterior Circulation Large-Vessel Occlusion Stroke: ETIS Registry Results. Cerebrovasc Dis. 2021;50(1):68-77.
82. Kobeissi H, Ghozy S, Turfe B, Amoukhteh M, Bilgin C, Kadirvel R, et al. Differences between males and females following endovascular therapy for stroke: A systematic review and meta-analysis. J of Stroke and Cerebrovas Dis. 2023;32(6).
83. Madsen TE, DeCroce-Movson E, Hemendinger M, McTaggart RA, Yaghi S, Cutting S, et al. Sex differences in 90-day outcomes after mechanical thrombectomy for acute ischemic stroke. J Neurointerv Surg. 2019;11(3):221-5.
84. Petrea RE, Beiser AS, Seshadri S, Kelly-Hayes M, Kase CS, Wolf PA. Gender differences in stroke incidence and poststroke disability in the Framingham heart study. Stroke. 2009;40(4):1032-7.

85. Mainz J, Andersen G, Valentin JB, Gude MF, Johnsen SP. Disentangling Sex Differences in Use of Reperfusion Therapy in Patients With Acute Ischemic Stroke. Stroke. 2020;51(8):2332-8.
86. Verschoof MA, Groot AE, de Bruijn S, Roozenbeek B, van der Worp HB, Dippel DWJ, et al. Clinical Outcome After Endovascular Treatment in Patients With Active Cancer and Ischemic Stroke: A MR CLEAN Registry Substudy. Neurology. 2022;98(10):e993-e1001.
87. Chen Z, Su M, Li Z, Du H, Zhang S, Pu M, et al. Metabolic Syndrome Predicts Poor Outcome in Acute Ischemic Stroke Patients After Endovascular Thrombectomy. Neuropsychiatr Dis Treat. 2020;16:2045-52.
88. Tiainen M, Martinez-Majander N, Virtanen P, Räty S, Strbian D. Clinical frailty and outcome after mechanical thrombectomy for stroke in patients aged ≥ 80 years. J Stroke Cerebrovasc Dis. 2022;31(12):106816.
89. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
90. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.
91. Hall RE, Porter J, Quan H, Reeves MJ. Developing an adapted Charlson comorbidity index for ischemic stroke outcome studies. BMC Health Serv Res. 2019;19(1):930.
92. Schmidt M, Jacobsen JB, Johnsen SP, Bøtker HE, Sørensen HT. Eighteen-year trends in stroke mortality and the prognostic influence of comorbidity. Neurology. 2014;82(4):340-50.
93. Benali F, Kappelhof M, Ospel J, Ganesh A, McDonough RV, Postma AA, et al. Benefit of successful reperfusion achieved by endovascular thrombectomy for patients with ischemic stroke and moderate pre-stroke disability (mRS 3): results from the MR CLEAN Registry. J Neurointerv Surg. 2023;15(5):433-8.
94. Tanaka K, Yamagami H, Yoshimoto T, Uchida K, Morimoto T, Toyoda K, et al. Endovascular Therapy for Acute Ischemic Stroke in Patients With Prestroke Disability. J Am Heart Assoc. 2021;10(15):e020783.
95. Ducroux C, Derex L, Nourredine M, Haesebaert J, Buisson M, Alesefir W, et al. Successful thrombectomy is beneficial in patients with pre-stroke disability: Results from an international multicenter cohort study. J Neuroradiol. 2023;50(1):59-64.
96. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. N Engl J Med. 1985;312(14):932-6.

97. Higashida RT, Furlan AJ. Trial Design and Reporting Standards for Intra-Arterial Cerebral Thrombolysis for Acute Ischemic Stroke. Stroke. 2003;34(8):e109-e37.
98. Tung EL, McTaggart RA, Baird GL, Yaghi S, Hemendinger M, Dibiasio EL, et al. Rethinking Thrombolysis in Cerebral Infarction 2b. Stroke. 2017;48(9):2488-93.
99. Noser EA, Shaltoni HM, Hall CE, Alexandrov AV, Garami Z, Cacayorin ED, et al. Aggressive Mechanical Clot Disruption. Stroke. 2005;36(2):292-6.
100. Goyal M, Fargen KM, Turk AS, Mocco J, Liebeskind DS, Frei D, et al. 2C or not 2C: defining an improved revascularization grading scale and the need for standardization of angiography outcomes in stroke trials. J Neurointerv Surg. 2014;6(2):83-6.
101. Liebeskind DS, Bracard S, Guillemin F, Jahan R, Jovin TG, Majoie CB, et al. eTICI reperfusion: defining success in endovascular stroke therapy. J Neurointerv Surg. 2019;11(5):433-8.
102. Nogueira RG, Liebeskind DS, Sung G, Duckwiler G, Smith WS. Predictors of Good Clinical Outcomes, Mortality, and Successful Revascularization in Patients With Acute Ischemic Stroke Undergoing Thrombectomy. Stroke. 2009;40(12):3777-83.
103. Karlsson A JK, Björkman-Burtscher I.M, Rentzos A. Extended treatment in cerebral ischemia score 2c or 3 as goal of successful endovascular treatment is associated with clinical benefit. Journal of Neuroradiology. 2024;51(2):190-5.
104. Chueh JY, Kang DH, Kim BM, Gounis MJ. Role of Balloon Guide Catheter in Modern Endovascular Thrombectomy. J Korean Neurosurg Soc. 2020;63(1):14-25.
105. Brinjikji W, Starke RM, Murad MH, Fiorella D, Pereira VM, Goyal M, et al. Impact of balloon guide catheter on technical and clinical outcomes: a systematic review and meta-analysis. J Neurointerv Surg. 2018;10(4):335-9.
106. Pederson JM, Hardy N, Lyons H, Sheffels E, Touchette JC, Brinjikji W, et al. Comparison of Balloon Guide Catheters and Standard Guide Catheters for Acute Ischemic Stroke: An Updated Systematic Review and Meta-analysis. World Neurosurg. 2024;185:26-44.
107. Wassélius J, Hall E, Ramgren B, Andersson T, Ullberg T. Procedural factors associated with successful recanalization in patients with acute ischemic stroke treated with endovascular thrombectomy-a nationwide register-based observational study. Interv Neuroradiol. 2024:15910199241248268.
108. Hansen BM, Hall E, Szolics A, Andersson T, Wassélius J. Balloon Guide Catheter Use and Outcomes After Endovascular Thrombectomy for Ischemic Stroke Due to Large Vessel Occlusions. Clin Neuroradiol. 2025.

109. Goldhoorn R-JB, Duijsters N, Majoie CBLM, Roos YBWEM, Dippel DWJ, van Es ACGM, et al. Balloon Guide Catheter in Endovascular Treatment for Acute Ischemic Stroke: Results from the MR CLEAN Registry. J of Vasc and Intervent Radiology. 2019;30(11):1759-64.e6.
110. Pederson JM, Reierson NL, Hardy N, Touchette JC, Medam S, Barrett A, et al. Comparison of Balloon Guide Catheters and Standard Guide Catheters for Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. World Neurosurg. 2021;154:144-53.e21.
111. Knapen RRMM, Goldhoorn RJB, Hofmeijer J, Lycklamaà Nijeholt GJ, van den Berg R, van den Wijngaard IR, et al. Balloon Guide Catheter Versus Non–Balloon Guide Catheter: A MR CLEAN Registry Analysis. Stroke: Vascular and Interventional Neurology. 2024;4(4):e001103.
112. Bourcier R, Marnat G, Labreuche J, Desal H, Maria FD, Consoli A, et al. Balloon Guide Catheter is Not Superior to Conventional Guide Catheter when Stent Retriever and Contact Aspiration are Combined for Stroke Treatment. Neurosurgery. 2021;88(1):E83-E90.
113. Dhillon PS, Butt W, Podlasek A, Bhogal P, Lynch J, Booth TC, et al. Effect of Proximal Blood Flow Arrest During Endovascular Thrombectomy (ProFATE): A Multicenter, Blinded-End Point, Randomized Clinical Trial. Stroke. 2025;56(2):371-9.
114. Liu J, Zhou Y, Zhang L, Li Z, Chen W, Zhu Y, et al. Balloon guide catheters for endovascular thrombectomy in patients with acute ischaemic stroke due to large-vessel occlusion in China (PROTECT-MT): a multicentre, open-label, blinded-endpoint, randomised controlled trial. Lancet. 2024;404(10468):2165-74.
115. Karlsson A, Jood K, Björkman-Burtscher I, Rentzos A. Stent retriever versus aspiration based thrombectomy: impact on first pass reperfusion, procedure time, and clinical outcomes in large vessel occlusion. Nationwide registry based cohort study. J Neurointerv Surg. 2025;17(e2):e245-e51.
116. Schartz DA, Ellens NR, Kohli GS, Akkipeddi SMK, Colby GP, Bhalla T, et al. A Meta-analysis of Combined Aspiration Catheter and Stent Retriever versus Stent Retriever Alone for Large-Vessel Occlusion Ischemic Stroke. AJNR Am J Neuroradiol. 2022;43(4):568-74.
117. Teo YN, Sia CH, Tan BYQ, Mingxue J, Chan B, Sharma VK, et al. Combined balloon guide catheter, aspiration catheter, and stent retriever technique versus balloon guide catheter and stent retriever alone technique: a systematic review and meta-analysis. J Neurointerv Surg. 2023;15(2):127-32.

118. Turk AS, 3rd, Siddiqui A, Fifi JT, De Leacy RA, Fiorella DJ, Gu E, et al. Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): a multicentre, randomised, open label, blinded outcome, non-inferiority trial. Lancet. 2019;393(10175):998-1008.
119. Lapergue B, Blanc R, Gory B, Labreuche J, Duhamel A, Marnat G, et al. Effect of Endovascular Contact Aspiration vs Stent Retriever on Revascularization in Patients With Acute Ischemic Stroke and Large Vessel Occlusion: The ASTER Randomized Clinical Trial. Jama. 2017;318(5):443-52.
120. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. New England Journal of Medicine. 2018;378(1):11-21.
121. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. N Engl J Med. 2018;378(8):708-18.
122. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, et al. First Pass Effect. Stroke. 2018;49(3):660-6.
123. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data. The Lancet Neurology. 2018;17(1):47-53.
124. Wiącek M, Tomaszewska-Lampart I, Dziedzic M, Kaczorowska A, Bartosik-Psujek H. Association between Transient-Continuous Hypotension during Mechanical Thrombectomy for Acute Ischemic Stroke and Final Infarct Volume in Patients with Proximal Anterior Circulation Large Vessel Occlusion. Journal of Clinical Medicine. 2024;13(13):3707.
125. Petersen NH, Ortega-Gutierrez S, Wang A, Lopez GV, Strander S, Kodali S, et al. Decreases in Blood Pressure During Thrombectomy Are Associated With Larger Infarct Volumes and Worse Functional Outcome. Stroke. 2019;50(7):1797-804.
126. Chen PR, Artime CA, Sheth SA, Pedroza C, Ortega-Gutierrez S, Wolfe S, et al. Sedation vs General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke: The SEGA Randomized Clinical Trial. JAMA Neurol. 2025.
127. Chia-Wei L, Yang-Pei C, Yen-Ta H, Chung-Hsi H, Yu-Li P, Min-Hsiang C, et al. General anesthesia but not conscious sedation improves functional outcome in patients receiving endovascular thrombectomy for acute ischemic stroke: A meta-analysis of randomized clinical trials and trial sequence analysis. Frontiers in Neurology. 2022;13.

128. Peng Z, Luo W, Yan Z, Zhang H. The effect of general anesthesia and conscious sedation in endovascular thrombectomy for acute ischemic stroke: an updated meta-analysis of randomized controlled trials and trial sequential analysis. Frontiers in Neurology. 2023;14.
129. Shenhui J, Wenwen D, Dongdong L, Yelong R. General anesthesia versus sedation for endovascular thrombectomy: Meta-analysis and trial sequential analysis of randomized controlled trials. Heliyon. 2024;10(13).
130. Uchida K, Shindo S, Yoshimura S, Toyoda K, Sakai N, Yamagami H, et al. Association Between Alberta Stroke Program Early Computed Tomography Score and Efficacy and Safety Outcomes With Endovascular Therapy in Patients With Stroke From Large-Vessel Occlusion: A Secondary Analysis of the Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism-Japan Large Ischemic Core Trial (RESCUE-Japan LIMIT). JAMA Neurol. 2022;79(12):1260-6.
131. Sarraj A, Hassan AE, Abraham MG, Ortega-Gutierrez S, Kasner SE, Hussain MS, et al. Trial of Endovascular Thrombectomy for Large Ischemic Strokes. N Engl J Med. 2023;388(14):1259-71.
132. Bendszus M, Fiehler J, Subtil F, Bonekamp S, Aamodt AH, Fuentes B, et al. Endovascular thrombectomy for acute ischaemic stroke with established large infarct: multicentre, open-label, randomised trial. Lancet. 2023;402(10414):1753-63.
133. Yoo AJ, Zaidat OO, Sheth SA, Rai AT, Ortega-Gutierrez S, Given CA, 2nd, et al. Thrombectomy for Stroke With Large Infarct on Noncontrast CT: The TESLA Randomized Clinical Trial. Jama. 2024;332(16):1355-66.
134. Costalat V, Jovin TG, Albucher JF, Cognard C, Henon H, Nouri N, et al. Trial of Thrombectomy for Stroke with a Large Infarct of Unrestricted Size. N Engl J Med. 2024;390(18):1677-89.
135. Huo X, Ma G, Tong X, Zhang X, Pan Y, Nguyen TN, et al. Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct. N Engl J Med. 2023;388(14):1272-83.
136. Sarraj A, Hassan AE, Savitz S, Sitton C, Grotta J, Chen P, et al. Outcomes of Endovascular Thrombectomy vs Medical Management Alone in Patients With Large Ischemic Cores: A Secondary Analysis of the Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT) Study. JAMA Neurol. 2019;76(10):1147-56.
137. Neuberger U, Kickingereder P, Schönenberger S, Schieber S, Ringleb PA, Bendszus M, et al. Risk factors of intracranial hemorrhage after mechanical thrombectomy of anterior circulation ischemic stroke. Neuroradiology. 2019;61(4):461-9.

138. Liu C, Abdalkader M, Sang H, Sarraj A, Campbell BCV, Miao Z, et al. Endovascular Thrombectomy for Large Ischemic Core Stroke: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Neurology. 2025;104(9):e213443.
139. Chen H, Lee JS, Michel P, Yan B, Chaturvedi S. Endovascular Stroke Thrombectomy for Patients With Large Ischemic Core: A Review. JAMA Neurol. 2024;81(10):1085-93.
140. Prabhakaran S, Gonzalez NR, Zachrison KS, Adeoye O, Alexandrov AW, Ansari SA, et al. 2026 Guideline for the Early Management of Patients With Acute Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association. Stroke.0(0):doi:10.1161/STR.0000000000000513.
141. Lindsberg PJ, Sairanen T, Nagel S, Salonen O, Silvennoinen H, Strbian D. Recanalization treatments in basilar artery occlusion-Systematic analysis. Eur Stroke J. 2016;1(1):41-50.
142. Schonewille WJ, Wijman CAC, Michel P, Rueckert CM, Weimar C, Mattle HP, et al. Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. Lancet Neurology. 2009;8(8):724-30.
143. Liu X, Dai Q, Ye R, Zi W, Liu Y, Wang H, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. Lancet Neurol. 2020;19(2):115-22.
144. Langezaal LCM, van der Hoeven E, Mont'Alverne FJA, de Carvalho JJF, Lima FO, Dippel DWJ, et al. Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion. N Engl J Med. 2021;384(20):1910-20.
145. Jovin TG, Li C, Wu L, Wu C, Chen J, Jiang C, et al. Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion. N Engl J Med. 2022;387(15):1373-84.
146. Ospel JM, Menon BK, Demchuk AM, Almekhlafi MA, Kashani N, Mayank A, et al. Clinical Course of Acute Ischemic Stroke Due to Medium Vessel Occlusion With and Without Intravenous Alteplase Treatment. Stroke. 2020;51(11):3232-40.
147. Goyal M, Ospel JM, Ganesh A, Dowlatshahi D, Volders D, Möhlenbruch MA, et al. Endovascular Treatment of Stroke Due to Medium-Vessel Occlusion. N Engl J Med. 2025;392(14):1385-95.
148. Menon BK, Hill MD, Davalos A, Roos Y, Campbell BCV, Dippel DWJ, et al. Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: meta-analysis of data from the HERMES Collaboration. J Neurointerv Surg. 2019;11(11):1065-9.

149. Clarençon F, Durand-Zaleski I, Premat K, Baptiste A, Chabert E, Ferrier A, et al. Evaluation of mechanical thrombectomy in acute ischemic stroke related to a distal arterial occlusion: A randomized controlled trial. Int J Stroke. 2024;19(3):367-72.
150. Goldman D, Mehta A, Majidi S, De Leacy R. Thrombectomy for MeVO and DVO: The End of the Road or Just a Detour? Stroke: Vascular and Interventional Neurology. 2025;5(3):e001785.
151. Psychogios M, Brehm A, Ribo M, Rizzo F, Strbian D, Räty S, et al. Endovascular Treatment for Stroke Due to Occlusion of Medium or Distal Vessels. N Engl J Med. 2025;392(14):1374-84.
152. Salsano G, Pracucci G, Mavilio N, Saia V, Bandettini di Poggio M, Malfatto L, et al. Complications of mechanical thrombectomy for acute ischemic stroke: Incidence, risk factors, and clinical relevance in the Italian Registry of Endovascular Treatment in acute stroke. International Journal of Stroke. 2021;16(7):818-27.
153. Balami JS, White PM, McMeekin PJ, Ford GA, Buchan AM. Complications of endovascular treatment for acute ischemic stroke: Prevention and management. Internat J of Stroke. 2018;13(4):348-61.
154. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. Lancet Neurol. 2016;15(11):1138-47.
155. Jickling GC, Liu D, Stamova B, Ander BP, Zhan X, Lu A, et al. Hemorrhagic transformation after ischemic stroke in animals and humans. J Cereb Blood Flow Metab. 2014;34(2):185-99.
156. Zhou Y, Zhang L, Cavalcante F, Suzuki K, Treurniet KM, Yan B, et al. Intracranial Hemorrhage in Patients With Stroke After Endovascular Treatment With or Without IV Alteplase: An Individual Participant Data Meta-Analysis. JAMA Neurol. 2025;82(10):1031-9.
157. Whiteley WN, Slot KB, Fernandes P, Sandercock P, Wardlaw J. Risk Factors for Intracranial Hemorrhage in Acute Ischemic Stroke Patients Treated With Recombinant Tissue Plasminogen Activator. Stroke. 2012;43(11):2904-9.
158. Lee YB, Yoon W, Lee YY, Kim SK, Baek BH, Kim JT, et al. Predictors and impact of hemorrhagic transformations after endovascular thrombectomy in patients with acute large vessel occlusions. J Neurointerv Surg. 2019;11(5):469-73.
159. Nogueira RG, Gupta R, Jovin TG, Levy EI, Liebeskind DS, Zaidat OO, et al. Predictors and clinical relevance of hemorrhagic transformation after endovascular therapy for anterior circulation large vessel occlusion strokes: a multicenter retrospective analysis of 1122 patients. J Neurointerv Surg. 2015;7(1):16-21.

160. Katsura K, Ekholm A, Siesjö BK. Coupling among changes in energy metabolism, acid-base homeostasis, and ion fluxes in ischemia. Can J Physiol Pharmacol. 1992;70 Suppl:S170-5.
161. Feldman MJ, Roth S, Fusco MR, Mehta T, Arora N, Siegler JE, et al. Association of asymptomatic hemorrhage after endovascular stroke treatment with outcomes. J Neurointerv Surg. 2021;13(12):1095-8.
162. Hao Y, Liu W, Wang H, Zi W, Yang D, Wang W, et al. Prognosis of asymptomatic intracranial hemorrhage after endovascular treatment. J Neurointerv Surg. 2019;11(2):123-6.
163. Tian B, Tian X, Shi Z, Peng W, Zhang X, Yang P, et al. Clinical and Imaging Indicators of Hemorrhagic Transformation in Acute Ischemic Stroke After Endovascular Thrombectomy. Stroke. 2022;53(5):1674-81.
164. Perez-Vega C, Domingo RA, Tripathi S, Ramos-Fresnedo A, Kashyap S, Quinones-Hinojosa A, et al. Influence of glucose levels on clinical outcome after mechanical thrombectomy for large-vessel occlusion: a systematic review and meta-analysis. J Neurointerv Surg. 2022;14(1).
165. Venditti L, Chassin O, Ancelet C, Legris N, Sarov M, Lapergue B, et al. Pre-procedural predictive factors of symptomatic intracranial hemorrhage after thrombectomy in stroke. J Neurol. 2021;268(5):1867-75.
166. Dong S, Yu C, Wu Q, Xia H, Xu J, Gong K, et al. Predictors of Symptomatic Intracranial Hemorrhage after Endovascular Thrombectomy in Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. Cerebrovasc Dis. 2023;52(4):363-75.
167. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Lancet. 1998;352(9136):1245-51.
168. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359(13):1317-29.
169. von Kummer R, Broderick JP, Campbell BC, Demchuk A, Goyal M, Hill MD, et al. The Heidelberg Bleeding Classification: Classification of Bleeding Events After Ischemic Stroke and Reperfusion Therapy. Stroke. 2015;46(10):2981-6.
170. Riksstroke. The Swedish Stroke Register. Access date: 2025-06-11. [Available from: https://www.riksstroke.org/general-information/].
171. Söderholm A, Stegmayr B, Glader EL, Asplund K. Validation of Hospital Performance Measures of Acute Stroke Care Quality. Riksstroke, the Swedish Stroke Register. Neuroepidemiology. 2016;46(4):229-34.

172. Evaluations of variables in Riksstroke, the Swedish Stroke Register. Access date: 2025-06-11. [Available from: https://www.riksstroke.org/wp-content/uploads/2015/06/Evaluations-of-variables-in-Riksstroke-rev-15-08-03.pdf].
173. EVAS register. Access date: 2025-06-11 [Available from: https://evas-registret.se/en/new-englishpage/].
174. EVAS annual report 2022. Access date: 2025-06-12 [Available from: https://evas-registret.se/wp-content/uploads/2023/09/EVAS_AR2022_230918-2.pdf].
175. EVAS annual report 2024. Access date: 2025-11-25. [Available from: https://evas-registret.se/wp-content/uploads/2024/10/EVASregistret_241002.pdf].
176. The Swedish National Patient Register. Access date: 2025-06-12 [Available from: https://www.socialstyrelsen.se/en/statistics-and-data/registers/national-patient-register/].
177. Socialstyrelsen. Access date: 2025-11-21. [Available from: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/dokument-webb/statistik/production-and-quality-of-the-patient-register.pdf].
178. The National Prescribed Drugs Register. Access date: 2025-06-12 [Available from: https://www.socialstyrelsen.se/en/statistics-and-data/registers/national-prescribed-drug-register/].
179. Production and quality of the National Prescribed Drugs Register. Access date: 2025-06-11. [Available from: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/dokument-webb/ovrigt/production-and-quality-lmed.pdf].
180. Eriksson M, Appelros P, Norrving B, Terént A, Stegmayr B. Assessment of functional outcome in a national quality register for acute stroke: can simple self-reported items be transformed into the modified Rankin Scale? Stroke. 2007;38(4):1384-6.
181. Heiss WD. Malignant MCA Infarction: Pathophysiology and Imaging for Early Diagnosis and Management Decisions. Cerebrovasc Dis. 2016;41(1-2):1-7.
182. Lantz B. Grundläggande statistisk analys. 3rd ed: Studentlitteratur AB; 2020.
183. Kotz S. BDL, Read C.B. Encyclopedia of Statistical Sciences Volume 3: Wiley-Interscience; 1999.
184. Kotz S. BDL, Read C.B. Encyclopedia of Statistical Science Volume 2: Wiley-Interscience; 1998.

185. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344-9.
186. The EQUATOR Network. Access date: 2026-01-25. [Available from: https://www.equator-network.org/about-us/equator-network-what-we-do-and-how-we-are-organised/].
187. Tian B, Tian X, Shi Z, Peng W, Zhang X, Yang P, et al. Clinical and Imaging Indicators of Hemorrhagic Transformation in Acute Ischemic Stroke After Endovascular Thrombectomy. Stroke. 2022;53(5):1674-81.
188. Hao Y, Yang D, Wang H, Zi W, Zhang M, Geng Y, et al. Predictors for Symptomatic Intracranial Hemorrhage After Endovascular Treatment of Acute Ischemic Stroke. Stroke. 2017;48(5):1203-9.
189. Katsanos AH, Malhotra K, Ahmed N, Seitidis G, Mistry EA, Mavridis D, et al. Blood Pressure After Endovascular Thrombectomy and Outcomes in Patients With Acute Ischemic Stroke. Neurology. 2022;98(3):e291-e301.
190. Yang P, Song L, Zhang Y, Zhang X, Chen X, Li Y, et al. Intensive blood pressure control after endovascular thrombectomy for acute ischaemic stroke (ENCHANTED2/MT): a multicentre, open-label, blinded-endpoint, randomised controlled trial. Lancet. 2022;400(10363):1585-96.
191. Nam HS, Kim YD, Heo J, Lee H, Jung JW, Choi JK, et al. Intensive vs Conventional Blood Pressure Lowering After Endovascular Thrombectomy in Acute Ischemic Stroke: The OPTIMAL-BP Randomized Clinical Trial. Jama. 2023;330(9):832-42.
192. Li Q, Abdalkader M, Siegler JE, Yaghi S, Sarraj A, Campbell BCV, et al. Mechanical Thrombectomy for Large Ischemic Stroke: A Systematic Review and Meta-analysis. Neurology. 2023;101(9):e922-e32.
193. Ospel JM, Dowlatshahi D, Demchuk A, Volders D, Möhlenbruch M, Nimjee S, et al. Endovascular treatment to improve outcomes for medium vessel occlusions: The ESCAPE-MeVO trial. Int J Stroke. 2024;19(9):1064-70.
194. Sheth SA. Is Mortality the Worst Outcome After Stroke? Stroke: Vascular and Interventional Neurology. 2024;4(4):e001332.
195. Bizhanov KA, Abzaliyev KB, Baimbetov AK, Sarsenbayeva AB, Lyan E. Atrial fibrillation: Epidemiology, pathophysiology, and clinical complications (literature review). J Cardiovasc Electrophysiol. 2023;34(1):153-65.
196. Mortezaei A, Al-Saidi N, Taghlabi KM, Mohammadzadeh I, Hajikarimloo B, Habibi MA, et al. Endovascular thrombectomy for distal medium vessel occlusion stroke: A meta-analysis of randomized controlled trials. Neurosurg Rev. 2025;48(1):691.

197. Schellinger PD, Tsivgoulis G, Frank B, Liebig T, Köhrmann M. Randomized controlled trials of endovascular therapy for acute ischemic stroke with medium or distal vessel occlusion: a study level metaanalysis. Neurol Res Pract. 2025;7(1):44.
198. Sheth SA, Saver JL, Starkman S, Grunberg ID, Guzy J, Ali LK, et al. Enrollment bias: frequency and impact on patient selection in endovascular stroke trials. J Neurointerv Surg. 2016;8(4):353-9.
199. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988;19(5):604-7.
200. Wilson JT, Hareendran A, Hendry A, Potter J, Bone I, Muir KW. Reliability of the modified Rankin Scale across multiple raters: benefits of a structured interview. Stroke. 2005;36(4):777-81.
201. Quinn TJ, Dawson J, Walters MR, Lees KR. Variability in Modified Rankin Scoring Across a Large Cohort of International Observers. Stroke. 2008;39(11):2975-9.
202. Glader E-L, Stegmayr B, Johansson L, Hulter-Åsberg K, Wester PO. Differences in Long-Term Outcome Between Patients Treated in Stroke Units and in General Wards. Stroke. 2001;32(9):2124-30.
203. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol. 2007;165(6):710-8.
204. Mundlia P, Sharma A, Kaur J, Chaubey B, Ranawat P, Sood V, et al. From antiretrovirals to curative therapies: Current developments in HIV treatment and prevention. European Journal of Medicinal Chemistry. 2025;300:118190.
205. Ospel JM, Hill MD, Demchuk A, Menon BK, Thornton J, Rempel J, et al. Clinical impact of EVT with failed reperfusion in patients with acute ischemic stroke: results from the ESCAPE and ESCAPE-NA1 trials. Neuroradiology. 2021;63(11):1883-9.
206. Broocks G, Flottmann F, Schönfeld M, Bechstein M, Aye P, Kniep H, et al. Incomplete or failed thrombectomy in acute stroke patients with Alberta Stroke Program Early Computed Tomography Score 0-5 - how harmful is trying? Eur J Neurol. 2020;27(10):2031-5.
207. White WL. Why I hate the index finger. Hand (N Y). 2010;5(4):461-5.

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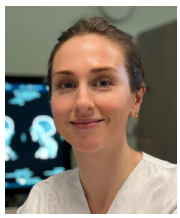
Denna avhandling bidrar med nya insikter om komplikationer och utfall relaterade till endovaskulär trombektomi genom att integrera kliniska och radiologiska perspektiv. Det övergripande syftet är att stödja välgrundade behandlingsbeslut och bidra till förbättrad patientvård.



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