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Original Article

Intracranial Atherosclerotic Disease: A Narrative Review of Its Role in Ischemic Stroke and Advances in Endovascular Therapy

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Abstract

Intracranial Atherosclerotic Disease (ICAD) is a significant global health challenge, causing ischemic stroke. The disease is prevalent in Asian, Hispanic, and African populations, with a higher prevalence observed. The mechanisms leading to stroke are complex, including artery-to-artery embolism, perforator occlusion, and impaired distal perfusion due to hemodynamic insufficiency. Aggressive medical management (AMM) is the cornerstone and first-line treatment for ICAD, demonstrating considerable effectiveness in mitigating stroke recurrence. However, landmark randomized controlled trials like SAMMPRIS, VISSIT, and CASSISS have generally not demonstrated the superiority of endovascular interventions over AMM as a primary treatment strategy due to associated periprocedural risks. Despite these challenges, endovascular therapies maintain a critical role, particularly in the acute management of large vessel occlusion (LVO) and for carefully selected patient cohorts who remain symptomatic despite optimal medical therapy. The field is poised for transformative advancements, including the development and refinement of novel devices, and a pivotal shift towards personalized medicine approaches. These ongoing efforts and the design of next-generation clinical trials are vital to address specific high-risk subgroups and refine treatment protocols, ultimately aiming to improve long-term outcomes for individuals affected by ICAD.

Key words: ICAD, AMM, SAMMPRIS, VISSIT, CASSISS, LVO

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1. Introduction to Intracranial Atherosclerotic Disease (ICAD)

1.1 Definition, Pathophysiology, and Clinical Presentation

Intracranial Atherosclerotic Disease (ICAD), also referred to as intracranial atherosclerosis (ICAS), is a chronic, progressive condition characterized by the accumulation of a sticky substance known as plaque within the arterial walls supplying blood to the brain.[1] This pathological buildup, composed of fat and cholesterol, leads to a gradual narrowing (stenosis) and potential blockage of these vital cerebral vessels.[1] It is important to recognize that ICAD is not an isolated phenomenon but rather an integral component of a systemic atherosclerotic process that affects arteries throughout the body, including those supplying the heart, which can lead to myocardial infarction, or the legs, causing peripheral artery disease.[1]

The pathophysiology of ICAD is complex, rooted in a progressive pathological process that culminates in cerebral hypoperfusion due to increasing stenosis.[4] Contemporary understanding emphasizes atherosclerosis as a chronic inflammatory process. Key systemic risk factors, such as hypertension, diabetes, and smoking, induce vascular endothelial dysfunction and heighten vascular permeability, thereby initiating and perpetuating plaque formation and growth.[4] Beyond the mere degree of luminal narrowing, the morphology of the atherosclerotic plaque itself is increasingly recognized as a crucial determinant of clinical events. Plaques deemed "unstable," characterized by a large lipid core, a thin fibrous cap, and evidence of inflammation, are particularly susceptible to rupture, which can trigger acute thrombosis and subsequent ischemic stroke.[5]

A significant challenge associated with ICAD lies in its often-insidious clinical presentation. Unlike extracranial carotid atherosclerosis, which frequently manifests with warning signs such as transient ischemic attacks (TIAs or "ministrokes"), intracranial atherosclerosis often remains clinically silent until a major ischemic stroke occurs.[1] This late presentation represents a substantial diagnostic hurdle, as it typically leads to a reactive rather than a proactive approach to diagnosis. When symptoms do emerge, they are typically abrupt and their specific nature depends on the affected brain region. Common signs and symptoms of a stroke or TIA include sudden onset of numbness or weakness, particularly on one side of the face, arm, or leg; confusion or dizziness; difficulties with speech or comprehension; visual disturbances in one or both eyes; problems with walking, balance, or coordination; severe headaches without an identifiable cause; or trouble swallowing. [1] In rare but severe instances, patients may also experience sudden loss of consciousness or seizures.[3] This pattern of late, often catastrophic, presentation underscores the urgent need for more effective screening strategies in high-risk populations, even in the absence of overt symptoms. It also highlights the imperative for the development of advanced non-invasive diagnostic tools capable of identifying hemodynamically significant or vulnerable ICAD lesions before a major cerebrovascular event. The fact that ICAD is frequently diagnosed in an acute or subacute phase profoundly influences the timing and associated risks of any potential interventional therapies.

Diagnosis of ICAD is most commonly established during the acute workup for stroke-like symptoms, often through computed tomography (CT) or magnetic resonance imaging (MRI) scans.[2] In some cases, ICAD may be an incidental finding on imaging studies performed for unrelated medical conditions.[2] While intra-arterial angiography has historically been considered the definitive gold standard for precisely delineating the extent of arterial stenosis. [6], non-invasive modalities such as transcranial Doppler (TCD) ultrasound and magnetic resonance angiography (MRA) are increasingly recognized for their reliability in detecting moderate to severe (50-99%) stenosis.[6] High-resolution MRI is also utilized for detailed evaluation of the intracranial arterial tree.[7] The understanding of atherosclerosis as a chronic inflammatory and systemic process further emphasizes the need for comprehensive risk factor modification. This extends beyond merely controlling blood pressure and cholesterol levels, suggesting that therapeutic strategies might also

need to address underlying systemic inflammatory conditions, given the disease's inflammatory basis. This interconnectedness explains why ICAD frequently co-occurs with other systemic cardiovascular diseases, underscoring the necessity of an integrated, multidisciplinary approach to patient management that addresses overall metabolic and vascular health.

1.2 Global Epidemiology and Key Risk Factors

Intracranial atherosclerotic disease (ICAD) is a significant and widespread cause of ischemic stroke across the globe.[3] In Western societies, including the United States, ICAD accounts for approximately 8-10% of all ischemic strokes, translating to an estimated 70,000 cases annually.[(11)] However, its prevalence is markedly higher in specific global populations, contributing to 33% to 50% of strokes in Asian, Hispanic, and African populations.[4] Globally, it is estimated that between 20 and 40 individuals per 100,000 experience a cerebral infarction directly attributable to ICAD.[12]

A well-documented epidemiological observation is the distinct racial and ethnic variation in the distribution of cervicocerebral atherosclerosis.[8] Atherosclerosis exhibits a greater propensity to affect intracranial arteries in Asian, Hispanic, and African populations.[(4)] Conversely, individuals of Caucasian descent tend to experience a higher incidence of extracranial carotid disease.[(8)] This observed disparity is likely a result of a complex interplay involving differences in genetic susceptibility, unique risk factor profiles, and lifestyle patterns prevalent within these diverse racial and ethnic groups.[(4)] The stark difference in prevalence between Western populations and Asian/Hispanic/African populations highlights ICAD as a disproportionately significant public health burden in specific global regions. This necessitates the development and implementation of regionally tailored public health interventions, targeted screening programs, and specific research priorities based on local demographics and risk factor profiles. Furthermore, it implies that findings from clinical trials predominantly conducted in Western populations, such as the SAMMPRIS trial, may not be directly generalizable or fully applicable to high-prevalence Asian populations, underscoring a critical need for more geographically and ethnically diverse research to inform global clinical practice.

A consistent set of modifiable risk factors are strongly associated with the development and progression of ICAD. These include:

- **High blood pressure (hypertension)**.[(1)]
- **Smoking (cigarette use)**.[(1)]
- **Diabetes mellitus**.[(1)]
- **High blood cholesterol levels (hyperlipidemia)**.[(1)]
- **Obesity**.[(1)]
- **Sedentary lifestyle and lack of exercise**.[(1)]
- **Other heart diseases** (e.g., heart attack, heart failure) and artery diseases outside the heart and major vessels.[(1)]
- **Metabolic syndrome** has also been identified as an independent predictor for ICAD.[(6)]

Several non-modifiable risk factors for ICAD have also been identified:

- **Increasing age**: ICAD is most frequently observed in patients 40 years and older, with its prevalence and severity distinctly increasing with advancing age.[(1)]
- **Gender**: The relationship between ICAD and gender is somewhat controversial, with some studies reporting a female predominance, while others indicate a higher prevalence in men, particularly in younger age groups.[1]
- **Family history of stroke and/or atherosclerosis**.[(1)]
- **Prior history of stroke and/or heart attack**.[(1)]
- **Race/ethnicity**, as detailed above.[(1)]

The consistent identification of these modifiable risk factors across numerous studies, coupled with the explicit association of metabolic syndrome with ICAD, points to a common underlying systemic pathological process, often linked to metabolic dysfunction. This understanding suggests that effective ICAD prevention and management must adopt a holistic, multi-factorial approach, aggressively target all components of metabolic syndrome and promote healthy lifestyles, rather than focusing on isolated risk factor control. This comprehensive strategy is crucial because ICAD is frequently a manifestation of broader systemic cardiovascular health issues, necessitating integrated care pathways that address the patient's overall metabolic and vascular well-being.

1.3 Significance of ICAD as a Cause of Ischemic Stroke

Intracranial atherosclerotic disease is unequivocally recognized as a leading and globally significant cause of ischemic stroke.[3] In the United States, it holds the distinction of being the third-leading cause of stroke, responsible for an estimated 70,000 cases annually.[7]

A critical and defining characteristic of ICAD is the significantly elevated risk of recurrent ischemic events and death observed among affected patients, a feature that distinctly differentiates it from other stroke subtypes.[4] The annual risk of stroke directly attributable to a stenosed intracranial vessel is approximately 8%.[5] For individuals presenting with high-grade stenosis, defined as 70-99% narrowing of the arterial lumen, the annual risk of stroke can escalate to between 10% and 20%.[8] Alarmingly, the 1-year recurrent stroke rate in this particularly vulnerable subgroup can exceed 20%, positioning it among the highest recurrence rates observed across common causes of stroke.[12] This persistently high recurrence risk, even in the context of optimal medical treatment, is a profound concern.[9] It highlights that while current medical management has undeniably improved outcomes, it remains insufficient for a substantial subset of ICAD patients, leading to considerable ongoing morbidity and mortality. This situation underscores the urgent need for more effective secondary prevention strategies, including the continuous refinement of medical therapies and the rigorous validation of advanced endovascular approaches that can safely and durably reduce this burden, particularly in those patients who continue to experience high risk despite receiving the best available medical care. The substantial long-term burden on patients, their caregivers, and healthcare systems due to repeated cerebrovascular events further emphasizes this critical need.

Furthermore, intracranial atherosclerotic disease-related large vessel occlusion (ICAD-LVO) constitutes a substantial proportion of acute ischemic stroke cases that necessitate endovascular therapy, accounting for 15-35% of such presentations.[13] This highlights the acute and severe manifestations of ICAD that often require immediate, advanced interventions.

2. Mechanisms of Stroke in ICAD

Stroke in patients with intracranial atherosclerotic disease can manifest through several distinct and often coexisting mechanisms, reflecting the complex pathophysiology of the disease. Understanding these mechanisms is crucial for tailoring effective treatment strategies.

One primary mechanism is **artery-to-artery embolization**.[9] This occurs when a fragment of an unstable atherosclerotic plaque, or a thrombus formed on its surface, detaches from the stenotic intracranial vessel and travels downstream, occluding a smaller, more distal artery. This typically results in territorial patterns of infarction, affecting larger areas of brain tissue.[16] The instability of the plaque, characterized by a large lipid core and a thin, inflamed fibrous cap, is a key factor in triggering such embolic events.[5]

Another significant mechanism is **perforator disease**, often referred to as **branch occlusion**.[5] In this scenario, the atherosclerotic plaque within the parent intracranial artery directly encroaches upon or occludes the ostium (origin) of small, penetrating arteries that supply deep brain structures. This leads to small, subcortical lacunar-like infarcts, often less than 1.5 cm in size.[5] This mechanism is particularly challenging as these small vessels are critical for localized brain perfusion.

Impaired distal perfusion, or **hemodynamic insufficiency**, represents a third major mechanism.[9] This occurs when severe stenosis significantly reduces blood flow to the brain tissue distal to the lesion, especially when collateral circulation is insufficient to compensate. Such hypoperfusion typically leads to "border zone" or "watershed" infarcts, which occur in areas at the periphery of major arterial territories, where blood supply is most vulnerable to drops in systemic blood pressure or severe local stenosis.[16] Patients with significant hemodynamic compromise, as identified by perfusion imaging, face a higher risk of stroke recurrence.[20]

Less common but equally impactful mechanisms include **in situ thrombotic occlusion** and **plaque extension**.[5] In situ thrombotic occlusion involves

the formation of a thrombus directly at the site of the atherosclerotic plaque, leading to complete blockage of the vessel.[18] Plaque extension refers to the growth of the atherosclerotic lesion itself, progressively narrowing the vessel lumen and potentially involving adjacent perforators.[10]

The diverse nature of these stroke mechanisms means that a single therapeutic approach may not be universally effective. For instance, an antiplatelet agent might be highly effective for preventing artery-to-artery embolism from an unstable plaque, but less so for a stroke caused by severe hemodynamic compromise. Conversely, revascularization procedures might be beneficial for hemodynamic insufficiency but carry risks if the primary mechanism is related to an unstable, highly thrombogenic plaque. Therefore, understanding the specific mechanism of stroke in an individual patient, often inferred from the pattern of infarction on MRI (e.g., lacunar, territorial, or border zone infarcts), is crucial for guiding personalized treatment strategies. This understanding informs the choice between different antiplatelet agents, the consideration of anticoagulants, or the decision to pursue revascularization procedures. The complexity of these mechanisms also explains why patients with ICAD often experience early progression of neurological deficits and new ischemic changes on imaging, even under aggressive medical management.[19]

3. Current Medical Management for ICAD

3.1 Aggressive Medical Management (AMM)

Aggressive Medical Management (AMM) stands as the cornerstone and current first-line treatment for patients diagnosed with intracranial atherosclerotic disease.[7] This comprehensive strategy is designed to reduce the high risk of recurrent stroke associated with ICAD by targeting multiple pathophysiological pathways and systemic risk factors.

A critical component of AMM is **antithrombotic therapy**. Aspirin is widely recognized as the most commonly used antiplatelet agent in ICAD management.[1] Historical trials, such as the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial, provided pivotal insights into antithrombotic choices. The WASID trial, which compared warfarin with aspirin for patients with symptomatic ICAD causing 50-99% stenosis, found no significant difference in the rates of recurrent stroke or death between the two arms. However, the warfarin group experienced significantly higher rates of major hemorrhage (8.3% vs. 3.2%) and death (9.7% vs. 4.3%) compared to the aspirin group, leading to the early cessation of the warfarin arm due to safety concerns.[9] Consequently, aspirin emerged as the preferred antithrombotic agent. More recent guidelines, particularly for patients with 70-99% symptomatic ICAD, recommend a short course of

dual antiplatelet therapy (DAPT), typically with aspirin (e.g., 325 mg/day) and clopidogrel (e.g., 75 mg/day) for up to 90 days, followed by long-term single antiplatelet therapy.[23] This approach is supported by trials like SAMMPRIS, which incorporated DAPT as part of its aggressive medical arm.[33] For Asian populations, cilostazol in combination with aspirin has shown promise in preventing the progression of symptomatic intracranial stenosis with fewer bleeding events.[5]

Beyond antithrombotic agents, stringent **risk factor modification** is paramount. This involves achieving and maintaining specific target levels for key cardiovascular risk factors:

- **Blood Pressure Management**: Current guidelines recommend maintaining systolic blood pressure below 140 mmHg.[22] For diabetic patients, a more aggressive target of less than 130/80 mmHg is often advised.[9] Thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin II receptor blockers (ARBs) are preferentially used.[24]
- **Lipid Management**: High-intensity statin therapy, such as atorvastatin (40-80 mg daily) or rosuvastatin (20-40 mg daily), is strongly recommended for all patients with atherosclerotic stroke, irrespective of baseline cholesterol levels.[9] The treatment target for low-density lipoprotein cholesterol (LDL-C) is typically below 70 mg/dL.[9] For patients who do not achieve target LDL-C levels or are statin intolerant, ezetimibe and PCSK9 inhibitors are beneficial adjunctive therapies.[24] Additionally, icosapent ethyl has shown promise in reducing ischemic events in patients with elevated

triglyceride levels and cardiovascular disease or diabetes.[9]

- **Diabetes Control**: For most diabetic patients, the goal is to achieve a hemoglobin A1c (HbA1c) level of ≤7%, managed through a combination of diet, insulin, and hypoglycemic medications.[23]
- **Lifestyle Modifications**: Comprehensive lifestyle changes are essential for both primary and secondary stroke prevention. These include strict smoking cessation [1], regular physical activity (with a minimum of 10 minutes of moderate-intensity aerobic activity four times a week recommended for capable patients)[2], adopting healthy dietary habits (emphasizing fruits, vegetables, whole grains, and limiting salt and saturated fats) [9], and achieving and maintaining a healthy weight.[1] Managing stress and ensuring adequate sleep are also recognized as important components of overall cardiovascular health.[35]

The evolution of AMM, particularly from the WASID trial's findings to the aggressive, multi-target risk factor control emphasized in SAMMPRIS, reflects a deepening understanding of ICAD's complex and systemic nature. This shift towards comprehensive, rather than isolated, risk factor management is a key paradigm change in ICAD therapy. While AMM has demonstrably improved outcomes and significantly reduced stroke rates over the years, a significant limitation remains the persistent high risk of stroke recurrence. Despite optimal medical treatment, the risk of stroke recurrence can still reach as high as 12% in the first year.[9] For patients with severe stenosis, the recurrence rates can be even higher.[19] This indicates that AMM, while foundational and highly effective, is not a complete solution, especially for those with severe stenosis. This ongoing challenge continues to drive the exploration and refinement of adjunctive therapies, including advanced endovascular interventions.

4. Advances in Endovascular Therapy

4.1 Historical Development and Early Trials

The journey of endovascular therapy for intracranial atherosclerotic disease has been marked by periods of both enthusiasm and significant setbacks, reflecting a continuous learning curve in managing this complex cerebrovascular condition. Early attempts at **intracranial angioplasty** were reported in the mid-1980s.[14] These initial procedures, however, were associated with alarmingly high complication rates, including vessel rupture, vasospasm, and dissection, with some studies reporting rates as high as 33-50%.[14] These complications were largely attributed to the use of oversized balloons and rapid inflation techniques, which were not well-suited for the delicate intracranial vasculature.[38]

The introduction of **stents**, initially bare metal stents (BMS) for coronary arteries in the 1980s, gradually led to their adaptation for intracranial applications.[39] The high stroke recurrence rates observed in the medical arm of the WASID trial (11-14% at 1-2 years overall, and a striking 23% at 1 year for patients with ≥70% stenosis) [19] fueled a renewed interest in endovascular stenting as a potential solution to reduce this substantial risk. This led to the development and eventual FDA approval of the

Wingspan Stent System in August 2005, under a Humanitarian Device Exemption (HDE).[29] Early trials and registries evaluating the Wingspan stent reported initial safety and feasibility, with periprocedural complication rates ranging from 4.5-6.2% and restenosis rates between 7-30% at 6 months.[29]

However, the landscape of ICAD treatment was dramatically reshaped by the results of the **Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Arterial Stenosis (SAMMPRIS) trial**, published in 2011. This landmark randomized controlled trial compared aggressive medical management (AMM) alone with AMM plus Wingspan stenting for patients with 70-99% symptomatic intracranial stenosis. The trial was prematurely halted due to a significantly higher 30-day rate of stroke or death in the stenting group (14.7%) compared to the AMM-alone group (5.8%).[19] This adverse outcome was primarily driven by periprocedural complications, including perforator occlusion and reperfusion hemorrhage.[25] Furthermore, long-term follow-up (1-3 years) also continued to favor AMM.[25]

The **Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) trial**,

published in 2015, yielded similar negative results for balloon-mounted stents compared to AMM. This trial reported higher 30-day (24.1% vs. 9.4%) and 1-year (36.2% vs. 15.1%) rates of stroke or TIA in the stent group.[25] More recently, the

China Angioplasty and Stenting for Symptomatic Intracranial Severe Stenosis (CASSISS) trial (2022) also found no significant benefit of stenting over AMM, although it reported comparable safety profiles between the two groups, indicating an improvement in procedural safety over time.[46]

The initial enthusiasm for endovascular therapy, spurred by the high medical failure rates observed in WASID, was profoundly tempered by the negative outcomes of SAMMPRIS and VISSIT. These pivotal trials fundamentally shifted the treatment paradigm, underscoring the critical importance of meticulous patient selection, the profound impact of operator experience, and the inherent risks associated with interventions, particularly in the acute phase of ICAD. The high rates of perforator occlusion and reperfusion hemorrhage observed in these trials highlighted specific vulnerabilities of the intracranial circulation to mechanical intervention. This historical progression has led to a more cautious and refined approach to endovascular therapy, emphasizing its role in specific clinical contexts rather than as a broad first-line treatment.

4.2 Current Endovascular Techniques and Devices

The field of endovascular therapy for ICAD has continued to evolve, spurred by the need to overcome the limitations identified in earlier trials. Current techniques predominantly involve **balloon angioplasty alone**, **balloon-mounted stenting**, and **self-expanding stent placement**, which may or may not be preceded by angioplasty.[15]

Balloon angioplasty aims to reduce luminal stenosis and increase downstream perfusion through mechanisms such as plaque redistribution and direct vessel dilation.[38] Lessons learned from early, high-complication rates have led to refined techniques, including slower inflation times over minutes (as opposed to seconds) and the use of undersized balloons, which have significantly reduced procedural complications.[15] The Gateway balloon is currently the only FDA-approved device specifically for intracranial angioplasty.[38]

Stent placement involves deploying a permanent metallic mesh tube within the artery to mechanically hold the vessel open and compress the plaque against the arterial wall, thereby improving blood flow and reducing the risk of plaque embolization.[1]

A variety of devices are currently employed:

- The **Wingspan Stent System** remains the only FDA-approved stent specifically for ICAD, but its indications have become more restrictive following the SAMMPRIS trial.[25]
- **Off-label self-expanding stents (SES)**, originally designed for other neurovascular conditions like aneurysms (e.g., Enterprise, Neuroform EZ, LVIS, Solitaire AB), have been used in some studies for ICAD with reports of fewer perioperative complications compared to the Wingspan stent in certain contexts.[46]
- **Drug-eluting stents (DES)**, which are coated with antiproliferative drugs, were developed to address the issue of in-stent restenosis, a common complication with bare metal stents.[39] While widely adopted in coronary artery interventions, their role in ICAD is still under investigation. Some studies suggest DES can reduce in-stent restenosis, particularly in vertebral arteries, but meta-analyses show less clear superiority over bare metal stents in intracranial arteries regarding postoperative stroke rates.[56]
- **Drug-coated balloons (DCB)** represent a newer therapeutic approach. These balloons deliver antiproliferative drugs directly to the vessel wall during angioplasty without leaving a permanent implant, potentially reducing restenosis while avoiding the long-term issues associated with permanent stents. DCB angioplasty is currently under investigation in randomized controlled trials, such as the DR. BEYOND trial, with promising early results for reducing restenosis.[45]

- **Flow diverters (FD)**, primarily developed for the treatment of intracranial aneurysms, are also being explored in specific ICAD contexts, particularly for intracranial aneurysms accompanied by parent artery stenosis.[61]

The procedural aspects of endovascular therapy typically involve accessing the arterial system via a small puncture in the femoral artery in the groin or, less commonly, the brachial artery.[1] Under fluoroscopic guidance, a catheter is advanced to the target intracranial artery. Antithrombotic medication is administered before, during, and after the procedure to prevent clot formation.[47] Balloon angioplasty is usually performed first to dilate the stenotic lesion, followed by stent deployment if indicated. Post-procedure, patients are monitored for complications, and antithrombotic therapy is continued.[(15)]

The continuous evolution of devices and techniques, particularly the emergence of drug-eluting technologies and the re-evaluation of submaximal angioplasty, reflects an ongoing commitment to mitigate the periprocedural risks and improve the long-term patency of treated vessels. These were significant limitations in earlier trials. The shift in focus from proving "superiority over medical therapy" to identifying endovascular interventions as "rescue therapy" or "treatment for specific high-risk subgroups" marks a more pragmatic and patient-centered approach. This refined perspective acknowledges the complexities of ICAD and aims to integrate interventions where they offer the most distinct and safest benefit.

4.3 Current Indications and Outcomes

Based on the cumulative evidence from major clinical trials and meta-analyses, endovascular interventions for ICAD are generally reserved for specific patient populations and clinical scenarios. They are not considered a primary, first-line therapy for most patients.

The primary role for endovascular interventions is now typically for patients who experience **recurrent ischemic events despite receiving maximal medical therapy (AMM)**, particularly those with high-grade stenosis (70-99%).[(7)] This reflects a shift in strategy, where intervention is considered a secondary option when AMM alone proves insufficient.

A crucial and expanding role for endovascular therapy is in the management of **acute ischemic stroke due to intracranial atherosclerotic disease-related large vessel occlusion (ICAD-LVO)**. ICAD-LVO accounts for a significant proportion (15-35%) of all large vessel occlusions requiring endovascular thrombectomy.[13] In these acute settings, mechanical thrombectomy is often performed, but ICAD-LVO is associated with a high rate of reocclusion (30-50%) following initial reperfusion.[(64)] Consequently,

rescue stenting is frequently considered in these cases to maintain vessel patency and prevent reocclusion.[45]

The outcomes of landmark randomized controlled trials (RCTs) have profoundly influenced current indications:

- The **SAMMPRIS trial** famously demonstrated that stenting plus AMM was inferior to AMM alone, with a significantly higher 30-day stroke or death rate in the stenting group (14.7% vs. 5.8%).[(27)] This negative outcome was largely attributed to periprocedural complications.

- The **VISSIT trial** similarly showed that balloon-mounted stenting resulted in higher 30-day (24.1% vs. 9.4%) and 1-year (36.2% vs. 15.1%) rates of stroke or TIA compared to AMM.[(27)]

- The more recent **CASSISS trial** (2022), while showing improved periprocedural safety for stenting compared to earlier trials, still found no significant difference in the primary outcome (stroke or death within 30 days or stroke in the qualifying territory from 30 days to 1 year) between the stenting and AMM groups (8.0% vs. 7.2%). [(46)]

Recent **meta-analyses** consolidate these findings, concluding that intracranial stenting as a first-line therapy offers no significant advantage over medical therapy in preventing stroke in symptomatic ICAS, while it does pose added early risks, particularly for stroke and

intracranial hemorrhage within 30 days. No significant differences in long-term outcomes (e.g., at 1 year) were found.[17] This consistency across multiple RCTs and meta-analyses provides a high level of evidence guiding current practice.

Regarding **patency rates**, restenosis remains a concern with intracranial stenting, with reported rates varying (e.g., 7-30% at 6 months for Wingspan).[29] However, newer

drug-eluting stents (DES) have shown promise in reducing in-stent restenosis compared to bare metal stents, particularly in vertebral arteries.[21] While DES exhibit a comparable safety profile to BMS for both intracranial and vertebral artery stenosis, their efficacy in reducing postoperative strokes is more pronounced in vertebral artery stenosis, with less clear benefits in intracranial arteries.[58]

The current body of evidence firmly establishes aggressive medical management as the default first-line therapy for most symptomatic ICAD patients. Endovascular therapy's role is shifting towards highly selected cases, particularly those presenting with acute large vessel occlusion or those who remain symptomatic despite rigorous AMM, and primarily within the context of ongoing clinical trials. This evolving understanding highlights a critical need for enhanced patient stratification and meticulous risk assessment before considering interventional procedures, as well as continued device refinement to further improve safety profiles and long-term efficacy.

5. Challenges and Future Directions

5.1 Limitations of Current Diagnostic and Treatment Methods

Despite significant advancements, the diagnosis and treatment of intracranial atherosclerotic disease continue to face several inherent limitations, contributing to the ongoing challenge of effectively managing this complex condition.

A primary diagnostic limitation is that ICAD often remains **asymptomatic until a major ischemic stroke occurs**, thereby limiting opportunities for early intervention and proactive prevention.[1] While traditional intra-arterial angiography offers detailed anatomical information, its invasive nature restricts its use as a routine screening tool.[6] Furthermore, current non-invasive imaging modalities, while improving, may not fully characterize the subtle features of plaque vulnerability or precisely quantify the degree of hemodynamic compromise, which are crucial for identifying patients at highest risk of future events.[55] The complexity of ICAD pathophysiology, with its diverse stroke mechanisms, means that a simple assessment of stenosis alone is often insufficient for guiding optimal management.

In terms of treatment, despite the demonstrated benefits of aggressive medical management (AMM), a **persistent high risk of stroke recurrence** remains, particularly in patients with severe stenosis.[9] This indicates that AMM, while foundational, is not a panacea for all ICAD patients.

The history of **endovascular therapy** for ICAD is marked by challenges related to periprocedural complications. Early randomized trials, notably SAMMPRIS and VISSIT, revealed unacceptably high rates of periprocedural stroke and death in the stenting arms. These complications were frequently attributed to factors such as perforator occlusion, reperfusion hemorrhage in vulnerable ischemic brain tissue, and mechanical disturbance of unstable plaques during the procedure.[19] Another persistent concern with stenting is

restenosis, the re-narrowing of the stented vessel, which can necessitate repeat interventions and contribute to recurrent ischemic events.[5]

The **optimal timing of intervention** remains a subject of debate. While early intervention might address acute ischemia, it carries a higher risk due to plaque instability in the acute phase. Conversely, delaying intervention, while potentially safer procedurally, may leave patients vulnerable during a high-risk period for stroke recurrence.[25] This dilemma highlights the need for precise patient selection and risk stratification. Furthermore, there is currently

no clear consensus on best practices for all aspects of ICAD management, particularly regarding the precise role and timing of endovascular interventio.[68] Significant gaps in knowledge also exist concerning the optimal duration of antithrombotic therapy and the impact of pharmacogenomic factors, such as the CYP2C19

genotype, on the efficacy and safety of medical management.[68]

These limitations collectively highlight the necessity for a more nuanced understanding of ICAD, moving beyond a simple assessment of stenosis degree to incorporate detailed plaque characteristics and the precise hemodynamic impact of the lesions. This complex interplay of factors necessitates the development of more advanced diagnostic tools and truly personalized treatment approaches to overcome current challenges and significantly improve patient outcomes.

5.2 Future Directions in Research and Therapy

The future of ICAD management is poised for transformative advancements, driven by ongoing research focused on overcoming current limitations and embracing a more personalized approach to patient care.

A key emerging direction is **personalized medicine**, which aims to tailor treatment strategies based on an individual's unique pathophysiology. This involves the integration of diagnostic and therapeutic approaches, often referred to as theranostics, to optimize stroke and cognitive impairment prevention.[70] This shift acknowledges the heterogeneity of ICAD and the need to move beyond a "one-size-fits-all" approach.

Advances in **imaging and biomarkers** are crucial for refining patient selection and guiding therapy. Future research will focus on:

- **High-resolution vessel wall imaging** to precisely characterize plaque morphology, identify vulnerable plaques, and assess inflammatory activity, which are critical determinants of stroke risk.[7]
- **Quantitative Magnetic Resonance Angiography (MRA)** and **CT perfusion** to accurately assess hemodynamic compromise and the adequacy of collateral circulation, providing a more functional assessment of stenosis.[55]
- The application of **computational fluid dynamics (CFD)** to model blood flow dynamics across stenoses, aiming to predict individual stroke risk and optimize therapeutic interventions.[21]
- Identification and validation of **novel serologic and neuroimaging biomarkers** that can predict stroke recurrence and guide treatment decisions.[20]

The development of **novel endovascular devices** is also a significant area of focus:

- **Drug-eluting balloons (DEB)** and **drug-eluting stents (DES)** are being refined to further reduce in-stent restenosis rates, which have been a persistent challenge with bare metal stents. These devices deliver antiproliferative agents directly to the vessel wall, aiming for sustained patency.[45] The DR. BEYOND randomized controlled trial is currently investigating the efficacy and safety of DEB angioplasty compared to bare-metal stenting.[60]
- **Submaximal angioplasty**, a technique involving less aggressive dilation, is being explored as a potentially safer alternative to stenting, with ongoing trials like the BASIS trial (Balloon Angioplasty for Symptomatic Intracranial Artery Stenosis) evaluating its efficacy and safety.[17]

Next-generation clinical trials are being meticulously designed to address the complexities and controversies in ICAD management:

- Future trials will increasingly focus on **hemodynamically compromised patients**, as these individuals are most likely to benefit from revascularization strategies.[67]
- Consideration of **specific high-risk subgroups**, such as those with posterior circulation involvement or lesions in perforator-rich vessels (e.g., basilar artery, MCA), is crucial for tailoring interventions and mitigating periprocedural risks.[34]
- Determining the **optimal timing of intervention** is a key research question, balancing the high risk of early stroke recurrence with the increased periprocedural risks associated with acute-phase interventions.[25]
- Trials will also emphasize **long-term follow-up** (beyond 3 months), as a significant proportion of recurrent strokes occur in this later period.[55]
- New studies are investigating **novel antithrombotic combinations**, such as low-dose rivaroxaban plus aspirin, to further reduce stroke risk in high-risk ICAD patients, as exemplified by the CATIS-ICAD study.[69]

The future of ICAD management hinges on a multi-pronged approach: refining patient selection through advanced diagnostic tools, developing safer and more effective interventional devices, and conducting rigorously designed clinical trials that precisely address the nuances of ICAD pathophysiology and patient heterogeneity. These concerted efforts are expected to pave the way for truly personalized and proactive stroke prevention strategies, ultimately improving the lives of individuals affected by this challenging disease.

Conclusions

Intracranial atherosclerotic disease (ICAD) remains a formidable cause of ischemic stroke worldwide, disproportionately affecting Asian, Hispanic, and African populations. Its insidious nature, often presenting with a major stroke without prior warning, underscores a critical diagnostic gap that necessitates more proactive screening strategies and advanced non-invasive imaging. The understanding of ICAD as a systemic, chronic inflammatory process, intricately linked to metabolic syndrome and other cardiovascular risk factors, emphasizes the imperative for holistic, multi-factorial aggressive medical management (AMM). AMM, encompassing stringent blood pressure and lipid control, diabetes management, and comprehensive lifestyle modifications, has significantly improved outcomes and is firmly established as the first-line therapy.

Despite these advancements in medical therapy, the persistently high rates of stroke recurrence, particularly in patients with severe stenosis, highlight the limitations of current AMM alone. The historical trajectory of endovascular therapy for ICAD, marked by the initial promise of angioplasty and stenting, was significantly tempered by the adverse outcomes of landmark trials such as SAMMPRIS and VISSIT. These trials revealed substantial periprocedural risks, including perforator occlusion and reperfusion hemorrhage, which largely outweighed any potential benefits of stenting as a primary treatment. Consequently, the role of endovascular intervention has evolved to a more targeted approach. It is now primarily considered for specific high-risk scenarios, such as acute large vessel occlusion due to ICAD (where rescue stenting may be necessary due to high reocclusion rates post-thrombectomy), and for carefully selected patients who continue to experience recurrent ischemic events despite optimal medical therapy.

The ongoing challenges in ICAD management—including the need for improved diagnostic tools to identify vulnerable plaques and hemodynamic compromise, the optimization of intervention timing, and the reduction of periprocedural complications and restenosis—are actively being addressed through innovative research. Future directions are centered on personalized medicine, leveraging advanced imaging techniques and novel biomarkers to enhance patient stratification. The development of next-generation devices, such as drug-eluting balloons and refined stent designs, coupled with rigorously designed randomized controlled trials focusing on specific high-risk subgroups, are crucial for advancing the field. These concerted efforts are essential to refine treatment protocols, improve safety profiles, and ultimately provide more effective and tailored stroke prevention strategies for individuals living with ICAD.

References

1. Intracranial Atherosclerotic Disease | University of Michigan Health, accessed July 24, 2025, https://www.uofmhealth.org/conditions-treatments/neurointerventional-radiology/intracranial-atherosclerotic-disease

2. Intracranial Atherosclerotic Disease (ICAD) | Hartford HealthCare | CT, accessed July 24, 2025, https://hartfordhealthcare.org/services/neurovascular/intracranial-atherosclerotic-disease

3. Intracranial Atherosclerotic Disease (ICAD) | National Institute of Neurological Disorders and Stroke, accessed July 24, 2025, https://www.ninds.nih.gov/health-information/disorders/intracranial-atherosclerotic-disease-icad

4. Intracranial atherosclerotic disease - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6363839/

5. Intracranial Atherosclerosis: Incidence, Diagnosis and Treatment ..., accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2854925/

6. Intracranial Atherosclerotic Disease. CiteSeerX. Accessed July 24, 2025. https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=f0bc6d84011e7f60e789a1fee4f0a6268f70f2b7.

7. Intracranial Atherosclerotic Disease (ICAD) - Cedars-Sinai, accessed July 24, 2025, https://www.cedars-sinai.org/programs/neurology-neurosurgery/specialties/neurovascular/icad.html

8. Epidemiology, diagnosis and management of intracranial atherosclerotic disease, accessed July 24, 2025, https://www.tandfonline.com/doi/pdf/10.1586/erc.10.129

9. Intracranial Atherosclerosis Treatment | Stroke - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/strokeaha.119.028528

10. Intracranial Atherosclerotic Diseases (ICAD) - University of Kentucky, accessed July 24, 2025, https://scholars.uky.edu/en/publications/intracranial-atherosclerotic-diseases-icad

11. Cedars-Sinai. “Treatment Advances for Common Cause of Ischemic Stroke.” Cedars-Sinai Pulse. Accessed August 19, 2025. https://pulse.cedars-sinai.org/news/treatment-advances-for-common-cause-of-ischemic-stroke.

12. Epidemiology, Pathophysiology, and Imaging of Atherosclerotic Intracranial Disease | Stroke, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.123.043630?doi=10.1161/STROKEAHA.123.043630

13. First-in-human trial of a self-expandable, temporary dilation system for intracranial atherosclerotic disease in patients presenting with acute ischemic stroke | Journal of NeuroInterventional Surgery, accessed July 24, 2025, https://jnis.bmj.com/content/16/12/1232

14. Endovascular Treatment of Symptomatic Intracranial Atherosclerotic ..., accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3040367/

15. Intracranial Stent and Angioplasty, accessed July 24, 2025, https://www.vnsc.org/procedures/intracranial-stent-and-angioplasty/

16. Intracranial Atherosclerotic Disease - Practical Neurology, accessed July 24, 2025, https://practicalneurology.com/diseases-diagnoses/stroke/intracranial-atherosclerotic-disease/30143/

17. Comparing Stenting with Medical Therapy Versus Medical Therapy Alone in Patients with Intracranial Atherosclerotic Stenosis: A Current Systematic Review and Meta-Analysis - ResearchGate, accessed July 24, 2025, https://www.researchgate.net/publication/392840417_Comparing_Stenting_with_Medical_Therapy_Versus_Medical_Therapy_Alone_in_Patients_with_Intracranial_Atherosclerotic_Stenosis_A_Current_Systematic_Review_and_Meta-Analysis

18. Caplan, Louis R. Caplan’s Stroke: A Clinical Approach. 5th ed. Cambridge: Cambridge University Press, 2016.

19. Intracranial Atherosclerotic Disease - Neurology.org, accessed July 24, 2025, https://www.neurology.org/doi/10.1212/WNL.0000000000012805

20. Intracranial Atherosclerosis: Current Understanding and Perspectives - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3961814/

21. Peritherapeutic intra-arterial flow changes predict long-term stent patency in patients with severe intracranial artery stenosis receiving PTAS | Request PDF - ResearchGate, accessed July 24, 2025, https://www.researchgate.net/publication/387581464_Peritherapeutic_intra-arterial_flow_changes_predict_long-term_stent_patency_in_patients_with_severe_intracranial_artery_stenosis_receiving_PTAS

22. www.ahajournals.org, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.124.050336?doi=10.1161/STROKEAHA.124.050336#:~:text=Current%20guidelines%20from%20the%20American,at%20least%20moderate%20physical

%20activity.

23. What are the current guidelines for treating symptomatic intracranial arterial stenosis?, accessed July 24, 2025, https://www.droracle.ai/articles/98638/are-there-any-new-guidelines-on-the-treatment-of-symptomatic-intracranial-stenosis-

24. Optimal Medical Management of Atherosclerotic Intracranial Stenosis | Stroke, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.123.043633

25. Endovascular Treatment of Intracranial Atherosclerotic Stenosis: Current Debates and Future Prospects - Frontiers, accessed July 24, 2025, https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2018.00666/full

26. Internal Carotid Artery Stenting for Intracranial Atherosclerosis - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4300064/

27. Endovascular Treatment of Intracranial Atherosclerotic Stenosis: Current Debates and Future Prospects - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6110852/

28. WASID Trial Summary: Warfarin and Aspirin for Symptomatic Intracranial Arterial Stenosis, accessed July 24, 2025, https://www.visualmed.org/wasid-trial-summary-warfarin-and-aspirin-for-symptomatic-intracranial-arterial-stenosis/

29. Long term clinical and angiographic outcomes with the Wingspan stent for treatment of symptomatic 50-99% intracranial atherosclerosis - ProQuest, accessed July 24, 2025, https://www.proquest.com/scholarly-journals/long-term-clinical-angiographic-outcomes-with/docview/1786800796/se-2

30. The Evolving Paradigm in the Management of Intracranial Atherosclerotic Disease - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3246764/

31. 6. Antiplatelet Therapy for Ischemic Stroke and Transient Ischemic Attack | Canadian Stroke Best Practices, accessed July 24, 2025, https://www.strokebestpractices.ca/recommendations/secondary-prevention-of-stroke/anti-platelet-therapy-in-ischemic-stroke-and-tia

32. www.ahajournals.org, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.124.047715#:~:text=The%20American%20Heart%20Association%2FAmerican,90%20days%20(2a%20moderate)%20followed

33. Critique of “Stenting Versus Aggressive Medical Therapy for Intracranial Arterial Stenosis” by Chimowitz et al in the New England Journal of Medicine | Stroke, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/strokeaha.111.641563

34. New Standards for Intracranial Atherosclerotic Disease Treatment - Frontiers, accessed July 24, 2025, https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2011.00077/full

35. Arteriosclerosis / atherosclerosis - Diagnosis and treatment - Mayo Clinic, accessed July 24, 2025, https://www.mayoclinic.org/diseases-conditions/arteriosclerosis-atherosclerosis/diagnosis-treatment/drc-20350575

36. Balloon Angioplasty for Symptomatic Intracranial Artery Stenosis (BASIS) - ClinicalTrials.gov, accessed July 24, 2025, https://clinicaltrials.gov/study/NCT03703635

37. Intracranial Angioplasty & Stenting for Cerebral Atherosclerosis: A Position Statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, and the American Society of Neuroradiology, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC7976119/

38. Endovascular Treatment of Intracranial Atherosclerosis - Neupsy Key, accessed July 24, 2025, https://neupsykey.com/endovascular-treatment-of-intracranial-atherosclerosis/

39. State of the art: coronary artery stents – past, present and future | EuroIntervention, accessed July 24, 2025, https://eurointervention.pcronline.com/article/state-of-the-art-coronary-artery-stents-past-present-and-future

40. Drug Eluting Stent Compounds - StatPearls - NCBI Bookshelf, accessed July 24, 2025,

https://www.ncbi.nlm.nih.gov/books/NBK537349/

41. Stent - Wikipedia, accessed July 24, 2025, https://en.wikipedia.org/wiki/Stent

42. Angioplasty and Stenting for Atherosclerotic Intracranial Stenosis: Rationale for a Randomized Clinical Trial - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2040119/

43. Wherefore Wingspan? - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8134132/

44. Study Details | An International Registry of the Wingspan™ Stent System for the Treatment of Intracranial Atherosclerotic Stenosis | ClinicalTrials.gov, accessed July 24, 2025, https://clinicaltrials.gov/study/NCT00929383

45. Intracranial atherosclerosis update for neurointerventionalists - PubMed, accessed July 24, 2025, https://pubmed.ncbi.nlm.nih.gov/37295944/

46. Intracranial angioplasty with a self-expandable stent for intracranial atherosclerotic stenosis: Systematic review and meta-analysis - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9870250/

47. Interventional procedure overview of endovascular stent insertion for intracranial atherosclerotic disease - NICE, accessed July 24, 2025, https://www.nice.org.uk/guidance/ipg429/documents/endovascular-stent-insertion-for-intracranial-atherosclerotic-disease-overview2

48. Does the Stenting Versus Aggressive Medical Therapy Trial Support Stenting for Subgroups With Intracranial Stenosis? | Stroke - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.115.009846

49. (PDF) Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis - ResearchGate, accessed July 24, 2025, https://www.researchgate.net/publication/274087914_Effect_of_a_Balloon-Expandable_Intracranial_Stent_vs_Medical_Therapy_on_Risk_of_Stroke_in_Patients_With_Symptomatic_Intracranial_Stenosis

50. CASSISS: No Benefit of Stenting for Intracranial Stenosis - TCTMD.com, accessed July 24, 2025, https://www.tctmd.com/news/cassiss-no-benefit-stenting-intracranial-stenosis

51. Effect of Stenting Plus Medical Therapy vs Medical Therapy Alone on Risk of Stroke and Death in Patients With Symptomatic Intracranial Stenosis: The CASSISS Randomized Clinical Trial - ResearchGate, accessed July 24, 2025, https://www.researchgate.net/publication/362584924_Effect_of_Stenting_Plus_Medical_Therapy_vs_Medical_Therapy_Alone_on_Risk_of_Stroke_and_Death_in_Patients_With_Symptomatic_Intracranial_Stenosis_The_CASSISS_Randomized_Clinical_Trial

52. Endovascular Therapy, Catheterization Procedures - Froedtert, accessed July 24, 2025, https://www.froedtert.com/heart-care/treatment/endovascular-therapy

53. Angioplasty and stent placement - carotid artery: MedlinePlus Medical Encyclopedia, accessed July 24, 2025, https://medlineplus.gov/ency/article/002953.htm

54. NCA - Intracranial Stenting and Angioplasty (CAG-00085R2) - Decision Memo - CMS, accessed July 24, 2025, https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=177&keyword=stent&keywordType=starts&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP&contractOption=all&sortBy=relevance&KeyWordLookUp=Doc&KeyWordSearchType=Exact&bc=AAAAAAQACAAAAAAA

55. The Future of Endovascular Therapy for Intracranial Atherosclerotic Disease | Stroke: Vascular and Interventional Neurology - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/SVIN.124.001053

56. Treatment of Intracranial Atherosclerotic Disease with a Balloon-Expandable Paclitaxel Eluting Stent: Procedural Safety, Efficacy and Mid-Term Patency - PMC, accessed July 24, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC3432207/

57. Abstract TP149: Balloon Mounted Drug Eluting Stents For Treatment Of Intracranial Atherosclerosis In Emergent Large Vessel Ichemic Stroke - American Heart Association Journals, accessed July 24, 2025,

https://www.ahajournals.org/doi/10.1161/str.54.suppl_1.TP149

58. Efficacy and safety of drug-eluting stents versus bare-metal stents in symptomatic intracranial and vertebral artery stenosis: a meta-analysis - Frontiers, accessed July 24, 2025, https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2024.1389254/full

59. Safety and efficacy of drug-eluting stents versus bare-metal stents in saphenous vein grafts lesions: a meta-analysis | EuroIntervention, accessed July 24, 2025, https://eurointervention.pcronline.com/article/safety-and-efficacy-of-drug-eluting-stents-versus-bare-metal-stents-in-saphenous-vein-grafts-lesions-a-meta-analysis

60. DRug-coated Balloon for Endovascular treatment of sYmptOmatic intracraNial stenotic Disease (DR. BEYOND): the protocol of a multicentre randomised trial | Stroke and Vascular Neurology, accessed July 24, 2025, https://svn.bmj.com/content/early/2024/07/23/svn-2024-003259

61. Outcomes of flow diversion in intracranial aneurysms accompanied by parent artery stenosis, accessed July 24, 2025, https://pubmed.ncbi.nlm.nih.gov/40527608/

62. Flow diverters for intracranial aneurysms - PubMed, accessed July 24, 2025, https://pubmed.ncbi.nlm.nih.gov/24967131/

63. Intracranial Stenting: Angioplasty Basic Technique, Indications, and Sizing: 2-Dimensional Operative Video - PubMed, accessed July 24, 2025, https://pubmed.ncbi.nlm.nih.gov/33956956/

64. Large Vessel Occlusion Stroke due to Intracranial Atherosclerotic Disease: Identification, Medical and Interventional Treatment, and Outcomes - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.122.040008

65. Endovascular Treatment of Large Vessel Occlusion Strokes Due to Intracranial Atherosclerotic Disease - :: Journal of Stroke, accessed July 24, 2025, https://www.j-stroke.org/journal/view.php?doi=10.5853/jos.2021.01375

66. Comparing Stenting with Medical Therapy Versus Medical Therapy Alone in Patients with Intracranial Atherosclerotic Stenosis: A Current Systematic Review and Meta-Analysis - PubMed, accessed July 24, 2025, https://pubmed.ncbi.nlm.nih.gov/40558231/

67. Future of Endovascular and Surgical Treatments of Atherosclerotic Intracranial Stenosis | Stroke - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.123.043634

68. ARISE II Consensus on the Management of Intracranial Atherosclerotic Disease | Stroke, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.124.050336?doi=10.1161/STROKEAHA.124.050336

69. Combination Antithrombotic Therapy for Reduction of Recurrent Ischemic Stroke in Intracranial Atherosclerotic Disease - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/STROKEAHA.124.047715

70. Our Health AI Medical Company Overview - iCAD, Inc., accessed July 24, 2025, https://www.icadmed.com/about/

71. Precision Medicine for ICAD - Frontiers, accessed July 24, 2025, https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2021.646734/epub

72. Balloon Angioplasty for Intracranial Atherosclerotic Disease | Stroke - American Heart Association Journals, accessed July 24, 2025, https://www.ahajournals.org/doi/10.1161/strokeaha.110.583245