5 Endovascular Treatment of Intracranial Atherosclerosis

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Introduction

One of the most common causes of ischemic stroke worldwide is intracranial atherosclerotic disease (ICAD). However, our understanding of the most appropriate treatment of this complex disease with a high recurrence rate of stroke remains limited. Although medical therapy has lowered the risk of stroke, the recurrence of stroke still remains overall high at 1- and 2-year follow-up. Certain high-risk ICAD patients may benefit from endovascular therapy. We will review the natural history, epidemiology, and current treatment options including surgical, medical, and endovascular management of ICAD while highlighting the recent literature in the field. We will concentrate and conclude with an in-depth look at endovascular treatment options including equipment and methods.

Natural History/Epidemiology

ICAD is a common cause of stroke worldwide, afflicting the Black, Asian, and Hispanic populations at a higher rate than Whites [1, 2]. ICAD is found in an estimated 10% of stroke patients in the USA, while in Asia, it accounts for approximately 30–50% [3, 4]. Age, hypertension, smoking, diabetes mellitus, hypercholesterolemia, and metabolic syndrome are all risk factors for ICAD [5, 6]. Although the high rate of uncontrolled risk factors partially accounts for the increased incidence of ICAD in some populations [7–10], this does not appear to be the case in others [11–13]. It stands to reason that management of risk factors alone may not be sufficient in controlling the disease.

The warfarin versus aspirin for symptomatic intracranial disease (WASID) trial data revealed that patients with symptomatic ICAD carry a high risk of subsequent stroke [14–16]. Despite the use of aspirin and management of risk factors, patients with a recent transient ischemic attack or stroke and a stenosis of ≥70% had a 23% risk of stroke at 1 year [15, 17–19]. Even with optimal medical therapy and lifestyle modification including blood pressure reduction, smoking cessation, weight loss, cholesterol reduction, and dual antiplatelet therapy, the risk of stroke in ICAD patients remains at a high 12.2–15% [16, 20].

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Clinical Presentations

Ischemic stroke or transient ischemic attack (TIA) is the classic presenting symptom of ICAD [21, 22]. There can be various clinical presentations including isolated motor or sensory involvement and/or cortical function impairments depending on the location of ischemia [16, 23–25]. Cognitive deficits, like impairment of executive function and anterograde amnesia, can occur with infarcts involving the anterior-medial thalamus, caudate nucleus, or cerebral cortical or white matter areas [26–28]. White matter degeneration, hypoperfusion, and hypometabolism may lead to cognitive changes in the absence of infarcts [1, 29].

Differential Diagnosis

Anatomic arterial narrowing detected on imaging studies may be due to a variety of pathologies, and determining the cause of narrowing can be challenging. Mimics include partially recanalized thrombus, intracranial dissection, vasculitis, vasculopathy, and vasospasm. A detailed history regarding prior peripheral atherosclerotic disease, diagnosis of coronary disease, or the presence of atherosclerotic risk factors can help in identifying non-atherosclerotic etiologies of stenosis [3, 30]. In the setting of acute stroke, partially recanalized thrombus will usually resolve on repeat imaging [5, 31, 32]. The presence of a severe headache and diffuse intracranial narrowing suggests reversible vasoconstrictive syndrome. Limited data exists, but studies of extracranial vessel imaging with pathologic correlation have shown inflammatory processes such as vasculitis are associated with concentric, circumferential wall thickening and enhancement, while ICAD is associated with eccentric wall thickening [7, 9, 33].

Mechanisms of Symptoms

Ischemia from ICAD can be due to hypoperfusion, in situ thromboembolism, or perforator orifice occlusion [11, 13, 34, 35]. Imaging may help in delineating the stroke mechanisms though sometimes one imaging pattern can be produced by a combination of mechanisms. Border zone infarcts are suggestive of hypoperfusion, territorial infarcts point to peripheral embolism, and deep subcortical infarcts are indicative of perforator artery orifice occlusion [17, 18, 36]. In one study over 80% of ICAD strokes showed combination of multiple mechanisms [16, 37]. The mechanism of the current stroke is predictive of the risk and mechanism of recurrent strokes. In an analysis of patients presenting with an index stroke in the WASID trial, the risk of recurrent stroke was similar in patients who presented with lacunar and non-lacunar strokes, and recurrent strokes in patients presenting with lacunar stroke were typically non-lacunar [21, 38].

Stenosis Characterization

Imaging including CTA, MRA, and digital subtraction angiography (DSA) can be used to detect intracranial stenosis. With this, one can ascertain the degree and length of stenosis, differentiate the atherosclerotic stenosis from mimics, and assess the state of collateral circulation.

DSA is considered the standard for the evaluation of intracranial stenosis. As standardized by the methods described in the WASID study, calculation of the degree of stenosis on DSA uses the following equation: $(1 - (D_{\text{stenosis}}/D_{\text{normal}})) \times 100$, where D_{stenosis} = the diameter of the artery at the site of most severe degree of stenosis and D_{normal} = the diameter of the proximal normal artery (Fig. 5.1) [23, 38].

For noninvasive modalities of evaluating large vessel ICAD, transcranial Doppler (TCD) and MRA compared with DSA were shown to have good negative predictive values of 86–91% but low positive predictive values of 36–59% [15, 26]. CTA was shown to have a higher sensitivity, specificity, and positive predictive value compared to MRA [29, 39]. The higher sensitivity and specificity of CTA have been observed for stenosis 50% or higher [30]. For ICAD in small intracranial arteries, a study showed that multidetector CT angiography depicted ≥90% of all examined small intracranial arteries compared

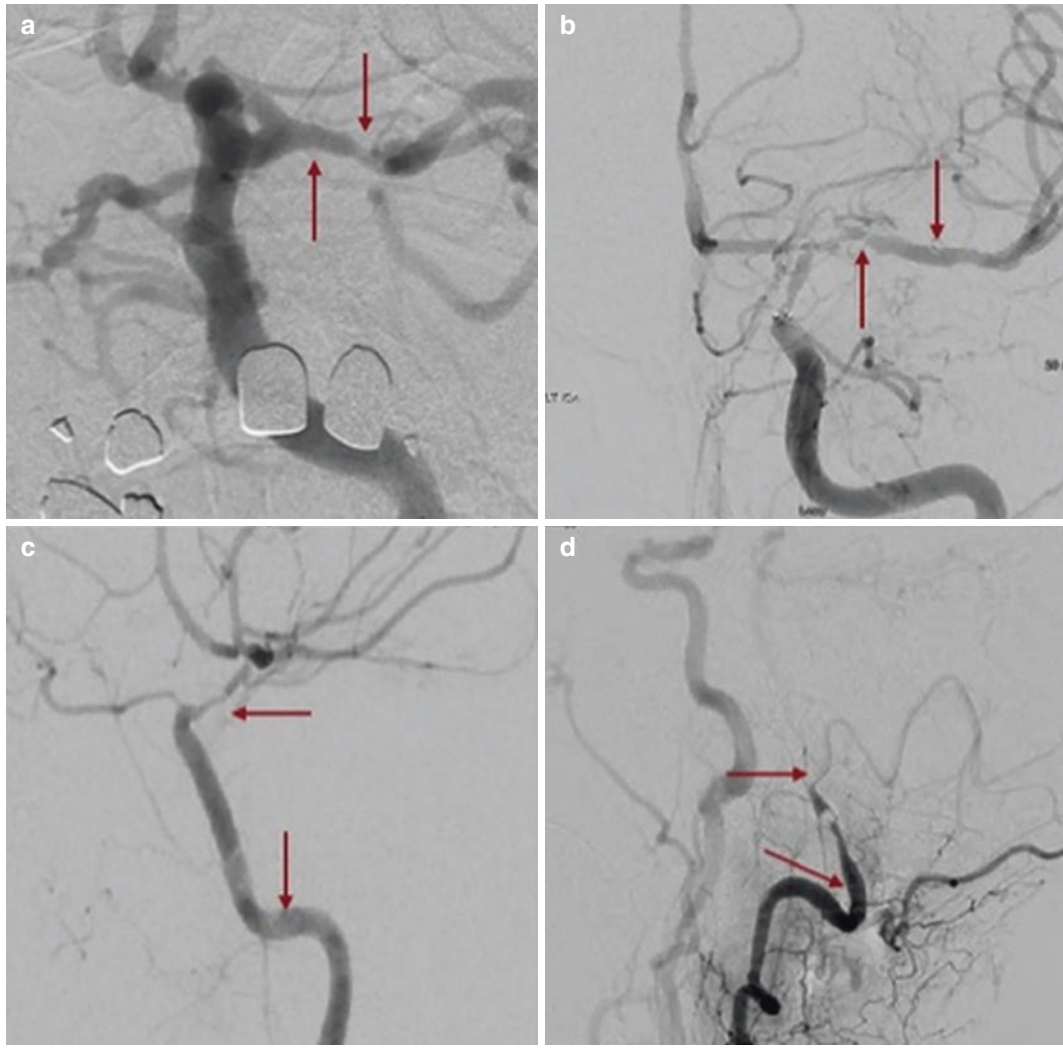

Fig. 5.1 Measurement of intracranial stenosis using the WASID method. (**a**) The diameter of the proximal part of the artery at its widest, non-tortuous, normal segment is chosen (first choice). (**b**) If the proximal artery is diseased, the diameter of the distal portion of the artery at its widest, parallel, non-tortuous normal segment is substituted (second choice). (**c**) For the internal carotid artery disease involving the pre-cavernous, cavernous, and post-cavernous segments, the petrous carotid segment with parallel margins is measured at its widest, non-tortuous, normal portion. If the entire petrous carotid is diseased, the most distal, parallel part of the extracranial internal carotid artery is substituted (second choice)—not shown. (**d**) If the entire intracranial artery is diseased, the most distal, parallel, non-tortuous normal segment of the feeding artery is measured (third choice)

to DSA, and the smallest arterial size reliably detected with CTA was 0.7 mm versus 0.4 mm for DSA.

Stenoses can be further characterized by the vessel tissue surrounding the luminal stenosis. Vessel wall imaging can be achieved with high-resolution MRI, intravascular ultrasound, and fat-suppressed T1-weighted MRI. High-resolution MRI can identify the thickness and pattern of protrusion [31, 32]. Identification of recent intraplaque hemorrhage and inflammation can be made with fat-suppressed T1-weighted MRI [34, 35, 40, 41]. Black-blood MRI with or without contrast allows for visualization of the heterogeneity of the thickened vessel wall due to various plaque components, lipid core,

Table 5.1 ASITN collateral score grade description

0 = no collaterals visible to the ischemic site
1 = slow collaterals to the periphery of the ischemic site with persistence of some of the defect
2 = rapid collaterals to periphery of ischemic site with persistence of some of the defect and to only a portion of the ischemic territory
3 = collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase
4 = complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion

fibrous cap, intraplaque hemorrhage, calcifications, and enhancement. Intravascular ultrasound can be used for distinguishing calcium and lipid deposits but is limited in its use due to its invasive nature [33].

The degree of collateral circulation is a powerful predictor of recurrent stroke in the setting of medical therapy for symptomatic ICAD [11, 42], impaired distal territory perfusion can be compensated for with good leptomeningeal collaterals. As with above, DSA remains the gold standard for assessing collaterals. CTA and MRA modalities offer less detailed but noninvasive alternatives. The ASITN collateral score (Table 5.1) is the most commonly used grading system [36, 43].

Surgical Treatment of Intracranial Stenosis

Surgical treatments have been used for decades to treat ICAD. In general, the current evidence does not favor surgical intervention. The EC/IC (extracranial to intracranial) bypass study showed no benefit of surgical bypass versus medical therapy for the reduction of overall ipsilateral major strokes or death in patients with intracranial or extracranial stenotic and occlusive diseases [38, 44].. The Carotid Occlusion Surgery Study (COSS) evaluated patients with ipsilateral ischemic events within 120 days in the setting of cervical carotid occlusion and increased oxygen extraction fraction. Patients were randomized to medical treatment versus EC/IC bypass surgery. Stroke and death at 30 days and 2-year ipsilateral stroke rates were not statistically different between the surgical and medical group (21% vs. 23%) [37, 43, 45, 46].

Medical Treatment of Intracranial Atherosclerotic Stenosis

Medical treatment has evolved over the years and is currently the first line of treatment for ICAD. The WASID trial compared aspirin versus warfarin in patients with ICAD. The primary endpoint of ischemic stroke, brain hemorrhage, or vascular death was similar in the aspirin (22.1%) and warfarin (21.8%) groups. However, the warfarin cohort had significantly more non-vascular death, major hemorrhage, and myocardial infarction or sudden death [15, 47]. The Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) trial compared maximal medical therapy to stenting in ICAD patients. At 1 year, the event rate was 17.6% in the stenting arm and 12.2% in the medical management arm [2, 6, 48]. The medical arm of SAMMPRIS is now considered the standard of care for first-time symptomatic ICAD patients: 325 mg aspirin and Plavix 75 mg daily for 3 months, followed by aspirin only. Additionally, patients were treated with a statin and blood pressure control and were enrolled in a lifestyle modification program. Goal systolic blood pressure was less than 140 mmHg and LDL was less than 70 mg per deciliter (1.81 mmol/L). In addition to the above regimen, management of secondary risk factors (diabetes, elevated non-high-density lipoprotein (non-HDL) cholesterol levels, smoking, excess weight, and insufficient exercise) was included.

Endovascular Treatment of Intracranial Atherosclerotic Stenosis

The results of the SAMMPRIS trial demonstrating medical management superiority compared to stenting have relegated endovascular treatment to a more secondary role, but new studies employing modern techniques and stricter selection of

Table 5.2 Possible indications and FDA indications for endovascular treatment

1. Hemodynamic symptoms
2. Poor collaterals
3. Large mismatch on imaging with signs of collateral failure
4. Recurrent symptoms despite best medical therapy
5. FDA wingspan use criteria: (1) Age 22–80 years (2), two or more strokes despite aggressive medical management (3), most recent stroke occurring more than 7 days prior to planned intervention (4), 70–99% stenosis due to atherosclerosis of the related intracranial artery, and (5) good recovery from previous stroke and modified Rankin scale score of ≤3 prior to intervention [49, 50]

patients show promising results. Endovascular treatment of intracranial stenosis aims to reduce luminal stenosis to improve downstream perfusion. This can be divided into three possible treatments: stand-alone balloon angioplasty, balloon-mounted stent (BMS), and self-expanding stent (SES) placement. Devices can also be drug-eluting, such as with drug-eluting stents (DES). Indications for each procedure (Table 5.2), outcomes from literature, and example case presentations are provided in the chapter.

Intracranial Balloon Angioplasty Without Stenting

Initially described with percutaneous transluminal angioplasty of the coronary arteries, the first reported cases of stand-alone balloon angioplasty in the 1980s saw high rates of dissections, emboli, and rupture [44, 51]. A small rupture or dissection not significant in the coronary circulation would result in devastating subarachnoid or parenchymal hemorrhage [47, 52–54]. In modern times improvement with technique and balloon selection have seen improved complication rates. Slow inflation over minutes as opposed to seconds and undersized balloons have decreased complication rates to as low as 5% [41, 55–57] (see Fig. 5.2). Defining technical success as less than 50% stenosis (established by the Practice Guideline Committee of the Society of Neurointerventional Surgery) puts modern series at a technical success rate of 60 to above 90% [3, 40, 41, 50, 51, 55, 56, 58–60].

Stand-alone intracranial balloon angioplasty has been advocated by some over stenting based on case series with low periprocedural complication rates [40, 41, 61]. Some studies have suggested that restenosis and outcomes in balloon angioplasty without stenting versus stenting are similar [49, 51].

There are several intracranial balloons used for treatment of ICAD. These include the Scepter (MicroVention; Tustin, CA, USA), HyperForm (Covidien, Irvine, CA), and TransForm (Stryker, Kalamazoo, Michigan, USA). These devices are designed for balloon-assisted coil embolization of aneurysms. The Gateway (Stryker, Kalamazoo, Michigan, USA) balloon is the only FDA-approved device for intracranial angioplasty. Coronary angioplasty balloons have also been used off-label to treat ICAD [48, 56]. Coronary balloons have been used with excellent technical success, and promising outcomes include Maverick balloon, NC Quantum Apex balloon, and drug-coated balloons [62–65].

Balloon-Mounted Stents

Balloon-mounted stents (BMS) have also been used in ICAD with some success. Most of the reported literature has used coronary BMS. NeuroLink, a dedicated intracranial BMS system, has been reported in the SYLLVIA trial. Results showed a 35% restenosis rate although 61% of these were asymptomatic [66]. The difficulty with the current BMS systems is that they are stiff and, therefore, harder to track in the tortuous intracranial circulation.

Self-Expanding Stents

Self-expanding nitinol stents have been the mainstay of intracranial stenting ever since the FDA approval of the Wingspan Stent (Stryker, Kalamazoo, Michigan, USA) (Fig. 5.3). They have had a high technical success rate: 98.8 and

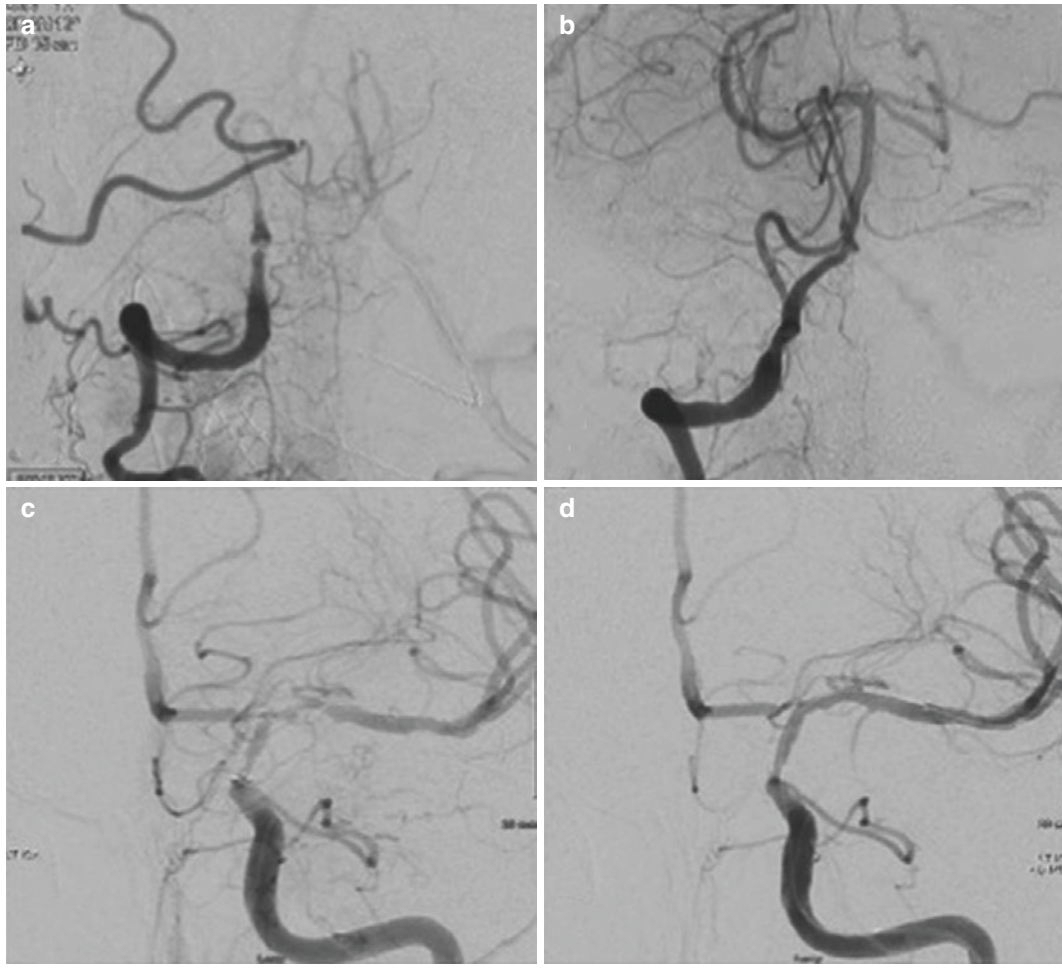

Fig. 5.2 (**a**, **b**) Patient with vertebral artery stenosis with recurrent strokes on optimal medical therapy before and after balloon angioplasty cerebral angiogram in AP projections, (**c**, **d**) patient with in-stent intimal hyperplasia before and after balloon angioplasty cerebral angiogram in AP projections

96.7% in the two large registries and 94.6% in the SAMMPRIS trial [3, 50, 51, 60]. Its small outward radial force (<0.1 atm) theoretically decreases chances of vessel rupture or dissection. It also does not need a balloon and can be delivered through a microcatheter, making it more trackable. Despite these advantages, the SAMMPRIS trial revealed better outcomes in the rate of stroke and death in the medically treated group compared to stenting [3, 20, 59]. Following criticism of the study that the stenting was not performed on-label by interventionalists of sufficient training, the WEAVE trial (Wingspan Stent System Post Market Surveillance) was conducted. The trial enrolled 152 patients, which was the largest on-label trial performed in the USA to date, and excellent results were seen. The periprocedural complication rate of 2.6% was also the lowest complication rate obtained compared to prior trials and registries. The trial inclusion protocol was stricter (criteria included age 22 to 80 years, symptomatic intracranial atherosclerotic stenosis of 70% to 99%, baseline modified Rankin Scale score ≤3, ≥2 strokes in the vascular territory of the stenotic lesion with at least one stroke while on medical therapy, and stenting of the lesion ≥8 days after the last stroke) [50, 60, 67, 68].

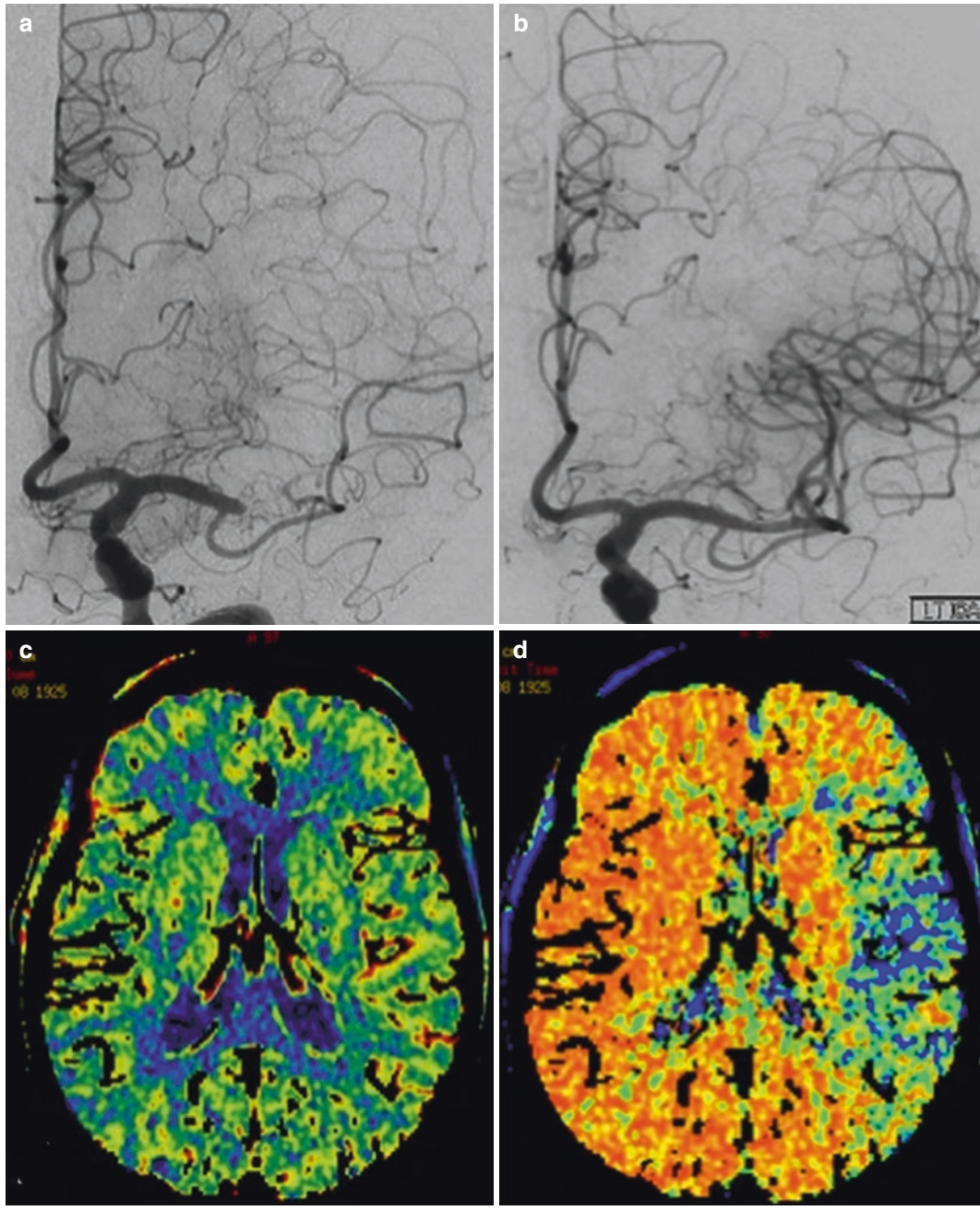

Fig. 5.3 Patient with near occlusion of M1 MCA who is symptomatic when her blood pressure is dropped. (**a**) Cerebral angiogram demonstrating the M1 MCA near occlusion before angioplasty and stenting, (**b**) cerebral angiogram after treatment with improved stenosis, (**c**) CBV (cerebral blood volume) increased in corresponding area, (**d**) MTT (mean transit time) decreased in corresponding area of symptoms and stenosis

Drug-Eluting Stents

Extracranial drug-eluting stents (DES) have been used off-label in the intracranial circulation. The devices are coated with antiproliferation drugs such as everolimus, sirolimus, and paclitaxel, which are designed to decrease intimal hyperplasia and restenosis of the stent. DES

have been used in both the anterior and posterior circulation with periprocedural complication rates ranging from 0% to 25% [3, 52–54]. Most DES are balloon mounted and difficult to track in the intracranial circulation. Other criticisms include the need for dual antiplatelet therapy for 6 months or longer as suggested by some of the cardiac literature [69, 70]. There is some literature on newer DES that points to a lower incidence of delayed thrombotic events, but research is still ongoing [55, 71]. The lack of long-term follow-up in patients treated with DES has limited their acceptance. A small case series ($n = 11$) with a mean follow-up period of 67 months has shown no patients with greater than 50% restenosis [57, 72].

Procedural Considerations

Patient Selection

It is important to remember that endovascular treatment of ICAD is a high-risk procedure, and care must be taken for patient selection and procedural preparation. Patients with recurrent symptoms in the setting of high-grade intracranial stenosis (≥70%) despite maximal medical therapy (dual antiplatelet agents, high-dose statin treatment, glycemic control, normotension, regular aerobic exercise, and smoking cessation) may be candidates for endovascular therapy. Other considerations include the location of stenosis and mechanism of stroke. Endovascular treatment of non-perforator-rich locations (intracranial internal carotid and vertebral arteries) is lower risk than perforator-rich locations (basilar and proximal middle cerebral arteries). Patients with hypoperfusion-related events are theoretically more likely to benefit from treatment.

Pre-procedure

It is important to perform a DSA for presurgical planning. A three-dimensional image is helpful to further characterize the lesion and to identify the optimal angle to utilize during endovascular surgery. It also allows for risk stratification by characterizing the extracranial and intracranial tortuosity that needs to be navigated in order to deliver the angioplasty balloon and/or stent to the desired location. The degree of angulation of the posterior and anterior genua of the cavernous carotid is a key determinant of success. Highly angulated genua may prohibit the navigation of a stent distally. The strategy must be tailored to the patient and his/her individual anatomy.

Dual antiplatelet agents (aspirin and clopidogrel) and high-dose statin therapy should be continued pre- and post-procedure. Consideration should be given to pre-procedural platelet function testing to screen for aspirin or clopidogrel resistance. The utility of these tests in reducing procedurally related stroke is controversial.

Anesthesia

Most neurointerventionalists currently perform intracranial angioplasty and stenting under general anesthesia. The arguments for this approach include the need for high-resolution imaging that is enhanced by decreased patient motion and mechanically induced apnea when needed. Elimination of the risk of sudden patient movement during a high-risk portion of the procedure is also achieved with general anesthesia. On the other hand, proponents of moderate sedation argue that the ability to monitor neurological function during the course of the procedure is invaluable. Additionally, the potential for medication-induced hypotension and subsequent hypoperfusion-related stroke may be less with moderate sedation. An arterial line should be in place both for peri- and post-procedure blood pressure monitoring.

Sheaths

A 6F or larger sheath is needed to perform these procedures. A long sheath (35 cm or greater) that bypasses the iliac artery and distal abdominal aorta is recommended due to the high incidence

of femoroiliac stenosis/tortuosity and abdominal aortic aneurysms in this population. When treating posterior circulation lesions, a radial access site may be advantageous. In this case a 6F 10 cm or shorter sheath is recommended. When intracranial stenting is planned, a 90 cm guiding sheath positioned in the distal common carotid artery or proximal internal carotid artery provides excellent support and allows the use of a "triaxial" system (guiding sheath, guiding catheter, and microcatheter) in the setting of difficult balloon/stent navigation.

Guiding Catheters

A 6F or larger guiding catheter is generally recommended. Standard guiding catheters can be safely positioned within the distal cervical carotid artery or at the V2/3 junction (e.g., Envoy XB (Codman Neurovascular, Raynham, MA)). A 45-degree tip catheter may help guide the force vector during the procedure. Alternatively, a more flexible, atraumatic tip guide catheter may be navigated into the petrous/cavernous carotid (e.g., Neuron (Penumbra Inc., Alameda, CA)). Some practitioners believe this more distal position outweighs the less supportive design of such catheters.

Intermediate Catheters

Intermediate or distal access catheter (DAC) can be navigated into the cavernous or supraclinoid segment. This can greatly facilitate accessing middle cerebral artery stenotic lesions by bypassing the cavernous segment.

Microcatheters

A low-profile microcatheter and microwire are used to cross the stenotic segment. There are many equally effective microcatheters available for this purpose such as the SL 10 (Stryker, Kalamazoo, MI).

Microwires

Two microwires are often used. The first is a standard length 0.014″ wire that, along with a low-profile microcatheter, is used to cross the stenosis. Ideal wire characteristics include 1:1 torque and a soft tip (e.g., Synchro-14; Stryker, Kalamazoo, MI). A headhunter shape to the distal wire tip often facilitates crossing the lesion. The second wire is an exchange length 0.014″ wire. This wire should be supportive proximally and highly shapeable distally (e.g., X-Celerator; Covidien, Irvine, CA). A J- or C-shaped wire tip will reduce the risk of micro-branch wire migration and perforation.

Balloons

Over-the-wire, semi-compliant balloons are generally preferred over monorail systems due to the greater trackability of the former through tortuous vessels. The Gateway balloon (Stryker, Kalamazoo, MI) is FDA approved for ICAD treatment. It is an over-the-wire, low-profile, and highly navigable balloon. Coronary angioplasty balloons have also been used off-label (e.g., Maverick; Boston Scientific, Natick, MA). With the use of balloon-mounted stents, a pre-dilation with a smaller balloon may facilitate stent passage.

With self-expanding stents, pre-stenting balloon diameters are generally sized to 80% or less of the normal luminal diameter. Balloon lengths are generally sized 5–10 mm greater than the lesion length. Extreme care must be taken to avoid overdistention of the vessel, as the fragile angio-architecture of the circle of Willis makes vessel rupture a real and catastrophic possibility.

Stents

The Wingspan Stent System is the only FDA-approved (HDE pathway) device for intracranial stenting in the setting of ICAD. It is used in conjunction with the Gateway balloon. These nitinol,

slotted tube, self-expanding stents are housed within a delivery catheter. The delivery catheter is generally navigated over an exchange wire and across the lesion. The delivery catheter is then withdrawn, allowing the stent to flower open. The diameter of the stent is generally close to that of the normal luminal diameter. The length is generally 5–10 mm greater than the lesion length. Over-the-wire, balloon-mounted coronary stents, both bare metal and drug-eluting, have been used off-label to treat ICAD. These devices are less navigable, but with a supportive proximal system, can generally cross the stenotic lesion. Stent sizing with these devices is 80% or less of the normal luminal diameter.

Procedural Steps

Anesthesia is induced. A sheath is placed within the access site. Heparin is administered to achieve an activated clotting time of >250 seconds and rechecked hourly. The guide catheter is navigated into the parent vessel. A low-profile microcatheter and standard length microwire are navigated intracranially and, under high-resolution road map guidance, used to cross the stenotic lesion. These devices are positioned in a large branch, a sufficient distance distal to the stenosis to allow support and access during subsequent steps (e.g., in the M3 angular branch or P2/3 segment). The standard length microwire is removed and replaced by an exchange length microwire. The microcatheter is then removed over the exchange wire. This step takes extreme care in order to avoid sudden movement of the wire. Sudden forward movement may lead to vessel perforation. A J- or C-shaped wire tip will reduce the tendency of the wire to enter small branch vessels. If the wire migrated proximally, trans-lesion access may be lost, or insufficient distal access may make balloon/stent navigation impossible. These exchanges generally require two operators. A repeat high-resolution road map is helpful to illustrate any changes in vessel angulation caused by the microwire. Next an over-the-wire angioplasty balloon is navigated across the lesion and inflated (see discussion above for balloon sizing tips), slowly deflated, and then removed from the arterial system.

If the Wingspan Stent System is being utilized, the delivery catheter is advanced over the exchange wire and across the lesion. Despite the hydrophilic coating and flexible design of this device, it is often a slow and laborious process to achieve the desired stent position across the stenotic lesion. The stent is deployed and the delivery catheter is removed (see above for stent sizing tips). An angiogram through the existing catheter is then performed. If insufficient luminal improvement is seen, a post-stent angioplasty can be performed, but is discouraged by the manufacturer.

If an over-the-wire, balloon-mounted coronary stent system is being utilized, a pre-stent angioplasty may not be needed, depending on the severity of the baseline lesion. Once the stent is navigated across the lesion, the balloon upon which it is mounted is inflated to nominal pressure (see above for stent sizing tips). A post-stent angioplasty can be performed if the desired luminal enlargement is not achieved. A final control angiogram will screen for thromboembolic complications or extravasation.

Post-procedural Considerations

It is important to carefully monitor and guard against spikes in blood pressure during the post-procedural period. High-risk points include awakening from anesthesia and extubation. Such spikes in blood pressure may precipitate hyperperfusion syndrome and intracranial hemorrhage. It is essential that dual antiplatelet therapy be maintained for at least 3 months. In the case of drug-eluting coronary stent use, 12-month to lifelong dual antiplatelet therapy is recommended.

Endovascular ICAD Studies

Despite having many options for treatment of ICAD with endovascular techniques, none has been established as primary treatment. Table 5.3 outlines some of the major literature on these approaches.

Table 5.3 Major[a] studies on endovascular treatment of intracranial atherosclerotic disease

Study	Groups compared	Endovascular txt, *location*	Pre- and post-txt stenosis	Restenosis rate (>50%)	Periprocedural complication rate	Outcome stroke or death
WEAVE trial [a] [68] VISSIT [a] [73] Miao [b] [48]	None BES plus medical therapy vs medical therapy alone medical	SES (Wingspan) ICA, MCA, VA, BA, and PCA Balloon-expandable stent PTA, stent *MCA*	83 → 28 NR 84 → NR	NR 26.5% NR	2.6% 24.1% 8.3%	2.6% stent 36.2% 19.4% stent 17.6% med
SAMMPRIS [b] (2011) [3]	Aggressive medical	SES *A and P circulation*	80 → NR	NR	19.2%	14.7% stent 5.8% med
Yu et al. [70]	MCA versus other locations	SES *MCA, ICA, BA, VA*	78 → NR	10%	2.4%—MCA 4%—Other	5.7% MCA 12% other
Nguyen et al. [55]	None	PTA *I, M, and ACA, B and VA*	79 → 34%	NR	5	8.5%
INTRASTENT [72]	None	Stenting (NR) *ICA, MCA, BA, VA*	NR	NR	NR	12.4%
Siddiq et al. (2008) [51]	PTA versus stent placement	PTA, stent (NR) *A and P circulation*	89 → NR 90 → NR	15% 4%	8% PTA 9% stent	8% PTA 11% stent
Mazighi et al. [59]	None	PTA, DES, BMS *ICA, MCA, BA, VA*	85 → 0%	16%	NR	10.1%
Zaidat et al. [50]	None	SES *ICA, MCA, BA, VA*	82 → 20%	25%	6.2%	14%
Fiorella et al. [60]	None	SES *ICA, MCA, BA, VA*	75 → 27%	NR	15.3%	6.1%
Marks et al. [41]	None	PTA, stent (NR) *I, M, and PCA, B and VA*	82 → 36%	NR	NR	5.8%
SSLYVIA [66]	None	BMS *I, M, and PCA, B and VA*	NR	32%	NR	9.3%

Txt treatment, *SES* self-expanding stent, *DES* drug-eluting stent, *BMS* balloon-mounted stent, *PTA* percutaneous transluminal angioplasty, *NR* not reported, *MCA* middle cerebral artery, *ICA* internal cerebral artery, *BA* basilar artery, *VA* vertebral artery, *ACA* anterior cerebral artery

[a] Major study has been defined as randomized, highly referenced, national registries or greater than 100 patients

[b] Indicates studies that were randomized and prospective

There have been positive results from non-randomized registries and case series, but there have been no positive randomized control trials to indicate its use as primary treatment of symptomatic patients with ICAD. The SAMMPRIS trial argues that it is likely harmful as first-line treatment [3, 8, 10]. VISSIT (the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy) randomized controlled trial showed increased 30-day risk of any stroke or TIA with stenting [73]. Despite this many experts still believe endovascular treatment of ICAD can play a role [12, 49].

Analysis of SAMMPRIS periprocedural strokes revealed that avoidance of perforator-rich areas, close monitoring of hemorrhages from wire perforation, Plavix loading, and close adherence to target activated clotting time could help produce better results from endovascular treatment [15, 74, 75]. Subsequent studies revealed lower complication rates and lower long-term stroke risk in well-selected patients undergoing angioplasty or stenting in ICAD (e.g., patients with poor collaterals, severe stenosis 70–99%, treated by an experienced operator at a high-volume center) [64, 76, 77]. Most recently, the WEAVE trial (Wingspan Stent System Post Market Surveillance) assessed the periprocedural safety profile of Wingspan Stent System to treat ICAD. This evaluated a strict on-label application of Wingspan Stent in 152 patients. On-label criteria included age 22 to 80 years, symptomatic ICAD stenosis of 70% to 99%, baseline modified Rankin Scale score ≤3, ≥2 strokes in the vascular territory of the stenotic lesion with at least 1 stroke while on medical therapy, and stenting of the lesion ≥8 days after the last stroke. A lower than expected periprocedural stroke, bleed, and death rate was achieved at 2.6% (4/152 patients) [68]. Currently patients should be evaluated on a case-by-case basis to determine if they would benefit from intracranial endovascular revascularization

Summary and Future Directions

Currently endovascular treatment is reserved for patients who have failed medical treatment. There is a need for future trials as even first-line maximal medical therapy has a 1-year 12% stroke rate and increased rate of stroke at follow-up [3, 20]. There is continued interest in endovascular ICAD treatment among experts [22, 49]. Imaging developments to assess intracranial arteries and identify high-risk plaque features are promising. Carefully selected patients with poor collaterals, hemodynamic symptoms, and recurrence despite medical therapy can potentially benefit from endovascular treatment. Future studies should focus on stricter selection of patients, which may utilize biomarkers from emerging imaging criteria or techniques. The endovascular technology also continues to evolve, with more devices tailored specifically for the intracranial vasculature rather than co-opted from cardiac applications.

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