Carotid Cavernous Fistula

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Contents

Abstract

Carotid cavernous fistulas (CCF) are complex lesions involving the abnormal shunting of arterial blood into the cavernous sinus. There are two distinct types: one is a direct communication between the internal carotid artery and the cavernous sinus, while the other is a dural shunt involving meningeal branches of the external and/or internal carotid arteries. Resulting patient symptoms as well as potential complications is determined primarily by the degree of arteriovenous shunting as well as the direction of venous outflow from the cavernous sinus. Catheter angiography remains the gold standard imaging evaluation of CCFs, although both MR and CT angiography can be used to screen patients in whom the diagnosis is suspected. Current treatment for these lesions consists primarily of conservative management and endovascular embolization. The latter can be performed via transarterial and/or transvenous approaches, using various materials such as detachable balloons, coils, and liquid embolic agents. A multidisciplinary approach, including neurointerventionalists, neurosurgeons, and ophthalmologists, is often required to achieve the best outcomes for patients.

Keywords

Carotid cavernous fistula • Endovascular embolization • Cortical venous reflux • Intracranial hemorrhage

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Introduction

A carotid cavernous fistula (CCF) is an abnormal arteriovenous shunt involving the cavernous sinus [1, 2]. The term actually applies to two distinct lesions, which vary in their etiology, potential clinical presentations, treatment, and outcomes. The first is a direct CCF, which consists of a tear in the cavernous segment of the internal carotid artery (ICA) with direct shunting of arterial blood into the sinus [2]. The second is an indirect CCF, which represents a dural arteriovenous fistula involving the cavernous sinus wall, which is fed by meningeal arterial branches that normally supply this region [1, 2]. Despite their differences, both lesions involve shunting of arterial blood into the normally low-pressure cavernous sinus, with resulting symptoms and complications determined primarily by the degree and route of venous drainage from the diseased sinus [3, 4]. The following chapter explores the characteristics of both types of CCF, highlighting their differences as well as similarities.

Types of Carotid Cavernous Fistula

- Direct fistulas: A direct fistulous communication between the cavernous segment of the internal carotid artery and the surrounding cavernous sinus
- Indirect fistulas: A dural arteriovenous fistula involving meningeal branches of the internal and external carotid arteries that normally supply the region of the cavernous sinus

Anatomy of the Cavernous Sinus and Cavernous Segment of the Internal Carotid Artery

Cavernous Sinus: The cavernous sinus is a contiguous network of trabeculated venous sinusoids surrounded by dura matter that is located centrally in the skull base adjacent to the pituitary sella and sphenoid sinus [5–7]. It contains both the cavernous segment of the ICA and cranial nerves III, IV, V1, V2, and VI [5–7]. Cranial nerves III, IV, V1, and V2 run in the lateral wall of the sinus, while VI is located within the sinus itself. The cavernous sinus normally receives venous blood from the ipsilateral orbit and brain, including the superior ophthalmic, inferior ophthalmic, superficial middle cerebral, and deep middle cerebral veins, as well as the sphenoparietal sinus [4, 8]. Venous outflow from the cavernous sinus is via superior and inferior petrosal sinuses to the transverse sinus and internal jugular vein respectively, as well as inferiorly via the pterygoid venous plexus as well as emissary veins associated with the foramina ovale and rotundum [4, 8]. Finally, the cavernous sinuses are interconnected via a venous network centered around the hypophysis, the so-called circular sinus [2, 9]. Although the circular sinus generally consists of a larger anterior and smaller posterior limbs, either may be absent or hypoplastic in a particular patient.

Contents of the Cavernous Sinus

- Cavernous segment of the internal carotid artery
- Cranial nerve VI
- Cranial nerves III, IV, V1, and V2 in the lateral wall of the sinus

Normal Hemodynamics of the Cavernous Sinus

- Venous inflow
  - Orbital veins: superior, inferior ophthalmic, and central retinal
  - Superficial and deep middle cerebral veins
  - Sphenoparietal sinus
- Venous outflow
  - Superior petrosal sinus
    Drains to transverse sinus
  - Inferior petrosal sinus
    Drains to internal jugular vein

(continued)

  - Pterygoid venous plexus
  - Emissary veins around foramina ovale and rotundum
- Intercavernous flow
  - Circular sinus

Internal Carotid Artery: The ICA ascends vertically in the skull base from the foramen lacerum into the cavernous sinus, before turning anteriorly into a horizontal segment approximately 2 cm in length [6]. The artery then ascends superiorly in a second vertical segment, extending along the medial aspect of the anterior clinoid process before exiting the sinus. The cavernous segment of the ICA can be divided into five segments, as detailed by Debrun et al. [10]. Going from caudal to cranial, these include the posterior ascending segment, junction of posterior ascending segment and horizontal segment, horizontal segment, junction of the horizontal segment and anterior ascending segment, and ascending segment [10]. Although any segment of the cavernous ICA may be involved by a direct CCF, the horizontal portion is the most common site of fistulization [10].

The cavernous segment of the ICA has two main branches that, along with distal branches of the internal maxillary artery from the external carotid, supply the dura surrounding the cavernous sinus as well as the nearby cranial nerves [2, 5, 11]. Small anastomoses between these branches of the external and internal carotid arteries are normally present in the surrounding dura and are responsible for the dural arteriovenous shunts found in indirect CCF [1, 5, 11]. The first is the meningohypophyseal trunk, present in 100 % of patients, which arises from the apex of the proximal curve of the vessel in the cavernous sinus [6]. This artery in turn has three main branches: the artery to the tentorium (Bernasconi-Cassonari), the dorsal meningeal artery to the clivus, as well as the inferior hypophyseal artery [5]. The second branch of the cavernous ICA is the inferolateral trunk (ILT), found in 84 % of patients, which originates from the distal horizontal segment of the vessel and is the most common branch to be involved by an indirect CCF [5, 6]. The ILT also has three main branches: superior or tentorial, anterior, and posterior branches, which supply dura as well as cranial nerves III, IV, V1, V2, and VI in and around the cavernous sinus and orbit [5]. Finally, the cavernous ICA may also give rise to McConnell's capsular arteries, although these vessels are inconstantly present [6].

Branches of the Cavernous Internal Carotid Artery

- Meningohypophyseal trunk
  - Artery to the tentorium (Bernasconi-Cassonari)
  - Dorsal meningeal artery
  - Inferior hypophyseal artery
- Inferolateral trunk
  - Superior or tentorial branch
  - Anterior branch
  - Posterior branch
- Capsular arteries

Pathophysiology

All CCFs demonstrate the same basic pathophysiologic mechanism of abnormal shunting of arterial blood into the normally low-pressure venous cavernous sinus. The resulting increase in pressure and volume results in reversal of blood flow in venous structures that normally drain the cavernous sinus, including the superior and inferior ophthalmic veins as well as the superior and inferior petrosal sinuses [4]. The resulting signs and symptoms associated with a CCF are determined both by the degree of arteriovenous shunting and the route of venous drainage from the cavernous sinus [3, 4]. The latter is determined by the location of the arteriovenous shunt, the presence of thrombus in the involved sinus, as well as stenosis or thrombosis of potential venous drainage pathways [10]. If the hemodynamic changes associated with a CCF persist over a long period of time, the involved veins may become arterialized with

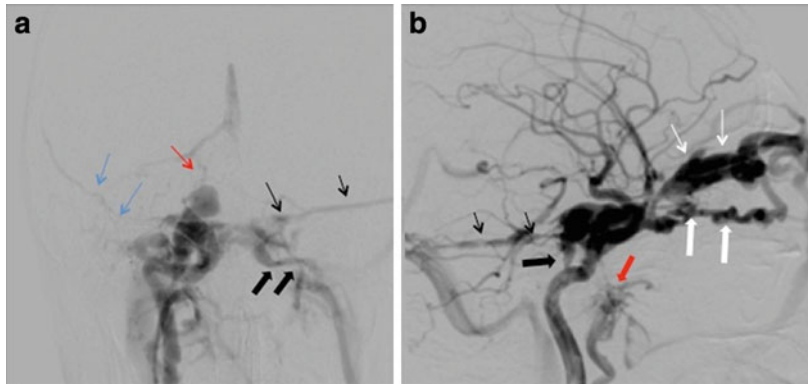

Fig. 1 Venous drainage pathways. (**a**) Frontal projection and (**b**) lateral projection of a right internal carotid artery angiogram demonstrating a direct right-sided CCF with bilateral venous drainage via the circular sinus. Multiple venous drainage pathways are illustrated, including the left superior petrosal sinus (*thin black arrows*), left inferior petrosal sinus (*thick black arrows*), right superior ophthalmic vein (*thin white arrows*), right inferior ophthalmic vein (*thick white arrows*), right superficial middle cerebral vein (*thin blue arrows*), right deep middle cerebral vein (*thin red arrow*), and pterygoid venous plexus (*thick red arrow*)

thickened, hyalinized walls [1]. Other chronic changes include recruitment of capillary connections in the conjunctiva of the eye, which are called specific limbal loops [1].

There are various patterns of venous drainage from the cavernous sinus that can be encountered with a CCF, which have important implications for patient symptomatology as well as the risk of intracranial complications (Fig. 1) [4, 10, 12]. Anterior drainage is commonly present, with reflux of blood into the ipsilateral orbit via the superior and inferior ophthalmic veins, with subsequent drainage into angular and facial veins [1, 12]. An additional anterior drainage route consists of the sphenoparietal sinus running along the anterior middle cranial fossa [2]. Posterior drainage from the cavernous sinus into the inferior and superior petrosal sinuses is also often encountered, either alone or in combination with anterior as well as contralateral drainage via the circular sinus [2, 4, 10, 12]. It has been speculated that the majority, if not all, of low-flow indirect CCF originally drain posteriorly, with anterior drainage only commencing once the posterior pathway becomes obstructed, often due to thrombosis [12]. Finally, superior and inferior venous drainage from the cavernous sinus can proceed via the Sylvian vein and pterygoid venous plexus, respectively [4].

Potential Routes of CCF Venous Drainage

- Anterior drainage via the orbital veins
  - Eventually draining into angular and facial veins
- Posterior drainage
  - Superior and inferior petrosal sinuses
- Contralateral drainage
  - Circular sinus
- Superior drainage
  - Superficial middle cerebral vein
- Inferior drainage
  - Pterygoid venous plexus & emissary veins

Classification

CCFs can be categorized using several criteria [5, 13]. These include classifications systems based on etiology (i.e., traumatic vs. spontaneous), hemodynamics (high-flow vs. low-flow shunts), as well as angiographic criteria [1, 5, 8, 13]. The latter was characterized by Barrow et al. [5] and is based on both the hemodynamics of the shunt as well as the arterial supply to the fistula as demonstrated on angiography [5].

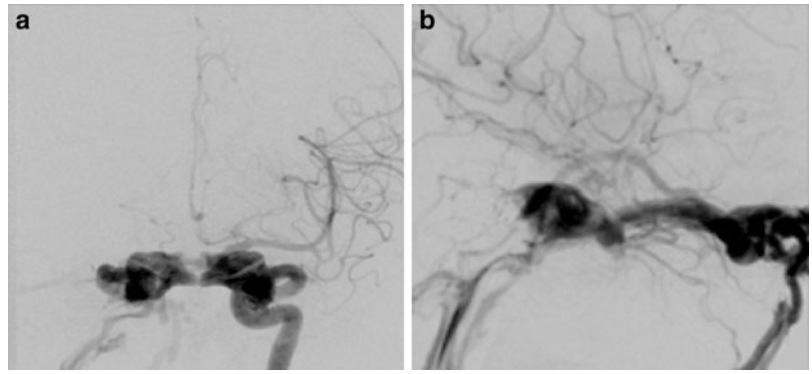

Fig. 2 Type A direct CCF. (**a**) Frontal projection and (**b**) lateral projection of a left internal carotid artery angiogram demonstrating a high-flow direct shunt between the left internal carotid artery and the ipsilateral cavernous sinus. Venous drainage is primarily via the circular and contralateral cavernous sinuses

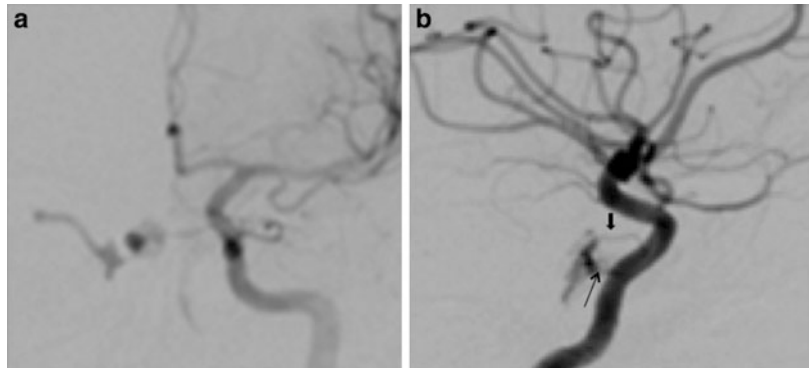

Fig. 3 Indirect type B CCF. (**a**) Frontal projection and (**b**) lateral projection of a left internal carotid artery angiogram demonstrating an indirect CCF supplied by meningeal branches of the ICA arising from the meningohypophyseal trunk (*thin black arrow*) and inferolateral trunk (*thick black arrow*)

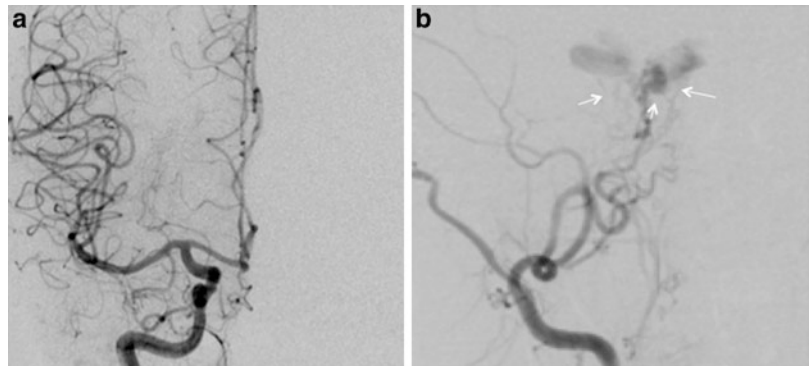

Fig. 4 Indirect type C CCF. (**a**) Frontal projection of a right internal carotid artery angiogram demonstrating no evidence of arteriovenous early cavernous shunting. (**b**) Frontal projection right external carotid artery angiogram demonstrating dural shunts between external carotid meningeal branches and the ipsilateral cavernous sinus (*white arrows*)

Type A CCFs are high-flow direct shunts between the ICA and the cavernous sinus (Fig. 2). Type B CCFs are dural shunts between meningeal branches of the cavernous ICA (arising from the meningohypophyseal or ILT trunks) and the cavernous sinus (Fig. 3). Type C CCFs are dural shunts between external carotid meningeal branches and the cavernous sinus (Fig. 4). Finally, type D CCFs are dural shunts with arterial supply from meningeal branches of both the ICA and ECA (Fig. 5) [5]. Rarely, a direct fistula between the ophthalmic artery and an ophthalmic vein can present in a similar fashion to a CCF, a so-called orbital shunt [1] (Fig. 6; Table 1).

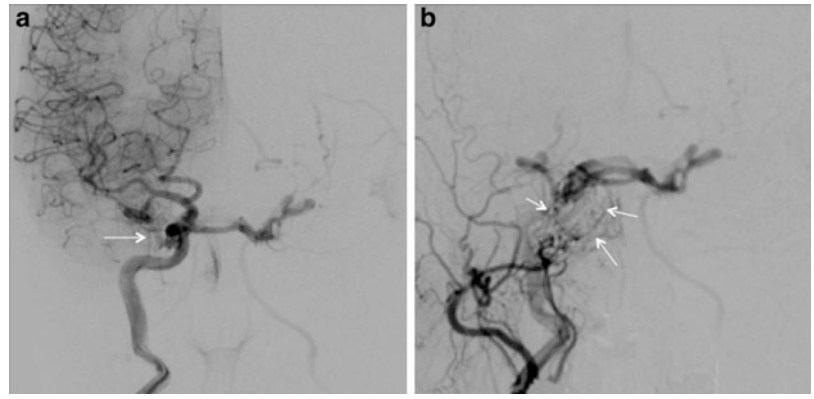

Fig. 5 Indirect type D CCF. (**a**) Frontal projections right internal carotid and (**b**) right external carotid artery angiograms demonstrating an indirect CCF with arterial supply from meningeal branches arising from both internal and external carotid arteries (*white arrows*)

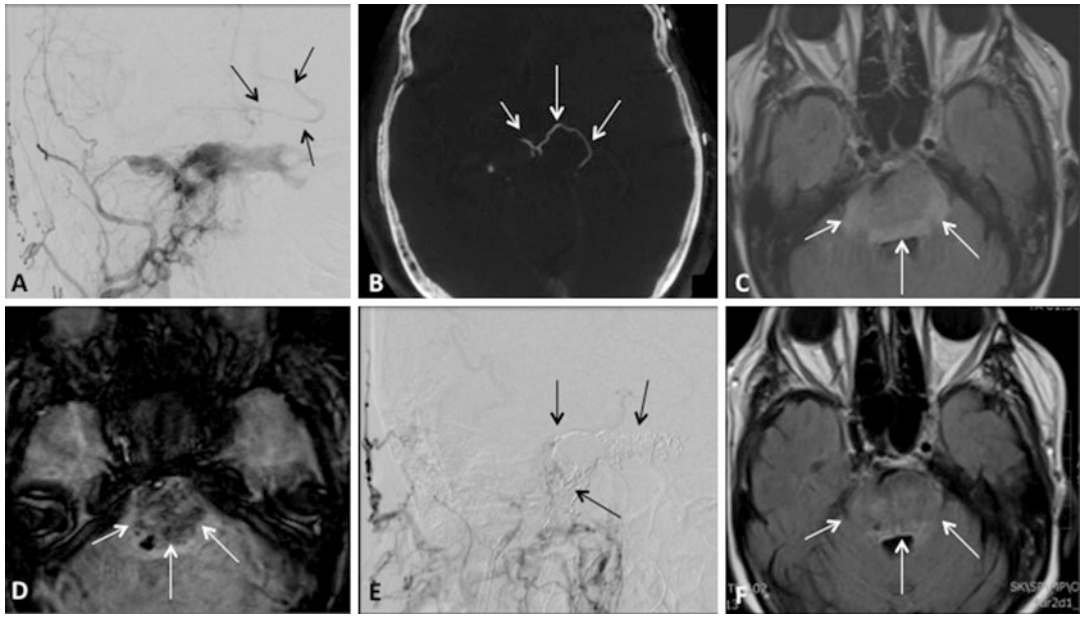

Fig. 6 Cortical venous reflux. (**a**) Frontal projection right external carotid artery angiogram and (**b**) flat panel computed tomography demonstrates a type C indirect CCF with cortical venous reflux (*black arrows* **a**, *white arrows* **b**). (**c**) Axial FLAIR and (**d**) susceptibility MR imaging demonstrates a resulting hemorrhagic brainstem venous infarct (*white arrows* **c**, **d**). (**e**) Lateral right external carotid artery angiogram and (**f**) axial FLAIR imaging following coil embolization demonstrates no residual arteriovenous shunting (*black arrows* **e**) as well as resolution of ischemic changes in the brain stem (*white arrows* **f**)

Etiology and Epidemiology

Direct Fistulas: Direct CCFs often result from blunt or penetrating trauma that results in a tear in the cavernous segment of the ICA, with resulting rapid arteriovenous shunting into the cavernous sinus [8, 10, 14]. These lesions are most commonly found in young males, presumably due to the increased prevalence of head trauma in this population [13–15]. Debrun et al. [10] found that the arterial tear in traumatic fistulas can vary in size anywhere from 1 to 5 mm, and rarely multiple rents may be present. Despite the high-flow arteriovenous shunting associated with direct fistulas, patients often present in a

Table 1 Barrow angiographic classification of carotid cavernous fistulas

	Fistula type	Arterial supply
Type A	Direct	Cavernous ICA
Type B	Indirect	Meningeal ICA branches
Type C	Indirect	Meningeal ECA branches
Type D	Indirect	Meningeal ICA and ECA branches

somewhat delayed fashion, anywhere from days to a few weeks following the inciting trauma [16]. The mechanism of vessel injury in many of these cases is likely a sudden increase in intraluminal arterial pressure associated with the traumatic event [17]. Penetrating trauma is another possible cause, as well as rarely arterial injury during skull base surgery [14–16, 18]. Finally, traumatic direct CCFs have been associated with fractures involving the skull base, with Liang et al. [16] in a retrospective review reporting an 8.3 % incidence of direct fistulas in patients with fractures involving the middle cranial fossa, particularly those with a transverse or oblique orientation.

Direct CCF fistulas can also be encountered in patients without a history of preceding trauma [8, 19]. These lesions are often encountered in middle-age women, but are not exclusive to this age group [20]. These spontaneous direct fistulas have several potential etiologies, the most common of which is rupture of a cavernous segment ICA aneurysm [18, 19]. Cavernous ICA aneurysms represent somewhere between 1.9 % and 9 % of all intracranial aneurysms, are more commonly associated with CCF development as opposed to subarachnoid hemorrhage, and give rise to roughly 20 % of direct CCFs [14, 19, 21]. In a retrospective review of all cavernous ICA aneurysms presenting to a single medical center, Kupersmith et al. [21] found that 13 of 193 lesions were associated with a CCF (6.7 %). However, it is important to remember that a predisposing cavernous aneurysm may not be identified following direct fistula formation due to the presence of high-flow arteriovenous shunting [22].

Etiologies of Direct Carotid Cavernous Fistulas

- Traumatic
  - Blunt
  - Penetrating
  - Iatrogenic
- Spontaneous
  - ICA aneurysm rupture
  - Collagen vascular disorders
    Ehlers-Danlos type IV syndrome
    Pseudoxanthoma elasticum
    Fibromuscular dysplasia
  - Minor episode of trauma or valsalva
    Coughing and sneezing

An additional cause of spontaneous direct CCFs includes various genetic syndromes that can weaken the arterial wall and predispose to rupture after minor trauma or episodes of valsalva, including coughing or sneezing [1, 18, 19]. Specific genetic conditions that can affect vascular wall structural integrity and have been associated with CCF include fibromuscular dysplasia, Ehlers-Danlos type IV syndrome, and pseudoxanthoma elasticum [23–25]. Finally, a direct CCF can be associated with a persistent trigeminal artery extending from the cavernous ICA to the basilar artery [22]. These so-called trigemino-cavernous fistulas may arise either from an inherent weakness in the aberrant vessel wall or due to aneurysm formation at the ICA-trigeminal artery branch point [22].

Indirect or Dural Fistulas: Indirect CCFs represent a subset of dural arteriovenous fistulas involving the cavernous sinus, which receive blood flow from meningeal branches of the internal and/or external carotid arteries that normally supply the cavernous sinus dura [2, 26]. These lesions most often occur spontaneously in postmenopausal women [15, 26, 27]. However, as is the case with direct CCFs, these lesions may present in all age groups, including children and infants, and can develop following minor trauma or episodes of valsalva [12]. Altogether, dural arteriovenous fistulas represent approximately

10–15 % of intracranial vascular malformations [28]. Potential arterial feeders to indirect CCFs include branches of the external carotid artery, such as the internal maxillary, middle meningeal, accessory meningeal, and ascending pharyngeal arteries, as well as internal carotid artery branches [26]. The latter include meningohypophyseal, capsular, inferolateral trunk arteries, as well as ethmoidal branches arising from the ophthalmic artery [26].

As is the case with dural arteriovenous fistulas found elsewhere in the intracranial compartment, the etiology of indirect CCF remains uncertain [12, 15]. One theory speculates that these fistulas may result from breakdown in small thin-walled dural arteries that normally cross the cavernous sinus [12]. Alternatively, venous thrombosis and/or elevated venous pressure may result in the opening of normally closed, small anastomotic channels in the dura [8, 12]. Risk factors for the development of these dural fistulas include atherosclerosis, hypertension, diabetes, sinusitis, pregnancy, and collagen vascular disease [8, 27, 29].

Etiology of Indirect Carotid Cavernous Fistulas

- Uncertain, two possible mechanisms
  - Breakdown of small thin-walled dural arteries that transverse the cavernous sinus
  - Opening of small anastomotic dural channels
    Venous sinus thrombosis
    Elevated venous pressure
- Risk factors
  - Atherosclerosis, diabetes, hypertension, and pregnancy

Clinical Presentations

The majority of symptomatic CCFs have anterior drainage via the ophthalmic veins, with resulting reflux of high-pressure arterial blood into the ipsilateral orbit [3, 12, 15]. This arteriovenous shunting results in orbito-ocular congestion and is responsible for the classic clinical triad associated with CCFs, namely, pulsatile exophthalmos, orbital bruit, and chemosis of the ipsilateral globe [1, 3, 4, 14, 19]. The contralateral orbit may also be affected due to reflux of blood across the circular sinus, occasionally in the absence of ipsilateral orbital symptoms depending on the pattern of venous drainage [1, 9, 12]. Other signs and symptoms of orbito-ocular congestion include medically refractory glaucoma, ophthalmoplegia, retro-orbital pain, vision loss, as well as dilatation and arterialization of conjunctival and episcleral veins on ophthalmologic exam [1, 12]. Although this latter finding may be seen in the setting of other diseases such as conjunctivitis, a tortuous corkscrew appearance of these vessels is highly specific for the diagnosis of CCF [12]. General differential considerations for physical exam findings suggestive of orbito-ocular congestion include vascular malformations involving the orbit or cavernous sinus, cavernous sinus thrombosis, as well as inflammatory processes such as scleritis, with vortex vein blockage [1].

Some CCFs may present without classic symptoms, depending on the pattern of venous drainage as well as the degree of arteriovenous shunting [3, 11, 15, 18, 28]. For example, low-flow indirect CCFs with exclusively posterior venous drainage characteristically lack signs and symptoms of orbito-ocular congestion, including pulsatile exophthalmos and orbital bruit [3, 4, 12, 29, 30]. Instead, these lesions often are either asymptomatic or associated with nonspecific symptoms including headache, tinnitus, trigeminal neuropathy, facial nerve palsy, or isolated oculomotor palsy due to the involvement of the corresponding cranial nerves [11, 12, 30]. In these instances, patient symptoms may be due, at least in part, to brainstem congestion resulting from the posterior venous drainage [12, 31]. The atypical presentation of these posteriorly draining fistulas often leads to a delay in their diagnosis, which is unfortunate given the association between drainage via the superior petrosal sinus and cortical venous reflux, a high-risk feature discussed subsequently in this chapter [1, 4].

Clinical Presentation of Carotid Cavernous Fistulas

- Fistulas with anterior drainage via orbital veins
  - Pulsatile exophthalmos
  - Chemosis
  - Glaucoma
  - Vision loss
  - Ophthalmoplegia
- Fistulas with exclusively posterior drainage via petrosal sinuses
  - Asymptomatic
  - Headache
  - Tinnitus
  - Trigeminal neuropathy
  - Isolated oculomotor palsy

Finally, symptom progression in CCFs is often determined by the degree of associated arteriovenous shunting, with high-flow lesions often presenting acutely with rapid deterioration, while low-flow fistulas may demonstrate an insidious onset and subsequent benign course [1, 15]. Low-flow shunts are most often encountered in the setting of an indirect, dural CCF, although direct lesions may also behave in a similar manner if the tear in the cavernous ICA is relatively small or if there is partial thrombosis of the involved cavernous sinus [1]. Recurrent fistulas following treatment may also present insidiously, again depending on the amount of residual arteriovenous shunting and available venous drainage pathways [22].

Complications and High-Risk Features

Ophthalmologic complications of CCFs include vision loss, ophthalmoplegia, and medically refractory glaucoma [1, 12]. Ophthalmoplegia can result from either entrapment of the extraocular muscles due to swelling of these structures or due to cranial nerve palsy secondary to mechanical compression of the corresponding nerve(s) [1, 12]. Glaucoma in CCFs may develop from high orbital venous pressure, congestion of the choroid or iris, displacement of the iris-lens diaphragm, or neovascularity secondary to chronic ischemia [12]. Finally, loss or deterioration of vision in the involved eye can be secondary to venous stasis retinopathy with resulting retinal ischemia, secondary glaucoma with optic nerve damage, or spontaneous choroidal detachment [1, 11, 12]. Vision loss is more commonly seen with direct CCF, although this finding may be encountered in as many as 20–30 % of indirect fistulas, particularly chronic lesions [12].

Ophthalmologic Complications of Carotid Cavernous Fistulas

- Glaucoma
  - Elevated orbital venous pressure
  - Choroid or iris congestion
  - Iris-lens diaphragm displacement
  - Neovascularity
- Ophthalmoplegia
  - Extraocular muscle swelling
  - Cranial nerve palsy
- Vision loss
  - Venous stasis retinopathy
  - Glaucoma with optic nerve damage
  - Spontaneous choroidal detachment

Additional complications of CCFs include intracranial hemorrhage, both intraparenchymal and subarachnoid, venous infarct, epistaxis (which may be fatal), as well as increased intracranial pressure with venous hypertension [18, 26, 32]. Intraparenchymal hemorrhage is often a result of reflux of high-pressure arterialized blood into cortical veins overlying adjacent brain parenchyma [1, 15, 18]. Posterior venous drainage of a CCF via the superior petrosal sinus has been associated with the development of this high-risk feature and may be precipitated by the spontaneous thrombosis or iatrogenic occlusion of alternative venous drainage pathways [1, 4, 15, 18]. Overall, cortical venous reflux has been reported in anywhere from 10 % to 55 % of CCFs, is often symptomatic due to increased intracranial pressure, and carries up to a 30–40 % chance of hemorrhagic stroke if untreated

[15, 18, 26, 33]. Furthermore, the reported annual mortality rate of intracranial dural arteriovenous fistulas with cortical venous reflux, regardless of location, is 10.4 % [33].

Subarachnoid hemorrhage from a CCF has been associated with the development of a cavernous sinus varix or pseudoaneurysm (Fig. 7) [18]. In a retrospective review of the angiographic features of 155 patients with CCFs, Halbach et al. [18] found that cavernous sinus venous varix was present in three of four patients who presented with subarachnoid hemorrhage, all of which were fatal. Although cavernous sinus varices were encountered in patients without intracranial hemorrhage, the authors argued the risk of fatal subarachnoid hemorrhage warranted emergent fistula treatment with this finding is present [18]. Finally, drainage into the sigmoid and transverse sinuses has been associated with elevation of intracranial pressure from resulting venous hypertension [18].

High-Risk Features of Carotid Cavernous Fistulas

- Cortical venous reflux
  - Between 10 % and 55 % of CCFs
  - Up to 30–40 % risk of hemorrhagic stroke untreated
  - Associated with superior petrosal sinus drainage
  - Can arise from blockage of venous drainage pathways
- Subarachnoid hemorrhage
  - Rare, but often fatal
  - Associated with cavernous sinus varix
- Drainage into sigmoid and transverse sinuses
  - Risk of elevated intracranial pressure from resulting venous hypertension

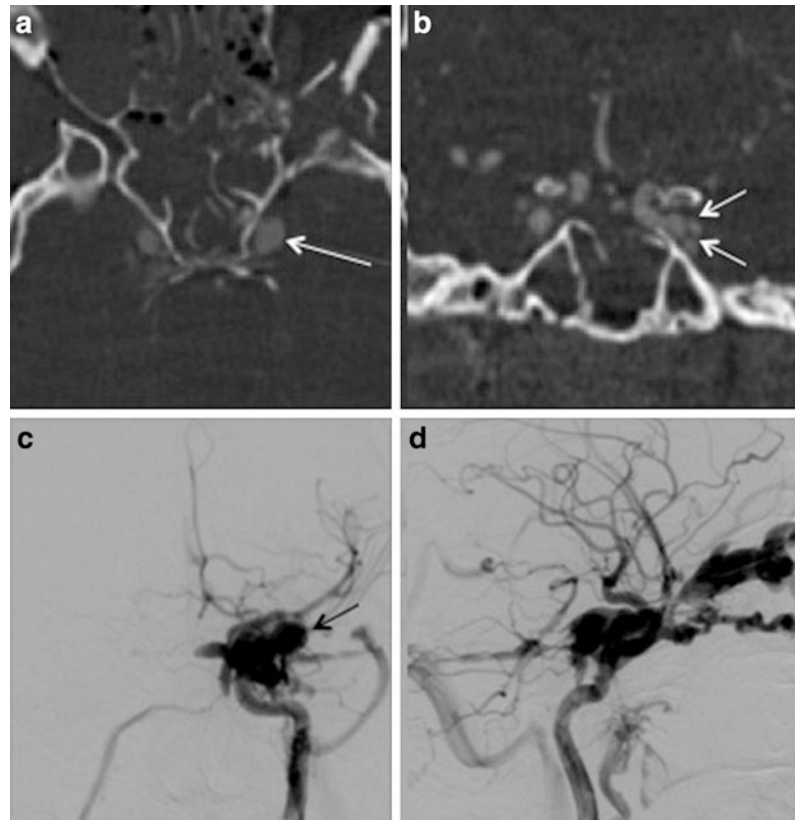

Fig. 7 Cavernous sinus pseudoaneurysm. (**a**) Axial and (**b**) coronal reconstructed CT angiography images show an ectatic left cavernous sinus (*white arrow* **a**) with multiple lateral projecting outpouchings (*white arrows* **b**), which may represent possible pseudoaneurysm and/or draining venous tributaries. (**c**) Frontal projection and (**d**) lateral projection of a left internal carotid artery angiogram demonstrate a direct CCF with associated pseudoaneurysm (*black arrow* **c**)

Imaging Evaluation

Noninvasive Cross-Sectional Imaging: Although many patients with a CCF present with classic signs and symptoms suggestive of the diagnosis, others may demonstrate either atypical symptomatology and/or an insidious, slowly progressive course [26]. In these instances, conventional MR, time-of-flight (TOF) and contrast-enhanced MR angiography (MRA), Doppler ultrasound, as well as CT angiography (CTA), may be used to screen patients for the presence of an arteriovenous fistula involving the cavernous sinus [34–36]. Conventional MR imaging finding suggestive of a CCF includes prominent flow voids in the involved cavernous or inferior petrosal sinuses on spin-echo sequences, dilated intercavernous venous channels, as well as the sequelae of orbito-ocular congestion including enlargement of the superior ophthalmic vein and extraocular muscles and proptosis [37–39]. However, these findings may only be present in high-flow fistulas, with conventional MR imaging being relatively insensitive for lesions demonstrating less rapid arteriovenous shunting [40].

3D TOF MRA can increase the sensitivity for detection of CCF by depicting flow-related enhancement in the involved cavernous sinus as well as arterial feeders in the setting of an indirect fistula [35, 37, 40]. It is important to note however that venous flow signal can be normally seen in the cavernous and inferior petrosal sinuses on 3D TOF MRA in the absence of a CCF [41]. In addition, 3D TOF MRA is limited by the lack of temporal resolution, which precludes full characterization of dynamic shunting lesions such as a CCF [40]. However, time-resolved contrast-enhanced MRA can help to overcome some of these challenges by imaging the suspected diseased cavernous sinus during passage of a gadolinium contrast bolus [40]. This technique has been shown to be both sensitive and specific for the diagnosis of CCF and is a promising tool both for screening patients as well as surveillance for fistula recurrence following treatment (Fig. 8) [40].

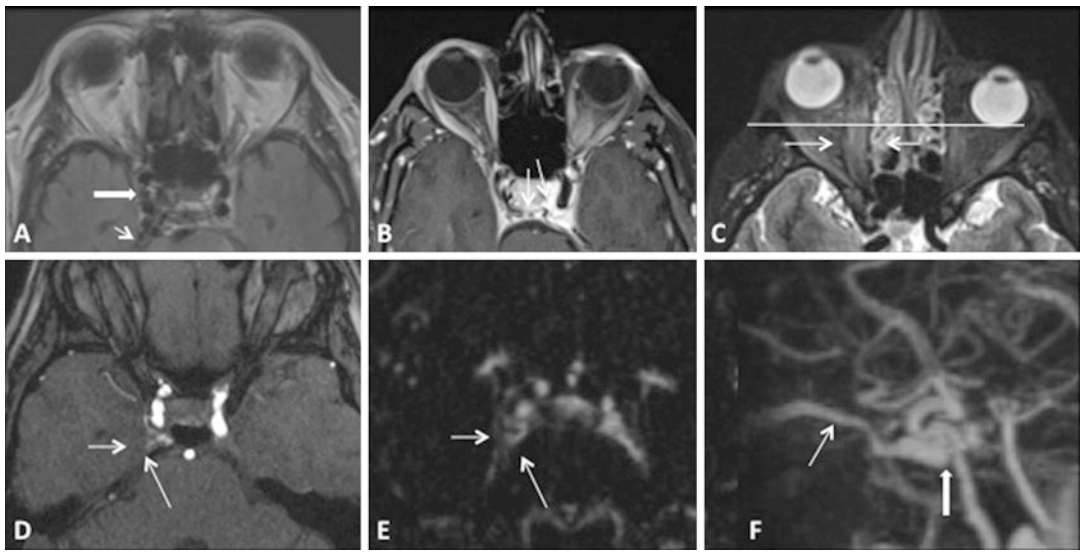

Fig. 8 Conventional MR and MRA finding suggestive of a right CCF. (**a**, **b**) Prominent flow voids are noted on spin-echo sequences in the right cavernous and inferior petrosal sinuses (*white thick* and *thin arrows* respectively **a**) as well as dilated intercavernous venous channels (*thin black arrows* **b**). (**c**) Sequelae of orbito-ocular congestion are present in the ipsilateral orbit with enlargement of the extraocular muscles (*white thin arrows*) and proptosis (*horizontal white line*). (**d**) Post-contrast MRA demonstrates enhancement of the involved cavernous sinus (*white arrows*). (**e**, **f**) Time-resolved contrast-enhanced MRA demonstrates early opacification of right cavernous sinus (*thin white arrow* **e**) as well as the fistulous shunt and drainage via the superior ophthalmic vein (*thick* and *thin white arrows*, respectively **f**)

CT angiography has also been demonstrated to be a promising technique for screening patients suspected of having a CCF [42]. With the availability of 256 and 320 slice CT scanners, excellent quality dynamic studies can be performed with high spatial and acceptable temporal resolution. CT and CT angiography findings of a CCF include an enlarged cavernous sinus that demonstrates early enhancement in the arterial phase, as well as dilatation of draining venous tributaries (e.g., superior ophthalmic vein) [42, 43]. Chen et al. [37] performed a retrospective study comparing noninvasive 3D TOF MRA and CTA to the gold standard of catheter angiography. They found that CTA performed better at detecting CCF than TOF MRA, particularly for fistula involving the more proximal aspect of the cavernous ICA (Table 2).

Catheter Angiography: Despite advances in cross-sectional imaging of CCF, catheter angiography remains the gold standard for the diagnosis and characterization of these lesions due to its superior spatial and temporal resolution [26, 40]. The diagnosis of a CCF is readily made on catheter angiography by the demonstration of abnormal arteriovenous shunting into the cavernous sinus from either the ipsilateral cavernous ICA or meningeal branches to the sinus wall in the case of an indirect fistula. Goals of catheter angiography when evaluating a CCF include the identification of the exact site of fistulization, evaluation of the degree of arteriovenous shunting, determination of arterial supply to the lesion, evaluation of the pattern of venous outflow, the presence of high-risk features including cortical venous reflux and venous varix, potential dangerous external or internal carotid artery anastomoses, as well as the presence of atherosclerotic disease if carotid compression is contemplated as a potential treatment [26].

Table 2 Noninvasive imaging modalities for evaluation of CCFs

Modality	Findings	Potential disadvantages
MRI	Flow voids, cavernous and petrosal sinuses	Insensitive for moderate- to low-flow fistulas
	Distension of the cavernous sinus	
	Dilated intercavernous channels	
	Sequelae of orbito-ocular congestion	
TOF MRA	Flow-related enhancement in cavernous sinus	Not 100 % specific
		No temporal resolution
CE MRA	Flow-related enhancement in cavernous sinus	Improved temporal resolution
		May not detect high-risk features
CTA	Distension of the cavernous sinus	Poor temporal resolution
	Early sinus enhancement in arterial phase	May not detect high-risk features
	Dilatation of draining venous tributaries	

Catheter Angiography Evaluation of Carotid Cavernous Fistulas

- Determination of type of fistula
- Arterial supply with indirect lesions
- Localization of fistulous tear with direct lesions
- Evaluation of degree of arteriovenous shunting
- Analysis of venous drainage pathways
- Identification of high-risk features, including cortical venous reflux

Huber's Maneuver: In the setting of a high-flow CCF, the tremendous arteriovenous shunting may obscure the underlying ICA tear, and the carotid artery more distally may not fill due to essentially complete diversion of blood flow into the cavernous sinus [2, 10, 22]. In these instances, injection of a vertebral artery during manual compression of the ipsilateral ICA may allow for better characterization of both the location and the size of the fistulous communication (Fig. 9) [10, 44]. This technique works by allowing a limited amount of contrast to reach the shunt via a posterior communicating artery with subsequent

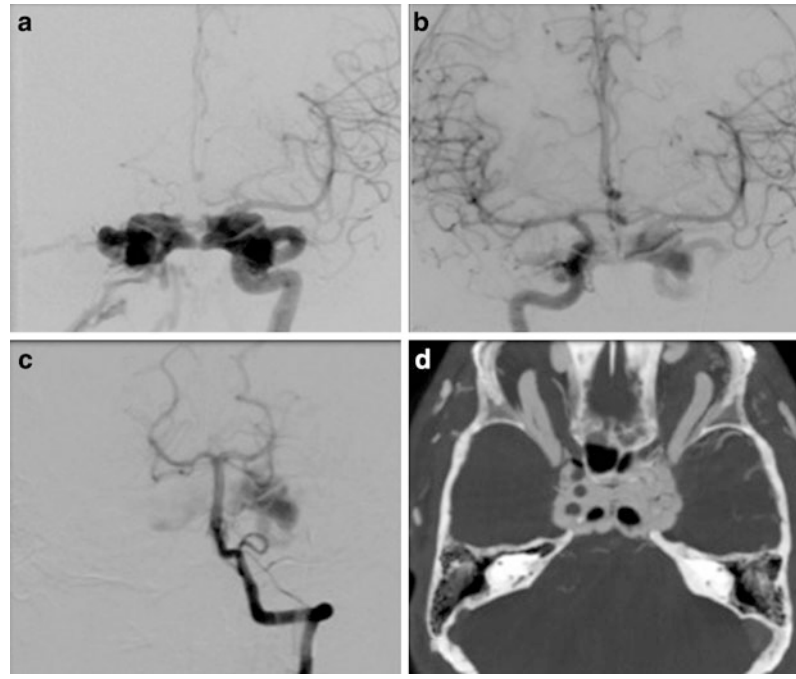

Fig. 9 Huber maneuver. (**a**) Frontal projection left internal carotid artery angiogram demonstrates a direct CCF with the high-flow arteriovenous shunting obscuring the underlying tear in the carotid artery. (**b**) Injection of the contralateral ICA or (**c**) vertebral artery during manual or balloon compression of the ipsilateral ICA (Huber's maneuver) may allow for better characterization of both the location and the size of the fistulous communication. (**d**) C-arm angiographic CT (flat panel rotational computed tomography) is also a exceptional technique for locating and studying the anatomy of fistula as well

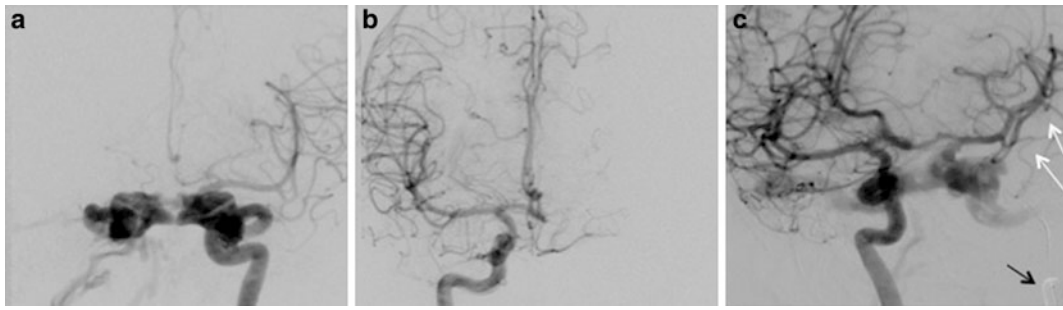

Fig. 10 Angiographic balloon occlusion test. (**a**) Frontal projection left internal carotid artery angiogram demonstrates high-flow arteriovenous shunting associated with a left direct CCF. There is relatively poor opacification of the more distal left internal carotid artery due to vascular steal. (**b**) Frontal projection right internal carotid artery angiogram opacifies the left anterior cerebral artery, but there is no significant filling of the left middle cerebral artery. (**c**) Frontal projection right internal carotid artery angiogram during balloon occlusion of the cervical left internal carotid artery (*black arrow*) demonstrates brisk collateral flow to the left middle cerebral artery territory (*white arrows*)

retrograde flow down the ipsilateral supraclinoid ICA [10]. Other maneuvers that can help delineate the fistula size and location include very high frame rate imaging and 3D subtraction angiography. Finally, C-arm angiographic CT (flat panel rotational computed tomography) is another exceptional technique for locating and studying the anatomy of fistula.

Balloon Occlusion Test (BOT): As a significant minority of direct CCFs may require ipsilateral ICA sacrifice for successful closure, performing a balloon occlusion test during the diagnostic workup can provide invaluable information to the treating physician (Fig. 10). First, a guide catheter is placed in the ipsilateral common carotid artery. Next, following full heparinization,

a soft, compliant balloon (typically a HyperForm or HyperGlide Occlusion Balloon, ev3, Irvine, California) is navigated into the cervical ICA proximal to the fistula. The balloon is then carefully inflated under fluoroscopic imaging, and a gentle injection is performed through the guide catheter to confirm vessel occlusion. Continuous neurologic monitoring, including testing of patient speech and contralateral strength, is then performed for a total of 30 min. The test is immediately stopped if the patient develops symptoms suggestive of ischemia involving the ipsilateral cerebral hemisphere. The patient can be further challenged during a balloon occlusion test by purposefully dropping the systolic blood pressure by 30 %, although all operators do not routinely perform this maneuver. Finally, collateral flow to the affected vascular territory via the Circle of Willis (i.e., an angiographic balloon occlusion test) can be performed during balloon inflation by injection of the contralateral carotid and vertebral arteries using a second diagnostic catheter.

Management

The management of CCFs is often determined by multiple interdependent factors, including the rate of arteriovenous shunting, the venous pathways recruited by the fistula, the degree of associated orbito-ocular congestion, as well as the presence of cortical venous reflux or venous varix [15, 45]. Treatment options include conservative management with close imaging follow-up as well as endovascular or surgical repair. Indications for aggressive fistula treatment include progressive vision loss, cranial nerve palsies, rapidly worsening proptosis with corneal exposure, cortical venous reflux, and intractable retro-orbital pain [14, 19]. It is important to note that these signs and symptoms may be reversible only when treatment is initiated early in the course of the disease, emphasizing the importance of prompt diagnosis and prompt treatment [1, 27, 46]. Liang et al. [16] found in their retrospective review of post-traumatic direct CCFs that the time from first symptom onset to treatment was significantly shorter in patients who had no fistula-related disability on follow-up compared to those who did (41.5 days compared to 140.8 days). Finally, although complete fistula cure is often attempted, partial occlusion/embolization may be adequate if it addresses either intolerable symptomatology or high-risk features such as cortical venous reflux.

The following sections further explore the various management options available to patients with CCFs.

Conservative Management

When discussing possible treatment of a CCF with a patient, the potential risks and benefits of therapy should be weighed against the natural history of the patient's particular lesion [18, 26]. Spontaneous closure of indirect CCF has been reported anywhere between 10 % and 73 % of cases, although spontaneous closure of direct fistulas is thought to be considerably more rare [9, 14, 18, 19, 26]. Interestingly, spontaneous fistula closure may be precipitated by catheter angiography [18, 19, 26]. Accordingly, low-flow fistulas without significant orbito-ocular congestion, high-risk angiographic features, or other intolerable symptoms can often be followed conservatively [1, 9, 15]. However, close clinical as well as periodic imaging follow-up is required though to exclude the development of aggressive fistula features [1]. Stiebel-Kalish et al. [9] found in a retrospective review that clinical signs suggestive of the presence of cortical venous reflux in indirect CCF include bilateral orbital symptoms as well as the presence of a postauricular bruit. Patients with these features should undergo catheter angiography for further evaluation.

During this time, patients may help to promote fistula closure by manually compressing the ipsilateral cervical carotid artery and internal jugular vein several times a day (Fig. 11) [47, 48]. Higashida et al. [48] found that this resulted in cure of indirect CCF in 30 % of patients anywhere from several minutes to 6 months. This maneuver can even result in lesion closure in a minority of direct CCF (17 %). Kai et al. [49] found that factors associated with a higher likelihood of achieving fistula closure

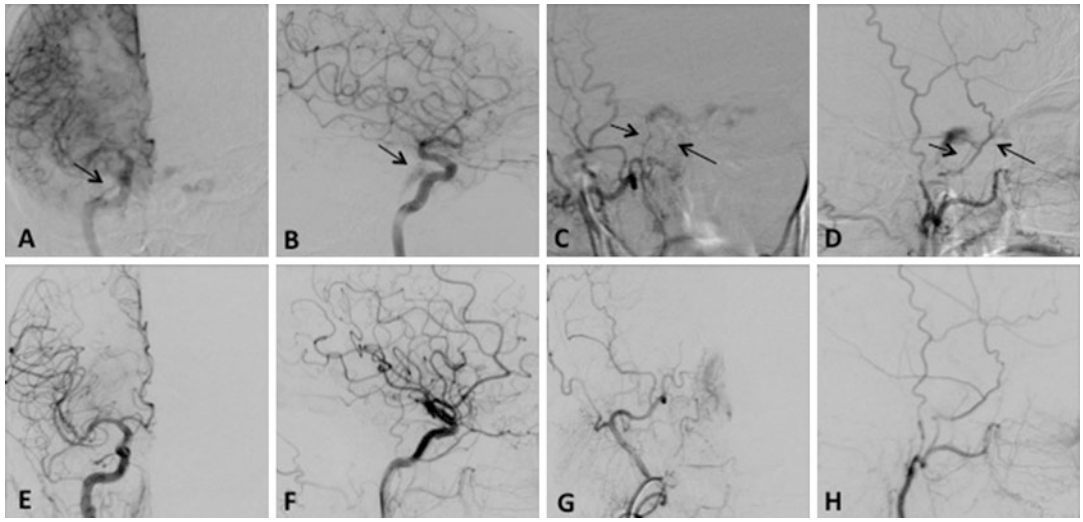

Fig. 11 Manual compression for treatment of a low-flow indirect type D CCF. (**a**) Frontal and (**b**) lateral projections of a right internal carotid and as well as frontal (**c**, **d**) lateral projections of a right external carotid artery angiogram demonstrating arterial supply to an indirect CCF from external and internal carotid meningeal branches (*black arrows*). Patient was managed conservatively and asked to perform intermittent manual carotid artery compressions. Follow-up right internal (**e**, **f**) and external carotid (**g**, **h**) artery angiogram performed 6 months later demonstrates resolution of the fistula

with manual compression for indirect lesions included a shorter time between symptom onset and initiation of treatment, lower ocular pressure, and venous drainage exclusively via the superior ophthalmic vein. Patients should be instructed to be sitting during the maneuver and to use the contralateral arm [49]. Otherwise, transient lack of blood flow to the ipsilateral cerebral hemisphere may lead to syncope as well as inadvertent prolonged compression if the ipsilateral arm is used (which would not be affected by the resulting ischemia).

Carotid Manual Compression of Carotid Cavernous Fistulas

- Appropriate for low-flow lesions without high-risk features or progressive symptoms.
- Patient should be sitting in case of syncope.
- Patients should perform maneuver several times a day.
- Patient should be instructed to use contralateral hand in case of ipsilateral cerebral ischemia.

General Considerations of Endovascular Treatment

A large majority of both direct and indirect CCFs can be successfully treated using modern endovascular techniques with a low rate of procedure-related complications [11, 50]. Embolization materials currently used for the treatment of CCFs include fiber and platinum microcoils, detachable latex balloons, as well as liquid embolic agents including n-butyl cyanoacrylate (nBCA) or ethylene vinyl alcohol (Onyx, ev3, Irvine, California) [50–52]. Transarterial, transvenous, as well as combined approaches may be utilized for fistula closure (Fig. 12) [11, 50, 53]. The endovascular method used to treat a given lesion often is determined by multiple factors, including the type of shunt (direct vs. indirect), the size of the ICA tear with direct fistulas, the rate of arteriovenous shunting, as well as the accessibility of venous pathways to the involved cavernous sinus [15].

General risks of endovascular treatment of CCFs include stoke, hemorrhage, vessel injury, and parent artery occlusion. In addition, patients

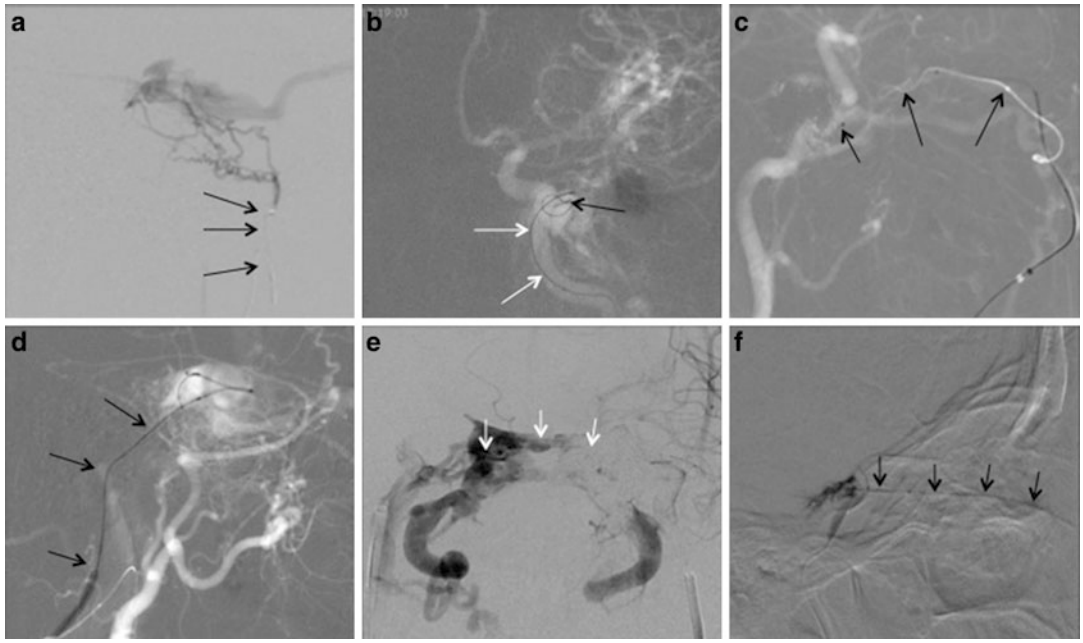

Fig. 12 Endovascular access routes. (**a**) Transarterial microcatheter injection of a distal external carotid artery branch supplying an indirect CCF. *Black arrows* demonstrate the distal aspect of the microcatheter. (**b**) Transarterial access of a direct left CCF with a microcatheter passing from the ipsilateral internal carotid artery (*white arrows*) and into the cavernous sinus (*black arrows*). (**c**) Transvenous access of a CCF through the superior ophthalmic vein (*black arrows*). (**d**) Transvenous access of a CCF through the inferior petrosal sinus (*black arrows*) (**e**) Transvenous access of a CCF with a microcatheter extending through the intercavernous channels (*white arrows*). (**f**) Direct cavernous sinus access through percutaneous of the inferior orbital fissure (*black arrows*)

should be counseled that their symptoms may temporarily, or rarely permanently, worsen following therapy as the fistula thromboses, with alterations of venous drainage [15]. Obtaining a complete diagnostic catheter angiogram prior to embolization is essential to define important fistula characteristics such as arterial supply and venous drainage, as well as to evaluate for high-risk features including cortical venous reflux [45]. In addition, the interventionalist must pay close attention to alterations of venous drainage from the cavernous sinus during embolization of a CCF. Inadvertent diversion of blood into the sphenoparietal or superior petrosal sinuses after partial fistula embolization may lead to cortical venous reflux and hemorrhagic stroke [15, 26, 45, 54, 55]. Similarly, redirection of venous drainage anteriorly into the ipsilateral orbit can lead to worsening of orbito-ocular congestion, with possible resulting loss of vision [28, 55]. Finally, patients should be advised that some symptoms, particularly cranial nerve palsies, may not improve despite successful fistula closure [46].

Endovascular Treatment of Carotid Cavernous Fistulas

- Materials
  - Detachable Balloons
  - Platinum or fiber coils
  - Liquid embolic agents
    n-Butyl cyanoacrylate (nBCA, glue)
    Ethylene vinyl alcohol copolymer (Onyx)
  - Covered Stents
- Endovascular Access
  - Ipsilateral carotid artery for direct fistula
  - Venous routes

(continued)

Inferior petrosal sinus
Facial and angular veins
Pterygoid venous plexus
Superior petrosal sinus
Percutaneous puncture of superior ophthalmic vein
– Transarterial catheterization of meningeal feeders of indirect fistulas

Endovascular Treatment of Direct CCF

Detachable Balloons: The goal of endovascular treatment of direct CCF is complete fistula closure with preservation of the ICA [14, 56]. Early endovascular approaches to direct CCF consisted of transarterially navigating a catheter with a detachable balloon mounted at its tip past the tear in the cavernous ICA and into the cavernous sinus. Once in position, one or more of these balloons were sequentially inflated and detached in the cavernous sinus to achieve fistula closure [12, 22, 33, 53]. Detachable balloons used for CCF treatment are made of latex and inflated with contrast medium in position [19]. Serbinenko [57] was the first to use such an approach for the treatment of CCFs, followed by Debrun et al. [58]. This method is very successful at achieving fistula closure, with high rates of ICA preservation and low procedure-related morbidity and mortality [10, 11, 14, 59]. Lewis et al. [14] demonstrated an 88 % rate of complete occlusion of direct CCF via the transarterial balloon embolization method, with a 75 % rate of ICA preservation. The permanent neurologic complication rate was only 4 %.

Challenges to transarterial balloon embolization of direct CCFs include difficulties navigating the relatively stiff balloon catheters, inability to cannulate small ICA tears, inability to inflate a balloon in small-sized venous compartments with the cavernous sinus, balloon compression and compromise of the cavernous ICA or cranial nerves, as well as subsequent balloon deflation or migration [10, 14, 55, 56, 59, 60]. Balloon deflation or migration could result in fistula recurrence, the development of an ICA pseudoaneurysm, or compression of the ICA and cranial nerves [14, 56, 60]. In addition, some patients following detachable balloon treatment have developed recanalization of a true cavernous ICA aneurysm, which was presumably responsible for development of the fistula [60]. Transarterial balloon embolization of direct CCFs has been abandoned in the USA due to the lack of commercially available detachable balloons.

Coils and Liquid Embolic Agents: An alternative endovascular treatment of direct CCFs is the placement of coils into the involved cavernous sinus via a transarterial approach [11, 19, 55]. Once the microcatheter is in position in the sinus, multiple fiber or platinum microcoils can be carefully deployed in the venous sinusoids closest to the point of arteriovenous fistulization [55]. Similar, to detachable balloons, challenges to coil embolization include difficulties navigating the microcatheter into the cavernous sinus if the ICA tear is small, as well as inadvertent coil prolapse into the ICA with larger rents [52, 55]. The latter may be particularly difficult to visualize in the setting of a high-flow shunt and can result in parent vessel occlusion and/or stroke. The risk of coil prolapse into the ICA may be mitigated by placement of an endovascular stent and/or non-detachable balloon in the vessel prior to embolization [13, 52]. Finally, it is possible to occlude a large majority of the diseased cavernous sinus with coils and still have residual arteriovenous shunting if the portion of the sinus closest to the fistula remains patent [50].

Embolization of a direct CCF may be supplemented or replaced by liquid embolic agents such as nBCA or ethylene vinyl alcohol (Onyx) [56, 61]. The non-adhesive nature of Onyx offers several advantages over nBCA, including the reduced risk of microcatheter retention, which allows for longer injection times and more thorough penetration of the liquid embolic agent into the lesion [50]. Potential risks of liquid embolic embolization of direct CCF include non-target embolization of the ipsilateral ICA and its branches as well as cranial neuropathy. The risk of reflux of liquid embolic agent may be mitigated by inflation of a balloon into the ipsilateral cavernous ICA during liquid embolic injection [62].

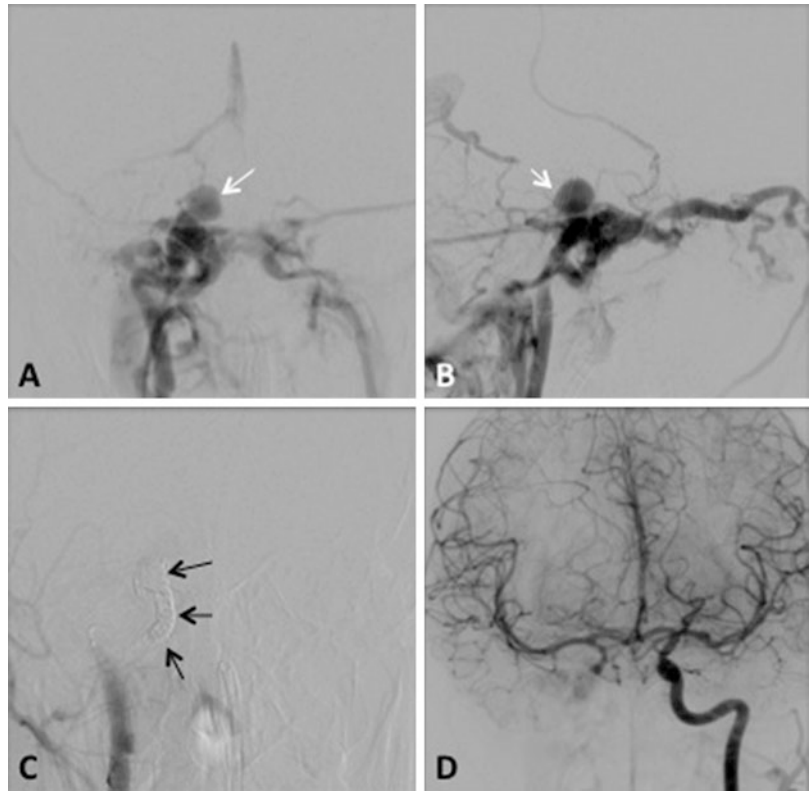

Fig. 13 Carotid artery sacrifice. (**a**) Frontal and (**b**) lateral projections of a right internal carotid artery angiogram demonstrate a post-traumatic right internal carotid artery pseudoaneurysm (*white arrows*) and associated direct CCF. (**C**) Frontal projection of a right internal carotid artery angiogram following vessel sacrifice by coil embolization demonstrates no residual filling of the fistula. Coil mass is outlined by *black arrows*. (**d**) Frontal projection of a left internal carotid artery angiogram following right internal carotid artery sacrifice demonstrates cross-filling of the contralateral right anterior and middle cerebral arteries

Alternative Routes to the Cavernous Sinus: If a transarterial approach is either not technically possible or fails to adequately close a direct CCF, transvenous treatment may be attempted [54]. A transvenous approach can be performed by placement of a guide catheter in the ipsilateral internal jugular vein followed by navigation of a microcatheter into the cavernous sinus via the inferior petrosal sinus [45, 53, 54]. However, it is not always possible to access the cavernous sinus via this route due to either thrombosis or stenosis of the inferior petrosal sinus [15, 53, 63]. In these instances, alternative routes to the cavernous sinus include the ipsilateral facial and angular veins, the contralateral pterygoid venous plexus, as well as the superior petrosal sinus via the transverse sinus [15, 29, 53, 63].

On occasion, it may only be possible to reach the involved cavernous sinus from a transvenous approach via direct surgical cannulation/percutaneous puncture of the ipsilateral superior ophthalmic vein [27, 28]. This method has been shown to be both safe and effective, with cannulation of the vein possible even if it appears thrombosed on imaging [27]. Once microcatheter access to the cavernous sinus has been achieved, embolization can then proceed with coils and/or liquid embolic agents [61]. Potential complications of direct puncture of the superior ophthalmic vein include rupture of the vessel with retroocular hemorrhage and rapid visual loss, infection, and damage to other orbital structures [28]. Finally, there are a few report of direct percutaneous cannulation of the inferior ophthalmic vein performed for fistula treatment [64].

Internal Carotid Artery Sacrifice: If other endovascular methods of closing a direct CCF fail, ICA sacrifice should be considered (Fig. 13)

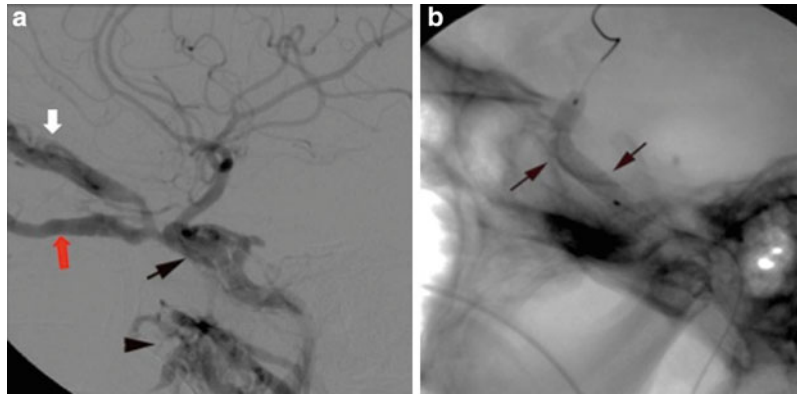

Fig. 14 Covered stent treatment of a direct CCF. (**a**) Lateral projection internal carotid artery angiogram demonstrates a high-flow direct CCF (*black arrow*) with extensive shunting into the superior ophthalmic (*white arrow*) and inferior ophthalmic veins (*red arrow*) as well as the pterygoid venous plexus (*arrow head*). (**b**) Lateral projection fluoroscopic native image demonstrates a covered stent (*black arrows*) placed in the cavernous internal carotid artery spanning the defect

[56]. The latter technique has proven to be highly successful in the treatment of direct CCFs, although there is a risk of ipsilateral cerebral hemispheric stroke. This risk may be mitigated, in part, by performing a balloon occlusion test prior to artery closure. However, a successful balloon occlusion test does not guarantee a good outcome. High-flow direct CCFs that demonstrate complete diversion of blood into the lesion with non-opacification of the supraclinoid ICA represent a special circumstance when carotid artery sacrifice should be considered [60]. If the patient has not suffered from stroke or TIA-like symptoms, the hemodynamics of the fistula provide strong evidence that carotid occlusion will be tolerated. On the other hand, as many of these patients are relatively young, carotid artery sacrifice must be weighed against the risk of the patient developing stenosis or occlusion of another major artery in the head and neck later in life.

Covered Stents: Covered stents have also been used to treat direct CCFs, either alone or in combination with coils and liquid embolic agents (Fig. 14) [51, 65, 66]. Gomez et al. [51] treated seven patients with post-traumatic CCFs with polytetrafluoroethylene (PTFE)-covered stents, all of which had successful fistula closure and no immediate procedure-related morbidity or mortality. However, one patient subsequently developed asymptomatic in-stent occlusion [51]. Tiewei et al. [65] reported similarly good results in a group of eight patients with traumatic direct CCF treated with covered coronary stents. Five of the eight patients had occlusion of their fistula following stent placement, while six went on to have resolution of their symptoms. However, once again, there was one case of subsequent asymptomatic in-stent occlusion [65]. Another group, Wang et al. [66], reported successful closure of 8 out of 10 direct CCF that failed more conventional endovascular therapy, with no in-stent stenosis or occlusion during the follow-up period of the study. These results suggest that covered stents are a promising new endovascular treatment of direct CCFs. However, more data is needed, particularly in regard to the long-term patency of these devices. Finally, as is the case with other endovascular stents, patients must be maintained on dual antiplatelet therapy for at least 3 months following treatment [51]. This is a

Table 3 Endovascular treatment options for direct carotid cavernous fistulas

Treatment modality	Potential advantages	Potential disadvantages
Detachable balloons	Proven, safe and effective method	Difficulty navigating stiff delivery catheter to fistula
	Extensive operator experience	Inability to inflate balloon in small venous compartments
		Potential for balloon deflation or migration following deployment
Coils	More controlled deployment compared to liquid embolic agents	Potential for coil prolapse into cavernous ICA, especially in setting of high-flow shunts or large rents
	Small, flexible microcatheters may be used for coil placement	Potential for residual fistula following coil embolization of majority of cavernous sinus
		Can be expensive if using platinum coils
Liquid embolic agents	Excellent penetration of small venous compartments of the cavernous sinus	Less controlled embolization with potential for nontarget closure of arterial supply to the brain, eye, cranial nerves
Carotid artery sacrifice	Effective method	Potential for ipsilateral ischemic stroke, even if patient passes BOT
	Relatively safe if fistula results in complete arterial steal or patient passes BOT	
Covered stents	Shown to be effective in small series	Concern for long-term patency of stents
	Option if more traditional endovascular methods fail	Need for antiplatelet therapy

significant drawback to treatment with covered stents, particularly in patients who recently experienced significant head trauma (Table 3).

Endovascular Treatment of Indirect or Dural CCF

Transvenous embolization of indirect, dural CCF is a safe and efficacious treatment for patients who have progressive symptoms and high-risks features on imaging or who fail conservative management (Fig. 15) [15, 28, 45, 50, 63, 67]. Similar to all intracranial dural arteriovenous fistulas, the goal of therapy is closure of the arteriovenous shunts connecting meningeal arteries to feeding veins [45]. For indirect CCF, this has been most commonly accomplished by placement of multiple coils in the diseased cavernous sinus [45, 50]. Kirsch et al. [46] reported either complete lesion closure or minor residual shunt without cortical or ocular drainage in 94 % of 141 patients treated using this approach. Meyers et al. [26] reported similar results with 90 % of patients cured following transvenous embolization of indirect CCF in a retrospective review of 135 patients.

However, transvenous coil embolization of indirect CCF may not always be successful due to the trabeculated structure of the cavernous sinus, which can preclude adequate coil placement in the venous compartment(s) involved by the shunt [45, 50]. In these instances, embolization may be successfully performed using liquid embolic agents, either alone or in combination with coils (Fig. 16) [45, 67, 68]. Furthermore, if a transvenous approach to an indirect CCF is not possible due to either venous stenosis or occlusion, a transarterial approach with a liquid embolic agent may also be utilized [50]. Onyx, with its ability to penetrate small arterial feeders during prolonged injections, is uniquely well suited to reach the small dural shunts from an arterial pedicle [50]. Care must be taken however

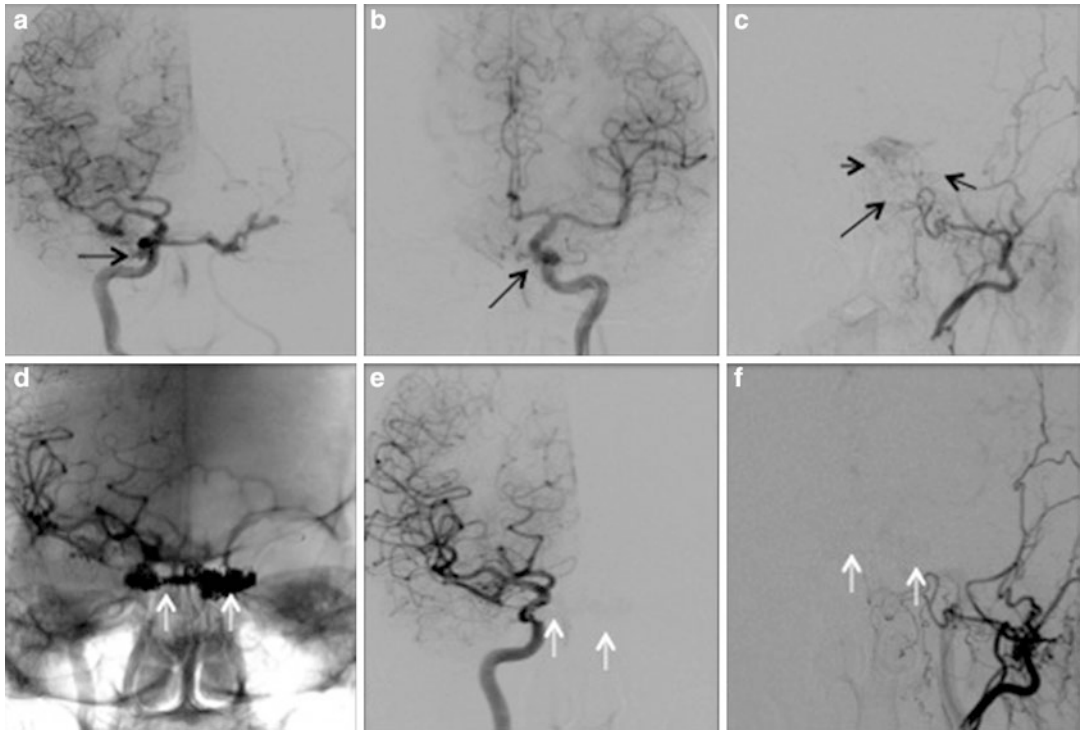

Fig. 15 Coil embolization of an indirect CCF. Frontal projections of a (**a**) right internal carotid artery, (**b**) left internal carotid artery, and (**c**) left external carotid artery angiograms demonstrating meningeal supply (*black arrows*) to a type D indirect CCF. The patient subsequently underwent transvenous coil embolization of the fistula. (**d**) Unsubtracted right internal carotid artery angiogram demonstrating coil mass in the bilateral cavernous and circular sinuses (*black arrows*). Follow-up frontal projections of (**e**) right internal carotid artery and (**f**) left external carotid artery angiograms demonstrate no residual arteriovenous shunting (*white arrows*)

as retrograde filling of non-catheterized arterial pedicles is possible with Onyx, which may lead to nontarget embolization of the arterial supply to the brain, eye, or other cranial nerves. Finally, other treatment options for indirect CCF include transarterial embolization using a particulate agent such as polyvinyl alcohol (PVA) (Fig. 17) [69]. A major limitation of this latter approach however is a high rate of fistula recurrence, which is less likely following embolization using coils or liquid embolic agents [69] (Table 4).

Surgical Treatment

Prior to the advent of modern endovascular techniques, surgical closure of CCFs was the standard of care [11]. Early surgical treatment for these lesions consisted primarily of carotid artery sacrifice by vessel trapping [10, 11, 70]. Parkinson [71] subsequently developed a direct surgical approach to the cavernous sinus via a triangular space in the lateral sinus wall demarcated by the III and IV cranial nerves superiorly and the V and VI cranial nerves inferiorly. With the aid of

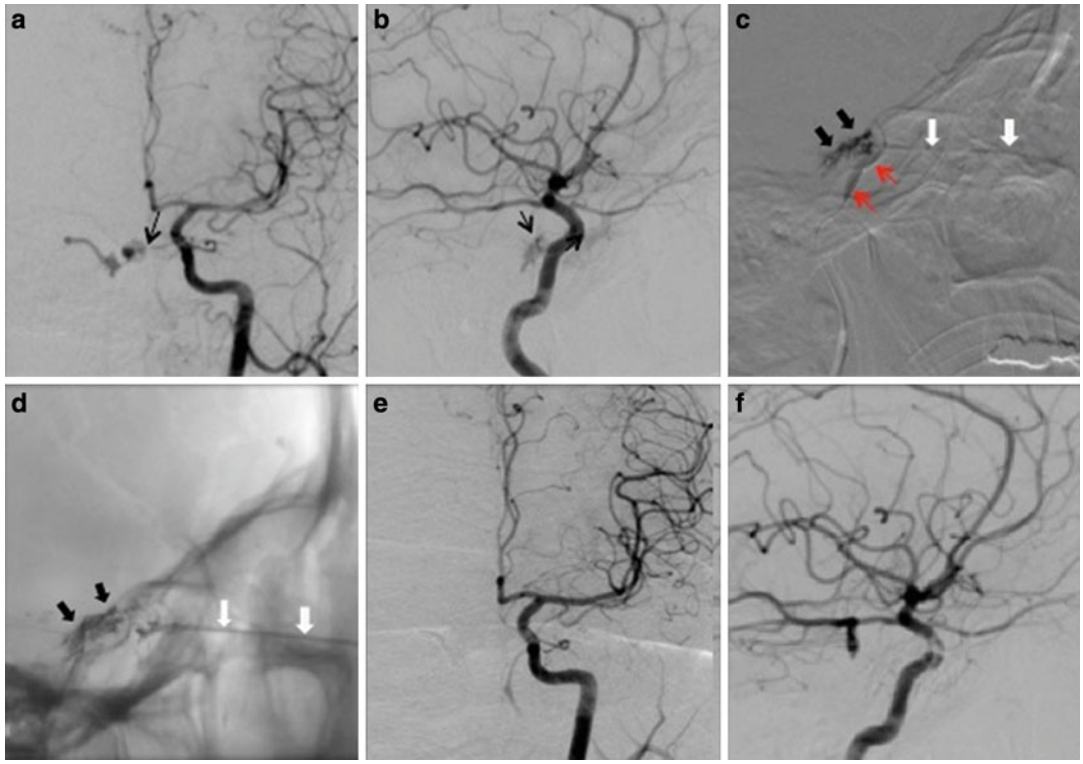

Fig. 16 Percutaneous onyx injection of an indirect CCF. (**a**) Frontal and (**b**) lateral projections of a left internal carotid artery angiogram demonstrate a type B CCF supplied by left internal carotid artery meningeal branches. Due to difficult access by transarterial or transvenous approaches, the lesion was accessed by direct transorbital puncture of the left cavernous sinus following by instillation of onyx. Lateral projections of a (**c**) subtraction road map and (**f**) native fluoroscopy demonstrate a needle coursing through the inferior orbital fissure (*white arrows* **c** and **d**) and onyx cast within the cavernous sinus (*black arrows* **c**, **d**). A balloon was inflated in the left internal carotid artery to prevent nontarget onyx embolization (*red arrows* **c**). Follow-up (**e**) frontal and (**f**) lateral left internal carotid artery angiograms demonstrates closure of the fistula

circulatory arrest and induced hypothermia, he went on to use this approach to treat both direct and indirect CCF, often preserving the carotid artery [72]. Modern surgical treatment of CCFs consists of a combined extradural-intradural approach to the cavernous sinus, with disconnection of arterial feeders in the case of indirect fistulas and clipping or suture repair of fistulous rents in the case of direct lesions [73, 74]. In addition, both direct and indirect fistulas may be indirectly occluded by packing the cavernous sinus with various materials, including muscle, glue, thrombus, and wires [18, 73, 74]. Due to the associated morbidity and technical challenges of surgical repair of CCFs, as well as the success of endovascular approaches, these procedures are most often performed only after failure of endovascular treatment [64].

Stereotactic Radiotherapy

Several small case series have demonstrated the efficacy of stereotactic radiosurgery for the treatment of indirect, low-flow CCFs without high-risk features [75–77]. Successful closure of the

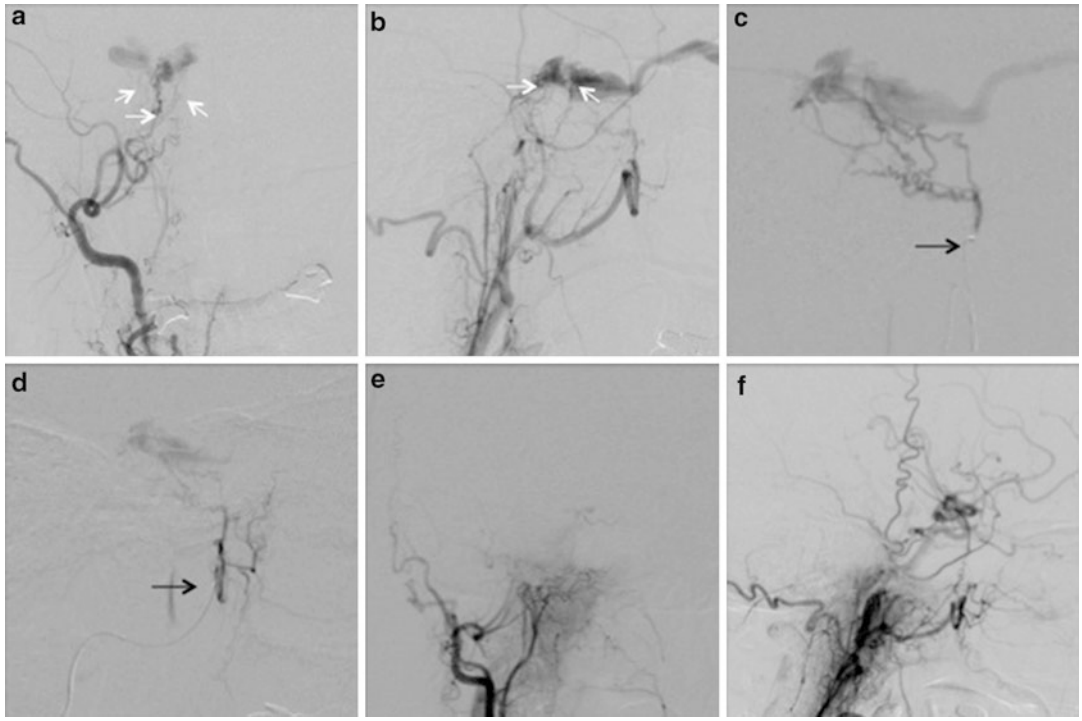

Fig. 17 Particulate embolization of a type C indirect CCF. (**a**) Frontal and (**b**) lateral projections of a right external carotid artery angiogram demonstrating dural shunts between external carotid meningeal branches and the cavernous sinus (*white arrows*). Microcatheter injections of two right external carotid artery pedicles (**c**, **d**) again demonstrate supply to the fistula, which were subsequently embolized with polyvinyl alcohol particles (PVA). (**e**) Frontal and (**f**) lateral projections of a right external carotid artery angiogram demonstrates occlusion of the fistula

arteriovenous shunt has been reported between 12 and 36 months following treatment [1]. Onizuka et al. [76] reported their results of a small case series consisting of four elderly women with symptomatic indirect CCF who received stereotactic radiosurgery targeted to the compartment of the involved cavernous sinus with a marginal dose of 13–15 Gy and a maximum dose of 36–30 Gy. All four fistulas were successfully closed, and patients experienced symptom relief in 1–3 months. There were no instances of lesion recurrence or adverse events from treatment during the follow-up period [76]. Pollock et al. [77] reported similarly high rates of symptom improvement and fistula closure in 20 patients with indirect CCF (95 % and 93 %, respectively). However, stereotactic radiotherapy was supplemented by transarterial particulate embolization in 13 of these patients [77].

Conclusion

Carotid cavernous fistulas are complex lesions that can be challenging to diagnose and manage. A multidisciplinary approach, including neurointerventionalists, neurosurgeons, and ophthalmologists, is often required to achieve the best outcomes for patients. The benefits as well as the risks of treatment need to be carefully weighed against the natural history of these lesions,

Table 4 Endovascular treatment options for indirect carotid cavernous fistulas

Treatment modality	Potential advantages	Potential disadvantages
Transvenous coiling	Proven, safe and effective method	Trabeculated cavernous sinus may preclude fistula closure
	More controlled deployment compared to liquid embolic agents	May not always be possible due to lack of venous access to cavernous sinus
Transvenous liquid embolic embolization	Excellent penetration of small venous compartments of the cavernous sinus	Potential for nontarget closure of arterial supply to the brain, eye, cranial nerves
	Can be used in combination of coils	May not always be possible due to lack of venous access to cavernous sinus
Transarterial liquid embolic embolization	Excellent penetration of small venous compartments of the cavernous sinus	Potential for nontarget closure of arterial supply to the brain, eye, cranial nerves due to either reflux of agent or retrograde filling of non-catheterized arterial pedicles
	Option when venous access to cavernous sinus not possible	
Particulate embolization	Safe method	High rate of fistula recurrence

particularly low-flow, indirect fistulas. Finally, identification of high-risk features on catheter angiography, including cortical venous reflux and cavernous sinus venous varix, is essential to appropriately triage these patients.

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