

# Embolization of Direct Carotid Cavernous Fistula With Onyx and Coils Under Transarterial Balloon Protection

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## Abstract

**Purpose** Endovascular management with good preservation of the internal carotid artery (ICA) has become the first-line choice for the treatment of direct carotid cavernous fistulas (CCFs). Multiple treatments have been tried with variable success. This article elucidates the effectiveness and safety of embolization with Onyx and coils under transarterial balloon protection.

**Materials and Methods** We reviewed 18 cases with direct CCFs in our case library. All cases were treated with transarterial or transvenous embolization with Onyx and coils under intra-arterial balloon protection.

**Results** Immediate angiography after embolization showed total occlusions in 16 patients and small residual fistulas in 2 patients. Good preservation of the ICA was observed in all cases. The average volume of Onyx was 2.6 ml, and the average length of bare coils was 102.0 cm.

Hydrogel-coated coils with an average length of 75.2 were used in five cases. Angiographic follow-ups of 16 patients showed no residual or recurrent fistula within 8 months (average 3.4). For the 2 patients with small residual fistulas, both received short-time angiographic follow-up within 3 month after the procedure. All follow-up angiograms showed no residual or recurrent fistula. Clinical follow-up of the other two recent patients showed no relapsing symptoms. There were no procedure-related complications, and no new symptoms occurred in any patient.

**Conclusion** The technique of embolization using Onyx and coils under intra-arterial balloon protection is feasible for the treatment of direct CCFs, especially for patients with large fistula ostium and large cavernous sinus. This technique is an effective and safe option with rare complications.

**Keywords** Direct carotid cavernous fistula · Endovascular embolization · Coils · Onyx

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Ying Yu and Qiang Li should be considered as co-first authors.

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## Introduction

Direct carotid cavernous fistulas (CCFs), according to the classification established by Barrow et al. [1], are direct arteriovenous communications between the internal carotid artery (ICA) and the cavernous sinus (CS), most of which result from a traumatic tear by skull fracture fragments after craniofacial trauma [2] or rupture of an aneurysm located on the cavernous segment of the ICA [3–6]. Because of the complex anatomy of the CS area, endovascular treatment was the previous choice for CCFs [7–9]. Detachable balloon, Onyx (ethylene vinylalcohol copolymer; ev3, Neurovascular, Irvine, CA), or coils has been used for the endovascular management for CCFs. Although Onyx has been reported as a feasible liquid embolic agent in the endovascular treatment for CCFs, it is still difficult to occlude the fistula with solely Onyx due to large, multiple fistula ostiums or an extremely dilated ICA. There are few case reports about Onyx and coils embolization for direct CCFs [10, 11]. This article elucidates the effectiveness and safety of transarterial balloon-protected endovascular treatment with Onyx and coils for direct CCFs.

## Materials and Methods

### Patient Population and Clinical Presentation

We reviewed all 18 patients with direct CCFs treated with Onyx and coils in our department between 2009 and 2013 (14 males and 4 females; age range 17–53 years; average 37.8). All clinical data are listed in Table 1. There were two spontaneous direct CCFs in this case series, and the others were of post-traumatic etiology. Ocular and/or orbital symptoms—including deterioration of visual acuity, chemosis, and proptosis—were most common. One patient had lost his sight completely before admission, and 11 patients complained about pulsatile bruit. Ophthalmoplegia due to CN III or CN VI palsy was found in six patients. In addition, there were two patients with massive epistaxis who were transferred from the Otolaryngological Department. Two patients with cranial trauma history had experienced seizure, and this was well-controlled on medication. However, we were not able to clarify the etiology of the seizure. It could have been either post-traumatic or cerebral ischemic due to direct CCFs. This study was reviewed and approved by the Institutional Review Board at our hospital.

### Angiographic Features

Complete cerebral vascular angiography (including the bilateral ICA, the external carotid artery, and the vertebral

artery) was performed for every patient to confirm the exact location of the fistula, drainage veins, compensatory blood supply, and other vascular disorders. Detailed angiographic features of each case are listed in Table 1. Compressing test (injection from the contralateral carotid or one vertebral artery while manually compressing the ipsilateral carotid artery) was performed if the main site of the fistula could not be confirmed due to large fistulous ostium. In this case series, there were 6 fistulas located on the left ICA and 12 on the right. Drainage veins—including the superior ophthalmic vein (SOV), the superior petrosal sinus (SPS), the inferior petrosal sinus (IPS), the cortex vein (CV), the contralateral CS (CCS), and the facial vein (FV)—were shown on angiograms. ICA dissection was observed in two cases of spontaneous direct CCFs.

### Endovascular Procedure

All endovascular procedures were performed with the patient under general anesthesia by way of standard transfemoral approach. After complete cerebral vascular angiography, a 6F guiding catheter (Envoy; Cordis, Miami Lakes, FL, USA) was positioned in the ascending petrous portion of the ICA. A Hyperglide balloon (ev3 Neurovascular), 4 mm in diameter and 20 mm in length, was navigated into the ICA at the main site of fistula; a microcatheter (Echelon-10; ev3 Neurovascular) was superselected into the CS through the fistula. For cases with unsuccessful transarterial approach (i.e., previous embolization of coils), audacious navigation lead to the migration of previous embolic agents. This is dangerous and will increase the risk of embolic events. We preset a microcatheter into the CS by way of transvenous approach (jugular vein–IPS) at the proximal origin of the ophthalmic vein and the CV in the CS for coiling or Onyx injection to avoid difficulty in navigation through coil mass by way of a transarterial approach (patient no. 17, Fig. 1). Detachable coils (Hydrogel-coated and/or bare; Microvention, Aliso Viejo, CA, USA) were deployed into the CS at the main site of fistula and near drainage venous outlets for partial embolization and as framework of subsequent Onyx embolization. Therefore, it was not necessary to densely pack the CS from front to back with coils. If necessary, the balloon was inflated to prevent coil herniation into the ICA. With the significant flow reduction of arteriovenous shunt after precoiling, Onyx injection could then be started. Before Onyx embolization, angiography from the guiding catheter in the ICA and/or microcatheter in the CS was performed to confirm occlusion of the fistula and protection of the balloon. Onyx-18 or -34 was injected under real-time road-mapping with the inflated balloon occluding the fistula. According to the unique features of Onyx solidification, Onyx 34 solidifies faster than Onyx 18. This decreases

**Table 1** Clinical data and outcomes of endovascular treatment with Onyx and coils in 18 patients with direct CCFs

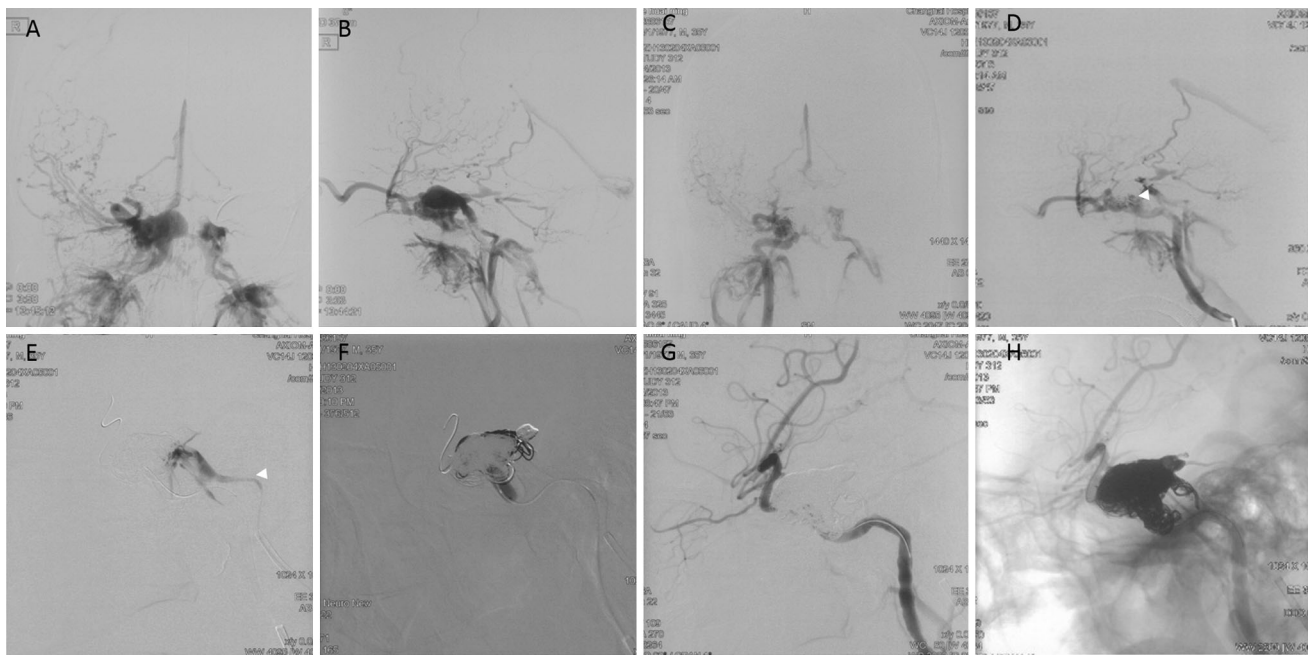
Patient no./age (year)/sex	Clinical presentation	Fistula position/drainage veins	Coil type/length (cm)	Onyx volume (ml)	Angiographic obliteration	Outcome	Follow-up (mo)
1/25/M	DVA, PB	L/SOV, CCS	Bare/152	3	Yes	Total visual loss <sup>a</sup>	3
2/46/F	DVA, PB, proptosis, chemosis, ophthalmoplegia	R/SOV, FV, CV	Bare/128	3	Small residual fistula with spontaneous cure	Cure	3
3/42/F	Proptosis, chemosis	R/SOV, FV, SPS, IPS, CCS	Bare/60	2.4	Yes	Cure	3
4/53/F	DAV, PB, ophthalmoplegia	R/SOV, SPS, CV, CCS	Bare/134	2	Small residual fistula with spontaneous cure	CN III palsy <sup>b</sup>	2/8
5/43/M	DVA, PB	R/SOV, IPS, CV, CCS	Bare/34, Hydro/92	3.3	Yes	Cure	3
6/28/M	Proptosis, PB	R/SOV, CV	Bare/55, Hydro/86	5	Yes	Cure	3
7/24/M	Epistaxis	L/SOV, CV, IPS	Bare/60, Hydro/125	2	Yes	Cure	3
8/32/F	PB	L/CCS, IPS	Bare/96	3.5	Yes	Cure	2
9/50/M	DVA, ophthalmoplegia	L/SOV, CCS	Bare/63, Hydro/28	0.3	Yes	CN III palsy <sup>b</sup>	2
10/49/M	DVA, PB, ophthalmoplegia	R/SOV, FV, SPS, IPS, CV	Bare/189	3	Yes	Cure	6
11/42/M	Proptosis, chemosis, PB	L/CV, IPS, CCS	Bare/76	2.5	Yes	Cure	8
12/22/M	DVA, chemosis, epistaxis	R/SOV, SPS	Bare/16	3	Yes	Cure	1
13/24/M	DVA, chemosis	R/SOV, CV	Bare/90	3.2	Yes	Cure	1
14/62/M	Chemosis, ophthalmoplegia	R/CV	Bare/20, Hydro/45	1.2	Yes	Cure	3
15/30/M	PB, seizure	R/SOV, CV	Bare/229	1.6	Yes	Cure	3
16/53/M	Proptosis, chemosis, seizure	L/IPS	Bare/80	1.3	Yes	Cure	3
17/38/M	PB, proptosis, chemosis	R/SOV, IPS, CCS	Bare/284	5	Yes	Cure <sup>c</sup>	1
18/17/M	PB, proptosis, chemosis, ophthalmoplegia	R/SOV, SPS, IPS, CCS	Bare/70	1.8	Yes	Cure <sup>c</sup>	1

DVA deterioration of visual acuity (indicates any level of visual loss, blurred vision, diplopia), PB pulsatile bruit, SOV superior ophthalmic vein, SPS superior petrosal sinus, /PS inferior petrosal sinus, CV cortex vein, CCS contralateral cavernous sinus, FV facial vein

<sup>a</sup> Total visual loss on admission

<sup>b</sup> CN III palsy on admission

<sup>c</sup> By clinical follow-up, there were no symptoms related to recurrent fistula



**Fig. 1** Patient no. 17 with failed coil embolization on admission (A through D white arrow shows coils from the previous embolization procedure). Transarterial and transvenous approaches were applied

(E, F white arrow indicates microcatheter in the CS). Post-procedure angiography shows complete occlusion of the fistula (G), and nonsubtraction angiogram shows the Onyx and coils (H)

the risk of migration when there is higher blood flow and also decreases balloon occlusion time. When Onyx injection started, we withdrew the microcatheter slowly and paid attention to the cast direction. It is important to preserve the normal drainage of the Sylvian vein and the SOV. To prevent Onyx from casting into any of those veins, we injected Onyx in the coil mass. Precoiling mass can trap the Onyx within it and thus decrease the risk of dangerous embolization of venous drainage. Onyx injection was held for  $\geq 30$  s to solidify the Onyx in the CS if it was about to exceed the coil mass or flow toward drainage venous outlets. Total angiographic obliteration was the perfect end point of embolization. Small residual shunt with the microcatheter slipping into the ICA, or with unassured or unsafe Onyx casting in the CS after a long time-hold, was another end point of embolization. In this case, short-time follow up was planned due to incomplete occlusion. All patients had 5- to 7-day postoperative observation and discharge assessment, including neurological deficits assessment, performed by the neurologist (Y. Z.) from the Neuroscience Center in our hospital.

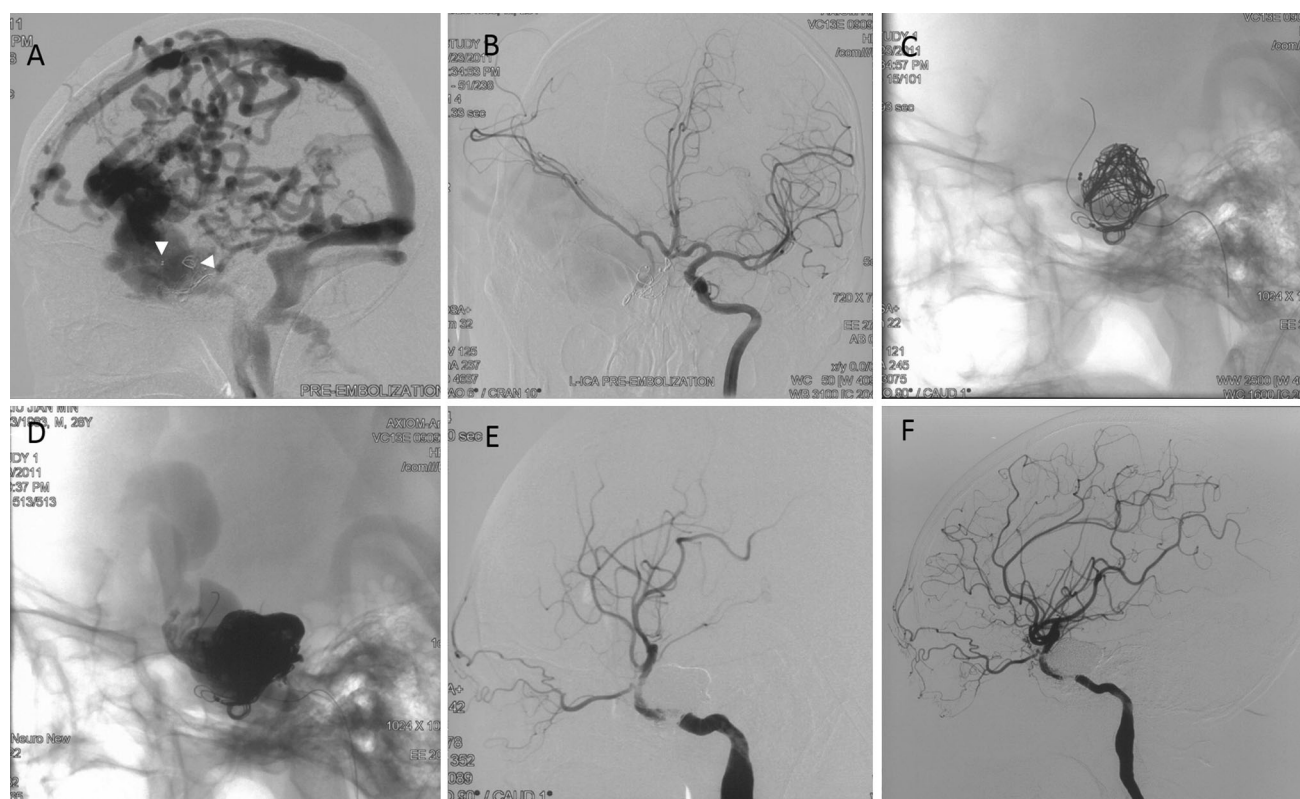
## Results

Angiographic results and follow-up findings are listed in Table 1. Immediate angiography after embolization showed total occlusions in 16 patients and small residual

fistulas in two patients. Good preservation of the ICA was observed in all cases. The average volume of Onyx was 2.6 ml, and the average length of bare coils was 102.0 cm. Hydrogel-coated coils, with an average length of 75.2 cm, were used in 5 cases. One patient had already had total visual loss before admission, and complete resolutions of ocular and orbital symptoms, pulsatile bruit, and epistaxis were observed in this case series, including the two patients with small residual fistulas. Six patients had ophthalmoplegia due to cranial nerve dysfunction, and this symptom resolved totally in four patients before discharge. Symptoms related to CN III palsy seemed irreversible in the other two patients. Angiographic follow-up was recorded for 16 patients at an average of 3.4 months. For the two patients with small residual fistulas, both received short-time angiographic follow-up within 3 months after the procedure. All follow-up angiograms showed no residual or recurrent fistula. Clinical follow-up within 1 month after discharge of the other two recent patients showed no relapsing symptoms. There were no procedure-related complications, and no new symptoms developed in any patient.

## Discussion

The goal in curing direct CCFs is to occlude the abnormal arteriovenous communication between the ICA and the CS



**Fig. 2** Patient no. 6 with embolization with a detachable balloon and coils 4 years previously (**A** white arrow shows the deflated balloon and migrated coils). Left ICA injection shows compensatory blood flow through the anterior communicating artery and abnormal shape

of the right middle cerebral artery (**B**). Coils and Onyx were used for embolization (**C**, **D**) in this case. Post-procedure angiography (**E**) and 3-month angiographic follow-up both show complete occlusion of fistula (**F**)

to decrease venous hypertension and improve cerebral perfusion. Currently, endovascular embolization is the first-line treatment for direct CCFs, and a number of embolic agents are available [12, 13]. The approaches and embolic agents for treatment are chosen differently from case to case depending on the specific anatomy of the fistula and operator preference. Because a larger fistulous ostium and greater flow rate in direct CCFs make microcatheter more easily navigated into the CS from the ICA, a transarterial approach may be superior to a transvenous approach. Due to forced removal of the detachable balloon for CCF embolization in United States during 2003 due to technical problems [13]—such as early detachment, deflation, and ruptured by bone fragments [14]—metallic coils have become the mainstay of endovascular embolization (patient no. 6, Fig. 2). Several reports exist about transarterial coils embolization for direct CCFs [15, 16]. However, theoretically, coils are not the ideal embolic materials for large fistulas and a dilated CS, which are common in direct CCFs. To completely occlude the fistula, dense packing in the CS is necessary, which might lead to cranial nerve palsy by coil mass compression. Retreatment might be required in some cases for recurrent or residual fistula due

to difficulties in dense packing [15]. Coil mass protruding into the parent artery through a large fistulous ostium is another potential disadvantage because it increases the risk of ICA occlusion. Stent-assisted technique seems to provide a solution; however, anticoagulation and/or antiplatelet therapy during the perioperative period may be counteractive to thrombus generation around the fistula and thus decrease the cure rate [17]. In addition, the huge expense of this procedure is hardly affordable.

We reported a series case of traumatic CCFs treated with solely Onyx [18]. It is an effective and economic option, but it is not universally applicable. A nondetachable balloon is used to prevent Onyx from leaking into arterial circulation. However, if the fistulous ostium is large enough, patients with imperfect circle of Willis might have a transient ischemic attack or acute infarction, the so-called “steal phenomenon” [19]. Long-term balloon occlusion within ICA during Onyx injection might make the hypoperfusion status worse and result in acute infarction. In addition, in some cases, inadequate apposition of the protective balloon to the arterial wall, due to compensatory dilation of the ICA as well as the extreme tortuous cavernous segment, makes it difficult to completely occlude

the fistula with the balloon, even if the balloon is highly conformable.

In the above-mentioned circumstances, precoiling before Onyx injection is an alternative option. Since the first embolization using Onyx and coils for direct CCFs reported by Baccin et al. in 2005 [10], this technique has been used for endovascular treatment of direct CCFs. Onyx, a liquid embolic mixture, casts in the coil mass adequately and solidifies when dimethyl sulphoxide (DMSO) solvent diffuses away in the blood. With this unique feature, the solidified Onyx and coils combine together in the form of a “reinforced concrete structure”, which then prevents the migration of coils and Onyx when deflating the protective balloon in the ICA. Precoiling before Onyx injection can decrease the dose and injection time of Onyx. In other words, precoiling decreased the ICA occlusion time, thus decreasing the risk of ischemic complications. The coil mass in the CS also slows down the blood flow rate and prevents Onyx from casting freely. It provides a “nest boundary” for Onyx. It is helpful to ensure proper position of the microcatheter tip as well as ensure that it is safe to inject Onyx within the coil mass to better preserve the ICA.

With the use of Onyx, coils become the framework, and dense packing is no longer necessary. This decreases the risk of cranial nerve palsy and the cost of the procedure. The key point to resolve the cranial nerve dysfunction due to CCFs is to remove the compression to the related cranial nerves (CN). For CCFs, this compression mainly comes from venous hypertension caused by large abnormal ICA-CS shunt. Compression is removed once the shunt is occluded. The fewer embolic agents we used in the CS, the lower risk of CN palsies occurring. In addition, we mainly focused on occluding the fistula site, not the entire CS. Also, direct CCFs are different from indirect ones. Ocular symptoms or CN palsy might take place in a few days after fistula formation. Development involves rapid progress, and most patients are treated urgently. This makes rapid regression of CN deficits possible. In addition, neurotropic and physical therapy after the procedure might promote recovery. However, for cases of CN damage symptoms lasting >2 weeks, such as patients nos. 4 and 9, CN palsies seem to be irreversible.

In direct CCFs, the fistula allows blood flow to enter the CS rapidly, thus leading to surged pressure in the CS and abnormal dilation in the SOV and CV and causing reverse flow in these veins. These abnormalities are thought to be responsible for ocular–orbital symptoms and intracranial hemorrhage [12]. The most concerning potential risk using liquid embolic agents during the procedure is mis-embolization of the drainage veins after abnormal reverse flow [18, 20, 21]. Before embolization, coils can slow down the flow rate and prevent Onyx from casting into drainage veins. Compared with the adhesive *N*-butyl-cyanoacrylate

(*N*-BCA), another liquid embolic agent widely used in brain arteriovenous malformation and dual arteriovenous fistula embolization [20, 22], the nonadhesive and solidification features of Onyx permits a long-time controllable injection and no microcatheter retention. Moreover, *N*-BCA always stays in a liquid state during injection and migrates into drainage veins more easily with blood flow [20], whereas Onyx solidifies in a coil mass.

Small residual fistulas can be tolerated if it is extremely difficult to achieve total occlusion for a fistula with this technique. For example, when we tried to adjust the tip of the microcatheter for better casting, the microcatheter slipped out of the CS at the end of Onyx injection due to the large fistula and could never be re-navigated back into the CS. In addition, during a long hold of Onyx injection, the casting direction of the Onyx may become undesirable and even dangerous in the CS, e.g., casting toward drainage veins. If the residual fistula is small (>95 % of the fistula has been occluded), we can end the procedure. The use of two types of embolic agents, i.e., Onyx and coils, greatly improves the capacity of thrombosis and slow down the flow rate of residual shunt around the fistula in the CS. Therefore, the possibility of spontaneous cure increases. There were two patients with small residual fistulas shown on post-procedure angiography; however, both patients had relief of their symptoms after procedure. Spontaneous cure and complete occlusion were shown at short-term angiographic follow-up for these two patients (nos. 2 and 4).

The use of an inflated balloon within the ICA during the procedure can serve as an important protection from solid or liquid embolic agents flowing into the ICA. Complete occlusion of the fistula should be confirmed by carotid and/or intra-CS injection angiograms. In contrast, the inflated balloon can assist to identify the location of the fistula by serial microangiography runs with temporary carotid occlusion [11]. Furthermore, during the precoiling process, the inflated balloon could prevent the protrusion of coils in parent artery with the balloon-remodeling technique. Although some physicians are concerned about the potential thromboembolic risk of using a balloon for temporary protective ICA occlusion, there were no embolic complications or new symptom related to nondetachable balloon in this case series. Emphatically, we should pay more attention when completing the injection and deflating the balloon. Because of the unique solidification feature, liquid Onyx might be flushed away if we deflate the balloon too quickly. Slow deflation will ensure a complete solidification of the Onyx by slowly diffusing DMSO away with the blood flow.

Above all, there is no absolute theoretical contraindication to this technique for treating direct CCFs. However, we should pay more attention during the procedure in the following circumstances:

- In cases of *compensatory dilation of the ICA* (diameter >5 mm) and *extreme tortuous cavernous segment*, carotid and intra-CS injection angiograms are helpful to confirm the protection of nondetachable balloon before Onyx injection. Onyx injection should be monitored intensely to prevent its leakage into the ICA.
- In cases of *multiple fistulas* in traumatic CCFs, the inflated balloon can assist to identify the location of the fistula by serial microangiography runs with temporary carotid occlusion.
- In patients with *incomplete circle of Willis*, most with direct CCFs have “steal phenomenon” of varying degree. Usually, patients can tolerate temporary ICA occlusion well. In this case series, there was no patient with intolerance of balloon occlusion. If necessary, a balloon occlusion test can be performed before procedure.

This is a preliminary summarization of endovascular embolization using Onyx and coils. More cases and results of longer follow-up are still needed for the evaluation of the efficacy and safety of this technique. The technique of embolization using Onyx and coils under intra-arterial balloon protection is feasible for direct CCFs, especially for patients with a large fistula ostium and large CS. It is an effective and safe option with rare complications.

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