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# Flow diversion for indirect carotid-cavernous fistula: Still an off-label indication?

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## ABSTRACT

**Background:** Flow diversion (FD) is an established treatment for large or giant wide-necked unruptured intracranial aneurysms. In the past few years, the use of flow diverter devices was extended to several other "off-label" indications, including solitary or adjunctive treatment to coil embolization for direct (Barrow A type) carotid cavernous fistulas (CCFs). The use of liquid embolic agents still represents the first-line treatment for indirect CCFs. Typically, the ipsilateral inferior petrosal sinus or superior ophthalmic vein (SOV) is the preferred transvenous routes to access CCFs. In some cases, vessel tortuosity or different features make the endovascular access challenging, thus requiring different approaches and strategies. The aim of the study is to discuss rational and technical aspect in treating indirect CCFs referring to the most up-to-date literature. An alternative experience-based endovascular strategy with FD is described.

**Methods:** We report the case of a 54-year-old woman diagnosed with indirect CCF and treated with flow diverter stent.

**Results:** After multiple unsuccessful attempts at transarterial right SOV catheterization, a right indirect CCF fed by a single trunk at the ophthalmic origin from the internal carotid artery (ICA) was treated by ICA stand-alone FD. Blood flow was redirect and successfully reduced through the fistula, with immediately postprocedure improvement of the patient's clinical status (ipsilateral proptosis and chemosis). Ten-months radiological follow-up showed the complete obliteration of the fistula. No adjunctive endovascular treatment was performed.

**Conclusion:** FD appears a reasonable alternative stand-alone endovascular strategy also for selected difficult-to-access indirect CCFs, when all conventional routes are judged unfeasible. Further investigations will be necessary to better define and support this potential lesson-learned application.

**Keywords:** Barrow B type fistulas, Carotid cavernous fistula, Endovascular treatment, Flow diversion, Indirect carotid cavernous fistula (Indirect CCF)

## INTRODUCTION

Flow-diversion is rapidly demonstrating its versatility in neurovascular procedures and its indication is progressively extending along with their technological advancements, sometimes outpacing the availability of reliable clinical evidence. The implant of flow diverter devices

(FDD) was approved for treating unruptured intracranial aneurysms in different topography.[5] Other indications are suggested by routine clinical practice and challenges. In some cases, the use of FDD was extended to certain off-label therapeutic approaches, ahead of long-term outcome data or regulatory approval, and markedly emphasizes a wheeling learning curve in the endovascular community. Among them, the treatment of carotid-cavernous fistulas (CCFs), mainly those classified as Barrow A-type or direct CCFs, is appealed when other typical therapeutic approaches have failed.[5] Off-label indications have been further extended to indirect CCFs taking into account the low-flow hemodynamic pattern, the complex anatomy of the vessels implicated, and the consequent challenging goal of fistula obliteration. The current experience of flow-diversion for the treatment of symptomatic indirect CCFs is based on very few cases, and there are no outcomes to reliably support the clinical decision-making. The appropriateness needs to be weighed case-by-case, considering experience and relative risks against standard approaches. In this paper, we present our experience in treating a patient with an indirect Barrow B-type CCF with flow-diversion through transarterial ipsilateral internal carotid artery (ICA) route along with related technical aspects and our decision-making algorithm.

## CASE DESCRIPTION

We report the case of a 54-year-old woman complaining progressively right proptosis, chemosis, conjunctival hyperemia, and intense eye pain [Figure 1] for a few days. No history of trauma was referred as well as no pathologies in her medical history, and no continue medications. A brain computed tomography (CT)-angiography (CTA) documented a significantly dilated vascular connection between inferolateral part of the cavernous internal carotid artery (ICA) and superior ophthalmic vein (SOV) suspected for a CCF; in Figures 2a, a brain CT shows significantly dilated right SOV and right exophthalmos, compared to the left side. A selective digital subtraction angiography (DSA) through a right femoral artery access with Vertebral 5F × 100 cm catheter confirmed the presence of a right indirect (Barrow B-type) CCF between the right ICA and the ipsilateral SOV, fed by a single arterial trunk coming from the inferolateral part of the cavernous ICA and draining into the ipsilateral SOV, associated with multiple congested facial and maxillary veins [Figures 2b-d]. After a multidisciplinary board consensus, we proceeded with endovascular treatment.

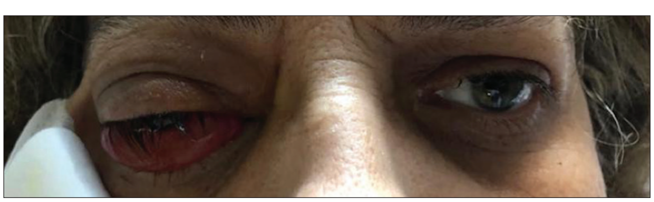

**Figure 1:** The patient consented to publication of her images. She complained progressively worsening of proptosis, chemosis, conjunctival hyperemia, and intense pain of her right eye, and diplopia.

### Description of the endovascular procedure

The first goal of the treatment was to reach the fistulous site through a transarterial route to occlude its distal (venous) part with coils delivery. Under general anesthesia, a selective cerebral digital subtraction angiography (DSA) was performed through a retrograde right transfemoral arterial access, catheterization of the right ICA, and microcatheterization of the right SOV through the fistulous site (long introducer 6F × 80 cm, guide catheter 5.6F × 132 cm, microcatheter 1,7F × 150 cm, microguides 0.014” × 205 cm, 0.08” × 220 cm). Several attempts of a selective microcatheterization of the SOV failed in multiple sessions. Because of the tortuosity of the fistulous feeder and distal stenosis of the fistulous site, it was no possible to introduce the microcatheter to reach the venous compartment. Then, a transvenous route through the ipsilateral inferior petrosal

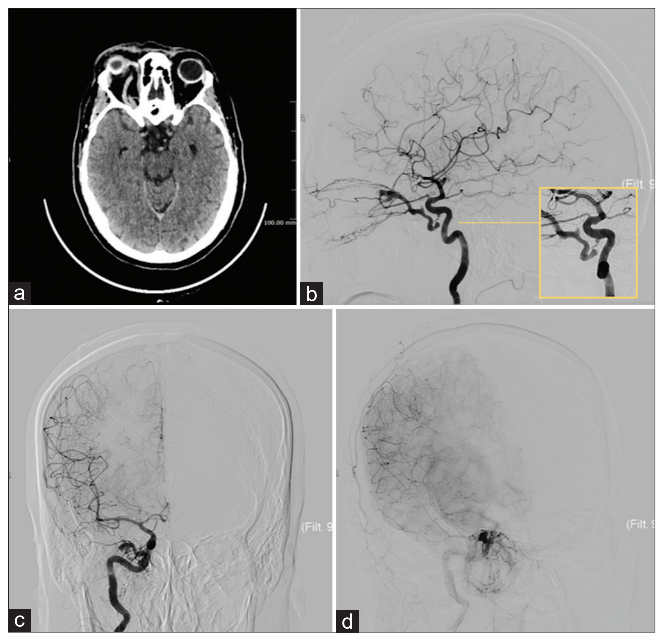


**Figure 2:** In (a) preoperative brain computed tomography scan shows significantly dilated right superior ophthalmic vein (SOV) and right exophthalmos, compared to the left side. Angiographic captures (lateral projection in [b], posterior-anterior projection in [c], and oblique projection in (d) show a right indirect carotid cavernous fistula (Barrow type “B”). In the yellow box in (b) the enlargement of the fistula documents the fistulous site filled by a single arterial trunk coming from the inferolateral part of the intracavernous right internal carotid artery and draining into the ipsilateral SOV, conditioning clinical congestion of the right eye, and multiple congested facial and maxillary veins. It should be noted intense SOV opacification during arterial pass of iodate contrast medium.

sinus (IPS) was considered, but the irregular appearance and partial thrombosis of the right IPS made no possible a venous catheterization. On the other and, a direct cannulation of the ipsilateral SOV was considered as a major invasive procedure with potential severe complications especially for oculomotor nerve function. After a second multidisciplinary board discussion, the alternative choice was to place a flow diverter stent to cover the segment of the ICA where the fistulous site arises. The rationale for an off-label flow diverter positioning is that flow forces may change becoming turbulent through the fistula, thus favoring a progressive process of thrombosis. Before the stent placement, a manual occlusion test of the left common carotid artery revealed a good compensation with no significant hemodynamic alterations in the anterior circulation. Under general anesthesia through retrograde right transfemoral arterial access, and selected microcatheterization of the right ICA (long introducer 6F × 80 cm, guide catheter 5.6F × 132 cm, microcatheter 2,9F × 150 cm, microguides 0.014" × 205 cm), the fistulous site was reaching. The flow-diverter stent (Derivo©) was correctly opened demonstrating a subsequent angiographic elimination of the CCF with preserved patency of ICA and ophthalmic artery [Figure 3a]. No complications were observed during the postoperative CT-scan. In Figure 3b, a sagittal bone-window head CT scan shows a view of the implanted stent. During the postoperative period, a gradual improvement in ipsilateral eye congestion and diplopia was observed [Figure 4]. The patient was under dual antiplatelet therapy for 3 months (aspirin and clopidogrel) followed by continue aspirin intake. At 10$^{th}$-month follow-up, magnetic resonance angiography showed the complete obliteration of the fistula [Figures 5a and 5b] with good neurological outcomes.

## DISCUSSION

The use of flow diverter stents is rapidly spreading as safe and effective treatment for intracranial aneurysms with different morphology and topography, showing a high rate of aneurysms obliteration over time and a reasonably low incidence of complications.[5] The rationale for flow diversion (FD) for aneurysms treatment is that it alters the hemodynamic forces reducing the sac inflow and redirects the physiological blood flow along the natural axes of the parent vessels. This usually causes intra-aneurysmal thrombosis while maintaining the patency of the parent vessels. As long-term effect, a neointima occurs along the latex of the device, increasingly embedding its wires into the remodeled vessel wall with complete isolation of the aneurysm from the intracranial circulation.[15] Relatively few studies reporting long-term outcomes of FD technique are available, but prototypes suggestions and implementations are evolving rapidly.[11] As a result, the use of these stents has been extended to some off-label indications in clinical practice, ahead of sparse clinical evidence, or long-term outcome data or regulatory approval.[5] Clinical evidences on CCFs are based mostly on case reports and empiric considerations. CCFs are abnormal connections between the ICA and cavernous sinus that causes blood flow shunt from ICA to the venous system, either directly (Type A CCFs) through an arterial cracking or less frequently indirectly (Type B, C, and D CCFs) with multiple fistulous sites in the dural wall of the cavernous sinus. It is supposed that fistulous shunts can occur spontaneously or as a result of trauma, but proofs of the exact mechanism are still missing. Sometimes, they were reported to develop spontaneously in elderly people and women.[6,22] Proptosis, chemosis, diplopia, ophthalmoplegia, and headache are typical symptoms of

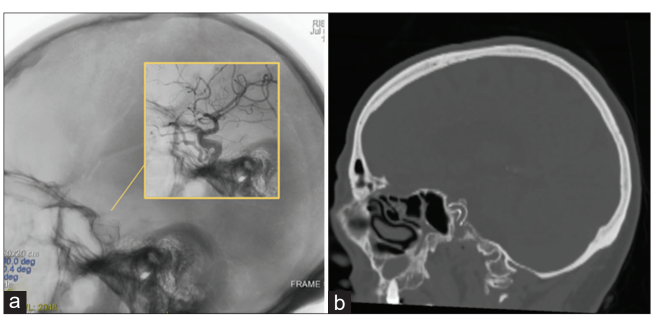


**Figure 3:** Intraoperative angiographic capture in lateral projection (a) shows the correct flow-diverter stent placement (Derivo©) within the right internal carotid artery (ICA), and subsequently angiographic elimination of the fistulous link and preserved patency of the vessels (ICA, ophthalmic artery) without complications (enlarged in the yellow box). In (b) sagittal bone-window head computed tomography scan a view of the implanted stent.

**Figure 4:** The patient consented to publication of her images. She complained progressively worsening of proptosis, chemosis, conjunctival hyperemia, and intense pain of her right eye, and diplopia: 10-month clinical follow-up is shown.

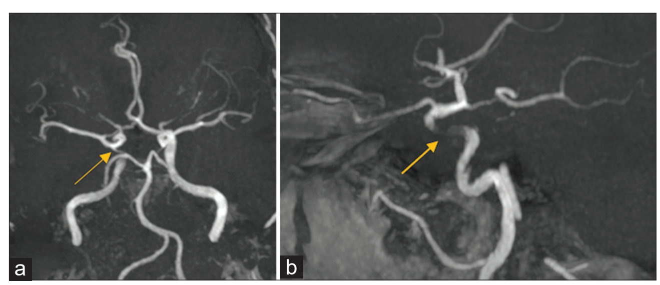


**Figure 5:** Intraoperative angiographic capture in lateral projection 10-months magnetic resonance angiography follow-up in (a and b) show normal preserved patency of the Circle of Willis' vessels, the lack of signal in the right ICA (yellow arrow in a and b) as an indirect sign of the flow-diverter stent placement, and the fistula line closed and entirely excluded.

acute presentation of direct high-flow CCFs usually due to ruptured intracavernous aneurysms causing direct passage of high-pressure arterial blood into the cavernous sinus and ophthalmic vein, and consequent venous hypertension. In case of indirect CCFs, the symptoms are usually milder because of slower blood flow into the minor vessels, and they depend on the fistula drainage into the superior and/or inferior ophthalmic veins or superior and/or IPSs;[6,19,22] symptomatic Barrow Type B CCFs are the least frequently represented among the three indirect CCF types. The goal of the treatment should be the occlusion of the fistula site or at least the reduction to minimum of the residual arterial blood flow into the venous system while preserving the patency of ICA and its arterial branches.[18,19] Therapeutic approaches for CCFs followed the same transition through technological development. Historically, traditional maneuvers included manual compression of the CCA and jugular vein, and external ocular compression of the angular vein with or without carotid compression, with a rate of complete occlusion around 30%.[4,7,9] This changed dramatically with the advent of endovascular treatment, which actually represents the first line treatment. Both transvenous and transarterial embolization are potential access routes to reach the fistulous site and deliver detachable balloons, coils, and liquid embolic agents.[4,8,11,17] Moreover, a combined approach using flow diverters with or without adjunct embolizing materials could be considered.[18] Usually, the transarterial approach is used, although in patients with tortuous or arteriosclerotic arteries reaching the fistula site may be extremely challenging; the risk of major complications such as migration of embolic agents into the cerebral circulation should not be forgotten.[4,8] On the other hand, transvenous approaches were proved to be a viable option with low risk and 90% of success rate, together with higher obliteration rate.[4,8] The transvenous approach through the IPS was the first established route and is still the most commonly used,[4,21] even when partially or completely thrombosed.[3,4] For a considerable proportion of the patients, the IPS cannot be catheterized because of complex architecture or lack of communication between the IPS and the fistula site.[4,10] In these cases, other transvenous routes can be considered, like the anterior approach through a facial vein or SOV. Some cases of blind direct cannulation of the SOV along with its potential complications[1,4] and direct surgical exposure of the SOV with anterior orbitotomy were described in the past.[4,16] The placement of a flow diverter in the ICA was previously described for the treatment of direct CCFs – or Barrow A-type – as un uncommon option only in some case reports.[2,4,12-14] Wendl *et al.* described 14 patients where complete occlusion was documented only in 21%, but a significant flow reduction occurred in the remaining cases.[20] However, 71% of patients were free from ocular symptoms at follow-up. A recent review of the literature reported 89.4% of patients having clinical improvement and long-term occlusion rate of 100%.[18] A postoperative residual flow could be expected and could be considered acceptable in these cases, and outcome considerations should be done on medium-long range, whereas a latency period can be explained as the time necessary for stent endothelization.[18] In fact, flow diverters are designed with specific properties and their composition enables to preserve side arterial branches from occlusion.[18] The time required for achieving a fistula occlusion represents a disadvantage in preventing a rapid symptoms improvement after treatment. As regards to indirect fistulas, Castaño *et al.* reported two cases of Barrow B-type of CCFs successfully treated with flow diverter stent in the left ICA in both cases.[4] In our case of Barrow B-type CCF, we faced many technical difficulties to reaching the fistula site. Thus, after numerous attempts to reach the target for embolization, we changed our therapeutic goal in reducing flow through the fistula by positioning a flow diverter stent in the ICA. An aspect we considered is that Barrow B-type are low flow fistulas and, in these cases, a clinical improvement may be achieved even without obtaining its complete closure. Since all the other roads were not viable, we considered it appropriate the off-label use of a flow diverter. Furthermore, for low-flow type CFFs as Barrow B-type, a long-term obliteration cannot be excluded from the study.

## CONCLUSION

Although further studies are needed to verify its effectiveness and safety, nowadays, a possible role of flow diverters implant should be taken in mind as a last choice also for indirect Barrow B type CC fistulas.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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