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Corresponding Author:	Shu Wan Zhejiang University Hangzhou, CHINA
Corresponding Author's Institution:	Zhejiang University
Corresponding Author E-Mail:	wanshu@zju.edu.cn
Order of Authors:	Shu Wan
	Jun Gu
	Weijian Fan
	Min Yan
	Ming Wang
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TITLE:

Transvenous Embolization of Carotid Cavernous Fistula through Inferior Petrosal Sinus with Detachable Coils and Ethylene Vinyl Alcohol Copolymer

AUTHORS & AFFILIATIONS:

Jun Gu[1*], Min Yan[1*], Weijian Fan[1], Wenchao Liu[1], Ming Wang[1], Shu Wan[2]

[1]Department of Neurosurgery, 1st affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, P.R. China

[2]Brain Center, Zhejiang Hospital, Hangzhou 310030, P.R. China

*These authors contributed equally to this work

Email Address of Corresponding Author

Shu Wan (wanshu@zju.edu.cn)

Email Addresses of Co-Authors:

Jun Gu (gujun66@163.com)

Min Yan (passerym@163.com)

Weijian Fan (fwj0111@aliyun.com)

Wenchao Liu (wenchao0729@126.com)

Ming Wang (wangminghz@yeah.net)

KEYWORDS:

Carotid cavernous fistula, Endovascular, Inferior petrosal sinus, Transvenous, Embolization, Cavernous sinus

SHORT ABSTRACT:

The purpose of the article is to present our experience in endovascular treatment via the inferior petrosal sinus of the carotid cavernous fistula with detachable coils and ethylene-vinyl alcohol copolymer.

LONG ABSTRACT:

Carotid cavernous fistula (CCF) is a rare disease caused by abnormal communications between the internal carotid artery (direct fistula) or meningeal branches of the external carotid artery (indirect fistula) and the cavernous sinus (CS). Trauma is the most common cause of CCF. The clinical presentation of CCF is closely related to the venous drainage pattern. Orbital and neuro-ophthalmological symptoms are the most common clinical presentation of CCF with drainage through the superior ophthalmic vein (SOV). Endovascular embolization by arterial or venous approaches is the most common management of CCF. Transvenous embolization using detachable coils and ethylene-vinyl alcohol copolymer (EVOH) is an alternative method for the treatment of CCF. Endovascular embolization offers different options to treat CCF by minimally invasive approach decreasing morbidity and residual fistulas. The purpose of this article is to report our treatment experiences via the inferior petrosal sinus (IPS), and immediate-term

outcomes of endovascular embolization of CCF by using detachable coils and EVOH.

INTRODUCTION:

Carotid cavernous fistula (CCF) is defined as abnormal arteriovenous communications between the internal carotid artery or meningeal branches of the external carotid artery and the cavernous sinus[1]. CCF can be classified based on the etiology (traumatic or spontaneous), flow rate (high or low flow), or the angiographic composition (direct or indirect)[1,2]. The clinical presentation of CCF is closely related to the venous drainage pattern: orbital and neuro-ophthalmological symptoms associated with drainage via the SOV, whereas neurological symptoms or intracranial hemorrhage related to leptomeningeal drainage[3,4].

The main treatment for CCF includes observation, intermittent manual compression of the common carotid artery (CCA), stereotactic radiosurgery and endovascular embolization[2,3]. Ethylene vinyl alcohol copolymer (EVOH) is a non-adhesive liquid embolic material that was firstly evaluated at UCLA Medical Center between January 1998 and May 1999[5]. The treatment has changed with the development of the transvenous approach in association with detachable coils and EVOH. CCF is treated by endovascular techniques evolved from unimodality (transarterial detachable balloon occlusion) to multimodality (transarterial/intravenous coils, detachable balloon, liquid embolic agents, endovascular stent, etc)[5,6,7]. Recently, transvenous endovascular embolization has become a standard treatment for CCF because of its feasibility and safety[3,6,7]. There are several venous approaches based on the type of venous drainage. If the CCF has a mainly posterior venous drainage, through the inferior petrosal sinus (IPS), this route is the simplest and shortest in most patients. Even if it cannot be shown on angiographical images or it is thrombosed, catheters can still be guided into the CS through it.

We report successful endovascular treatment of 7 CCF patients using detachable coils and EVOH via the inferior petrosal sinus. The technical details are described in this protocol. The final decision to treat with a transarterial or transvenous approach was made after the analysis of the clinical images, and angiographic findings in each case. Based on our prior experience of treating CCF procedures by transarterial or transvenous approaches, we have found that endovascular embolization via the inferior petrosal sinus is a very good option with good outcomes, also safer and more effective than that via arterial access[3,6].

PROTOCOL:

The protocol has been approved by the local medical and ethics committees. All patients provided written informed consent.

1. Preoperative Preparation

1.1. Ensure the patients are diagnosed with CCF: All patients undergo digital subtraction angiography (DSA), routine bilateral internal and external carotid angiography, vertebral arteriography for assessment of feeding arteries, sizes, venous drainage patterns of CCFs, and carotid artery compression test with three-dimensional rotational angiographic capability.

1.2. Ensure all the procedures are executed under general anesthesia.

2. Vascular catheterization

2.1. Catheter and sheath preparation

2.1.1. Prepare a 5F vascular sheath and a 6F vascular sheath, a 100-cm length of 4F H1 catheter and a 90-cm length of 6F or 5F guiding catheter, two 150-cm length of microcatheters with the inner diameter of 0.017'.

2.1.2. Prepare a 150-cm guidewire with the diameter of 0.035' and a 200-cm length of microwire with the diameter of 0.014'.

2.2. Confirm the pulse of the femoral artery below the middle segment of the inguinal ligament, which is the site of puncture.

2.3. Puncture the left femoral artery via percutaneous approach and put a 5F vascular sheath into it with modified Seldinger technique. Position a 4F H1 catheter into the common carotid artery related to the CCF through the sheath with continuous heparinized saline solution (1000 U heparin diluted per 500 mL) perfusion for angiography during the procedure.

2.4. Puncture the right femoral vein via percutaneous approach and put a 6F vascular sheath into it with modified Seldinger technique. Position a 6F or 5F guiding catheter through the sheath with continuous heparinized saline solution (1000 U heparin diluted per 500 mL) perfusion in the internal jugular vein nearby the IPS.

2.5. Confirm the IPS by delayed arterial roadmap with three-dimensional rotational angiographic capability. The IPS is a main draining vein of CS, which flows into the internal jugular vein.

2.6. Coaxially navigate two microcatheters with a microwire into the CS through the IPS progressively step by step under the road mapping, and then gently inject the contrast medium (2 mL at 150 pounds per square inch) with the high-pressure injector from the microcatheter (selective venography) to confirm the position.

2.6.1. To do this, position one microcatheter into the proximal side of the superior ophthalmic vein (SOV) through the IPS and another into the middle capacity of the CS.

2.6.2. In cases of occluded IPS, use another stiffer microwire to pass through the sinus. Inject 2000 U heparin after the femoral artery puncture.

3. Embolization of CCF with detachable coils and EVOH

3.1. Detach several coils into the proximal SOV and the anterior position of the CS through the microcatheters. However, identify the residual fistulas on the control angiogram after coil detachment. Place the tips of the microcatheters among the detached coils.

3.2. Flush the microcatheter with 10 mL normal saline, followed by 0.25 mL dimethyl sulfoxide (DMSO) to fill the microcatheter dead space. Slowly inject 0.25 mL EVOH by hand into the dead space of the microcatheter and then start the embolization with the persistent injection of EVOH. The procedure is shown on angiography.

NOTE: The EVOH is initially injected into the coil mesh and proximal position of the SOV. It penetrates the anterior compartment followed by the posterior compartment of the CS through two microcatheters with manually persistent injection.

3.3. Ensure preserving the blood flow of the ICA by digital subtraction angiography.

4. Estimation of treatment

4.1. Immediately perform angiography after the procedure to check for the occlusion of the CCF[6,7].

NOTE: The immediate angiographic result is defined as complete disappearance, minor residual fistula, and significant residual fistula[6,7].

5. Postoperative Care

5.1. Let the patient recover from general anesthesia.

5.2. Check the patient on the following days for any discomfort, and for the improvement of symptoms in the hospital.

5.3. Follow up the patients admitted to hospital accordingly for the digital subtraction angiography at 3-month, 1-year and 2-year after treatment to confirm further improvement or recurrence.

REPRESENTATIVE RESULTS:

In our study, all 7 patients underwent angiographic evaluation and successful endovascular embolization. All patients presented with more than one symptom, conjunctival congestion and chemosis were the most common symptoms. No patient presented with seizures or hemorrhagic/ischemic stroke.

Table 1 describes clinical and angiographic baseline characteristics with the technique of transvenous embolization. A transvenous approach via the IPS was successful in 7 patients.

For endovascular embolization, we put the two microcatheters into the CS through inferior petrosal sinuses. For the embolic materials used for treatment, coiling by venous approaches was firstly indicated. Then EVOH was injected through the microcatheter into the residual capacity of

CS (**Figure 1**). Finally, angiographic complete occlusion was achieved.

FIGURE AND TABLE LEGENDS:

Figure 1: Digital subtraction angiography of CCF embolization. (A) and (B) Digital subtraction angiography (DSA) of CCF, frontal and lateral view, the black arrow shows fistula and cavernous sinus. (C) Selective DSA of the cavernous sinus through the microcatheter to confirm the site of the microcatheter, lateral view. (D) DSA of common carotid arteries, lateral view, showing the image after embolization with coils, lateral view. (E) X-rays showing the final cast of coils and Onyx, lateral view. (F) the final image of complete occlusion of CCF, lateral view.

Table 1: Summary of information in 7 patients by the transvenous approach via IPS. The CCF patients including 4 females and 3 males were all successfully treated by the transvenous approach.

DISCUSSION:

Recently, endovascular treatment has become the most common therapy for CCFs. Successful treatment of CCFs is to occlude the abnormal shunts between the ICA or meningeal branches of the external carotid artery and the CS while keeping the ICA unobstructed. The treatment can be achieved with transarterial or transvenous approach to obliterate the affected side CS with coils or other embolic materials. Some patients with direct CCFs can be cured with the deployment of a covered stent across the fistula through ICA. The disadvantage of the covered stent is its stiffness making it difficult to navigate into the distal segment of ICA, particularly in those patients with tortuous ICAs[7,8]. A Flow Diverter has also been used for the treatment of direct carotid-cavernous sinus fistulas, but it constitutes a new challenge and needs long term follow-up[9,10].

Now the most common transvenous route is via the inferior petrosal sinus. The critical step is to identify the IPS and navigate the microcatheters into the CS through the IPS. However, sometimes this route is not available (either due to anatomic variation or thrombosis). If one tries to get through the IPS, complications may occur, especially bleeding. The treatment can be completed via other venous routes such as the superior ophthalmic vein (SOV), the vein of Labbe[11,12].

Coils can be delivered into the CS through the microcatheter into the CS via the IPS, leading to fistula occlusion. However, the disadvantages of mere coils are that they are very expensive in our country and because the cavernous sinus often contains multiple septae, the residual fistula may occur. Furthermore, in CCFs with large CS, lots of coils are needed and space occupying effect of coils lead to difficulty in evaluating the patency of the nearby parent artery[6,14].

The physical properties of mechanical occlusion but non-adherent to the vessel wall of EVOH are excellent to fill minor fistulous spaces in CCFs. The treatment of a CCF case with EVOH was reported by Arat et al. in Turkey, where EVOH has been approved for clinical use since 1999[7,15].

We report successful transvenous treatment of seven CCF patients using detachable coils and

EVOH, three males and four females with a mean age of 48.6 years old admitted into the Department of Neurosurgery, 1st Affiliated Hospital of Zhejiang University between 2014 and 2017. The details are shown in **Table 1**.

The final decision to treat with a trans-arterial or transvenous approach was made after analysis of the clinical, images, and angiographic findings in each case. All patients underwent digital subtraction angiography (DSA), routine bilateral internal and external carotid angiography, vertebral arteriography for assessment of feeding arteries, sizes, venous drainage patterns of CCFs, and carotid artery compression test, and all the procedures were executed under general anesthesia.

Two microcatheters were navigated coaxially into the CS because of the large capacity of CS. One microcatheter was put into the proximal position of the SOV, and the other into the center of the CS, which could make the coils well-distributed.

Results of our study suggest that angiographic and clinical outcomes of endovascular embolization by the transvenous approach remain relatively effective at midterm follow-up, but more cases and long-term follow-up for at least 2 years are needed. Fortunately, there are no complications during our procedures. But complications are reported in some articles, for example, cranial nerve palsy, ICA dissection, blurred vision and so on, and the overall procedure-related complication rate was 10.6%, with a permanent complication rate of 3.5%[2,6,16].

This study presents the technique of endovascular treatment of CCFs by the transvenous approach through IPS, illuminating the feasibility and safety of the approach.

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DISCLOSURES:
The authors have nothing to disclose.

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Figure 1: Digital Subtraction Angiography of CCF embolization

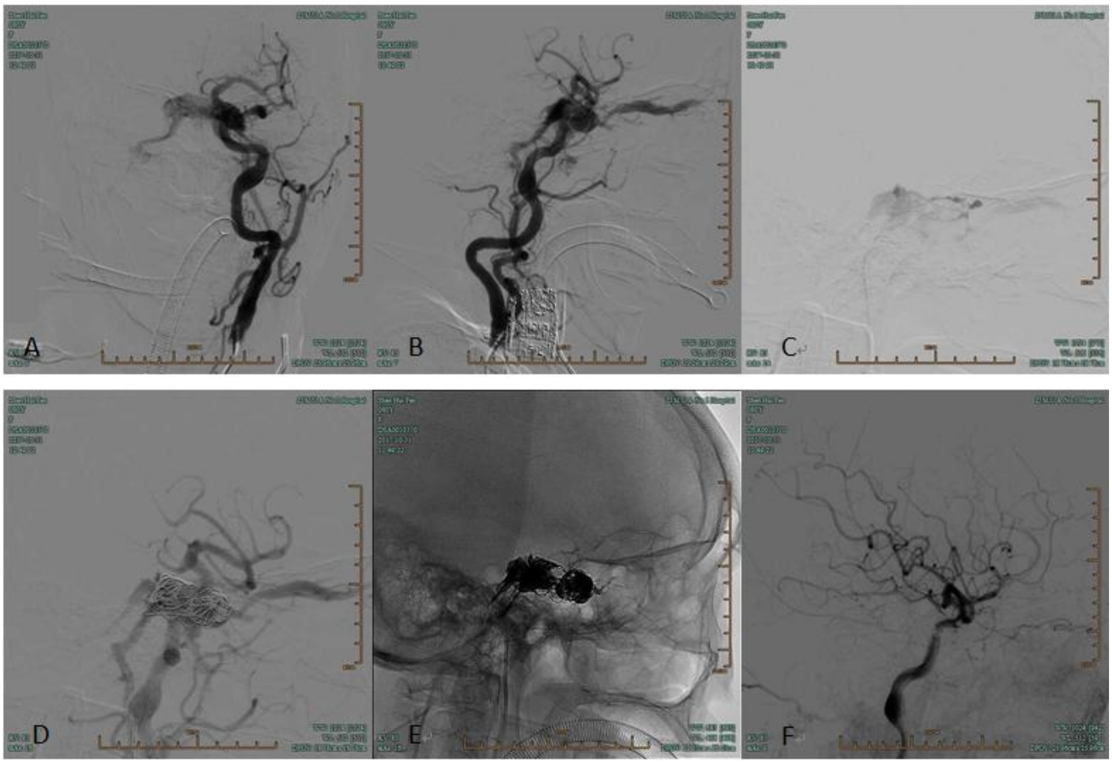

Table 1

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Table 1 Summary of information in patients by transvenou:

No.	Age(y)	Sex	Signs and Symptoms	Arteries	Veins
1	62	F	Lt. eye redness and chemosis, tinnitus	ICA/MMA	Opht /IPS
2	80	F	Lt. eye redness and chemosis	ICA/MMA	Opht /IPS
3	35	F	Lt. eye redness and chemosis	ICA	Opht /IPS
4	43	F	Lt. eye redness and chemosis, tinnitus	ICA	Opht /IPS
5	29	M	Rt. eye redness and chemosis, tinnitus	ICA	Opht /IPS
6	45	M	Lt. eye redness and chemosis	ICA	Opht /IPS
7	36	M	Rt. eye redness and chemosis	ICA/MMA	Opht /IPS

F: female; ICA: internal carotid artery; IPS: inferior petrosal sinus; Lt: left; M: male; MN
to inf): ophthalmic vein (superior to Inferior); Rt: right.

s approach	
Complications	Outcome
–	complete occlusion
–	complete occlusion
–	complete occlusion
–	complete occlusion
–	complete occlusion
–	complete occlusion
–	complete occlusion

MA: middle meningeal artery; Opht (s

Name of Material/ Equipment	Company	Comments/Description
EV3 coil	Medtronic, Irvine, California, USA	material for endovascular treatment
MicroPlex coil	MicroVention, California, USA	material for endovascular treatment
EVOH	Medtronic, Irvine, California, USA	material for endovascular treatment
Echelon/microcatheter	Medtronic, Irvine, California, USA	interventional material
Envoy/guiding catheter	Johnson & Johnson Company,USA	interventional material
vascular sheath	Terumo Corporation, Tokyo, Japan	interventional material

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CORRESPONDING AUTHOR:

Name: Wan Chu

Department: Department of Neurosurgery

Institution: the first affiliated Hospital of Zhejiang University

Article Title: Transvenous embolization of carotid cavernous fistula with detachable coils and ethylene vinyl alcohol copolymer

Signature: Wan Chu

Date: 2018. 9. 25

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Dear Professor:

The manuscript is revised in accordance with the referee's suggestions in the comments as follows:

Reviewer #1:

Major Concerns:

While the authors' description of transvenous embolization being the primary treatment of choice for embolization of CCFs, this statement needs qualification. First, the treatment approaches varies between direct and indirect CCFs. This can dramatically affect the way to treat these lesions. It can also affect how necessary curative obliteration is. Additionally, EVOH embolization can be quite dangerous and should be reserved for only those cases in which it is truly needed. As such, further clarification of why this was pursued should be described. The first reference cited (Meyers et al) has recently been expanded on (pmid 30418600). The complications found with EVOH and other liquid embolics in this manuscript should be addressed in this proposed paper. Specifically, when and why should EVOH be used? The vast majority of cases can be cured with coils alone.

Response:

CCFs can be classified into direct and indirected. Direct CCFs were usually treated in our department with detachable balloons in the past from a transarterial approach. But the detachable balloons were failed to obtain Food and Drug Administration approval and withdrew from the USA market in 2003. In our country, we also can not use detachable balloons now. For approximately 30 years transvenous approch has been considered the most common technique for indirect CCFs. Sometimes, microcatheter can not be put into the proper position in cavernous sinus for treatment of direct CCFs from a transarterial approach, and liquids may reflux into ICA. So we also try to treat direct CCFs using detachable coils and EVOH by the transvenous approach. Additionally, the disadvantages of coils alone are that they are very expensive and residual fistula may occur because of insufficient filling of the fistula and CS. Furthermore, in CCFs with large CS, lots of coils are needed and space occupying effect of coils lead to difficulty in evaluating the patency of the nearby parent artery. EVOH can penetrate into the entire dural fistula site and block blood flow. Our study presented the technique of endovascular treatment of CCFs by the transvenous approach, illuminating the feasibility and safety of the approach.

Please write to us if the manuscript has any problems. Thank you for your consideration.

Dear Professor:

The manuscript is revised in accordance with the referee's suggestions in the comments as follows:

Reviewer #2

Major Concerns:

You say you had no complications, but you should discuss a little bit more about the potential complications of the method proposed.

Minor Concerns:

You say that in your series 1 patient underwent the facial vein route, but the patient is not shown in the table1.

Response:

I added some contents about complications in the discussion

The table1 just shows the venous drainage patterns of CCFs, not the venous approaches. I deleted the data about the patient underwent the facial vein route later, because I just wanted to describe the venous approach via IPS.

Please write to us if the manuscript has any problems. Thank you for your consideration.

Dear Professor:

The manuscript is revised in accordance with the referee's suggestions in the comments as follows:

Reviewer #3

Manuscript Summary:

Line 89: "dimethylsfloxide (DMSO)" : mistyping.

Line 91: "proximal position of the SOV": need to define 'proximal' or distal of a vein.

Line 151: the statement "..were detached after no shunt..." is not understandable.

Major Concerns:

Why do you use 02 microcatheters at the same time for embolization? Please explain in discussion.

Response:

"dimethylsfloxide (DMSO)": I modified this in revision.

"proximal position of the SOV": the position that the SOV communicated with CS.

"..were detached after no shunt...": I deleted some contents about detached balloon to simplify the manuscript .

Two microcatheters were navigated coaxially into the CS, which could make the coils well-distributed. I mentioned in discussion in revision.

Please write to us if the manuscript has any problems. Thank you for your consideration.