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ORIGINAL ARTICLE

Onyx as an adjunctive embolic material for transvenous embolization of cavernous sinus dural arteriovenous fistula after coiling

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Abstract

Background: Transvenous coil embolization (TVCE) is a common and effective treatment for cavernous sinus dural arteriovenous fistulas (CSDAVFs). However, some patients may experience residual fistulas or worsening visual symptoms after the procedure. This study aimed to compare the effectiveness of transvenous coil and Onyx embolization (TVCOE) with TVCE in treating CSDAVFs.

Methods: The study included 207 patients with 222 CSDAVFs referred for TVCE, all of whom had complete angiographic follow-up over 9 years. Ninety patients (mean age, 65.3 years) with 97 CSDAVFs underwent TVCOE after coiling. Clinical data, angioarchitecture, and outcomes were retrospectively assessed and compared to 125 CSDAVFs treated with TVCE.

Results: Key reasons for selecting TVCOE included improvement in immediate complete obliteration of CSDAVFs (n = 47, 48.5%), presence of cranial nerve palsy (n = 26, 26.8%), residual fistula with persistent pial venous reflux (n = 22, 22.7%), and redirection of fistula flow to pial venous reflux (n = 2, 2.1%). The average volume of Onyx used in TVCOE was 1.7 mL per CSDAVF. The mean coil lengths for TVCOE and TVCE were 143 and 228 cm, respectively, with a statistically significant difference ($p < 0.05$). Immediate digital subtraction angiography showed complete obliteration or nearly complete obliteration of CSDAVFs in TVCOE and TVCE at rates of 97.9% and 76.8%, respectively, indicating statistical significance in immediate complete obliteration ($p < 0.05$). Transient hemodynamic instability occurred in 81 (90.0%) patients due to Onyx toxicity, and one patient (1.1%) experienced hemorrhagic complications during TVCOE.

Conclusion: The use of a small volume of Onyx as an adjunctive embolic material in TVCOE resulted in reduced coil use and improved immediate complete obliteration. This technique is viable for patients with pial venous reflux. Aside from the transient hemodynamic instability, periprocedural complications and follow-up angiographic outcomes did not show significant differences between the two groups.

Keywords: Cavernous sinus dural arteriovenous fistula; Embolization; Onyx; Transvenous coil embolization; Treatment outcomes

1. INTRODUCTION

Cavernous sinus dural arteriovenous fistulas (CSDAVFs) are abnormal connections between arteries and veins within the cavernous sinus, supplied by dural branches of the internal and/or external carotid arteries. Most CSDAVFs are low-flow shunts that exhibit antegrade flow to the inferior petrosal sinus (IPS) and retrograde flow to the ophthalmic vein. These fistulas typically manifest with benign orbital or cavernous symptoms.[1,2] However, some CSDAVFs with restricted or inadequate venous drainage may exhibit pial venous reflux (PVR), which poses risks for cerebral symptoms and neurologic deficits.[3,4] Transvenous coil embolization (TVCE) is a standard treatment with encouraging angiographic cure rates of 80% to 90%.[5–9] A potential drawback of coiling CSDAVFs is the risk of worsening or causing new cavernous symptoms, including third and/or sixth cranial nerve palsy (CNP).[5,6] In some cases with multiple dural feeders and relatively high-flow fistulas, coils may not achieve complete obliteration (CO) of the CSDAVF.[5,9]

This study reports our experiences in using nonadhesive liquid materials to address residual CSDAVFs after coiling and compares the angioarchitecture and treatment outcomes with those of CSDAVFs treated solely by TVCE.

2. METHODS

2.1. Patients

A total of 207 patients with 222 CSDAVFs were referred for transvenous embolization (TVE) between July 2013 and June 2022, all with more than 6 months of clinical and angiographic follow-up. This study was approved by the Institutional Review Board before its initiation. Patient symptoms were identified

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through chart reviews and classified into categories: orbital symptoms (eg, chemosis, exophthalmos), cavernous symptoms (eg, ptosis, diplopia), ocular symptoms (eg, glaucoma), and cerebral symptoms indicative of stroke or neurological deficits.[7] From this cohort, 90 (43.5%) patients with 97 (43.7%) CSDAVFs underwent transvenous coil and Onyx embolization (TVCOE) due to residual CSDAVF following TVCE. The ages of these patients ranged from 45 to 84 years, with a mean age of 65.3 years. They were referred for TVE due to CSDAVF-related symptoms, including orbital (n = 71, 78.9%), cavernous (n = 51, 56.7%), ocular (n = 37, 41.1%), and/or cerebral symptoms (n = 15, 16.7%).

2.2. Angioarchitecture analysis

Digital subtraction angiographies (DSAs) of the bilateral carotid and vertebral arteries were conducted on the same day as the embolization and used for angioarchitecture analysis. The classifications by Barrow et al[10] and Suh et al[11] were applied. Two senior neuro-interventionists independently evaluated the clinical manifestations and angioarchitecture, including the patterns of dural feeders, venous drainage, patency of the IPS, and angiographic types. Any discrepancies between their evaluations were discussed until consensus was achieved.

2.3. Endovascular treatment

The trans-IPS approach is the primary method for TVE, even in cases where the IPS is occluded. In 19 patients with occlusive IPS draining exclusively to the superior ophthalmic veins, transfacial venous access was utilized. Two Onyx-compatible microcatheters (MC, Headway 17; Microvention, Austin, CA) were navigated into the cavernous sinus (CS) and/or proximal ophthalmic vein when access was feasible, allowing for better packing and subsequent TVCOE. If navigating to the fistula site was challenging, one MC was positioned at that location. A bolus of 3000 units of heparin and a continuous infusion of 1000 units per hour were administered intravenously after diagnostic DSA to maintain the bleeding time at 1.5 to 2 times the baseline. TVE commenced from the TVCE at fistula sites with risky angioarchitecture (eg, PVR). TVCOE was selected for residual fistulas to improve the CO of CSDAVFs (n = 47, 48.5%, Fig. 1), particularly in patients presenting with cavernous symptoms of CNP (n = 26, 26.8%, Fig. 1), residual flow with persistent PVR (n = 22, 22.7%, Fig. 2), or redirection of the residual fistula to PVR (n = 2, 2.1%, Fig. 3). TVCOE was initiated in CSDAVF using a single MC, as continued coiling could lead to the MC recoiling from the fistula site. Onyx-34 (Medtronic, Irvine, CA) was selected to obliterate the residual fistula. Hand-injection DSA of the MC was performed to evaluate the angioarchitecture of the residual CSDAVF before TVCOE. The tip of the MC was positioned optimally for the subsequent TVCOE as needed. A protective balloon (Scepter XC, Microvention, Austin, CA) was inflated at the origins of the dural feeders of the internal carotid arteries (ICAs) in 80 (82.5%) CSDAVFs classified as Barrow's type B and D to prevent Onyx from refluxing from the CS to the ICA through the dural feeders. DSA was intermittently used to assess the treatment outcome every 5 minutes during balloon deflation. The procedure's endpoint was defined as achieving angiographic CO or nearly CO of the CSDAVFs or the expectation of spontaneous thrombosis in small residual fistulas as seen in the controlled DSA.

The patient's vital signs, including blood pressure and heart rate, were monitored during the periprocedural period. Hemodynamic instability associated with TVCOE or TVCE was defined as an elevation or reduction in blood pressure of 30 mmHg and/or a change in heart rate of 20 beats/min from baseline before the initiation of TVCOE. The mean coil length and volume of Onyx used per CSDAVF were recorded. Demographic data, clinical manifestations, angioarchitecture, and outcomes of TVCE were analyzed in 117 patients with 125 CSDAVFs treated solely by TVCE and compared with 90 patients with 97 CSDAVFs who underwent TVCOE.

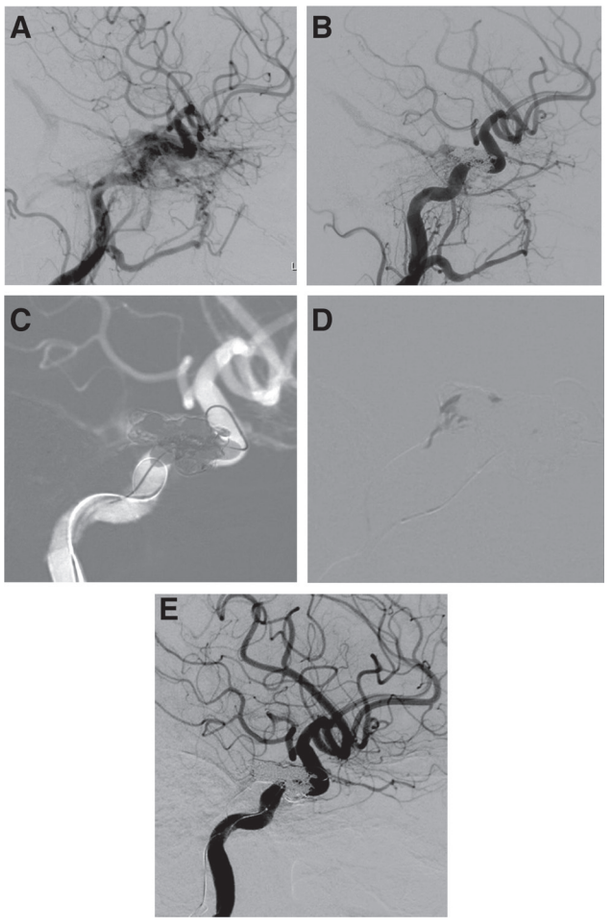

Fig. 1 A 55-y-old female patient presented with cavernous symptoms due to a Barrow type D and proliferative-type left CSDAVFs. A, Left lateral carotid DSA showed a left CSDAVF draining into the superior petrosal sinus. B, The patient underwent TVCE, but a residual fistula persisted. C–E, Balloon-assisted TVCOE (2.1 mL of Onyx) was performed on the residual fistula. C, Balloon inflation in the cavernous segment of the ICA before Onyx embolization. D, Onyx embolization during balloon inflation. E, Postembolization DSA of the left lateral carotid demonstrated CO of the CSDAVF. CO = complete obliteration; CSDAVF = cavernous sinus dural arteriovenous fistula; DSA = digital subtraction angiography; ICA = internal carotid artery; TVCE = transvenous coil embolization; TVCOE = transvenous coil and onyx embolization.

2.4. Treatment outcome evaluation

CO or nearly CO was defined as the complete disappearance or minimal residual fistula observed on immediate postembolization and follow-up DSA. All enrolled patients underwent clinical and DSA follow-up for over 6 months. A complication was defined as any newly developed neurologic deficit post-TVE, confirmed by computed tomography or magnetic resonance imaging (MRI). CNP was defined as the worsening or new onset of CNP after the initial treatment.

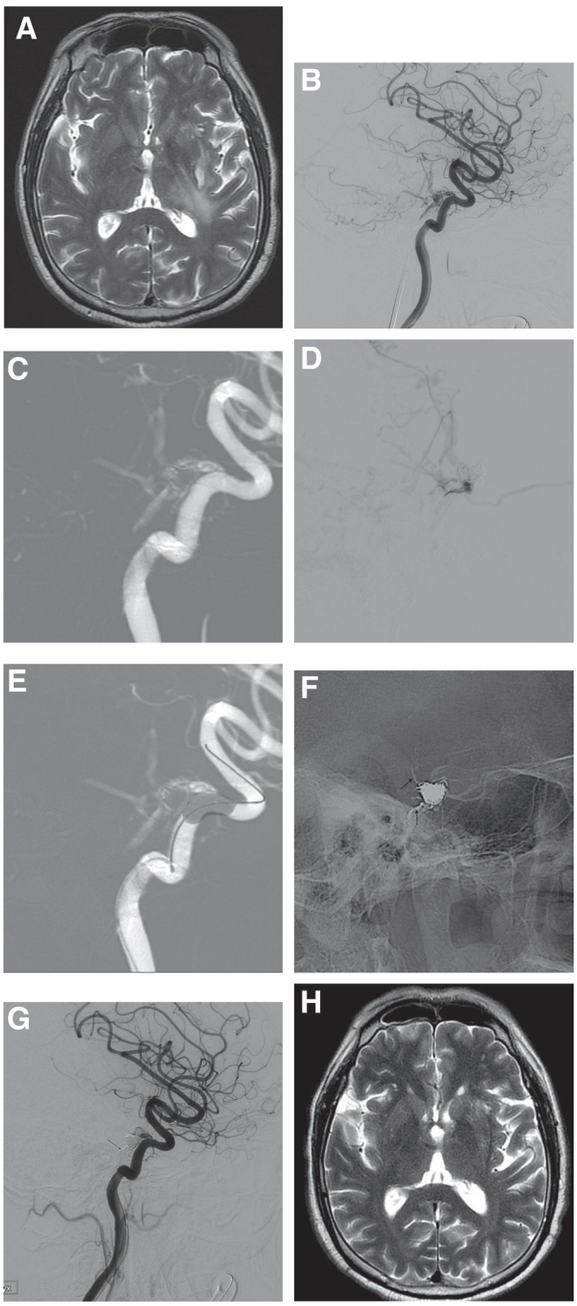

Fig. 2 A 62-y-old male patient presented with cerebral and cavernous symptoms due to left CSDAVFs. A, Axial T2 MRI showed edema in the left basal ganglia and thalamus. B, Left lateral carotid DSA revealed Barrow type B and late restrictive CSDAVFs with occlusive IPS and PVR. C and D, The patient underwent TVCE via the occlusive IPS, resulting in partial fistula occlusion with persistent PVR. E–G, He then received balloon-assisted TVCOE for the residual fistula. E, Balloon inflation in the cavernous segment of the ICA before Onyx embolization. F, Onyx embolization, with Onyx casts retained at the fistula and proximal venous drains. G, Postembolization DSA of the left lateral carotid demonstrated nearly CO of the CSDAVFs. H, MRI performed 4 wk after embolization revealed total regression of brain edema. CO = complete obliteration; CSDAVF = cavernous sinus dural arteriovenous fistula; DSA = digital subtraction angiography; ICA = internal carotid artery; IPS = inferior petrosal sinus; MRI = magnetic resonance imaging; PVR = pial venous reflux; TVCE = transvenous coil embolization; TVCOE = transvenous coil and onyx embolization.

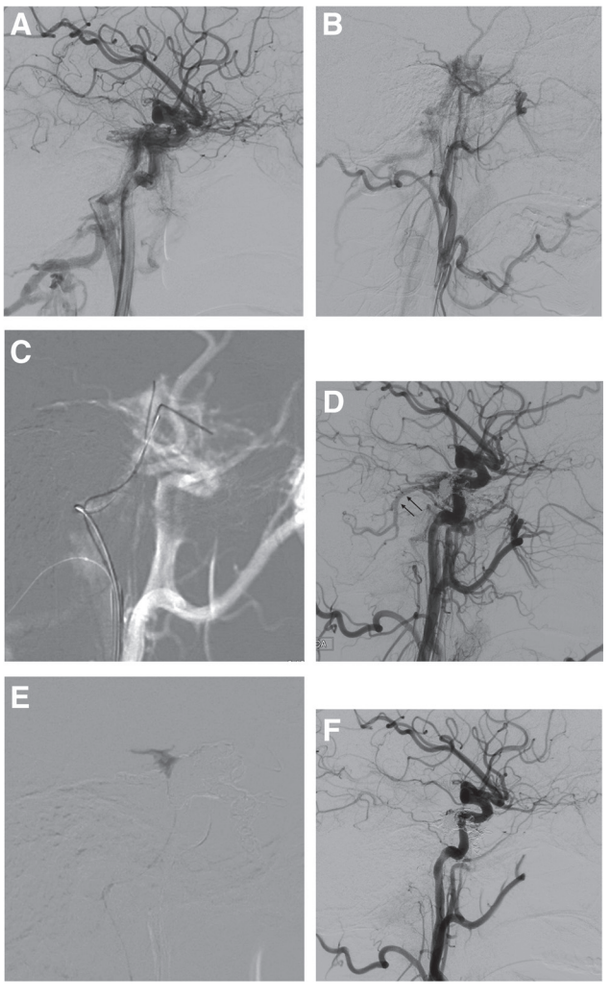

Fig. 3 A 46-y-old female patient presented with orbital and ocular symptoms due to left CSDAVFs of proliferative/Barrow type D. A and B, Lateral carotid DSA. A, The left lateral ICA DSA demonstrated CSDAVFs. B, The left lateral external carotid artery DSA also demonstrated CSDAVFs without fistula reflux to the cerebellar veins. C and D, The patient underwent TVCE via IPS. C, Two MCs were navigated to the CS. D, Coiling of the left CSDAVF redirected the fistula flow to the cerebellar veins (arrows). E and F, The patient then underwent TVCOE. E, Onyx embolization was performed for the residual fistula. F, The left lateral carotid DSA after Onyx embolization demonstrated nearly CO of the CSDAVFs. CO = complete obliteration; CS = cavernous sinus; CSDAVF = cavernous sinus dural arteriovenous fistula; DSA = digital subtraction angiography; ICA = internal carotid artery; IPS = inferior petrosal sinus, MC = microcatheter; TVCE = transvenous coil embolization; TVCOE = transvenous coil and onyx embolization.

2.5. Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences for Windows (version 20; IBM-SPSS, Chicago, IL). Results are presented as means and counts (percentages) for categorical and continuous variables, respectively. Chi-square tests were used to analyze gender, various symptoms, IPS occlusion, PVR, and both immediate and final treatment outcomes. Kendall's tau was utilized to assess Barrow and Suh classifications, while independent *t* tests were employed to compare the ages of patients undergoing TVCOE and TVCE. Cox regression analysis was conducted as needed to identify the CO/nearly CO rates in relation to treatment options, symptoms, Suh's classification, PVR, and the embolization agent. Final CO rates were compared using a χ^2 test. Statistical significance was set at a p value of <0.05.

Table 1

Demography, angioarchitecture, and outcomes of 90 of 97 and 117 of 125 patients/CSDAVFs treated by TVCOE and TVCE

CSDAVF	TVCOE (n = 97)	TVCE (n = 125)	*p*
No of patient/CSDAVF	90/97	117/125	0.810
No of female patients (%)	63 (70.0%)	78 (66.7%)	0.610
No of male patient (%)	27 (30.0%)	39 (33.3%)	
Mean age (y)	65.3	64.5	0.936
Symptoms (patient)			
Orbital symptoms	71 (78.9%)	90 (76.9%)	0.843
Cavernous symptoms	51 (56.7%)	18 (15.4%)	<0.05*
Ocular symptoms	37 (41.1%)	39 (33.3%)	0.279
Cerebral symptoms	15 (16.7%)	12 (10.3%)	0.185
Angioarchitecture analysis (lesion)			
Barrow classification			0.804
Type B	9 (9.3%)	10 (8.0%)	0.736
Type C	17 (17.5%)	26 (20.8%)	0.540
Type D	71 (73.2%)	89 (71.2%)	0.742
Suh's classification			<0.05*
Proliferative type	45 (46.4%)	12 (9.6%)	<0.05*
Restrictive type	32 (33.0%)	69 (55.2%)	<0.05*
Late restrictive type	20 (20.6%)	44 (35.2%)	<0.05*
IPS occlusion	29 (29.9%)	58 (46.4%)	0.05*
PVR	38 (39.2%)	25 (20.0%)	<0.05*
Access and treatment outcomes (lesion)			
Multiple MCs	52 (53.6%)	56 (44.8%)	0.193
Mean coil length (cm)	143	228	<0.05*
Immediate CO or nearly CO	95/97 (97.9%)	96/125 (76.8%)	<0.05*
CO on follow-up	97/97 (100%)	119/125 (95.2%)	0.077
Peri-procedure complications (patient)			
New-onset or aggravating CNP	2 (2.2%)	10 (8.5%)	0.052
Transient hemodynamic instability	81 (90.0%)	3 (2.6%)	<0.05*
Hemorrhagic/ischemic complication	1 (1.1%)	1 (0.9%)	1.000

CNP = cranial nerve palsy; CO = complete obliteration; CSDAVF = cavernous sinus dural arteriovenous fistula; IPS = inferior petrous sinus; MC = microcatheter; PVR = pial venous reflux; TVCE = transvenous coil embolization; TVCOE = transvenous coil and onyx embolization.

*Statistically significant.

3. RESULTS

Table 1 presents the demographics, angioarchitecture, and outcomes of 90 patients with 97 CSDAVFs treated with TVCOE. Barrow type D was the most common, accounting for 71 cases (73.2%, Figs. 1 and 3), followed by type C with 17 cases (17.5%) and type B with 9 cases (9.3%). In Suh's classification, the proliferative type was the most prevalent (n = 45, 46.4%, Figs. 1 and 3), followed by the restrictive type (n = 32, 33.0%) and the late restrictive type (n = 20, 20.6%, Fig. 2). IPS occlusion was observed in 29 (29.9%, Fig. 2A) CSDAVFs. Aggressive CSDAVFs with PVR were identified in 38 (39.2%, Fig. 2) cases, of which 15 (16.7%) exhibited cerebral symptoms (Fig. 2). Two MCs were successfully navigated to the fistula site in 52 (53.6%, Fig. 3C) cases. The lengths of detachable coils used for TVCOE ranged from 43 to 218 cm, with a mean length of 143 cm. Balloon-assisted TVCOE was utilized in 80 (82.5%, Figs. 1 and 2) CSDAVFs with dural feeders originating from the ICA (Barrow types B and D). The volume of Onyx used for TVCOE ranged from 1.1 to 3.3 mL, averaging 1.7 mL. Transient hemodynamic instability was observed in 81 (90.0%) patients, predominantly manifesting as elevated blood pressure (n = 70, 86.4%), followed by bradycardia (n = 6, 7.4%), and both bradycardia and elevated blood pressure (n = 5, 6.2%). The rates of immediate and follow-up angiographic CO or nearly CO of CSDAVFs were 97.9% and 100%, respectively. New-onset (n = 1) and aggravated (n = 1) sixth CNP occurred in two (2.2%) CSDAVFs, both of which showed almost complete regression during the 6-month clinical follow-up. One patient experienced a postprocedural headache attributed to a small amount of subarachnoid hemorrhage, believed to be caused by injury to the dura from the guidewire/catheter system during manipulation. There were no other significant major complications in the remaining 87 patients, all of whom showed improvement in their orbital, cavernous, ocular, and/or cerebral symptoms; one patient with sixth CNP remained stable. No recurrent CSDAVFs were detected in any patients during angiographic follow-up, which ranged from 6 to 13 months (mean, 11 months).

Table 1 presents a comparison of the demographics, angioarchitecture, and outcomes between the TVCOE (n = 97) and TVCE (n = 125) groups. The mean age and percentage of male patients were similar in both groups. Cavernous symptoms (56.7% vs 15.4%, $p < 0.05$) and PVR (39.2% vs 20.0%, $p < 0.05$) were more prevalent in the TVCOE group, showing statistical significance. Angiographic IPS occlusion was more common in the TVCE group (29.9% vs 46.4%), with statistical significance ($p < 0.0$). The average coil length for TVCOE was 143 cm, compared with 228 cm for TVCE, which was statistically significant ($p < 0.05$). Immediate angiographic near CO or CO of CSDAVFs occurred more frequently in the TVCOE (97.9%) group than in TVCE (76.8%) group, also with statistical significance ($p < 0.05$). Follow-up angiographic CO of CSDAVFs was similar in both groups (100% vs 95.2%). Transient unstable vital signs were observed in 90.0% of patients undergoing TVCOE, while

three (2.60%) patients in the TVCE group experienced transient hemodynamic instability, which was thought to be due to coil mass stimulation of the dura in the CS, resulting in pain and elevated blood pressure. New-onset or aggravated CNP occurred in 2.2% of TVCOE patients, which was lower than the 8.5% seen in the TVCE group, although this difference was not statistically significant. Excluding transient hemodynamic instability, there was no statistically significant difference in periprocedural complications between the two groups.

4. DISCUSSION

TVCE using a detachable coil is a safe and effective approach for managing CSDAVFs in most patients. The main advantage of the detachable coil is its ease of control compared with other embolic materials, allowing for precise placement within the CS to occlude the fistula. However, limitations of TVCE include the difficulty of placing the coil at the ideal fistula site due to challenging anatomy and the inability to access certain locations with the MC, as well as the potential for residual fistula after coiling. Achieving immediate CO or near CO of CSDAVF may require dense packing at the fistula site with a larger coil mass, which can be time-consuming and costly.[5] Additionally, the coil mass can lead to new-onset or aggravated third and/or sixth CNP in some patients.[6] Intermittent DSA is necessary to prevent over-packing of the CS, which can exacerbate or complicate cavernous symptoms. Although TVCE with a single MC is the traditional treatment, if the MC is recoiled out of the CS with a residual fistula, it becomes difficult to re-enter the ideal site due to obstruction by the previously placed coil mass. The multi-MC technique offers the advantage of increasing packing density and enhancing the immediate CO of TVCE. In our series, we usually attempted to navigate multiple MCs within the CS. However, navigating additional MCs can be challenging and risky in certain complex fistula anatomies, especially in cases of angiographic IPS occlusion, where the irregular and narrow pathway may already be occupied by the first MC. We successfully navigated two MCs to the fistula site in 52 (53.6%) of the CSDAVFs in our series. This success rate for navigating two MCs in the CS was comparable to the 44.8% success rate observed in patients undergoing TVCE alone.

Onyx is a nonadhesive, radiopaque, and permanent liquid embolic material that offers advantages such as excellent penetration, easy delivery through a dimethyl sulfoxide (DMSO)-compatible MC, and rapid occlusion of fistulas. Furthermore, Onyx allows for slow, repeated injections with a reduced risk of the MC becoming stuck, compared to adhesive embolic materials. Several studies have reported promising angiographic and clinical outcomes from trans-arterial Onyx embolization of pial and dural arteriovenous malformations/fistulas.[12–18] TVCOE using Onyx in combination with coils has been documented in a few case reports or small series to enhance the CO of CSDAVFs.[19–21] This study included patients treated over a 9-year period. Onyx was introduced at our institute in 2015, and prior to that, only detachable coils were used for CSDAVF embolization. Since 2015, Onyx has been used as an adjunctive embolic material in certain challenging cases, as noted in the text. If the CSDAVFs are slow-flow fistulas and detachable coils can achieve CO, there is no need to use Onyx, as this could increase the risk of additional periprocedural complications. In this series, the volume of Onyx used for TVCOE ranged from 1.1 to 3.3 mL, with a mean of 1.7 mL. This amount is relatively small compared to what is typically used for embolizing cranial arteriovenous malformations. Instead of Onyx-18, we chose Onyx-34 for TVCOE due to its ability to penetrate distant venous drains, making long reflux unnecessary for the intended propagation, as seen in traditional trans-arterial Onyx embolization of pial or dural arteriovenous malformations. A nondetachable balloon was used at the site of the dural feeders from the ICA in 80 (82.5%) of the CSDAVFs in Barrow types B and D. This technique was used to protect the ICA during TVCOE. The primary advantage is that it prevents Onyx reflux from the CS to the dural feeders of the ICA, thereby reducing the risk of ischemic stroke. In addition, balloon inflation helps in contouring and localizing the ICA lumen during Onyx injection. Although there is a risk of thromboembolic stroke with this technique, none were observed in our series. This complication can be minimized through intravenous heparin administration and intermittent inflation/deflation of the balloon to restore ICA blood flow.

TVCOE was utilized in 47 (48.5%) cases of residual CSDAVFs after coiling to achieve CO or near CO, as spontaneous thrombosis of the residual fistula was unlikely. This technique is particularly beneficial for proliferative-type CSDAVFs that have multiple dural feeders and a relatively high-flow fistula. In such cases, the coil mass may not be sufficient to achieve immediate CO, even with dense packing.[5] Onyx can fill the residual spaces within the coil mass, thereby enhancing immediate CO or near CO of the CSDAVF. In our series, the selection of TVCOE was statistically significant for the proliferative type. This approach is particularly valuable and can serve as a viable procedure. Untreated partial fistula occlusion with persistent PVR (n = 22, 22.7%) or residual fistula flow redirected to PVR (n = 2, 2.1%) may lead to severe intracranial hemorrhage.

Cavernous symptoms, particularly involving sixth or third CNP, are common clinical manifestations that may occur in up to 72% of patients due to the hemodynamic effects of CSDAVFs on the cranial nerves within the CS.[5,6,22] Hemodynamic changes and normalization of the CS following TVCE can lead to improvements or resolution of CNP within a few months after the procedure.[23] However, the coil mass may exert pressure on CN6 and/or CN3, resulting in new or worsening CNP.[24] In our series, cavernous symptoms with CNP were observed in 51 (56.7%) of 90 patients with 97 CSDAVFs. We aimed to use TVCOE to minimize coil usage and reduce the risk of worsening CNP in 26 (26.8%) patients. The mean coil length for TVCOE was 143 cm, compared to 228 cm for TVCE, indicating statistical significance. New-onset or worsening CNP occurred in 2.2% of patients undergoing TVCOE, which is lower than the 8.5% seen with TVCE, likely due to reduced coil utilization, although this difference was not statistically significant.

DMSO may induce histopathological inflammation of target vessels during rapid injection in animal model. However, slow infusion into vascular structures has been shown not to have toxic effects on neural and arterial tissues, as demonstrated in numerous studies over the past 20 years. The primary concern regarding TVCOE for residual CSDAVFs in this series is the potential toxicity of Onyx to cranial nerves in the CS, particularly the DMSO component affecting the trigeminal nerve. This can trigger a vagal response and trigeminocardiac reflex, leading to bradycardia, which was noted in 44% of patients in previously published data on trans-arterial embolization. Another common transient adverse effect was the stimulation of the CS dura by Onyx, resulting in painful sensations and elevated blood pressure, observed in 90.0% of patients in our series. This was thought to be more sensitive to the dura and/or cranial nerves of the CS than to the artery. Most of these adverse effects were reversible with a temporary pause in Onyx injection. Additionally, they could be managed with the intravenous administration of muscle relaxants, antihypertensive agents, and/or atropine. In our series, we usually paused the Onyx injection for about 30 seconds, followed by a slower injection along with muscle relaxants. Only two patients required atropine to address their bradycardia. No complications related to Onyx were observed in our series.

In conclusion, our findings indicated no significant Onyx-related morbidity or mortality, despite transient hemodynamic instability in most patients. The small amount of Onyx used for TVCOE can reduce coil utilization and enhance the immediate CO of CSDAVFs. Due to the potential toxicity of DMSO, TVCOE should not be the first-line treatment for CSDAVFs. This technique is particularly beneficial as a viable procedure for cases with persistent PVRs or redirection of the fistula to PVRs.

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