Transvenous Embolisation of Dural Arteriovenous Fistulas with Combination of Guglielmi Detachable Coils and Onyx: Preliminary Experience and Evaluation of the Clinical Outcomes

VWT Chan, SSM Lo, DPH Wong, KF Fok, KW Tang
Department of Radiology and Imaging, Queen Elizabeth Hospital, Jordan, Hong Kong

ABSTRACT

Introduction: The current mainstay treatment strategy for dural arteriovenous fistulas (DAVFs) is endovascular therapy. The use of transarterial Onyx 18 for treatment of DAVFs has been established, but there is limited literature on transvenous embolisation of DAVFs using Onyx 18 and Guglielmi detachable coils (GDCs). We herein present our preliminary experience of combined use of Onyx 18 and GDCs in treatment of DAVFs using a transvenous approach. Endovascular techniques, clinical and angiographic outcomes, and complications are discussed. We aimed to share our experiences to provide a foundation for future studies to improve patient care.

Methods: We retrospectively analysed all patients with DAVF (n=5, age 23-60 years) with endovascular treatment using Onyx 18 and GDCs performed in the same session, who were treated in our institution between 2014 and 2015. The double-catheter technique with transvenous approach was performed in all five cases. Treatment response and complications were evaluated clinically. We assessed the treatment outcomes with digital subtraction angiogram at 6 months and 18 months after embolisation, assessing the degree of residual arteriovenous shunting and presence of cortical venous reflux.

Results: Among the five reviewed cases, all achieved symptom alleviation. In two (40%) cases of DAVFs complete obliteration was achieved in the first session of embolisation; in one case significant reduction of arteriovenous shunting was achieved. In two (40%) cases, significant reduction of flow into DAVF was achieved after two separate sessions of embolisation. There were no reported cases of new neurological deficits after the procedures.

Conclusion: Onyx 18 in combination with GDCs using transvenous approach for DAVF treatment is a safe and feasible method, with a reasonably high success rate in a small sample. As DAVF is a spectrum of diseases with different severities and locations, treatment approaches should be highly individualised and a multidisciplinary approach should be adopted.

Key Words: Central nervous system vascular malformations; Dimethyl sulfoxide

Correspondence: Dr VWT Chan, Department of Radiology and Imaging, Queen Elizabeth Hospital, Jordan, Hong Kong, Email: chanwaitat@gmail.com

Submitted: 14 Jun 2017; Accepted: 28 Sep 2017.

Disclosure of Conflicts of Interest: All authors have disclosed no conflicts of interest.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics Approval: Requirement for patient consent was waived by the ethics board.
INTRODUCTION

Dural arteriovenous fistulas (DAVFs) are abnormal vascular shunts between the dural arteries and dural venous sinuses. They can occur anywhere along the intracranial dura mater, although they are most frequently found involving the transverse, cavernous, and superior sagittal sinuses and the tentorium cerebelli.\(^1,2\)

The exact incidence is unknown, but DAVFs account for 10% to 15% of intracranial arteriovenous malformations.\(^3\) Whereas some cases of DAVFs may remain clinically silent, some may involute spontaneously\(^4\) or present with different symptoms.

Before the mid-1970s, DAVFs were thought to be congenital in origin. In the late 1970s, an acquired aetiology of DAVFs was proposed.\(^5\) Since then, different aetiologies have been postulated, including venous sinus thrombosis, prior head trauma or transcranial surgery, hormonal influences (e.g. pregnancy, use of oral contraceptives) that may affect angiogenesis, tumours (causing obstructing of dural venous outflow), and prior ear infection.\(^6\) In 1995, Cognard et al\(^7\) and Borden et al\(^8\) proposed that DAVFs are not benign lesions, and the clinical aggressiveness of DAVFs depends on the degree of cortical venous reflux (CVR). The Cognard and Borden classifications of DAVFs are the most commonly used, and both emphasise the importance of site of venous drainage and the presence of CVR.

As described by Borden and Cognard, the lack of cortical venous drainage (Borden Type I, Cognard types I, IIa) is a favourable feature for DAVFs and these cases are associated with a benign natural history.\(^7,8\) There is a low risk of conversion of type I DAVFs into higher grade, and a low risk of intracranial haemorrhage or death.\(^9,10\) In contrast, for DAVFs with CVR, the reported annual risks of non-haemorrhagic neurological deficits, intracranial haemorrhage, and mortality are up to 10%.\(^5,10\)

The presence of CVR is considered the most important determinant for management.\(^11\) These patients may present with aggressive symptoms such as intracranial haemorrhage or neurological deficits. Other intolerable symptoms that may warrant treatment such as bruit, severe headache, seizures, and neuropsychiatric...
Symptoms have also been reported.2

Weighing the risk of treatment and natural history of DAVFs, most studies advocate treatment for high-grade lesion to avoid risks of haemorrhage and non-haemorrhagic neurological defects. Low-grade lesions with debilitating symptoms (such as severe visual symptoms or tinnitus) may also be considered candidates for therapy.

In the past, DAVFs have been treated with many different approaches. Recent studies have shown an increased success rate of transcatheter embolisation, which can achieve a high occlusion rate, and is now considered as one of the primary treatment modalities.

Onyx (ev3 Endovascular Inc., Plymouth [MN], US) is a non-adhesive liquid embolic agent comprised of ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide (DMSO), and was approved by the US Food and Drug Administration in 2005 for presurgical embolisation of brain arteriovenous malformations.12 Since then, transarterial Onyx has gained favour over n-butyl cyanoacrylate (NBCA) in the treatment of DAVFs, with promising results.15,16 However, limited studies have been performed on the combined use of transvenous Onyx and Guglielmi detachable coils (GDCs) for treating DAVFs.

In this paper, we present our preliminary experience in combined use of transvenous Onyx 18 and GDCs in treatment of intracranial DAVFs. The techniques, angiographic and clinical outcomes are discussed. We aimed to share our experience and provide a foundation for future studies to be performed for improving patient care.

METHODS
Patients
We retrospectively analysed all patients with DAVFs treated with combined use of Onyx 18 and GDCs performed in the same embolisation session, who were treated in our institution between 2014 and 2015. Five consecutive patients (three men and two women; mean age 37.2 years, range 23-60 years) were recruited. All DAVF shunts were located along the venous sinus wall or tentorial bridging vein with non-direct and non-exclusive leptomeningeal venous reflux, and retained venous sinus antegrade flow (Cognard classification type IIb). Two of these patients received prior embolisation treatment (one with transarterial Onyx, one with transarterial NBCA) but they presented with persistent symptoms related to residual DAVFs. The main presenting symptoms included: headache (n=4, 80%), seizure (n=2, 40%), visual symptoms (n=2, 40%), altered mental status due to underlying intraventricular haemorrhage (n=1, 20%), and pulsatile scalp mass (n=1, 20%). The baseline characteristics of the patients are summarised in Table 1.

Pretreatment angiography, including selective bilateral external and internal carotid arteries digital subtraction angiographies, were performed for diagnosis and classification of the intracranial DAVFs.

Embolisation Procedures
Embolisation procedures were performed in our endovascular operating room with biplanar digital subtraction angiography facilities. Each patient was put

Table 1. Dural arteriovenous fistula patient characteristics.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Symptoms</th>
<th>Location of DAVF</th>
<th>Cognard classification</th>
<th>Arterial supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>31</td>
<td>Headache, seizure (mRS 2)</td>
<td>Torcular herophili</td>
<td>IIb</td>
<td>Multiple branches from bilateral ECA and ICA, and left VA</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>42</td>
<td>Headache, visual blurring (mRS 1)</td>
<td>Superior sagittal sinus</td>
<td>IIb</td>
<td>Angiogenesis from bilateral ACA</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>60</td>
<td>Headache, altered mental status (mRS 3)</td>
<td>Junction of vein of Galen and straight sinus</td>
<td>IIb</td>
<td>Bilateral ECA, bilateral ICA meningohypophyseal branches, posterior meningeal branch of left VA</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>23</td>
<td>Pulsatile occipital mass (mRS 1)</td>
<td>Occipital, transosseous venous drainage into intracranial bulge then to transverse sinus</td>
<td>IIb</td>
<td>Right occipital artery, right STA</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>30</td>
<td>Headache, seizure, visual blurring (mRS 3)</td>
<td>Superior sagittal sinus</td>
<td>IIb</td>
<td>Multiple branches from bilateral ECA and ICA</td>
</tr>
</tbody>
</table>

Abbreviations: ACA = anterior cerebral artery; DAVF = dural arteriovenous fistula; ECA = external carotid artery; ICA = internal carotid artery; MMA = middle meningeal artery; mRS = modified Rankin Scale; STA = superficial temporal artery; VA = vertebral artery.
under general anaesthesia. Intravenous heparin bolus followed by infusion was given to maintain an activated clotting time of between 200 and 300 s. The right common femoral artery was catheterised with a 5F arterial sheath. The artery supplying the DAVF was cannulated by a 5F diagnostic catheter for arterial control. The right common femoral vein was subsequently catheterised with a 6F venous sheath. A 6F Benchmark™ 071 guiding catheter (Penumbra Inc., Alameda [CA], US) was introduced into the internal jugular vein, and superselective canulation of the target venous sinuses was achieved using an Excelsior® 1018® (Stryker Neurovascular, Fremont [CA], US) or an Excelsior® SL10® (Stryker Neurovascular) microcatheter aided by Transend® 0.014 (Stryker Neurovascular) guidewire. A Marathon™ flow directing microcatheter (ev3 Endovascular Inc.), with Mirage™ 0.008 (ev3 Endovascular Inc.) or Hybrid 0.007 (Balt Extrusion, Montmorency, France) microguidewires, was subsequently used to cannulate the target venous sinus using the parallel co-axial technique. The microcatheter tip was placed as close as possible to the DAVF site.

The DAVF outflow venous tracts and target venous sinuses were first embolised with GDCs (Target® 360 coils, Stryker Neurovascular). Onyx vials were pre-prepared by placing an Onyx shaker for 20 minutes prior to use. Onyx was aspirated into the Onyx Delivery Syringe and attached to the Syringe Catheter Interface Adaptor (SCIFA; ev3 Endovascular Inc., Plymouth [MN], US). DMSO was used to fill the catheter dead space. The SCIFA was then attached to the catheter hub, and pre-prepared Onyx 18 (6% ethylene vinyl alcohol) was slowly injected into the DAVFs in a controlled manner, under biplane road-mapping technique with fluoroscopic guidance. This allows direct visualisation of filling of the venous side of the DAVF. The Onyx injection was stopped when the DAVFs venous outflow tract was completely embolised, or there was persistent Onyx reflux into the distal venous sinus.

A post-embolisation angiogram was performed via the artery control catheter. All catheters were removed, and heparin infusion was discontinued and reversed with protamine at the end of the procedure.

Follow-up digital subtraction angiography at 6 months postoperatively was performed to assess the degree of residual arteriovenous shunting and presence of CVR. Cases with residual DAVF were reassessed with digital subtraction angiography at 18 months postoperatively. Patients clinical outcomes were evaluated using the modified Rankin Scale.

RESULTS
Successful embolisation of the DAVF venous outflow and involved venous sinuses was achieved in all five cases. There was no non-target embolisation.

Among the five cases, complete obliteration (total disappearance of arteriovenous shunting) of the DAVFs were achieved in two (40%) cases, and near-total occlusion (significant reduction of arteriovenous shunting with a small residual shunt) in one (20%) case, in single-stage embolisation procedure. In the other two (40%) cases, near-total occlusion of the DAVF was achieved after two separate sessions of embolisation with slow flow residual arteriovenous shunt (Figures 1 and 2). All patients reported symptom alleviation after the procedure(s).

The angiographic findings of DAVF location, total volume of Onyx injected, coil volume, angiographic and clinical outcome were summarised in Table 2. In all five cases, no residual CVR was observed on follow-up angiogram. No fistula recanalisation was observed at 6- or 18-month follow-up angiography. There were no reported cases of new neurological deficits after the procedure(s). There were no reported cases of unintentional reflux of Onyx 18 into the normal vasculature. Results from other case series are summarised and compared with the those from the present study in Table 3.15,17-19

DISCUSSION
Many different approaches have been used to treat DAVFs, including conservative treatment,4 gamma knife surgery,20 surgery,21 transarterial or transvenous catheter embolisation,19 or a combination of these techniques. The main aim of current endovascular treatments for DAVFs is to completely obliterate the arteriovenous shunt, which can be achieved via a transarterial or transvenous approach.20

Oh et al17 reported nine patients undergoing conservative treatment of cavernous sinus DAVF, in which three patients showed complete obliteration. The other six developed new or recurrent symptoms. Conservative treatment could be considered in cases with a benign natural history (Borden Type I, or Cognard types I or IIa), and when treatment risks outweigh the potential benefits. In these cases, the aim of treatment would be clinical improvement rather than complete angiographic
Transvenous Embolisation of Dural Arteriovenous Fistulas

Figure 1. Case 3. Patient presented with headache and altered mental status. (a) Computed tomography of the brain showing intraventricular haemorrhage (arrow). Cranial AP (b) and lateral (c) views of left external carotid digital subtraction angiographies showing an extensive dural arteriovenous fistulas (white arrows) at junction of vein of Galen and straight sinus, with venous varices (straight black arrows) at vein of Galen. Cortical venous reflux (curved arrows) is identified. (d) Intra-operative image showing a Marathon microcatheter (white arrow) inserted through the Benchmark™ 071 guiding catheter. The pouch-like venous outflow is being embolised with multiple coils (black arrows), followed by Onyx 18. Cranial AP (e) and lateral (f) views of left external carotid digital subtraction angiographies performed 6 months after embolisation, showing complete occlusion of the dural arteriovenous fistulas, and no cortical venous reflux.

cure. However, if patients present with progressive neurological symptoms, more aggressive treatment should be considered even for benign types of DAVFs.

Studies have reported high success rate (up to 87%) of complete occlusion of DAVFs with the use of gamma knife surgery. However, compared with endovascular treatment, which provides an immediate effect, gamma knife surgery has a latent period of up to 3 years before treatment effects are observed. Such delay is considered unacceptable in DAVFs with CVR, as these lesions are prone to bleeding during this latent period.

Wachter et al reported different surgical approaches of treatment of DAVFs, with a high success rate for direct interrupting of the draining vein for non-sinus-type DAVFs. However, those authors also demonstrated comparable treatment outcomes between surgery and endovascular embolisation for sinus-type DAVFs, with the latter favoured for their lower complication rate.

The transarterial approach requires superselective catheterisation of the arterial feeders. This method is particularly useful when the fistula site involves severely stenotic venous outflow or isolated venous sinus. However, many cases of DAVFs present with multiple small feeders derived from external and internal carotid arteries, which are mostly small fine and tortuous vessels. This makes the transarterial approach extremely difficult, if not impossible. Even with successful superselective catheterisation of the small arterial feeders, there is still a high risk of retrograde reflux or migration of liquid embolic agent into arterialised draining veins, which may cause subsequent venous infarction. In these cases,
the transvenous approach is considered safer when the diseased sinus segment can be completely occluded, as long as the diseased segment has minimal contributions to the normal venous drainage.

Transvenous embolisation involves retrograde catheterisation of the involved dural venous sinus or the cortical veins, followed by obliteration of the arteriovenous shunt by use of liquid embolic agents and/or coils. Previous studies have suggested obliteration of the fistula site solely with coils; however, complications such as postoperative cranial nerve palsy have been reported. Furthermore, despite dense packing of coils, residual fistulas may still occur. Therefore, in our cases, we first deployed detachable coils into the venous outflow, and followed by slow injection of Onyx 18.

By first employing coils and then Onyx injection, the coils achieved initial flow reduction within the venous channels and form a scaffold for Onyx cast anchorage. The use of Onyx enables infiltration into the fistula site and smaller total volume of coils required. Long et al. described their initial experience in the combined use of transvenous Onyx 18 together with coils in treatment of cavernous sinus DAVFs in eight cases. That study demonstrated promising results for the combined transvenous use of Onyx 18 and detachable coils in the management of cavernous sinus DAVFs; however, that technique for management of non-cavernous sinuses DAVFs has not been reported.

The use of Onyx involves some risks. The slow injection rate of Onyx implies a prolonged fluoroscopic time, where potential radiation-induced complications may occur. Furthermore, despite dense packing of coils, residual fistulas may still occur. Therefore, in our cases, we first deployed detachable coils into the venous outflow, and followed by slow injection of Onyx 18.

By first employing coils and then Onyx injection, the coils achieved initial flow reduction within the venous channels and form a scaffold for Onyx cast anchorage. The use of Onyx enables infiltration into the fistula site and smaller total volume of coils required. Long et al. described their initial experience in the combined use of transvenous Onyx 18 together with coils in treatment of cavernous sinus DAVFs in eight cases. That study demonstrated promising results for the combined transvenous use of Onyx 18 and detachable coils in the management of cavernous sinus DAVFs; however, that technique for management of non-cavernous sinuses DAVFs has not been reported.

The use of Onyx involves some risks. The slow injection rate of Onyx implies a prolonged fluoroscopic time, where potential radiation-induced complications may occur. Other complications have also been reported, including cranial nerve injury, catheter entrapment, rupture, and vasospasm due to angiotoxicity caused by both Onyx 18 and DMSO. The risk of catheter entrapment can be avoided by positioning the catheter tip in a relatively straight vessel segment to avoid reflux around the catheter tip, although this is not always technically feasible. DMSO-induced angiotoxicity and vasospasm
Transvenous Embolisation of Dural Arteriovenous Fistulas

Table 2. Treatment summary and outcomes.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Location of Onyx injection and coil deployment</th>
<th>Total volume of Onyx injected (ml)</th>
<th>Total volume of coils deployed (mm³)</th>
<th>Angiographic outcome</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Distal end of SSS, torcular, occipital sinus; left transverse sinus</td>
<td>13.5</td>
<td>235.27</td>
<td>Near-complete occlusion (with small slow flow residual shunt)</td>
<td>No symptoms (mRS 0)</td>
</tr>
<tr>
<td>2</td>
<td>SSS</td>
<td>5.5</td>
<td>24.52</td>
<td>Complete occlusion</td>
<td>No symptoms (mRS 0)</td>
</tr>
<tr>
<td>3</td>
<td>Junction between the vein of Galen and straight sinus</td>
<td>18</td>
<td>646.97</td>
<td>Complete occlusion</td>
<td>No symptoms (mRS 0)</td>
</tr>
<tr>
<td>4</td>
<td>Venous bulge draining into transverse sinus</td>
<td>15</td>
<td>145.33</td>
<td>Near-complete occlusion (with small slow flow residual shunt)</td>
<td>Decreased occipital fullness (mRS 1)</td>
</tr>
<tr>
<td>5</td>
<td>Falcine sinus, SSS</td>
<td>34</td>
<td>171.93</td>
<td>Near-complete occlusion (with small slow flow residual shunt)</td>
<td>Occasional breakthrough seizures (mRS 2)</td>
</tr>
</tbody>
</table>

Abbreviations: mRS = modified Rankin Scale; SSS = superior sagittal sinus.

Table 3. Review of literature and comparison of treatment results.

<table>
<thead>
<tr>
<th>Series</th>
<th>No. of cases</th>
<th>Modality of treatment</th>
<th>Complete/near-complete occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lv et al 17</td>
<td>31</td>
<td>Transarterial Onyx embolisation</td>
<td>61% Complete, 39% partial</td>
</tr>
<tr>
<td>Chew et al 15</td>
<td>12</td>
<td>Transarterial Onyx embolisation</td>
<td>75% Complete</td>
</tr>
<tr>
<td>Kirsch et al 19</td>
<td>96</td>
<td>Transarterial NBCA embolisation</td>
<td>30% Complete</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined transarterial NBCA and transvenous coil embolisation</td>
<td>54% Complete</td>
</tr>
<tr>
<td>Choi et al 18</td>
<td>5</td>
<td>Transvenous coil embolisation</td>
<td>80% Complete, 20% partial with residual symptoms</td>
</tr>
<tr>
<td>Our study</td>
<td>5</td>
<td>Transvenous coil plus Onyx embolisation</td>
<td>40% Complete, 60% near complete with no recurrence</td>
</tr>
</tbody>
</table>

Abbreviation: NBCA = n-butyl cyanoacrylate.

can also be prevented by slow Onyx injection, at a cost of prolonged operation time. One possible limitation of Onyx is that there are limited numbers of DMSO-compatible delivery systems available for clinical use. Onyx-related complications may also affect the success of this approach. For instance, large amounts of Onyx and DMSO may be required and complications related to this are possible. Furthermore, reflux of Onyx distally into normal venous sinuses will affect the treatment end-point.

Our study has some limitations. We performed our new approach in only five patients; generalisation of this treatment approach requires further evaluation. Another limitation is that our approach was performed in only selected patients where the transarterial approach was considered extremely difficult or not feasible; thus, exact comparison of the current approach with the transarterial approach is impossible.

Compared with our prior experience of transarterial embolisation, we noticed an increased rate of complete or near-complete occlusion of the shunting using our new approach. Between 2008 and 2013 we performed 12 embolisation operations for DAVFs using the transarterial approach (4 with NBCA and 8 with Onyx 18). Of them, only seven (58%) cases were able to achieve complete or near-complete occlusion, owing to the presence of multiple small and tortuous arterial feeders not-accessible by microcatheters and microguidewires.

**CONCLUSION**

Onyx 18 in combination with GDCs using a transvenous approach is a safe and feasible method for treating DAVFs, with a reasonably high success rate in a small sample. With our preliminary experience, we aim to improve outcome for patients with DAVF. As DAVF is a spectrum of diseases with different severities and locations, treatment approaches should be highly individualised, and a multidisciplinary approach should be adopted for treatment for each patient. Future study is recommended for selected cases where both transarterial and transvenous approaches are considered technically feasible, to compare the success rate of each modality.
REFERENCES


