Embollization of peripheral high-flow arteriovenous malformations with Onyx


Abstract

Purpose: The aim of this study was to report our experience in embolization of high flow peripheral arteriovenous malformations (AVMs) with Onyx.

Material and methods: Nineteen patients (10 men, 9 women) with peripheral high-flow AVMs who were treated with arterial embolization using Onyx were retrospectively included. AVMs were located in the head and neck (6), extremities (5), chest (2), kidney (2), uterus (2), pelvis (1) and parietal (1). In 13 patients, embolization was done using Onyx only. One patient underwent embolization by direct puncture, the others by transarterial approach. Embolization was performed in one or multiple sessions (up to 5). A total of 28 sessions were performed. Follow-up was performed with a delay between 10 and 34 months.

Results: Technical success was achieved in all patients. Complete devascularization was obtained in 12 patients. Surgical excision was performed in 9 patients. Non-target Onyx embolization was not observed. One patient developed stroke. In 1 patient microcatheter
Arteriovenous malformations (AVMs) are vascular lesions that consist of arteriovenous microfistulae through a vascular nidus. They can occur anywhere in the body. Symptoms and signs of AVMs depend on the site, size, and degree of arteriovenous shunting through the lesion. Their etiology is commonly congenital [1]. Trauma may sometimes reveal underlying dormant AVM. The management of peripheral AVMs (pAVMs) is very challenging. Curative surgical treatment is feasible in early stage lesions; however, during these stages AVMs are usually quiescent and asymptomatic, so conservative treatment seems to be a reasonable choice [2]. With various stimuli (hormonal, traumatic, incomplete surgery or embolization), lesions may rapidly progress to higher stages, associated with more complex and difficult management. In case of diffuse lesions, surgery is associated with significant morbidity and carries a high likelihood of recurrence [3]. Ligation of feeding arteries is only temporarily effective and is almost obsolete nowadays as it clearly stimulates neangiogenesis and cuts off any possible further endovascular access.

Endovascular embolization has been suggested as a treatment option since the early 1970s. Its aim is either palliative in symptomatic patients with impossible surgical resection or to minimize intra-operative hemorrhage and facilitate complete resection [4]. The ethylene vinyl alcohol copolymer (EVOH: Onyx; ev3-Covidien, Irvine, CA, USA) is a non-adhesive liquid embolic agent that has been used since the early 1990s [5]. Onyx is proved to be safe and efficient embolic agent in management of brain AVMs [6]. Peripheral use of Onyx has been published in few case reports with promising results [7–9].

The aim of this study was to report our experience in embolization of pAVMs with Onyx.

**Materials and methods**

A retrospective review of the medical records and imaging studies of patients treated by embolization with EVOH (Onyx) from July 2008 to March 2012 for pAVMs in the department of interventional radiology (Hôpital La Timone, Marseille, France) was performed. All patients were managed by a multi-disciplinary team dealing with peripheral vascular malformations (plastic surgeons, interventional radiologists, pathologists and dermatologists). Patients were encountered by the team with previous dynamic magnetic resonance angiography (MRA) study and/or Doppler ultrasound. A consensus decision of embolotherapy followed or not by surgery were decided upon patient’s complaint and angioarchitecture on dynamic contrast-enhanced MRA study. The patient’s consent (or parents’ consent in minor patients) was always obtained after explanation of the treatment and its potential complications. This study included 19 consecutive patients (10 men, 9 women) with a mean age of 36.5 years (range: 2–72 years). Data concerning lesion location, clinical presentation and previous interventions (surgery or embolizations) were reviewed. Number of embolization sessions and their technical details (approach, material used, type and quantity of Onyx used, association to other embolic agent) were analyzed. Technical results and complications of the procedures were registered. Patients were followed-up for an average period of 19 months (range 10–34 months) by clinical examination, imaging (ultrasound and/or MRI) or phone communication for clinical success (relief, persistence or recurrence of symptoms) or delayed complications.

Table 1 summarizes patients’ age, gender, AVM location, clinical presentation, Schobinger clinical stage, previous interventions, number of embolization sessions, quantities and concentrations of Onyx used, other embolic agents used, complications, technical and clinical results and follow-up duration.

**Embolization technique**

Eighteen patients underwent preliminary diagnostic angiography via a percutaneous transarterial approach. During the same session, the embolization procedure was performed. One patient underwent embolization at a second session after the diagnostic angiography because a second multidisciplinary discussion was required. All embolization procedures were performed by a transarterial approach. In one patient, this was changed into direct percutaneous puncture of the nidus due to difficult navigation of the microcatheter secondary to vasospasm that occurred before Onyx injection. Transvenous approach, external compression, and balloon protection techniques were never used. In 18 patients, the procedure was performed by right femoral puncture with introduction of a 6 Fr sheath followed by the introduction of a 6 Fr guiding catheter to allow per- procedure angiograms with the microcatheter in place. Patient No. 1 required a 4 Fr introducer and a 4 Fr vertebral catheter because of his young age (2 years). No anticoagulation was done during the procedures. A dimethyl sulfoxide (DMSO)-compatible microcatheter (Echelon-14 or Echelon-10, ev3, Irvine, CA, USA) was used to perform
Table 1  Patients’ age, sex, AVM location, clinical presentation, Schobinger clinical stage, previous interventions, number of embolization sessions, quantities and concentrations of Onyx used, other embolic agents used, complications, technical and clinical results and follow-up duration.

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Age/ gender</th>
<th>Lesion site</th>
<th>Signs and symptoms</th>
<th>Clinical Stage</th>
<th>Previous interventions</th>
<th>No. of sessions</th>
<th>Onyx concentration, quantity</th>
<th>Other Embolic agent used</th>
<th>Technical result</th>
<th>Clinical result</th>
<th>Complications</th>
<th>FU months</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2/F</td>
<td>Facial</td>
<td>Epistaxis</td>
<td>III</td>
<td>No</td>
<td>2</td>
<td>18, (0.8 &amp; 0.9 ml)</td>
<td>Microspheres 500–700 μm</td>
<td>Partial, &gt; 80%, (ICA feeders not embolized)</td>
<td>Partial</td>
<td>Embolic stroke</td>
<td>21</td>
<td>Few epistaxis</td>
</tr>
<tr>
<td>2</td>
<td>33/M</td>
<td>Right kidney</td>
<td>Hematuria</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>20, (0.8 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Complete</td>
<td>No</td>
<td>12</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>36/M</td>
<td>Right thigh</td>
<td>Pain</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>20, (4 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Complete</td>
<td>No</td>
<td>24</td>
<td>Operated, good</td>
</tr>
<tr>
<td>4</td>
<td>14/M</td>
<td>Left gluteal</td>
<td>Pain, increase in size</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>30, (3.8 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Complete</td>
<td>No</td>
<td>24</td>
<td>Operated, good</td>
</tr>
<tr>
<td>5</td>
<td>33/F</td>
<td>Right parietal (thoraco-abdominal wall)</td>
<td>Severe pain</td>
<td>III</td>
<td>2 embolizations with coils B NBCA + surgery 10 years ago Surgery 2 years ago</td>
<td>3</td>
<td>18, (7 ml, 6.5 ml &amp; 4.2 ml)</td>
<td>No</td>
<td>Partial</td>
<td>Temporary relief of pain, recurrence 3 weeks later</td>
<td>No</td>
<td>18</td>
<td>Persistence of pain</td>
</tr>
<tr>
<td>6</td>
<td>27/F</td>
<td>Right temporal</td>
<td>Pain, swelling</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>18, (1.1 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>No</td>
<td>24</td>
<td>Operated, good</td>
</tr>
<tr>
<td>7</td>
<td>17/M</td>
<td>Mandible</td>
<td>Gingival hemorrhage, pulsatile mandibular mass</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>18, (5.8 ml)</td>
<td>Microspheres 700 μm + coils</td>
<td>Partial, &gt; 80% (very small feeders difficult to catheterize)</td>
<td>Success</td>
<td>No</td>
<td>17</td>
<td>Operated, good</td>
</tr>
<tr>
<td>8</td>
<td>72/M</td>
<td>Right Pulmonary</td>
<td>Deteriorating hypoxia</td>
<td>II</td>
<td>2 embolizations with coils 1 year ago</td>
<td>1</td>
<td>20, (9 ml), 34 (4.5 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>No</td>
<td>12</td>
<td>Good</td>
</tr>
<tr>
<td>9</td>
<td>51/M</td>
<td>Right Pulmonary</td>
<td>Recurrence of hemoptysis</td>
<td>III</td>
<td>1 coils embolization</td>
<td>1</td>
<td>20 (4.5 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>No</td>
<td>18</td>
<td>Good</td>
</tr>
<tr>
<td>10</td>
<td>39/M</td>
<td>Left kidney</td>
<td>Hematuria</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>18 (1.5 ml), 34 (1.5 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>No</td>
<td>34</td>
<td>Good</td>
</tr>
<tr>
<td>Pt. No.</td>
<td>Age/ Gender</td>
<td>Lesion site</td>
<td>Signs and symptoms</td>
<td>Clinical Stage</td>
<td>Previous interventions</td>
<td>No. of sessions</td>
<td>Onyx concentration, quantity</td>
<td>Other Embolic agent used</td>
<td>Technical result</td>
<td>Clinical result</td>
<td>Complications</td>
<td>FU months</td>
<td>Outcome</td>
</tr>
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</tr>
<tr>
<td>11</td>
<td>25/M</td>
<td>Left maxillary</td>
<td>Gingival hemorrhage with chewing</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>34 (0.6 ml)</td>
<td>Coils</td>
<td>Complete</td>
<td>Success</td>
<td>No.</td>
<td>16</td>
<td>Operated. Good outcome</td>
</tr>
<tr>
<td>12</td>
<td>25/F</td>
<td>Uterine</td>
<td>Recurrent metrorrhagia</td>
<td>III</td>
<td>3 Gelfoam embolizations</td>
<td>1</td>
<td>20 (3 ml)</td>
<td>No</td>
<td>Partial, 50% reduction</td>
<td>Severely</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>31/F</td>
<td>Right palpebral</td>
<td>Swelling of right eyelid, rapid increase in size</td>
<td>II</td>
<td>No</td>
<td>1</td>
<td>20 (1.5 ml), 34 (1.5 ml)</td>
<td>Coils</td>
<td>Partial, &gt; 80% (ICA feeders not embolized)</td>
<td>Success</td>
<td>Severe pain &amp; bradycardia during injection</td>
<td>29</td>
<td>Operated, Good outcome</td>
</tr>
<tr>
<td>14</td>
<td>46/F</td>
<td>Uterine</td>
<td>Recurrent metrorrhagia</td>
<td>III</td>
<td>1 Gelfoam embolization</td>
<td>2</td>
<td>20 (9 ml), 20 (7.5 ml)</td>
<td>Coils (AVF)</td>
<td>Partial, 50%</td>
<td>Success</td>
<td>—</td>
<td>10</td>
<td>Good</td>
</tr>
<tr>
<td>15</td>
<td>38/F</td>
<td>Left knee</td>
<td>Post-traumatic painful swelling</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>20 (1.5 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>—</td>
<td>18</td>
<td>Good</td>
</tr>
<tr>
<td>16</td>
<td>33/M</td>
<td>Left forearm</td>
<td>Digital ischemia and pain due to steal phenomena</td>
<td>III</td>
<td>Amputation of ring finger</td>
<td>5</td>
<td>20 (7.5 ml, 11 ml, 4.5 ml, 6 ml, 6 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>—</td>
<td>15</td>
<td>Operated, Good outcome</td>
</tr>
<tr>
<td>17</td>
<td>29/F</td>
<td>Superior labial</td>
<td>Pain, increase in size with pregnancy</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>34 (3 ml)</td>
<td>Coil</td>
<td>Complete</td>
<td>Success</td>
<td>Mild pain during injection</td>
<td>12</td>
<td>Operated</td>
</tr>
<tr>
<td>18</td>
<td>16/F</td>
<td>Left shoulder</td>
<td>Pain</td>
<td>III</td>
<td>No</td>
<td>2</td>
<td>18, 34 (6, 3 ml), 18, 34 (4.5–1.5 ml)</td>
<td>No</td>
<td>Incomplete, &gt; 80% (small feeders difficult to catheterize)</td>
<td>Success</td>
<td>Minimal reflux to brachial artery, no ischemia</td>
<td>26</td>
<td>Operated, shoulder prosthesis, No pain</td>
</tr>
<tr>
<td>19</td>
<td>69/M</td>
<td>Right pelvic</td>
<td>Pain</td>
<td>III</td>
<td>No</td>
<td>1</td>
<td>Onyx 20, 34 (3, 1.5 ml)</td>
<td>No</td>
<td>Complete</td>
<td>Success</td>
<td>No.</td>
<td>13</td>
<td>Good</td>
</tr>
</tbody>
</table>
superselective catheterization. The microcatheter was placed as near as possible to the nidus. According to operator judgment depending on microcatheter tip position in relation to the nidus and the flow within the AVM, Onyx type to be used was decided. If distal penetration is needed, lower concentration and viscosity of the copolymer were preferred (Onyx 18 or 20) as in case of tiny feeding branches with difficult navigation and unstable superselective catheterization. Higher concentration of the copolymer (Onyx 34) was preferred in high-flow lesions with microcatheter tip was very close or in the nidus to avoid the risk of pulmonary migration. Before Onyx embolization, flushing of the microcatheter with saline solution was first performed prior to filling the microcatheter's "dead space" with adequate volume of DMSO. The vials of Onyx were shaken during 20 mins using a shaker (Vortex-Genie, Scientific Industries, Bohemia, NY) to make the tantalum powder homogenous within the suspension. Onyx was then injected with a 1-ml syringe slowly during 60 s to fill the microcatheter dead space replacing the DMSO. First, Onyx injection was performed under fluoroscopic guidance. Further Onyx injections were performed under serial negative roadmap imaging. The injection was maintained and repeated until the feeding arteries and the nidus were completely occluded on control angiogram or until major reflux towards the parent artery was seen. When reflux was noted along the microcatheter in the catheterized feeder, injection was stopped and repeated few minutes later in order to approach the proximal Onyx cast to solidify and thus distal penetration of Onyx in the nidus could be obtained (reflux hold-reinjection technique). If reflux persisted catheterization of another feeding branch was performed and injections repeated in order to occlude consecutively all the feeding branches and the nidus. Completion angiogram was realized through the guiding catheter with the microcatheter in place to evaluate the degree of devascularization. In head and neck lesions we did not embolize feeders originating from the internal carotid artery (ICA) to reduce the risk of neurological complications.

Definitions and procedure endpoints

Complete technical success was defined as absent flow through the nidus with disappearance of the early opacification of draining veins. Incomplete technical success was defined as reduced flow through the AVM with persistent early opacification of the venous outflow drainage. We quantified the approximate percentage reduction of flow through the AVM in case of incomplete success subjectively by 2 experienced interventional radiologists (average value was retained).

Clinical success was defined as complete in case of complete disappearance of initial clinical signs and symptoms. An unsuccessful clinical result was defined by unchanged clinical signs and symptoms or appearance of new symptoms related to procedure complications. Major complications were defined as arrhythmia, non-target embolization or severe pain necessitating morphine analgesia. Minor complications included pain responding to simple analgesia, skin discoloration, vasospasm or retained microcatheter extremity in Onyx cast.

Results

We performed 28 embolization procedures in 19 patients. Only one embolization session was performed in 14 patients; two sessions in three patients; three sessions in one and five sessions in one patient). Eight sessions were performed under local anesthesia. The others were performed under general anesthesia.

Patient 5 had undergone 2 previous embolizations and surgical excision of a large thoraco-abdominal wall AVM 10 years ago that recurred 3 years later. Both patients with pulmonary AVMs (patients 8 and 9) had undergone coil embolization 1 and 16 years ago respectively with recurrence of symptoms. Both patients with uterine AVMs had undergone previous embolizations with gelatine sponge (3 times for patient 12 and once for patient 14) with recurrence of metrorrhagia. Patient 16 had undergone previous amputation of his left ring finger as a partial treatment of his AVM.

The mean volume of injected Onyx in each procedure was 5.9 ml (range 0.6–11.5 ml). We used Onyx alone in 13 patients. Onyx was combined with coils in 5 procedures. We associated 500–700 μm microspheres (Embosphere; Biosphere Medical, Roissy, France) in patient No. 1 and 700 μm microspheres (Embozene, CeloNova Biosciences, Newnan, GA, USA) in patient No. 8. In patient No. 8, we used Onyx with both microcoils and microspheres.

Postembolization angiogram revealed total occlusion in 12/19 patients (63%) (Figs. 1 and 2). Embolizations were incomplete but resulted in marked flow reduction (> 80%) through the malformation in 5 patients (26%). This was due to non-embolized feeding vessels originating from ICA (patients 1 and 13), or due to very tiny feeding vessels that were difficult to catheterize with important risk of reflux (patients 5, 7 and 18). In two patients with uterine AVMs, embolization was incomplete and achieved moderately reduced flow through the malformation (50%). Nine patients were operated on day 1 or 2 after the embolization.

In 16 patients clinical symptoms completely disappeared after embolization and/or surgery. In patient 1, there was persistent but less frequent and less severe epistaxis. In patient 5, pain improved only 2 weeks after embolization and recurred later with the same severity. Patient 12 had incomplete exclusion of the lesion but was lost to follow-up. Patient 1 developed altered level of consciousness after the first session of embolization for facial AVM with Onyx and microspheres. Unenhanced CT brain was performed and revealed no abnormalities. On diffusion-weighted MR images there were multiple lacunar areas of restricted diffusion in both cerebral hemispheres suggestive of embolic stroke. No long-term neurological deficit was noted during the period of follow-up (21 months).

Patient 13 presented severe pain and bradycardia during Onyx injection that resolved within one minute after administration of atropine and morphine analgesia.

In patient 14, we had difficulty in microcatheter retrieval from the Onyx cast during the second session of embolization for the left uterine artery. Excessive traction on the microcatheter led to its fracture. We decided to push the fractured fragment (about 10 cm) distally within the branches of the left internal iliac artery. No ischemic symptoms were noted during follow-up.
Patient 15 developed dark skin discoloration after embolization due to subcutaneous superficial location of the nidus (Fig. 3). Six months later, this discoloration markedly regressed with persistence of only faint discoloration.

In patient 16, we were unable to perform superselective catheterization due arterial spasm that occurred before Onyx injection. We decided to perform direct percutaneous puncture of the nidus and achieved complete technical success.

Patients 6, 11 and 17 developed mild non-specific pain during the procedure that responded to simple analgesia (1 g of intravenous paracetamol). In patient No. 18 (left shoulder AVM), we observed minimal reflux to the brachial artery that remained localized and adherent to the wall with no significant stenosis or occlusion. The patient did not develop any ischemic complaint. No off-target embolization with Onyx® was noted. No pulmonary embolism or respiratory distress was observed following embolization. We did not experience any arterial spasm related to DMSO injection.

Discussion

Endovascular transcathe ter embolization of pAVMs followed or not by surgical excision is a validated therapeutic option. It is frequent that multiple embolization sessions are necessary [10–14].

Different embolic agents can be used for endovascular transcatheter embolization. Coils and detachable balloons cause proximal occlusion with no distal penetration into the nidus. When used, even in preoperative setting, coils may preclude further endovascular access, especially in case of recurrence after surgery. Polyvinyl alcohol (PVA) particles may be used, however, the choice of the size of particles is difficult and migration through large arteriovenous shunts may result in distal pulmonary embolism [15,16]. Recanalization or recruitment of other arterial feeders is another potential disadvantage after PVA embolization [17]. In our series, we combined Onyx to microspheres in patients 1 and 8. Patient 1 developed embolic stroke after the first session of embolization. Lacunar areas of restricted diffusion were seen on diffusion-weighted MR imaging. The presumed etiology retained was off-target embolization with particles through shunts between external and internal carotid branches feeding the facial AVM or by reflux. The possibility of Onyx migration was not considered due to absence of intracerebral hyperdense material seen on the unenhanced CT images. The patient recovered progressively uneventfully with no late neurological deficit. In deep tissue location, Onyx may be used alone without further surgery. In relatively small superficial pAVMs, preoperative embolization with particles can be considered. Onyx can be a good alternative in large arteriovenous shunts in high-flow lesions.

No anticoagulation was used in any of the procedures. Some authors recommend anticoagulation systematically in any cervicofacial endovascular intervention even in external carotid territory.

Among different available embolic agents, liquid agents seem most appropriate to AVMs because of their ability to form a cast penetrating the nidus and occluding the different feeders. Ethanol is a very effective embolic agent described in embolization of AVM [12]. However, severe local and systemic complications such as inflammatory necrotic tissue damage, nerve palsy or acute pulmonary hypertension with cardiopulmonary collapse have been described.
Onyx embolization for AVMs

[18]. This technique requires operator experience in handling ethanol and pulmonary artery pressure monitoring by Swan-Ganz catheter which is a relatively invasive technique.

The tissue-adhesive NBCA is one of the preferred agents currently available for AVMs embolization. Precise use of NBCA and safe embolization is almost impossible due to unpredictable behavior when it comes in contact with blood (reflux, migration or immediate polymerization). Complications such as off-target embolization and catheter gluing can occur [19,20]. In addition, after injection of NBCA, the microcatheter should be removed immediately to avoid gluing the catheter to the vessel wall, which may require restarting a difficult catheterization in case of incomplete embolization [21]. In order to avoid these potential complications, some authors proposed the use of diluted NBCA, which seems have a similar tissue response to that of the high-concentration form [22].

Onyx may represent a promising alternative to the use of NBCA. It has been used successfully for cerebral AVMs embolizations [23]. Recently, case series of embolization of pAVMs with Onyx have been published due to its ability to penetrate and conform to the tortuous arteries supplying the AVM as well as the foci of the nidus [24—26].

The viscosity of Onyx depends on the concentration of the EVOH dissolved in DMSO. If distal penetration is needed, lower concentration and viscosity of the copolymer are preferred. This is especially useful in case of tiny feeding branches with difficult navigation and unstable superselective catheterization. Higher concentrations of the copolymer undergo rapid polymerization which can be interesting in high-flow lesions to avoid the risk of pulmonary embolism in case of superselective catheterization very close or in the nidus. Once the mixture comes in contact with blood, precipitation of the polymer is started after dissipation of DMSO. This process begins on the surface while the core is still liquid, resulting in a soft, and nonadherent mass [27]. In comparison with NBCA, Onyx has several advantages.

The microcatheter tip is not glued within the vessel, and thus it is possible in case of reflux to interrupt the injection for few minutes without retrieving the microcatheter which will allow polymerization of the proximal Onyx cast; then, when injection is restarted, Onyx will penetrate distally towards the low-resistance areas of the nidus. It is also possible to interrupt injection to analyze the actual Onyx casting and review angiographic images while leaving the microcatheter in the same place with no risk of gluing. However, there are cases reported in the literature of difficult retrieval of the microcatheter from the Onyx cast after embolization of brain AVMs or dural arteriovenous fistulas (AVFs) if a long segment of the microcatheter is entrapped.

Figure 2. Patient 2 with: right renal AVM: A: non-enhanced CT shows spontaneous hyperdensity of right renal pelvis compatible with blood clots; B: contrast-enhanced CT shows multiple abnormal vessels in the mid-zone of right kidney, no active contrast extravasation; selective digital subtraction angiogram (DSA) of the right renal artery in early (C) and late (D) arterial phases show a nidus of abnormal vessels with early venous filling compatible with high-flow AVM; E: non-subtracted image after embolization with Onyx shows filling of the nidus and feeding branches; F: post-embolization DSA shows complete exclusion of the AVM with limited loss of renal parenchyma.
Proximal pulling force may not be adequately translated to the distal end, resulting in an entombed microcatheter tip. The monorail snare technique was described to overcome this problem [28]. The use of detachable microcatheter tip is also an alternate option [29]. We experienced one occurrence of retained microcatheter in the Onyx cast after embolization of a uterine AVM (patient 14). Excessive traction on the microcatheter resulted in its fracture. We pushed the retained microcatheter distal tip in the branches of the left internal iliac artery and the patient did not develop any ischemic symptoms.

Another potential advantage of Onyx® is that it seems to be easier to handle during surgery by comparison with NBCA [30]. The complete filling of embolized vessels by Onyx and the lower inflammatory reaction makes surgical dissection easier. In vivo evaluation of inflammatory reaction in histologic specimens of Onyx®-embolized vessels in humans showed that they were essentially located intravasally, with no reaction of the surrounding tissues depicted [31].

One of disadvantages of Onyx® is its relatively high cost compared with other embolic agents. Another disadvantage is that if the operator does not have enough experience with its use, the time and complexity of the procedure may be excessively increased. However, after a learning curve, its handling is probably easier and safer for the treatment of peripheral AVMs and vascular anomalies compared to other liquid embolic agents [7,32]. Some authors reported severe vasospasm in case of rapid injection [33]. This is especially important during the early stages of the embolization procedure when the DMSO is being replaced by Onyx® in the catheter dead space. Thus, the first milliliter of the embolic agent must be injected very slowly. We never experienced severe vasospasm related to DMSO injection. Chemical irritation by DMSO may be very painful. It is recommended to use moderate to deep sedation or general anesthesia to ensure patient comfort during embolization. In our series, 3 patients developed non-specific pain during the procedure which responded well to simple analgesia medication. We did not attribute this pain to DMSO injection as these were not synchronized. On the other hand, one patient developed severe pain and bradycardia during DMSO injection that persisted for about 1 min and necessitated administration of morphine analgesia and atropine. This patient recovered completely with normal rhythm and disappearance of pain. This was attributed to trigemino-cardiac reflex due to chemical or mechanical irritation of the trigeminal nerve, or of the structures innervated by it. It has been described in embolization of dural AVF with Onyx with an incidence rate around 11% [34]. The reflex stops as soon as

Figure 3. Patient 15: Digital subtraction angiogram of the left popliteal artery during arterial (A) and early venous phase (B) show a nidus of abnormal dysplastic vessels with early venous filling compatible with AVM; C: superselective DSA with microcatheter shows multiple small branches feeding the nidus; D: non-subtracted image following superselective embolization with Onyx shows the cast filling all the feeding branches and the nidus; E: DSA post-embolization shows complete exclusion of the AVM; F: dark discoloration of the infero-medial aspect of the left knee appeared after embolization; patient became free of any pain; G: 6 months later, the discoloration markedly regressed.
the triggering factor is removed [35]. We did not experience any significant non-target embolization caused by reflux or migration through the AVM. In our study, despite the fact that AVMs in 7 patients were embo lized incompletely, only 2 patients had persisting symptoms. We observed complete clinical success in 2 patients despite the fact that AVM was not completely occluded.

Aret et al. [26] reported one case of permanent black discoloration of the overlying skin after embolization with Onyx that persisted after simple excision of the AVM and necessitated a second surgery. One patient developed dark skin discoloration after embolization of subcutaneous AVM of left knee. Six months later, this discoloration faded spontaneously with only faint mark left. Other potential disadvantage is that the slow Onyx injection can be time-consuming and may increase the radiation dose given to the patient in case of large AVM. Also DMSO is eliminated via respiration and sweat. This has a garlic-like smell that may last for a few days. The patient and ward staff should be warned to expect this. The use of Onyx requires specific DMSO-compatible microcatheters. Most of microcatheters currently available on the market are DMSO-compatible.

We used transarterial approach in all patients. In one patient, we were not able to perform superselective catheterization due to spasm. We transformed our technique to direct percutaneous puncture. We never used transvenous approach neither balloon protection. These techniques were proposed by some authors in case of fine, diffuse, serpiginous arterial supply, important normal arterial branches arising in very close proximity to the malformation, extreme arterial tortuosity with difficult stable catheterization, previous therapy (embolization or surgery) with occlusion of arterial access to the central portion of the malformation precluding a transarterial approach [36]. We did not have any of these indications in our patients.

Our study is limited by the relatively small number of patients with heterogenous nature of lesions. This corresponds to the real-life incidence of this disease. Relatively good results presented may be biased by the high experience of the operators using Onyx and by meticulous preselection of patients during multidisciplinary meeting. Embolization was only performed if a relatively high rate of technical success was predicted. This highlights the importance of multidisciplinary approach when managing this type of patients. Another limitation is that patients were followed-up mainly on clinical basis, so any asymptomatic recurrence even if rare could have been non-depicted. Further prospective studies are needed, however, these cases are relatively rare and are managed on a case-by-case basis depending mainly on the angioarchitecture of the lesion which is extremely variable and almost non-comparable from one case to another, which constitute a major obstacle for this type of study.

In conclusion, transcatheter embolization with Onyx is a promising treatment option of pAVMs followed or not by surgical excision. Onyx seems to provide controlled embolization due to slow polymerization, which enables deep penetration in the nidus with less risk of catheter gluing due to its non-adhesive nature. Currently, available data in the literature are very limited. Further studies are needed to better characterize its safety profile in peripheral vasculature.

Disclosure of interest
V.D. reported action of Proctoring (EV3-Covidien), outside the submitted work.
M.S.K., V.L., P.P., G.M., D.C. and J.-M.B. declare that they have no competing interest.

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