Surgical outcome of carotid body tumour resection after percutaneous embolization using Onyx®, an ethylene-vinyl alcohol copolymer†

T Abdel-Aziz1*, M Lehmann1, U Dietrich2, J Ebmeyer1, H Sudhoff1

Abstract

Introduction
Carotid body tumours (CBTs) are highly vascularised tumours that can only be treated curatively by complete surgical resection. Preoperative embolization is widely used to reduce intraoperative bleeding and minimise surgical complications.

Objective
To assess the surgical outcome of CBT resection after percutaneous embolization using Onyx®.

Methods
Retrospective analysis of five consecutive patients with CBTs was performed from August 2008 until December 2011 after embolization via percutaneous intratumoural injection using Onyx®, and the results were compared with those available in the literature.

Results
In four of five patients, complete devascularisation was achieved. No complications occurred during embolization. All CBTs were resected completely. Duration of surgery varied between 35 and 289 min, with an average of 148 min. Mean estimated intraoperative blood loss was 327 mL (range, 40–1400 mL). We experienced one Horner’s syndrome, one temporary hypoglossal nerve paresis and a permanent paressis of the recurrent laryngeal nerve.

Conclusion
Preoperative embolization reduces intraoperative blood loss, improves operative field visualisation and consecutively diminishes damage to the nerval and vascular structures. Percutaneous embolization via direct intratumoural puncture appears to achieve a higher degree of devascularisation by affecting arterial vessels, capillary bed and venous drainage. Existing data suggest a decrease in intraoperative blood loss and fluoroscopy times over transarterial embolization.

Introduction
Carotid body tumours (CBTs) are highly vascularised tumours and belong to a group of paragangliomas. They are considered a rarity, with a 0.001% overall incidence and 0.6% proportion of all head and neck tumours. CBTs have a female to male ratio of 3:1. Further, 90% of all CBTs occur sporadically, whereas 10% are of familial origin. To date, several mutations of succinate dehydrogenase subunits have been identified. Although CBTs can arise at any age, incidence increases from the 4th decade in sporadic and between the 2nd and 3rd decade in hereditary CBTs. Bilaterality is seen in 5% of sporadic cases and up to 30% of familial CBT cases.

The carotid body is located in the posterosomedical portion of the carotid bifurcation within the adventitia. It serves as a vascular chemoreceptor, detecting changes in O₂- and CO₂-partial pressure as well as changes in acid–base balance. Innervation is supplied by the glossopharyngeal nerve. Although vascular supply of the carotid body occurs via the carotid artery or the vertebral arteries, CBTs are most commonly supplied by branches of the external carotid artery, especially the ascending pharyngeal and occipital arteries. Additional vascular supply may also occur via branches of the internal carotid or vertebral arteries.

Clinically, most CBTs present as slow growing, painless masses in the lateral neck. Of 75% CBTs that are incidentally diagnosed, only 25% cause medical conditions such as a thrill, dysphagia, cranial nerve deficits, carotid sinus syndrome or cerebrovascular complications.

Most CBTs are hormonally inactive. Further, 94% CBTs are benign; only 6% CBTs undergo malignant transformation. However, even benign tumours have the potential to locally invade and destruct adjacent cranial nerves, leading to permanent nerve palsies.

Complete surgical resection is the only curative therapy, and therefore, it is the therapeutic gold standard. Radiation therapy is considered a treatment option only in elderly patients and in patients with vital contraindications to surgical intervention.

While intraoperative mortality has declined below 1%, the greatest perioperative risk for the patient is extensive blood loss, which also impairs adequate visualisation of the surgical field, thus increasing the risk for nerve injury. However, it is important to emphasise that due to potential tumour invasion of nervous structures, sometimes the sacrifice of nerves...
regardless of surgical field visibility, is inevitable in order to achieve complete tumour resection.

To minimise intraoperative blood loss (IBL) and its complications, many surgeons prefer preoperative tumour embolisation.

Two different strategies of embolisation have been proposed: transarterial, first described by Schick et al. in 1980 and direct percutaneous intratumoural puncture, first described by Casasco et al. in 1994.

Comparison of both routes of embolisation reveals several advantages for the percutaneous approach. While transarterial embolisation only affects the arterial blood supply, direct intratumoural application of the embolic agent is able to occlude arterial supply, the capillary vessels, and the venous vessels, resulting in an overall higher degree of devascularisation. Furthermore, tortuous vascular architecture can make microcatheterisation of feeding vessels very difficult or even impossible. Additionally, in case of multiple feeding vessels, time-consuming microcatheterisation of every vessel is required. These difficulties are bypassed in direct intratumoural embolisation, leading to reduced fluoroscopy times.

For these reasons, at our institution, we prefer preoperative embolisation of CBTs via direct intratumoural puncture.

Most reports of direct intratumoural embolisation have used n-butyl cyanoacrylate (n-BCA) or polyvinyl alcohol. In the past several years, a few reports have been published propagating the use of Onyx® (ev3, Irvine, CA, USA), a non-adhesive liquid embolic agent. It consists of ethylene-vinyl alcohol copolymer (EVOH) dissolved in dimethyl sulfoxide (DMSO) and suspended micronized tantalum powder as a contrast agent for visualisation during fluoroscopy. On contact with blood, DMSO dissipates, leading to precipitation of EVOH (Figure 1).

Several advantages of Onyx® over n-BCA have been proposed. Onyx® polymerises slower than n-BCA, allowing intratumoural application in a more controlled and precise manner. Additionally, injection can be halted if needed to evaluate the achieved degree of devascularisation or to repostion the injection needle for larger sized tumours.

Figure 1: Histologic image of embolized CBT. Blood vessels filled with Onyx®, arrow (H/E staining, 40×).

For these reasons, we considered the use of Onyx® for preoperative percutaneous tumour embolisation as favourable.

Methods and material

In our setting, percutaneous embolisation was performed in collaboration with the Department of Diagnostic and Interventional Radiology and Neuroradiology at the Evangelic Hospital in Bielefeld, Germany. Generally, embolisation is performed 24 h prior to surgery under general anaesthesia. The detailed procedural description has been previously published. After angiographic display of the common carotid artery (Figure 2A), a protective microballoon is inserted into the internal carotid artery until the level of the observed tumour blush. The microballoon can be temporarily inflated to avoid retrograde penetration of the embolic agent into the carotid artery. Subsequently, the tumour is percutaneously punctured using the road-map technique and intratumoural access is confirmed using contrast dye injection (Figure 2B). Finally, percutaneous injection of Onyx® was performed under fluoroscopic roadmap guidance. Intraprocedural angiography was used to control the achieved degree of devascularisation (Figure 2C).

Results

From August, 2008 to December, 2011, five CBTs were preoperatively embolised and subsequently resected completely by subadventitial tumour dissection. All patients were female with a mean age of 58.2 (32–78) years. All CBTs were benign and occurred sporadically. No CBTs displayed endocrine activity (Table 1).

An average of 4.4 (1–9) mL of Onyx® was needed for devascularisation. In four of five cases, complete devascularisation could be achieved; in one case devascularisation was nearly complete, as controlled by angiography. No complications were observed during embolization (Table 1).

Licensee OA Publishing London 2013. Creative Commons Attribution License (CC-BY)

Duration of surgery varied between 35 and 289 min, with an average of 148 min. Mean estimated IBL was 327 mL (range, 40 to 1400 mL; Table 2). In the case with 1400 mL blood loss, surgical resection proved exquisitely difficult due to an unusual cranial localisation of the carotid bifurcation. Additionally, complete preoperative embolization had not been achieved with feeding branches of the carotid bifurcation in remaining patients (Table 1). Excluding this case as a runaway value yielded an average IBL of 54 mL. Carotid arteries were not injured in any case, and no vascular reconstruction was required. Postoperatively, one patient suffered from Horner’s syndrome, and the patient with the unusual anatomy suffered from a permanent paralys is of the recurrent laryngeal nerve and a temporary paralysis of the hypoglossal nerve that resolved completely within 9 months after surgery. The nerves themselves had not been sacrificed during surgery as confirmed by intraoperative nerve stimulation.

### Discussion

Only few reports exist on the surgical outcome after preoperative direct intratumoural embolization of CBTs using Onyx®. They all cover only small case series, but results seem to resemble the ones obtained at our institution.

Shah et al.15 retrospectively reviewed a consecutive series of seven CBTs that had undergone preoperative direct percutaneous Onyx® embolization. An average of 8.7 (4.2–18) mL of Onyx was used. Average estimated IBL was 55 (15–80) mL. Complications during embolization did not occur, surgical complications were not addressed.

Wanke et al.14 in a case series of four patients with six CBTs required an average of 4.75 (3–9.1) mL Onyx for complete devascularisation. Mean surgical duration was 151 (80–280) min. In two patients with bilateral CBTs, surgical resection was performed one at a time. No complications occurred during embolization or surgical resection.

Compared with older literature reports in which CBTs were resected either without prior embolization or after transarterial embolization, the data available so far indicate a benefit of the aforementioned preoperative intratumoural Onyx® embolization over such methods. LaMuraglia et al.16 retrospectively investigated a series of 17 patients with 19 CBTs treated in a 10-year period from 1982 to 1991. In 11 CBTs, complete preoperative transarterial embolization of all afferent vessels was performed using polyvinyl alcohol beads and gel foam. Average IBL differed significantly ($P < 0.02$) among both cohorts, with 373 ± 213 mL in the embolized and 609 ± 564 mL in the non-embolized cohort. Both cohorts did not differ significantly in tumour surface area. Surgical time did not differ significantly, with 4.1 h in the embolized and 4.5 h in the non-embolized group. One attempt of preoperative embolization had to be terminated due to extreme tortuosity of feeding vessels, making stable catheter positioning impossible. This patient developed a transient episode of aphasia. Regarding surgical complications, two cases of Horner’s syndrome and two cases of tenth nerve injuries resulting in vocal cord paresis were reported.

CBTs are highly vascularised tumours that require surgical excision for curative treatment. Preoperative embolization has proved to significantly reduce IBL and therefore is helpful in improving visualisation of the operative field. This reduces the likelihood of damage to nerve and vascular structures15–17.
Percutaneous embolization via direct intratumoural puncture appears to achieve a higher degree of devascularisation by affecting arterial vessels, capillary bed and venous drainage. Additionally, it shortens fluoroscopy time and under certain conditions, even impossible micrcatheterisation of small tortuous feeding vessels is no longer necessary.

Although our group, similar to Shah et al.\textsuperscript{15} and Wanke et al.\textsuperscript{14}, could not observe any complications during percutaneous Onyx\textsuperscript{®} embolization, one interesting complication was reported by Wiegand et al.\textsuperscript{11} in 2010. After embolization of a large CBT measuring $7 \times 3 \times 4$ cm and necessitating the use of 20 mL Onyx\textsuperscript{®}, postembolic tumour swelling was observed that caused a permanent Horner’s syndrome and transient paresis of the hypoglossal and glossopharyngeal nerves, which recovered within 7 days after tumour resection.

One case of embolization of the superior sagittal sinus with subsequent haemorrhagic venous infarct requiring emergency decompression craniectomy and frontal lobectomy after Onyx\textsuperscript{®} embolization of an intracranial frontal parasagittal meningioma raised the question of a possible increased risk for venous spread of the embolic agent when compared with the transarterial approach\textsuperscript{12}.

Only few case series have investigated the efficacy of preoperative percutaneous Onyx\textsuperscript{®} embolization, and existing data suggest a decrease in IBL and fluoroscopy times over transarterial embolization.

Reduced blood loss is a prerequisite to facilitate visualisation of the surgical field and avoid unintended injury of adjacent nerval and vascular structures. It shortens the duration of surgery and consequently reduces perioperative morbidity, leading to an accelerated postoperative recovery. However, it is important to emphasise that due to the possible tumour invasion of nerves, nerval sacrifice sometimes is inevitable to achieve complete tumour resection.

The few existing case series only comprise a small number of patients. To date, there is no study from a single institution directly comparing the two techniques of embolization, transarterial vs. percutaneous. Similarly, among the different agents applicable for percutaneous embolization, such as n-BCA and Onyx\textsuperscript{®}, no comparative clinical trial from a single institution exists. Blinded studies will hardly be accomplishable due to the characteristic garlic-like breath and taste of Onyx\textsuperscript{®}\textsuperscript{11}. However, more and larger case series are required to definitely determine the value of percutaneous preoperative Onyx\textsuperscript{®} embolization of CBTs.

### Table 1: Patients and embolization results

<table>
<thead>
<tr>
<th>Patient/age (years)/sex (M, F)</th>
<th>CBT size (cm)</th>
<th>Onyx (mL)</th>
<th>Devascularisation</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/32/F</td>
<td>$2.9 \times 3.9 \times 2.2$</td>
<td>9</td>
<td>Complete</td>
<td>No</td>
</tr>
<tr>
<td>2/41/F</td>
<td>$2.3 \times 1.9 \times 2.8$</td>
<td>4</td>
<td>Complete</td>
<td>No</td>
</tr>
<tr>
<td>3/35/F</td>
<td>$2.5 \times 2.5 \times 3.5$</td>
<td>4</td>
<td>Complete</td>
<td>No</td>
</tr>
<tr>
<td>4/78/F</td>
<td>$3.2 \times 2.0 \times 1.4$</td>
<td>1</td>
<td>Complete</td>
<td>No</td>
</tr>
<tr>
<td>5/48/F\textsuperscript{a}</td>
<td>$2.8 \times 2.0 \times 1.5$</td>
<td>4</td>
<td>Almost complete</td>
<td>No</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Difficult anatomy due to unusual cranial location of the carotid bifurcation.

### Table 2: Surgical results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Duration of surgery (min)</th>
<th>IBL (mL)</th>
<th>RBC transfusion</th>
<th>Surgical complications</th>
<th>Surgical removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>289</td>
<td>50</td>
<td>0</td>
<td>None</td>
<td>Complete</td>
</tr>
<tr>
<td>2</td>
<td>133</td>
<td>75</td>
<td>0</td>
<td>Horner’s syndrome</td>
<td>Complete</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>50</td>
<td>0</td>
<td>None</td>
<td>Complete</td>
</tr>
<tr>
<td>4</td>
<td>106</td>
<td>40</td>
<td>0</td>
<td>None</td>
<td>Complete</td>
</tr>
<tr>
<td>5\textsuperscript{a}</td>
<td>176</td>
<td>1400</td>
<td>2</td>
<td>Recurrent laryngeal nerve (permanent)</td>
<td>Complete</td>
</tr>
<tr>
<td>AVG</td>
<td>148</td>
<td>327 (54\textsuperscript{b})</td>
<td></td>
<td>Hypoglossal nerve (temporary)</td>
<td>Complete</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Difficult anatomy due to unusual cranial location of the carotid bifurcation.

\textsuperscript{b}Average IBL with 1400 mL considered a runaway value.

References

15. Shah HM, Gemmte J, Chaudhary N, Pandey AS, Ansari SA. Preliminary experi-
ence with the percutaneous embolization of paragangliomas at the carotid bifurca-