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Preoperative embolization of skull–base tumors: Indications, utility, and concerns

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ABSTRACT

Skull-base tumors are generally difficult to access compared with many other cranial lesions. Usually surgery remains the gold standard treatment for the majority of these tumors. However, in many cases, surgical resection is a challenge because the disease usually is already in the advanced stage by the time of diagnosis. Additionally, there are hypervascular lesions which cause excessive loss of blood, then results in multiple blood transfusions and prolonged operative time, increases the risk of neural injury and prevents complete excision. In order to reduce blood loss intraoperatively, many alternatives were available with the neurosurgical armamentarium, such as head elevation, intravenous use of tranexamic acid, total intravenous anesthesia and even preoperative embolization of tumors. However, preoperative embolization carries variable results, potentially aggravating edema and increasing tumor size. To ascertain the current status and the up-to-date indications, an evaluation of the therapeutic role of preoperative embolization was performed in the current study.

1. Introduction

Embolization of the vascular tumors during the preoperative phase may lead to a reduction of tumor vascularity and the intraoperative loss of blood, finally aiding in surgical resection[1-4]. Benefits of preoperative embolization have been only partially demonstrated, which include reduction in blood loss, intra-operative time, hospital stay after surgery, blood transfusions and morbidity and mortality of the procedure[5,6] (Figure 1). On the other hand, some authors reported an increased risk of tumor growth and tumor edema when subtotal resection was performed after embolization[7].

Despite potential problems, this strategy is widely used where endovascular therapy facilities are available, although the indications for embolization of some skull-base tumors remain controversial. As a rule, there are two techniques of tumor embolization: direct arterial catheterization or direct puncture of the main tumor artery.

The most commonly embolized skull-base tumors are juvenile nasopharyngeal angiofibroma, hemangioblastoma, hemangiopericytomas, meningiomas, metastatic deposits, glomus tumors and other paragangliomas[8].

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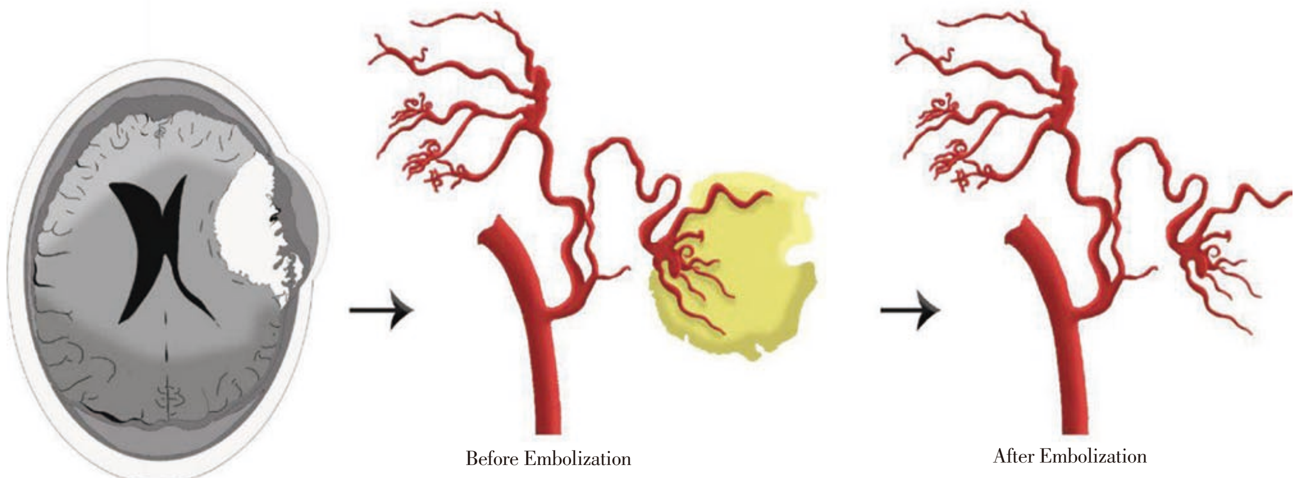

Figure 1. Preoperative embolization facilitates tumor resection.

Although few case series have analyzed preoperative embolization of intracranial tumors, overall published sources on endovascular management of skull base tumors are remarkably scarce, and no randomized controlled study has been conducted[9,10].

The objectives of this review are to update the current available information, to describe the role of preoperative embolization of skull base tumors, and to discuss the most frequent hypervascular tumors from the view of specific vascular anatomy according to different types and locations of tumors and types of embolizing materials.

2. Initial evaluation–radiological imaging

The development of non-invasive perfusion imaging methods like magnetic resonance or tomography provide a safe estimate of the vascularity of tumor, but angiographic evaluation is still the best choice[11-15]. Non-invasive perfusion imaging methods should be routinely performed to decrease the costs and potential morbidities associated with cerebral angiography, hence the cerebral angiography may overestimate the vascularity of the target lesion for embolization[14].

Generally, hypervascular skull-base tumors receive their blood supply through the arteries that also supply the adjacent dura mater with blood. In meningiomas, blood supply generally originates from the branches of the middle meningeal artery and external carotid artery[14]. The results of the endovascular treatment of skull base tumors have shown a relatively constant blood supply pattern, which varies with different tumor locations (Figure 1)[16].

Most of the tumors are medially located in the anterior cranial fossa, such as meningiomas of the tuberculum sellae, planum sphenoidale, and olfactory sulcus. They are supplied by ethmoidal branches of the ophthalmic artery whose embolization carries the risk of amaurosis due to occlusion of the central retinal artery in the event of reflux of the embolizing material or sub-occlusive catheterization[4,17-20]. Although successful embolization of the ophthalmic artery without producing visual complications have been reported, the evidence for this practice is not enough to allow the routine use, considering the high risk of visual injury[4,20].

Although tumors embolization of the anterior cranial fossa is not commonly indicated, juvenile nasopharyngeal angiofibroma is the most notable exception, since their vascular supply generally originates from branches of the internal maxillary artery and the embolization before surgery is effective[21].

The perfect delimitation of the dural pedicle is especially important in the cases in which tumors arise from middle fossa in relation to the sphenoid wing and these tumors are supplied from many branches of the internal and external carotid artery. It has been demonstrated that tumors located in parasellar and clinoid region are supplied by dural branches of the meningo-hypophyseal trunk and the inferolateral trunk of the internal carotid artery, which makes an adequate embolization of the meningiomas in the middle and inner third of the sphenoid wing difficult[14]. In contrast, meningiomas involving the outer third, which are mostly supplied by anterior and petrosal branches of the middle meningeal artery, as well as by the recurrent artery and accessory meningeal branch of the internal maxillary artery, can be treated with preoperative embolization with higher success rate[16].

3. Evaluation and indications

The preoperative embolization of tumors is a tool in the neurosurgical armamentariums, and can reduce blood loss and improve surgical results. The results of previous studies involving tumors of the skull base have shown that most of the complications are related to the complete angiographic devascularization. In relation to this, there are a few reports of morbidity and mortality rate associated with preoperative embolization of skull-base tumors[4,9,22]. The results of these studies demonstrated the importance of the location and type of tumor in the appearance of complications. Regarding that meningiomas locate in the skull base, the risk of complications can vary by 20%[4,9]. These findings are similar with those found in the retrospective study of Rosen *et al*. in 2002, who analyzed 167 cases of meningiomas, and found that 21% of the patients developed complications due to the procedure. However, only 9% of these events presenting major neurological complications were not resolved in the following 24 h; while the rest of the patients presenting diplopia, focal deficits, and sensory disturbances were treated within a day[9].

A systematic review involved 503 persons (include both patients and control group) diagnosed as intracranial hemangioblastoma, among whom 111 patients underwent preoperative embolization, while 392 patients were treated with surgery alone. The result showed complication rate was 11.7% in patients with embolization and up to 20% after surgery. These complications involved ischemic and hemorrhagic events, symptoms associated with increased intracranial pressure and neurological deficit, showing that preoperative embolization did not lead to better results and increased the risk of adverse events[1].

This high occurrence of complications can be significantly reduced by avoiding the embolization of arteries dependent on the internal carotid artery, such as the ophthalmic artery and meningo-hypophyseal branches. Considering this, complication rates can be reduced from 21% to 2.5%. The performance of a digital subtraction angiography, supported by the CT and MRI evaluation findings, allows an integral analysis of the lesion and its vascularization [8,14].

The study by Trivelatto *et al*. showed complications of bleeding around the lesion and transient paralysis of the left oculomotor nerve in 1 out of 5 patients with meningiomas supplied by the ophthalmic artery, However, it should be noted that the patients did not present visual alteration after the embolization on branches of ophthalmic artery[4]. The deposit of the embolizing material into the vasculature of the tumor can induce thrombosis and ischemic necrosis, which ultimately causes softening, and facilitates its resection[23].

The possibility of good resection (Simpson Ⅰ and Ⅱ) for giant meningioma, is increased by 8 to 10 folds when preoperative embolization is added to the treatment. This can be attributed to the reduction of intraoperative bleeding and decreasing the vascularity of the friable necrotic tissue, hence improving the final outcome[23,24]. Additionally, another study showed that in those patients who did not undergo extensive resections, the preoperative embolization was associated with a longer progression-free period during long-term follow-up[6]. Finally, tumor embolization has also been proposed as an alternative method in palliative treatment for those patients who are not surgical candidates for definitive resections; however, the evidence about its efficacy and safety is not enough to be recommended by routine treatment policy[24,25]. The preoperative embolization can reduce intra-operative bleeding, surgical time, and the risk of injury to neighboring neurovascular structures, increase the probability of performing a total resection, and decrease tumor recurrence. However, the disadvantages are the risks of angiography and the procedure of embolization. The publications of preoperative management algorithms for the management of tumors in the skull base are scarce. We propose an algorithm to provide an overview of the potential benefits of preoperative embolization. Our algorithm allows all tumors of the skull base to be treated (Figure 2). On the other hand, we propose that a pre-embolization score mechanism should be applied, which will contains the most relevant elements in the angiographic evaluation of the lesions in the skull base. The Proposed score for embolization of skull-base tumors include three parameters:

(1) The access feasibility to vascular branch (YES: 2 scores, NO: zero score);

(2) The presence of Risks anastomosis (YES: zero score, NO: 1 score);

(3) Absence of irrigation to unscratched structures (YES: 1 score, NO: zero score);

With the total collected score interpreted as the following: 0-1: High-risk of failed embolization; 2-3: Moderate risk of embolization; 4: Low risk of failed embolization.

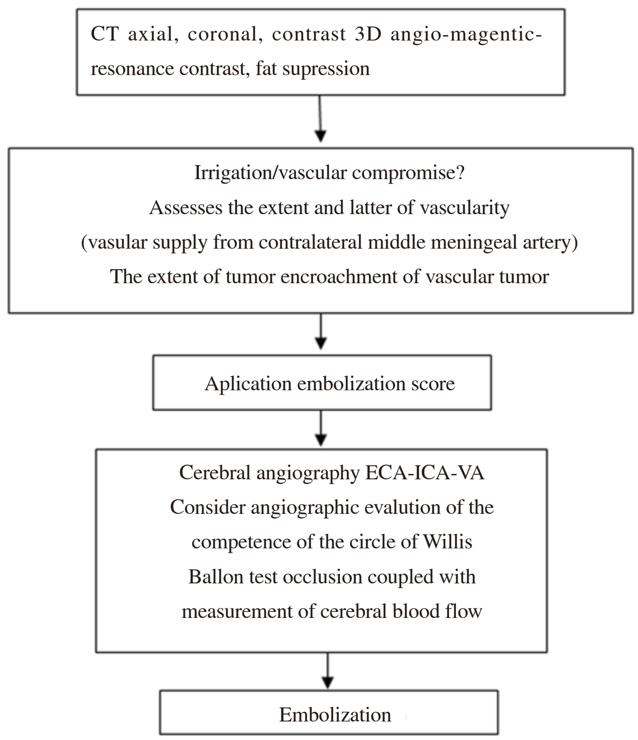

Figure 2. Algorithm of approximation for tumors of the base of the skull including the anterior cranial fossa. CT: computerized tomography; ECA: external carotid artery; ICA: internal carotid artery; VA: vertebral artery.

4. Morphological changes induced by embolization of a tumor

The alterations of the tumor structure induced by embolization have been studied almost exclusively in meningiomas. These changes include the presence of necrosis and increased cell proliferation, and may modify the graduation and finally the treatment and postoperative follow-up. The findings of a grade Ⅰ embolized meningioma are confused with an atypical meningioma (grade Ⅱ), due to the loss of cell size and relative cytoplasmic volume; cytoplasmic vacuoles can simulate a clear cell meningioma, and the loss of cell cohesion can represent features of a rhabdoid meningioma[1,4].

At the cytological level, there is a prominent cell dissociation, with cellular isolation or formation of small cell groups, great infiltration of neutrophils and macrophages load with cellular detritus, as observed in other ischemic events. The most prominent cellular changes are the increase in the nuclear/cytoplasm ratio, reduction in total cell volume, nuclear pyknosis and karyorrhexis[26]. Despite all these characteristics, in most cases, tumor areas that preserve the histological and cytological architecture can be identified, and allow accurate diagnosis[26]. However, it has been described that immuno-labeling with Ki-67 may help in differentiation since it does not increase in previously embolized grade Ⅰ tumors[22,27].

5. Case selection

The success of pre-surgical embolization of intracranial tumors largely depends on the appropriate selection of the case, histology, location, size and tumor vascularity. The magnitude of the benefits and the potential risks can be estimated.

Similar with all invasive procedures, preoperative embolization of tumors can cause risks. Initially, the potential complications related to vascular access, the injection of the contrast medium and the inadvertent occlusion of arteries that also cause healthy tissues must be taken into consideration.

According to the histological lineage, a group of identified tumors have been identified, which could benefit the most from the preoperative treatment including meningiomas, juvenile angiofibroma, hemangiopericytoma, metastatic lesions, hemangioblastoma, jugular glomus, and other paragangliomas[8]. However, the histology should be considered because not all tumors of a certain histological type will necessarily be provided with an abundant vasculature, which is especially relevant in the case of meningiomas, hemangiopericytoma and metastatic lesions.

However, some patients may not be suitable for preoperative procedure due to tortuous feeding vessels, unavailability of the endovascular facility. In the cases where preoperative embolization cannot be carried out, and in event of intraoperative severe bleeding despite embolization, the patients need emergency surgical intervention. Waldron *et al*. analyzed 119 patients suffering from skull-base meningiomas, who were evaluated by cerebral angiography. Only 54% were able to perform the embolization and about 10% were angiographically avascular[14]. To avoid unnecessary invasive procedure on relatively avascular tumors, prior to cerebral angiography, perfusion image by tomography or magnetic resonance should be considered, and the study of the anatomical relationships of the tumor with the neighboring arteries should be preserved in the subsequent surgical procedure.

Most intracranial tumors susceptible to preoperative embolization are attached to the dura and receive their vascular supply through vessels that adhere to it. Therefore, the anatomical relationships of the lesion with the dura should be carefully analyzed to establish the feasibility of the procedure.

Before planning the procedure, it should be taken into account that practically all of the dura matter of the supratentorial convexity is irrigated by the anterior and posterior divisions of the middle meningeal artery, whose endovascular occlusion is usually technically possible[10]. This artery also irrigates the dura mater that covers the lateral aspect of the anterior cranial fossa. The infratentorial convexity, on the other hand, is predominantly irrigated by the hypoglossal and jugular branches of the ascending pharyngeal artery, and the mastoid branch of the occipital artery. The meninges of the anterior cranial fossa are supplied medially by the anterior ethmoidal artery, posterior ethmoidal artery, olfactory branches of the anterior cerebral artery, recurrent branch of the ophthalmic artery, while more posterior aspect of the dura of the cranial fossa anterior is irrigated through the McConnell capsular arteries and the meningo-lacrimal artery[16]. We proposed a new algorithm of approximation for skull-base tumors including anterior cranial fossa (Figure 2).

In general, most of the vascularity of the lesions located in the middle cranial fossa gets supply from both the branches of the internal carotid artery (ICA) and the external carotid artery (ECA). Lateral dura of the middle fossa receives its irrigation more through the petrosal branch of the middle meningeal artery and the accessory meningeal and peri carotid arteries from the ascending pharyngeal artery. On the other hand, the sellae and retro lateral dura are supplied almost entirely by the McConnell capsular arteries, the dorsal meningeal branches and the inferolateral trunk of the internal carotid artery. In the infratentorial space, the dura is supplied by branches of the vertebral arteries and the ascending pharyngeal; the first supplies the suboccipital surface and the last supplies the dura mater that surrounds the lateral aspect of the cerebellopontine angle[16]. The tentorium, a relatively frequent site of hypervascular lesions, is mainly irrigated by the medial tentorial artery of Bernasconi-Cassinari and the lateral tentorial artery.

In the indication of preoperative embolization, realistic expectations of the procedure must be maintained[28]. Although most of the convexity tumors irrigated by the middle meningeal artery can be devascularized in entirety. In regard to tumors of the skull base, the risks can be unacceptably high. Medial tumors of the anterior fossa usually cannot be embolized safely because the supply comes from direct or indirect branches of the ICA, whose diameter is usually very small and its occlusion can lead to high risk of injuring healthy structures. There are, however, multiple reports of cases that have reported satisfactory occlusion of branches from the ophthalmic artery or branches of the cavernous segment of the internal carotid artery[29,30] either using particles 11 or embolizing liquid agents such as Onyx[4]. In a published series by Waldron *et al*. the occlusion of branches of the internal carotid could be performed in 18% of the identified nutritional vessels[14]. However, in other studies with similar percentages of occlusion, the complication rate was up to 12.6%, of which the majority are permanent[9]. The neurological sequelae are unacceptably high, considering that it is an optional procedure aiming to improve the results of definitive surgical treatment.

Some authors recommended that in attempt to occlude these branches, the balloon occlusion procedure can be performed according to the technique of Abdel-Karim *et al*., to achieve a stable catheterization and avoid the migration or reflux of the embolizing material from the target artery to its parent vessel; however, this practice has not been widely validated and, therefore, cannot be recommended[29].

6. Technical requirements

To ensure the effectiveness and safety of the procedure, the availability of angiographic equipment with the capability of real-time digital subtraction images, "road-mapping", as well as a detailed analysis of the angiographic images during the procedure is necessary.

All conventional projections of the internal and external carotid arteries and vertebral arteries should be carried out systematically, to determine the tumor vascularity and exclude the presence of anastomosis between the different arterial systems that can lead to the occlusion of a vessel and have implications when selecting the embolizing material.

Subsequently, we proceed with superior selective angiography, through which we can identify the angioarchitecture of the tumor in detail and confirm once again the absence of risky anastomoses or anatomical variants. Possible anastomoses between branches of the internal, external and vertebral carotid artery[30] of the most frequency and risk are as follows:

(1) Distal maxillary artery (ICA);

(2) Neuro meningeal trunk of the ascending pharyngeal (IX, X, and XI);

(3) Odontoid branch of the ascending pharyngeal (VA);

(4) Meningo lacrimal branch (ECA);

Once the branch to be embolized is supra-selectively catheterized, it is advisable to perform functional tests, which are essential when treating tumors at the skull base, particularly when they are related to exiting foramen of the cranial nerves. It can be performed by intermittent occlusion with balloons or with the injection of small doses of lidocaine or propofol when the patient is under neuroleptanalgesia. It is possible to induce permanent neurological deficits in a transitory and reversible way. Once these tests are done, it is possible to proceed with the application of the embolizing agent. During angiography, the contrast within the ICA and ECA will be performed to identify the blood supply, the type, number and geometry of the arteries directly related to the tumor, in the same way to evaluate the collateral circulation, the arterial complex anastomosis, relationship with cranial nerves, skin tissue involvement, flow dynamics, venous drainage among other aspects, which is crucial for correct performance of the procedure. The options available for these procedures are: Onyx at 18% and 34%; polyvinyl alcohol (Calibrated particles and ambo-spheres) -150-300 microns; Ethanol; gel Foam; coils of platinum.

7. Dangerous anastomosis

It has been suggested that if the occlusion is not complete, the benefit of embolization treatment appears to be minimal or non-existent. Suyama[31] Motozaki[32] and Watanabe[33] have experience of peritumoral hemorrhage as performing preoperative meningioma embolization and described other complications of tumor embolization including facial paralysis, pain in the scalp, skin necrosis. Embolization material towards the ICA has been reported, the presence of brain and tumor hemorrhage associated with embolization is rare. We also proposed a new score mechanism for embolization of skull-base tumors and we consider that this score mechanism must be validated, and should be carried out in an appropriate way to the tumor lesions of the skull base.

8. Conclusions

Preoperative vascularity reduction of skull-base tumors is a useful neurosurgical adjunct to minimize intra-operative blood loss, shorten the operative time and reduce risk of injury to neighboring neurovascular structures. Dural blood supply in relation to the tumor must be meticulously analyzed before selection of endovascular embolization procedure. The main objective of preoperative embolization of tumors is to produce tumor devascularization, augmentation of tumor necrosis at the precapillary level to reduce intra-operative bleeding, contributing to a more radical and feasible resection and minimizing chances of recurrence. After embolization, the surgery should be carried out only after 24 h at least, and within 7 d and never be delayed beyond that period, as the effect of embolization gradually vanishes due to the re-revascularization phenomenon of skull-base tumors. In relation to meningiomas, embolization can be considered as a low-risk procedure because vascular supply usually derived from the external carotid artery. The detailed anatomical knowledge of vascular anatomy is a prerequisite for the neuro-interventionist to carry out successful therapeutic embolization in the preoperative period.

Conflict of interest statement

The authors report no conflict of interest.

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