



Review

Preoperative embolization of carotid paragangliomas as a bridge to surgical resection: is the risk justified?

Embolización de paragangliomas carotídeos como terapia puente a la cirugía: ¿un riesgo necesario?

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Abstract

Carotid paragangliomas are neurocrine tumors of the carotid body, usually asymptomatic and benign but with the potential for local invasion. Due to their nature with highly vascularized stromal tissue and the risk of intraoperative bleeding, especially in larger ones (greater than 30 mm or Shamblyn II-III), preoperative endovascular embolization has become increasingly common. Recent reviews and meta-analyses analyze the benefits in terms of reduced bleeding, shorter surgical time, and lower postoperative complication rates, but the lack of solid evidence due to the absence of randomized studies does not allow for definitive recommendations on this matter. Our work aims to delve into the evidence regarding the risks and benefits behind this procedure and will attempt to establish a guideline for indications and management.

Keywords: Carotid paraganglioma. Carotid body tumor. Shamblyn. Transarterial embolization. Percutaneous embolization.

Resumen

Los paragangliomas carotídeos son un tipo de tumores poco frecuentes del cuerpo carotídeo de estirpe neuroendocrina, habitualmente asintomáticos y benignos, pero con capacidad de invasión local. Debido a su tejido estromal altamente vascularizado y al riesgo de hemorragia operatoria, sobre todo en aquellos de gran tamaño (mayores de 30 mm o Shamblyn II-III), es cada vez más frecuente la realización de un tratamiento mediante embolización endovascular preoperatoria. Las revisiones y los metaanálisis recientes analizan el beneficio en términos de disminución de sangrado, del tiempo quirúrgico y de la tasa de complicaciones posoperatorias, pero la ausencia de una evidencia sólida por la falta de estudios aleatorizados no permite llegar a recomendaciones absolutas sobre este tema. Nuestro trabajo busca ahondar en la evidencia sobre los riesgos y los beneficios que hay detrás de este procedimiento e intentará establecer una pauta de indicaciones y manejo.

Palabras clave: Paraganglioma carotídeo. Glomus carotídeo. Shamblyn. Embolización transarterial. Embolización percutánea.

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INTRODUCTION AND OBJECTIVE

Carotid body paragangliomas (CBPs) are a rare entity with complex management that is often shared with other specialties, such as otolaryngology or maxillofacial surgery. They are characteristically highly vascularized tumors with usually benign histopathological features but with the capacity for local invasion, which confers a risk of malignancy due to involvement of adjacent structures. Surgical resection is the treatment of choice. Radiotherapy is reserved as a suppressive (noncurative) alternative in inoperable cases. Conservative management in selected cases (small tumors, elderly patients, or those with significant comorbidities) may be beneficial, although the available evidence is limited (1).

The expansion of endovascular treatments has also changed management trends for these tumors, as it allows for a sequential approach aimed at reducing afferent vascular flow and, in theory, decreasing the risk of hemorrhage and perioperative complications associated with surgical resection.

Recent studies comparing outcomes in patients undergoing preoperative embolization (PE) vs those treated with direct surgical resection (SR) have yielded conflicting results and have not established clear recommendations to guide clinical decision-making.

The objective of this work is to review the available literature and update the evidence regarding preoperative endovascular management of this disease.

DEVELOPMENT

CBPs are rare neuroendocrine tumors arising from the carotid body. They are typically asymptomatic and benign but have the capacity for local invasion. They are located in the subadventitial plane of the carotid bifurcation and are characteristically highly vascularized. From an anatomical standpoint, CBP blood supply arises mainly from branches of the external carotid artery (ascending pharyngeal, superior thyroid, facial, and occipital arteries), although they may also receive supply from direct branches of the internal or external carotid artery (glomeric artery). Among these, the ascending pharyngeal artery is the most frequent source (2).

Shamblin and colleagues from the Mayo Clinic developed an anatomical classification for CBPs based on tumor extension and vascular involvement (3), which allows prediction of intraoperative technical difficulty and a higher risk of complications (Fig. 1). Type I tumors are localized at the bifurcation without encasing the internal or external

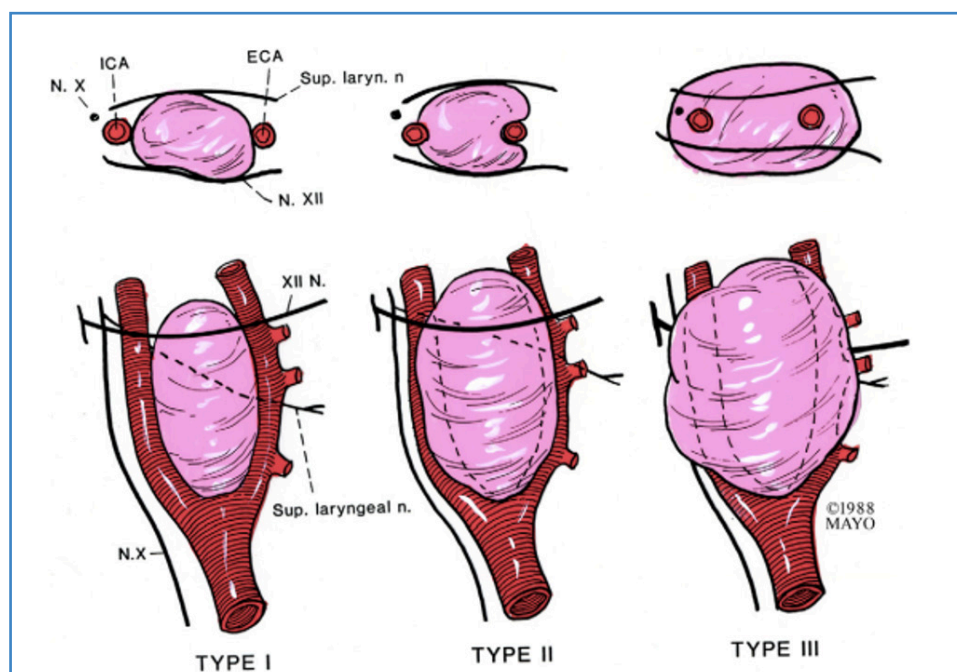


Figure 1. Shamblin classification of CBPs (3).

carotid arteries. Type II tumors partially surround the bifurcation, and in type III tumors both the internal and external carotid arteries are encased within the tumor. Surgical resection is the treatment of choice and has traditionally represented a challenge, particularly for large tumors and Shamblin II and III lesions, due to their high vascularity and proximity to neural structures.

The main complications associated with SR that have been studied include 30-day mortality, stroke rate, cranial nerve injury, and the need for surgical revision due to cervical hematoma. When stratified by Shamblin classification, complication rates are higher in type II and type III tumors, as demonstrated in a meta-analysis by Robertson et al. (4).

Embolization can be performed via transarterial approach (usually femoral access) or by direct percutaneous puncture of the tumor using an 18–22 G needle under fluoroscopic guidance, according to techniques described in detail by García Gutiérrez and González-Fajardo (5). Inflation of an occlusion balloon at the origin of the external carotid artery may be used as an adjunct to prevent retrograde passage of embolic materials into the internal carotid artery. The most widely used embolic agents include *n*-butyl cyanoacrylate (Magic Glue®; Balt, Montmorency, France), Glubran 2® (GEM Srl, Viareggio, Italy), ethylene-vinyl alcohol copolymer (EVOH) such as Onyx® (Medtronic, Irvine, CA, USA), Easyx® (Qmedics, Zurich, Switzerland), SquidPeri® (Emboflu, Zurich, Switzerland), polyvinyl alcohol (PVA), Gelfoam® (Pfizer, New York, NY, USA), microspheres, and coils (Fig. 2). Ethanol has shown good results for nidus occlusion; however, the risk of damage to adjacent tissues (tissue necrosis and nerve injury) makes it unsuitable as an embolic agent in this disease (6).

Although PE was first described in 1980 by Schick et al. (7), it is noteworthy that publications from the early 2000s rarely addressed embolization as a preoperative treatment; its mention becomes more frequent in later years. Given the rarity of this pathology, it is exceptional to find studies larger than case series or retrospective observational studies.

Among case review articles, the study by Cobb et al. (8) stands out due to patient volume. They conducted a retrospective cross-sectional review of patients treated with SR and those undergoing PE

between 2006 and 2013 across 5 US states considered representative of population characteristics. A total of 547 patients were identified, of whom 13.7% ($n = 75$) underwent preoperative embolization. The analyzed complications included overall mortality, stroke, cranial nerve injury, and blood loss. Mortality was very low, with only one death in the SR group, which did not result in statistically significant differences. Stroke rates were identical in both groups (4.1%), and cranial nerve injury rates were very low, with only 2 cases documented in the surgery-only group and none in the PE group, which the authors attributed to underreporting or coding limitations in the analyzed databases. Paradoxically, intraoperative blood loss was higher in the PE group, although this did not reach statistical significance. Analysis of the length of stay revealed longer admissions in the PE group; however, the authors did not specify whether embolization was performed on an outpatient basis or during hospitalization, nor the interval between embolization and surgery.

Several points are highlighted in this study. From a cost-effectiveness perspective, it is worth questioning whether the costs associated with longer lengths of stays and the embolization procedure outweigh the theoretical benefits of reduced complication rates (bleeding or cranial nerve injury), especially given that the study data did not demonstrate statistically significant differences. Additionally, the database did not allow stratification of patients by Shamblin classification or tumor size; larger or Shamblin III tumors are those most likely to undergo embolization. This could explain longer lengths stays or greater blood loss, although this remains speculative due to the lack of available data. The authors therefore conclude that PE does not confer benefits in terms of intraoperative blood loss, stroke rate, cranial nerve injury, or the length of stay.

Jackson et al. (9) published the first meta-analysis in 2015 to address the lack of evidence on this topic. They included 22 studies comprising a total of 578 patients and 607 tumors. Their results showed lower estimated intraoperative blood loss and shorter operative time in patients treated with PE vs DR. Subgroup analyses according to embolization technique, Shamblin classification, or length of hospital stay were limited by insufficient data in the included

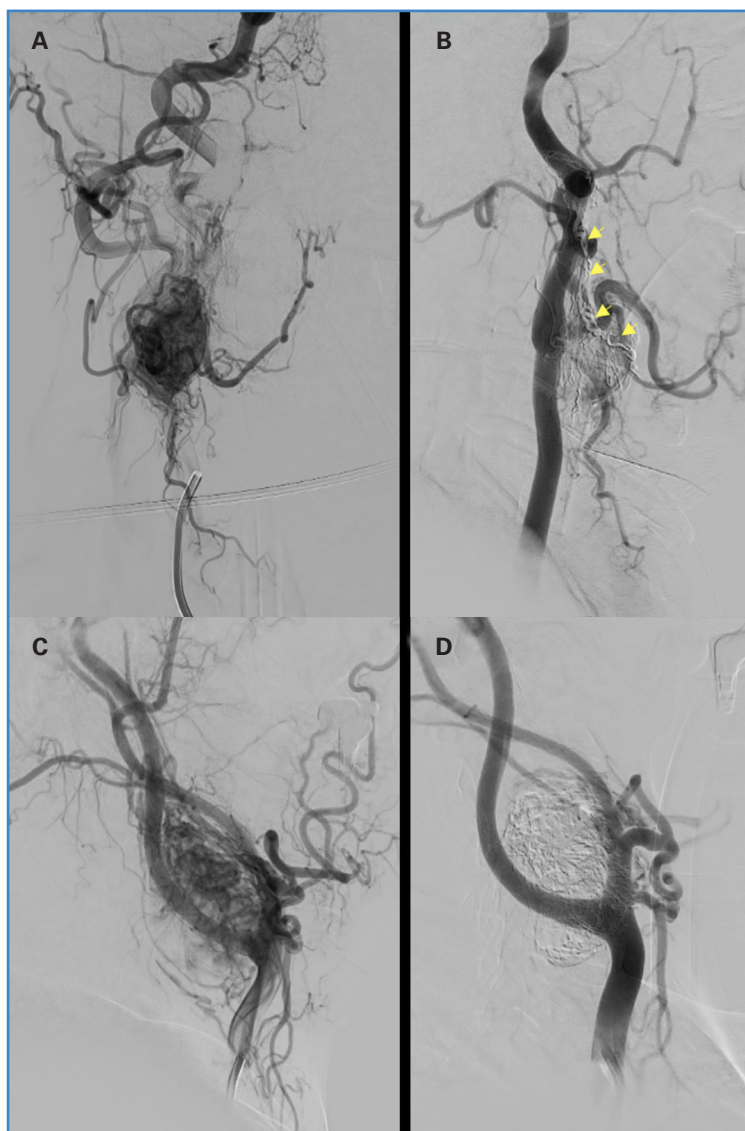


Figure 2. Pre- and post-embolization angiography of carotid body paragangliomas. A. Angiography of a Shamblin II paraganglioma. B. Embolization of a Shamblin II paraganglioma with Onyx® and protection of a neuromeningeal branch using coils (yellow arrows). C. Angiography of a Shamblin III paraganglioma. D. Post-embolization control angiography with Onyx®.

studies. No statistically significant differences were found with regard to surgical complications; the most frequent were vascular and nerve injuries. With respect to embolization-related complications, a rate of 2.5% (4 of 160 patients) was reported, including hypoglossal nerve palsy, transient aphasia, permanent vocal cord paralysis, and arterial dissection.

In parallel, Abu-Ghanem et al. (10) conducted a systematic review and meta-analysis published in 2016 with the same objective: to establish evidence on the benefits and risks of preoperative embolization. This analysis included 15 retrospective studies with a total of 470 patients. No statistically significant differences were found between PE and SR in estimated intraoperative blood loss, operative time,

or length of hospital stay. Although the PE group showed a higher risk of nerve injury and a lower risk of vascular injury and stroke compared with the SR group, these differences did not reach statistical significance.

Subsequently, in 2019, Robertson et al. (4) performed a systematic review and meta-analysis addressing the presentation, management, and periprocedural complications of CBPs according to the Shamblin classification. Among 4418 patients and 4743 documented tumors, approximately one-fifth (21%) were treated with PE. In the comparative analysis between SR and PE, no statistically significant differences were observed in reintervention for hematoma or wound bleeding, although the

authors noted difficulties in calculating odds ratios and potential bias due to the small number of patients. A subanalysis of 16 patient series, including 472 individuals, found no statistically significant differences in blood loss between patients undergoing PE and those treated with DR. Other outcomes, such as perioperative complications according to embolization status, length of stay, and operative time, were not analyzed.

Furthermore, in 2019, Texakalidis et al. (11) published a systematic review and meta-analysis evaluating the role of preoperative embolization, including 25 retrospective observational cohort studies with a total of 1326 patients, of whom 830 underwent PE and 496, DR. The results were heterogeneous. The analysis demonstrated significantly lower intraoperative blood loss and shorter operative time in the PE group. However, funnel plot analysis suggested publication bias. Other variables, including cranial nerve injury, risk of stroke or transient ischemic attack (TIA), and length of stay, did not show statistically significant differences. Two subgroup analyses were performed: one according to Shamblin classification and another according to the interval between embolization and surgical resection. No differences were found among Shamblin I, II, and III tumors with or without PE. Regarding timing, only the subgroup undergoing surgery 24 to 48 hours after embolization was available vs DR, and this subgroup showed a significantly shorter length of stay. A meta-regression analysis assessing the effect of tumor size on postoperative outcomes confirmed that tumor size, regardless of embolization status, was a predictor of greater blood loss. Other complications, such as cranial nerve injury, vascular injury, and stroke rate, were not influenced by tumor size. Importantly, the authors emphasized that although greater blood loss was observed in the SR group, this difference did not appear to be clinically relevant.

González-Urquijo et al. (12) sought to address the lack of multicenter studies on PE outcomes by establishing an international registry for Spanish-speaking countries (CAPACITY), including patients with CBPs treated with or without PE. The analysis published in 2023 included patients from 11 hospitals in Mexico, Ecuador, Bolivia, and Spain who were treated from January 2010 through December 2019. A total of

1432 patients were included, with an approximate 6:1 ratio of SR to PE. PE was performed at the discretion of the treating surgeon, primarily in Shamblin II and III tumors. The results demonstrated a statistically significant association between PE and reduced perioperative blood loss and lower hematoma rates, with similar operative times in both groups and no differences in perioperative stroke or nerve injury rates.

Most studies attempting to clarify the benefit of PE analyze outcomes irrespective of Shamblin classification, which may introduce bias given the intrinsic surgical complexity of Shamblin III tumors. For this reason, Napoli et al. (13) published a meta-analysis specifically evaluating the effect of PE separately in Shamblin II and Shamblin III tumors. Five studies involving a total of 245 patients were included; 121 underwent PE and 124 underwent DR. When data were analyzed collectively, lower blood loss was observed in the PE group, with no difference in operative time. However, when stratified by Shamblin grade, no statistically significant differences were found in surgical blood loss or operative duration, although a clear trend favoring PE was noted in both groups. The authors highlighted several limitations, including the small number of studies and patients available for subgroup analysis, publication bias detected by funnel plot analysis, and the potential influence of the learning curve. In addition, details regarding embolic materials and techniques were largely unavailable, although PVA appeared to predominate in the included studies.

Finally, the most recent and comprehensive analysis was published by Wang et al. (14). This systematic review included 155 studies with 9291 patients and 9862 tumors. Regarding preoperative embolization, the authors reported a higher incidence of stroke in the PE group, without an associated increase in mortality compared with DR. Statistically significant differences were also observed in favor of PE with respect to lower estimated intraoperative blood loss and shorter operative time. Other outcomes—including length of stay, need for carotid repair, TIA rate, hematoma formation, cranial nerve injury, need for transfusion, and other adverse events—did not differ significantly between groups. The authors concluded that routine embolization

of paragangliomas is not recommended due to the increased risk of stroke, despite reductions in blood loss and operative time.

Table I illustrates the main parameters evaluated in the abovementioned studies.

The interval between embolization and surgery has also been investigated and remains a matter of debate. Inflammation and edema following embolization typically resolve within 1 to 2 days; however, partial reperfusion of embolized vessels may occur during this period. In a retrospective study by Li et al. (15), patients undergoing carotid body paraganglioma resection after embolization were divided into three groups according to the interval between embolization and surgery (1, 2, or 3 days), and surgical parameters were analyzed. Non-embolized patients were not included in the comparison, and differences according to embolic material were not assessed. Among the 103 patients included, most underwent surgery 24 hours after embolization ($n = 76$), with no significant differences in patient characteristics or tumor size among groups. A progressive increase in blood loss and operative duration was observed from group 1 to group 3. No differences were found in the need for vascular repair or in the rate of adverse events.

Several Japanese groups have proposed early SR, performed approximately 3 hours after embo-

lization, and have compared their outcomes with those of studies in which surgery was delayed for more than 24 hours. Katagiri et al. (16) reported a series of 16 patients who underwent PE via transfemoral transarterial access using gelatin particles (Gelpart®; Nippon Kayaku, Tokyo, Japan). Their analysis demonstrated a mean tumor volume reduction of 46% (range, 7%–76%) and showed reduced intraoperative blood loss, although no reduction in surgical time was observed. Using a similar embolization technique, Tamura et al. (17) concluded that PE was associated with shorter surgical time and lower blood loss vs previously published series, and they demonstrated a statistically significant reduction in tumor size. In contrast, Acuña-Pinzón et al. (18) conducted a retrospective study of 33 patients with CBPs, of whom 51.5% underwent PE with Gelfoam® via transfemoral transarterial access 3 hours prior to surgery, and compared them with patients who did not undergo embolization. In this study, no statistically significant differences were observed in complication rates, intraoperative blood loss, or operative time across groups.

Regarding embolization materials, there are few comparative studies that clarify the superiority of one agent over another, and this variable is not analyzed in detail in the previously cited meta-analyses and systematic reviews. Overall, PVA is the most fre-

Table I. Statistically significant differences between embolization and non-embolization groups in major meta-analyses

Study	<i>n</i>	Blood loss	Length of stay	Surgical time	Complications
Jackson et al.	607	Yes	Inconclusive	Yes	No
Abu-Ghanem et al.	407	No	No	No	No
Robertson et al.	4743	No	Not evaluated	Not evaluated	Not evaluated
Texakalidis et al.	1326	Yes	No	Yes	No
González-Urquijo et al.	1432	Yes	Not evaluated	No	No
Napoli et al.	245	Yes	Not evaluated	No	Not evaluated
Wang et al.	9862	Yes	No	Yes	Yes*

NC: inconclusive due to insufficient data; NE: not evaluated. *Wang et al. reported a higher rate of stroke in the PE group (statistically significant), but did not find a lower rate of postoperative complications in the embolization group vs the non-embolization group.

quently reported embolic agent. However, in recent years, a growing trend toward the use of Onyx® has been observed. The study by Economopoulos et al. (19) (2015) reviewed all embolized cases published up to that time but did not perform comparisons between embolic materials. In the CAPACITY registry reported by González-Urquijo et al. (12), PVA was the most widely used agent (54 patients, 68.4%), followed by microcoils ($n = 21$; 26.6%) and Onyx® ($n = 4$; 5%). No comparative analysis between embolic agents was performed, and because the embolization-related complication rate was 0%, no assessment of relative risk according to material was possible. The use of occlusion balloons to prevent embolic material migration has been described in several reports; however, no comparative studies have evaluated the systematic efficacy of this technique (6).

Regarding embolization access routes (transarterial vs transcatheter direct puncture), Griauszde et al. (20) compared transarterial embolization using various materials (particles, coils, and Onyx®) with direct percutaneous Onyx® embolization in 17 patients. Intraoperative blood loss was greater in the transarterial embolization group than in the percutaneous group. Other outcomes, including length of hospital stay and operative time, did not differ significantly. Although the percentage of tumor embolization did not differ significantly between techniques, there was a trend toward higher technical success with direct puncture Onyx® embolization (98%) vs transarterial embolization (84%).

CONCLUSIONS

PE of CBPs is an increasingly used strategy that is not without risk. Based on the current literature, PE may reduce intraoperative blood loss and operative time, but it has not consistently demonstrated a reduction in postoperative complication rates.

Recent advances in embolization techniques and materials are not adequately reflected in the available retrospective studies, which may lead to underestimation of their true benefit. Currently, the embolic agents and approaches with the greatest supporting evidence are PVA and Onyx®, delivered via transarterial embolization (most common-

ly through femoral access) or transcatheter direct puncture. Selected cases may benefit from the use of coils or protective balloon occlusion to prevent embolic migration. Minimizing the interval between embolization and surgery may reduce hospital stay and intraoperative bleeding, particularly in patients undergoing transcatheter embolization.

Ultimately, appropriate patient selection based on tumor size and Shamblin classification, together with prospective studies evaluating modern embolic materials and techniques performed by experienced operators who have surpassed the learning curve, may yield results more consistent with the anticipated clinical benefit. Until such evidence is available, and given the ongoing controversy, selective and individualized use of PE based on a careful assessment of risks and benefits appears to be the most appropriate approach.

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