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Meta-Analysis of the Effects of Preoperative Embolization on the Outcomes of Carotid Body Tumor Surgery

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Abstract: Background: Carotid body tumors (CBTs) are situated at the bifurcation of the common carotid artery within the adventitia, and are reported to be the most common head and neck paragangliomas. Surgery is the gold standard for curative treatment of respectable CBTs and is recommended in otherwise healthy patients because of the risk of local complications related to tumor size and a small but definite risk of malignancy. Preoperative embolization has been shown to reduce potential intraoperative blood loss and provide the surgeon with greater ease and safety in excising the tumor, thus reducing the operation time and morbidity. However, other physicians have stated that although blood loss may be reduced after preoperative embolization, transfusion requirements are not affected, and that the embolization procedure adds a significant risk for stroke. Therefore, the purpose of the current study was to compare the surgical outcomes of patients undergoing CBT surgical resection with and without preoperative embolization. Aim: To evaluate the need for preoperative embolization for the treatment of carotid body tumour. Methodology: A meta-analysis study is done to compare the surgical outcomes of patients undergoing CBT surgical resection with and without preoperative embolization. Results: Our meta-analysis for evaluation of the effects of preoperative embolization on the outcomes of carotid body tumour surgery, included (14) studies with a total number of patients (n=477). The results of these studies showed no statistically significant difference between preoperative embolization group and non embolization group in carotid body surgery for (blood loss & operation time). Preoperative embolization did not reduce risk of postoperative complications. Conclusion: Preoperative embolization shows no statistically significant reducing in blood loss and operation time, also embolization does not decrease incidence of postoperative complications.

[Mohamed Magdy Samir, Tamer Abd ElWahab Abo Elezz, Peter Milad Mikahail and Mohamed Khaled Shafeek Bassam. **Meta-Analysis of the Effects of Preoperative Embolization on the Outcomes of Carotid Body Tumor Surgery.** *Nat Sci* 2019;17(11):158-163]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 19. doi:10.7537/marsnsj171119.19.

Keywords: Carotid Body Tumor, Preoperative Embolization, Vascular Tumors Management, Carotid Body Tumor Surgery, Carotid Body Tumor Radiotherapy

1. Introduction

Carotid body tumors (CBT) are rare tumor originating from carotid body. Carotid body lies in the adventitia at the bifurcation of common carotid arteries. Most of the blood supply of carotid body originates from external carotid artery through Mayer ligament.

CBT are the commonest paragangliomas of head and neck region and have been variously named chemodectomas and glomus tumors as well. [(1)]

Surgery is considered most effective mode of treatment. Surgery of these tumors can be challenging and used to be associated with significant mortality and morbidity because of their vascularity, involvement of internal carotid artery and proximity to cranial nerves. [(2)]

It is known that the indications of angiography with embolization performed less than 48 hr before surgery include a reduction in tumor size, which reduces blood loss, operating time, and that also facilitates the surgical dissection. [(3)]

In this study, the researchers will compare the surgical outcomes of patients undergoing CBT surgical resection with and without preoperative embolization.

Aim of the Work

The aim of this study is to point out the surgical outcomes (operation time, intraoperative blood loss, postoperative complications) of patients undergoing CBT surgical resection with and without preoperative embolization.

2. Material and Methods

This study was done in the following steps:

- Determination of the target subject.
- Identification and Location of articles.
- Screening and evaluation of the articles.

- Data collection.
- Data analysis.
- Reporting and interpretation (of the results).
- Discussion and conclusion.

I) Target subject: patients with carotid body tumor and underwent surgical resection.

II) Identification and location of articles: We will revise and sort Published medical studies about the effects of preoperative embolization on carotid body tumor surgery, Medline database and Cochrane library in English language and in the last 30 years (1988-2018) then choose suitable ones according to mentioned criteria.

Using a combination of the following key words:

1- Carotid body tumors.
2- Preoperative embolization .
3- Vascular tumors .
4- Surgery for carotid body tumors

III) Screening and evaluation of articles: The screening form of articles was used to screen the articles, which were yielded by the Medline search after blinding the author name and journal name.

The inclusion criteria included articles:

- Published in English language.
- In the last 30 years.
- Conducted on human subjects.
- Patients with a diagnosis of carotid body tumors.
- Patients underwent surgical resection of carotid body tumor.

Excluded articles:

Articles which miss one or more of the above mentioned inclusion criteria, like articles not concerned in outcome evaluation; articles not in English and articles of other vascular tumor or radiotherapy treatment

IV) Data collection:

Information was gathered for each individual study about effects of preoperative embolization on carotid body tumor surgery.

Statistical methods:

Statistical considerations:

Evaluation and sorting of outcome results from included trials will be combined using the Review Manager Software, statistical bias will be considered and evaluated, collective statistical analysis will be done in a single arm statistical results.

Testing for heterogeneity:

Studies included in meta-analysis were tested for heterogeneity of the estimates using the following tests: **Cochran** <0.1) denoted heterogeneity among the studies, **I-square (I^2) index which is interpreted as follows:** I^2 = 0% to 40%: unimportant heterogeneity, I^2 = 30% to 60%: moderate heterogeneity, I^2 = 50% to 90%: substantial heterogeneity, I^2 = 75% to 100%: considerable heterogeneity.

Examination of publication bias:

Publication bias was assessed by examination of funnel plots of the estimated effect size on the horizontal axis versus a measure of study size (standard error for the effect size) on the vertical axis.

3. Results

1- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of intraoperative blood loss.

Comparison between intraoperative blood loss in preoperative embolized group and non embolized group, included (8) studies with a total number of patients (n=276). Studies included in meta-analysis were tested for heterogeneity of the estimates using Cochran Q chi square test: A statistically significant test (p-value <0.1) denoted heterogeneity among the studies. Incidence of events was presented as proportions with their 95% confidence limits (95% CI) were pooled using the DerSimonian laird random-effects method (REM) and the Mantel-Haenszel fixed-effects method (FEM). Because of the presence of significant heterogeneity, there is no significant difference between intraoperative blood loss in embolized group and non embolized group (Table 1). Pooling with random effects model (REM) shows no statistically significant difference between embolization and non-embolization (SMD = -0.22, 95% CI = -0.85 to 0.40, P-value = 0.48). Funnel plot for blood loss. There is no evidence of publication bias.

2- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of operation time.

Comparison between operation time in preoperative embolized group and non embolized group, included (5) studies with a total number of patients (n=209). Studies included in meta-analysis were tested for heterogeneity of the estimates using Cochran Q chi square test: A statistically significant test (p-value <0.1) denoted heterogeneity among the studies.

Incidence of events was presented as proportions with their 95% confidence limits (95% CI) were pooled using the DerSimonian laird random-effects method (REM) and the Mantel-Haenszel fixed-effects method (FEM). Because of the presence of significant heterogeneity, there is no significant difference between operation time in embolized group and non embolized group (Table 2).

Pooling with random effects model (REM) shows no statistically significant difference between embolization and non-embolization (SMD = -0.33, 95% CI = -0.88 to 0.23, P-value = 0.25). Funnel plot

for operative time. There is no evidence for publication bias.

Table 1. Meta-analysis for blood loss

Study	SMD	SE	Variance	95% CI		Z-Value	p-Value
				Lower limit	Upper limit		
Dardik 2002 [8]	-0.89	0.51	0.26	-1.89	0.11	-1.75	0.08
Ikeda 2017 [15]	1.11	0.27	0.08	0.58	1.65	4.06	<0.01
Kasper 2006 [9]	0.03	0.40	0.16	-0.75	0.82	0.08	0.93
LaMuraglia 1992 [5]	-0.64	0.52	0.27	-1.66	0.38	-1.24	0.22
Li 2010 [11]	-0.72	0.26	0.07	-1.24	-0.21	-2.74	0.01
Little 1996 [6]	0.32	0.44	0.19	-0.54	1.18	0.72	0.47
Ozay 2008 [10]	-0.13	0.56	0.31	-1.23	0.96	-0.24	0.81
Ward 1988 [4]	-1.23	0.56	0.31	-2.33	-0.13	-2.19	0.03
REM	-0.22	0.32	0.10	-0.85	0.40	-0.71	0.48
Test of heterogeneity							
Q-value	33.675						
df (Q)	7						
P-value	<0.001						
I-squared	79.213%						

SMD = standardized mean difference, SE = standard error, 95% CI = 95% confidence interval, REM = random effects model, df (Q) = degree of freedom

Table 2. Meta-analysis for operative time

Study	SMD	SE	Variance	95% CI		Z-Value	p-Value
				Lower limit	Upper limit		
Ikeda 2017 [15]	-0.16	0.26	0.07	-0.67	0.36	-0.61	0.54
Law 2017 [16]	-0.03	0.46	0.21	-0.93	0.86	-0.08	0.94
Li 2010 [11]	-0.57	0.26	0.07	-1.08	-0.06	-2.18	0.03
Little 1996 [6]	0.57	0.45	0.20	-0.31	1.44	1.27	0.20
Ward 1988 [4]	-1.79	0.61	0.37	-2.98	-0.61	-2.96	<0.01
REM	-0.33	0.28	0.08	-0.88	0.23	-1.14	0.25
Test of heterogeneity							
Q-value	11.54						
df (Q)	4						
P-value	0.021						
I-squared	65.339%						

SMD = standardized mean difference, SE = standard error, 95% CI = 95% confidence interval, REM = random effects model, df (Q) = degree of freedom

3- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of postoperative complications.

Comparison between postoperative complications in preoperative embolized group and non embolized group, included (12) studies with a total number of patients (n=435).

Studies included in meta-analysis were tested for heterogeneity of the estimates using Cochran Q chi square test: A statistically significant test (p-value <0.1) denoted heterogeneity among the studies.

Incidence of events was presented as proportions with their 95% confidence limits (95% CI) were pooled using the DerSimonian laird random-effects method (REM) and the Mantel-Haenszel fixed-effects method (FEM).

Because of the presence of significant heterogeneity, there is marginal significant difference between postoperative complications in embolized group and non embolized group favours non embolized group (Table 3).

Table 3. Meta-analysis for incidence of complications

Study	Odds ratio	95% CI		Z-Value	p-Value
		Lower limit	Upper limit		
Bercin 2015 [14]	6.667	0.487	91.331	1.421	0.155
Dardik 2002 [8]	2.286	0.216	24.140	0.687	0.492
Ikeda 2017 [15]	1.533	0.546	4.304	0.812	0.417
LaMuraglia 1992 [5]	0.200	0.014	2.876	-1.183	0.237
Law 2017 [16]	1.000	0.127	7.893	0.000	1.000
Li 2010 [11]	0.625	0.128	3.060	-0.580	0.562
Liapis 2000 [7]	1.667	0.109	25.433	0.367	0.713
Little 1996 [6]	1.200	0.216	6.676	0.208	0.835
Power 2012 [13]	3.035	1.183	7.784	2.311	0.021
Ward 1988 [4]	0.300	0.025	3.626	-0.947	0.344
Zeitler 2010 [12]	2.786	0.373	20.819	0.998	0.318
Zhang 2018 [17]	2.000	0.382	10.482	0.820	0.412
REM	1.613	1.002	2.597	1.968	0.049
Test of heterogeneity					
Q-value	9.096				
df (Q)	11				
P-value	0.613				
I-squared	0.000%				

SMD = standardized mean difference, SE = standard error, 95% CI = 95% confidence interval, REM = random effects model, df (Q) = degree of freedom

Pooling with random effects model (REM) shows marginally significant difference between embolization and non-embolization that favours non-embolization (OR = 1.613, 95% CI = 1.002 to 2.597, P-value = 0.049).

Funnel plot for incidence of complications. There is no evidence for publication bias.

4. Discussion

Carotid body tumor (CBT) is a rare disease derived from carotid body paraganglion cells. The characteristic feature of this tumor is a rich vascular network in its contents and capsule supplied by many feeding arteries.

Angiography of the carotid system was the final diagnostic method for these lesions. Today, the diagnosis can be made with MR imaging in axial and coronal planes. The settings should include gadolinium-enhanced three-dimensional time-of-flight sequences, which demonstrates the extension of the tumor in relation to the carotid arteries and the involvement of the base of the skull. Additionally, MR imaging provides a perfect screening tool for multifocal (i.e., occult) head and neck paragangliomas.

Magnetic resonance imaging and MR angiography provide good insight into the vascularization of the tumor and the origin and contribution of the several branches of the external carotid. Differential diagnosis, including other vascular or nonvascular tumors in the neck, can also be made. This includes branchial cleft cysts, metastatic carcinomas, lymphomas, schwannomas, salivary gland tumors, and carotid artery aneurysms.

Angiography, though no longer the first-line imaging method, remains valuable for preoperative evaluation, and the possibility of preoperative embolization. Angiography can confirm the diagnosis and can provide information about the vascular supply of the paraganglioma, the status of the carotid arteries (e.g., stenosis, irregularity), and the patency of the circle of Willis.

Shamblin classification has been widely used by physicians as a predictor of vascular morbidity and for surgical decision-making. A directly proportional relationship of the Shamblin group with blood loss and surgical time has also been reported.

Surgery is the only curative treatment for carotid body tumors. Surgery of carotid body tumors should not be undertaken without careful preparation and the patient's consent.

Alternatively, radiotherapy has been advocated with good results in local tumor control, although the definition of successful treatment is difficult in such an indolent neoplasm**.** Other investigators claim the tumor is not radiosensitive because there is no direct cell-killing effect, and report regrowth of initially regressed carotid body tumor. Moreover, radiation therapy rapidly leads to substantial sclerosis and

fibrosis that complicate future surgery and in the long run may carry the risk of an induced malignancy.

The primary purpose of tumor embolization is to allow a successful complete resection of such a vascular tumor, as the control of bleeding can be quite challenging.

Our meta-analysis for evaluation of the effects of preoperative embolization on the outcomes of carotid body tumor surgery included (14) studies with a total number of patients (n=477). The results of these studies showed no statistically significant difference between preoperative embolized group and non embolized group in carotid body surgery regarding blood loss or operation time. Preoperative embolization did not reduce the risk of postoperative complications.

1- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of intraoperative blood loss.

Comparison between intraoperative blood loss in preoperative embolized group and non embolized group, included eight studies with a total number of patients (n=276), there was no significant difference between intraoperative blood loss in embolized group and non embolized group.

Our results are supported by ***Law et al.*** [16], ***Zeitler et al.*** [12], whom studies showed that there were no significant difference in operative bleeding between those patient who underwent preoperative embolization before CBT surgical excision and those who did not undergo preoperative embolization. Their patients were equally matched for tumor size to eliminate the possibility of confounded results. These studies showed that Shamblin classification was significant in predicting difficulty of the operation but could not predict the occurrence of postoperative complications.

Conversely, ***Ikeda and his group*** [15], ***Ward et al.*** [4] proved that, the most frequent feeding artery of these CBTs was the ascending pharyngeal artery. Preoperative embolization of these feeding arteries was effective to reduce blood loss. However, no statistical analysis was performed for these small cohorts of patients.

2- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of operation time.

Comparison between operation time in preoperative embolized group and non embolized group included five studies with a total number of patients (n=209). there is no significant difference between operation time in embolized group and non embolized group.

Our results is supported by ***Zeitler et al.*** [12], ***Ozay et al.*** [10] whom studies showed that the intraoperative blood loss and operation time was reduced in patients who underwent preoperative embolization, but the difference did not reach statistical significance. These studies showed that, angiography can provide an "arterial map" that can assist in surgical planning, also it can aid in the identification of prognostic variables such as carotid wall abnormalities, luminal compromise, and tumor size. Surgical resection is the treatment of choice for carotid body tumors. Observation of these tumors is not recommended because progressive growth is associated with increased risk of neurological deficits.

Conversely, ***Liapis et al.*** [7], ***La Muraglia et al.*** [5] their results proved that, preoperative embolization is helpful by decreasing intraoperative bleeding & operation time and showed a significant reduction in intraoperative bleeding in patients who underwent embolization before surgical resection of CBTs in comparison to patients who had surgery alone. Diminishing intraoperative blood loss & operation time through complete and careful embolization and use of intraoperative EEG monitoring along with surgical technique. The limitations of the these studies were the retrospective nature of the publications and the small number of study groups available for inclusion.

3- Comparison of preoperative embolized group vs. non embolized group in carotid body surgery as regards incidence of postoperative complications.

Comparison between postoperative complications in preoperative embolized group and non embolized group, that included twelve studies with a total number of patients (n=435).

There was marginal significant difference between postoperative complications in embolized group and non embolized group favours non embolized group, so embolization did not reduce risk of postoperative complications.

Our results are supported by **Bercin et al.** [14], ***Power et al.*** [13], whom studies showed that, the benefits of transarterial embolization before surgical excision of carotid body tumor are controversial, and also it does not appear to be an advantage in reducing intraoperative blood loss, ease of dissection, and reducing the duration of the operative procedure following embolization. Furthermore, the risk of vascular rupture rate is increasing during dissection. According to the results of their study, transarterial preoperative embolization of CBT does not seem to be helpful.

Conversely, ***Zhang et al.*** [17] showed reduction in rate of complications after angiography or embolization. The median blood loss, operation time, and hospital stay of the embolized group were significantly reduced ($P < 0.05$), in comparison to the non embolized group. These results suggest that preoperative embolization can reduce intraoperative

blood loss significantly and that hemostasis can easily be achieved during resection of CBTs when the course of the ascending pharyngeal artery is taken into consideration. Preoperative angiography with embolization showed less nerve injury compared with the non embolized group. Their study showed no evidence of significant heterogeneity or publication bias.

Conclusion

Preoperative embolization can non significantly reduce blood loss and shorten operation time but does not decrease incidence of postoperative complications.

References

1. Joseph, Terry A, John DK. Primary Neoplasms of the neck. [Book Auth.] Bruce Haughey, Regan Thomas and Lee Harker Charles Cummings. Cummings Otolaryngology: Head & Neck Surgery. St Louis: 4th Ed. St Louis: Elsevier-Mosby; 2005.
2. Kim GY, Lawrence PF, Moridzadeh RS, Zimmerman K, Munoz A, Luna- Ortiz K. New predictors of complications in carotid body tumor resection. J Vasc Surg 2017; 65(6): 1673-79.
3. Persky MS, Setton A, Niimi Y, Hartman J, Frank D, Berenstein A. Combined endovascular and surgical treatment of head and neck paragangliomas—a team approach. Head Neck 2002;24:423–31.
4. Ward PH, Liu C, Vinuela F, Bentson JR. Embolization; an adjunctive measure for removal of carotid body tumors. Laryngoscope 1988;98:1287–91.
5. La Muraglia GM, Fabian RL, Brewster DC, Pile-Spellman J, Darling RC, Cambria RP, et al. The current surgical management of carotid body paragangliomas. J Vasc Surg 1992;15:1038–45.
6. Little VR, Reilly LM, Ramos TK. Preoperative embolization of carotid body tumors: when is it appropriate. Ann Vasc Surg 1996;10:464–8.
7. Liapis CD, Evangelidakis EL, Papavassiliou VG, Kakiskas JD, Gougoulakis AG, Polyzos AK, et al. Role of malignancy and preoperative embolization in the management of carotid body tumors. World J Surg 2000;24:1526–30.
8. Dardik A, Eisele DW, Williams GM, Perler BA. A contemporary assessment of carotid body tumor surgery. 2002 Jul-Aug;36(4):277-83.
9. Kasper GC, Welling RE, Wladis AR, Ca Jacob DE, Grisham AD, Tomsick TA, et al. A multidisciplinary approach to carotid paragangliomas. Vasc Endovascular Surg 2006–2007;40:467–74.
10. Ozay B, et al. Acta chir Belg. surgery of carotid body tumor: 14 cases in 7 years 2008: 107-11.
11. Jiaping Li, MD, Shenming Wang, MD, Chishing Zee, MD, Jianyong Yang, MD, Preoperative Angiography and Transarterial Embolization in the Management of Carotid Body Tumor: A Single-Center, 10-Year Experience 2010: 947-8.
12. Zeitler DM, Glick J, Har-El G. Preoperative embolization in carotidbody tumor surgery: is it required? Ann Otol Rhinol Laryngol 2010;282-5.
13. Adam H. Power, MD, Thomas C. Bower, MD, Jan Kasperbauer, MD, Michael J. Link, MD, Impact of preoperative embolization on outcomes of carotid body tumor resections 2012: 987:34.
14. Sami Bercin, Togay Muderris, Ergun Sevil, Fatih Gul, Aydan Kılıcarslan, Muzaffer Kiris, Efficiency of preoperative embolization of carotid body tumor 2015: 226: 5.
15. Ikeda A, Shiga K, Katagiri K, Saito D, Miyaguchi J, Multi-institutional survey of carotid body tumors in Japan. 2017: 5324-7.
16. Law Y, Chan YC and Cheng SW. Surgical management of carotid body tumor – Is Shamblin classification sufficient to predict surgical outcome. 2017: 189-6.
17. Zhang WJ, Yong-Li L, Bing L and Tatsuo Y. Perioperative management of carotid body tumor Approach in the Surgical 2012; 780-8.

9/3/2019