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REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY

ISSN: 1507-1367

e-ISSN: 2083-4640

Debulking surgery prior to stereotactic radiotherapy for head and neck paragangliomas

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DOI: 10.5603/rpor.101802

Article type: Research paper

Published online: 2024-08-12

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Running title: Surgery for head and neck paragangliomas

DOI: 10.5603/rpor.101802

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Abstract

Background: Surgery has been used as standard treatment for head and neck paragangliomas. Stereotactic radiotherapy (SRT) has also been increasingly used for this disease. The results for combined modality are not well described. This analysis aims to describe the results for combined modality of debulking surgery and SRT for head and neck paragangliomas (HNP).

Materials and and methods: Retrospective cohort of patients treated in a large university hospital between 2008 and 2023.

Results: Fifty-one patients had their charts reviewed. Mean age was 56.3 years. Most were female (82.3%). Most lesions arose from the skull-base (84.3%) and not the inner ear. Most lesions were larger than 3 cm (51.0%) and mean lesion size was 4.4 cm. 36 (70.6%) were treated with radiotherapy alone while 15 (29.4%) were treated with combined modality treatment. Median follow-up was 42.5 months (7.1–112.8 months). There were no reported deaths nor disease progression. Debulking surgery did not impact response rate for SRT

(52.8% *vs.* 47.2% for SRT alone and debulking surgery, respectively, p = 0.971). There was no impact on new neurological deficits after SRT (25.0 *vs.* 13.3%, respectively, p = 0.356).

Conclusion: Debulking surgery did not improve response rate for SRT. In our sample, it also did not impact new neurological deficits for SRT. Prospective data regarding HNP treatment is needed.

Key words: paraganglioma; tumor; carotid body; stereotactic radiosurgery

Background

Treatment for head and neck paragangliomas (HNP) is still a debatable issue due to the lack of good quality data. These tumors arise from cells derived from the neural crest and its anatomical distribution follows the migration of such cells in close relation to the sympathetic nervous system [1]. However, the data supporting any approach has always been of low quality.

The natural first option for treatment of these highly vascular lesions was surgery, particularly smaller lesions with easy surgical access, with a lower burden of expected residual deficit. A large systematic review with meta-analysis of over 3498 patients has assessed the impact of surgery compared to stereotactic radiotherapy (SRT) [2]. Even though surgery is far more favored over SRT, chances of control by surgery are lower (85% compared to 93%), and chances of complication for surgery are over 25%. The quality of this evidence, however, is poor and based mostly on retrospective data of small studies.

Previous systematic reviews have assessed the role for SRT in this setting. Another systematic review based on retrospective data compared a small number of patients and described outcomes for disease control (achieved in 92% of patients and symptom control in 93%) and toxicities (8% rate) from SRT [3]. The results, however, must be considered with caution due to the low quality of the data.

None of those reviews, nonetheless, have addressed results for combined modality treatment of debulking surgery and SRT. In this study, we aim to retrospectively compare the results for combined modality and SRT to treat HNP.

Materials and methods

We retrospectively reviewed all patients with diagnosis of head and neck paraganglioma treated with radiation in a single university hospital from July 2008 to January 2023.

Patients were divided into two groups based on radiosurgery technique. Group 1 was treated with radiotherapy (RT) only while Group 2 was treated with surgery before RT. Biopsies were not routinely done due to the bleeding risks involved with paragangliomas. Debulking surgery was considered as any attempt of removal of the primary tumor that resulted in a macroscopic residue that was still symptomatic. RT could be delivered by either single-dose stereotactic radiosurgery with dose of 15 Gy, in a hypofractionated regimen of 25 Gy in 5 fractions or fractionated stereotactic RT in 20 to 30 fractions of 1.8 to 2 Gy in a total of 40 to 54 Gy. The choice for which method [stereotactic radiosurgery (SRS) or fractionated radiotherapy (FRT)] would be performed was decided in a multidisciplinary board. The choice between methods was based on total volume, proximity to organs at risk (OAR) to respect dose constraints and topography of the lesion and anatomical relation to vital structures; all of which could impact planning and dose delivery.

Follow-up was done by either computed tomography (CT) scans or magnetic resonance imaging (MRI). Survival was calculated from date of first treatment, either surgery or radiotherapy. This imaging study was requested twice a year for the first two years and annually afterwards. Response was assessed by Response Evaluation Criteria in Solid Tumours (RECIST 1.1) guidelines.

All new reported deficits were considered after RT. Patients that had already prior deficits from their surgical treatment and maintained those deficits were not included as new deficits.

Statistical analysis was performed. Fisher Exact-test and Chi-square tests were performed to address differences between both groups.

This retrospective study was approved by the local ethics committee in March 2022. This report follows the STROBE [4] statement guidelines for publication.

Results

Fifty-one (51) patients were retrospectively reviewed. Mean age at treatment was 56.8 years. Most were female (82.3%). Treatment and demographic characteristics were assessed. Demographics are described in Table 1.

Group 1 and 2 were compared in Table 2 to differences in clinical characteristics, the use of RT and outcomes. We assessed the difference between groups, but no variable was statistically significant.

Median follow-up was 42.5 months (7.1–112.8 months). There were no reported deaths.

RT used on both groups was similar. More patients were treated with fractionated RT (90.2%) than SRS. Patients in Group 1 and 2 had no difference in total dose given. Patients receiving either single dose or hypofractionated regimens had their dose equivalent in 2 Gy fractions (EQD2) calculated before analysis. There was also no difference in the use of SRS between groups.

There was no difference in disease response after surgery. There were no complete responses achieved. The group treated with only RT had a trend to better responses than patients that had undergone surgery, but that was not statistically significant.

There was no difference in late toxicities between groups. Out of surgical patients, 53.3% (8/15) of patients had prior deficit before RT. Amongst the new toxicities reported there were six cases of hearing loss as per Gardner-Robertson scale (9.8%), four cases of tinnitus (7.8%), two cases of facial palsy (3.9%) and one case of diminished ipsilateral visual acuity (1.9%).

Discussion

This is a small, retrospective study on the impact of debulking surgery prior to radical radiotherapy for head and neck paragangliomas. The retrospective nature of this study is a limitation, as is a relatively small sample. Another source of bias in our sample is that we are a university hospital whose cases are mostly referred after previous treatment in other facilities. Our cases, as a result, are usually of higher risk. Nevertheless, its results must be addressed.

Even though the sample is small in statistical terms, it is large compared to most prior publications on the matter. Most prior publications about the use of SRT for HNP have limited-sized samples, varying under 50 patients [5–8], whereas our sample is comparatively large. Our results are also compatible with data from systematic review, with a control over 95% (there were no reported disease progressions in this study) and chances of new deficits under 25% (in this study it was 23.5%) [9].

Data also gathered from retrospective studies show that stereotactic radiosurgery (SRS) is superior to fractionated SRT. In a large systematic review of over 2740 patients [10], the reported control for fractionated SRT was 89.1%. A very small number of our patients had smaller lesions which could be treated with SRS (9.8%) and that is a limitation for our findings. Our sample is mostly composed of larger lesions compared to the literature since our mean lesion size was 4.4 cm, whereas most publications with SRS, particularly those that report results for Gamma-Knife SRS, limit their lesion size to 3 cm.

Most publications, in fact, report findings for Gamma-Knife and Cyber-Knife SRS. A large meta-analysis of retrospective data reported the findings for 335 patients that were treated for HNP with SRS and reported that only 17.0% of those patients were treated in a LINAC-based setting [11]. Most of those publications, however, are also small, although they report over 95.0% of disease control [12–17]. Nevertheless, for over 58.8% of our sample, this approach would not be possible due to lesions size or location.

Even though SRT has been used for HNP, surgery is still the main treatment. A large meta-analysis from Campbell et al. [2] showed the higher frequency of surgery as a primary approach for HNP, even though it still finds that the control with surgery was lower compared to SRT, and with a high incidence of complications. Surgical complications, particularly the chances of vessel damage and stroke, are reported to be as high as 22.2% [18]. This evidence also comes from small, retrospective data [19,20]. A few strategies have been reported to ease surgical burden on the patient, particularly staged treatment with Gamma-Knife SRS [21] and preoperative embolization, with disappointing results [22,23]. Results for surgery, though, as described by a large meta-analysis of retrospective data, have shown that postoperative mortality could be as high as 2.3% and the risk of persistent neurological deficits after surgery as high as 17% [24], with control results comparable to SRT alone.

A different strategy that could be adopted for larger lesions that are unable to be completely removed is surgical debunking followed by SRT. This strategy was assessed by a study on a comparatively large retrospective cohort that reported that control for SRT alone could be even better than a combined modality, even though the addition of SRT to residual disease could mean less surgical complications than those reported for surgery alone [25]. Differently from that report, our report did not include patients that underwent only surgery; therefore, we report a better control rate and a lessen neurological damage rate. Our cases, as stated before, were often referred from other institutions and, frequently, had already received a previous surgical treatment elsewhere. Therefore, the incidence of pre-treatment deficits was higher in our sample, even though it did not impact results. Also, both samples are comparable in terms of size, but we also included a skull base lesion that would be excluded from the report from Jansen et al. Their conclusion that radiotherapy alone should be the treatment of choice for the elderly and frail patients, and surgical approach should be followed by radiotherapy for relapsed lesions mirrors our own findings. We did not find any specific reportable benefit from surgery for patients with larger lesions.

The impact of treatment burden for HNP has been assessed before. In a public health approach, surgery and SRT seem to have the same impact after the first 30 days of perioperative morbidity [26]. Quality of life has also been assessed, with good results [27] following SRT. Surgery, however, is still linked to more frequent complications.

Conclusion

Results of debulking surgery before SRT for HNP were assessed. We found that in a sample of larger lesions, debulking surgery did not show superior results to SRT alone, but in cases where there is a neurological deficit or central nervous system invasion it still should be a standard option. Prospective data for this disease is needed.

Conflict of interest

Authors declare no conflict of interest.

Funding

None declared.

Table 1. Demographic description

Patients' characteristics	**N = 51**
Age	
< 50 years	16 (31.4%)
> 50 years	35 (68.6%)
Sex	
Male	9 (17.6%)
Female	42 (82.3%)

Side	
Left	25 (49.0%)
Right	22 (43.1%)
Bilateral	4 (7.8%)
Localization	
Skull base	43 (84.3%)
Inner ear	8 (15.7%)
Size	
≤ 3 cm	20 (39.2%)
> 3 cm	31 (69.8%)

Table 2. Treatment results by surgical group

Variables	**Treatment**		
	RT only **N = 36 (70.6%)**	**Previous surgery** **N = 15 (29.4%)**	**p**
Age (at diagnosis)			
< 50 years	10 (27.8%)	5 (40.0%)	0.391
≥ 50 years	26 (72.2%)	10 (60.0%)	
Gender			
Male	5 (13.8%)	4 (11.1%)	0.275
Female	31 (86.2%)	11 (88.9%)	
Size			
≤ 3 cm	13 (36.1%)	7 (27.3%)	0.957
> 3 cm	23 (63.9%)	8 (72.7%)	
Laterality			
Left	17 (47.2%)	8 (53.3%)	0.920
Right	16 (44.5%)	6 (40.0%)	
Bilateral	3 (8.3%)	1 (6.7%)	
Localization			0.083
Head and neck	33 (91.7%)	10 (66.7%)	
	3 (8.3%)	5 (33.3%)	

Inner ear			
RT characteristics			
RT dose			
< 50 Gy	8 (22.2%)	5 (33.3%)	0.407
≥ 50 Gy	28 (77.8%)	10 (66.7%)	
RT regimen			
SRS	4 (11.1%)	1 (6.7%)	0.627
FRT	32 (88.9%)	14 (93.3%)	
Outcomes			
Response to treatment			
Complete response	0	0	
Partial response	19 (52.8%)	8 (53.3%)	0.971
Stable disease	17 (47.2%)	7 (46.7%)	
Progressive disease	0	0	
New neurological deficit			
No	27 (75.0%)	13 (86.7%)	0.356
Yes	9 (25.0%)	2 (13.3%)	

RT — radiotherapy; SRS — stereotactic radiosurgery; FRT — fractionated radiotherapy

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