Tumour Resection Volumes and Facial Nerve Outcomes for Vestibular Schwannomas

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Abstract The objective of this study is to correlate tumour volume relationship with surgical outcomes in subtotal resections and accepted nomenclature through a retrospective study at Charing Cross Hospital, London, a tertiary referral centre. The participants were 16 patients with vestibular schwannoma managed with subtotal resection between 2002 and 2011. The main outcome measures were surgical technique; tumour volume; recurrence and post-operative facial nerve function. Mean pre-operative and post-operative volumes for all patients were 14.7 and 3.7 cm³ respectively. Tumour volumes do not correlate with diameter ($p < 0.05$). Mean reduction in volume of these subtotal resections was 75 %. Long term facial nerve outcome was good in the majority of patients: House–Brackmann Grade I/II in 12 (75 %), Grade III/IV in 2 (12.5 %) and Grade V/VI in 2 patients (12.5 %). Notably, two patients with Grade I/II House–Brackmann grading later developed Grade V/VI palsy following adjunctive radiotherapy. Seven of the 16 subtotal resections had subsequent radiotherapy or microsurgery. Mean follow up was 26.5 months. In conclusion, subtotal resections lead to good facial nerve outcomes but may require further

treatments. Radiation treatment can worsen facial nerve function. There is no standardised use of tumour volumes or accepted guidelines for resection terminology. We propose the use of tumour volumes to define this further.

Keywords Vestibular schwannoma · Acoustic neuroma · Recurrence · Facial nerve · Volume

Introduction

Vestibular schwannoma is a benign tumour of the nerve sheath, originating from the vestibulo-cochlear nerve and accounting for 6 % of all intracranial tumours with a reported incidence of 13/million/year [1]. Patients characteristically report gradual, unilateral hearing loss and tinnitus [1]. A small proportion present with cerebellar involvement, hydrocephalus, facial numbness or otalgia [2].

Management options include watchful waiting with interval scanning, radiosurgery or microsurgery [1–3]. All vestibular schwannomas are managed in a multi-disciplinary team setting with decisions dependent on size of the tumour, the extent of hearing loss, patient co-morbidities and preferences. The principal aim is to minimise morbidity, preserving functions of surrounding structures, particularly the facial nerve [4, 5].

Despite progress in the understanding and management of vestibular schwannomas, there remain discrepancies and uncertainties regarding optimal patient outcomes [6]. Whilst historically the main aim was for complete tumour removal, this has now been superseded with achieving the best patient outcome—by optimising post-operative cranial nerve function whilst safeguarding for tumour re-growth [5].

There is evidence that shows gross total resections cause more harm than good, particularly in large vestibular

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schwannomas, with increased risks of cranial nerve damage [7, 8]. Furthermore, the extent of resection does not correlate with long term tumour control [9].

It is difficult to correlate the results of the many studies comparing gross total, near total and subtotal resections, and use them to outline management as there is disparity between the limits, despite internationally agreed guidelines [6, 10]. There is also no volumetric software in place for regular assessment of patients to elucidate these limits [6, 11].

The aim of this study is twofold; firstly to measure pre and post-operative tumour volume and secondly to use this data to evaluate surgical outcomes in particular recurrence and facial nerve function.

Materials and Methods

A retrospective study assessing all patients that underwent subtotal resection microsurgery for vestibular schwannoma was performed at our tertiary referral centre between 2002 and 2011. All patients with Neurofibromatosis type-2 (NF-2) tumours were excluded.

We collected data to include patient demographics, presenting symptoms, operative technique and outcomes. Facial nerve function was contemporaneously recorded using the House–Brackmann grading [12]; both immediately post-operatively and at latest follow up.

Tumour volumes were calculated by summation of consecutive cranio-caudal magnetic resonance imaging (MRI) slice volumes. Each slice volume was generated by multiplying slice interval thickness by the two-dimensional area of tumour [13]. Slice interval thickness was dependent on the MRI sequencing protocol but typically 1 mm. Areas were calculated via the standard hospital imaging system (Picture Archiving and Communication System, PACS) and use of an irregular polygon perimeter correlating to the tumour edge. Pre-operative, post-operative and latest follow up imaging was examined.

Statistical analysis was performed using GraphPad Prism^R v5.0 (GraphPad Software Inc., La Jolla, CA, USA). A *p* value of less than 0.05 was considered significant.

Ethical approval was not required by the London—Fulham Research and Ethics committee due to the retrospective nature of the study.

Results

Patient Database

From 2002 to 2011, a prospectively maintained database incorporated 122 patients managed with vestibular schwannoma. These patients underwent surgery in 77 cases

(42 total and 35 subtotal resection), primary radiation treatment in 43 cases and one patient declined further treatment. Patients with subtotal resections, available imaging and case notes were selected.

Patient Demographics

Sixteen patients were identified with a mean age of 48.3 years (range 22–78). There were 8 female (50 %) and 8 male (50 %) patients.

Presentation

The majority of patients (*n* = 13) had a gradual onset of symptoms over at least 6 months. There were three acute presentations with two patients presenting with hydrocephalus requiring ventriculo-peritoneal shunting.

The most common complaint was of hearing loss (81 %, *n* = 13), followed by vestibular symptoms (63 %, *n* = 10). Tinnitus was described by 31 % (*n* = 5) and trigeminal symptoms were present in 6 % (*n* = 1) of patients. Five patients had symptoms that included visual complaints, limb weakness/numbness and headaches. All patients had normal facial function pre-operatively and all underwent translabrynthine approach surgery.

Resections and Tumour Volumes

The mean and median volume of all tumours pre-procedure was 14.7 cm³ (95 % CI range 7.78–21.6) and 13.4 cm³ respectively.

These subtotal resections had a 75 % reduction in volume overall with a mean and median post-procedure value of 3.67 cm³ (95 % CI range 1.81–5.53), (*p* = 0.0012) and 2.49 cm³. Median reduction in volume was 69 %.

Thirteen subtotal resections also had a volume measurement from MRI scans during follow up (Mean 20.2 months). There was no statistical difference between post-operative and latest follow up volumes (*p* = 0.52).

Seven patients (of 16) required subsequent gamma/steereotactic radiotherapy (*n* = 6) or microsurgery (*n* = 1).

One case was abandoned due to adherence of the facial nerve to the tumour following radiotherapy.

Correlation Between Diameters and Tumour Volumes

Table 1 illustrates the actual tumour volumes as compared to the largest tumour diameters (*d*) from the imaging. The predicted tumour volume (*V*) was estimated by assuming a spherical mass ($V = \pi d^3/6$). When comparing the predicted and actual tumour volumes there was a statistically significant difference (*p* < 0.006) indicating that tumour diameters do not correlate with actual volumes. The

Table 1 Correlation between diameter, predicted and actual pre-operative tumour volumes ($p < 0.006$)

Diameter (cm)	Actual volume (cm ³)	Predicted volume (cm ³)	Difference in volume (cm ³)
1.3	0.379	1.150	0.771
1.5	0.216	1.767	1.551
2.0	2.607	4.189	1.582
2.5	3.471	8.181	4.71
2.5	4.217	8.181	3.964
2.5	7.572	8.181	0.609
3.0	17.087	14.137	2.950
3.5	10.053	22.449	12.396
4.0	2.209	33.510	31.301
4.0	16.793	33.510	16.717
4.0	19.597	33.510	13.913
4.0	21.885	33.510	11.625
4.0	35.442	33.510	1.932
4.5	41.027	47.713	6.686
5.0	22.844	65.450	42.606
5.0	29.858	65.450	35.592

predicted volumes overestimate by a median of 5.7 and mean of 11.2 cm³ (95 % CI range 3.7–18.6). Furthermore, the same diameters produce widely ranging actual volumes (e.g. 4 cm diameter 2.2–35.4 cm³ volumes).

Facial Nerve Function Post-Op

Pre- and post-operative facial nerve function was determined using the House–Brackmann (HB) classification and graded by the same surgeon to minimise intra-observer bias [13, 14, 15]. For simplicity and to allow data analysis, these were then divided into three groups reflecting severity: HB I/II (good), HB III/IV (moderate) and HB V/VI (poor).

Post operatively, 11 (69 %) had a HB grade I/II and 5 (31 %) were grade V/VI. At long term follow up, the 5 Grade V/VI cases had improved to Grade III/IV in two patients and Grade I/II in one patient (Table 2). In addition, two patients with Grade I/II HB grade post-operatively later developed Grade V/VI palsy following adjunctive radiotherapy (Gamma-Knife radiosurgery), given due to continuing tumour growth. Three patients have subsequently been referred for facial reanimation surgery.

Follow Up and Complications

The mean follow up was 26.5 months (95 % CI range 19.8–33.1). There were two non-surgery related mortalities from metastatic breast cancer and cardiac events, both at least 6 months following intervention. Other complications are listed in Table 3.

Table 2 Facial nerve outcomes

HB grade	I/II	III/IV	V/VI
Post-op	11	0	5
Current	12	2	2

This data excludes 2 patients with HB I/II who later developed HB V/VI following adjunctive radiation therapy

Table 3 Post-operative complications

Acute	Number	Long term	Number
CSF leak	2 (1 requiring surgical repair)	Residual balance dysfunction	4
Intracerebral haematoma	1	Headaches	2
Meningocele	1	Trigeminal paraesthesia	2
Wound infection	1		

Discussion

Vestibular schwannomas are the commonest lesion of the cerebopontine angle. Management depends on tumour size, ability to preserve cranial nerve function, extent of hearing loss, patient preference and co-morbidities [1, 4–6, 8].

Whilst improved surgical techniques have led to reduction in mortality rates, as a consequence, the morbidity, in particular facial nerve function post-operatively is under increasing scrutiny [8]. Lee et al. [8] noted in his study that the social impact on facial nerve disability in patients does not correlate with the degree of facial nerve damage and this varies from individual to individual. This makes it more important for us, as clinicians, to ensure the post-operative nerve function is optimal. Our patient database reflects this in that our surgical aim was for total excision but we maintained a low threshold for subtotal resection if the facial nerve was liable to damage.

Our case series highlights that significant macroscopic clearance of disease is possible in subtotal resection despite varying tumour size (with an overall mean reduction in tumour bulk of 75 %) with good long term outcomes. Seven out of 16 (44 %) had further intervention in the form of stereotactic surgery (STS) or repeat microsurgery indicating that patients undergoing subtotal resection are likely to require adjuvant therapy or repeat surgery. This is in contrast to recently published literature indicating that extent of resection has little effect on the recurrence rate [6, 9]. This may, in part, be due not only to larger tumours in this subgroup but also cystic or mixed tumour pathologies.

In our series, facial nerve function was better in the long term with higher grades of palsy improving with time (i.e.

over half or 50 % of the HB V/VI grades improved). Although most studies report overall better facial nerve function [2, 6, 16] with subtotal resections, there were still substantial numbers with HB grade 3 or greater including those who had cystic schwannomas [7, 17, 18].

Many studies have mentioned or demonstrated that STS is more suited to preserving facial nerve function [2, 5, 9]. Interestingly and in contrast, our follow up series demonstrated two patients with initial HB grade I/II developing grade V/VI palsy following adjuvant radiation treatment. However, better predictors to good facial nerve function include tumour volume less than 15 mm in diameter, patient age younger than 60 years, and radiation dose <13 Gy [5]. Facial nerve function was also seen to deteriorate further in those who had microsurgery following STS but a small study of 15 patients demonstrated that planned STS for tumours over 3 cm showed no post-operative facial nerve nerve dysfunction [5]. Nevertheless, Gormley et al. [7] concluded that microsurgery is still the primary therapy option and may be more cost-effective due to its low recurrence rates leading to fewer long term surveillance and adjunct therapies.

There are a number of published studies using new volumetric software such as Vitrea imaging software (Toshiba Medical Systems) to perform detailed studies for vascular tumours, colonic tumours or even to establish the area on tibial heads for bone harvesting [19–21]. Varughese et al. [22] have prospectively observed conservatively managed vestibular schwannomas using a three growth model and found that a volume-doubling model was the most realistic model in predicting tumour growth. Other studies have used magnetic resonance based volume calculations similar to our study [11, 13, 23]. They all show a promising future for the use of volumetric assessments to measure tumour growth and can significantly impact on clinical management of vestibular schwannomas from surveillance times to resection volumes when planning surgery. This can have a positive impact on post-operative sequelae and improve the complication rates. Perhaps, thereafter, a new standardisation of tumour volumes and measurements can be devised and improve upon the model already established by Kanzaki et al. [10].

This study has demonstrated that volume measurements can be used more readily in the treatment of vestibular schwannomas. Volumetric measurement can lead to a better understanding of growth patterns and aid clinical management. Tumour volumes are potentially more reliable than using diameters and could be used to define total, gross total, near total and subtotal resections by volume [24]. This would then enable management algorithms to be generated to decide on long term follow up and the need for adjuvant therapy. We propose reduction in volume by 100, 98, 95 and 90 % as the limits for total, gross total, near total and

subtotal resections in keeping with previous consensus [10]. This series of patients (Table 1) highlights the range of actual volumes produced by the same diameters, suggesting volume calculations and the use of volume software would be preferable. The diameters alone do not provide adequate volume estimates as shown by the predicted volume data and as such reinforces the need for a volumetric programme [24]. Varughese et al. highlight that maximal diameters should be avoided in approximating tumour size, preferring the technique we have employed as a gold standard reference methodology, although it is more time consuming. Furthermore, it is well recognised that tumour diameters are measured quite differently across departments despite internationally agreed criteria, for example by inclusion of the intracranial components of tumours [10, 24].

The main limitations of this study include its lack of power due to small case numbers and lack of longer term follow up, attributable to lack of available imaging and case notes. In addition, the predicted volume calculation is based on the assumption of a spherical lesion. We also did not differentiate between the cystic or mixed solid-cystic or solid tumours (which has an impact on the recurrence rates). Patients with NF-2 in whom tumour biology is largely different, although we appreciate that this group may comprise the majority in larger centres, were also excluded. The main aim of this study was to re-open the debate of volumetric analysis as opposed to diameter measurements and its potential utility in assessing, planning and prognosticating vestibular schwannoma patients.

Conclusion

This study adds to the debate of using volume measurements when treating patients with vestibular schwannomas. Measuring tumour volumes can be beneficial when predicting tumour growth rates, planning management/post-operative surveillance and tumour resection amounts. MRI based volume calculations or volumetric software has a definite role in the future and they should be used more regularly. Further, long term prospective studies are then required using standardised data collection techniques to be better able to compare post-operative outcomes.

Conflict of interest The authors report no conflict of interest regarding the publication of this article.

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