ORIGINAL ARTICLE

THE OUTCOMES OF FRACTIONATED CYBER KNIFE STEREOTACTIC RADIOSURGERY FOR VESTIBULAR SCHWANNOMAS

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ABSTRACT

INTRODUCTION: Vestibular Schwannomas cause significant morbidity and quality of life can be affected in major way if not promptly managed. There are various therapeutic options available to cure the disease but cyber knife stereotactic radiosurgery is one of leading therapeutic option to manage vestibular schwannomas with minimal to or no complications. **OBJECTIVE:** To evaluate radiological tumor control, hearing preservation status and complication rates by use of fractionated stereotactic radiosurgery / radiotherapy, specifically cyber knife device in patients with vestibular schwannomas. **METHODS:** It is a retrospective review of patients treated at Jinnah Postgraduate Medical Centre treated between December 2018 to April 2021, and patient's charts and radiological images were reviewed from medical record and symptom control and complication rate was assessed from clinical follow up notes after giving a certain dose of SRT for vestibular schwannomas. **RESULTS:** 130 (56.52%) were women and 100 (43.47%) were men, among 230 cases. After stereotactic radiosurgery/ radiotherapy the median follow-up duration was 24 months (interquartile range: 10-42 months). With the median follow-up the radiographic control evaluation ratio was 95.7% (IQR: 18.5 months). Among 230 patients, results of 129 (56%) patients showed stable response, 98 (42%) showed improving response and three (1.3%) showed worsening response. However there were no statistically significant changes between pre and post treatment symptoms ($p>0.05$). New onset facial paresis was noted in two (1%) patients. **CONCLUSION:** The outcome of treatment of vestibular schwannomas by using stereotactic radiosurgery resulted in good ratio of tumor control. Ratios of toxicity and hearing preservation status were approximate to the published literature.

Keywords: Vestibular schwannomas, cyber knife, stereotactic radiosurgery/radiotherapy.

Introduction

Vestibular schwannomas (VS) constitute about 6% of all brain tumours with incidence of 9-13 per million people per year. These are benign tumours originating from the vestibular part of the vestibulocochlear nerve. When these tumours grow large enough, exert mass effect on cranial nerve V,VII and VIII as well as the brain stem leading to hearing loss, tinnitus, and vertigo and gait instability. The most common vestibular schwannomas are unilateral and sporadic tumours making up 95% of VS.[1-3] The most common preliminary symptom is hearing loss which is generally followed by disequilibrium, tinnitus, trigeminal nerve dysfunction, facial nerve dysfunction, headache, vertigo and diplopia. Tumour progression and extension occur into external auditory canal through cerebellopontine angle and symptoms generally occur

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due to the compression of neighboring cranial nerves and brainstem.[4,5]

Observation, radiation therapy and microsurgery are the treatment options for VS. On the basis of size and location of tumour, patient age as well as hearing level should be determined for useful indication of treatment. For the treatment of VS alternative approaches have been usedto target the tumour by using highly conformal radiation therapy techniques. These consist of Cyber knife (CK) or stereotactic radiosurgery (SRS) by using CK or a linear accelerator (LINAC) and stereotactic radiosurgery (SRS) by using Gamma knife (GK).[1,6,7] albeit surgical operation affords that the potential morbidity of surgical resection of acoustic neuromas can be meaningful inspite of instancy and low rates of reoccurrence after surgery. The non-invasive and single session treatment by SRS or SRT spares the operative morbidity, Although SRS for acoustic neuromas (ANs) may give high rates of tumor control but can also give rise torisk to the neighboring cranial nerves.[8,9] The rationale of this study was to evaluate tumor control, hearing preservation status and complication ratio after fractioned SRS/SRT by using CK device in patient with VS.

Material and Methods

From December 2018 to April 2021, this prospective study was conducted at Jinnah Postgraduate Medical Centre, Karachi. Informed consents were taken from patients and data consists of patients with VS who have been treated with Stereotactic radiosurgery with exception of patients with neurofibromatosis was collected after approval from IRB (No.F.2-81-IRB/2018-GENL/6880/JPMC). Eligible criteria for the treatment was evidenced by MRI or audiogram in the patients who have radiological evidence of ANs with deterioration in hearing and documented increase in size of tumours within 12 months prior to SRS/SRT. Records were looked for gender, age, volume of tumour, fractioned dose, fraction no: dosage of total radiotherapy, pretreatment hearing status, tinnitus, headache, vertigo and facial nerve status.

Each patient had to undergo individualized treatment plan. Patients were immobilized by using thermoplastic head andmasks and treated by using CK (Accuracy, Sunnyvale, California) system. By using contrast study (CT) (Toshiba, Aquilion, Japan) was performed during the procedure using 1.2mm thick slices. MR T1 weighted images with contrast were also obtained and transferred to the planning system of CK computer. Super imposition/ fusion of CT and MRI images were done for the better assessment of the target volume. For the better contrast absorption in tumour also better imaging quality, fusion of MR images was performed using gadolinium dependent T1 weighted slices. The important viscera and gross tumour volume were outlined by using CT or MR images. The dose to normal tissue, particularly the cochlea and the vestibular organ were determined by using inverse planning factors such as homogeneity index and conformity index were taken into consideration for evaluating the selected treatment plan.[10]

For the first 2 years after completion of SRS/SRT patient underwent post treatment monitoring by using MRI scan, audiogram and clinical visits every six months and then yearly thereafter. Evaluation of patients undergoes neurological examination and tumour volume response wave done by using MRI technique. >2mm reduction in tumour volume was considered as regression response, >2mm increase in tumour volume was considered as progression response and no change in tumour volume after therapy was considered as stable response. The cause of selecting this type of treatment was asked by patients and they were asked about advancement of symptoms, development of any new symptoms and if their hearing had changed since the treatment. Gardner Robertson scale was used for evaluation of hearing loss.[11]

For statistical analysis SPSS 17 was used A neuro-radiologist was asked to interpret the MRI findings stating progression or regression of the tumor. At the time of their last follow up Kaplan-Meir product-limit method was used to calculate tumour control rate and patient were censored at that time. Maintenance of Gardner-Robertson had grade 1-2 hearing after SRS was considered as hearing preservation. To compare the clinical parameter between group Pearson's Chi-square and paired t test were used. $P<0.05$ was considered statistically significant.

Results

130 (56.52%) of the 230 patients were women and 100 (43.47%) were men. The overall median age was

49 years (interquartile range [IQR]: 16-80 years) (Tab.1). (Tab.2) demonstrates treatment characteristics of patients.

Age (Median, Range, Years)	49, 16-80
Gender	**n (%)**
Male	130 (56.52)
Female	100 (43.47)
Location	**n (%)**
Left	95 (41.30)
Right	125 (54.34)
Bilateral	10 (4.34)
Prior Surgery rate	**n (%)**
Yes	70 (31)
No	156 (69)
Hearing lost rate	**(%)**
Pre-FSR	
Partial	68.88
Complete	31.11
Hearing lost rate	**(%)**
Pre-FSR	
Partial	68.88
Complete	31.11
Post-FSR	
Partial	55
Complete	42

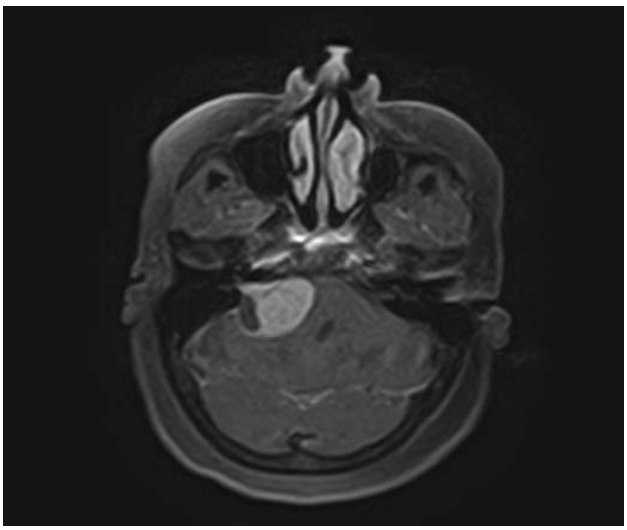
Table 1: Characteristics of patients

Characteristics	Range	Median
Fraction number	1-7	3
Fraction dose (Gy)	4.25-13	6
Tumor volume (mm)	3.5-36	20
Homogeneity Index (HI)	1.08-1.32	1.16
Conformity Index (CI)	1.14-1.69	1.28
new Conformity Index (nCI)	1.09-1.47	1.20
Dose Prescription isodose line (%)	75-92	85
Coverage (%)	96.23-99.88	98.80

Table 2: Treatment characteristics of patients

Mean tumour size was 21 ± 8.8 mm (range: 3.4-41mm). 51 (22%) patients underwent surgery prior to SRS/SRT. In the other 179 (78%) patients, SRS/SRT was administered as the initial therapy. Prior to SRS/SRT Gardner-Robinson score for patients

Figure 1: SRT treatment planning in a patient with VS



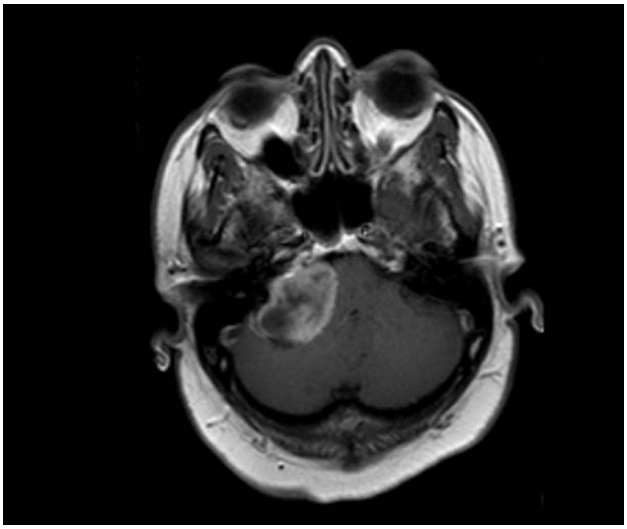


Figure 2: Pre Cyber Knife and Post Cyber Knife treatment MRI images respectively in VS

was 1 in 79 (34%) patients. The median follow-up time was 24 months (IQR: 10-42 months). Results of 129 (56%) patients showed stable disease, 98 (42%) regression and three (1.3%) showed progre

-ssive disease. Radiological tumour control ratio was 95.7% at a median follow-up of three years [(IQR: 18.5 months). Planning tumour volume (PTV) was calculated as GTV+2mm margin on right side (Fig.1). (Fig.2) demonstrates vestibular schwannoma on right side in a patient. The pre cyber knife therapy image is showing homogenous and diffuse enhancement in tumor while post cyber knife therapy image demonstrates most of the tumor has developed necrosis as evidenced by lack of enhancement on post contrast MRI images following treatment. (Fig.3) is showing treatment planning in a patient with bilateral VS by calculating and planning tumor volume while (Fig.4), demonstrates bilateral vestibular schwannomas smaller on right side and larger on left side in a patient. The pretreatment image is showing homo-

Figure 3: SRT treatment planning in a patient with bilateral VS

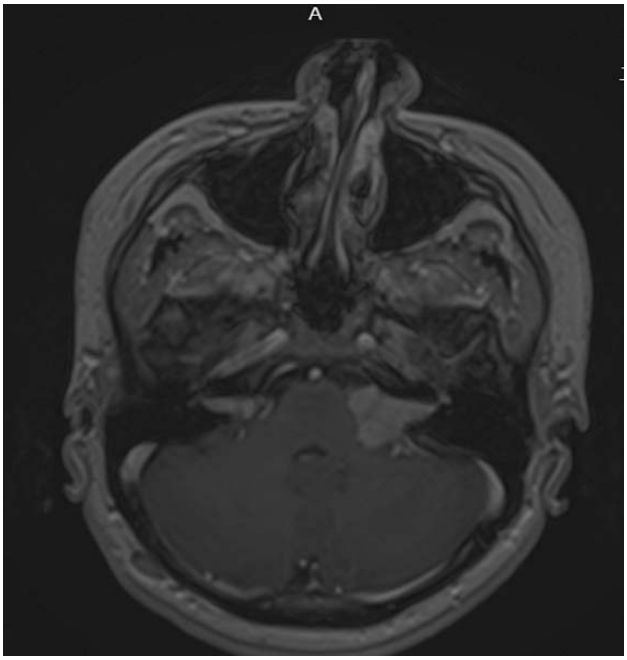


Figure 4: Pre Cyber Knife and Post Cyber Knife treatment MRI images respectively in a patient with bilateral VS

genous and diffuse enhancement in bilateral tumors while post treatment image demonstrates that most of the tumor has developed necrosis bilaterally as evidenced by lack of enhancement on post contrast MRI images following SRS / SRT.

Overall, 168 (73%) patients were given three fractions and total 18Gy dose. It was noted that 12 (5%) patients had good hearing, 125 (54%) had non-serviceable hearing and 97 (42%) had poor hearing after SRS/SRT. Moreover, 17 (7.3%) patients who had poor hearing before SRS/SRT presented worsening hearing. Patients who had good and non-serviceable hearing before SRS/SRT showed no changes in hearing. Hearing preservation rate was 81.7% with follow-up of three years (IQR: 18.5 months). There was hydrocephalus secondary to tumor progression in six (2.4%) cases. Ventriculoperitoneal (VP) shunt had to be placed in these patients. There were no statistically significant difference between pre- and post-SRS/SRT symptoms of patients. But two (1%) patients presented a new onset facial paresis. Some of the cases who reported tinnitus, facial paresis, disequilibrium and headache presented resolution of symptoms. There were no reports of trigeminal neuralgia (TGN) (Tab.3).

Pre-treatment [n (%)]	Post-treatment [n (%)]	p	
Disequilibrium	125 (54)	79 (34)	0.478
Tinnitus	145 (63)	102 (44)	0.337
Headache	118 (51)	85 (37)	0.565
Facial paresis	47 (20)	51 (22)	0.853

Table 3: Treatment complications of non-auditory

Discussion

Various treatment options are available for the treatment of acoustic neuromas few of them include surgery, radiosurgery and fractioned SRT. In about 90% of patients, both anatomical and functional preservation can be obtained after complete tumour resection using modern surgical alternatives, however this preservation of facial nerve is inversely related to the size of acoustic neuroma in term of surgery. Safety of facial nerve function and preservation was provided by Gormley et al (House Brackman grade I or II). In 96% of small tumours (<2 centimeters diameter), 74% of medium tumours (2.0-3.9cm), and 38% of large tumours (4.0cm and greater). Sterkers et al. provided that the ratio of preserved facial function (grade I or II) accelerated from 20% to 52% for large tumours (larger than 3cm), from 42% to 81% for medium tumours (2-3cm in diameter) and from 70% to 92% for small tumours (as much as and concerning 2cm in diameter).[12-14]

Traditionally surgical resection was indicated for VS. Nowadays there has been increase awareness of vestibular schwannomas and continuous advancement in imaging technology for diagnosis of these tumours helps in early detection of even small and medium-sized intracranial VS tumours. Due to this advancement in imaging technologies current management strategy for VS has shifted to observation, microsurgery and radiation therapy with an emphasis on safety of facial nerve.[15]

There has been significant progress in radiosurgery as a treatment option for VS in the past few years. The essential tools and requirements to achieve the successful radiosurgical treatment have become available with several platforms (GK, numerous LINACs and, maximum recently, CK). The gold standard in the SRS system is represented by gamma radiosurgery and seems to be effective clinically in controlling VS tumours, however its hearing preservation rate doesn't seems to be satisfactory ranging from 55-79%, as a functional preservation-oriented treatment option.[16] Owing to its robotic arm and computerized image processing, the CK system has recently emerged as a revolutionary treatment not only for VS but also for the whole body due to real time image guidance and its dynamic monitoring software allow it for precise irradiation for the target volume. There has been limited published articles that has discussion over treatment of VS with CK. So, the main purpose of our study was to assess the clinical outcomes, including tumor control and hearing retention and possible prognostic factors of hearing loss in patients with VS who has been treated with CK.[1,17,18]

High ratio of tumour control with various radiation treatment technique was reported in recent studies. These techniques include GK-based SRS, LINAC-based SRS, conventionally fractionated SRT, proton-beam radiation therapy. Various publications have been seen with the frameless CK-based fractioned stereotactic radiotherapy (FSR) by using the CK system and identical outcomes were observed.[11,19,20] The same system was used by Ishihara et al. who showed that there is 94% radiographic tumour control ratio at a median follow up of 27 months. While the Stanford series showed that there is 98% radiographic tumour control ratio at a mean follow up of 48 months.[19] With the use of multisession SRS outcomes, the standford group presented an interventional tumour control ratio of 99% and 96% at three and five years respectively in their last update. With the median follow up of 24 months our study showed that 129 (56%) of patients had stable response, 98 (42%) of patients showed regression response and three (1.3%) of patients showed progression response. The average radiographic tumour control rate seemed to be 95.7% at three years in our patients. The various toxicities can occur after VS radiotherapy and SRS have been developed to reduce these toxicities. However several adverse effects can be encountered after SRS in treatment of Vestibular schwannomas, such as hearing loss, headache, tinnitus, facial nerve damage, radiation induced trigeminal neuropathy and imbalance. In our study three patients had poor hearing before SRS who had hearing loss after undergoing SRS. However no change in hearing

status of patients was observed who had good or non-serviceable hearing before SRS. Hydrocephalus secondary to tumour progression was observed in one patient. Few symptoms were decreased before SRS treatment like tinnitus, headache, imbalance and facial paresis.[20]

There are various treatment options for patients with VS, the major treatment options are microsurgery and radiosurgery. An alternative treatment to microsurgery for VS is radiosurgical treatment. No statistical significance was noted among these two modalities for tumour control between the two groups. Radiosurgery is associated with lower rate of immediate and long term development of trigeminal and facial neuropathy, hospital stay and postoperative complications. In comparison to microsurgery radiosurgery provides better hearing preservation and tumour growth control.[21]

Conclusion

With the help of SRS treatment of patients with vestibular schwannomas there is an outstanding tumor control and good hearing preservation with minimal toxicity to cranial nerves so the preferable treatment choice of patients with VS is SRS/SRT using Cyber Knife.Also, FSR can also be indicated for residual or re-developing tumours in patients who had preceding surgical resection.

Conflicts of Interest: Authors have no conflicts of interest.

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