Patient-Centered Neurosurgery: Improved Outcomes after Subtotal Surgical Resection and Nonframe-Based Fractionated Stereotactic Radiotherapy for Large Cerebellopontine Angle Vestibular Schwannoma

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Background The novel paradigm in neurosurgery for large vestibular schwannomas (VSs) involves a combination of planned subtotal resection (STR) and scheduled postoperative fractionated stereotactic radiotherapy (FSRT).

Methods This retrospective observational study aimed to evaluate and compare the outcomes of patients who underwent either near-total resection (NTR) or were treated with STR and scheduled FSRT over 6 years. We systematically coded and analyzed the data to obtain comprehensive insights into the results.

Results Our study included 65 patients diagnosed with large VS, who underwent retrosigmoid craniotomy and NTR or STR for tumor removal. The mean age of the cohort was 42.6 (standard deviation: 16.2) years, with 40 (61.5%) female patients. All patients presented with asymmetrical sensory neural hearing loss and other prevalent symptoms such as headache (58) and tinnitus (58). Cerebellar signs, speech abnormalities, and pyramidal signs were also observed. Ten patients underwent NTR, and 55 underwent STR followed by an FSRT at 3 months or later based on the physical and radiological findings. Facial nerve palsy was noted in all cases of those who underwent NTR, while no instances of facial nerve palsy, lower cranial nerve palsy, posterior fossa, or brain stem injury were noted in the STR group. One patient undergoing STR experienced meningitis and died despite best possible medical management. The majority of patients showed symptom improvement, and none of the patients reported recurrence at 3-year follow-up.

Conclusion The combined approach of STR and FSRT ensures safety, high tumor control rates, and favorable outcomes. It provides a sensible alternative to NTR for managing large tumors, emphasizing tumor debulking while preserving neurological function for overall benefit.

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Introduction

Vestibular schwannomas (VSs) are benign neoplasms originating from the nerve sheath, constituting 6 to 8% of all intracranial tumors.1-3 These tumors are also called acoustic neuromas, acoustic neurinomas, vestibular neuromas, or acoustic schwannomas.4 They predominantly originate from the vestibular portion of the eighth cranial nerve (CN), constituting 80 to 94% of all cerebellopontine angle (CPA) tumors, with meningiomas and epidermoid cysts comprising the rest.4-6 They may be confined within the internal auditory canal or extend into the CPA, resulting in symptoms related to the compression of adjacent CNs, brain stem, or posterior fossa (PF) structures.5,7,8 Most VSs exhibit an intracanalicular component, characterized by the widening of the porus acusticus internus, observed in approximately 90% of cases. As these tumors grow, they extend beyond the canal.7,8

Despite being benign, these tumors can significantly impact the quality of life of an individual. They can cause hearing loss, tinnitus, balance issues, facial paralysis, and facial paresthesia, and in cases of large VS, may exert a mass effect on the brain stem and cerebellar peduncle, leading to other serious neurological manifestations.7-9 Asymmetrical sensorineural hearing loss, confirmed by audiometry, or other CN deficits typically raises suspicion of VS. These symptoms often prompt further investigation using contrast-enhanced computed tomography (CECT) or magnetic resonance imaging (MRI).6,10 The increase in the reported cases over the years is likely due to the more frequent use of radiographic imaging for other medical purposes. VSs constitute the majority (80-90%) of PF lesions detected through these imaging methods.11

The main treatment choices for VS include observation with annual follow-up and imaging, surgery, and radiotherapy, with a high likelihood of tumor control and favorable functional outcomes. Surgery is the main treatment for removing symptomatic or potentially life-threatening VS, and may also be considered for smaller tumors.12,13 Achieving complete or near-total resection (NTR) or gross total resection is associated with local control rates of 80 to 90%; however, it comes with its own set of consequences.14-16 Similarly, using stereotactic radiotherapy (SRT) as a first-line approach is not feasible due to the increased risk of radiation-induced complications associated with large-volume targets.17 Therefore, a tailored clinical approach is often feasible, considering both the characteristics of the tumor and the patient. The approach entails a subtotal resection (STR) of the tumor, carefully handling and preserving the facial nerve, lower CNs, PF, and brain stem structures during the procedure. The remaining tumor can then be effectively treated with subsequent nonframe-based fractionated stereotactic radiotherapy (FSRT), which can be administered using different technical methods.12,18-21

This retrospective observational study was conducted to analyze and compare the clinical outcomes of patients who underwent both NTR or STR followed by FSRT, as a treatment sequence that has been practiced in recent times for large tumor size. The study’s findings not only contribute to the existing literature on this topic but also enrich the broader discourse concerning this condition.

Materials and Methods

Study Setting and Design

This retrospective observational study was conducted in two distinguished neurological and radiation oncology centers in eastern India. The study spanned over 7 years, from 2012 to 2019.

Study Participants

This study involved patients with VS who had a maximum diameter of 4 cm or larger. Patients who underwent STR (i.e., 90–95% total volume resection) or had more than 3 mL residual tumor volume, or partial excision (i.e., <90% of total volume resection), and had a Ki-67 proliferative index (histopathological findings > 2 were selected for additional adjuvant FSRT. On the other hand, patients with NTR (i.e., >95% of the total tumor volume resection with less than 3 mL residual tumor) were monitored through yearly serial MRI to assess tumor regrowth or recurrence. Patients scheduled for FSRT were referred to the radiation oncology center after 3 months.

Variables

Data of the patients were obtained from the medical records of in- and outpatients. A standardized data collection sheet was used to document the demographic and baseline characteristics of the participants, including the symptoms observed at the presentation, clinical examination findings, medical history, and image findings. Moreover, the immediate postoperative outcomes and subsequent outcomes at 3 months, 6 months, 1 year, 2 years, and 3 years were recorded as available. Postoperative image findings along with the overall outcome including complications were recorded as well.

Surgery

Each patient underwent a retrosigmoid craniectomy and tumor excision. Before the intraoperative opening of cisterna magna, a preoperative ventriculoperitoneal shunt or an external ventricular drain was placed to relax the brain. The cerebellum was then retracted to access the CPA. Tumor resection was done using the Opmi Pentero 900 neurosurgery microscope by Carl Zeiss Meditec. We used the NIM intraoperative neuromonitoring system to identify, confirm, and monitor motor nerve function of the facial and lower CNs, minimizing the risk of nerve damage. To assess nerve function, nonrelaxant anesthetic agents, namely propofol or sevoflurane, were used as the principal agents, with dexmedetomidine being used in cases where sevoflurane is contraindicated. During the surgery, we maintained normotension, normocarbia, or slightly elevated EtCO2 levels (40–45 mm Hg), and maintained normothermia to mild hypothermia. We refrained from
attempting to address the intracanalicular part of the tumor around the facial nerve. Similarly, we left the tumor capsule located at the root entry zone and around the facial nerve, and the tumor segment of the brain stem, aiming to reduce the potential risk of facial nerve and brain stem damage. The decompression of the remaining part of the tumor was achieved using cavitron ultrasonic surgical aspirator. Special care was taken while handling the surrounding brain to avoid any structural damage. The facial nerve, petrosal vein, anterior inferior cerebellar artery, lower CNs, and the capsule were all preserved intact. Adjuvant FSRT was utilized for the residual tumor and the capsule.

**Postoperative Period and Follow-up**
Following surgery, each patient was monitored in the intensive care unit (ICU) for at least 48 to 72 hours. Any complications that arose were managed on a case-by-case basis by the critical care team. None of the patients experienced immediate complications necessitating surgical intervention. Within 24 hours after the surgery, or earlier if the patient’s clinical condition worsened, a repeat CECT scan or MRI was conducted to evaluate the surgical outcome. Each patient was administered intravenous antibiotics, antiedema measures, and steroids for the first 3 days, after which the treatment was switched to oral medication. The transition of patients from the ICU to the regular ward beds was done gradually, guided by their hemodynamical and clinical conditions. Facial nerve function was assessed using the House–Brackmann (HB) score before the surgery at the time of discharge, and during follow-up. A useful hearing was defined as hearing loss of less than 50 dB, based on the Gardner–Robertson modification of the Silverstein and Norell classification. After evaluating the image findings and the patients’ hemodynamical condition at 3 months, selected patients were directed to the radiation oncologist for FSRT.

**Nonframe-Based Fractionated Stereotactic Radiotherapy**
Patients were positioned supine, with their head secured using a double-layered face mask and clamps followed by CECT and T1–weighted MRI of the brain for CT simulation. The imaging data were fused using Siemens SOMATOM® go. Sim and coregistered to delineate the gross tumor volume and calculate the planning target volume with a 0.3-cm margin. Dose constraints, based on guidelines from the American Association of Physicists in Medicine Task Group 101 (TG 101), were applied to ensure dose homogeneity and minimize risks to organs at risk. In our group of patients, the FSRT plan evaluation criteria were based on the TG 101 guidelines, including parameters such as the Radiation Therapy and Oncology Group (RTOG) conformity index (where the prescription isodose volume is divided by the target volume, typically ranging between 1 and 2), the dose gradient index (calculated as the equivalent radius of the 50% isodose minus the equivalent radius of the prescription isodose, predominantly within 0.3–0.9 mm), and the distance between various isodose lines (with the optimal distance between 80 and 60% isodose lines being < 2 mm, and the ideal distance between 80 and 40% isodose lines being < 8 mm). Additionally, considerations extended to the RTOG homogeneity index (defined as the maximum dose to the target volume divided by the prescription dose, typically < 2) and the gradient index (calculated as the volume receiving half the prescription isodose divided by the volume receiving the full prescription isodose, typically ≥ 3 cm). The RTOG coverage index, indicating the minimum isodose in the target divided by the prescription isodose covering 100% of the target volume, was also accounted for, with a threshold acceptance of more than 0.9. Furthermore, we ensured that parameters such as V95% (representing the dose received by 95% of the target volume) and V100% (indicating the dose received by 100% of the target volume) were at least 100 and 90%, respectively, in relation to the prescribed dose. Radiation therapy was delivered using the Varian Medical Systems, Inc. (NYSE: VAR) Clinac iX linear accelerator, administering a prescribed dose of 25 Gy in five fractions over 5 days. Throughout the treatment period, patients were closely monitored and subsequently discharged with a scheduled follow-up appointment in the neurosurgeon’s outpatient department (OPD), where repeat imaging (CECT or MRI) was conducted to assess treatment response.

**Data Source and Analysis**
The data were entered into Microsoft Excel version 16.75, Microsoft, and used to create simple diagrams/tables illustrating both the initial presentation and postoperative outcomes.

**Results**
In this study, a cohort of 65 patients diagnosed with large VS, with tumor diameters exceeding 4 cm, underwent retrosigmoid craniotomy for tumor removal. Among them, 10 patients underwent NTR, while the remaining patients underwent STR followed by FSRT (Fig. 1). The mean age of the cohort was 42.6 (standard deviation: 16.2) years and a majority of 40 (61.5%) patients were females, with most (n = 24; 36.9%) falling within the age group of 41 to 50 years. All 65 patients presented with asymmetrical sensory neural hearing loss, characterized by nonserviceable hearing, based on a hearing loss of less than 50 dB, as per the Gardner–Robertson modification of the Silverstein and Norell classification. In addition to hearing loss, other prevalent symptoms included headache (58 patients) and tinnitus (58 patients). Cerebellar signs such as ataxia, nystagmus, and intention tremor, as well as speech abnormalities such as slurring, were observed in 56 patients. Furthermore, pyramidal signs such as weakness, slowing of rapid alternating movements, hyperreflexia, and a positive Babinski sign were noted in 55 patients. Lower CN dysfunction was seen in 14 patients, and facial nerve palsy was detected in 6 patients (Table 1).

NTR was possible for 10 patients (Figs. 2 and 3), while 55 patients underwent STR (Figs. 4 and 5). As mentioned earlier, patients who underwent NTR were monitored for a
period of up to 3 years, and there were no cases of tumor recurrence or regrowth observed among them. Unfortunately, facial nerve palsy was observed in all cases, despite anatomical preservation. Among these patients, eight had grade II HB facial nerve palsy, which indicates slight dysfunction only noticeable upon close inspection, with normal symmetry and tone at rest. Additionally, two patients presented with grade III/IV dysfunction, indicating moderate dysfunction with obvious but not disfiguring asymmetry, and possible weakness and dysfunction. Moreover, lower CN palsy was noted in two patients who required RT feeds and long-term speech and swallow rehabilitation therapy. However, there were no cases of brain stem dysfunction or mortality in this group. On the other hand, among patients undergoing STR, none developed facial nerve palsy, lower CN palsy, PF, or brain stem injury, although there was a single case of meningitis observed on the third postoperative day. Despite the best possible medical management, the patient could not be revived and succumbed to the illness. This highlights the differences in outcomes between NTR and STR procedures, with potential implications for treatment decision-making and patient care.

The majority of patients were discharged from the hospital on the 7th or 8th day after surgery, and they were scheduled for a follow-up visit in the OPD within 15 days or sooner if any symptoms worsened. Table 2 corroborates that most patients showed improvement in their initial presenting symptoms and signs at 3 months and 3 years. Among the 55 patients who underwent STR and FSRT, utilizing the previously mentioned technique (Fig. 6), none of them has reported any recurrence or deterioration of their condition during the follow-up period of at least 3 years (Fig. 1). These findings demonstrate favorable postoperative outcomes and sustained symptom relief in this set of studied patient populations.

### Discussion

The ongoing debate revolves around the limited publications describing outcomes in patients with VS undergoing NTR and STR with FSRT. This study presents our own experience on this matter, aimed at achieving successful local tumor control while minimizing treatment-related complications, with results that align with recent literature. The decision-making process considers individual patient factors, such as tumor size, clinical presentation, patient age, and the importance of preserving hearing. Our study
comprises 10 patients who underwent NTR and 55 patients who underwent STR with nonframe-based FSRT, making it a distinctive and valuable addition from India to the overall database.

NTR has been considered the preferred treatment for various cerebral and skull base tumors. This surgical approach provides numerous benefits, including histologic confirmation of the tumor, reduction of local compression on

Fig. 2 Pre- and postoperative MRI of the brain of a 55-year-old man, who sought outpatient care for complaints of asymmetrical sensorineural hearing loss, ataxia, and headaches. (A) Preoperative MRI of the brain, enhanced with a gadolinium-based contrast agent, revealed a hyperintense mass in the cerebellopontine angle region (red arrow). Notably, there was an evident impression on adjacent brain structures, indicative of a mass effect. (B) Postoperative MRI at 2 months showed minimal residual enhancement in the operative bed is observed, signifying tissue scarring (red arrow). The extent of resection appears to be near total, and the previously noted mass effect on the fourth ventricle and surrounding cerebellar tissue has resolved. MRI, magnetic resonance imaging.

Fig. 3 Pre- and postoperative MRI of the brain of a 62-year-old woman, presenting with nonserviceable hearing, gait ataxia, nystagmus, and progressively worsening headaches over 2 months. (A) Preoperative MRI of the brain revealed a well-defined, enhancing mass in the right cerebellar hemisphere with a heterogeneous pattern (red arrows). This mass exerts a significant effect on surrounding tissue, impacting the fourth ventricle, and causing hydrocephalus. (B) Postoperative MRI, taken 1 month after surgery, shows evident changes with a resection cavity. The original mass has been reduced to a cavity with a rim of enhancement (red arrows). The fourth ventricle appears decompressed, relieving the previously noted mass effect and indicating a successful reduction in intracranial pressure. The surrounding edema diminished, and the midline shift was corrected, affirming the effectiveness of the intervention (near-total resection). MRI, magnetic resonance imaging.

Fig. 4 Pre- and postoperative MRI of the brain of a 58-year-old woman with asymmetrical sensorineural hearing loss, headache, gait ataxia, slurred speech, and pyramidal signs. An initial neurological examination showed lower cranial nerve dysfunction, grade II facial nerve palsy, and papilledema. (A) Preoperative MRI of the brain unveiled a well-defined, enhancing mass in the left cerebellar hemisphere with a heterogeneous pattern, exerting a notable mass effect on the fourth ventricle and adjacent tissue, raising concerns of hydrocephalus and brain stem compression (red arrows). (B) Postoperative MRI after 3 months showed a resection cavity with diminished mass effect and partial restoration of the fourth ventricle, signaling alleviation from hydrocephalus. Minimal residual enhancement in the cavity suggests successful lesion removal, while some at the margins imply residual tumor (subtotal resection) (red arrows). Notably, no significant edema is observed in postoperative images.
surrounding neurovascular structures, and alleviation of mass effect.\textsuperscript{14,25,26} Moreover, for benign lesions, NTR offers the potential for complete cure as an additional advantage, however, has its consequences. The available studies comparing CN morbidity between patients who underwent NTR and STR for large-volume VS yield varying outcomes. Skilled surgical centers show a 50 to 75% probability of hearing preservation in patients with small lesions and normal hearing after 5 years and 25 to 50% after 10 years of surgery.\textsuperscript{27,28} The risk of persistent facial palsy ranges from 3 to 15%. However, in this study, a group of 10 patients underwent NTR while preserving the anatomical integrity of the facial nerve. Despite diligent efforts, all patients experienced postoperative facial nerve palsy. However, it improved to near normal at 3 months, indicating an favourable outcome in terms of both functional and cosmetic aspects, as well as their reported quality of life, which aligns with previous findings in the literature.\textsuperscript{4,26}

Stereotactic radiosurgery (SRS) has revolutionized radiation therapy, providing an innovative approach to treating neurological and oncological conditions.\textsuperscript{17,29} Its historical origins date back to the early 20th century, with the development of stereotactic principles by Sir Victor Horsley and Robert H. Clarke.\textsuperscript{30} Technological advancements have diversified SRS techniques, leading to the emergence of notable modalities such as Gamma Knife, CyberKnife, and linear accelerator-based systems.\textsuperscript{29,31,32} Concurrently, FSRT has evolved as a complementary strategy in precision radiation therapy, addressing challenges associated with single-fraction treatments.

\begin{table}[h]
\centering
\caption{Clinical outcome of patients undergoing near-total resection versus subtotal resection followed by fractionated stereotactic radiotherapy at both 3-month and 3-year follow-up periods}
\label{table:clinical_outcome}
\begin{tabular}{|l|c|}
\hline
\textbf{Variables} & \textbf{Frequency: 65 (%)} \\
\hline
Near-total resection & 10 (15.4) \\
Subtotal resection followed by fractionated stereotactic radiotherapy & 55 (84.6) \\
Complications following near-total resection ($n = 10$) & 10 (100) \\
Facial nerve palsy (HB\textsuperscript{a} grade II) & 8 (80.0) \\
Facial nerve palsy (HB\textsuperscript{a} grade III/IV) & 2 (20.0) \\
Lower cranial nerve palsy & 2 (20.0) \\
Brain stem dysfunction & 0 \\
Mortality & 0 \\
Complications following subtotal resection ($n = 55$) & 1 (1.8) \\
Facial nerve palsy (HB\textsuperscript{a} grade II) & 0 \\
Facial nerve palsy (HB\textsuperscript{a} grade III/IV) & 0 \\
Lower cranial nerve palsy & 0 \\
Brain stem dysfunction & 0 \\
Mortality (secondary to meningitis) & 1 (1.8) \\
Observed amelioration of symptoms ($n = 64$) & \\
Asymmetrical sensorineural hearing loss & 60 (58) \\
Headache & 55 (58) \\
Tinnitus (intermittent) & 53 (55) \\
Ataxia & 14 (16) \\
Nystagmus & 34 (38) \\
Slurring of speech & 9 (13) \\
Pyramidal signs & 49 (55) \\
Observed amelioration neurological examination & \\
Lower cranial nerve dysfunction & 9 (12) \\
Facial nerve palsy (cases with postoperative complications are excluded) & 4 (6) \\
Papilledema & 5 (5) \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a}House–Brackmann (HB) score to assess facial nerve function. Following near-total resection, patients with postprocedure facial nerve palsy achieved significant improvement through regular physiotherapy, with remarkable progress evident at the 3-month follow-up, approaching a near-normal state. Patients with lower cranial nerve palsy required an average of 15 days of Ryle’s tube feeding before initiating swallow therapy. Subsequently, oral feeds were introduced based on their clinical improvement.
adaptive planning reintegration of advanced imaging, real-time monitoring, and outcomes while minimizing potential side effects. Contrast, FSRT provides greater as tumor size, location, and patient characteristics. Selecting between these techniques, considering factors such underscore the importance of a tailored approach in or anatomically complex targets. Recent recommendations CT, computed tomography; MRI, magnetic resonance imaging.

Fig. 6 CT scan of the brain showing the planning fractionated stereotactic radiotherapy. The planning of residual lesions involved a CT scan of the brain with 95% isodose coverage for the planning target volume, as depicted by the colored contours. The central area received doses up to (A) 105.1%, (B) 105.3%, and (C, D) 104.4%, respectively, albeit not of the same patients as those shown before. CT, computed tomography; MRI, magnetic resonance imaging.

particularly in limiting doses to surrounding healthy tissues. Various FSRT techniques, including intensity-modulated radiotherapy and volumetric-modulated arc therapy (VMAT), allows the delivery of radiation in multiple fractions, dispersing doses and reducing normal tissue toxicity. While FSRT offers enhanced normal tissue sparing, improved radiobiological effectiveness, and flexibility in treating larger or irregularly shaped tumors, its extended treatment duration poses challenges in patient compliance and resource utilization.

A comparative analysis between single-fraction SRS and FSRT highlights specific advantages for each. Single-fraction SRS excels in cases where precise, high-dose radiation can be delivered in a single session, ideal for smaller lesions. In contrast, FSRT provides greater flexibility in managing larger or anatomically complex targets. Recent recommendations underscore the importance of a tailored approach in selecting between these techniques, considering factors such as tumor size, location, and patient characteristics. The integration of advanced imaging, real-time monitoring, and adaptive planning refines the application of both techniques, emphasizing an ongoing commitment to optimize therapeutic outcomes while minimizing potential side effects. In the dynamic interplay between historical foundations, evolving technologies, and contemporary guidelines, these noninvasive treatment modalities continue to progress within the field of stereotactic radiation strategies. Recent developments have sparked growing interest in planned subtotal resections combined with adjuvant FSRT. This strategy involves careful planning of a partial tumor resection to minimize surgical morbidity, followed by targeted FSRT to treat the remaining tumor based on preestablished plans. The combined approach aims to leverage the advantages of both surgical and FSRT methods. However, this approach requires a comprehensive understanding of both treatment methods and their individual effectiveness and safety aspects. The strategic approach focuses on surgically removing a smaller tumor volume while preserving CN and brain stem function, making it an ideal target for subsequent radiosurgery. A comprehensive meta-analysis conducted by Rykaczewski and Zabek on treatment modalities for large VS included SRS/FSRT and STR followed by FSRT. The analysis covered 28 studies conducted between 2007 and 2011, involving a total of 3,233 patients. Remarkably, the study revealed a noteworthy mean tumor control rate of 92.7% at an average follow-up period of 51.24 months for patients who underwent STR followed by FSRT. These findings strongly support the concept of achieving excellent tumor control rates while preserving desired facial nerve function. Despite its logical advantages, this paradigm shift has not been widely adopted, both practically and conceptually. However, in the study group, consisting of 55 patients who underwent STR, none experienced facial nerve palsy, lower CN, PF, or brain stem injuries. Approximately 3 months after discharge, they received FSRT. Over 3 years, with annual imaging, none of the patients exhibited tumor recurrence or growth, achieving a 100% rate of tumor control. These results indicate that this treatment approach is safe and can be considered for further implementation.

Conclusion

Planned subtotal resection and scheduled postoperative FSRT for residual tumors offer patients an optimal combination of exceptionally high tumor control rates and favorable clinical outcomes. While achieving NTR may lead to significant CN morbidity. It is essential to clarify that this approach does not endorse leaving large-volume residual tumors after surgery, but instead, the primary treatment goal is tumor debulking and preservation of neurological function, ultimately seeking the patient’s overall benefit.

Conflict of Interest

None declared.

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