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Research Article

Treatment Strategies and Survival Outcomes of Vestibular Schwannoma: A Comparative Study Based on SEER Database

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Abstract

Background: Treatment strategies for vestibular schwannoma (VS) vary widely, and selecting the optimal approach based on individual patient characteristics remains challenging. This study systematically evaluated the impact of different treatment modalities on survival outcomes and treatment-related risks using the SEER database, and analyzed temporal trends and tumor size influences on treatment selection.

Methods: A total of 10,119 patients diagnosed with vestibular schwannoma (VS) between 2004 and 2021 were identified from the SEER database. Patients were categorized into four treatment groups: no treatment, surgery alone, radiotherapy alone, and combined surgery plus radiotherapy. To minimize baseline confounding, inverse probability of treatment weighting (IPTW) was employed. Comparative analyses of overall survival and treatment-related mortality risks were conducted across the four groups using Kaplan-Meier survival curves and cumulative incidence functions (CIF). Additionally, temporal trends and tumor size influences on treatment groups were examined to provide clinical insights into individualized therapeutic strategies.

Results: The surgery group showed the highest overall survival, with a 5-year survival rate of approximately 94%, compared to 78% in the no-treatment group (log-rank $p < 0.001$). Combined therapy and radiotherapy alone had intermediate 5-year survival rates of about 89% and 85%, respectively. These differences remained significant after IPTW adjustment. Short-term treatment-related mortality was slightly higher in the surgery (sub-HR=1.14, $p<0.001$) and combined therapy groups (sub-HR=1.27, $p=0.030$), while radiotherapy alone showed no significant increase. Treatment choices evolved over time and were strongly influenced by tumor size.

Conclusions: Surgical treatment remains the cornerstone of VS management. Treatment decisions should be individualized based on patient age, tumor size, and clinical symptoms. Future research integrating multicenter clinical data is warranted to advance precision therapy and functional preservation, ultimately improving patient quality of life.

INTRODUCTION

Vestibular Schwannoma (VS), also known as acoustic neuroma, is a benign, slow-growing tumor originating from the Schwann cells of the vestibulocochlear nerve (cranial nerve VIII) [1]. Although histologically benign, VS can cause significant morbidity due to its proximity to critical neurovascular structures, leading to symptoms such as hearing loss, tinnitus, balance disturbances, and, in advanced cases, brainstem compression [2,3]. The incidence of VS has been rising, partly attributable to advances in diagnostic imaging and increased clinical awareness [4].

Currently, management options for VS include observation (no active treatment), microsurgical resection, radiation therapy (RT), or a combination of surgery and RT [5]. Observation is typically reserved for small, asymptomatic tumors or patients with significant comorbidities, aiming to minimize treatment-related morbidity [6]. Surgical resection remains the definitive treatment for large or symptomatic tumors, offering immediate tumor removal but carrying risks such as cranial nerve injury and other complications [7]. Radiation therapy, including stereotactic radiosurgery, provides a less invasive alternative with favorable tumor control

rates, though it may involve delayed adverse effects [8]. Combined surgery and RT are generally considered for select cases, such as residual or recurrent tumors [8,9]. Despite these options, no universally accepted treatment algorithm exists; clinical decisions are often individualized based on tumor size, patient age, symptoms, and institutional expertise [4-10].

Previous studies have reported variable survival outcomes and treatment-related risks associated with different modalities, but many suffer from limitations including small sample sizes, single-center designs, or short follow-up periods [11,12]. Furthermore, the impact of temporal trends and tumor characteristics on treatment selection has not been comprehensively assessed in large, population-based cohorts. Understanding these patterns is essential for optimizing patient outcomes and guiding evidence-based practice [13].

In this context, the Surveillance, Epidemiology, and End Results (SEER) database provides a valuable resource for analyzing large-scale, real-world data on VS patients across diverse demographics and clinical settings. Utilizing this database, our study aims to systematically compare overall survival and treatment-related mortality among VS patients receiving no treatment, surgery alone, RT alone, or combined surgery plus RT. Additionally, we explore how treatment choices have evolved over time and vary according to tumor size. These insights will contribute to refining therapeutic strategies and promoting personalized management of VS.

METHODS

Study design and participants

This retrospective study utilized data from the SEER 18 registries cohort of the National Cancer Institute. Patient records were retrieved through SEER*Stat software version 8.4.4, identifying individuals diagnosed with Vestibular Schwannoma between 2004 and 2021. The study was conducted in accordance with the Declaration of Helsinki (2013 revision). Cases were selected based on the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) code 9560/0 for benign schwannoma, coupled with the topography code C72.4, which specifies the auditory and vestibular nerves. Patients with alternative coding or those reported exclusively from laboratory sources, physician offices, nursing or convalescent homes, hospice, autopsy, or death certificates were excluded. Tumor size was stratified into three categories according to the dataset: less than 1.5 cm, 1.5 to 3 cm, and greater than 3 cm. Treatment modalities were classified based on SEER's site-specific surgery, radiotherapy, and radiation-surgery sequence variables. Microsurgery encompassed both gross total and subtotal resections, whereas "radiation alone" referred to patients who did not undergo microsurgery but received radiation therapy documented as administered in hospital inpatient radiation treatment centers or medical oncology facilities.

Data Processing and Variable Categorization

In this study, multiple clinical and demographic variables were extracted and systematically processed for analysis. Records with invalid or unknown survival times were excluded to maintain data quality. Tumor size data were carefully cleaned by removing entries marked as "Unknown," as well as those with implausible values—specifically, tumor sizes ranging from 401 to 989 mm—and the code 990, which denotes microscopic focus. Age was categorized into two groups based on actual patient age: under 65 years and 65 years or older. Race was classified into three categories: White, Black, and Other, with all races other than White and Black grouped under Other. The year of diagnosis was stratified into two intervals, 2004–2012 and 2013–2021, using the median year as the cutoff. Tumor laterality was categorized as Left, Right, Bilateral, or Other/Unclear. Radiation therapy (RT) was dichotomized into Yes or No, irrespective of the specific treatment modality or sequence. Surgery is classified as either "No" or "Yes" .The SEER database classifies chemotherapy into "No" and "Yes". It is important to note that no data were collected regarding pathological diagnostic subtypes. The variable "COD to site rec" (Cause of Death to Site Record) was used to classify death causes as follows: (1) deaths due to treatment-related accidents and adverse effects, (2) patients alive at last follow-up, and (3) deaths from other causes unrelated to the primary tumor. This classification enabled a more precise assessment of cause-specific event probabilities.

The primary outcome of the study was overall survival (OS), defined as the length of time from the date of first diagnosis until the date of death from any cause, or the last follow-up if the patient was still alive at the end of the study period.

Statistical Analysis

Patients were stratified into four treatment groups according to therapeutic modality: No treatment, Radiation Therapy (RT) alone, Surgery alone, and combined RT plus Surgery. Baseline demographic and clinical characteristics among these groups were compared using Pearson's chi-squared test or Fisher's exact test for categorical variables. Survival outcomes, including survival time and status, were analyzed using complete-case data.

Univariate survival analyses were conducted using the Kaplan-Meier method with log-rank tests to compare survival distributions across treatment groups. Competing risk analyses were performed by estimating cumulative incidence functions (CIF), and Fine-Gray proportional subdistribution hazard models were employed to assess the impact of covariates on cause-specific hazards.

Subgroup analyses examined the relationships between diagnosis period, tumor size, and treatment selection. To mitigate confounding and selection bias, inverse probability of treatment weighting (IPTW) based on propensity scores was applied, and weighted analyses were subsequently performed.

All statistical tests were two-sided, with significance defined as $p < 0.05$. Analyses were carried out using R software (version 4.4.0).

RESULTS

Patient characteristics

A total of 10,119 patients diagnosed with VS were identified from the SEER database. These patients were categorized into four treatment groups based on therapeutic modality: No treatment (n = 4,539), Surgery alone (n = 3,807), Radiation Therapy (RT) alone (n = 1,620), and combined Surgery plus RT (n = 153) (Figure 1. Baseline demographic and clinical characteristics are summarized in Table 1.

Before propensity score adjustment, significant differences were observed among groups in age distribution, year of diagnosis, race, tumor size, and chemotherapy administration (all $p < 0.05$). Notably, younger patients (<65 years) predominated in the Surgery group (87%) compared to the No treatment group (55%). Tumor size also varied markedly, with smaller tumors (<1.5 cm) more frequent in the No treatment group (75%), while larger tumors (>3 cm) were more common in the combined Surgery plus RT group (67%).

To reduce confounding and balance baseline covariates across treatment groups, inverse probability of treatment weighting (IPTW) was applied. Post-IPTW adjustment, all key covariates—including age, tumor size, year of diagnosis, laterality, race, and sex—were well balanced among the four groups, with no statistically significant differences observed (all $p > 0.05$) (Table 2). This indicates that IPTW effectively minimized baseline imbalances, thereby enhancing the comparability of treatment groups for subsequent outcome analyses.

Overall, 89% of patients were alive at last follow-up, with the highest survival rate in the Surgery group (94%). These findings provide a comprehensive overview of the study population and confirm the robustness of the IPTW approach in balancing confounders.

Survival analyses

Kaplan-Meier survival curves were generated to compare overall survival among the four treatment groups: No treatment, Surgery alone, Radiation Therapy (RT) alone, and combined Surgery plus RT.

Before IPTW adjustment Figure 2A, significant differences in survival were observed across groups (log-rank $p < 0.0001$). The Surgery group demonstrated the highest survival probability over time, followed by the combined Surgery plus RT group, RT alone, and No treatment group. At 5 years, survival rates were approximately 94% for Surgery, 89% for Surgery plus RT, 85% for RT alone, and 78% for No treatment. These results suggest a survival benefit associated with surgical intervention.

After IPTW adjustment Figure 2B, the survival differences among groups remained statistically significant (log-rank $p < 0.0001$), confirming the robustness of the findings after balancing baseline covariates. The adjusted survival curves showed a similar pattern, with Surgery alone and Surgery plus RT groups maintaining superior survival compared to RT alone and No treatment groups. This indicates that the observed survival advantage is unlikely to be due to confounding factors.

Competing Risks Analysis of Treatment-Related Mortality

Figure 3 shows the cumulative incidence function (CIF) curves for three competing events based on the SEER variable “COD to site rec”: treatment-related death, survival, and death from other causes. Patients undergoing surgery (with or without radiotherapy) had a lower cumulative incidence of treatment-related death compared to those receiving radiotherapy alone or no treatment. The no-treatment group had the highest risk, highlighting the benefit of active treatment.

The Fine-Gray subdistribution hazard model (Table 3), further quantified these effects. Age ≥65 (sub-HR=0.58, $p<0.001$) and male sex (sub-HR=0.92, $p=0.003$) were associated with reduced risk of treatment-related death. Diagnosis in 2013–2021 increased risk substantially (sub-HR=5.26, $p<0.001$). Tumor size 1.5–3 cm showed a slight risk reduction (sub-HR=0.90, $p=0.036$), while >3 cm tumors showed no significant difference.

Regarding treatment, surgery alone (sub-HR=1.14, p<0.001) and surgery plus radiotherapy (sub-HR=1.27, p=0.030) were linked to increased short-term risk compared to no treatment, whereas radiotherapy alone showed no significant difference (sub-HR=1.03, p=0.550). Combined with the CIF results, these findings suggest that despite early risks, surgery may offer long-term benefits.

In summary, the CIF curves and Fine-Gray model together highlight differences in treatment-related mortality and key prognostic factors, providing guidance for personalized treatment decisions.

Treatment Selection Trends by Diagnosis Year and Tumor Size

Figure 4 illustrates the distribution of treatment modalities stratified by diagnosis year Figure 4A and tumor size Figure 4B.

As depicted in Figure 4A, the proportion of patients undergoing Surgery alone steadily increased over successive diagnosis year groups, while the percentage of patients receiving No treatment declined correspondingly. The use of RT alone remained relatively stable throughout the study period, and combined Surgery plus RT consistently represented the smallest treatment group. These trends suggest a growing clinical preference for surgical intervention in the management of Vestibular Schwannoma over time.

Figure 4B shows treatment patterns according to tumor size. Patients with smaller tumors (<1.5 cm) were more likely to receive No treatment or RT alone, whereas those with larger tumors (>3 cm) predominantly underwent Surgery alone or combined Surgery plus RT. Patients with intermediate tumor sizes (1.5–3 cm) exhibited a more varied distribution of treatment modalities. This pattern reflects clinical decision-making tailored to tumor burden, with more aggressive treatments favored for larger tumors.

Collectively, these findings highlight evolving treatment preferences influenced by both temporal factors and tumor characteristics, emphasizing the importance of individualized therapeutic strategies in Vestibular Schwannoma management.

DISCUSSION

This study utilized the large-scale SEER database to systematically evaluate the survival outcomes and treatment-related mortality risks among patients with VS receiving different treatment modalities, as well as to analyze temporal trends and tumor size influences on treatment selection. Our findings not only highlight the significant survival benefit associated with surgical intervention but also reflect dynamic adjustments in clinical practice, providing valuable insights for personalized management of VS.

From a clinical perspective, the choice of treatment strategy for VS must be individualized, taking into account patient age, tumor size and location, as well as current symptomatology [13,14]. These factors critically influence both the feasibility and expected outcomes of different therapeutic approaches. For example, younger patients with larger or symptomatic tumors may benefit more from surgical resection, whereas older patients or those with small, asymptomatic tumors might be better candidates for observation or radiotherapy.

For patients requiring surgery, particular attention must be paid to preserving facial nerve function to avoid postoperative facial paralysis, which significantly impacts quality of life [15]. Microsurgical resection via the translabyrinthine approach under the operating microscope has proven effective in achieving minimally invasive tumor removal while maximizing facial nerve preservation. However, the suitability of this approach depends heavily on preoperative imaging assessments to evaluate tumor extension and anatomical considerations. This tailored surgical planning is essential to optimize outcomes and minimize complications [16,17].

It is important to note that the translabyrinthine approach necessitates removal of the labyrinth, resulting in complete ipsilateral hearing loss postoperatively [18]. To address this, some scholars have proposed simultaneous cochlear implantation during the same surgical session, aiming to restore auditory function and improve postoperative quality of life [19]. This combined strategy represents a promising direction for comprehensive management of VS patients undergoing translabyrinthine surgery.

Our survival analysis demonstrated that patients undergoing surgery had the highest overall survival rates, which remained significant after IPTW adjustment. This suggests a clear survival advantage conferred by surgical treatment, consistent with previous studies that regard surgery as a definitive curative approach for VS [20,21]. Although the combined surgery plus radiotherapy group showed slightly lower survival than the surgery-alone group, it still outperformed the radiotherapy-alone and no-treatment groups. This may reflect selection bias, as combined therapy is often reserved for larger or recurrent tumors. The RT-alone group exhibited better survival than the no-treatment group, supporting radiotherapy

as an effective option for patients who are not surgical candidates [22].

In the competing risk analysis of treatment-related mortality, surgical and combined treatment groups showed a slightly increased short-term risk, but long-term survival benefits were evident. This underscores the balance between early treatment risks and long-term gains, emphasizing that clinical decisions should integrate patient age, tumor size, and overall health status [23]. Notably, patients aged ≥65 years and males had lower treatment-related mortality risks, potentially due to selection factors or physiological differences, warranting further investigation.

Regarding temporal trends, the proportion of patients undergoing surgery has gradually increased in recent years, while the no-treatment group has declined, reflecting growing confidence in surgical intervention and improved safety due to technological advances [24]. RT usage remained relatively stable, and combined therapy was consistently a minority choice, indicating a clinical preference for monotherapy. Tumor size significantly influenced treatment decisions: smaller tumors were more often managed with observation or radiotherapy, whereas larger tumors favored surgery or combined treatment, aligning with clinical considerations of tumor burden and treatment risk [25,26].

The strengths of this study include the extensive coverage and large sample size of the SEER database, combined with IPTW to effectively control baseline confounders, enhancing the reliability and generalizability of the results. However, limitations exist. The SEER database lacks detailed clinical information such as tumor location, symptom severity, and postoperative functional outcomes, limiting comprehensive assessment of treatment efficacy. Treatment selection may also be influenced by patient preference, healthcare resources, and physician experience, introducing potential selection bias. Additionally, detailed radiotherapy modalities and dosages were unavailable, precluding analysis of differential effects among radiotherapy techniques.

In summary, our study confirms the pivotal role of surgery in managing VS and highlights the necessity of individualized treatment decisions based on patient characteristics and tumor size. Incorporating clinical considerations such as facial nerve preservation and hearing rehabilitation strategies, especially in surgical candidates, is crucial for optimizing patient outcomes. Future research should integrate multicenter clinical data to further explore the impact of treatment modalities on quality of life and neurological function, advancing precision and personalized care for vestibular schwannoma patients.

CONCLUSIONS

This study, based on a large-scale SEER database, systematically evaluated the survival outcomes and treatment-related risks of different therapeutic modalities for VS. The results demonstrate that surgical treatment significantly improves overall survival and remains the preferred curative option when patients are appropriately selected. Treatment strategies should be individualized by integrating patient age, tumor size, location, and clinical symptoms to optimize management.

Future efforts should focus on integrating multicenter clinical data to further explore the impact of different treatment modalities on patients' quality of life and neurological function, advancing precision and personalized care in VS management to achieve optimal therapeutic efficacy and functional preservation.

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ETHICAL STATEMENT

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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