Pre-treatment Tumor Growth Does Not Affect Radiosurgery Control Rates for Sporadic Vestibular Schwannomas

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Introduction

Numerous studies have reported excellent control rates (>95%) with stereotactic radiosurgery (SRS) for vestibular schwannomas, but have not accounted for pretreatment tumor growth. Studies examining the impact of pretreatment growth on SRS control rates have had conflicting results, some suggesting better control with slower growing tumors and other showing no significant impact of pretreatment growth (Marston 2016, Niu 2014, Timmer 2011, Varughese 2012). The goal of this study was to determine the SRS control rate for growing vestibular schwannomas.

Methods

This retrospective single-institution study included all sporadic vestibular schwannomas treated primarily with Gamma Knife radiosurgery between 2002 -2014. Patients with < 2 years follow -up were excluded. Volumetric analysis was performed on the initial, treatment, and latest follow-up MR T1 post-contrast imaging, from which the pre- and post-treatment percent volume change was calculated.

Univariate analysis was performed to identify demographic, clinical, and radiographic factors significantly associated with the presence of pretreatment growth. Factors included in this analysis were age, sex, laterality, prior surgery, treatment volume, and pre- and post-treatment symptoms (hearing loss, word recognition scores, facial nerve palsy, facial numbness/parasthesias, and dizziness). A univariate analysis was then performed to test for association between pretreatment growth and the three outcomes of interest: 1) radiographic stability, 2) need for salvage treatment. This analysis was stratified by follow-up duration (1.5 to 4 years and > 4 years), treatment volume (< 1.2cm3 or ~1cm diameter, 1.2 – 4cm3 or ~ 1-2cm diameter, and > 4cm3 or ~2cm diameter), and history of prior surgical resection. A p-value <0.05 was considered a significant association.

A stepwise mixed direction multivariate logistic regression was performed to identify factors with significant predictive value for the outcome of radiographic progression. Predictor variables with p-values <0.05 were retained in the model.

Results

Patients & Treatments

213 patients underwent Gamma Knife radiosurgery for a vestibular schwannoma between 2002 and 2014. 89 patients were excluded due to insufficient follow-up. 11 patients were excluded due to planned upfront radiosurgical treatment after surgical resection. 6 additional patients were excluded due to a history of NF2. The remaining 118 patients included in the study included 67 women. The median treatment tumor volume was 0.74 ± 1.8 cm3. Fifteen patients had undergone prior surgical resection with clinical progression prompting radiosurgical treatment. The overall median follow-up was 4.1 ± 2.6 years. Interval pretreatment imaging was available for 93 patients (median pretreatment observation interval 1 ± 1.6 years). Thirty three patients (28%) had documented significant pretreatment tumor volume increases (0.53±1.1cm3/year, 34±41% per year). Demographic, radiographic, and clinical characteristics are compared for patients with and without documented pre-treatment growth in Table 1. The two cohorts were similar, with the exception of larger tumor treatment volumes being significantly associated with the presence of pre-treatment growth.

Pretreatment Growth and Radiographic Control Rate

Significant radiographic growth at last follow-up occurred in 26 patients (22%). There was no radiographic growth in 70% and 81%, respectively, of patients with and without documented pretreatment growth (p = 0.22, Table 2). When patients were stratified by follow-up duration, there was a non-significant trend towards better radiographic stability (58% vs. 74%, p = 0.24) in patients without pretreatment growth on short–term follow-up (1.5-4 years). However, in patients with > 4 years of follow-up, the rate of radiographic stability were similar (86% and 87%, with and without pretreatment growth, respectively, p = 1). When stratified by tumor size (Table 3), there was a non-significant trend towards improved radiographic stability associated with the absence of pretreatment growth (43% vs. 80%, p= 0.29), in patients with large tumors (> 4cm3). Rate of radiographic stability were similar for groups with and without pretreatment growth, regardless of a history of prior surgical resection (Table 4).

Results (continued)

Average pretreatment growth rates are shown in Figure 1 for tumors with > 4 years follow-up; the median pretreatment percent volume change per year for tumors with radiographic growth after therapy was 57 36 % per year (0.290.79 cm3/yr), compared with 28 80 % per year (0.291.3 cm3/yr) for tumors which were radiographically stable after therapy (p = 0.38 and 0.99, respectively).

Pretreatment Growth and Rate of Salvage Treatment

The overall clinical control rate (no need for a salvage treatment) was 94%. Of the 7 failures, 6 patients received salvage surgery and one patient underwent a second radiosurgical treatment, all at a median of 2.7 ± 1.1 years. The rate of salvage treatment was 3% and 7% for patients with and without pretreatment growth, respectively (p = 0.67, Table 1). Stratification by follow-up duration, tumor volume (Table 2), and history of prior surgical resection (Table 3) did not reveal any significant associations between pretreatment growth and rate of salvage treatment.

Predictors of Radiographic Growth

Tumor volume at the time of treatment was the only predictor variable with significant predictive value in a multivariate logistic regression (Table 5 & 6). This analysis was stratified by follow-up duration due to a highly significant difference in follow-up times between tumors showing significant volume increases at last follow-up (2.71.4) and those without (4.62.7, p = 0.002). Between 1.5 and 4 years of follow-up, treatment volume (cm3) had a unit odds ratio of 1.6 (95% CI 1.1 – 2.3) favoring significant increase in tumor volume. With greater than 4 years of follow-up, treatment volume was no longer a significant predictor of radiographic growth.

Conclusions

Pretreatment growth was not associated with a reduced clinical or radiographic control rates following Gamma Knife radiosurgery in this series of 118 patients. Larger tumor volume was predictive of volume increase in the first 4 years after SRS treatment however beyond the four year mark there were no predictors of tumor control. Further studies are needed to better understand the impact of pretreatment tumor behavior on response to SRS, and to characterize the volumetric behavior over time of tumors after treatment.