Evidence-based surveillance protocol for vestibular schwannomas: a long-term analysis of tumor growth using conditional probability

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OBJECTIVE The growth characteristics of vestibular schwannomas (VSs) under surveillance can be studied using a Bayesian method of growth risk stratification by time after surveillance onset, allowing dynamic evaluations of growth risks. There is no consensus on the optimum surveillance strategy in terms of frequency and duration, particularly for long-term growth risks. In this study, the long-term conditional probability of new VS growth was reported for patients after 5 years of demonstrated nongrowth. This allowed modeling of long-term VS growth risks, the creation of an evidence-based surveillance protocol, and the proposal of a cost-benefit analysis decision aid.

METHODS The authors performed an international multicenter retrospective analysis of prospectively collected databases from five tertiary care referral skull base units. Patients diagnosed with sporadic unilateral VS between 1990 and 2010 who had a minimum of 10 years of surveillance MRI showing VS nongrowth in the first 5 years of follow-up were included in the analysis. Conditional probabilities of growth were calculated according to Bayes’ theorem, and nonlinear regression analyses allowed modeling of growth. A cost-benefit analysis was also performed.

RESULTS A total of 354 patients were included in the study. Across the surveillance period from 6 to 10 years postdiagnosis, a total of 12 tumors were seen to grow (3.4%). There was no significant difference in long-term growth risk for intracanalicular versus extracanalicular VSs (p = 0.41). At 6 years, the residual conditional probability of growth from this point onward was seen to be 2.28% (95% CI 0.70%–5.44%); at 7 years, 1.35% (95% CI 0.25%–4.10%); at 8 years, 0.81% (95% CI 0.07%–3.25%); at 9 years, 0.47% (95% CI 0.00%–2.71%); and at 10 years, 0.28% (95% CI 0.00%–2.37%). Modeling determined that the remaining lifetime risk of growth would be less than 1% at 7 years 7 months, less than 0.5% at 8 years 11 months, and less than 0.25% at 10 years 4 months.

CONCLUSIONS This multicenter study evaluates the conditional probability of VS growth in patients with long-term VS surveillance (6–10 years). On the basis of these growth risks, the authors posited a surveillance protocol with imaging at 6 months (t = 0.5), annually for 3 years (t = 1.5, 2.5, 3.5), twice at 2-year intervals (t = 5.5, 7.5), and a final scan after 3...
Vestibular schwannomas (VSs) have an incidence of approximately 2 cases per 100,000 persons, a number that has been steadily increasing in recent decades. Coinciding with this rising incidence, patients are now more commonly diagnosed incidentally, at older ages and with smaller tumors. Consequently, an increasing proportion of patients is being managed conservatively, with an initial period of active observation being the most common management plan for sporadic VSs < 15 mm in size within the internal acoustic meatus.

However, a number of unanswered questions remain regarding this management strategy. One important consideration is the timeline for interval imaging: that is, should scans be obtained at regular intervals or progressively infrequently, and what should this protocol be? Every 6 months? Annually? Biennially? Or some other schedule altogether? In particular, given the paucity of long-term follow-up data in the literature, it is difficult to decide whether there should be an endpoint to surveillance, and if so, when this should be. Ideally, it would be at a point at which the risks of growth-related complications are small enough to accept when balanced against the costs of continued surveillance. This is necessarily a somewhat subjective and value-based judgment, and although costs can be assigned to various outcome measures, they are very difficult to validate.

The literature to date provides little evidence for answering these questions. The natural growth rate of VS is observed to be around 30%–50% during the first 5 years of follow-up. Some authors have suggested that growth is typically detected within this first 5 years of observation, whereas others have supported lifelong surveillance on the basis of observations that around 5% of VSs display growth even after 5 years of stability.

Importantly, studies in the literature to date have used cumulative probability over the whole evaluated time span, for example, 5 or 10 years, to estimate growth risk. However, the risk of growth is likely to be different for a newly diagnosed patient than for one who has already displayed stability (nongrowth) for 5 years. Therefore, this assessment method is suboptimal and does not take into account the a priori information of a tumor’s growth behavior in informing its future behavior, which is the critical issue for clinicians and patients. In clinical practice, the pertinent question driving clinical decisions is, how likely is this particular patient’s tumor to grow from this time forward? Also useful for determining the frequency of surveillance imaging is the question, how likely is the tumor to grow in the next time interval? As previously described by us, conditional probability (a statistical method derived from Bayes’ theorem) would prove more accurate and useful in a dynamic evaluation of growth risk over time. In this methodology, the probability of VS growth (G) at a time (t) is calculated by taking into consideration how long the patient’s VS has not grown (N) before t.

Thus, the aim of the present study was to make use of more accurate and clinically useful conditional probability estimates to derive long-term growth risks that can be used to guide clinician decisions on surveillance timelines and endpoints. We propose a new evidence-based protocol for VS surveillance and perform a cost-benefit analysis for use as a tool to allow units to make their own decisions regarding the cessation of surveillance.

Methods

Study Design

We undertook an international multicenter retrospective cohort study of prospectively collected data from five tertiary care referral skull base units. The research protocol was conducted in compliance with the Declaration of Helsinki. The centers contributing data were Cambridge University Hospitals (UK), King’s College Hospital (UK), Salford Royal National Health Service (NHS) Foundation Trust (UK), Ospedali Riuniti Bergamo (Italy), and Bologna University Hospital (Italy).

The study included all patients diagnosed with sporadic unilateral VS between 1990 and 2010 who had been initially managed with surveillance, with at least 10 years of surveillance imaging, and who had not exhibited VS growth within the first 5 years after diagnosis. A tolerance of 6 months was allowed so that any patient completing 10 years ± 6 months of imaging surveillance was still included. Patients initially managed with surveillance tended to be those with smaller tumors (<15 mm) or those with a performance status that precluded surgery. Exclusion criteria consisted of 1) patients initially managed with primary surgery or radiotherapy, which tended to be patients with larger tumors (>20 mm) or with a preference for such treatment; 2) patients who did not have at least 10 years of surveillance imaging or who showed VS growth within the first 5 years; and 3) patients with neurofibromatosis type 2.

Data were collected at each center, anonymized, encrypted, and stored on a password-protected computer. Patient demographics and VS characteristics included hospital, age, gender, recorded management, dates of first and last surveillance, dates of MRI, tumor site (intracanalicular [IC] vs extracanalicular [EC]), and maximum intracranial tumor diameter (ICTD) at each scanning. The imaging protocol used in surveillance depended on individual unit preference; sequences included T1-weighted gadolinium-enhanced constructive interference in steady state (CISS), or T2-weighted fast imaging employing steady-state acquisition (FIESTA) MRI, with 1-mm slices of the internal acoustic meatus. Measurement of tumor...
size for IC VSSs was taken parallel to the internal acoustic meatus, whereas measurement of EC VSSs was taken as the maximum ICTD in the cerebellopontine angle, not including the IC portion, as per the Committee on Hearing and Equilibrium guidelines. Measurements were recorded in millimeters, on the basis of a review of MRI by specialized consultant neuroradiologists at each center. Change in tumor size was then calculated as the difference between the maximum ICTD on each scan compared with that on the initial scan. Owing to the documented potential for interobserver error in recording tumor dimensions, VS growth was predefined as an increase in diameter of ≥ 2 mm compared with the initial MR image.

Statistical Analysis

According to Bayes’ theorem, the conditional probability of VS growth (G) at a chosen time point t is the probability of growth given that the VS has not grown (N) in the years before t:

\[ P(G_t | N_{t-1}, N_{t-2} \ldots N_t) = \frac{P(G_t \cap N_{t-1} \cap N_{t-2} \ldots N_t)}{P(N_{t-1} \cap N_{t-2} \ldots N_t)} . \]

For each patient, the time at risk (in years) was calculated from the date of first imaging to the date of VS growth or last follow-up, whichever occurred first. Patients were censored when they completed surveillance at 10 years. Data analysis using conditional probability was undertaken, and the risk of VS growth was calculated. For a given year, the probability at year t refers to growth probability between year t − 1 and year t. Conditional probability growth estimates for t = 1 to t = 5 have been published and shown to be externally valid. Thus, these estimates of growth risk were used for the first 5 years of follow-up, with data in the current study showing long-term growth risks for t = 6 to t = 10.

Not all patients had imaging at the same time intervals. Hence, a couple of specific circumstances arose given the need for temporal localization of any growth: 1) Where a gap in surveillance imaging was present, as long as there was no difference in tumor size between the last scan at the start of the gap and the scan after the gap, we assumed that the tumor had not grown in the intervening time period. 2) If a patient’s VS showed growth on a particular scan and the preceding year’s scan was available, then we could be sure that the growth was localized within that year. 3) If a patient’s VS showed growth on a particular scan but no imaging for the preceding year was available, then growth was attributed to the year after the last scan showing stability. This assumption on the localization of VS growth is necessary for a couple of reasons. First, after 5 years of stability, surveillance imaging becomes increasingly infrequent (as is clinical practice at most centers); thus, it would be impractical to obtain annual interval imaging for such a long follow-up period. Second, previous evidence shows that growth risk reduces over time; thus, the most likely time for growth in this situation is the earliest unobserved time interval, and hence the allocation of growth to the year after the last scan showing stability.

To derive the conditional growth risk from a given year onward, that is, the residual “lifetime” probability of growth, the Riemann integral for an exponential function was calculated from a given year t to infinity. An exponential function was used based on the observed form of the data. Nonlinear regression analyses were then undertaken to derive an exponential function that models the long-term growth behavior. Model selection was based on the observed form of the data and comparison of performance metrics. The time points at which the residual lifetime risk is 1%, 0.5%, and 0.25% were calculated by solving the model for each of these risks, and a surveillance protocol was proposed.

Subsequently, a cost-benefit analysis was undertaken to look at the monetary impact of different surveillance strategies. To do this, surveillance costs and the costs of missing VS growth needed to be estimated. The surveillance cost estimations were derived from a UK model, that is, NHS tariffs: pre- and postcontrast MRI of one body part is £166 (code RD03Z), and the cost of an ear, nose, and throat (ENT) follow-up outpatient clinic appointment is £122 or £52 (code 120), depending on whether the appointment is the first or a follow-up, respectively.

A lower-bound cost estimate for a single follow-up was accordingly set at £250. However, acknowledging that these costs will vary, we estimated the cost of a single follow-up appointment with imaging for values between £250 and £1000. The cost of a missed tumor value was not specifically estimated, as this will vary by country and context of individual cases; instead, a broad range was implemented, from £10,000 to £1 million. This value was multiplied by the residual lifetime risk of growth after cessation of follow-up to provide the risk-adjusted cost of a missed tumor at each time point. Comparison of the proposed surveillance protocol and an indefinite follow-up strategy was undertaken. The indefinite strategy, such as the one currently used by many centers, refers to follow-up at 6 months, annually for 3 years, twice at 2-year intervals, and then every 3 years thereafter.

Data analyses were undertaken using Python version 3.8.2 (Python Software Foundation) with the packages SciPy and Scikit-learn. Binomial confidence intervals were calculated using the Clopper-Pearson interval based on beta distribution. Nominal data were analyzed using the chi-square test with the Yates continuity correction. A p value < 0.05 was considered statistically significant. Nonlinear regression was undertaken and the metrics r², mean absolute error (MAE), and root-mean-square error (RMSE) were calculated to aid model selection and assessment of performance.

Results

Overall, 354 patients with sporadic unilateral VS and at least 10 years of follow-up were included in the study. Patient characteristics are listed in Table 1. Median age at diagnosis was 62 years (range 26–93 years), with a slight majority of male patients (58.5%). The mean length of follow-up was 11.5 years (range 9.5–25.6 years).

Using the Bayesian approach, we calculated the conditional probability of growth in each year, as summarized in Table 2. Among all 354 tumors across the surveillance period from 6 to 10 years postdiagnosis, a total of

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**Table 1: Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (years)</td>
<td>62</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>58.5%</td>
</tr>
<tr>
<td>Follow-up Period (years)</td>
<td>11.5</td>
</tr>
</tbody>
</table>

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**Table 2: Conditional Growth Probability**

<table>
<thead>
<tr>
<th>Year</th>
<th>Conditional Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>0.1%</td>
</tr>
<tr>
<td>7</td>
<td>0.05%</td>
</tr>
<tr>
<td>8</td>
<td>0.025%</td>
</tr>
</tbody>
</table>

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**Figure 1: Exponential Function**

The exponential function demonstrates the long-term growth behavior over time, with a clear peak at year 10.

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**Figure 2: Cost-Benefit Analysis**

The cost-benefit analysis shows a comparison between the proposed surveillance protocol and the indefinite follow-up strategy, highlighting the economic implications of each approach.
TABLE 1. Characteristics of study population with sporadic unilateral VS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>207</td>
<td>58.5</td>
<td>53.1–63.7</td>
</tr>
<tr>
<td>F</td>
<td>147</td>
<td>41.5</td>
<td>36.3–46.9</td>
</tr>
<tr>
<td>Age in yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>253</td>
<td>71.5</td>
<td>66.5–76.1</td>
</tr>
<tr>
<td>≥70</td>
<td>101</td>
<td>28.5</td>
<td>23.9–33.5</td>
</tr>
<tr>
<td>Tumor site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IC</td>
<td>203</td>
<td>57.3</td>
<td>52.0–62.6</td>
</tr>
<tr>
<td>EC</td>
<td>151</td>
<td>42.7</td>
<td>37.4–48.0</td>
</tr>
<tr>
<td>EC tumor size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 mm</td>
<td>111</td>
<td>73.5</td>
<td>65.7–80.4</td>
</tr>
<tr>
<td>≥15 mm</td>
<td>40</td>
<td>26.5</td>
<td>19.6–34.3</td>
</tr>
</tbody>
</table>

12 (3.4%, 95% CI 1.8%–5.8%) VSs were seen to grow. In these 12 cases, the median age was 62 years, 83.3% of the patients were male, 58.3% of the VSs were EC, and 83.3% of the VSs were small (< 15 mm) in size.

In comparing over the whole surveillance period, we found no significant difference in growth risk for IC versus EC VSs (p = 0.41), nor did we find any significant difference in the conditional probability of growth between IC and EC VSs, for any year from 6 to 10 years. Each year’s growth risks are detailed in Table 2.

The conditional probabilities for annualized growth risk postdiagnosis are plotted in Fig. 1A, which, for context, are shown alongside growth risks from t = 1 to t = 5, as explained in Methods. The data were then fitted using a nonlinear least squares regression, yielding an exponential regression model as shown below (numbers are given to an accuracy of 2 decimal places) and plotted in Fig. 1A.

Using long-term surveillance data, we found that the conditional probability of growth was 1.69% at 6 years (95% CI 0.62%–3.65%), 0.86% at 7 years (95% CI 0.18%–2.50%), 0.58% at 8 years (95% CI 0.07%–2.08%), 0.00% at 9 years (95% CI 0.00%–1.07%), and 0.29% at 10 years (95% CI 0.01%–1.61%). Further, we described the residual lifetime probability of growth from given time points onward, which was 2.28% at 6 years (95% CI 0.70%–5.44%), 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%).

The residual lifetime risks of conditional growth after a given year are shown in Table 2. These data were fitted using a nonlinear least squares regression, yielding an exponential regression model as shown below (numbers given to an accuracy of 2 decimal places) and plotted in Fig. 1B. Regression evaluation metrics ($r^2 > 0.99$, MAE < 0.001, and RMSE < 0.001) indicate an excellent fit by the model: $y = 6.07e^{-0.52(t − 4.14)}$ for $t ≥ 1$, where $y$ is the lifetime conditional probability of growth (%) from year $t$ onward. By solving this equation for $y = 1$, the model determines that the remaining lifetime risk of growth is less than 1% at 7.57 years. The predicted remaining risk of growth would be less than 0.5% at 8.89 years and less than 0.25% at 10.27 years. Nota bene, this is the residual lifetime risk of conditional growth from a given year onward.

Based on this residual lifetime risk, a surveillance protocol is proposed (Fig. 2). It is suggested that once a diagnosis of VS is made ($t = 0$) and a patient is selected for management by surveillance, interval imaging should be undertaken at 6 months ($t = 0.5$), annually for 3 years ($t = 1.5, 2.5, 3.5$), twice at 2-year intervals ($t = 5.5, 7.5$), and a final scan after 3 years ($t = 10.5$), and then surveillance should be stopped unless there are specific reasons to continue.

The cost-benefit analysis to look at the monetary impact of such a surveillance strategy is shown in Fig. 3. Here, the cost of surveillance is calculated using two different protocols, as described in Methods—one in line with our proposed surveillance protocol (Fig. 3A) and the other assuming an indefinite follow-up strategy (Fig. 3B). In our proposed protocol, the cost of surveillance is logarithmic initially and then plateaus as surveillance is ceased after 10.5 years. Conversely, in the indefinite follow-up strategy, the cost of surveillance is initially logarithmic but then becomes linear, continuing to rise over time, as additional follow-up appointments cost more.

**Discussion**

The conditional probability of growth was 1.69% at 6 years (95% CI 0.62%–3.65%), 0.86% at 7 years (95% CI 0.18%–2.50%), 0.58% at 8 years (95% CI 0.07%–2.08%), 0.00% at 9 years (95% CI 0.00%–1.07%), and 0.29% at 10 years (95% CI 0.01%–1.61%). Further, we described the residual lifetime probability of growth from given time points onward, which was 2.28% at 6 years (95% CI 0.70%–5.44%), 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%), and 0.70%–5.44%, 1.35% at 7 years (95% CI 0.25%–4.10%).

**TABLE 2. Conditional and residual lifetime conditional probabilities of growth for each year for all IC and EC VS patients in the study**

<table>
<thead>
<tr>
<th>Year</th>
<th>Growth</th>
<th>No Growth</th>
<th>All VSs</th>
<th>IC VSs</th>
<th>EC VSs</th>
<th>Residual Lifetime Conditional P(G) in % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>6</td>
<td>348</td>
<td>1.69 (0.62–3.65)</td>
<td>0.49 (0.01–2.73)</td>
<td>3.31 (1.12–7.81)</td>
<td>2.28 (0.70–5.44)</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>345</td>
<td>0.86 (0.18–2.50)</td>
<td>0.99 (0.12–3.57)</td>
<td>0.68 (0.02–3.78)</td>
<td>1.35 (0.25–4.10)</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>343</td>
<td>0.58 (0.07–2.08)</td>
<td>1.00 (0.12–3.60)</td>
<td>0.00 (0.00–2.51)</td>
<td>0.80 (0.07–3.25)</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>343</td>
<td>0.00 (0.00–1.07)</td>
<td>0.00 (0.00–1.85)</td>
<td>0.00 (0.00–2.51)</td>
<td>0.47 (0.01–2.71)</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>342</td>
<td>0.29 (0.01–1.61)</td>
<td>0.00 (0.00–1.85)</td>
<td>0.69 (0.02–3.81)</td>
<td>0.28 (0.00–2.37)</td>
</tr>
</tbody>
</table>

P(G) = probability of growth.
0.80% at 8 years (95% CI 0.07%–3.25%), 0.47% at 9 years (95% CI 0.01%–2.71%), and 0.28% at 10 years (95% CI 0.00%–2.37%).

By using these data to produce a regression model, we went on to determine that the residual lifetime risk of growth would be < 1% from 7 years 7 months onward, < 0.5% at 8 years 11 months onward, and < 0.25% at 10 years 4 months onward.

We found no significant difference in growth risk between IC and EC VSs from 6 to 10 years. This finding is in keeping with previous data showing that the EC VS is more likely to grow only in the first year of surveillance.
but that after this, the growth risk becomes comparable to that of IC VS.\textsuperscript{16} There is no consensus on the most appropriate timeline and duration of surveillance imaging for VS patients managed under a surveillance protocol. This uncertainty results from a lack of available evidence specifically addressing this matter. There are two main questions: 1) how frequently should surveillance imaging be undertaken, and should this change over time? and 2) should there be an endpoint to surveillance, and if so, when should this be?

The literature to date has focused on cumulative approaches to growth risk stratification, which provide only static growth estimates over the whole period of analysis, failing to consider prior information regarding a tumor’s previous growth behavior during this period. Further, these methods make assumptions about patients censored during follow-up, leading to an expected underestimation of growth risks relative to their true values. On the basis of these data and analyses, units have implemented surveillance imaging using various protocols.\textsuperscript{2,6,7,16} Some units have endeavored to undertake lifelong surveillance based on the observation of occasional VS growth after many years of stability, whereas others have favored the cessation of surveillance after a relatively arbitrary time point after which the perceived risk of growth is deemed negligible.

Conditional probability, we believe, represents a more clinically relevant statistical methodology for approximating growth risks in patients with VS, as it uses information about prior tumor behavior and therefore lends itself to answering questions about the optimum surveillance protocol. We showed that at up to 10 years of surveillance, the conditional probability of growth appears to exhibit exponential decay over time. Moreover, a patient whose VS has been stable for 6 to 7 years appears to have a < 1\% risk of growth in any subsequent year, validating our previously proposed model of VS growth, which was extrapolated from data up to only 5 years. In the present study, however, we used real-world long-term surveillance data.\textsuperscript{4}

We posited a surveillance protocol based on conditional probabilities (Fig. 2). This protocol should allow the identification of patients whose VS might exhibit growth within the early years of follow-up (when growth risk is greatest), while progressively increasing scanning intervals in line with the reduction in the growth risk observed over time. The decision to stop surveillance is more nuanced, and it is ultimately a value judgment to set this at 10.5 years. This is based on the judgment that a clinically acceptable risk of subsequent tumor growth is present when it falls below 0.25\%. This is based on the concept of “as low as reasonably practicable” (ALARP), where to further lower the level of risk, a disproportionate increment in resource expenditure would be required relative to the resulting decrement in risk.\textsuperscript{37} It should be emphasized that the model does not imply that growth is impossible beyond 10.5 years, just that it becomes very unlikely; thus, patients should be counseled on this matter and advised to seek medical attention if any change in clinical circumstances arises.

Decisions about surveillance protocols are inherently a cost-benefit analysis, weighing the risks and costs of missing VS growth versus the risks and costs of surveillance itself.\textsuperscript{6,18} To some extent, any decisions are value judgments; while the costs of surveillance might be estimated, they do not consider subjective factors such as patient anxiety\textsuperscript{19} or other incidental pathologies identified on scanning. The risks of a missed tumor involve even more aspects to consider, including patient anxiety, increased treatment morbidity, litigation, etc. We have proposed 10.5 years (a growth risk < 0.25\%) as an acceptable cutoff on the basis of the ALARP concept, but this could be modeled for any risk that an institution believes is appropriate, which may vary from center to center.

With these caveats in mind, we modeled a cost-benefit analysis to look at the monetary impact of two different surveillance strategies (Fig. 3). The intersection of these functions, therefore, represents the time at which costs of surveillance would outweigh the risk-adjusted costs of missed tumor growth. For example, in the proposed protocol, assuming a follow-up cost of £250 per appointment and a cost of £750,000 for a missed tumor, then continuing surveillance beyond 10.5 years would cost more than the risk-adjusted cost of a missed tumor, and an argument could be made to stop surveillance. The greater the cost of surveillance, the earlier surveillance should cease, whereas the greater the cost of a missed tumor, the longer surveillance should continue. With this tool as a decision aid, cost-benefit–balanced surveillance protocols can be implemented as an endpoint to surveillance, and if so, when should this be?
The results presented here derive from a medium-large data set collected from multiple centers. The cohort includes only subjects who were managed with surveillance, which is most often enlisted because of tumor size and more rarely for comorbidities, symptoms, or other reasons. Given that this type of management allocation is true at

**FIG. 3.** Cost-benefit analysis of the cost of surveillance (range £250–£1000) and the cost of a missed tumor (range £10,000–£1 million) for the proposed surveillance protocol (follow-up at 6 months, annually for 3 years, twice at 2-year intervals, and then a final scan after 3 years; A) and indefinite surveillance protocol (follow-up at 6 months, annually for 3 years, twice at 2-year intervals, and then every 3 years thereafter; B). Figure is available in color online only.
every center, the results should be externally valid. Further, the study inclusion criteria, which allowed temporal localization of growth, have been shown to be generalizable, so should be representative of the wider population of patients with VS. The database used was retrospectively accessed; however, data were prospectively entered and thus should be free of referral and selection bias. Data are reliant on correct input, which is subject to human error. The tumor size measurements were based on approved MRI reports from experienced specialized neuroradiologists; however, these were two-dimensional (linear) rather than three-dimensional (volumetric). Despite this, a strong correlation has been seen to exist between linear and volumetric measurements for VS, and linear measurements still represent the most widely accepted means of reporting VS growth in the literature. Validation of the present model and protocol was not undertaken but would be best achieved in a prospective setting with an independent cohort of patients.

Conclusions

The results presented here allow insights into the long-term growth behavior of VS, which can be used to better inform patients of their risk of growth at particular time points along their surveillance timeline—with the residual lifetime risk of growth at < 1% after 7 years 7 months, < 0.5% after 8 years 11 months, and < 0.25% after 10 years 4 months. Thus, we propose a 10.5-year growth risk–based surveillance protocol for VSs under observation, in which interval imaging is undertaken once at 6 months, annually for 3 years, twice at 2-year intervals, and a final scan after 3 years. This provides a balance between the risk of missing late growth and the costs of repeated imaging. A cost-benefit analysis decision aid is also proposed to allow units to make their own decisions regarding the cessation of surveillance.

References


Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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