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Screening for vestibular schwannoma in the context of an ageing population

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Abstract

Objective. To review the literature regarding screening for vestibular schwannoma in the context of demographic changes leading to increasing numbers of elderly patients presenting with asymmetric auditory symptoms.

Methods. A systematic review of the literature was performed, with narrative synthesis and statistical analysis of data where appropriate.

Results. Vestibular schwannomas diagnosed in patients aged over 70 years exhibit slower growth patterns and tend to be of smaller size compared to those tumours in younger age groups. This fact, combined with reduced life expectancy, renders the probability of these tumours in the elderly requiring active treatment with surgery or stereotactic radiotherapy to be extremely low. Vestibular schwannomas in the elderly are much more likely to be managed by serial monitoring with magnetic resonance imaging. The weighted yield of magnetic resonance imaging in the diagnosis of vestibular schwannoma in all age groups is 1.18 per cent, with almost 85 scans required to diagnose 1 tumour.

Conclusion. An evidence-based approach to the investigation of asymmetric hearing loss and tinnitus in the elderly patient can be used to formulate guidelines for the rational use of magnetic resonance imaging in this population.

Review Article

Mr S Basu takes responsibility for the integrity of the content of the paper

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Introduction

Acoustic neuroma or vestibular schwannoma is a benign neoplasm arising from the enveloping sheath of the vestibular (VIIIth cranial) nerve. Considerable resources in terms of clinical time and diagnostic investigations are consumed in the diagnosis of these neoplasms. There are two varieties: a sporadic form and a genetic form called neurofibromatosis type 2 (NF2). In this study, unless otherwise specified, vestibular schwannoma will refer to the sporadic form.

Magnetic resonance imaging (MRI) is considered to be the 'gold standard' in the diagnosis of vestibular schwannoma.[1] Among different neuro-otological symptoms and signs produced by vestibular schwannoma, asymmetrical sensorineural hearing loss (SNHL) is the most common, followed by tinnitus.[2] The MRI scans are very commonly requested for patients presenting to ENT clinics with these symptoms. These neoplasms exhibit a spectrum of clinical manifestations. A minority of tumours can undergo significant and rapid growth, passing out of the internal auditory meatus into the cerebellopontine angle, where they can cause brainstem compression and ultimately death. The majority of vestibular schwannomas, however, show indolent and slow growth, with symptoms of asymmetric deafness and tinnitus being the only presenting features.

The change in the demographic pattern of the world population has seen an increase in the proportion of people aged over 60 years (8 per cent in 1950 *vs* 11 per cent in 2010).[3]

This article aimed to examine the cost-effectiveness of MRI as a screening tool in the diagnosis of vestibular schwannoma in patients aged over 70 years and presenting with asymmetrical SNHL or unilateral tinnitus, by collecting and analysing data from published materials obtained through a literature search.

Materials and methods

A literature search covering the period from 2008 to 2018 was performed, by the first author, using the Medline, Embase, Cumulative Index to Nursing and Allied Health Literature ('CIHNAL'), PubMed and Google Scholar databases. The key words 'acoustic neuroma' or 'vestibular schwannoma' were used in combination with: 'epidemiology' or 'natural history'; 'growth rate', 'rate of growth' or 'size'; 'asymmetrical hearing loss', 'asymmetrical sensorineural hearing loss' or 'tinnitus'; and 'pick up rate', 'screening', 'diagnosis' or 'test'. All searches were repeated to confirm the results.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') flow charts were used in the selection of articles relevant for this study. These were articles involving sporadic vestibular schwannoma in adults, and epidemiological studies on its incidence rate, growth rate, change in its management with time, conservative

management outcome, and reported incidence of vestibular schwannoma based on MRI in patients presenting with asymmetrical SNHL or unilateral tinnitus.

Articles not published in the English language or not available in English translation were excluded. Studies based solely on NF2 and patients aged below 16 years were also excluded. However, some articles included both sporadic and NF2 vestibular schwannoma groups; where the data from each group were given separately, only those from the former group were included in our study. Duplicate results were excluded.

The articles were excluded if the abstracts indicated that the main subject of the study focused on: vestibular schwannoma therapy; the epidemiology of the tumour in a societal group or discussion of the regional distribution of vestibular schwannoma; the tumour risk factors; the characteristics of incidental vestibular schwannoma only; a comparison of different protocols defining asymmetrical SNHL; or a comparison of MRI with other methods of diagnosing vestibular schwannoma.

Relevant meta-analyses and systematic reviews were used for reference and comparison with our results. For statistical analysis, those articles reporting observational studies on the epidemiology, size and growth rate of tumours, a change in management of vestibular schwannoma, and the pick-up rate of vestibular schwannoma from audiological tests were included.

In the next step, the articles selected were requested from the library of the first author's institution. Only when full articles were obtained were they included in this study, after screening and applying the same exclusion criteria. Abstracts from presentations were used for reference only and were not included in the statistical analysis.

Statistical analysis

Weighted averages, using the number of patients in each article as weight, were calculated in Microsoft Excel® spreadsheets for: tumour size at diagnosis (millimetres), percentage of tumours showing growth, growth rate (millimetre per year), and percentage of patients who completed conservative management and did not need any switch to active treatment during the follow-up period. These data were obtained from the papers included for statistical analysis for this article.

To calculate the pick-up rate of vestibular schwannoma from MRI scans performed for asymmetrical SNHL in pure tone audiograms, we used: scans per diagnosis (number of scans required to obtain one positive result) and yield (percentage value of positive results divided by the total number of scans performed). The reason for using this method is described later.

Results

Epidemiology

The search of the epidemiology literature was performed to investigate: the incidence of vestibular schwannoma in the general and elderly populations, the size of tumours at diagnosis and how this has changed with time, and the relationship between age and tumour size.

Our search revealed 1022 studies. By following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart, 11 papers were included that met our criteria.[4–14] The results are shown in Figure 1, and Tables 1 and 2.

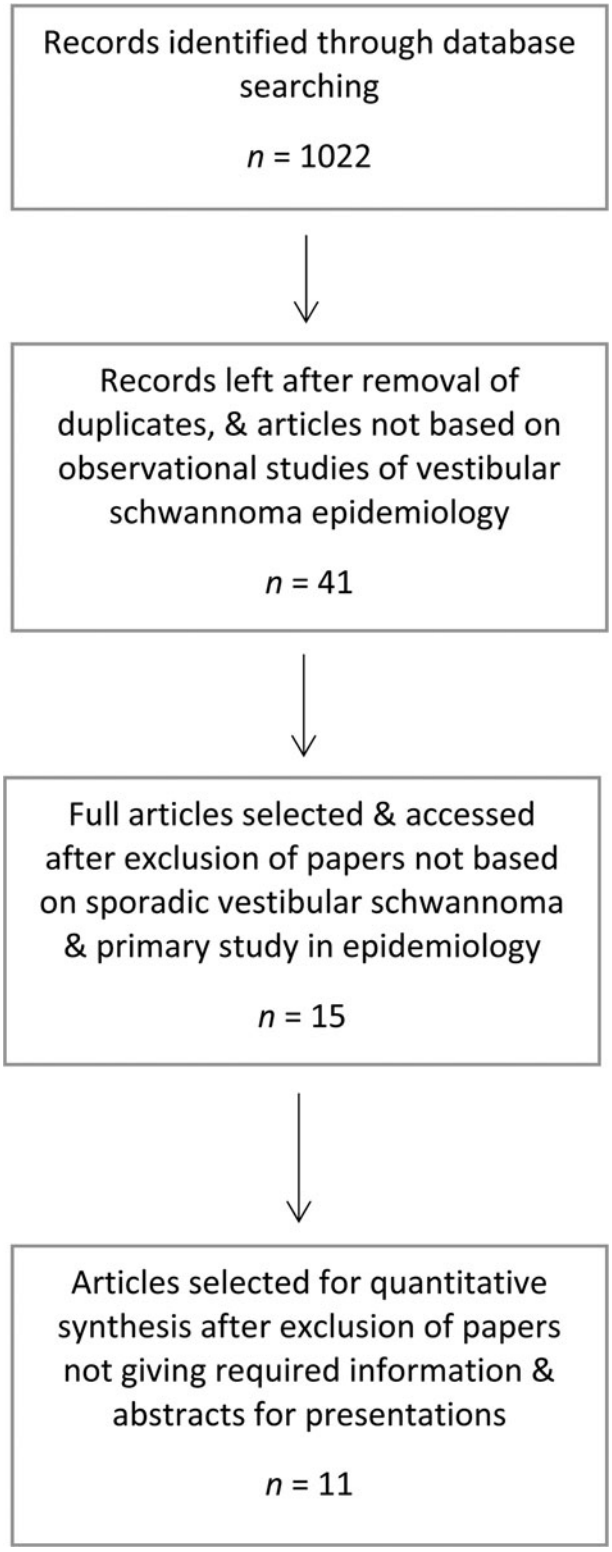

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') 2009 flow diagram for epidemiology of vestibular schwannoma.

The main reasons for excluding 1011 papers were as follows: the articles did not perform an epidemiological study themselves, but quoted figures from other sources; the main topics of discussion were vestibular schwannoma treatment, risk factors or change in management; the articles compared incidence of vestibular schwannoma between males and females, between people from different races or of different ethnicities, between different socio-economic classes; or the articles reported a regional comparison of vestibular

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Table 1. Epidemiology of vestibular schwannoma – incidence rate and percentage of older patients

Study (year)	Study type	Years assessed	Incidence per 100 000 per year	% of population with vestibular schwannoma aged over 65 or 70 years
Gal *et al.* (2010)[4]	National database (SEER) study, USA	2004–2005	1.1	21 (65 years)
Stangerup & Caye-Thomasen (2012)[5]	National database (Denmark) study	1976–2008	0.78 in 1976; 2.3 in 2004; 1.9 in 2008	12 (70 years) (in 2008)
Lau *et al.* (2012)[6]	Data from National Cancer Institute, USA	2004–2007	1.1–1.3	
Kleijwegt *et al.* (2016)[7]	Data from National Cancer Registry, Netherlands	2001–2012	1.03–1.55	15.9 (70 years)
Stepanidis *et al.* (2014)[8]	National database (Denmark) study	1976–2012	3.07 (2011)	25–30 (65 years)
Carlson *et al.* (2015)[9]	Retrospective analysis of SEER data	2004–2011	1.1	
Babu *et al.* (2013)[10]	National database (SEER) study	2004–2009	1.2	14.01 (70 years)

SEER = Surveillance, Epidemiology, and End Result Program

Table 2. Epidemiology of vestibular schwannoma – tumour size and relationship with age

Study (year)	Years assessed	Patients in study (*n*)	Average tumour size at diagnosis & change with time	Relationship between tumour size & age
Patel *et al.* (2014)[11]	1966–1998	1834	Small tumour (<1.5 cm), 23.8%; medium (1.5–2.5 cm), 38.7%; large (>2.5 cm), 37.6%	
	1999–2008	1471	Small tumour (<1.5 cm), 45.3%; medium (1.5–2.5 cm), 29.1%; large (>2.5 cm), 25.6%	
Gal *et al.* (2010)[4]	2004–2005	1621	56% had tumour <2 cm (1119 patients)	Risk of larger tumours (>2 cm) reduced by 23% for every 10-year increase of age
Stangerup *et al.* (2012)[5] & (2010)[12]	1976–2008	2283*	Mid 1970: mean extra-meatal tumour size, 30 mm; no intra-meatal. Large & giant tumours, 40%	Size decrease with age; at end of study average tumour size was 13 mm in patients aged 70+ years
	2003–2008		Mean tumour size, 10 mm; intra-meatal, 33%. Large & giant tumours, 6%	
Stepanidis *et al.* (2014)[8]	1976–2012	2739	Average diameter: 28.6 mm, 1976–1984; 9.9 mm, 2003–2011	
Kleijwegt *et al.* (2016)[7]	2001–2012	3663	Koos VS grade I, 34.9%; Koos VS grade IV, 14% (for 129 patients)	
Carlson *et al.* (2015)[9]	2004–2011	8330	Rate of tumours sized 0–2 cm increased over study period, from 38.3% to 50.7% (for 6331 patients)	
Babu *et al.* (2013)[10]	2004–2009	6225	Median, 1.6 cm; most frequent group (27.71%) had tumours 1–1.9 cm	Statistically, older age associated with smaller tumours†
Harun *et al.* (2012)[13]	1997–2010	1269		Increasing age associated with decrease in tumour size
Foley *et al.* (2017)[14]	1992–2015	945	Tumour <1.5 cm, 48%; tumour 1.5–2.4 cm, 25%	Proportion of tumours <2.5 cm increased with time

*Number obtained from 2010 study. †Study included 0.26 per cent neurofibromatosis type 2 patients. VS = vestibular schwannoma

schwannoma incidence within a country. It was not possible to determine the total number of cases across the entire population studied from the data in these papers.

The results for incidence rates of vestibular schwannoma in the general population came from studies conducted in the USA, Denmark and the Netherlands. We found seven papers in this section.[4–10] The incidence rates varied from 1.1[4] to 3.07[8] per 100 000 population per year. A long-term study carried out by Stangerup and Caye-Thomasen[5] showed that, after a steady increase, vestibular schwannoma incidence started to decline. The figure quoted by the British Acoustic Neuroma Association is 2 per 100 000 per year.[15] An earlier study, by Tos *et al.*,[16] showed an increase in vestibular schwannoma incidence between 1976 and 2001.

Out of these seven papers, five[4,5,7,8,10] showed the percentage of patients aged over 65–70 years when they were first diagnosed with vestibular schwannoma. Two papers[4,8] published the percentage of patients aged over 65 years, giving figures of 21 per cent and 25–30 per cent respectively. Three papers[6,7,10] showed the percentage of patients aged over 70 years; the respective results were 12 per cent, 15.9 per cent and 14.01 per cent. It appears that most of the patients were

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Table 3. Change in management of vestibular schwannoma with time

Study (year)	Years assessed	Patients (*n*)	Change of management with time
Patel *et al.* (2014)[11]	1966–2008	3305	Surgery, from 92.7% to 53,4%; radiosurgery, from 5% to 24.2%; observation, from 2.3% to 22.4%
Kleijwegt *et al.* (2016)[7]	2001–2012	3363	Surgery, from 31.9% to 24%; radiosurgery, from 5% to 1.6%; observation, from 63% to 74.4%
Lau *et al.* (2012)[6]	2004–2007	3650	Major decrease in surgery, with an increase of radiosurgery; observation remained unchanged
Carlson *et al.* (2015)[9]	2004–2011	8330	Surgery, from 55.6% to 44.5%; radiosurgery, from 21.5% to 20.5%; observation, from 22.9% to 34%
Babu *et al.* (2013)[10]	2004–2009	6225	Surgery, from 56% to 48.8%; radiosurgery, from 21.6% to 25.2%; observation, from 20.7% to 24.4%
Ferri *et al.* (2008)[17]	1981–2006		During 1981–1990, all VS patients had surgery; observation started in 1990, & by 2005–2006 it outnumbered surgery
Moffat *et al.* (2012)[19]	1988–2007	381	Increase in observation, which had superseded microsurgery by 2005
Foley *et al.* (2017)[14]	1992–2015	945	>80% had surgery at beginning of study, compared with <20% in last 7 years
Suryanarayanan *et al.* (2010)[20]	1992–2006		From 1978, all had surgery; this started changing in 1992. By 2003, 50% had conservative management
Mackeith *et al.* (2013)[21]	1990–2009	1308	Change in UK between 2001 & 2011: surgery, from 51% to 19%; radiosurgery, from 8% to 12%; observation, from 41% to 69%

VS = vestibular schwannoma

younger than 65 years when they were diagnosed with vestibular schwannoma.

A long-term epidemiological study conducted in Denmark[5] showed that the mean age of vestibular schwannoma diagnosis increased from 49 in 1976 to 58 in 2008, but the number of patients aged under 40 years did not change significantly. This indicates that more vestibular schwannoma cases are diagnosed at an older age, but the percentage of those aged over 70 years is still low compared to the total diagnosed.

An assessment was made of the average vestibular schwannoma size at diagnosis, how this has changed with time, and the relationship between patient age and tumour size at diagnosis. Results were obtained from 10 studies and are shown in Table 2.[4,5,7–14] The focus was mainly directed on the change in tumour size with time and the age of patients.

It is clear that the tumour size at diagnosis decreased over time. This suggests that an increasing number of people were diagnosed with smaller tumours. This is mainly attributed to improved technology used in investigations for vestibular schwannoma. It was also found that, generally, older people were more likely to have smaller tumours.[4,5,10,12,13]

A long-term study by Stangerup and Caye-Thomasen[5] found that, by 2008, the average size of tumours in people aged 70 years or more was 13 mm. A study from the same centre, published in 2010,[12] found that the number of intra-meatal tumours and extra-meatal tumours sized 1–10 mm was highest in people aged over 70 years. A study by Harun *et al.*[13] showed that, for each additional year of age at diagnosis, the mean tumour size decreased by 0.244 mm. Papers from Kleijwegt *et al.*[7] and Babu *et al.*[10] reported that, irrespective of age, the proportion of smaller tumours was higher than that of larger ones.

In summary, we can see from the published papers that the incidence of vestibular schwannoma has increased with time, and the size of the tumour at diagnosis has decreased with time. The percentage of people first diagnosed with vestibular schwannoma when aged over 70 years was reported as 12–15.9 per cent. In addition, elderly people had smaller sized tumours.

Change in vestibular schwannoma management

As the average patient age and vestibular schwannoma size at initial diagnosis changed, so did the management of this neoplasm. Factors considered when making decisions about treatment included tumour size, patient's age, health and hearing status, and the patient's preference.[9] However, the same authors also mentioned that sometimes the mode of treatment was influenced by the opinion and preference of the doctor(s) who saw these patients.

Generally, younger patients and larger tumours were treated with surgery, while older patients and those with smaller tumours received conservative management.[10] Conservative management involved a 'wait and scan' method, with serial MRI, to observe any tumour growth, and to check the symptoms and signs, in order to determine whether any change in treatment was required. There is also an argument in favour of active treatment for hearing preservation,[17] but this has been strongly challenged by Møller *et al.*[18]

Overall, our literature search revealed a decline in the rate of surgery and an increase in conservative management with time, which is shown in Table 3.[6,7,9–11,14,17,19–21] Carlson *et al.*[9] predicted that, by 2017, conservative management would become the most common method of treatment, and, by 2026, at least 50 per cent of tumours would be at least initially managed using the wait and scan method. The same paper proved (with a statistically significant correlation) that both surgery and radiotherapy were more commonly used for younger patients and larger tumours.

Tumour growth and conservative management outcome

With the changes in vestibular schwannoma epidemiology (an increase in the number of smaller tumours diagnosed; Table 2) and management (more cases of conservative management than active treatment; Table 3), the rate of vestibular schwannoma growth and the factors contributing to growth are two major topics of interest. These two topics can predict which

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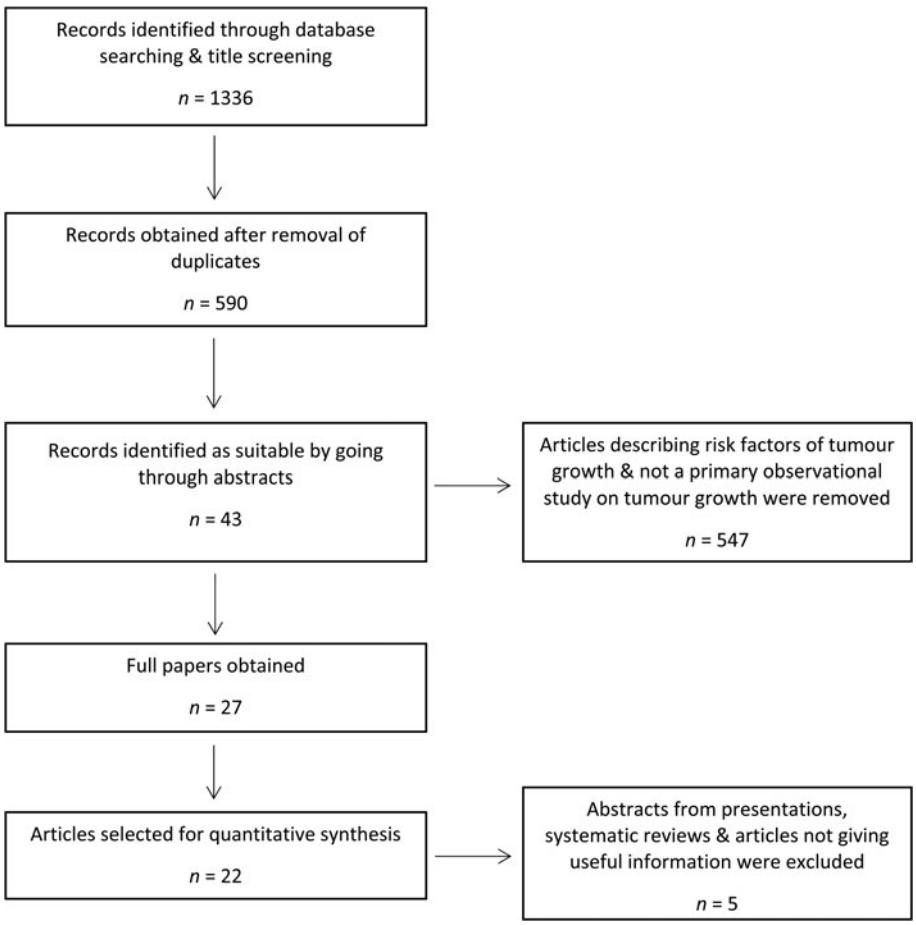

Fig. 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') 2009 flow diagram for growth and conservative management outcome of vestibular schwannoma.

of those tumours that are small at diagnosis will need active treatment during the observation period. This has led to many articles being published on the subject of tumour growth.

Our search in this section identified 1336 records. Twenty-two papers[17,19,20,22–40] were ultimately included by following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart (Figure 2); these are summarised in Table 4. In addition to these, a systematic review on tumour growth – published during the search period – was identified, along with two other systematic reviews published before 2008; these are summarised separately[42,43,45] (Table 5).

Our review of the included papers revealed a lack of uniformity in measuring tumour growth. While most papers considered an increase in extra-canalicular diameter as growth,[17,19,20,22–29,31,32,35,40] some studies used an increase in tumour volume or volume doubling time.[34] Even when diameter was considered, some papers defined growth as 2 mm or more per year,[17,19,22,23,25,29,33,36] while others defined it as 1 mm or more.[20,27,31,37] The time interval used to measure growth was also variable. While most considered growth per annum,[19,20,22,23,25,27,29,31,33,36,37] others considered the growth between two successive scans,[17,26,32,38,39] although imaging is not always conducted at one-year intervals.

The average tumour size at diagnosis varied from 5.1 mm[20] to 20.1 mm.[26] No average value was reported in five articles;[22,29,35,36,38] two articles[30,33] included intra-canalicular tumours only, two articles[23,39] included intra-canalicular tumours and up to 2 cm of extra-canalicular tumours, while one article[34] considered tumour volume. We calculated the weighted average diameter of tumours at diagnosis as 9.32 mm. This is based on data gathered from 12 papers.[17,19,20,24–28,31,32,37,40] We must remember that these tumours were treated using a conservative approach.

Great disparity was apparent in the percentage of tumours showing growth during the observation period, ranging from 11.9 per cent[39] to 79.8 per cent.[34] This raises a serious question regarding how vestibular schwannoma growth is measured. The weighted mean percentage of tumours showing growth was approximately 33.79 per cent. This was calculated using data obtained from 22 papers.[17,19,20,22–40]

The growth rate was also variable, ranging from 0.3 mm per year[17] to 4 mm per year.[23] This figure was reported as low as 0.16 mm per year for intra-canalicular tumours.[29] Data on average growth rates were missing from six articles.[30,33,36–39]

Lastly, the rate of conservative management success (i.e. the patient did not have to switch treatment to surgery or radiosurgery during the study period) ranged from 26 per cent[32] to 100 per cent[24] (follow-up period not available) or 96.9 per cent[40] (known follow-up period). These data were not available in two articles.[28,39] The weighted mean for this (from 20 articles[17,19,20,22–27,29–38,40]) was 73.66 per cent.

Next, we investigated published studies that had carried out systematic reviews on the growth and success of conservative management. Two papers[41,42] were published between 2018 and 2008, and three[43–45] were published before that time. Of these five systematic review papers, three[42,43,45] used a weighted average (the number of patients in the included articles was used as weight), one[41] did not give any average value and another[44] used mean value. In order to avoid any confusion in comparing data with our article, only values from those articles that used weighted averages[42,43,45] are given, in Table 5. These three articles reported the percentage of tumours showing growth as between 43 per cent and 50 per cent. The growth

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Table 4. Tumour growth and conservative management outcome

Study (year)	Patients (*n*)	Tumour size at diagnosis (range)	Cases showing growth (%)	Follow-up period	Average growth rate (mm/year)	Measurement parameter	Successful conservative management (%)
Younes *et al.* (2017)[22]	53	Not mentioned	27	Mean, 32 months	2.43	≥2 mm/year	77.35
Martin *et al.* (2009)[23]	276	Intra-canalicular or ≤2 cm	22	Mean, 43 months	4	≥2 mm/ year	82.25 (12 (4%) lost to follow up)
Escorihuela-García *et al.* (2014)[24]	27	8 mm (5–16 mm)	66.66	Not mentioned	<0.5	Not mentioned	100*
Fayad *et al.* (2014)[25]	114	10.5 mm (2–28 mm)	38	4.8 years – radiological follow up; 6.4 years – clinical follow up	3.1	≥2 mm/year	69
Ferri *et al.* (2008)[17]	123	10.7 mm (2–28 mm)	35.5	Mean, 57.4 months	0.3	≥2 mm between 2 scans	79.67†
Reddy *et al.* (2014)[26]	45	20.1 mm (15–31 mm)	24.4	Median, 36 months	1.2 ± 3.6 mm	2 mm between 2 scans	55.6
Hajioff *et al.* (2008)[27]	72	Median, 9.8 mm	40	Median, 121 months	1	≥1 mm/year	72.22‡
Oddon *et al.* (2017)[28]	26	Mean, 11.65 mm	53.8	Mean, 25.8 months	2.22	Not mentioned	Not mentioned
Hughes *et al.* (2011)[29]	59	No average**	20	Mean, 68 months (duration of successful conservative management)	0.16 – intra-canalicular; 1.52 – extra-canalicular, extending to cerebellopontine angle	≥2 mm/year	81.4
Lee *et al.* (2014)[30]	31	All intra-canalicular	22.5	Median, 31 months	Not mentioned	≥2 mm between 2 scans	77.5
Whitehouse *et al.* (2010)[31]	88	Mean, 10.9 mm	51.1	Mean, 3.7 years	1.2	≥1 mm/year (tumour measured by both CT & MRI)	75
Régis *et al.* (2010)[32]	47	Mean, 8.1 mm	77 (RT for intra-canalicular tumour	Mean, 43.8 months	2.1	Not mentioned	26
Kirchmann *et al.* (2017)[33]	156	All intra-canalicular	37	Mean, 9.5 years	Not mentioned	≥2 mm/year	85
Moffat *et al.* (2012)[19]	381	Mean, 9.9 mm	32.5	Mean, 4.2 years	0.7	≥2 mm/year	74.3
Varughese *et al.* (2012)[34]	178	0.71 cm^3	79.8 (when measured by single diameter	43.3 months	0.66	Given in volume doubling time§	59 (35.4 months)
Bakkouri *et al.* (2009)[35]	325	Mean not mentioned	42.2	1–9 years	1.15	No values given	76.3
Ferri *et al.* (2013)[36]	162	Not available	35.8	6.1 years	Not available	≥2 mm/year	77.78
Agarwal *et al.* (2010)[37]	180	Mean, 10 mm	37	32 months	Not available	≥1 mm/year	65
Eljamel *et al.* (2011)[38]	53	Not available	29.8	5 years	Not available	≥2 mm between 2 scans	69.8
Daultrey *et al.* (2016)[39]	555	Intra-canalicular or ≤2 cm	11.9	Not available	No mean available for all tumours	≥1 mm between 2 scans	Not available
Suryanarayanan *et al.* (2010)[20]	327	5.1 mm	32	Mean, 3.6 years	1.1	≥1 mm between 2 scans	63#
Klersy *et al.* (2018)[40]	65	9.34 mm	18.5	Mean, 41.72 months	0.74	Not defined	96.9

*Only picked up patients who completed conservative management between 2007 and 2013. †Two patients lost to follow up, one died, 47.6 per cent of tumours were intra-canalicular. ‡Excluding those who showed tumour growth but did not have any treatment, and one who died from cerebral oedema. **Number of patients according to tumour size: intra-canalicular = 34; 1–10 mm = 14; 11–20 mm = 10; 21–30 mm = 1. §Mean volume doubling time was 4.4 years; any tumour showing volume doubling time of more than 0 years was considered in the growing group. #Article involved neurofibromatosis type 2, but data for sporadic tumours were given separately. CT = computed tomography; MRI = magnetic resonance imaging; RT = radiotherapy

Table 5. Systematic reviews on vestibular schwannoma growth

Study (year)	Tumours showing growth (%)	Rate of growth (mm/year)	Successful conservative management (%)
Paldor *et al.* (2016)[42]	Up to 50 (during 5-year follow up)	Average of 1.11; for growing tumours, 2.83	–
Smouha *et al.* (2005)[43]	43	1.9	80
Yoshimoto (2005)[45]	46	1.2	82

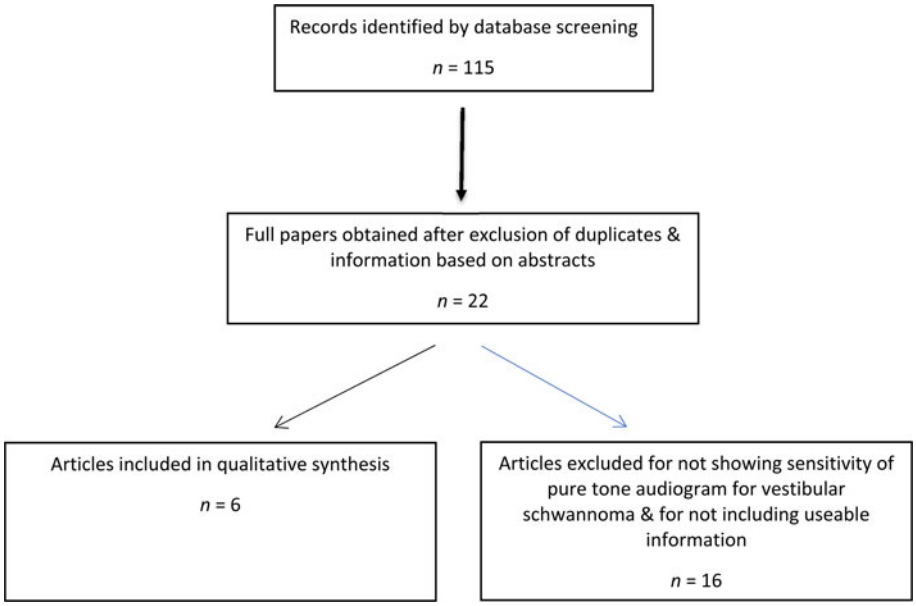

Fig. 3. Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') flowchart for sensitivity of pure tone audiogram, showing asymmetrical sensorineural hearing loss, for vestibular schwannoma.

rate was 1.11–1.9 mm per year, and the conservative management success rates were 80 per cent[43] and 82 per cent.[45]

Asymmetrical sensorineural hearing loss and vestibular schwannoma

Here, we tried to determine the chance of detecting vestibular schwannoma from MRI scans that were requested on the basis of asymmetrical SNHL and unilateral tinnitus. A literature search using the key words mentioned earlier revealed 115 studies. By following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart (Figure 3), we included six articles[7,46–50] for our qualitative synthesis. All of these were based on asymmetrical SNHL. One paper was found to be a systematic analysis.[51] Three out of six articles[46,49,50] in the study by Egan[51] were included, and that is why the data from this article are not included in weighted mean calculation. The results of these articles are shown in Table 6.

It must be mentioned that there was a lack of consensus on how asymmetrical SNHL should be defined. A guideline from the USA[52] recommended a 10 dB or more difference at two or more contiguous frequencies, or a 15 dB or more difference at one frequency. The article also states that a 15 dB or more difference at 3 kHz was the most reliable guideline. Nine different types of definition for asymmetrical SNHL were found in the thesis by Egan.[51]

As mentioned earlier, 6 studies[7,46–50] included in our qualitative analysis showed that the number of scans per diagnosis (the number of MRI scans per 1 diagnosis of vestibular schwannoma) ranged from 247 scans[46] to 23.3 scans.[47] The diagnostic yield (the percentage of positive scans against the total number of scans performed) ranged from 4.2 per cent[47] to 0.4 per cent.[46] The systematic review by Egan showed the average number of scans per diagnosis as 19.53 and the diagnostic yield as 5.1 per cent.[51]

When calculating the weighted mean using the data from these 6 articles, there were 84.15 scans per diagnosis, with a diagnostic yield of 1.18 per cent. When the total number of patients ($n = 4791$) and positive scans ($n = 149$) in these six studies was added, and assuming each MRI scan was requested for one asymmetrical SNHL result in a pure tone audiogram, the positive predictive value for asymmetrical SNHL in the diagnosis of vestibular schwannoma was 3.1 per cent.

In addition to the above six papers, our literature search also identified two abstracts for which we could not access the full papers; the yields quoted in those were 1.3 per cent[53] and 2.4 per cent.[54]

'Yield' or 'pick-up rate' were the terms used by different authors[46,47,51,53] to describe the effectiveness of MRI, requested for asymmetrical SNHL cases, in diagnosing vestibular schwannoma; we selected the former term for use in our study. Some papers have used the terms 'sensitivity' and 'specificity' in this context, but those papers were mainly focused either on comparing MRI with other non-imaging diagnostic tools for vestibular schwannoma or comparing the best predictive value of different audiological protocols for asymmetrical SNHL.[1,55,56]

The results of our literature search for vestibular schwannoma and unilateral tinnitus were sparse. The incidence rate quoted was very low in most of the published articles. One systematic review[52] gave this as less than 1 per cent for patients whose presenting symptom was unilateral tinnitus. Another article[57] found that the incidence of vestibular schwannoma in patients with tinnitus was 0.3 per cent. Choi *et al.*[48] found no vestibular schwannoma in patients with unilateral

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Table 6. Vestibular schwannoma detection rate from MRI scans requested on basis of asymmetrical SNHL

Study (year)	Study type	Total patients (*n*)	Patients with positive scans (*n*)	Scan sensitivity*		Asymmetrical SNHL parameter
				Scans per diagnosis (*n*)	Yield (%)	
Kleijwegt *et al.* (2016)[7]	Study of National Cancer Registry, Netherlands	2644	82	32.2	3.1	Not mentioned
Wilson *et al.* (2010)[46]	Retrospective chart review	247	1	247	0.4	≥30 dB difference in 3 contiguous frequencies
Pan *et al.* (2016)[47]	Retrospective review	1050	45	23.3	4.2	Not mentioned
Choi *et al.* (2015)[48]	Retrospective review	218	6	36.3	2.75	≥15 dB difference in 2 contiguous frequencies
Newton *et al.* (2010)[49]	Retrospective review	132	2†	66	1.5	Comparison of different pure tone audiogram protocols for asymmetrical SNHL
Suzuki *et al.* (2010)[50]	Retrospective review	500	13	38.6	2.6	≥15 dB difference at any 1 frequency
Egan (2015)[51]	Systematic analysis of 14 papers	5783 (MRI scans)		19.53	5.1	No correlation between degree of asymmetrical SNHL & MRI scan positive for vestibular schwannoma

*Scans per diagnosis reflect the number of scans required to obtain one positive result, and yield represents the percentage value of positive results divided by the total number of scans performed. †Paper states number of scans, not patients (presumed one scan per patient). MRI = magnetic resonance imaging; SNHL = sensorineural hearing loss

tinnitus and with no hearing loss or symmetric hearing loss. One article[26] with a small number of patients reported detecting vestibular schwannoma in 4.4 per cent of patients with tinnitus as the only presenting symptom.

Discussion

The reported incidence of vestibular schwannoma has increased over time.[4] The reasons for the rising number of tumours diagnosed include: the increased use of advanced MRI, with higher accuracy and easier access to MRI for patients; an increased awareness among physicians and patients regarding vestibular schwannoma symptoms; and the increasing life span of the population.[58]

An MRI scan of the internal auditory meatuses is frequently obtained in the investigation of patients who present with various otological symptoms, in order to diagnose (or refute the likelihood of) vestibular schwannoma. The most common symptom requiring MRI scanning in this way is asymmetrical SNHL.[59] However, the indiscriminate use of MRI scanning has been criticised in an article from the Congress of Neurological Surgeons.[52] Another article[1] suggested more rational use of MRI in the diagnosis of vestibular schwannoma. Unfortunately, at the present time, no investigation other than MRI has shown higher sensitivity and specificity in the diagnosis of vestibular schwannoma.

An article by Wilson *et al.*,[46] published in 2010, calculated that the average cost of each MRI scan for people presenting with asymmetrical SNHL was $1800 USD. The amount quoted by Pan *et al.*[47] was $11 436 USD per new diagnosis (with each scan costing $490.10 USD), and the figure quoted by Aaron *et al.*[54] for the same was $42 294 USD. The estimated cost of this imaging in the UK National Health Service was £130 GBP.[60]

Of note, some vestibular schwannomas can regress after diagnosis, in as many as 22 per cent of cases.[6] Some papers have shown that the quality of life and life expectancy of patients who followed a conservative management pathway were not inferior to those of patients who underwent surgery or radiotherapy, or to the general population.[40,61–63]

We have determined the cost-effectiveness of MRI via statistical analysis of the data collected. The weighted mean of the yield of MRI was 1.18 per cent. This means that, out of 100 MRI scans, 1.18 patients will be diagnosed with vestibular schwannoma. Considering that the estimated cost of MRI is £130 GBP,[60] the cost per diagnosis of one vestibular schwannoma would be £11 016.95 GBP (based on the calculation: $(130 \times 100) / 1.18$).

We found that: the number of small sized tumours has increased with time,[4,5,8–14] elderly people are more likely to have smaller tumours,[4,5,10,12,13] there has been a shift in the management strategy of vestibular schwannoma over time (Table 3), and conservative management is favoured for small tumours and in elderly patients.[10] Given the above, most of the patients aged 70 years or older will have small tumours managed by the wait and scan method.

Our statistical analysis also showed that, among patients who followed a conservative management pathway, only 33.79 per cent (weighted mean) of the tumours will show growth, and 73.66 per cent (weighted mean) of patients will not need to switch treatment to surgery or radiotherapy.

All of the above shows that, as a screening tool for vestibular schwannoma, more than £11 000 GBP needs to be spent on MRI scans to detect one patient with vestibular schwannoma whose tumour will be less likely to grow and will, most likely, not need any treatment.

There are other potential negative aspects of indiscriminate MRI scanning of the brain and internal auditory meatus in the elderly, including anxiety, and the extra work caused by the finding of incidental pathologies, such as old infarcts, cerebral atrophy and meningiomas, that almost never need treatment.[64]

The cost-effectiveness for patients with unilateral tinnitus will be even lower, as the quoted yields[48,52,57] are lower than those found for asymmetrical SNHL.

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Conclusion

An appreciation of the natural history of vestibular schwannoma has led to the majority of tumours being managed by observation with serial MRI scanning. In addition, the growth rate of vestibular schwannoma appears to be lower in the elderly population, with the implication that the overwhelming proportion of vestibular schwannomas in this population group will never require active treatment. A prospective analysis of elderly patients presenting with asymmetric auditory symptoms needs to be undertaken from both a clinical and cost–benefit standpoint. We hope that this article will stimulate discussion among clinicians who encounter these patients, so that management decisions can be taken and discussed with patients on a rational basis.

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