

Main Article

Georgios Kontorinis takes responsibility for the integrity of the content of the paper

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Corresponding author:

Georgios Kontorinis;
Email: gkontorinis@gmail.com

Abstract

Objective. Magnetic resonance imaging of the internal auditory meatus is a highly sensitive and specific way to diagnose vestibular schwannoma. However, the rate of incidental findings with this method is believed to be high and can lead to increased patient anxiety and health interventions with unclear benefit.

Method. A systematic review of the literature was performed using the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines to identify incidental findings from magnetic resonance imaging of the internal auditory meatus; 12 studies were identified for inclusion within this review.

Results. A total of 10 666 patients were included within the review. The overall rate of diagnosis of vestibular schwannoma was 0.87 per cent; 21 per cent of the study population had incidental findings on magnetic resonance imaging of the internal auditory meatus, and 9.56 per cent had clinically significant incidental findings.

Conclusion. Standardised pre-scan counselling may mitigate the risks of overdiagnosis, but future work should be undertaken to assess the benefits of such a strategy as well as the exact significance of some incidental findings.

Introduction

Magnetic resonance imaging of the internal auditory meatus (MRI IAM) or the head enhanced with intravenous gadolinium administration has revolutionised the diagnosis of vestibular schwannoma. Magnetic resonance imaging of the IAM or the head has a sensitivity and specificity approaching 100 per cent¹ for the identification of this rare but potentially life-threatening condition. As such, this imaging technique is now considered the ‘gold standard’ for the diagnosis of vestibular schwannoma.²

Vestibular schwannoma is a relatively rare benign growth of the vestibulo-cochlear nerve with a reported incidence of approximately 1 in 100 000 patients.³ Approximately two thirds of all vestibular schwannoma demonstrate no significant growth, and in those that do grow the average rate of growth is 1.2 mm per year.⁴ However, in cases where the cerebellopontine angle becomes compressed, patients can experience severe neurological symptoms, which can also be life threatening.⁵ In such cases, patients are offered treatment with stereo-tactic radiosurgery or skull base surgery.^{4,5} Owing to the slow rate of growth and the high rate of spontaneous cessation of growth and even regression, many patients are offered serial MRI scans as part of a conservative ‘scan and wait’ management of the condition, indicative of the importance of imaging in vestibular schwannoma management.⁶

Symptoms of vestibular schwannoma are largely split into early audiological symptoms followed by late neurological symptoms.⁴ As such, current recommendations in the UK recommend early MRI IAM scanning in patients who present with localised symptoms of the IAM (such as unilateral tinnitus and facial nerve palsy) or those with asymmetric sensorineural hearing loss.⁷ Although MRI IAM has a high specificity and sensitivity, it is not without its disadvantages, mainly the associated cost and waiting times for scanning.^{1,3,8} Another significant aspect to consider is the rate of incidental findings that MRI IAM can identify. Previous studies have quoted that rates of incidental findings in patients meeting criteria for MRI IAM are as high as 40–45 per cent.^{9,10} Even in healthy volunteers, the rate of incidental findings has been reported to be 13.5–18 per cent,^{11,12} with one study showing that the risk of identifying a clinically serious incidental finding on MRI was approximately 1.7 per cent.¹³ The identification of such incidental findings, particularly the ones with limited clinical impact, can cause increased patient anxiety and increase the burden of work load in secondary care and primary care services.¹⁴

Given the absence of any systematic reports on MRI IAM incidental findings, we conducted a systematic review of the literature with respect to the identification of incidental findings on MRI IAM in patients presenting with symptoms suggestive of vestibular schwannoma. We aimed to identify the rate and nature of such findings as well as the

incidence of serious incidental findings of MRI IAM and the diagnostic yield of vestibular schwannoma in the included studies.

Materials and methods

Basic settings and search strategy

We carried out a systematic review using the Preferred Reporting Items for Systematic Review and Meta-Analyses ('PRISMA') 2020 guidelines.¹⁵ The primary literature search was conducted via the library team in our tertiary, academic setting.

Our research question was on the nature and significance of incidental findings on MRI IAM. The literature search was conducted on two separate databases: Embase and Medline. The literature search included papers published at any point (no starting point) up to 4 April 2022.

Our search terms for the literature review were 'internal auditory canal', 'internal auditory meatus', 'magnetic resonance imaging' and 'incidental finding'. We included studies reporting incidental findings on MRI IAM. We excluded case reports and conference abstracts as well as papers not in the English language.

Study selection

This initial search yielded a total of 76 records, and these were screened for duplicates. This led to the removal of 14 records leaving 62 for review. All records were then screened by two independent reviewers (PS, GK). Accepted study designs included: retrospective cohort, retrospective case-control series, retrospective cross-sectional, prospective cohort, prospective observational studies and large case series. Single case reports and conference abstracts were excluded. Studies on paediatric populations and on asymptomatic or 'normal' volunteers were also excluded. Following screening, full text review was undertaken by the same reviewers to assess for suitability for inclusion in the systematic review. The references of all full text articles were also reviewed to assess for any other records that would meet inclusion criteria.

Data collection and analysis

The following data points were then analysed from the included records: study date and place of origin, study design, study size and population, indication for imaging, rate of vestibular schwannoma diagnosis, incidental finding rate, breakdown of incidental findings, and rate of serious or clinically significant incidental findings as defined by each study. We followed the Joanna Briggs Institute guidance for narrative data synthesis, pending adequate data homogeneity.

Risk of bias and heterogeneity assessment

The risk of bias for each included study was assessed using the Joanna Briggs Institute checklist for observational studies.¹⁶ This is a nine-point checklist, and each element of the checklist can be answered yes or no with an answer of yes scoring 1 point and an answer of no scoring 0. Studies were then placed into one of three categories depending on this score; these were: low risk of bias, moderate risk of bias and high risk of bias. The Joanna Briggs Institute review document is included in Table 1 in the supplementary material, available on *The Journal of Laryngology & Otology* website.

Results

Following initial screening, 18 records were deemed appropriate for full text review. Following review of the references of these full text records, a further three records were deemed suitable for full text review. Following the full text review of the 21 records, 9 papers were excluded leading to 12 eligible papers. The reasons for these exclusions are demonstrated within the Preferred Reporting Items for Systematic Review and Meta-Analyses ('PRISMA') flowchart diagram in Figure 1.

Geographic origin

A total of 12 studies were included in the final review. The earliest study date was from 2000, and the latest was from 2021; 7 of the studies originated from the UK, 1 from the USA, 1 from The Netherlands, 1 from Canada, 1 from the Republic of Ireland and 1 from India.

Indication for imaging

Seven studies assessed all patients who met local guidelines for MRI IAM for audiovestibular symptoms, three studies assessed only patients presenting with unilateral non-pulsatile tinnitus, one study assessed only asymmetric sensorineural hearing loss and one study only assessed individuals presenting with acute onset asymmetric sensorineural hearing loss.

Study design and risk of bias

Ten of the 12 studies were retrospective cross-sectional studies, and the remaining 2 were prospective cross-sectional studies. On assessment of the risk of bias, 9 of the 12 studies scored 9 out of 9 utilising the Joanna Briggs Institute guidance, and the remaining studies (Kalsotra *et al.*, Htun *et al.* and Powell and Choa) scored 8 out of 9.¹⁷⁻¹⁹ All included studies thus fell into the category of being low risk of bias.

Vestibular schwannoma identification rates and incidental findings

A total of 10 666 patients were included in the review; 93 patients were found to have a newly diagnosed vestibular schwannoma with an overall identification rate of 0.87 per cent. A total of 2245 patients had incidental findings on the MRI IAM scan, which equated to 21 per cent of the study population. Seven of the studies reported the rate of serious or clinically significant findings. Of this sub-population, 9.56 per cent were identified as having a clinically important finding. However, there was no uniform criteria across the studies as to what constituted a clinically significant finding. A breakdown of the included studies is shown in Table 1.

Only one study (Powell and Choa) did not provide a breakdown of the incidental findings.¹⁹ The most common incidental findings were multiple high signal white matter changes or small vessel disease ($n = 671$) followed by paranasal sinus mucosal thickening or disease ($n = 575$) and then cerebral atrophy ($n = 246$). Other common incidental findings included: middle-ear or mastoid mucosal thickening or disease ($n = 193$), vascular loops ($n = 161$) and arachnoid cyst ($n = 77$). Two of the included studies did not include sino-nasal disease as an incidental finding (Hoekstra *et al.* and Wong *et al.*), and two studies did not include multiple high signal white matter changes or small vessel disease as an incidental finding (Ahsan *et al.* and

Table 1. Included studies with vestibular schwannoma identification and incidental finding rates

| Study | Year of publication | Country of origin | Study design | Scans (n) | Indication for imaging | VS identification rate (%) | Incidental findings rate (%) | Clinically significant findings rate (%) |
|--|---------------------|---------------------|-------------------------------|-----------|--|----------------------------|------------------------------|--|
| Mirza <i>et al.</i> ²⁰ | 2000 | UK | Retrospective cross-sectional | 644 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 4 | 41.3 | 2 |
| Chisholm <i>et al.</i> ³⁰ | 2006 | UK | Retrospective cross-sectional | 672 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 1.4 | 32.9 | Not reported |
| Powell and Choa ¹⁹ | 2010 | UK | Retrospective cross-sectional | 152 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 1 | 29.6 | Not reported |
| Papanikolaou <i>et al.</i> ¹⁰ | 2010 | Republic of Ireland | Retrospective cross-sectional | 200 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 0.5 | 45 | 2.5 |
| Hoekstra <i>et al.</i> ⁹ | 2015 | Netherlands | Retrospective cross-sectional | 308 | Unilateral non-pulsatile tinnitus patients | 2.2 | 42.5 | 4.9 |
| Ahsan <i>et al.</i> ²¹ | 2015 | USA | Retrospective cross-sectional | 451 | Patients presenting with acute sensorineural hearing loss | 4.7 | 20.4 | Not Reported |
| Htun <i>et al.</i> ¹⁸ | 2015 | UK | Retrospective cross-sectional | 109 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 0.9 | 43.1 | Not reported |
| Kalsotra <i>et al.</i> ¹⁷ | 2015 | India | Prospective cross-sectional | 62 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 1.6 | 41.9 | 0 |
| Amiraraghi <i>et al.</i> ⁸ | 2018 | UK | Retrospective cross-sectional | 6978 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 1.6 | 15.7 | 11.2 |
| Wong <i>et al.</i> ¹ | 2020 | Canada | Retrospective cross-sectional | 324 | Sensorineural hearing loss patients only | 5.8 | 2.2 | Not reported |
| Saxby <i>et al.</i> ³ | 2021 | UK | Retrospective cross-sectional | 566 | Unilateral non-pulsatile tinnitus patients | 0.5 | 23.7 | Not reported |
| Sajid <i>et al.</i> ² | 2021 | UK | Prospective cross-sectional | 200 | All patients presenting with audiovestibular symptoms meeting local criteria for MRI | 0.5 | 44.5 | 0 |

VS = vestibular schwannoma; MRI = magnetic resonance imaging

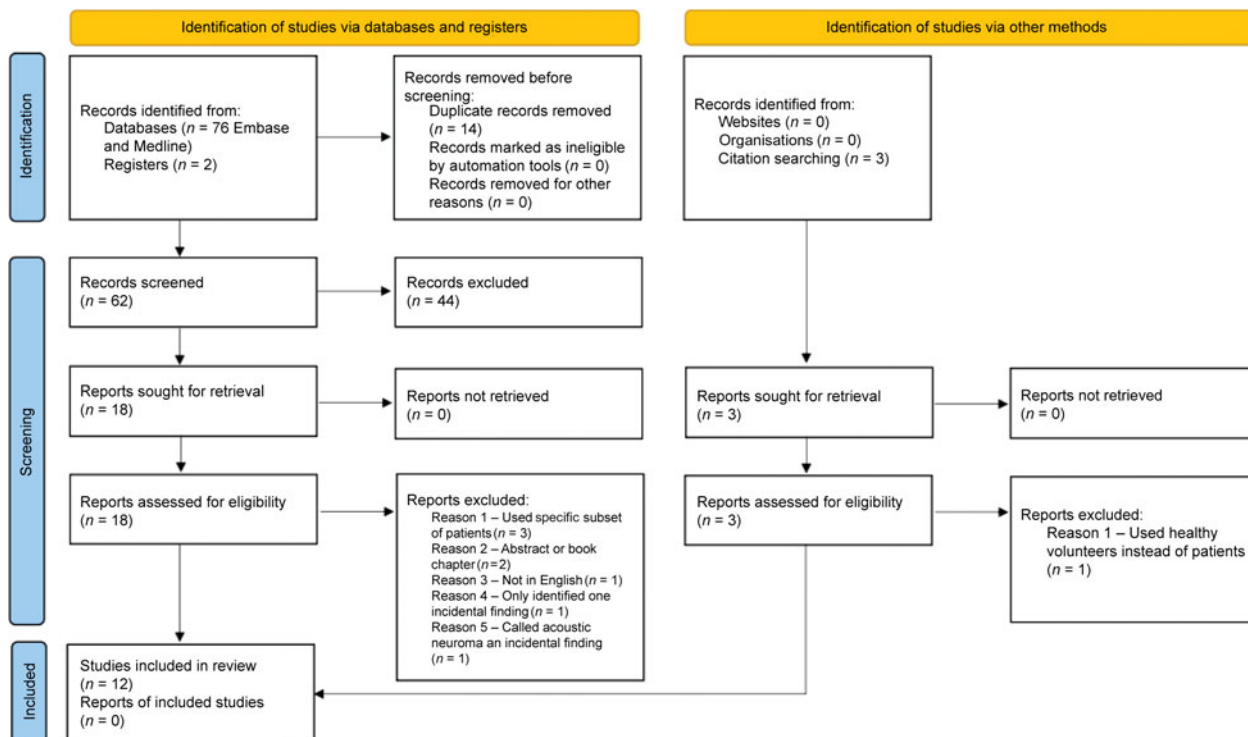


Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analyses (‘PRISMA’) flowchart.

Wong *et al.*).^{1,9,20} A detailed breakdown of the results is shown in Table 2. A complete breakdown of all specific incidental findings is included in Table 1 in the supplementary material, and the conclusions of each included study are shown in Table 2 in the supplementary material, both available on *The Journal of Laryngology & Otology* website.

From our analysis, the diagnostic yield of MRI IAM for vestibular schwannoma was low. Less than 1 per cent of all patients scanned received a new diagnosis of vestibular schwannoma. This is in stark contrast to the rate of patients who have a new incidental finding, at 21 per cent of all

patients. This may also represent a conservative estimate of the incidental findings rate because three studies did not include either sino-nasal disease or white matter changes as incidental findings. Five of the included studies (Mirza *et al.*, Papanikolaou *et al.*, Htun *et al.*, Hoekstra *et al.* and Sajid and Frost)^{2,9,10,18,20} reported incidental finding rates in excess of 40 per cent of all scanned patients. Although these figures sound high and variable, it is worth addressing that the definition of the term ‘incidental finding’ varies widely. If one looks closer at incidental findings with potential clinical significance, the reported numbers are lower but still significant.

Table 2. Detailed breakdown of the most common incidental findings

| Study | Year | Scans (n) | Incidental findings (n) | Vascular loops | Small vessel disease / white matter changes (n) | Sinus disease (n) | Mastoid / middle ear-disease (n) | Arachnoid cysts (n) | Other (n) |
|--|------|-----------|-------------------------|------------------------|---|-------------------|----------------------------------|---------------------|-----------|
| Mirza <i>et al.</i> ²⁰ | 2000 | 644 | 266 | 30 | 135 | 56 | 34 | 0 | 39 |
| Chisholm <i>et al.</i> ³⁰ | 2006 | 672 | 221 | 0 | 74 | 42 | 38 | 10 | 39 |
| Powell & Choa ¹⁹ | 2010 | 152 | 45 | No breakdown available | | | | | |
| Papanikolaou <i>et al.</i> ¹⁰ | 2010 | 200 | 90 | 2 | 66 | 8 | 6 | 2 | 0 |
| Hoekstra <i>et al.</i> ⁹ | 2015 | 308 | 131 | 70 | 0 | 0 | 4 | 5 | 7 |
| Ahsan <i>et al.</i> ²¹ | 2015 | 451 | 92 | 3 | 0 | 69 | 1 | 9 | 5 |
| Htun <i>et al.</i> ¹⁸ | 2015 | 109 | 47 | 7 | 29 | 9 | 0 | 0 | 3 |
| Kalsotra <i>et al.</i> ¹⁷ | 2015 | 62 | 26 | 5 | 8 | 4 | 0 | 3 | 1 |
| Amirraghi <i>et al.</i> ⁸ | 2018 | 6978 | 1097 | 63 | 284 | 331 | 83 | 40 | 188 |
| Wong <i>et al.</i> ¹ | 2020 | 324 | 7 | 0 | 0 | 0 | 0 | 0 | 3 |
| Saxby <i>et al.</i> ³ | 2021 | 566 | 134 | 0 | 43 | 40 | 18 | 3 | 8 |
| Sajid <i>et al.</i> ² | 2021 | 200 | 89 | 11 | 32 | 16 | 9 | 5 | 12 |

Potential impact of incidental findings

Sajid and Frost discussed some of the healthcare consequences of incidental findings. This group identified that between 23–37 per cent of their sample population was referred to secondary care and that these referrals had a clear temporal relationship with the timing of the MRI scan.² This will have clear implications for secondary care services and will exact a deleterious effect of appointment burden. The group also discussed the consequences to the patient. Within the sample, they deduced that nearly 20 per cent of patients would be exposed to a diagnosis of small vessel disease. This would also expose them to further treatment cascades, referrals, treatment burden (with difficult to estimate but potential iatrogenic harm), financial or health-insurance harm, and anxiety. It was also stated that treatment in such a circumstance was of unclear benefit; however, both the benefit and harm of treating such a condition are unclear.

Additionally, it should be noted, that we did not identify any specific data on the risk of overdiagnosis.² The financial implications were, however, discussed in several of the studies. Saxby *et al.* stated that the average cost of an MRI IAM within the National Health Service system would cost approximately £200.³ Applying this number to our sample size, this would equate to £2.13 million spent on MRI scans, or approximately a cost of £23 000 per vestibular schwannoma diagnosed on MRI. This represents a significant financial burden to nationalised or public healthcare systems. With the costs of MRI being much higher in other health systems across the globe, the question to scan or not to scan becomes of even more interest, not only from the patients' but also from a financial perspective.

Clinically significant findings

Over half of the included studies discussed clinically significant or serious incidental findings found on MRI IAM in patients presenting with audiovestibular symptoms. A total of 9.6 per cent of the patients included in this analysis were diagnosed with a new serious or significant incidental finding. As above, there was no agreed criteria as to what constituted a serious or clinically significant finding, and thus individual authors were left to classify incidental findings, and there was some crossover between the included studies. This particular finding was heavily influenced by the Ammiraghi *et al.* study, with 781 of the 815 serious findings being identified within this one study, which included the largest cohort of nearly 7000 scans.⁸ Interestingly, the rate of serious incidental findings in this review was slightly higher than previously described in the general population. Vernooij *et al.* studied the MRI brains of 2000 healthy volunteers and found clinically significant findings in 7.3 per cent of patients, but a larger meta-analysis by Gibson *et al.* found this to be 1.4 per cent.^{12,22}

This discrepancy can be explained by several factors: (1) more detailed imaging and MRI evolution allowed the diagnosis of more incidental findings, (2) a vague and variable definition of 'incidental', 'clinically significant' or 'serious' finding, (3) the retrospective nature of most of these studies and the inevitable lack of reliability in data collection, (4) the enrolled number of scans or patients, and (5) the indication for imaging in each study.

In particular, when it comes to the definition of 'incidental', this is vaguely defined not only in the included studies but also throughout the literature. Certain findings that were defined as incidental in some studies could be of significance in a

different clinical context. As addressed in supplementary Table 1, relatively uncommon radiological findings such as meningiomas or arterio-venous malformations can be incidental for certain patients or studies but were considered significant by the reporting studies.

Specific findings

The most common incidental finding that was identified in our review was small vessel disease or multiple T2-weighted high signal areas within white matter (a more accurate radiological term as it also includes non-specific white matter changes).²³ Several studies discussed the significance of these findings. Changes related to small vessel ischaemia become increasingly common in older populations, particularly in older adults where their prevalence can approach 95 per cent of the population. They are also associated with individuals who have risk factors for cerebro-vascular disease and are more common in stroke patients, although it should be noted that they are also present in a significant proportion of non-stroke patients. They have also been associated with symptoms of poor mobility and cognitive decline. It is worth noting that T2-weighted high signal white matter changes are not specific to cerebro-vascular disease and can be linked to demyelination, migraine or other neurological conditions in a patient with an appropriate history.^{24–26}

It was recommended in the study by Mirza *et al.* that patients who are noted to have white matter changes should be screened for stroke risk and appropriate preventative therapy considered.²⁰ However, to our knowledge there is no evidence that T2-weighted high signal white matter changes are directly linked to future stroke or that therapeutic intervention in this patient confers benefit to patients.²⁰ A similar observation was made in the Ammiraghi *et al.* study.⁸ Given the commonality of this finding, it is a matter of priority to further understand the significance of these changes. At present, we could only recommend that the identification of multiple high signal white matter changes should prompt a clinical review to further define the likely underlying cause of the white matter changes.²³ If the changes are deemed to be because of small vessel ischaemia, evaluation and treatment of vascular risk factors would confer a benefit to patients.

The second most common incidental finding identified was paranasal sinus disease. This was identified in a total of 575 patients in our review. The incidence of incidental or sub-clinical sinusitis identified on cross-sectional imaging is high, with papers quoting 25–50 per cent.^{27–29} No specific recommendations were made in any of the included studies, but previous studies recommend correlating the findings on imaging with those reported in the history and examination findings. The correlation between patients with sinusitis symptoms and cross-sectional imaging has been found to be poor, and it could be expected that in the absence of nasal or paranasal symptoms that this correlation would be even poorer, although we cannot find any published evidence to support this claim.³⁰

Vascular loops around the IAM were seen in 161 patients within our review. A vascular loop is an anatomical variant usually of the anterior inferior cerebellar artery where it passes in close proximity to the vestibular-cochlear nerve. The management of these loops has historically been controversial in the literature. Several studies in our review discussed the importance of these loops. In particular, the Hoekstra *et al.* study conducted auditory brainstem response (ABR) testing

on all patients that were identified with a vascular loop within their sample. They noted a generally poor correlation with the presence of a vascular loop and any changes on ABR testing. They also noted a poor correlation between the side of the vascular loop and ipsilateral audiovestibular symptoms; this finding was similarly reported within the Amiraraghi *et al.* paper.^{8,20} Hoekstra *et al.* concluded that the presence of these vascular loops likely represents a true incidental finding and is of doubtful clinical significance.

Pre-imaging counselling

Four of the included studies specifically discussed the benefit of pre-scan counselling (Papanikolaou *et al.*, Htun *et al.*, Amiraraghi *et al.* and Kalsootra *et al.*) in an attempt to mitigate the risks discussed above.^{8,10,17,18} The aim of this counselling would be to educate patients about the low chance of diagnosis versus the much higher risk of the identification of a non-relevant clinical finding or a significant clinical finding. They also discussed the need for this counselling to be as standardised as possible. Furthermore, specific emphasis on pre-existing conditions or symptoms that could result in 'incidental' findings would be worth considering as part of pre-imaging counselling. For example, changes in the paranasal sinuses should be expected in patients with known rhinosinusitis or polyposis nasi; this could perhaps be discussed, particularly with the more anxious patients, in advance.

Practical considerations should also be taken into account. Clinic appointments are unlikely currently to be long enough for effective face-to-face pre-scan counselling to occur. A patient information leaflet may be helpful but then also places burden on the patient to communicate the decision back to the clinician, with the disadvantage of lack of personal communication with the health professional. However, in the long-term, a strategy of detailed pre-scan counselling could provide time and financial benefits to public healthcare systems. It should also be mentioned that we were unable to identify any evidence that any unit has adopted such a strategy and what benefits it confers to a healthcare service. Further research should focus on this strategy, when it comes to health services and policies.

Our review identified that a patient undergoing MRI for audiovestibular symptoms is nearly 20 times more likely to be diagnosed with an incidental significant finding (10 times more likely when it comes to incidental findings of potentially clinical significance) than being diagnosed with a vestibular schwannoma; this fact raises an ethical dilemma. Multiple authors advocate for pre-scan counselling to mitigate these risks. However, in studies where serious findings were discussed, the outcomes of the patients diagnosed with serious findings and also any possible benefits that early diagnosis may have conferred versus the harm of missed diagnosis was not discussed. Further work into this area should be undertaken before concluding that pre-scan counselling would be directly beneficial to patients.

Study inclusion, quality and limitations

All of the included studies were cross-sectional in nature, with only 2 of the 12 being prospective. This represents level 4 evidence for this review. Although this represents a relatively low quality of evidence, the risk of bias from each study was deemed to be low across all the studies. Inappropriate sample size was the only reason why included studies did not score nine out of nine using the Joanna Briggs Institute appraisal

tool. This likely is a reflection of the rarity of vestibular schwannoma in the general population.

Most of the included studies looked at all patients who met local guidance for MRI scanning for audiovestibular symptoms. As stated, five of the included studies looked at a specific sub-population of audiovestibular symptoms (tinnitus and/or asymmetric sensorineural hearing loss). We decided to include these studies within this review as it was felt that these patients would still have met criteria for MRI IAM scanning within most secondary care units. However, we accept that this may have increased the risk of bias in increasing the rate of incidental findings and decreasing the rate of vestibular schwannoma diagnosis. Additionally, some of the studies did not define the exact indications for imaging and whether broader criteria than asymmetric sensorineural hearing loss or unilateral tinnitus, such as pulsatile tinnitus, were used.

As most of the studies were retrospective in nature, our review is open to some element of bias. Also, the majority of our papers originated from the UK where a nationalised global health service exists. Many of these papers discussed the pressures that incidental findings exerted on the global health service as a whole, which may not be present in other healthcare services. This may have also added further bias to our results.

Irrespectively, this review represents a large-scale review of multiple international studies examining the results of over 10 000 MRI scans suggesting that incidental findings should be taken into account within the appropriate clinical context.

Conclusion

Magnetic resonance imaging of the IAM or the head is a highly specific and sensitive tool for the detection of vestibular schwannoma. However, the overall diagnostic yield of this condition is low, around 1 per cent. The rate of any incidental finding is relatively high at 21 per cent, with nearly 10 per cent of patients having a clinically significant incidental finding. The exact significance of these findings remains unclear, but overall such findings should be assessed within the appropriate clinical context. Effective and standardised pre-scan counselling may mitigate some of the risks of overdiagnosis, but further published evidence is needed to identify the adoption of such a strategy and the benefits that it would confer to this patient population.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0022215122002596>.

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Competing interests. None declared.

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