The association of vascular loops within the internal auditory meatus or contacting the vestibulo-cochlear nerve with audio-vestibular symptoms. A systematic review and meta-analysis.

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ABSTRACT

Background: Intrameatal vascular loops (IVL) entering the internal auditory meatus (IAM) and neurovascular contact (NVC) with the vestibulo-cochlear nerve (CN VIII) have been proposed to have a relationship with audio-vestibular symptoms.
Purpose: This systematic review and meta-analysis aimed to determine whether the presence of IVLs and CN VIII NVC on magnetic resonance imaging (MRI) is associated with tinnitus, sensorineural hearing loss (SNHL) or vertigo and any specific subtypes.
Data Sources: All studies comparing the presence of IVL or CN VIII NVC in ears with these audio-vestibular symptoms and controls were identified through MEDLINE, EMBASE, Web of Science Core Collection, Scopus and Cochrane Register of Controlled Trials databases.
Study Selection: 16 studies and 3,455 ears (1526 symptomatic ears and 1929 control ears) were included.
Data Analysis: Meta-analysis was performed using a bivariate random effects model. Pooled odds ratios (ORs) were calculated, and heterogeneity was evaluated with Cochran's Q test with statistical significance defined as $p<0.05$.
Data Synthesis: There was no significant association between the presence of undefined tinnitus or SNHL and that of IVL (OR 0.90 95% CI 0.47, 1.70; OR 0.67, 95% CI 0.36, 1.25) or CN VIII NVC (OR 1.15, 95% CI 0.68, 1.95; OR 0.89, 95% CI 0.33, 2.40). However, the subgroup of sudden onset SNHL was associated with IVL (OR 1.34, 95% CI 1.04, 1.73) ($p=0.02$). There was no significant difference in the prevalence of IVL (OR 0.97, 95% CI 0.64, 1.48) or CN VIII NVC (OR 0.99, 95% CI 0.42, 2.32) between ears with undefined vertigo and control ears. However, there was an association between the presence of CN VIII NVC and the specific diagnosis of vestibular paroxysmia (OR 13.19, 95% CI 2.09, 83.16) ($p=0.006$).
Limitations: Our meta-analysis is limited by selection bias, small number of eligible studies and moderate heterogeneity.
Conclusions: IVL or CN VIII NVC on MRI are unrelated to symptoms of undefined tinnitus, SNHL and vertigo. However, CN VIII NVC is associated with vestibular paroxysmia whilst IVL is associated with sudden onset SNHL.

ABBREVIATIONS: AICA = anterior inferior cerebellar artery, CI = confidence interval, CN = cranial nerve, CPA = cerebellopontine angle, IAM = internal auditory meatus, NVC = neurovascular contact, OR = odds ratio, SNHL = sensorineural hearing loss, SoSNHL = sudden onset sensorineural hearing loss.

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INTRODUCTION

Vascular loops are frequently identified within the internal auditory meatus (IAM) on magnetic resonance imaging (MRI). Whilst this is most commonly due to the anterior inferior cerebellar artery, the posterior inferior cerebellar artery, superior cerebellar artery, or venous structures may also be responsible [1]. Authors have speculated that these intrameatal vascular loops (IVL) may be responsible for tinnitus, sensorineural hearing loss (SNHL) and vertigo [2]. It is hypothesised that such audio-vestibular symptoms may result from altered neural conduction due to CN VIII neurovascular contact (NVC), reduced

vascular perfusion of the nerves due to disturbed blood flow or increased transmission of sound through the CSF of the IAM [1-2]. Symptoms due to NVC are considered to be most common when a vessel contacts the centrally myelinated portion of the cranial nerve or the transition zone between central and peripheral myelin [3].

Determining an association between the presence of an IVL or CN VIII NVC and audio-vestibular clinical presentations would guide the selection of appropriate diagnostic MRI sequences and interpretation of the imaging findings. There are also potential therapeutic implications since vascular decompression surgery has been performed to alleviate such symptoms [4]. An association between these vascular variants and audio-vestibular clinical presentations remains uncertain, with variable outcomes from previous case-controlled studies and with no contemporary pooling of the statistical outcomes.

This systematic review and meta-analysis aimed to determine whether there is an association between IVLs or CN VIII NVC and specific audio-vestibular symptoms.

MATERIALS AND METHODS

This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [5] and enrolled on the Prospective Register of Systematic Reviews (PROSPERO), CRD42023447065.

Search strategy

The search strategy was designed using PICOS (population; intervention or exposure; comparator/control; outcome; study design). Population was defined as ears with specific audio-vestibular symptoms; exposure as the presence of a IAM vascular loop or CN VIII NVC; control as ears without audio-vestibular symptoms; outcome as the presence of an IAM vascular loop or CN VIII NVC relative to the reporting of audio-vestibular symptoms; and study design as case-controlled cross-sectional studies. Search terms were adapted after a pilot search to include relevant synonyms (supplementary 1).

Searches were performed in MEDLINE, EMBASE, Web of Science Core Collection, Scopus and Cochrane Register of Controlled Trials databases. The search was performed from database inception onwards. The searches were last performed on 01/08/2023. Manual forward and backward searches were performed for all eligible review articles. The five most frequently cited journals were hand searched (2009–2023) (supplementary 1). EndNote Web© was used as a reference manager to identify and collate the literature and allow for the manual removal of duplicates.

Selection of studies

Two independent reviewers (JC, MST) applied the piloted screening tool to the titles and abstracts with the following inclusion criteria: a defined patient group with audio-vestibular symptoms; analysis using MRI; reference to a vascular loop/variant or anomaly. Case studies, review articles, foreign language literature and duplicated studies were excluded. The full text was independently assessed for eligibility by both reviewers according to the PICOS criteria. Studies were included when there were data that could be extracted into a 2x2 contingency table comparing the presence of an IVL or CN VIII NVC in ears with and without tinnitus, SNHL or vertigo. Since vertigo is not lateralised to either ear, patients with vertigo were compared to

subjects without vertigo, with the prevalence of an IVL or CN VIII NVC in either ear being recorded. When a symptomatic subtype was defined by specific criteria then this was analysed separately.

Reasons for exclusion are listed in supplementary 2. Discrepancies were resolved by discussion (JC, MST, SC).

Data extraction

Two reviewers (JC, MST) independently extracted data regarding (a) study characteristics: authors, year of publication, retrospective v prospective, case and control group size, IVL classification scale applied, specified audio-vestibular symptom(s); (b) control group type: asymptomatic contralateral ears, healthy volunteer ears, or ears of patients with an unrelated condition; (c) demographic and clinical characteristics: age and sex of the case and control groups, unilateral or bilateral cases. Contingency tables (2x2) were constructed comparing the presence of the audio-vestibular symptom (reference standard) and the presence of an IVL or CN VIII NVC on MRI (index test). Details of specific classifications for the assessment of IVL and CN VIII NVC are provided in supplementary 3. Any discrepancies in the data collection were resolved by revisiting the article in a consensus meeting.

Quality assessment

The methodological quality of the eligible studies was evaluated using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) tool by two independent reviewers (JC, MST) [6]. The signaling questions were tailored specifically to the review (supplementary 4).

Statistical analysis

Bivariate random-effects meta-analysis was performed with R 4.3.1 (package “meta”) and R Studio (Version 2023.09.0+463) to evaluate the association between audio-vestibular symptoms and the presence of an IVL or CN VIII NVC. The results were tabulated with corresponding forest plots. Pooled odds ratios (ORs) were calculated with 95% confidence intervals and p values. Heterogeneity was assessed by Cochran’s Q test. Further quantification of heterogeneity was provided with tau^2 and I^2 statistics. Statistical significance was defined as $p<0.05$.

RESULTS

Systematic review

The screening tool identified 77 potentially eligible articles. After full text review, 15 studies were included. One additional relevant article was identified via citation searching, totaling 16 eligible studies (Fig 1).

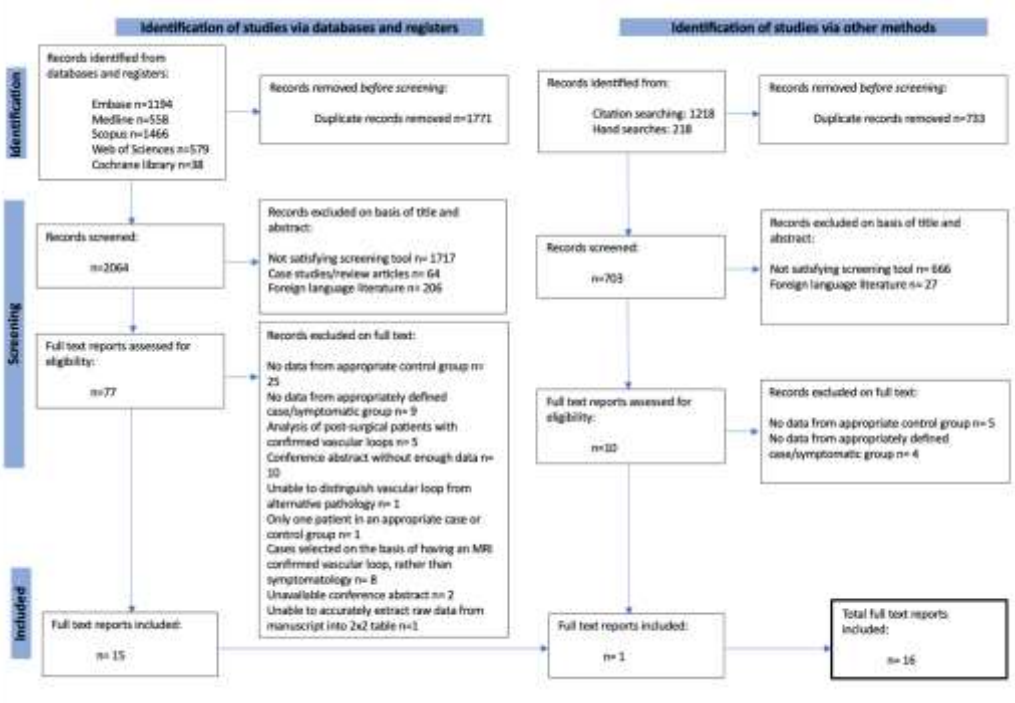


Figure 1. Flow chart summary of the systematic literature review process.

Study characteristics

The demographics of the patients from eligible studies and the number of case (with audio-vestibular symptoms) and control ears are documented in Table 1[1][7-21]. A total of 1526 symptomatic ears and 1929 control ears were included. Mean ages ranged between 43 and 54.1 years. Study characteristics are demonstrated in Table 2. Eligible studies comprised ears with tinnitus (n=5), SNHL (n=7) and vertigo (n= 6). Specific symptomatic subtypes studied were “typewriter tinnitus”, sudden onset sensorineural hearing loss (SoSNHL) and vestibular paroxysmia (VP). The diagnostic criteria for these subtypes are defined in Table 2. Control groups comprised of the contralateral ear (n=8), a normal, asymptomatic patient cohort (n=5) or a patient cohort with an unrelated condition (e.g. trigeminal neuralgia) (n=3).

Eleven papers analysed the relationship of audio-vestibular symptoms with IVL whilst 13 papers analysed the association with CN VIII NVC. The most adopted classification with regard to position of the IVL was that proposed by Chavda in McDermott et al [22]. A standardised classification for NVC was more seldom used, with that established by Gorrie et al adopted in 3 papers [11][Supplementary 3].

Table 1. Eligible studies patient demographics.

Author (year)	Case ears/Control ears (n)	Bilateral cases included Y/N (n)	Age (cases)	Sex (cases)	Age (controls)	Sex (controls)
Bae (2017) [7]	16/14	Y (1 bilateral)	54.1 (27-84)	5 m/10 f	N/A	N/A
Best (2013) [8]	40/40	N/A	47.2 ± 14.7 (17-78)	8 m/12 f	48.4 ± 14.9 (25-77)	8 m/12 f
Beyazal Celiker (2017) [9]	356/478	N/A	50.1 ± 17.3	63 m/ 115 f	42.1 ± 18.9	119 m/120 f
Ezerarslan (2019) [10]	68/76	N	45.3 ± 14.6 (18-77)	36 m/ 32 f	48.6 ± 14.0 (26-81)	21 m/17 f
Gorrie (2009) [11]	58/56	N	NR	31 m/ 27 f	N/A	N/A
Gultekin (2008) [12]	68/128	Y (13 bilateral)	48.5 (18-78)	23 m/ 32 f	42.2 (19-88)	9 m/34 f
Kierig (2023) [1]	36/36	N/A	52.6 ± 18.1 (28-84)	12 m/ 6 f	50.3 ± 16.5	5 m/ 13 f
Kim (2019) [13]	49/49	N	45.0 ± 15.3	58 m/ 40 f	N/A	N/A
Leng (2022) [14]	136/136	N	43 ± 13	60 m/ 76 f	N/A	N/A
Maruyama (2020) [15]	248/392	N	51.1 ± 17.2 (8-84)	121 m/ 127 f	55.2 ± 16.8 (10-84)	77 m/67 f
Ozan (2017) [16]	92/85	N/A	53.6 ± 14.2 (20-84)	42 m/ 50 f	52.2 ± 15 (23-79)	39 m/46 f
Peters (2020) [17]	48/49	N	52 (23-76)	24 m/ 25 f	N/A	N/A
Sivarasan (2019) [18]	9/20	N	48.4 ± 14.0	5 m/ 4 f	N/A	N/A
Yoo (2011) [19]	85/173	Y (29 bilateral)	47.3 ± 12.7	30 m/ 44 f	N/A	N/A
Zhang (2023) [20]	77/77	N	47.6 ± 14.3	45 m/ 34 f	N/A	N/A

Zidan (2020) [21]	140/120	N	47.6 ± 15 (11-73)	47 m/ 51 f	45.6 ± 11.7 (19-88)	28 m/ 32 f

n – number of patients
Y – yes, N – no
± standard deviation
(range)
[IQR]
m - male, f – female
N/A – not available

Quality of studies

QUADAS-2 evaluation showed high bias within the 'patient selection' and 'flow and timing' domains. 'Patient selection' always resulted in high bias due all included studies being case-controlled. High bias was reported for 'index test' when there it was unclear whether readers were blinded to the clinical details. Since the diagnosis of an audio-vestibular symptom (reference standard) always preceded index test evaluation, all studies were low bias in this domain. Only 1/16 studies were deemed low risk with the regard to 'flow and timing' since others were either retrospective or included post hoc exclusions (Fig 2).

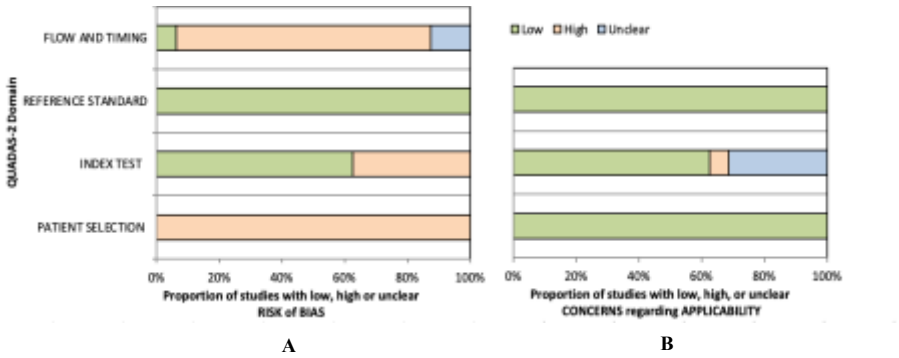


Figure 2. QUADAS-2 tool. Bar charts quantify studies by (a) risk of bias and (b) applicability concerns for the 16 eligible studies included in the meta-analysis.

Relationship between audio-vestibular symptoms and an IAM vascular loop or CN VIII neurovascular contact

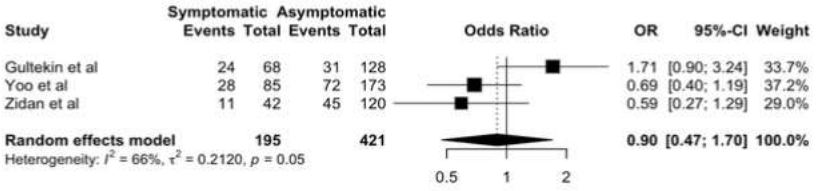
Pooled odds ratios are presented in Table 3. Forest plots are shown in Figure 3.

There was no significant association demonstrated between the presence of tinnitus (undefined) and that of IVL (OR 0.90 95% CI 0.47, 1.70) or CN VIII NVC (OR 1.15, CI 0.68, 1.95) ($p>0.05$). The single study of the 'typewriter tinnitus' subtype showed no significant difference in the prevalence of symptoms in ears with IVL ($p=0.73$) or NVC ($p=0.15$) [7].

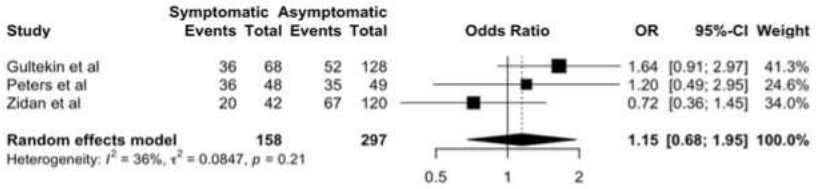
There was no relationship demonstrated between ears with SNHL (undefined) and the presence of IVL (OR 0.67, 95% CI 0.36, 1.25) or CN VIII NVC (OR 0.89, 95% CI 0.33, 2.40) ($p>0.05$). In studies of the SoSNHL subtype alone, there was also no relationship between symptomatic ears and CN VIII NVC (OR 1.16, 95% CI 0.61, 2.20) ($p>0.05$) however and there was an association with an IVL (OR 1.34, 95% CI 1.04, 1.73) ($p=0.02$).

There was no significant difference in the prevalence of IVL or CN VIII NVC between ears with vertigo (undefined) and control ears (OR 0.97, 95% CI 0.64, 1.48), (OR 0.99, 95% CI 0.42, 2.32) ($p>0.05$). However, there was a strong association between the presence of CN VIII NVC and the specific diagnosis of vestibular paroxysmia subtype (OR 13.19, 95% CI 2.09, 83.16) ($p=0.006$). No included studies investigated the association of IVL and vestibular paroxysmia.

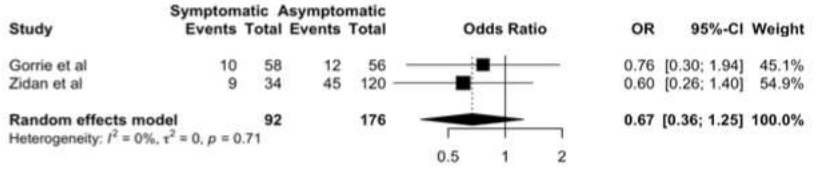
Forest plot for tinnitus (undefined) and presence of an IVL



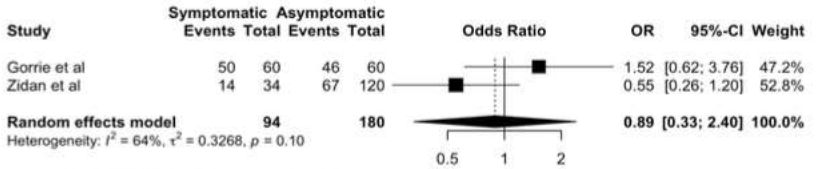
Forest plot for tinnitus (undefined) and CN VIII NVC



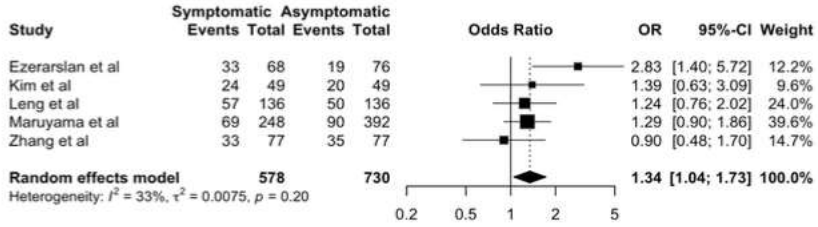
Forest plot for SNHL (undefined) and presence of an IVL



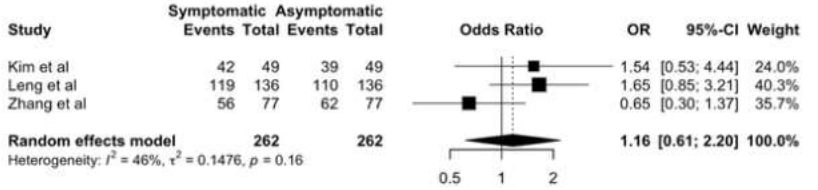
Forest plot for SNHL (undefined) and CN VIII NVC

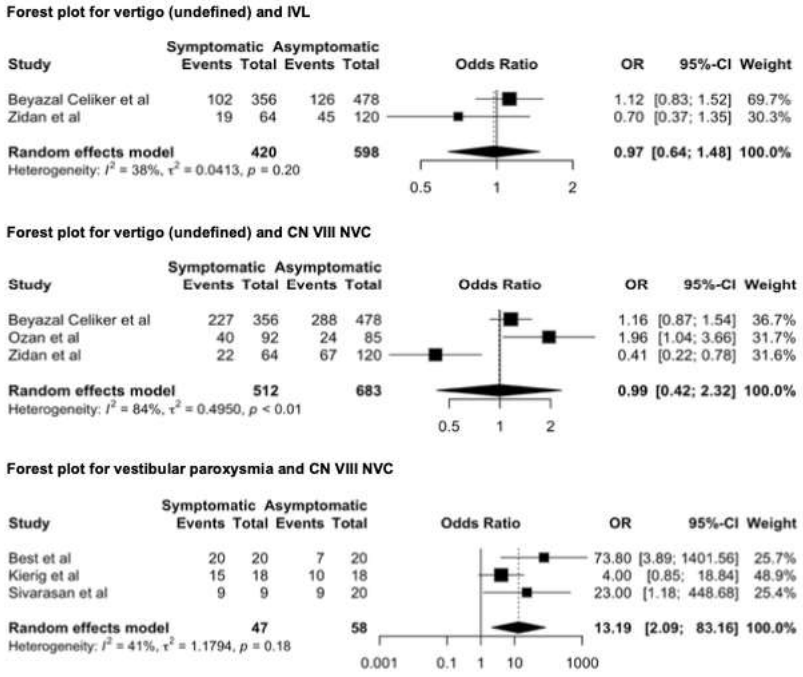


Forest plot for SoSNHL and presence of an IVL



Forest plot for SoSNHL and CN VIII NVC





Events – presence of a vascular loop within the IAM or CN VIII contact
OR – odds ratio
CI – confidence interval
IVL – intrameatal vascular loop
NVC – neurovascular compression

Figure 3. Forest plots for each audio-vestibular symptom and corresponding MRI variable (IVL or CN VIII NVC).

Table 3. Pooled odds ratio, 95% confidence intervals and p values for the association between IVL or CN VIII NVC and audio-vestibular symptoms.

Audio-vestibular symptom	MRI vascular loop variable	Number of studies	Pooled OR (95% CI)	p
Tinnitus (undefined)	IVL	3	0.90 (0.47, 1.70)	0.73
Tinnitus (undefined)	NVC	3	1.15 (0.68, 1.95)	0.60
SNHL (undefined)	IVL	2	0.67 (0.36, 1.25)	0.21
SNHL (undefined)	NVC	2	0.89 (0.33, 2.40)	0.82
SoSNHL	IVL	5	**1.34 (1.04, 1.73)**	**0.02**
SoSNHL	NVC	3	1.16 (0.61, 2.20)	0.65
Vertigo (undefined)	IVL	2	0.97 (0.64, 1.48)	0.90
Vertigo (undefined)	NVC	3	0.99 (0.42, 2.32)	0.98
Vestibular Paroxysmia	NVC	3	**13.19 (2.09, 83.16)**	**0.006**

OR – odds ratio
CI – confidence interval
IVL – position of an intrameatal vascular loop within the IAM
NVC – neurovascular compression of CN VIII

Heterogeneity

Considerable heterogeneity was detected in one sub-group for papers comparing the presence of CN VIII NVC in patients with vertigo (undefined) ($p<0.01$), with an I^2 of 84%. All other analyses demonstrated non-significant p-values (0.05-0.71). I^2 quantification suggested moderate heterogeneity for five sub-group analyses, and substantial heterogeneity for a further 2 sub-analyses. The subgroup analysis comparing IVL and SNHL demonstrated I^2 of 0%. A guide for the interpretation of I^2 has been included in supplementary 5.

DISCUSSION

This systematic review and meta-analysis sought to quantify the relationship between intrameatal vascular loops (IVL) or CN VIII neurovascular contact (NVC) and specific audio-vestibular symptoms. Pooled data from 16 case-controlled studies demonstrated no statistically significant association between the presence of an IVL or CN VIII NVC and either tinnitus (undefined) or SNHL (undefined), whilst there was also no relationship between IVL or vertigo (undefined) or CN VIII NVC and vertigo (undefined). However, the symptomatic subtype of sudden onset sensorineural hearing loss (SoSNHL) demonstrated a significant association with the presence of an IVL whilst that of vestibular paroxysmia was associated with CN VIII NVC (fig 3) (table 3).

Few attempts have been made to formally synthesise the body of literature before now. Chadha and Weiner performed a systematic review of five papers in 2008, but this comprised studies with heterogenous and largely non-comparable methodology [28]. Two of the eligible studies concurred with our finding of no significant association between CN VIII NVC

and unilateral tinnitus, however an association was demonstrated between CN VIII NVC and sensorineural hearing loss ($p<0.05$, OR 1.99) [28]. In addition, a more recent meta-analysis found no significant association between ipsilateral SoSNHL and NVC, although substantial differences in eligibility criteria and interpretation of IVL/NVC grading exists between their work and the present study [29].

The results of the current study should serve to inform both radiology and surgical colleagues alike. Whilst dedicated three dimensional T2-weighted sequences will be required to exclude other pathologies in patients with undefined audio-vestibular symptoms, there will not be a requirement for the radiologist to report either CN VIII NVC or IVL. Similarly, our analysis indicates that IVL and CN VIII NVC are unlikely to be an aetiology for undefined SNHL, tinnitus and vertigo, and would not benefit from surgical intervention. A previous meta-analysis of 35 studies and 572 patients who underwent microvascular decompression of CN VIII NVC found that only 28% of tinnitus patients and 32% of vertigo patients reported complete relief of symptoms and with substantial complication rates following treatment [4].

The results of the current study demonstrate an association between an IVL and SoSNHL. Identifiable causes of SoSNHL are found in a minority of patients, with a vascular aetiology and altered neural perfusion in the context of an IVL a possible pathophysiological explanation [30]. However, we note that of the five papers included in the sub-analysis, only one paper demonstrated an OR greater than 1 suggesting low statistical power for this association. Moreover, there may be several confounding factors responsible for altered vascular supply to the inner ear with a recent meta-analysis demonstrating increased rates of concomitant diabetes, hypertension, and increased cholesterol in patients with SoSNHL [31].

The demonstrated association of CN VIII NVC with vestibular paroxysmia also warrants a consideration of potential pathophysiology. Whilst this study indicates an association rather than causality, it may be postulated that the association of CN VIII NVC with the characteristic short lived paroxysmal vertigo of vestibular paroxysmia is more likely to be related to direct pulsatile compression of the vulnerable long VIII transition zone resulting in ephaptic discharges [32].

Limitations of the current study should be appreciated. Firstly, a body of non-English language literature was not reviewed which may have missed some eligible or noteworthy studies. Secondly, the low number (2-5) of eligible studies for each analysis and the generally small study cohorts have the potential to increase type II error. In this regard, some substantial case-controlled studies were not considered eligible since it was not possible to identify the specific audio-vestibular symptom experienced. For instance, Makins et al studied “auditory symptoms”, and Lei et al investigated a cohort with Meniere’s Disease, neither of which showed a significant association with IVLs [33-34]. Thirdly, it should be noted that case-controlled studies analysing IVL or CN VIII NVC were not available for all relevant symptom subgroups, including that for pulsatile tinnitus. Finally, despite attempts to reduce heterogeneity in our meta-analysis and a p-values ≥ 0.05 in 7/8 plots, there remained a moderate-substantial degree of variance with I^2 ranging from 0-84% for each sub-analysis. Reasons for this are likely multifaceted and comprise clinical heterogeneity between studies and a small number of included papers. Any future studies should aim to collect patients consecutively, with a sample size which allows for appropriate power, adopt an established grading system for vascular loops and a control group of healthy volunteers.

CONCLUSIONS

This systematic review and meta-analysis evaluated the association between the presence of a vascular loop within the IAM (IVL) or contacting the vestibulo-cochlear nerve (CN VIII NVC) and audio-vestibular symptoms. There was no statistically significant correlation between IVL or CN VIII NVC and tinnitus, sensorineural hearing loss or vertigo with the exception of the specific subtypes of vestibular paroxysmia and sudden onset sensorineural hearing loss.

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SUPPLEMENTAL FILES

Online Supplemental Data. Study characteristics.

Author (year)	Study Design	Case symptom	Definition	Control type	Intrameatal vascular loop or CN VIII NVC	Vascular loop/NVC Classification (s) [11][22][23][27]
Bae (2017) [7]	R/C	Typewriter tinnitus	"typewriter," "machine gun," or "crackling" sounds.	Contralateral ear	IVL, NVC	Chavda
Best (2013) [8]	U/U	Vestibular paroxysmia	'Definite' VP patients included	Other Subject*	NVC	N/A
Beyazal Celiker (2017) [9]	R/U	Vertigo	Patients admitted with dizziness, BPPV excluded	Unspecified	IVL, NVC	Chavda
Ezerarslan (2019) [10]	R/U	SoSNHL	As per American Society of Otolaryngology [24].	Other Subject	IVL	Kazawa
Gorrie (2009) [11]	R/C	SNHL	i) the difference between the pure-tone audiometry average of the symptomatic ear when compared with the asymptomatic ear >70%. ii) the difference between the pure-tone audiometry average of the	Contralateral ear	IVL, NVC	Chavda

			symptomatic ear and the asymptomatic ear > 20 dB.			
Gultekin (2008) [12]	P/U	Tinnitus	'Unexplained' tinnitus Pulsatile/non-pulsatile not specified	Other subject, Contralateral ear	IVL, NVC	Chavda
Kierig (2023) [1]	P/U	Vestibular paroxysmia	Diagnosis of VP was based on the Classification Committee of the Bárány Society 2016 [25]	Other subject	NVC	N/A
Kim (2019) [13]	R/C	SoSNHL	As per American Society of Otolaryngology [24].	Contralateral ear	IVL, NVC	Chavda, Gorrie
Leng (2022) [14]	R/U	SoSNHL	As per American Society of Otolaryngology [24].	Contralateral ear	IVL, NVC	Chavda, Gorrie, Kazawa
Maruyama (2020) [15]	R/C	SoSNHL	As per American Society of Otolaryngology [24].	Other subject**, Contralateral ear	IVL	Kazawa
Ozan (2017) [16]	R/U	Vertigo	Short duration episodic peripheral vertigo	Other subject	NVC	N/A
Peters (2020) [17]	R/C	Tinnitus	Non-pulsatile tinnitus (83%) or Pulsatile tinnitus (17%)	Contralateral ear	NVC	Sirikci
Sivarasan (2019) [18]	R/C	Vestibular paroxysmia	All cases of 'probable' or	Other subject	NVC	N/A

			‘definite’ VP included [25]			
Yoo (2011) [19]	R/U	Tinnitus	‘Unexplained’ tinnitus Pulsatile/non-pulsatile not specified	Other subject***, Contralateral ear	IVL	Chavda
Zhang (2023) [20]	U/U	SoSNHL	As per Chinese guidelines 2015 [26]	Contralateral ear	IVL, NVC	Chavda, Gorrie
Zidan (2020) [21]	R/U	Tinnitus, SNHL, Vertigo	Undefined Pulsatile/non-pulsatile not specified	Other subject	IVL, NVC	Chavda

P – prospective, R – retrospective, U – unclear / C – consecutive sampling, U – unclear
SoSNHL – sudden onset sensorineural hearing loss
SNHL – sensorineural hearing loss
IVL – position of an intrameatal vascular loop within the IAM
NVC – neurovascular compression of CN VIII
American Society of Otolaryngology definition of SoSNHL - hearing loss of ≥30 dB affected at least three consecutive frequencies within a 72-hour period.
*Subjects with trigeminal neuralgia
** Contralateral ears of patients with bell’s palsy
*** Subjects with headache

Supplementary 1. Search strategy

Database search terms

Key words (Thesaurus/index and MESH terms) and free text search terms were adapted for each database search.

EMBASE

#1 exp artery/

#2 exp anterior inferior cerebellar artery/

#3 exp nerve compression/

#4 vascular.mp.

#5 vascular loop.mp.

#6 arterial loop.mp.

#7 AICA.mp.

#8 neurovascular compress*.mp.

#9 exp nuclear magnetic resonance imaging/

#10 magnetic resonance imag*

#11 MRI

#12 exp vestibulocochlear nerve/

#13 exp vestibular nerve/

#14 exp cochlear nerve/

#15 exp internal auditory canal/

#16 exp pons angle/

#17 exp inner ear/

#18 IAM.mp.

#19 IAC.mp.

#20 CPA.mp.

#21 vestibul*.mp.

#22 cochle*.mp.

#23 exp vestibular disorder/

#24 exp hearing impairment/

#25 exp tinnitus/

#26 otologic*.mp.

#27 audio*.mp.

#28 dizz*.mp.

#29 vert*.mp.

#30 hear*.mp.

#31 deaf*.mp.

#32 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

#33 #9 OR #10 OR #11

#34 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22

#35 #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31

#36 #32 AND #33 AND #34 AND #35

MEDLINE

#1 artery.mp.
#2 vascular.mp.
#3 vascular loop.mp.
#4 arterial loop.mp.
#5 anterior inferior cerebellar artery.mp.
#6 AICA.mp.
#7 nerve compress*.mp.
#8 neurovascular compress*mp.
#9 exp magnetic resonance imaging/
#10 magnetic resonance imag*.mp.
#11 MRI.mp.
#12 exp vestibulocochlear nerve/
#13 exp vestibular nerve/
#14 exp cochlear nerve/
#15 exp cerebellopontine angle/
#16 exp ear, inner
#17 internal auditory canal.mp.
#18 internal acoustic meat*.mp.
#19 internal auditory meatus.mp
#20 CPA.mp.
#21 IAC.mp.
#22 IAM.mp.
#23 vestibul*.mp.
#24 cochle*.mp.
#25 exp vestibular diseases/
#26 exp hearing loss/
#27 exp tinnitus/
#28 exp vertigo/
#29 otologic*.mp.
#30 audio*.mp.
#31 dizz*.mp.
#32 hear*.mp.
#33 deaf*mp.
#34 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 #8
#35 #9 OR #10 OR #11
#36 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24

#37 #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33

#38 #34 AND #35 AND #36 AND #37

Scopus and Web of Science

#1 artery

#2 vascular

#3 vascular loop

#4 arterial loop

#5 anterior inferior cerebellar artery

#6 AICA

#7 nerve compress*

#8 neurovascular compress*

#9 MR imag*

#10 MRI

#11 magnetic resonance imag*

#12 cerebellopontine angle

#13 inner ear

#14 internal auditory*

#15 internal acoustic*

#16 CPA

#17 IAM

#18 IAC

#19 vestibul*

#20 cochle*

#21 tinnitus

#22 vert*

#23 otologic*

#24 audio*

#25 dizz*

#26 hear*

#27 deaf*

#28 SNHL

#29 ear*

#30 balance

#31 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

#32 #9 OR #10 OR #11

#33 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20

#34 #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30

#35 #31 AND #32 AND #33 AND #34

Cochrane Register of Controlled Trials databases

#1 MeSH descriptor: [Arteries] explode all trees
#2 vascular
#3 vascular loop
#4 arterial loop
#5 anterior inferior cerebellar artery
#6 AICA
#7 neurovascular compress*
#8 nerve compress*
#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#11 MRI
#12 MR
#13 magnetic resonance imag*
#14 #10 OR #11 OR #12 OR #13
#15 MeSH descriptor: [Vestibulocochlear Nerve] explode all trees
#16 MeSH descriptor: [Vestibular Nerve] explode all trees
#17 MeSH descriptor: [Cochlear Nerve] explode all trees
#18 MeSH descriptor: [Cerebellopontine Angle] explode all trees
#19 MeSH descriptor: [Ear, Inner] explode all trees
#20 internal auditory canal
#21 internal auditory meatus
#22 internal acoustic meat*
#23 CPA
#24 IAC
#25 IAM
#26 vestibul*
#27 cochle*
#28 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
#29 MeSH descriptor: [Vestibular Diseases] explode all trees
#30 MeSH descriptor: [Hearing Loss] explode all trees
#31 MeSH descriptor: [Tinnitus] explode all trees
#32 MeSH descriptor: [Vertigo] explode all trees
#33 otologic*
#34 audio*
#35 dizz*
#36 hear*
#37 deaf*
#38 #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37
#39 #9 AND #14 AND #28 AND #38

Hand Searched Journals

1. World Neurosurgery
2. Otology and Neurotology
3. Journal of The Neurological Sciences
4. Journal of Neurosurgery
5. Laryngoscope

Supplementary 2. Principle reasons for exclusions of database and register reports after full text review for eligibility.

A No data from appropriate control group

B No data from appropriately defined case/symptomatic group

C Analysis of post-surgical patients with confirmed vascular loops

D Conference abstract without enough data

E Unable to distinguish vascular loop from alternative pathology

F Only one patient in an appropriate case or control group

G Inclusion criteria included an MRI confirmed vascular loop, rather than symptomatology alone

H Unavailable conference abstracts

I Unable to accurately extract raw data from manuscript into 2x2 table

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Supplementary 3. Classification systems for vascular loop assessment.

IVL

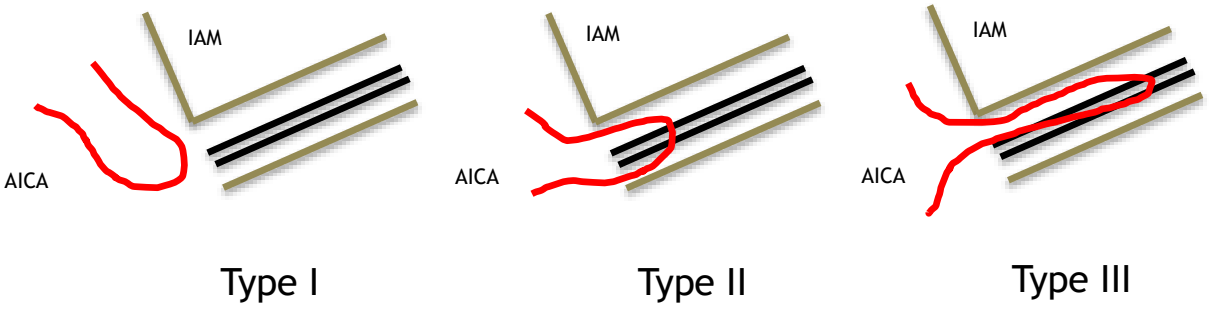
Chavda

I - AICA loop located at the CPA but not entering the IAM

II - AICA loop located within the proximal 50% of the IAM

III - AICA loop located extending within the distal 50% of the IAM

Grade II or III – taken as positive for an IVL



Kazawa

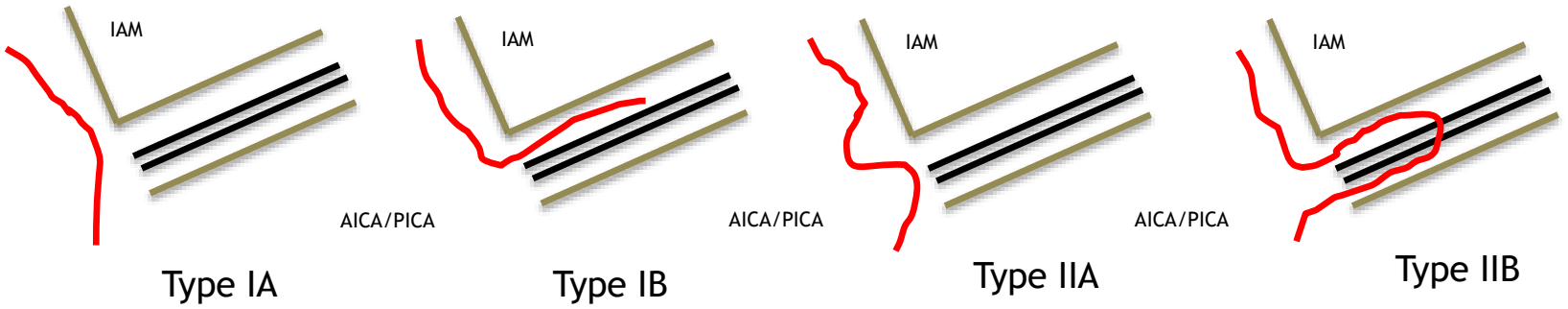
IA – non loop AICA/PICA located in the CPA cistern

IB – non loop AICA/PICA entering the IAM

IIA – loop type AICA/PICA located in the CPA cistern

IIB – loop type AICA/PICA entering the IAM

IB and IIB taken as positive for an IVL and IA and IIA taken negative for an IVL



CN VIII NVC

Gorrie

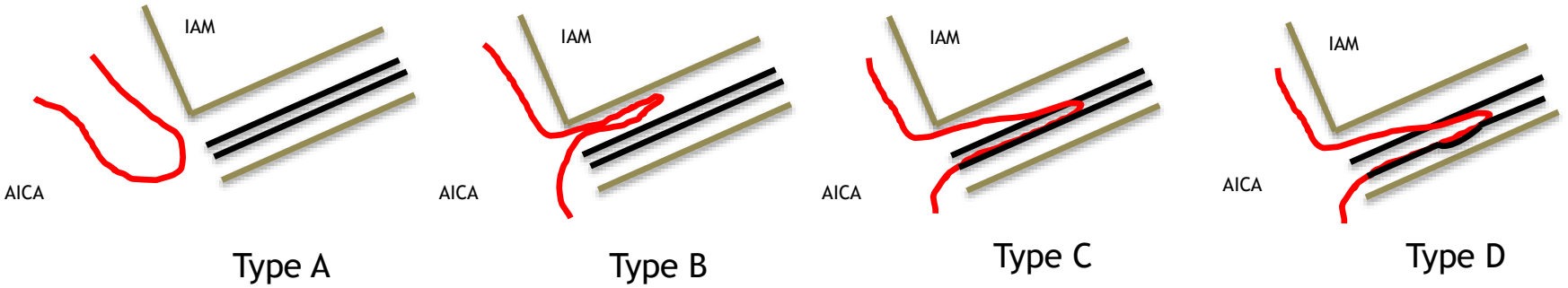
A – an AICA loop without contact with adjacent nerves

B – an AICA loop that runs adjacent to the nerves

C – an AICA loop that courses between VII and VIII cranial nerves

D – an AICA loop that displaces the VIII cranial nerve

B, C or D interpreted as positive for CN VIII NVC, A taken as negative.



Sirikci

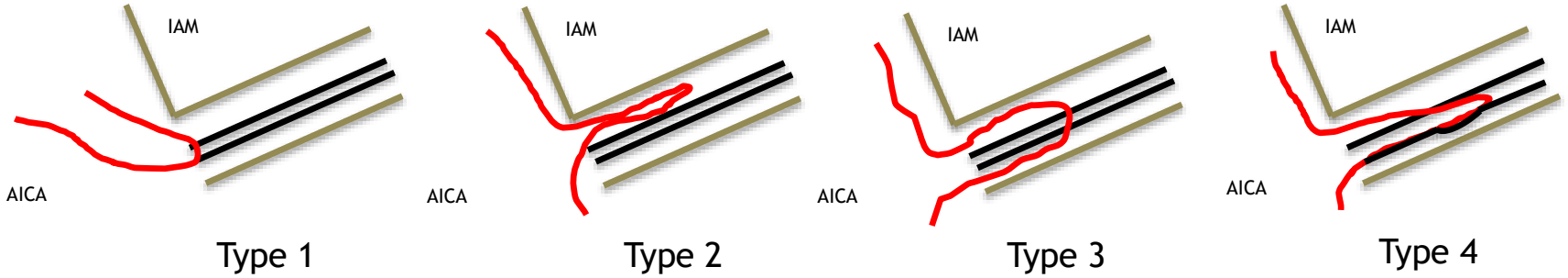
1 – Point compression – the AICA compresses only a limited portion of the cochleovestibular nerve

2 – Longitudinal compression - the AICA approaches the CVN as both traverse parallel to each other

3 - Loop compression - vascular loop of the AICA encircles the cochleovestibular nerve

4 – Indentation - the AICA compresses the CVN so as to make an indentation in the nerve

All grades (1-4) taken as positive for CN VIII NVC.



Supplementary 4. **QUADAS-2 signalling questions.**

Patient selection
Risk of bias
Could the selection of patients have introduced bias? (Low/High/Unclear risk)
• Was a consecutive or random sample enrolled?
• Was a case-control methodology avoided?
• Did the study avoid inappropriate exclusions?
Notes: All included studies are case-control and therefore all included studies are high risk
Concerns regarding applicability
Are there concerns that the included patients and setting do not match the review question? (Low/High/Unclear risk)
Notes: Studies were considered low risk if there was a clear inclusion and exclusion criteria which was deemed to suitably match the review question.
Conduct and interpretation of index test
Risk of bias
Could the conduct or interpretation of the index test introduce bias? (Low/High/Unclear)
• Were the index test results interpreted without knowledge of the results of the reference standard?
• If a threshold was used, was it pre-specified?
• Were two or more independent reviewers involved in interpreting the index test?
Notes: Studies were considered low risk if the reader/readers of the index test were blinded to the clinical details of the patient.
Concerns regarding applicability
Are there concerns that the index test or its conduct or interpretation differs from the review question? (Low/High/Unclear risk)
Notes: Studies were considered low risk if they included thin (≤1 mm) T2/CISS/FIESTA slices in the MRI protocol.
Reference standard conduct and interpretation
Risk of bias
Could the reference standard or its conduct or interpretation have introduced bias? (Low/High/Unclear risk)

• Are the reference standard's likely to correctly classify the target condition?
• Was the reference standard's result interpreted without knowledge of the index test?
Notes: Application of the reference standard (diagnosis or acknowledgement of an audiovestibular symptom always preceded the index test (MRI) in the included studies. Therefore, all included studies were deemed low risk.
Concerns regarding applicability
Are there concerns that the target condition as defined by the reference standard does not match the review question? (Low/High/Unclear risk)
Notes: Studies considered low risk if the reference standard was met i.e., the investigation of an audiovestibular symptom(s) was sought.
Flow and Timing
Risk of bias
Could the patient flow have introduced bias? (Low/High/Unclear risk)
• Was there an appropriate interval between index test and reference standard?
• Did all patients receive the same reference standard?
• Were all patients included in the analysis?
Notes: An appropriate interval index test and reference standard was only considered low risk if a prospective study. If patients within the same cohort were classified with a range of different clinical criteria, then the patients were not deemed to receive the same reference standard. Post hoc exclusions such as technically inadequate MRI was considered high risk of bias.

Supplementary 5. I^2 Interpretation.

A guide to interpreting I2 has been published in the Cochrane Handbook for Systematic Reviews of Interventions (2011).

It is noted that thresholds can be misleading since the interpretation of inconsistency depends on several factors. They suggest the following rough guide:

- 0% to 40%: might not be important.
- 30% to 60%: may represent moderate heterogeneity.
- 50% to 90%: may represent substantial heterogeneity.
- 75% to 100%: considerable heterogeneity.

J Higgins. S Green. Cochrane Handbook for Systematic Reviews of Interventions. [Online]. 2011. Available from: https://handbook-5-1.cochrane.org/front_page.htm.