

**UTILITY OF VIDEO HEAD IMPULSE TEST IN MENIERE'S DISEASE:
A SYSTEMATIC REVIEW**

Jijinu P S

19AUD020

A Dissertation Submitted in Part of Fulfilment of The Degree of

Master of Science

(Audiology)

University of Mysore



All India Institute of Speech and Hearing,

Manasagangothri, Mysuru-570006

September 2021

CERTIFICATE

This is to certify that this dissertation entitled “**Utility of video head impulse test in Meniere’s disease; A systematic review**” is a bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student with Registration Number 19AUD020. This has been carried out under the guidance of the faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru

September 2021

Dr. M. Pushpavathi

Director

All India Institute of Speech and Hearing

Manasagangothri, Mysuru-570006

CERTIFICATE

This is to certify that this dissertation entitled “**Utility of video head impulse test in Meniere’s disease; A systematic review**” has been prepared under my supervision and guidance. It is also certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru

September 2021

Dr. Sujeet Kumar Sinha

Associate Professor

Department of Audiology

All India Institute of Speech and Hearing

Manasagangothri, Mysuru-570006

DECLARATION

This is to certify that this dissertation entitled “**Utility of video head impulse test in Meniere’s disease; A systematic review**” is the result of my own study under the guidance of Dr. Sujeet Kumar Sinha, Associate Professor, Department of Audiology, All India Institute of Speech and Hearing, Mysuru, and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru,

Registration No: 19AUD020

September 2021

Dedicated to My Guide &

My Family

ACKNOWLEDGEMENT

The path I have traveled has not always been an easy one, but I am still here. I know the only reason I could make it this far is that the almighty was walking the path with me every step of the way... This dream would not be a reality without the blessings from above, so I begin by thanking God for the blessings that have brought me here.

“At times, our light goes out and is rekindled by a spark from another person. Each of us has cause to think with deep gratitude of those who have lighted the flame within us...”

***Sujeet sir...** your words “strive not to be a success, but rather to be of value” has always been a motivation. You opened the world of vestibular to me. A mentor like you is always precious, and I am blessed to have you as my guide. And I thank you for being patient, supporting, and guiding me to fly high to capture my dreams...*

*I extend my gratitude to all the faculties of this institute, especially **Sandeep sir**, for molding me and inspiring me to grow up in professional skills.*

***Acha, Amma & Chettan ...** thank you for always believing in me.. Without you, I might not be the person I am today... **Kannetta...** the love of my life.... Thanks for being the shoulder that I can always depend on. Thank you for always supporting me and my dreams and never trying to hold me back from what I want in life... I extend my thanks to **Kunju, Ammama, Ammayi & Maman** for all the moral support. My **Ponnan** for being my stress buster... Love you all....*

*It's wonderful how God brings the right person into your life when you need them. And I have got the most amazing person who keeps me in all her prayers... who makes me mentally strong when I am down... **Sr. Annsmaria...** my **Annsutty...** It's hard to find words to express my gratitude... All my love and thanks to you...*

***Friends....** I just have the right ones...**Jesiüü... (My technical supporter)** you have seen the best and worst part of mine... Thank you so much for always listening patiently and helping me in all possible ways through miles apart. **Joeluu... Jayamma... Alishaa... Yaalu... & Krupechiüü...** Thank you for your unconditional support.*

*My other bunch of friends, who can never be forgotten-**Aadii, Fagye, Appu, Kruthika, and Joanna chechi, and my lovely juniors** especially, **Silpa, Nammu, Krishna, Nivi, Leya, and Neha...** Thanks for always cheering me on... A special thanks to my senior, **Hannah chechi** for always helping me to clear my kuttu kuttu doubts... I also thank my dissertation partners **Shraddha and Ankit**, for all your help...*

*I thank all my friends in Bachelors, **Renovators**, and in Masters, **Renovators 2.0**, for all the motivation and support they have given. My batchmates, **mAudiolus**, the best bundle of future audiologists. Thank you, guys, for all your immense support.*

Thank you one and all...

ABSTRACT

Introduction: Meniere's disease is an inner ear disorder characterized by low-frequency sensorineural hearing loss, episodic vertigo, and tinnitus. Video head impulse test is a recent tool that assesses all the six semi-circular canals in individuals with various vestibular pathology.

Aim: To systematically review the articles related to video head impulse test findings in patients with definite Meniere's disease.

Method: Initially, a review search was performed in different databases. Searches across different databases resulted in 93 topic-related articles. Total nineteen articles met the inclusion and exclusion criteria to meet the objectives of the study. The quality and potential risk associated with each article were evaluated using the QUADAS-2 risk of bias assessment tool.

Results: The results of these studies are unequivocally indicating increased, decreased, or normal VOR gain on the side affected with Meniere's disease. Few studies have found an abnormal decrease in VOR gain as the disease duration increases and also in the advanced stages of the disease. Some authors have reported that the chances of showing reduced VOR gain are more for the posterior semi-circular canals, whereas some other authors showed it on the lateral canals. Presence of a higher proportion of saccades on the affected side compared to the unaffected side. The occurrence of saccades is more in the horizontal canals. Overt saccades are seen more than covert saccades. The majority of the studies showed a dissociation between the vHIT and caloric test results in patients with Meniere's disease.

Conclusion: The video head impulse test is a valuable tool in the diagnosis of Meniere's disease when used along with other vestibular tests. When there is an involvement of vertical canals, especially the posterior canal, vHIT provides essential information by showing abnormality in at least one of the parameters.

TABLE OF CONTENTS

Contents	Page number
List of tables	i
List of figures	ii
Chapter I Introduction	1-4
Chapter II Method	5-9
Chapter III Results	10-32
Chapter IV Discussion	33-38
Chapter V Summary and Conclusions	39-41
References	I-XI

LIST OF TABLES

No.	Title	Page number
3.1	Risk of Bias assessment for the 19 studies included in the study	12
3.2	Characteristics of the different studies	16
3.3	Summary of findings	27

LIST OF FIGURES

No.	Title	Page number
3.1	PRISMA chart for Systematic Reviews and Meta-Analyses (PRISMA)	11
3.2	QUADAS-2 (Risk of bias)	15
3.3	QUADAS-2 (Applicability concerns)	15

Chapter-I

INTRODUCTION

The balance and spatial orientation are maintained by the ear's innermost important portion, called the vestibular system. Along with its projections to various central pathways, it also sends signals to the neural structures which control eye movements. This connection between the vestibular system and the eyes is called vestibulo-ocular reflex (VOR). The VOR helps in gaze fixation during the head movement (Lysakowski et al.,1998).

Initially, the Head Impulse Test (HIT), a bedside technique, was used to evaluate the VOR. HIT was later upgraded to an objective test, i.e., video Head Impulse Test (vHIT). vHIT test elicits the responses from the vestibular system using brisk head movements instead of using unnatural stimulus. These movements make the vestibular system more sensitive and provide a quantitative measure of VOR function in 3 planes; lateral, RALP, and LARP. vHIT assesses all the six semi-circular canals in individuals with various vestibular disorders (Halmagyi et al., 2017; Jerin et al.,2019; Rubin et al.,2018).

There are two test protocols for testing the semi-circular canal function, i.e., Head Impulse (HIMP) and Suppression Head Impulse (SHIMP) paradigms. In the HIMP protocol, the person is asked to fix his eyes on the earth-fixed target, and 20 head impulses are given in lateral, RALP, and LARP planes to assess the various semi-circular canal functions. Individuals with a properly functioning vestibular system have a normal VOR gain and absence of corrective saccades. In contrast, individuals with peripheral vestibular disorders have reduced VOR gain and the presence of corrective saccades. In contrast, the SHIMP protocol is precisely the opposite of the HIMP paradigm and is restricted to lateral

canals' assessment only (Halmagyi et al., 2017; McDougall et al., 2013; Alhabib & Saliba, 2017).

There are unequivocal findings regarding the VOR gain in individuals with Meniere's disease. Some studies have reported a reduced VOR gain whereas, some other studies have reported a normal VOR gain in individuals with Meniere's disease. The reduced VOR gain in Meniere's disease is because of the damage to the vestibular hair cells. It has been reported that if the distention of the membranous duct due to endolymphatic hydrops does not obstruct the VOR, VOR gain will be normal in individuals with Meniere's disease (Cordero-Yanza et al., 2017). Also, the VOR gain gets normalized or increased between MD attacks in the 1st and 2nd stages of Meniere's disease, whereas it is expected to increase or decrease during MD attacks. But, in stage 3 of MD, the VOR gain remains abnormal (Manzari et al., 2011; Lee et al., 2017). The literature review also shows a disagreement between caloric test results and vHIT results as an indication of vestibular dysfunction in Meniere's disease (McGarvie et al., 2015; McCaslin et al., 2015).

In several patients with Meniere's disease, re-fixation saccades are the only abnormal finding in vHIT. Deficits in vestibulo-ocular reflex function associated with the presence of re-fixation saccades in individuals with Meniere's disease is considered as a compensatory mechanism (Shugyo et al., 2020). Blodow et al. (2013) reported an abnormal vHIT in fifty-five percent of the patients with Meniere's disease, where sixteen percent of them had isolated covert saccades. Bharadwaj et al. (2020) indicated that the corrective saccades are significantly higher in Meniere's disease patients, showing the importance of corrective saccades in diagnosing Meniere's disease.

1.1 NEED OF THE STUDY

Video head impulse test (vHIT) is a relatively latest test reported in Paris by the Barany society in 2004 and then described in detail by Ulmer and Chays (2005). Reviews regarding vHIT are important for audiologists specializing in vestibular assessment because vHIT has become more useful clinically. It is a non-invasive, easy-to-use test with high sensitivity and specificity. vHIT possesses several advantages over search coil and caloric tests. vHIT is a quick physiological test without causing nausea or dizziness and studies the response of each semi-circular canal at high frequency, thus detecting a mono or multi canals pathology, with no need for a darkroom. The capability of vHIT to test all the six semi-circular canals individually or independently has made it more useful in diagnosing vertigo patients (Alhabib & Saliba, 2017).

Though time-consuming, systematic reviews help reduce many scientific studies into a single piece of literature. In a systematic review, these unmanageable amounts of data in the form of experimental studies undergo several series of selection procedures. Then, different studies will be compiled in a well-ordered manner (Khan et al., 2003). It also helps in reducing the potential risks and biases seen in individual studies (Henderson et al., 2010). Vertigo is one of the classic symptoms of Meniere's disease, and several vestibular tests are carried out to confirm vestibular dysfunction. Several studies report a disparity between different vestibular function tests in Meniere's disease (Fukushima et al., 2018; Hannigan et al., 2019). Also, the results of vHIT in Meniere's disease are contrasting in different studies. Thus, systematically reviewing and summarising the findings regarding video head impulse test results in individuals with Meniere's disease will provide the information under a single title. It would be beneficial for those who work in this

research area. Integration of these accumulating data will also act as a quick guide that provides direct insight into the topic rather than searching all the relevant articles related to the same (Aromataris & Pearson, 2014).

1.2 AIM OF THE STUDY

The present study aims to systematically review the articles related to video head impulse test findings in patients with definite Meniere's disease.

1.3 OBJECTIVES OF THE STUDY:

The objective of the study was to systematically review and find out the diagnostic test accuracy of the video head impulse test in the detection of vestibular dysfunction in individuals with definite Meniere's disease using the following parameters:

1. Vestibulo-ocular reflex gain
2. Presence or absence of re-fixation saccades
3. Vestibulo-ocular reflex gain asymmetry
4. Correlating the vHIT parameters with caloric test results

Chapter-II

METHOD

2.1 Searches

A literature search was conducted in databases, including Google Scholar, PubMed, and Web of Science. All the articles that define vHIT and definite Meniere's disease according to the criteria given by the American Academy of Otolaryngology-Head and Neck Surgery (AAO HNS), 2015 (Lopez-Escamez et al., 2015), compared vHIT with other clinical tests, studied the power of vHIT as diagnostic tools with Meniere's disease and other vestibular disorders were considered for the preliminary search. No limits were placed on the date of publication. The searches were limited to studies with full-text availability, published in English, and including human subjects. The search was also conducted just before the final analysis to identify more studies to be included. Search words such as "head impulse test, video head impulse test, vestibular ocular reflex, Meniere's disease, definite Meniere's disease, etc." were entered into different databases in different combinations with the use of Boolean operators such as AND, OR, NOT.

2.2 The study types included: Study designs such as retrospective and prospective observational studies, cross-sectional studies, longitudinal studies, and randomized clinical trials were included. Studies that do not report direct or indirect observations or original data, case studies, and reviews were excluded from the present study.

2.3 Condition or domain being studied

1. Evaluation of six semi-circular canals functions in individuals with Definite Meniere's disease,

2. VOR gain, VOR gain asymmetry, and compensatory saccades were taken as assessing parameters.

2.4 Participants/Population

Inclusion: Individuals of any age presenting with signs and symptoms of definite Meniere's disease to evaluate vertigo. The study that defined the definite Meniere's disease as per AAO-HNS (2015) criteria was included. Studies also included normal individuals without Meniere's disease as control groups.

Exclusion: Individuals with other neurological disorders and other comorbid disorders were excluded from the study.

2.5 ANALYSIS

2.5.1 Data extraction (selection and coding)

Titles and abstracts of all the obtained articles from different databases were screened by two review authors independently. The articles fulfilling the inclusion criteria were only included. Other studies were excluded. The reference list of the included studies was further reviewed to obtain additional relevant articles. Any discrepancies or disagreements for the methodology of the article were resolved through discussions between two authors. A full-text screening of the included studies was done in the second stage of analysis through the same process. Reasons for exclusion were documented and reported at this phase in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Page et al., 2021). The risk of bias was considered, and the assessment for the same was carried out independently by the two reviewers. Abnormal or normal VOR gain, VOR gain asymmetry, presence, or absence of re-fixation saccades were taken as the data elements of interest.

2.5.2 Risk of bias (quality) assessment

Reviewer bias was overcome by involving two independent reviewers at each stage of screening, and the disagreements were dealt with through discussions. Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2), an evidence-based quality assessment tool, was used to assess the risk of bias of the included studies by two independent authors. QUADAS-2 has been specifically developed to be used in systematic reviews of diagnostic accuracy studies, with four critical domains, including patient selection, index test(s), reference standard, and flow and timing (Whiting et al., 2011). Studies with a higher risk of bias were excluded from further analysis and interpretation, or their results were qualified depending on the nature and potential impact of the bias.

QUADAS, was explicitly developed for systematic reviews in 2003, upgraded to QUADAS-2 in 2011. It consists of four key domains: patient selection, index test, reference standard, and flow and timing. All four domains were assessed regarding their risk of bias, and the initial three domains regarding their concerns about applicability. The assessment provided the degree to which estimates of diagnostic accuracy avoided the risk of bias and the extent to which the primary studies are applicable to this review. Each of these domains has a set of signaling questions making a total of 11 questions in the entire tool, which are listed below. Each question assessing the risk of bias was rated either yes/no or unclear. If the domains have maximum 'yes' responses, it was judged as having a low risk of bias, and if it has more 'no' responses, it was considered having a high risk of bias. If the signaling questions lead to 'unclear' responses, the domain was judged as having an unclear risk of bias. Concerns regarding applicability were also evaluated as 'low/high/unclear' concerns.

Domain 1: Patient selection

1. Was a consecutive or random sample of patients enrolled?
2. Was a case-control design avoided?
3. Did the study avoid inappropriate exclusions?

Domain 2: Index test (s)

1. Were the index test results interpreted without knowledge of the results of the reference standard?
2. If a threshold was used, was it pre-specified?

Domain 3: Reference standard

1. Is the reference standard likely to correctly classify the target condition?
2. Were the reference standard results interpreted without knowledge of the results of the index test?

Domain 4: Flow and timing

1. Was there an appropriate interval between index test (s) and reference standard?
2. Did all patients receive a reference standard?
3. Did all the patients receive the same reference standard?
4. Were all the patients included in the analysis?

After obtaining the rating for each question, the percentage of yes was calculated for each study as a whole by finding the total number of 'yes' out of 11 questions. This was further used to categorize the studies according to the percentage of positive answers in the questions which is extrapolated from the risk of bias assessment guidelines given by The Joanna Briggs Institute (Moola et al., 2015). They considered a higher risk of bias when

only up to 49% of the answers were “yes”, moderate when 50%–69% of the answers were “yes”, and low when more than 70% of the answers were “yes”.

2.5.3 Strategy for data synthesis

The data synthesis was carried out by analyzing the homogeneity of the data, and different analysis parameters such as VOR gain, saccades (covert and overt saccades), and Asymmetry ratio were considered. The detail of all the three parameters for all the articles was analyzed.

2.5.4 Analysis of subgroups or subsets

The correlation between vHIT and other tests or discrepancies between vHIT and other Meniere’s Disease tests was also investigated.

Chapter-III

RESULTS

3.1 Studies selection

Searches across different databases, including Google Scholar, Web of Science, and PubMed, resulted in 93 topic-related records. Sixty-one records were identified and screened after duplicate removal. Considering the exclusion criteria including, unavailability of full text, studies reported in languages other than English, case reports, reviews, and participants having other comorbid conditions, 32 articles were excluded, which led to the full-text screening of 29 articles. In three articles, the type of Meniere's Disease was unspecified, and in two articles, the patients had Vestibular migraine and Meniere's disease.

Among the remaining studies, five were excluded due to the following reasons; a study conducted in certain Meniere's group, data of definite and probable Meniere's disease was mixed. In other studies, patients were performed with IT-Gd, the comparison was made between two Meniere's disease groups, and data of two different conditions were not separately mentioned. Finally, the full-text screening led to the exclusion of 10 articles. Total of 19 articles were included for this systematic review. The screening process and the reasons for exclusion are depicted in the PRISMA flow diagram (Figure 3.1)

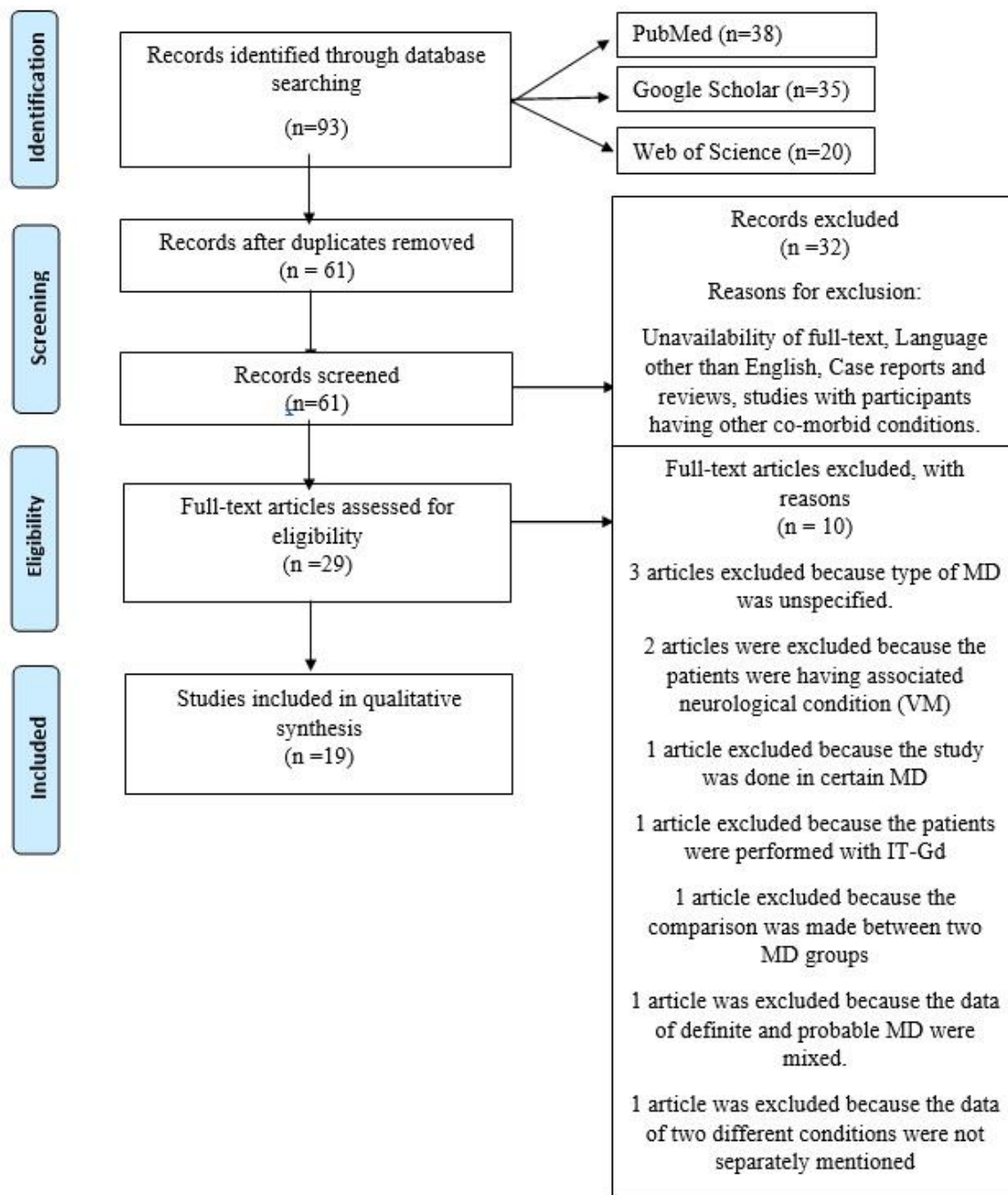


Figure 3.1. PRISMA chart for Systematic Reviews and Meta-Analyses (PRISMA)

3.2 Risk of bias

Quality appraisal of the selected studies using QUADAS-2 led to the categorization of 19 studies according to the risk of bias involved in different domains, including patient

14	McGarvie et al. (2015)	☹	☹	😊	😊	☹	😊	😊	45.45 %
15	Oliveria et al. (2019)	😊	😊	😊	😊	😊	😊	😊	63.63 %
16	Rubin et al. (2018)	😊	😊	😊	😊	😊	😊	😊	72.72 %
17	Yacovino et al. (2020)	😊	😊	😊	😊	😊	😊	😊	54.54 %
18	Yilmaz et al. (2020)	😊	😊	😊	😊	😊	😊	😊	72.72 %
19	Zulueta-Santos et al. (2014)	😊	😊	😊	😊	😊	😊	😊	54.54 %

Icon illustration: ☹ Indicates domains with a high risk of bias and 😊 indicates domains with a low risk of bias.

The proportion of studies with a low or high risk of bias and the proportion of studies with low or high concerns regarding applicability are graphically represented in Figures 3.2 and 3.3, respectively.

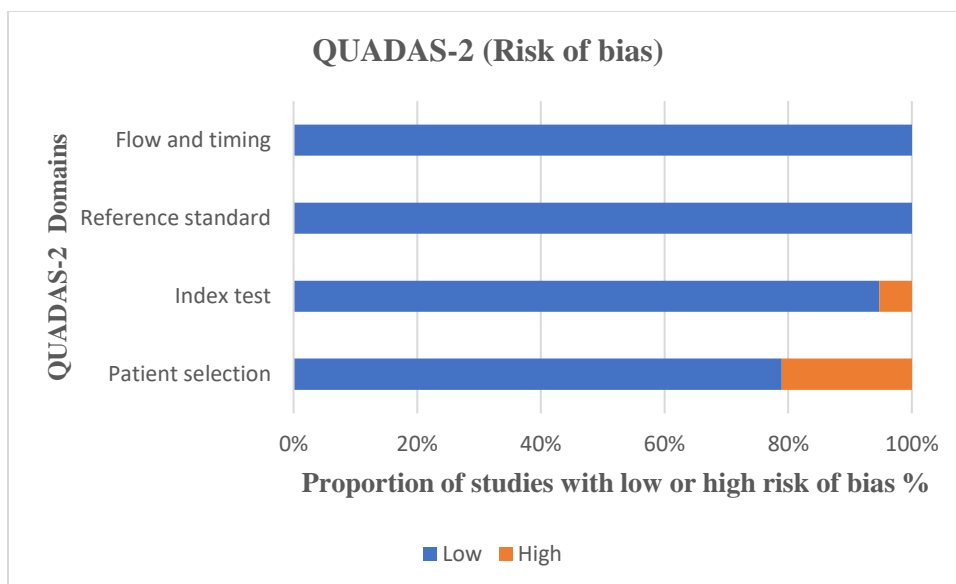


Figure 3.2 Proportion of studies with a low or high risk of bias.

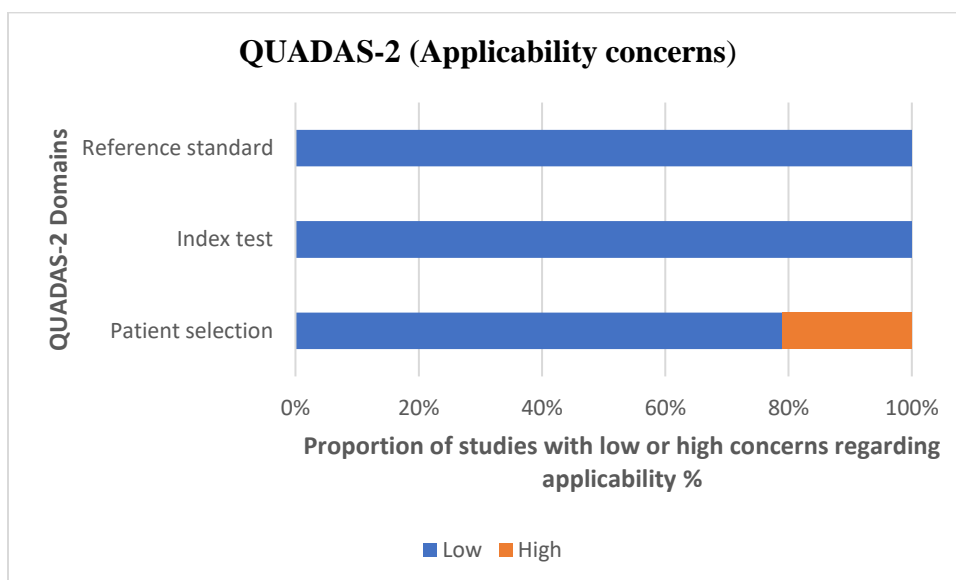


Figure 3.3 Proportion of studies with low or high concerns regarding applicability.

3.3 Characteristics of the selected studies:

All the records included in this study have compared vHIT results with either normal groups or other tests. The number of participants with Meniere's disease varied between 24 to 250 in each study. Among 19 included studies, re-fixation saccades were

assessed in 13 studies, and VOR gain asymmetry was evaluated in 4 studies, whereas vestibulo ocular reflex gain value was assessed in all the 19 studies. The characteristics of studies including participants, control groups, groups with other conditions, and the parameters of vHIT used for diagnosis of MD are mentioned in Table 3.2

Table 3.2. Shows the Characteristics of the different studies

Sl no.	Authors & Year	No. of patients with definite MD	No. of healthy subjects in CG	Other study groups	Other Audio-vestibular tests	Diagnosis using vHIT	VOR	RS	AR	Correlation with CVT/VEMP
1	Bharadwaj et al. (2020)	40	40	None	PTA, CVT, vHIT	VRG	✓	VRG	asymmetry	*(GA and UCW) **(RS and UCW)
2	Choi et al. (2017)	24	None	VN: 22	CVT, vHIT	✓	✓	---		*
3	Cordero-Yanza et al. (2017)	88	None	None	CVT, vHIT	✓	✓	Ga		*
4	van Esch et al. (2018)	250	None	None	PTA, CVT, vHIT	✓	✓	---		Not applicable

5	Fukushima et al. (2018)	90	None	None	PTA, CVT, vHIT	✓	✓	---	** (HSCC) * (PSCC)
6	Grigol et al. (2019)	29	21	None	PTA, cVEMP, vHIT	✓	✓	---	Not applicable
7	Hannigan et al. (2019)	73	None	---	CVT, vHIT	✓	✓	---	*
8	Huang et al. (2020)	80	None	None	DHI, vHIT, RCT, VEMP	✓	---	---	Not applicable
9	Jerin et al. (2019)	54	None	None	PTA, vHIT, CVT, cVEMP	✓	✓	---	*
10	Jung et al. (2016)	76	None	EVA-10 AVN-19	CVT, vHIT	✓	---	---	Not applicable
11	Kahn et al. (2019)	31	26	None	PTA, vHIT,	✓	---	---	Not applicable

					oVEMP, cVEMP				
12	Lee et al. (2020)	55	None	VN/Labyrinthis-36	CVT, vHIT	✓	✓	---	Not applicable
13	Limviriyakul et al. (2020)	51	None	None	PTA, CVT, vHIT	✓	✓	✓	*
14	McGarvie et al. (2015)	22	None	None	CVT, vHIT	✓	---	---	*
15	Oliveria et al. (2019)	32	20	None	CVT, vHIT	✓	✓	---	*
16	Rubin et al. (2018)	37	None	None	CVT, vHIT	✓	✓	---	*
17	Yacovino et al. (2020)	210	None	None	CVT, vHIT	✓	---	---	Not applicable
18	Yilmaz et al. (2020)	59	None	VM-50	CVT, vHIT	✓	✓	---	*
19	Zulueta-Santos et al. (2014)	36	None	None	PTA, vHIT, DHI	✓	---	---	Not applicable

*CG: Control Group, VOR gain: Vestibulo Occular Reflex gain, RS: Refixation Saccades, AR: Asymmetry Ratio, Ga: Gain Asymmetry, VRG: Velocity Regression Gain, PTA: Pure Tone Audiometry, CVT: Caloric Vestibular Test, cVEMP: cervical Vestibular Evoked Myogenic Potential, oVEMP: ocular Vestibular Evoked Myogenic Potential, DHI: Dizziness Handicap Inventory, RCT: Rotatory Chair Test, VN: Vestibular Neuritis, AVN: Acute Vestibular Neuritis, EVA: Enlarged Vestibular Aqueduct, VM: Vestibular Migraine, HSCC: Horizontal Semi-circular canal, PSCC: Posterior Semi-circular canal, UCW: Unilateral Canal Weakness, **- correlation, *- no correlation*

3.4 Vestibulo Ocular Reflex gain (VOR gain)

The most studied video Head Impulse Test parameter is the VOR gain, calculated by taking the area under the eye velocity curve to the area under the head velocity curve during the head impulse (Halmagyi et al., 2017). All the studies included in this systematic review process have evaluated the VOR gain, but the cut-off criteria vary from study to study.

Bharadwaj et al. (2020) used velocity regression gain (VRG) as a parameter of horizontal VOR, which is calculated from the regression slopes of left and right head impulses. It provides a more accurate representation of VOR gain by taking a time window of -10 ms to 100 ms with respect to the head impulse to avoid other interfering factors such as cervical ocular reflex and smooth pursuit. They established normative VRG for 40 healthy individuals in the age range of 24 to 69 years, and the normative range was 1.21 to 0.81. They found that in patients with Meniere's disease, the mean VRG was 0.99+/-0.07 SD and 0.87 +/- 0.18 SD for the unaffected and affected ear, respectively. Bharadwaj et al.

(2020) reported that the side affected with Meniere's disease had statistically reduced mean VRG, and statistically greater standard deviation than that of the unaffected side or healthy subjects.

Choi et al. (2017), considered VOR gain values of <0.8 and <0.7 as abnormal for horizontal and vertical canals, respectively. The authors reported that the sensitivity of VOR gain values in diagnosing individuals with Meniere's disease are lower. Only 12.5 percent of the Meniere's disease patients exhibit abnormality in VOR gain value, which is significantly lower than the abnormality seen in the patients with vestibular neuritis.

Jerin et al. (2019) considered VOR gain values lower than 0.7 as pathological in individuals with Meniere's disease. The authors reported no statistically significant difference in VOR gain between Meniere's ears and non-Meniere's ears in the same patient. The authors also suggested using VOR gain at different times. When the VOR gain at 60ms was taken, thirty-three out of fifty-four Meniere's disease patients were reported to have abnormal VOR gain. On the other hand, when averaged VOR gain at 40ms, 60ms and 80 ms was taken, the VOR gain reduction was noted in five out of fifty-four Meniere's disease patients. Furthermore, the authors found no correlation between VOR gain and the duration of the disease.

Lee et al. (2020) reported bilaterally positive vHIT results with VOR gain values being less than 0.8 for horizontal canals in 4 patients with Meniere's disease. Rubin et al. (2018) defined the threshold for normal VOR gain as 0.64 for vertical canals and 0.78 for lateral canals. Rubin et al. (2018) found that the VOR gain was normal in all thirty-seven patients with Meniere's disease. Yilmaz et al. (2020), considered VOR gain value lower than 0.79 as pathological for lateral canals. The authors reported that when the VOR gain value lesser

than 0.79 was considered as pathological, thirty-nine percent of the patients with Meniere's disease exhibited abnormal VOR gain. Thirty-four percent of MD patients in a study by Cordero- Yanza et al. (2017) showed normal VOR gain values for all the canals when they took VOR greater than 0.8 as normal criteria for horizontal canals and VOR gain of more than 0.7 for vertical canals. They found that the right posterior canal was most involved (30%), followed by the left posterior canal (23%) in individuals with Meniere's disease.

van Esch et al. (2018) studied VOR gain values concerning the duration and stage of the disease. The authors reported that twenty-five percent of patients with Meniere's disease, with a disease duration of more than ten years, are more likely to have an abnormal VOR gain with a VOR gain value of <0.8 . However, they could not find a statistically significant difference across different durations of Meniere's disease progression. Though the possibility of having abnormal VOR gain in Meniere's disease stages III and IV was more than that of stages I and II, a statistically significant difference was not obtained between different stages of the disease.

Fukushima et al. (2018) considered median VOR gain values of 0.8 or more for horizontal canals and 0.7 or more for vertical canals as normal. The VOR gain was found to be reduced more on the side affected with Meniere's disease than the unaffected side. The reduction in VOR gain was more evident for the lateral and posterior canals. 56.7 % of their patients with MD were found to have canal paresis according to reduced VOR gain.

Grigol et al. (2019) have set the VOR gain cut-off of <0.77 and <0.61 VOR gain values for lateral and vertical canals, respectively, as abnormal VOR gain. The VOR gain values of horizontal canals of symptomatic ears and the control group were statistically different. Symptomatic ears had lower VOR gain values than the control group. In contrast, there

was no difference in VOR gain between symptomatic and asymptomatic ears of Meniere's disease individuals and between the asymptomatic ears of MD and the healthy individuals.

Huang et al. (2020) have taken the VOR gain values less than 0.8 for lateral canals and less than 0.7 for superior and posterior canals as pathological. Among 80 patients with definite Meniere's disease, the abnormal rate of vHIT was maximum for the posterior semi-circular canals (36.25%), followed by superior semi-circular canals (35%). When the abnormality in vHIT is considered, the lateral semi-circular canals were the least affected semi-circular canal in individuals with Meniere's disease. The authors also considered the number of vestibular end organs involved (ranging from 0 to 5) as a measure of Meniere's disease progress. They observed a negative association between the number of involved vestibular end organs and the VOR gains of superior and posterior canals.

Vestibulo-ocular reflex gain thresholds of 0.64 for vertical canals and 0.78 for lateral canals were considered by Kahn et al. (2019). In their 31 definite Meniere's disease patients, the symptomatic ears obtained mean VOR gain values as follows; 0.78 +/- 0.15 for anterior canals, 0.86 +/- 0.15 for horizontal canals, and 0.81 +/- 0.12 for the posterior canals.

An abnormality in vHIT was considered by Limviriyakul et al. (2020) when the VOR gain was dropped below 0.8 for horizontal canals and 0.7 for vertical canals. A normal VOR gain was found for all the semi-circular canals in approximately 53% of the patients with Meniere's disease, whereas abnormal VOR gain was found in at least one of the semi-circular canals in 47% of the patients. They reported a statistically significant difference in the VOR gain on the affected side of posterior semi-circular canals of active and inactive MD groups ($p=0.048$).

Yacovino et al. (2020) have categorized the vertigo attack into initial, acme, and recovery stages in patients with Meniere's disease. The VOR gain was defined as abnormal when the value was less than 0.80 or more than 1.11 for the lateral canals. Interictal and post-attack stages did not show a significant difference in the mean ipsilesional hVOR gain. Ipsilesional hVOR gain was considerably lower during the attack in all the nine definite Meniere's disease patients than the hVOR of contralesional and healthy ears. Though the values of hVOR gain had returned to the normal range during the period between attacks, it was substantially lower on the affected ear than the unaffected ear and healthy controls. Such differences in VOR gain were not seen on the contralateral side during all stages of vertigo attack.

Zulueta-Santos et al. (2014) set the VOR gain value >0.8 for horizontal canals and >0.7 for anterior and posterior canals to consider it normal. In a study group of 36 subjects with Meniere's disease, 33.3% had VOR gain values within normal limits. Another 33.3 % of the subjects showed abnormal VOR gain value in at least one of the semi-circular canals. Among the remaining subjects, 30.5% indicated pathological VOR gain value in at least one of the semi-circular canals in the ipsilesional and contra-lesional ears. They reported that abnormal VOR gain was more commonly seen in the posterior canal and least in the horizontal canal of Meniere's ear.

Most studies have considered VOR gain values less than 0.8 and 0.7 as pathological for horizontal and vertical semi-circular canals, respectively. Though the VOR gain is not reduced in all the patients with Meniere's disease, nearly 30 to 50 percent of the population showed a reduction in the VOR gain value. A more noticeable VOR gain reduction is observed during the vertigo attacks, with the VOR gain values returning to the normal

values in post-Meniere's attack stages. Another critical observation is the more frequent occurrence of VOR gain reduction in the posterior semi-circular canal plane, indicating the most affected in Meniere's disease progression. Superior canals follow this, and then lateral canals being the least affected. At present, vHIT is the only test capable of evaluating all the six semi-circular canals; it indicates the pathology by showing decreased VOR gain value in at least one semi-circular canals.

3.5 Presence or absence of Refixation Saccades:

The presence/absence of re-fixation saccades, including both covert and overt saccades, can be identified with vHIT. A covert saccade happens along with the head movement, and an overt saccade occurs after the head movement. Bharadwaj et al. (2020) evaluated the diagnostic accuracy of re-fixation saccades in patients with Meniere's disease. An acceleration criterion of >2000 degree/s² was used to identify the catch-up saccades. The catch-up saccade was defined when the occurrence was more than two with similar amplitude and latency with $>50\%$ of head impulse velocity. The Meniere's ear had a significantly higher proportion of corrective saccades, including both covert and overt saccades than the non-pathological side or healthy subjects.

Choi et al. (2017) considered the presence of saccade when the velocity of the saccade was greater than 50 degree/s and reported that only 12.5 percent of their Meniere's disease patients had abnormal results compared to vestibular neuritis. Cordero-Yanza et al. (2017) reported the presence of corrective saccades, majorly overt saccades, in individuals with Meniere's disease. Fukushima et al. (2018) reported the presence of large-amplitude re-fixation saccades in the lateral and posterior semi-circular canals in patients with

Meniere's disease. Fifty-seven percent of the individuals with Meniere's disease have the presence of re-fixation saccades.

Jerin et al. (2020) defined saccade as any peak outside of the band of recorded eye movements to include even small saccades (velocity of the smallest saccade was $60^{\circ}/s$). They studied three saccade parameters: the mean saccade velocity($^{\circ}/s$), latency (ms after the onset of head movement), and frequency in individuals with Meniere's disease. The mean velocity of re-fixation saccades ($104^{\circ}/s$ versus $97^{\circ}/s$, $p = 0.19$), or the mean saccade latency (198ms versus 214ms, $p = 0.17$) was not significantly different between ears affected with Meniere's disease and the unaffected ears. However, saccadic frequency shows a significant difference between Meniere's ear and non-Meniere's ear. Infrequent re-fixation saccades were found in 14 out of 54 patients in less than 50 percent of performed vHIT curves in the presence of normal VOR gain. A significant increase in saccade latency with increasing VOR gain is seen in contralateral ears but not for Meniere's ears. The relationship between saccade frequency, velocity, and latency in pathological and non-pathological ears indicates an increase in the percentage of vHIT curves with saccades within one individual. The saccades' velocity for Meniere's ears increased significantly, and the latency decreased for unaffected ears.

Yilmaz et al. (2020) showed re-fixation saccades in 37.3 percentage of their Meniere's disease patients. The percentage of re-fixation saccade is higher in individuals with Meniere's disease compared to the vestibular migraine group. Grigol et al. (2019) found that saccades were detected more in the horizontal canals of the Meniere's ear but not in the unaffected ear or control group. At the same time, such saccades are absent in the posterior and anterior canals. Though there is no significant difference, lateral overt

saccades were more seen than the covert variant. The absence of saccades is more commonly seen in the asymptomatic ears of the study group than the control group.

Oliveria et al. (2019) reported a more frequent cover/overt saccades in the horizontal canals of the individuals with Meniere's disease. These studies indicate that re-fixation saccades can be considered a valuable parameter as it makes the diagnosis of Meniere's disease more accurate using vHIT. The frequency of catch-up saccades is more in the Meniere's ears than the asymptomatic ears, even in the presence of other vHIT parameters being normal. Most of the studies have considered the occurrence of saccades when the velocity is more than 50 degrees/sec. These studies also report the higher prevalence of saccades in the horizontal plane than superior and posterior canals.

3.6 Vestibulo-ocular reflex Gain Asymmetry

The number of studies that have evaluated the VOR gain asymmetry in individuals with Meniere's disease is considerably low. Among the 19 studies included, only four studies have discussed the VOR gain asymmetry value. All these studies compared the VOR gain asymmetry of vHIT and canal paresis of the caloric test. Bharadwaj et al. (2020) showed no good correlation between the velocity regression gain asymmetry and the percentage of unilateral canal weakness, suggesting that VOR gain asymmetry may not be a good indicator of semi-circular canal function in patients with Meniere's disease.

Limviriyakul et al. (2020) also indicated a lack of correlation between VOR gain asymmetry and caloric weakness for the horizontal canal of the affected side in patients with Meniere's disease. Yilmaz et al. (2020) reported VOR gain asymmetry in 35.6% of Meniere's disease patients. However, the authors could not find a statistically significant

difference for the VOR gain asymmetry between Meniere's disease and vestibular migraine groups. Cordero-Yanza et al. (2017) reported that VOR gain asymmetry could not be considered a good indicator of Meniere's disease. The VOR gain asymmetry value does not correlate with caloric weakness.

In contrast to these studies, Cordero-Yanza et al. (2017) revealed a moderate linear correlation between VOR gain asymmetry and canal paresis in Meniere's disease individuals. More the canal paresis, the larger the values of VOR gain asymmetry. The authors also observed that the median VOR gain asymmetry value was five percentage and 12 percentage in individuals with normal and abnormal caloric test results.

The summary of findings concerning all the vHIT parameters is provided in table no 3.3

Table no. 3.3. Summary of findings

Sl. No	Author & Year	Summary of findings
1	Bharadwaj et al., 2020	<ul style="list-style-type: none"> ☛ Reduced VRG in the ear affected with MD (0.87 +/- 0.18). ☛ A higher proportion of corrective saccades in the pathological ear. ☛ No correlation between VRG asymmetry and unilateral canal weakness.
2	Choi et al., 2017	<ul style="list-style-type: none"> ☛ 12.5 percent of MD patients exhibited abnormal vHIT results.
3	Cordero-Yanza et al., 2017	<ul style="list-style-type: none"> ☛ 34 percentage of MD patients showed normal VOR gain values. ☛ The right posterior canal is involved more commonly than the left posterior canal.

- Observed the presence of corrective saccades with normal VOR gain in the MD group.
 - Moderate linear correlation between VOR gain asymmetry and canal paresis of horizontal canals.
- 4 van Esch et al., 2018
- Abnormal VOR gain as the course of the disease progresses and in stages III and IV of MD.
- 5 Fukushima et al., 2018
- More reduction of VOR gain in lateral and posterior canals of subjects affected with Meniere's disease.
 - Fifty-seven percent of patients had the presence of large-amplitude re-fixation saccades in lateral and posterior canals.
- 6 Grigol et al., 2019
- Less VOR gain was seen in lateral canals of Meniere's ears and the presence of corrective saccades, especially overt saccades in the lateral canals.
- 7 Hannigan et al., 2019
- Less chances of showing pathological VOR gain in MD.
- 8 Huang et al., 2020
- Abnormal rate of vHIT was maximum for posterior SSC, followed by superior SCC.
 - The number of involved vestibular end organs showed a negative association with the vertical canals' VOR gains.
- 9 Jerin et al., 2019
- 33 out of 54 MD patients showed abnormal VOR gain.
 - More frequent occurrence of re-fixation saccades in MD patients.
- 10 Jung et al., 2016
- hVOR gain was lower in the Canal Paresis group.

- 11 Kahn et al., 2019
 - ☛ Meniere's ears showed mean VOR gain values as follows; 0.78 +/- 0.15 for anterior canals, 0.86 +/- 0.15 for horizontal canals, and 0.81 +/- 0.12 for the posterior canals.
- 12 Lee et al., 2020
 - ☛ A significantly fewer number of MD patients with bilateral positive vHIT.
- 13 Limviriyakul et al., 2020
 - ☛ Abnormal VOR gain in at least one of the SCC in 47 percentage of MD patients.
 - ☛ No correlation between VOR gain asymmetry and canal weakness of horizontal canals.
- 14 McGarvie et al., 2015
 - ☛ VOR gain values were within the normal range for patients with MD.
- 15 Oliveria et al., 2019
 - ☛ Most of the vHIT results were within the normal range for MD patients.
 - ☛ More frequency of occurrence of saccades is in the lateral SCCs.
- 16 Rubin et al., 2018
 - ☛ All MD patients had normal VOR gain.
- 17 Yacovino et al., 2020
 - ☛ Reduced hVOR gain on the ipsilesional side but not on the contralateral side during all stages of the attack.
- 18 Yilmaz et al., 2020
 - ☛ 39 percent of subjects with MD showed abnormal VOR gain in horizontal canals.
 - ☛ Presence of re-fixation saccades in 37.3 percentage of MD patients.
 - ☛ Presence of re-fixation saccades with normal VOR gain in the horizontal SCCs.

- ☛ Reported VOR gain asymmetry in 35.6% of MD patients.
- 19 Zulueta-Santos et al., 2014
- ☛ 33.3% of patients showed abnormal VOR gain value in at least one of the SCC.
 - ☛ Abnormal VOR gain is more commonly seen in the posterior canal and least in the horizontal canal.
-

3.7 Correlation of vHIT with caloric test results in Meniere's disease

The vestibular system consists of five sensory systems. The video head impulse test assesses the six semi-circular canals. The video head impulse test does not evaluate the otolith organs. The vestibular evoked myogenic potentials provide information about both the otolith organs, i.e. utricle and saccule. In patients with Meniere's disease, there is a possibility of isolated damage to the otolith organs. Hence, a comprehensive evaluation of the vestibular system would require the administration of video head impulse test along with the vestibular evoked myogenic potentials. Few studies have compared the video head impulse test findings with other vestibular tests findings in Meniere's disease diagnosis.

Bharadwaj et al. (2020) reported a weak correlation between the absolute VOR gain asymmetry and absolute unilateral canal weakness in individuals with Meniere's disease. However, the authors reported a moderate correlation between the presence of re-fixation saccades and unilateral caloric weakness in Meniere's ears. Choi et al. (2017) also reported a dissociation between vHIT and caloric test in twenty-four Meniere's disease patients. Choi et al. (2017) reported a normal VOR gain in the presence of abnormal caloric test results in 87.5% of the Meniere's disease patients.

Cordero-Yanza et al. (2017) reported a moderate correlation between the VOR gain asymmetry and canal paresis values. The median VOR gain asymmetry for the horizontal semi-circular canal in patients with the normal caloric test was 5%, whereas it was 12 percentage for patients with the abnormal caloric test. VOR gain was normal in 45% of Meniere's disease patients with abnormal caloric test results. In most cases, the pathological side identified through caloric tests did not correspond to that obtained in vHIT. 13% and 3.4% percent of their patients showed pathological VOR gain values for posterior and anterior semi-circular canals in the presence of normal caloric results. They have reported that abnormal caloric test results do not imply an abnormal vHIT, making both the tests complementary in patients with Meniere's disease. They also found normal caloric test results in the presence of an abnormal vHIT result where re-fixation saccade was the only abnormal finding in such patients.

Fukushima et al., (2018) also reported no correlation between vHIT and caloric tests results. Hannigan et al. (2019), reported discordant results in twenty-seven Meniere's disease patients where the VOR gain was normal, and the caloric test result was abnormal with canal paresis value $>30\%$. A chi-square test revealed a significant relationship between a diagnosis of MD and the presence of a vHIT caloric dissociation ($p < 0.001$). Jerin et al. (2018) did not find any correlation between vHIT VOR gain, saccade frequency or saccade velocity, and caloric irrigation canal paresis. Jung et al. (2016), McGarvie et al. (2015), and Yilmaz et al. (2020) also reported discrepancies between the caloric and vHIT test results.

To summarize, the overall results suggest no correlation between caloric test results and the video head impulse test in Meniere's disease patients. This suggests that the two

tests assess a different aspect of the vestibular system. Video head impulse test cannot be a replacement for the caloric test results. It can complement the findings of the caloric test in individuals with Meniere's disease.

Chapter-IV

DISCUSSION

Meniere's disease is characterized by episodes of vertigo along with hearing loss and tinnitus. The diagnosis of Meniere's disease is made based upon the clinical sign and symptoms and several test findings. Video head impulse test has become one of the important tools in the assessment of semi-circular canal dysfunction in Individuals with Meniere's disease. The aim of the systematic review was to identify the clinical utility of the video head impulse test in the diagnosis of Meniere's disease. For this purpose, nineteen studies were evaluated under three parameters; vestibulo-ocular reflex gain, re-fixation saccades, and vestibulo-ocular reflex gain asymmetry.

4.1 Vestibulo-ocular reflex gain and Gain asymmetry

The results regarding VOR gain show that the VOR gain is not necessarily abnormal in all the patients with Meniere's disease, but the majority of the studies indicate an abnormality in the VOR gain (either increased or decreased VOR gain) for up to 30 to 50 percent of their subjects. Patients who exhibited reduced VOR gain indicated a prevalence of posterior and lateral semi-circular canals getting affected more than the anterior semi-circular canal.

McCall et al. (2009) have reported different degrees of degeneration of the vestibular structures in individuals with Meniere's disease. There is a presence of monolayer epithelial cells in Meniere's disease. The membrane thickening is more in the cristae of the semi-circular canals than in the utricular maculae. Loss of stereocilia is more frequent in the lateral semi-circular canals (McCall et al., 2009). This could be one of the

reason for more prevalence of the vestibular disorder in the lateral canal of the Meniere's disease than in other canals.

Yacovino et al. (2020), reported secondary development of BPPV followed by Meniere's disease. This leads to obstruction of the semi-circular canals and hence resulting in vestibular hypofunction. The presence of persistent spontaneous nystagmus characterizes it without any change in direction (Castellucci et al., 2019; Luis et al., 2013). The otoconia may get expelled into the semi-circular canals from the otolith organs resulting in the ampullopetal movement of the cupula. This would create excitatory nystagmus (Yacovino et al., 2020). "Drainage theory," as stated by Gibson & Arenberg (1997), points that the vertigo attack could be related to the malfunctioning of the endolymphatic sac and impeding the endolymphatic flow. This results in excessive endolymph reflexes through the utricular valve of Bast into the ampullae, eventuating in cupular deflection and finally vertigo causing hypofunction of horizontal VOR. A relatively new theory for explaining the vertigo attack and variation in hVOR is associated with the inner ear vasculature at the time of the attack. The hydrops may result in episodic and reversible ischemic attacks affecting the nerve and hair cells (Foster & Breeze, 2013).

vHIT results are also associated with the stage of disease and the duration of symptoms indicating abnormal VOR gain in later stages of disease (van Esch et al., 2018). In the early stages, the VOR gain is more towards the affected side with the presence of ipsilateral nystagmus, and also prominence in the VOR gain is seen on the affected side before the attack (Funabiki et al., 1999). Over-excitability of the cristae due to increased load within the ampulla resulting from increased endolymphatic space could be the possible reason for such elevation (Manzari et al., 2013; Rey-Martinez et al., 2018).

Manzari et al. (2012) also reported an increased VOR gain before, during, and after the attack of vertigo. Though there is a reduction in the VOR gain during vertigo, it remains above the normative and returns to the enhanced initial value after the attack. High values for VOR gain can also be obtained due to the improper placement of the goggles, miscalibration, pseudo saccades by eye blinks, activation of the convergence system, or Meniere's disease itself (Limviriyakul et al., 2020).

Due to its rigid walls, semi-circular canals are more resistant to the expansion caused by fluid accumulation. Semi-circular canals are the last structure to get affected and results in normal VOR function when assessed using vHIT, at least in the initial stages of Meniere's disease (Pender, 2015). The semi-circular canals have greater marginal space, vertical canals are more resistant to volume expansion than lateral canals resulting in more abnormal findings in the latter (Zulueta-Santos et al., 2014).

4.2 Re-fixation saccades

Saccades are found present alone or with a reduced VOR gain in Meniere's disease. The most noticeable finding in a few studies is a normal caloric test and abnormal vHIT test, with re-fixation saccade being the only abnormality that is correlated with the affected ear (Cordero-Yanza et al., 2017).

The catch-up saccades are meant to compensate for the reduced VOR gain. The gaze instability resulting from the deficient VOR is compensated by the occurrence of re-fixation saccades. (Blodow et al., 2013). The presence of re-fixation saccades, saccadic latency, frequency and amplitude/velocity are important parameters to provide information regarding the VOR functioning. The authors have reported that overt saccades were seen

in 33.3%, covert saccades in 16.7%, and a combination of both in 50% of the subjects with Meniere's disease.

Grigol et al. (2019) also reported a higher prevalence of overt saccades than the covert saccades in Meniere's disease patients. The re-fixation saccades occur to compensate for the reduced VOR gain. The covert saccades arise when there is difficulty stabilizing the eyes on the target. In contrast, overt saccades occur as a central compensation when the eyes cannot reach the target. This was also supported by the findings of Anson et al. (2016). The authors indicated a reduced VOR gain with the presence of overt saccades, which is of higher amplitude and shorter latency. They suggested that the compensatory saccades are capable of indicating gaze instability which may not be correctly identified through VOR gain. Re-fixation saccades with larger amplitude and shorter latency is seen in individuals with reduced VOR gain. This is because of the likelihood in response to increased retinal slip and a greater gaze position error. Importantly, even if not all vHITs had a re-fixation saccade, the re-fixation saccades, when present, were associated with underlying VOR gain (Anson et al., 2016).

According to Weber et al., 2008, the residual VOR and the re-fixation saccades work in a collaborative way for gaze stabilization. So, in individuals with vestibular disorders, the reduction in VOR gains on the affected side is compensated by the occurrence of re-fixation saccades, and hence keeping the eyes on the target. They also reported the presence of large re-fixation saccades on the ipsilesional and smaller contralesional saccades. As the latency of the re-fixation saccades reduces, the chances of gaze deviation from the target also reduce. The occurrence of covert saccades helps the

patients to reduce oscillopsia, as it occurs during the head impulse and making the gaze fixation at an earlier stage.

4.3 Correlation of vHIT and Caloric test results

Most of the studies have reported a dissociation between caloric vestibular test and video head impulse test, a marker for Meniere's disease.

Rubin et al. (2018) reported a discrepancy between the two even in advanced definite MD. It was made clear by three possible explanations; vHIT assesses all six semi-circular canals, whereas caloric test assesses only lateral canals, differential stimulation of the hair cell, and lastly, due to the anatomical orientation of the hair cells.

Type I hair cells are innervated by irregular nerve fibers, responding to high-frequency head movements vHIT (2.5 Hz). On the other hand, the type II hair cells are innervated by regular nerve fibers, responding for extremely low-frequency movements as in caloric testing (0.003-0.008 Hz) (Halmagyi et al., 2017). VOR is primarily mediated via regular fibers in the presence of low-frequency stimuli or via irregular fibers in the presence of high-frequency stimuli. The anatomical position of the type I and type II hair cells of cupulae is in such a way that the central zone is made up of type I, and the peripheral zone is made up of type II hair cells. This kind of arrangement leads to selective damage of type II hair cells, leaving the type I hair cells intact. Hence, it disables the low-frequency response, i.e., caloric, and spares high-frequency responses (vHIT). This clearly explains the reason for the dissociation between the caloric test and vHIT. In cases where there is an abnormality in both the tests, it indicates more general destruction of the hair cells (McCaslin et al., 2015). Hence, the functional preservation of type I hair cells as marked by vHIT and the destruction of type II hair cells, as noted in the caloric test, could be

considered a diagnostic criterion for Meniere's disease. However, histological studies using fresh tissues from the inner ear in individuals with MD contradicted this dual-frequency viewpoint. Studies pointed that both type I and II hair cells are affected equally in MD, and both the cells send signals to regular and irregular neurons (Tsuji et al., 2000; Eatock et al., 2011). The caloric responses and VOR gain in initial stages and during attacks fluctuated with the possibility of recovery to normal values (Manzari et al., 2011; Proctor et al., 2000).

'Hydrostatic temperature dissipation' hypothesis developed by McGarvie et al. (2015) explains that thermally induced dilation of the membranous duct resulting in a non-convective endolymphatic flow, same as in MD where membranous expansion happens due to hydrops. This could also be a possible reason for the deficits seen in the caloric test, which is not the case in vHIT. Head turn, a physiological stimulus, elicits cupular deflection due to inertia of the endolymph in vHIT whereas, the deflection resulted in the caloric test is due to the expansion of endolymph from the thermal stimulation, which is a non-physiological stimulus. The endolymphatic volume has an effect on the caloric test, i.e., the larger the volume, the smaller the cupula amplitude resulting in canal paresis. As vHIT generates large cupula amplitude, it is not affected by endolymph volume (Fukushima et al., 2018).

Chapter-V

SUMMARY & CONCLUSIONS

The objective of the study was to systematically review and find out the diagnostic accuracy of video head impulse tests in the detection of semi-circular canal dysfunction in individuals with definite Meniere's disease. Three parameters: Vestibulo-ocular reflex gain, presence or absence of re-fixation saccades, and Vestibulo-ocular reflex gain asymmetry in individuals with Meniere's disease were evaluated. The study also aimed at determining the association or dissociation of video head impulse test with the caloric test. Initially, a review search was performed in different databases. Searches across different databases resulted in 93 topic-related articles. Total nineteen articles met the inclusion and exclusion criteria to meet the objectives of the study. The quality and potential risk associated with each article were evaluated using the QUADAS-2 risk of bias assessment tool.

A detailed review of all the articles revealed that vestibulo-ocular gain is the most extensively studied parameter of video head impulse test in individuals with Meniere's disease. In contrast, the VOR gain asymmetry ratio being the least studied one. The results of these studies are unequivocally indicating increased, decreased, or normal VOR gain on the side affected with Meniere's disease. Few studies have found an abnormal decrease in VOR gain as the disease duration increases and also in the advanced stages of the disease. Some authors have reported that the chances of showing reduced VOR gain are more for the posterior semi-circular canals, whereas some other authors showed it on the lateral canals.

Re-fixation saccades, the second parameter, were more accurately identified through the video head impulse test. There was a higher proportion of saccades on the affected side compared to the unaffected side. Refixation saccade is more important findings compared to the VOR gain and VOR gain asymmetry. The occurrence of saccades was more in the horizontal canals. Overt saccades are seen more than covert saccades. VOR gain asymmetry being the least studied parameter, only Cordero-Yanza et al. (2017) showed a linear correlation between VOR gain asymmetry and canal paresis.

Evaluation of studies that reported other vestibular tests to diagnose Meniere's disease, especially caloric tests, showed a dissociation in its results with that of vHIT. The majority of the studies showed that the results of caloric tests were abnormal in individuals with Meniere's disease, whereas the findings of vHIT were normal. A wide variety of reasons were stated to support this disagreement.

Based on the above findings, it can be concluded that the video head impulse test is a valuable tool in the diagnosis of Meniere's disease when used along with other vestibular tests. Video head impulse test provides information about the pathologies related to all the six semi-circular canals where other vestibular tests fail to do so. When there is an involvement of vertical canals, especially the posterior canal, vHIT provides essential information by showing abnormality in at least one of the parameters. The VOR gain and corrective saccades are the most critical parameters that help to diagnose semi-circular canal dysfunction in Meniere's disease. Video head impulse test cannot replace the caloric test. Both the video head impulse test and caloric test complement each other, making the diagnosis of Meniere's disease more accurate.

IMPLICATIONS OF THE STUDY

- ❖ The study provides knowledge about the diagnostic accuracy or usefulness of video head impulse test in individuals with Meniere's disease.
- ❖ The study also provides insight into the different parameters of video head impulse test that can be used while diagnosing the semi-circular canal dysfunction in individuals with Meniere's disease.
- ❖ The study also helps in understanding the various mechanisms responsible for the VOR gain abnormality and re-fixation saccades in individuals with Meniere's disease.
- ❖ This systematic review also enabled one to understand the association or dissociation between vHIT and caloric test results in assessing Meniere's disease.

REFERENCES

- Alhabib, S. F., & Saliba, I. (2017). Video head impulse test: a review of the literature. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 274(3), 1215–1222. <https://doi.org/10.1007/s00405-016-4157-4>
- Anson, E. R., Bigelow, R. T., Carey, J. P., Xue, Q. L., Studenski, S., Schubert, M. C., & Agrawal, Y. (2016). VOR Gain Is Related to Compensatory Saccades in Healthy Older Adults. *Frontiers in aging neuroscience*, 8, 150. <https://doi.org/10.3389/fnagi.2016.00150>
- Aromataris, E., & Pearson, A. (2014). The systematic review: an overview. *The American journal of nursing*, 114(3), 53–58. <https://doi.org/10.1097/01.NAJ.0000444496.24228.2>
- Bharadwaj, S., Petrak, M. R., Bahner, C. M., Sharp, L. E., Mosey-Claycomb, S. F., & Matsuoka, A. J. (2020). Diagnostic value of refixation saccades in the Video Head Impulse Test (vHIT) in unilateral definite Meniere's disease. *Acta oto-laryngologica*, 140(7), 537–543. <https://doi.org/10.1080/00016489.2020.1744720>
- Blödow, A., Blödow, J., Bloching, M. B., Helbig, R., & Walther, L. E. (2015). Horizontal VOR function shows frequency dynamics in vestibular schwannoma. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 272(9), 2143–2148. <https://doi.org/10.1007/s00405-014-3042-2>

- Blödown, A., Pannasch, S., & Walther, L. E. (2013). Detection of isolated covert saccades with the video head impulse test in peripheral vestibular disorders. *Auris, nasus, larynx*, 40(4), 348–351. <https://doi.org/10.1016/j.anl.2012.11.002>
- Castellucci, A., Malara, P., Brandolini, C., Del Vecchio, V., Giordano, D., Ghidini, A., Ferri, G. G., & Pirodda, A. (2019). Isolated horizontal canal hypofunction differentiating a canalith jam from an acute peripheral vestibular loss. *American journal of otolaryngology*, 40(2), 319–322. <https://doi.org/10.1016/j.amjoto.2018.12.005>
- Choi, J. E., Kim, Y. K., Cho, Y. S., Lee, K., Park, H. W., Yoon, S. H., Kim, H. J., & Chung, W. H. (2017). Morphological correlation between caloric tests and vestibular hydrops in Ménière's disease using intravenous Gd enhanced inner ear MRI. *PloS one*, 12(11), e0188301. <https://doi.org/10.1371/journal.pone.0188301>
- Cordero-Yanza, J. A., Arrieta Vázquez, E. V., Hernaiz Leonardo, J. C., Mancera Sánchez, J., Hernández Palestina, M. S., & Pérez-Fernández, N. (2017). Comparative study between the caloric vestibular and the video-head impulse tests in unilateral Ménière's disease. *Acta oto-laryngologica*, 137(11), 1178–1182. <https://doi.org/10.1080/00016489.2017.1354395>
- Eatock, R. A., & Songer, J. E. (2011). Vestibular hair cells and afferents: two channels for head motion signals. *Annual review of neuroscience*, 34, 501–534. <https://doi.org/10.1146/annurev-neuro-061010-113710>
- Foster, C. A., & Breeze, R. E. (2013). Endolymphatic hydrops in Ménière's disease: cause, consequence, or epiphenomenon?. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society*

[and] *European Academy of Otolology and Neurotology*, 34(7), 1210–1214.
<https://doi.org/10.1097/MAO.0b013e31829e83df>

Fukushima, M., Oya, R., Nozaki, K., Eguchi, H., Akahani, S., Inohara, H., & Takeda, N. (2019). Vertical head impulse and caloric are complementary but react opposite to Meniere's disease hydrops. *The Laryngoscope*, 129(7), 1660–1666.
<https://doi.org/10.1002/lary.27580>

Funabiki, K., Naito, Y., & Honjo, I. (1999). Vestibulo-ocular reflex in patients with Meniere's disease between attacks. *Acta oto-laryngologica*, 119(8), 886–891.
<https://doi.org/10.1080/00016489950180225>

Gibson, W. P., & Arenberg, I. K. (1997). Pathophysiologic theories in the etiology of Meniere's disease. *Otolaryngologic clinics of North America*, 30(6), 961–967.

Grigol, T., Lopes, K. C., & Ganança, F. F. (2020). Cervical vestibular evoked myogenic potentials and video head impulse test in Ménière disease. *Brazilian journal of otorhinolaryngology*, 86(5), 534–544. <https://doi.org/10.1016/j.bjorl.2019.02.002>

Halmagyi, G. M., Chen, L., MacDougall, H. G., Weber, K. P., McGarvie, L. A., & Curthoys, I. S. (2017). The Video Head Impulse Test. *Frontiers in neurology*, 8, 258. <https://doi.org/10.3389/fneur.2017.00258>

Hannigan, I. P., Welgampola, M. S., & Watson, S. (2021). Dissociation of caloric and head impulse tests: a marker of Meniere's disease. *Journal of neurology*, 268(2), 431–439. <https://doi.org/10.1007/s00415-019-09431-9>

Henderson, L. K., Craig, J. C., Willis, N. S., Tovey, D., & Webster, A. C. (2010). How to write a Cochrane systematic review. *Nephrology (Carlton, Vic.)*, 15(6), 617–624. <https://doi.org/10.1111/j.1440-1797.2010.01380.x>

- Huang, S., Zhou, H., Zhou, E., Zhang, J., Feng, Y., Yu, D., Shi, H., Wang, J., Wang, H., & Yin, S. (2020). A New Proposal for Severity Evaluation of Menière's Disease by Using the Evidence From a Comprehensive Battery of Auditory and Vestibular Tests. *Frontiers in neurology*, *11*, 785. <https://doi.org/10.3389/fneur.2020.00785>
- Janky, K. L., Patterson, J., Shepard, N., Thomas, M., Barin, K., Creutz, T., Schmid, K., & Honaker, J. A. (2018). Video Head Impulse Test (vHIT): The Role of Corrective Saccades in Identifying Patients With Vestibular Loss. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, *39*(4), 467–473. <https://doi.org/10.1097/MAO.0000000000001751>
- Jerin, C., Maxwell, R., & Gürkov, R. (2019). High-Frequency Horizontal Semicircular Canal Function in Certain Menière's Disease. *Ear and hearing*, *40*(1), 128–134. <https://doi.org/10.1097/AUD.0000000000000600>
- Jung, J., Suh, M. J., & Kim, S. H. (2017). Discrepancies between video head impulse and caloric tests in patients with enlarged vestibular aqueduct. *The Laryngoscope*, *127*(4), 921–926. <https://doi.org/10.1002/lary.26122>
- Kahn, L., Hautefort, C., Guichard, J. P., Toupet, M., Jourdain, C., Vitaux, H., Herman, P., Kania, R., Houdart, E., Attyé, A., & Eliezer, M. (2020). Relationship between video head impulse test, ocular and cervical vestibular evoked myogenic potentials, and compartmental magnetic resonance imaging classification in menière's disease. *The Laryngoscope*, *130*(7), E444–E452. <https://doi.org/10.1002/lary.28362>

- Khan, K. S., Kunz, R., Kleijnen, J., & Antes, G. (2003). Five steps to conducting a systematic review. *Journal of the Royal Society of Medicine*, *96*(3), 118–121. <https://doi.org/10.1258/jrsm.96.3.118>
- Lee, J. Y., Kwon, E., Kim, H. J., Choi, J. Y., Oh, H. J., Koo, J. W., & Kim, J. S. (2020). Dissociated Results between Caloric and Video Head Impulse Tests in Dizziness: Prevalence, Pattern, Lesion Location, and Etiology. *Journal of clinical neurology (Seoul, Korea)*, *16*(2), 277–284. <https://doi.org/10.3988/jcn.2020.16.2.277>
- Lee, S. U., Kim, H. J., Koo, J. W., & Kim, J. S. (2017). Comparison of caloric and head-impulse tests during the attacks of Meniere's disease. *The Laryngoscope*, *127*(3), 702–708. <https://doi.org/10.1002/lary.26103>
- Limviriyakul, S., Luangsawang, C., Suvansit, K., Prakairunghong, S., Thongyai, K., & Atipas, S. (2020). Video head impulse test and caloric test in definite Ménière's disease. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, *277*(3), 679–686. <https://doi.org/10.1007/s00405-019-05735-8>
- Lopez-Escamez, J. A., Carey, J., Chung, W. H., Goebel, J. A., Magnusson, M., Mandalà, M., Newman-Toker, D. E., Strupp, M., Suzuki, M., Trabalzini, F., Bisdorff, A., Classification Committee of the Barany Society, Japan Society for Equilibrium Research, European Academy of Otology and Neurotology (EAONO), Equilibrium Committee of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), & Korean Balance Society (2015). Diagnostic criteria

for Menière's disease. *Journal of vestibular research: equilibrium & orientation*, 25(1), 1–7. <https://doi.org/10.3233/VES-150549>

Luis, L., Costa, J., Vaz Garcia, F., Valls-Solé, J., Brandt, T., & Schneider, E. (2013). Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials. *Otology & neurotology: official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, 34(4), 743–747. <https://doi.org/10.1097/MAO.0b013e318287f343>

Lysakowski A, McCrea RA, Tomlinson RD. Anatomy of vestibular end organs and neural pathways. In: Cummings CW, editor. *Otolaryngology- Head and Neck Surgery*. 2. St. Louis, MO: Mosby; 1993. pp. 2525–2547

MacDougall, H. G., McGarvie, L. A., Halmagyi, G. M., Curthoys, I. S., & Weber, K. P. (2013). Application of the video head impulse test to detect vertical semicircular canal dysfunction. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, 34(6), 974–979. <https://doi.org/10.1097/MAO.0b013e31828d676d>

Manzari, L., Burgess, A. M., & Curthoys, I. S. (2012). Vestibular function in Lermoyez syndrome at attack. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 269(2), 685–691. <https://doi.org/10.1007/s00405-011-1657-0>

- Manzari, L., Burgess, A. M., MacDougall, H. G., Bradshaw, A. P., & Curthoys, I. S. (2011). Rapid fluctuations in dynamic semicircular canal function in early Ménière's disease. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 268(4), 637–639. <https://doi.org/10.1007/s00405-010-1442-5>
- Manzari, L., MacDougall, H. G., Burgess, A. M., & Curthoys, I. S. (2013). New, fast, clinical vestibular tests identify whether a vertigo attack is due to early Ménière's disease or vestibular neuritis. *The Laryngoscope*, 123(2), 507–511. <https://doi.org/10.1002/lary.23479>
- McCall, A. A., Ishiyama, G. P., Lopez, I. A., Bhuta, S., Vetter, S., & Ishiyama, A. (2009). Histopathological and ultrastructural analysis of vestibular endorgans in Meniere's disease reveals basement membrane pathology. *BMC ear, nose, and throat disorders*, 9, 4. <https://doi.org/10.1186/1472-6815-9-4>
- McCaslin, D. L., Rivas, A., Jacobson, G. P., & Bennett, M. L. (2015). The dissociation of video head impulse test (vHIT) and bithermal caloric test results provide topological localization of vestibular system impairment in patients with "definite" Ménière's disease. *American journal of audiology*, 24(1), 1–10. https://doi.org/10.1044/2014_AJA-14-0040
- McGarvie, L. A., Curthoys, I. S., MacDougall, H. G., & Halmagyi, G. M. (2015). What does the dissociation between the results of video head impulse versus caloric testing reveal about the vestibular dysfunction in Ménière's disease?. *Acta oto-laryngologica*, 135(9), 859–865. <https://doi.org/10.3109/00016489.2015.1015606>

- Moola S, Munn Z, Sears K, et al. Conducting systematic reviews of association (etiology): The Joanna Briggs Institute's approach. *International Journal of Evidence-based Healthcare*. 2015 Sep;13(3):163-169. DOI: 10.1097/xeb.000000000000064. PMID: 26262566.
- Oliveira, L., Oliveira, C., Lopes, K. C., & Ganança, F. F. (2019). Diagnostic assessment of patients with Meniere's disease through caloric testing and the video-head-impulse test. *Brazilian journal of otorhinolaryngology*, S1808-8694(19)30141-7. Advance online publication. <https://doi.org/10.1016/j.bjorl.2019.10.008>
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., ... Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ (Clinical research ed.)*, 372, n71. <https://doi.org/10.1136/bmj.n71>
- Pender D. J. (2015). Membrane Stress in the Human Labyrinth and Meniere Disease: A Model Analysis. *International archives of otorhinolaryngology*, 19(4), 336–342. <https://doi.org/10.1055/s-0035-1549157>
- Proctor L. R. (2000). Results of serial vestibular testing in unilateral Ménière's disease. *The American journal of otology*, 21(4), 552–558.
- Rey-Martinez, J., Burgess, A. M., & Curthoys, I. S. (2018). Enhanced Vestibulo-Ocular Reflex Responses on vHIT. Is It a Casual Finding or a Sign of Vestibular Dysfunction?. *Frontiers in neurology*, 9, 866. <https://doi.org/10.3389/fneur.2018.00866>

- Rubin, F., Simon, F., Verillaud, B., Herman, P., Kania, R., & Hautefort, C. (2018). Comparison of Video Head Impulse Test and Caloric Reflex Test in advanced unilateral definite Menière's disease. *European annals of otorhinolaryngology, head and neck diseases*, *135*(3), 167–169. <https://doi.org/10.1016/j.anorl.2017.08.008>
- Shugyo, M., Ito, T., Shiozaki, T., Nishikawa, D., Ohyama, H., Fujita, H., Yamanaka, T., & Kitahara, T. (2020). Comparison of the video head impulse test results with caloric test in patients with Meniere's disease and other vestibular disorders. *Acta oto-laryngologica*, *140*(9), 728–735. <https://doi.org/10.1080/00016489.2020.1766700>
- Tsuji, K., Velázquez-Villaseñor, L., Rauch, S. D., Glynn, R. J., Wall, C., 3rd, & Merchant, S. N. (2000). Temporal bone studies of the human peripheral vestibular system. Meniere's disease. *The Annals of otology, rhinology & laryngology. Supplement*, *181*, 26–31. <https://doi.org/10.1177/00034894001090s505>
- Ulmer, E., & Chays, A. (2005). "Head Impulse test de Curthoys & Halmagyi". Un dispositif d'analyse [Curthoys and Halmagyi Head Impulse test: an analytical device]. *Annales d'oto-laryngologie et de chirurgie cervico faciale: bulletin de la Societe d'oto-laryngologie des hopitaux de Paris*, *122*(2), 84–90. [https://doi.org/10.1016/s0003-438x\(05\)82329-1](https://doi.org/10.1016/s0003-438x(05)82329-1)
- van Esch, B. F., Abolhosseini, K., Masius-Olthof, S., van der Zaag-Loonen, H. J., van Benthem, P., & Brintjes, T. D. (2018). Video-head impulse test results in patients with Menière's disease related to duration and stage of disease. *Journal of*

vestibular research: equilibrium & orientation, 28(5-6), 401–407.
<https://doi.org/10.3233/VES-190654>

Weber, K. P., Aw, S. T., Todd, M. J., McGarvie, L. A., Curthoys, I. S., & Halmagyi, G. M. (2008). Head impulse test in unilateral vestibular loss: vestibulo-ocular reflex and catch-up saccades. *Neurology*, 70(6), 454–463.
<https://doi.org/10.1212/01.wnl.0000299117.48935.2e>

Whiting, P. F., Rutjes, A. W., Westwood, M. E., Mallett, S., Deeks, J. J., Reitsma, J. B., Leeflang, M. M., Sterne, J. A., Bossuyt, P. M., & QUADAS-2 Group (2011). QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Annals of internal medicine*, 155(8), 529–536.
<https://doi.org/10.7326/0003-4819-155-8-201110180-00009>

Yacovino, D. A., Schubert, M. C., & Zanotti, E. (2020). Evidence of Large Vestibulo-Ocular Reflex Reduction in Patients With Menière Attacks. *Otology & neurotology: official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, 41(9), e1133–e1139. <https://doi.org/10.1097/MAO.0000000000002746>

Yilmaz, M. S., Egilmez, O. K., Kara, A., Guven, M., Demir, D., & Genc Elden, S. (2021). Comparison of the results of caloric and video head impulse tests in patients with Meniere's disease and vestibular migraine. *European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, 278(6), 1829–1834.
<https://doi.org/10.1007/s00405-020-06272-5>

Zulueta-Santos, C., Lujan, B., Manrique-Huarte, R., & Perez-Fernandez, N. (2014).

The vestibulo-ocular reflex assessment in patients with Ménière's disease: examining all semicircular canals. *Acta oto-laryngologica*, *134*(11), 1128–1133.

<https://doi.org/10.3109/00016489.2014.919405>