Diagnostic Value of Vestibular Evoked Myogenic Potentials in Endolymphatic Hydrops: A Meta-Analysis

In this study, we evaluated the clinical diagnostic value of vestibular evoked myogenic potentials (VEMPs) for endolymphatic hydrops (EH) by systematic review and Meta-analysis. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and area under summary receiver operating characteristic curves (AUC) were calculated. Subgroup analysis and publication bias assessment were also conducted. The pooled sensitivity and the specificity were 49% (95% CI: 46% to 51%) and 95% (95% CI: 94% to 96%), respectively. The pooled positive likelihood ratio was 18.01 (95% CI: 9.45 to 34.29) and the pooled negative likelihood ratio was 0.54 (95% CI: 0.47 to 0.61). AUC was 0.78 and the pooled diagnostic odds ratio of VEMPs was 39.89 (95% CI: 20.13 to 79.03). In conclusion, our present meta-analysis has demonstrated that VEMPs test alone is not sufficient for Meniere’s disease or delayed endolymphatic hydrops diagnosis, but that it might be an important component of a test battery for diagnosing Meniere’s disease or delayed endolymphatic hydrops. Moreover, VEMPs, due to its high specificity and non-invasive nature, might be used as a screening tool for EH.

Meniere’s disease (MD) is a well-known inner ear disorder. Its symptoms include recurrent episodes of self-limiting vertigo, fluctuating or progressive sensorineural hearing loss, fullness and tinnitus of the affected ear. Previous studies showed that endolymphatic hydrops (EH) is a major histopathological characteristics of MD. Over the past two decades, mounting evidence has demonstrated that MD may present a variety of clinical symptoms and respond differently to treatment and possesses a wide array of phenotypical and endophenotypical features of inner ear disorders1–3.

Delayed endolymphatic hydrops (DEH) is defined as delayed development of episodic vertigo following either ipsilateral or contralateral ear with profound sensorineural hearing loss4.

Underlying pathological state of MD is idiopathic EH, while, DEH is one form of secondary EH. Therefore, pathophysiological, both DEH and MD have EH1–4. Previous studies suggested that development of EH involves a set of environmental, genetic and epigenetic factors. However, the underlying pathogenesis of EH remains poorly understood. Up to date, no single method, neither physical examinations nor diagnostic tests, can identify EH with significant certainty5.

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Currently, MD and DEH are principally diagnosed on the basis of the typical clinical symptoms, pure tone audiometry and the presence of EH. However, the objective in vivo confirmation of EH is difficult and it might be subject to constant change during a vertigo attack and between attacks. Since vestibular or cochlear symptoms may occur separately at the early stage of EH, clinical diagnosis of EH can be difficult. Previous studies indicated that the remission rate of stood somewhere between 60% to 80% in MD patients receiving treatments. To improve the effectiveness of clinical treatment, it is of great importance to establish a reliable technique for diagnosing EH.

Vestibular evoked myogenic potentials (VEMPs) can be used for assessing the otolith organ and peripheral vestibular function. Cervical vestibular evoked myogenic potentials (c-VEMPs) can serve as an indicator of vestibular function. c-VEMPs are elicited via a special pathway that goes from the saccule, inferior vestibular nerve, vestibular nucleus, medial, lateral vestibulospinal tract and finally to the ipsilateral sternocleidomastoid muscle (SCM). Moreover, ocular vestibular evoked myogenic potentials (o-VEMPs), another indicator of vestibular function, are evoked through the pathway that starts from utricle, superior vestibular nerve, vestibular nucleus, the medial longitudinal fasciculustill, oculomotor nuclei and ends at the contralateral extraocular muscles. Distortion of the membranous labyrinth, labyrinthine ruptures, and complete collapse of the membranous labyrinth may disturb the homeostasis of the inner ear. These may explain symptoms in auditory and vestibular systems in EH, the histopathological hallmark of MD and DEH, tends to develop in the cochlea. It then extends to the saccule and utricle and eventually involves the semicircular canals. In fact, anatomic studies of temporal bone suggested that the functional impairment in the cochlea, saccule, utricle, and semicircular canals may be the consequence of sequential development of EH.

Moreover, abnormal VEMPs can also be recorded in other vertigo diseases, such as vestibular neuritis, superior canal dehiscence, benign paroxysmal positional vertigo, sudden hearing loss, vestibular Schwannoma, multiple sclerosis, Miller Fisher syndrome and so on. In all these conditions, the saccule or inferior vestibular nerves are involved. Differentiation diagnosis relies on detailed history-taking, physical examinations, a battery of audio-vestibular function tests including pure tone audiometry, VNG, MRI on inner ear and brain and CT scan on temporal bone. In this study, we focused on EH, a histopathological hallmark of both MD and DEH, to explore the diagnostic value of VEMPs.

Since VEMPs can be used for detecting EH, we were led to assume that VEMPs test would be helpful in the diagnosis of EH. VEMP is complementary caloric test, rotation test and pure tone audiometry for EH diagnosis. Previous studies have intensively explored the diagnostic value of VEMPs for MD or DEH, and the findings varied substantially with different researches. In this meta-analysis, we comprehensively summarized the results of prior results with an attempt to precisely evaluate the usefulness of VEMPS in the diagnosis of EH due to MD or DEH.

Results

Literature search and eligible studies. Initially, 102 studies were identified after elimination of duplicates (Fig. 1). By screening titles or abstracts against our inclusion/exclusion criteria, 53 articles were excluded (Irrelevant: 33, Reviews: 16, Case reports: 3, News: 1), with 49 full-text articles left. Then another 18 articles were removed for failure to providing sufficient data and 1 animal study was excluded. Our effort to contact the original authors for detailed data failed. In the end, 30 eligible articles were included for our meta-analysis. The features of all eligible studies are presented in Table 1.

Quality assessment of the included studies. To evaluate the quality of the eligible studies, we employed the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. The overall quality of the included studies was high, as shown in Fig. 2.

Meta-analysis. Our analysis revealed that the pooled sensitivity and the specificity of all studies were 49% (95% CI: 46% to 51%) and 95% (95% CI: 94% to 96%), respectively (Figs 3 and 4). The pooled
| Author                        | Country | Study design | Case N | Control N | TP  | FN  | FP  | TN  | Funding  |
|------------------------------|---------|--------------|--------|-----------|-----|-----|-----|-----|----------|
| 2003 Yi-Ho Young             | Taiwan  | prospective  | 40     | 40        | 16  | 24  | 0   | 40  | Government |
| 2008 Seok Min Hong           | Korea   | prospective  | 29     | 29        | 20  | 9   | 0   | 29  | No funding |
| 1999 catherine de waele      | France  | retrospective| 59     | 37        | 27  | 32  | 4   | 33  | No funding |
| 2012 CHI-HSUAN HUANG         | Taiwan  | prospective  | 50     | 50        | 22  | 28  | 0   | 50  | No funding |
| 2012 CHI-HSUAN HUANG         | Taiwan  | prospective  | 50     | 50        | 19  | 31  | 0   | 50  | No funding |
| 2011 Stephanie M Winters     | Netherlands | prospective  | 31     | 55        | 14  | 17  | 1   | 54  | No funding |
| 2011 Stephanie M Winters     | Netherlands | prospective  | 37     | 55        | 27  | 10  | 1   | 54  | No funding |
| 2008 Giuseppe Magliulo       | Italy    | prospective  | 22     | 22        | 8   | 14  | 0   | 22  | No funding |
| 2008 Giuseppe Magliulo       | Italy    | prospective  | 22     | 22        | 7   | 15  | 0   | 22  | No funding |
| 2008 Giuseppe Magliulo       | Italy    | prospective  | 22     | 22        | 7   | 15  | 0   | 22  | No funding |
| 2006 Gu‘zin Akkuzu           | Turkey   | prospective  | 20     | 34        | 10  | 10  | 2   | 32  | No funding |
| 2005 Shih-Wei Kuo            | Taiwan   | prospective  | 12     | 12        | 8   | 4   | 0   | 12  | No funding |
| 2005 Shih-Wei Kuo            | Taiwan   | prospective  | 12     | 12        | 4   | 8   | 0   | 12  | No funding |
| 2012 M. Geraldine Zuniga     | USA      | prospective  | 20     | 56        | 4   | 16  | 0   | 56  | Government |
| 2012 M. Geraldine Zuniga     | USA      | prospective  | 20     | 56        | 10  | 10  | 2   | 54  | Government |
| 2012 M. Geraldine Zuniga     | USA      | prospective  | 20     | 56        | 2   | 18  | 2   | 54  | Government |
| 2006 Ming-Yee Lin            | Netherlands | prospective | 17     | 24        | 17  | 0   | 0   | 24  | Government |
| 2006 Ming-Yee Lin            | Netherlands | prospective | 6      | 24        | 5   | 1   | 0   | 24  | Government |
| 2012 ANA PAULA SERRA         | Brazil   | prospective  | 12     | 66        | 6   | 6   | 0   | 66  | Government |
| 2012 Jaswinder S. Sandhu     | UK       | prospective  | 12     | 16        | 12  | 0   | 0   | 16  | No funding |
| 2012 HSUN-MO WANG            | Taiwan   | retrospective| 79     | 60        | 49  | 0   | 60  | No funding |
| 2011 TOSHHISA MUROFUSHI      | Japan    | prospective  | 20     | 14        | 11  | 9   | 0   | 14  | No funding |
| 2011 TOSHHISA MUROFUSHI      | Japan    | prospective  | 20     | 14        | 9   | 11  | 0   | 14  | No funding |
| 2002 Yi-Ho Young             | Taiwan   | prospective  | 10     | 16        | 3   | 7   | 0   | 16  | No funding |
| 2007 V OSEI-LAH              | UK       | prospective  | 11     | 36        | 2   | 9   | 0   | 36  | Government |
| 2007 V OSEI-LAH              | UK       | prospective  | 9      | 36        | 5   | 4   | 0   | 36  | Government |
| 2007 V OSEI-LAH              | UK       | prospective  | 20     | 36        | 5   | 15  | 0   | 36  | Government |
| 2013 Min-Beom Kim            | Korea    | prospective  | 41     | 66        | 14  | 27  | 0   | 66  | No funding |
| 2013 Chuan-Yi Lin            | Taiwan   | prospective  | 30     | 32        | 31  | 19  | 0   | 32  | No funding |
| 2013 Chuan-Yi Lin            | Taiwan   | prospective  | 50     | 32        | 40  | 10  | 0   | 32  | No funding |
| 2006 CHUN-NAN CHEN           | Taiwan   | prospective  | 14     | 14        | 10  | 4   | 0   | 14  | Government |
| 2009 T Murofushi             | Japan    | prospective  | 11     | 16        | 5   | 6   | 0   | 16  | No funding |
| 2009 Chen-Han Chou           | Taiwan   | prospective  | 7      | 40        | 3   | 4   | 0   | 40  | Government |
| 2009 Chen-Han Chou           | Taiwan   | prospective  | 7      | 40        | 4   | 3   | 0   | 40  | Government |
| 2010 Naoya Egami             | Japan    | retrospective| 26     | 26        | 19  | 7   | 19  | 7   | Government |
| 2010 Naoya Egami             | Japan    | retrospective| 7      | 7         | 4   | 3   | 4   | 3   | Government |
| 2011 Chi-Hsuan Huang         | Taiwan   | prospective  | 20     | 20        | 13  | 7   | 8   | 12  | Government |
| 2011 Chi-Hsuan Huang         | Taiwan   | prospective  | 20     | 20        | 5   | 15  | 0   | 20  | Government |
| 2011 Chi-Hsuan Huang         | Taiwan   | prospective  | 20     | 20        | 9   | 11  | 3   | 17  | Government |
| 2011 Chi-Hsuan Huang         | Taiwan   | prospective  | 20     | 20        | 5   | 15  | 0   | 20  | Government |
| 2013 Naoya Egami             | Japan    | prospective  | 114    | 94        | 57  | 57  | 22  | 72  | Government |
| 2013 Naoya Egami             | Japan    | prospective  | 22     | 94        | 21  | 1   | 22  | 74  | Government |
| 2012 Mei-Chun Lin            | Taiwan   | prospective  | 20     | 20        | 14  | 6   | 11  | 9   | No funding |
| 2012 Mei-Chun Lin            | Taiwan   | prospective  | 20     | 20        | 9   | 11  | 6   | 14  | No funding |
| 2011 Rachael L. Taylor       | Australia| prospective  | 60     | 70        | 30  | 30  | 0   | 70  | Government |
| 2011 Rachael L. Taylor       | Australia| prospective  | 60     | 70        | 24  | 36  | 0   | 70  | Government |
| 2006 Timmer Ferdinand C A    | USA      | retrospective| 82     | 24        | 11  | 71  | 0   | 24  | Government |
Table 1. Characteristics of included eligible studies.

| Author                | Country   | Study design | Case N | Control N | TP | FN | FP | TN | Funding           |
|-----------------------|-----------|--------------|--------|-----------|----|----|----|----|-------------------|
| 2002 Yi-Ho Young      | Taiwan    | prospective  | 20     | 20        | 11 | 9  | 0  | 20 | Government        |
| 2009 Bernhard Baier   | Germany   | prospective  | 16     | 126       | 11 | 5  | 0  | 126 | No funding        |
| 2013 Young Joon Seo   | South Korea| prospective | 26     | 26        | 25 | 1  | 0  | 26 | No funding        |

Figure 2. Evaluation of the methodological quality of the included studies according to quality assessment diagnostic accuracy studies tool (QUADAS) criteria.

Figure 3. Forest plot of the sensitivity of included studies, summary sensitivity and I^2 statistic for heterogeneity.
positive likelihood ratio was 18.01 (95% CI: 9.45 to 34.29) and the pooled negative likelihood ratio was 0.54 (95% CI: 0.47 to 0.61). The area under the summary receiver operating characteristic curve was 0.78 and the pooled diagnostic odds ratio estimate for VEMP was 39.89 (95% CI: 20.13 to 79.03). The SROC graph with the 95% confidence region and with the 95% prediction region is shown in Fig. 5.

**Subgroup Analysis.** A subgroup analysis was conducted to identify potential sources of heterogeneity among the included studies (Caucasian patients vs. Asian patients, prospective design vs. retrospective design, healthy controls vs. patient controls, period between attacks vs. period during attacks, air conduction vs. bone conduction, o-VEMP vs. c-VEMP, comparison among different stages, tone burst vs. click, and funded projects vs. non-funded projects). As shown in Table 2, the sensitivity, specificity and diagnostic accuracy of VEMP test were higher in Caucasian patients, prospective studies, healthy controls, period during attacks, bone conduction, c-VEMP, stage II–IV, tone burst and funded projects, respectively, than in Asian patients, retrospective studies, patient controls, period between attacks, air conduction, o-VEMP, stage I, click and non-funded projects.

**Assessment of Publication Bias.** To evaluate potential publication bias among the included studies, Deeks’ funnel plot was obtained on the basis of the log diagnostic odd ratios (DOR) and sample size of individual studies. The funnel plot for VEMP is shown in Fig. 6.

**Discussion**

Accurately distinguishing between the affected and non-affected sides of EH is crucial for stage assessment, therapeutic planning, disease monitoring and treatment efficacy. In clinical practice, diagnosis of EH remains a great challenge and this is especially true when the auditory symptoms are independent of vestibular ones. Hence, it is of great significance to find a test battery that provides comprehensive assessment of clinical conditions. Conventional vestibular function test (including caloric test and rotation test) detects horizontal semicircular canal involvement while audiometry measures cochlear involvement. Different from these two techniques, VEMP tests access the involvement of saccule and utricule. Recently, VEMPs have emerged as a non-invasive approach for diagnosing EH due to MD or DEH\(^\text{10}\).

Since VEMPs are not affected by ipsilateral hearing impairment, some researchers believed that it might be valuable tool for diagnosing, staging and even predicting EH.
Our meta-analysis showed that the sensitivity of VEMPs test in EH patients was 49%. A previous study exhibited that VEMPs had moderate sensitivity and relatively higher specificity as compared with the conventional vestibular function test. Hence, VEMPs might serve as a useful diagnostic tool for EH. The diagnostic odds ratio (DOR) is an accurate measure, which integrates both sensitivity and specificity. A DOR of 1.0 shows that the test does not distinguish between patients and healthy individuals. In this meta-analysis, the DOR value was 39.89 (95% CI: 20.13 to 79.03), indicating that the accuracy was significant. Moreover, the area under the SROC curve reflects the overall performance of the test for assessing the trade-off between sensitivity and specificity.

Our subgroup analysis demonstrated that the sensitivity, specificity and diagnostic accuracy of VEMP test were higher in Caucasian patients, prospective studies, healthy controls, period during attacks, bone conduction, c-VEMP, stage II–IV, tone burst and funded projects, respectively, than in Asian patients, retrospective studies, patient controls, period between attacks, air conduction, o-VEMP, stage I, click and non-funded projects.

Manzari et al. measured cervical and ocular VEMPs in MD patients during an acute attack and between attacks. Their data illustrated that the signals of both cervical and ocular VEMPs were higher during the vertigo attack than between the attacks. c-VEMP and oVEMP can be applied for assessing the function of different otolith organs. Therefore, the patients with both utricular and saccular disorders tend to have abnormal c-VEMP and o-VEMP amplitudes. Furthermore, for patients with conductive hearing loss, despite presence of middle ear dysfunction, the bone-conducted stimuli are transmitted to the vestibular organs directly through the skull bones. VEMPs of tone burst stimuli are more sensitive and stable than those of click stimuli.

Then, we compared the VEMPs data of various MD stages and found that the diagnostic sensitivity increased with the progression of MD. However, this stage system for MD cannot be applied to DEH cases, since the latter represents as profound sensorineural hearing loss on the lesion ear. In this meta analysis, only one research with DEH stage information was included. With the conventional staging system, the status of MD is assessed only by the means of hearing measurement. In some cases of late stage MD, vestibular function is intact while with the progression of MD, the vestibular function and hearing level fluctuate. Some patients with minimal hearing loss may have sustained saccular hydrops. On the other hand, a patient with maximum hearing loss may have normal saccular function. Hence, clinically, Meniere's disease falls into two categories: typical MD and atypical one, in terms of cochlear and vestibular symptoms. Since the VEMPs test assesses saccular function, the VEMPs may not be correlated with ipsilateral audiometric thresholds. The status of the vestibular system can not be audiometrically determined. Therefore, VEMPs may act as a new staging tool in MD diagnosis. It is complementary to the conventional tests such as pure tone audiometry. However, VEMPs result should be interpreted in combination with other clinical features (recurrent episodes, degree of endolymphatic hydrops, timing
of detection, disease stages and treatment protocols). Furthermore, a test battery comprising detailed history taking, pure tone audiometry, caloric test, o-VEMP or c-VEMP and image examination may provide an overall assessment of patients’ status.

| Subgroup       | N | Sensitivity | Specificity | DOR  | AUC  |
|----------------|---|-------------|-------------|------|------|
| **Race**       |   |             |             |      |      |
| Caucasian      | 12| 0.43        | 0.99        | 57.25| 0.95 |
| Asian          | 18| 0.53        | 0.92        | 28.59| 0.69 |
| **Study design**|   |             |             |      |      |
| prospective    | 26| 0.52        | 0.95        | 50.54| 0.81 |
| retrospective  |  4| 0.36        | 0.94        | 10.62| 0.78 |
| **Control**    |   |             |             |      |      |
| health         | 20| 0.49        | 0.96        | 44.93| 0.82 |
| patients       | 10| 0.48        | 0.94        | 35.37| 0.78 |
| **Attacks**    |   |             |             |      |      |
| Yes            | 30| 0.49        | 0.95        | 38.44| 0.78 |
| No             |  2| 0.44        | 1.00        | 30.43| —    |
| **Methods**    |   |             |             |      |      |
| Air conduct    | 29| 0.48        | 0.95        | 36.48| 0.76 |
| Bone conduct   |  3| 0.54        | 1.00        | 59.46| 0.99 |
| o-VEMP         | 10| 0.48        | 0.96        | 20.96| 0.45 |
| c-VEMP         | 27| 0.49        | 0.95        | 39.36| 0.81 |
| Click          |  6| 0.45        | 0.95        | 22.18| 0.59 |
| Tone burst     | 23| 0.48        | 0.99        | 60.66| 0.97 |
| **Stage(c-VEMP)** | | | | | |
| I              |  4| 0.47        | 0.85        | 4.01 | 0.64 |
| II             |  5| 0.49        | 0.86        | 16.32| 0.65 |
| III            |  5| 0.46        | 0.86        | 11.15| 0.31 |
| IV             |  4| 0.54        | 0.85        | 12.13| 0.39 |
| **Funding**    |   |             |             |      |      |
| Government     | 13| 0.45        | 0.94        | 27.60| 0.77 |
| No             | 17| 0.52        | 0.97        | 53.63| 0.80 |

Table 2. Subgroup analysis for accuracy of VEMP for MD detection. DOR = Diagnostic Odds Ratio; AUC = the area under the summary receiver operating characteristic curve.

Figure 6. Publication bias was evaluated by Deek’s funnel plots.
This study had some limitations. First, the studies included had some heterogeneity. Second, so far, there has been no established gold standard for MD or DEH diagnosis yet. In this meta-analysis, we used clinical history and close follow-up instead as the reference standard. Third, the potential publication bias might exist and Deeks’ funnel plot was employed for evaluating publication bias based on DOR and sample sizes of selected studies. The publication bias among the included studies suggested that the diagnostic value of VEMP on MD identification might be over-estimated, since positive data were prone to being published. Forth, it should be emphasized that these findings were mainly based upon studies of small sample size, and thus further extrapolation should be cautious. Well-designed prospective studies with large patient’s cohorts are warranted to further evaluate the value of VEMP for identifying EH due to MD or DEH.

**Conclusion**

In conclusion, our present meta-analysis has demonstrated that VEMPs test alone is not sufficient for MD or DEH diagnosis, but that it might be an important component of a test battery for diagnosing MD or DEH. Moreover, VEMPs, due to its high specificity and non-invasive nature, might be used as a screening tool for endolymphatic hydrops.

**Methods**

**Search strategy and study selection.** PubMed and Embase were searched to identify eligible studies published before 2015. We used terms “vestibular evoked myogenic potential”, “Meniere’s Disease”, “Endolymphatic hydrops”, “Delayed Endolymphatic hydrops” and “vestibular hypofunction”. In addition, we also manually searched reference lists from related reviews and all retrieved articles. The language was restricted to English. Duplicate publications were removed.

**Selection criteria.** Studies included in this meta-analysis met the following criteria:

1. They were about the assessment of the diagnostic accuracy of vestibular evoked myogenic potentials in Meniere's disease, endolymphatic hydrops or delayed endolymphatic hydrops;
2. They were about the measurement of the sensitivity and specificity of vestibular evoked myogenic potentials.
3. They included detailed case history, follow-up observations and pure tone audiometry as the reference standard. All subjects were identified as either definite Meniere's disease according to the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) 1995 or delayed endolymphatic hydrops based on Schuknecht's definition.
4. They defined abnormal VEMPs (absent or decreased) as follows:
   - When the latencies of c-VEMP, each peak (p13, n23) and amplitude (p13 to n23) were measured, the interaural amplitude difference ratio was greater than the mean of normal range plus 2 × standard deviation (SD);
   - The peak-to-peak c-VEMP amplitude was absent or decreased;
   - c-VEMP threshold shifts exceeded the mean of normal range plus 2 × standard deviation (SD) (delayed response).
   - Biphasic waveform of o-VEMP was absent after at least 50 responses;
   - o-VEMP asymmetry ratio > 40%.

Studies were excluded if:

1. They were reviews, editorial comments, case reports or letters;
2. They did not provide sufficient data;
3. They were animal studies.

**Data extraction.** Two reviewers independently reviewed the eligible studies and extracted the relevant data, including first author, publication year, country of origin, race, study design, gender, mean age, clinical profiles, sample size, measurement protocol, and funding source. Moreover, they recorded the number of true-positive, false-positive, true-negative, and false-negative data for each study. Discrepancies, if any, were resolved by mutual discussion or the judgement of a third reviewer.

**Quality Assessment.** The quality assessment of diagnostic accuracy studies (QUADAS) tool was used for quality evaluation. The QUADAS tool included 14 items, each being judged by yes, no, or unclear.

**Data analysis.** If heterogeneity existed, a random-effects model was performed to examine the summary sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio (DOR).
Furthermore, the summary receiver operating characteristic (sROC) curve summarized each pair of sensitivity and specificity into a single measure of accuracy and the diagnostic odds ratio. sROC curve were delineated and the area of SROC (AUC) was calculated to evaluate the diagnostic accuracy and consistency of VEMPs in the context of a meta-analysis15–17. We delineated and the area of SROC (AUC) was calculated to evaluate the diagnostic accuracy and sensitivity and specificity into a single measure of accuracy and the diagnostic odds ratio. SROC curve (Stata Corp, College Station, Texas) and Meta-Disc, Version 1.4 (Unit of Clinical Biostatics, the Ramón y Cajal Hospital, Madrid, Spain).

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**Author Contributions**

W.K. conceived and designed the work; S.Z. conducted the experiment; H.S. and M.L. analyzed data; S.Z. drafted the paper; W.K. and Y.L. revised the paper; B.L. prepared the figures. All authors reviewed and approved the manuscript.

**Additional Information**

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