Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Turk Arch Otorhinolaryngol 2016; 54: 124-30

Validity and Reliability of the Diagnostic Tests for Ménière's Disease

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Review

Abstract

Ménière's disease is defined as an idiopathic syndrome characterized by endolymphatic hydrops. Various tests and measurement methods have been employed for the diagnosis of Ménière's disease. These include audiological, vestibular, radiological, clinical, and biochemical tests. However, the lack of a definitive or gold standard diagnostic test sometimes complicates the process of diagnosis. Hence, the clinician should be well-experienced in deciding when to perform a test and how to interpret the results of the test. Furthermore, having the knowledge of the validity and reliability of these tests plays a critical role. This review particularly emphasizes on remarking the validity and reliability of each test performed for the diagnosis of Ménière's disease and discussing the results according to the up-to-date literature.

Keywords: Ménière's disease, diagnostic tests, diagnosis, reliability and validity

Introduction

The success of a clinical test is expressed by the reliability and validity of that test. The reliability of a test refers to the consistency of the test (stability of measurement values) and the presence of a common consensus. The most frequently used methods for the evaluation of reliability include the investigation of whether new results obtained from repeated successful measurements compatible with previous measurements and the observation of consistency among the results obtained by different researchers using the same diagnostic tools (1).

The validity indicates whether a test measures what it intends to measure, if the measurements are accurate and how to interpret the results of these measurements. Validity is measured by sensitivity and specificity. Sensitivity refers to the possibility of a positive test result when a disease exists. i.e., the percentage of sick people who are correctly identified as having the condition. Specificity indicates the probability of being test negative when disease is absent and identifies only sick people (1, 2).

Ménière's disease (MD) is not a rare condition, but it is difficult to differentiate it from other diseases of the inner ear. Because of the occurrence of non-specific symptoms in the early stages of MD and the absence of MD-specific tests, Establishing the diagnosis of MD is difficult and usually delayed. Moreover, the fluctuating course of MD complicates the interpretation of the diagnostic tests. Therefore, diagnosing MD has always been confusing and the diagnosis is generally established clinically. Patients with hearing loss and balance disorders are commonly diagnosed of MD, a misdiagnosis, due to the lack of sensitive and specific diagnostic tests. (3, 4).

Clinical and Research Effects

In this review, the reliability and validity of diagnostic tests used for the diagnosis of MD were evaluated and each test was discussed separately.

1. Medical History of the Patient: The most common and effective diagnostic test is a well-taken medical history. Recurrent episodes of vertigo that continues for minutes or hours (often 2-3 h) (96.2%), tinnitus (91.1%), and hearing loss in the affected ear (87.7%) are the most frequent symptoms of MD (5). The attacks of vertigo generally follow aural fullness, increased tinnitus, and de-

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Received Date: 05.05.2016
Accepted Date: 22.06.2016
Available Online Date: 15.08.2016

DOI: 10.5152/tao.2016.1697

creased hearing. For the results obtained from various treatment methods to be more reliable and comparable with each other, it was necessary to establish diagnostic criteria and to stage the disease. Therefore, the American Academy of Otolaryngology Head and Neck Surgery Committee on Hearing and Equilibrium Guidelines (AAO HNS CHE), which was last revised in 1995, is used at present (4). In these guidelines, the clinical diagnosis of MD is divided into four groups: possible MD, probable MD, definite MD, and certain MD. The AAO HNS CHE criteria are used in 80% of the current publications on MD, but the actual diagnostic utility of these criteria has been reported to be approximately 50%. The main limitation in these guidelines is that either the diagnosis of MD or the success of any treatment method can be evaluated only according to the patient's subjective definitions. This situation necessitates the clinician to differentiate the real attacks of vertigo from other imbalance symptoms, and confirm the accurate number of attacks while taking the patient's medical history. The second limitation of the medical history is the confounding effect of the counter ear's symptoms. Because bilateral disease can occur with the involvement of the opposite ear in 50% of patients in the advanced disease, it is generally impossible to understand which ear causes the complaints that develop after a long remission period by only considering the patient's medical history (6).

There are also some notable inconsistencies between the original diagnostic criteria defined by Prosper Ménière and the AAO HNS CHE criteria. All cases exactly meeting the original criteria also meet the AAO HNS CHE criteria. However, it has been reported that when the AAO HNS CHE guidelines are used for diagnosis, the number of patients diagnosed with MD is three times higher than that with the original criteria. Therefore, the diagnostic criteria of Prosper Ménière seems more specific (but less sensitive) and the AAO HNS CHE guidelines is more sensitive (but less specific) (7).

Another diagnostic method based on medical history, is the Gibson scoring system (6, 8). In this scoring system, which evaluates the symptoms of vertigo with the feeling of rotation of the surrounding environment, hearing loss, tinnitus, and aural fullness, a score of 7 and above is required for the diagnosis of MD, whereas a score below 3 excludes MD. In a study combining the Gibson score with the AAO HNS CHE criteria, the diagnostic reliability was raised to a rate of 80%. It was stated that patients without MD could be better identified with the Gibson system, and patients with MD could be better identified with the AAO HNS CHE criteria. According to the results of this study, the AAO HNS CHE criteria are more sensitive, but the Gibson scoring system is more specific (6).

2. Pure Tone Audiometry: Pure tone audiometry is the basic test used in the process of diagnosis and follow-up. It also plays a determining role in disease staging and treatment decisions. Progressive and sensorineural hearing loss that affects low frequencies and displays fluctuation is typically observed in MD. Besides that, different audiometric patterns can be encountered and variations in hearing loss can be seen in association with the stage of the disease. Although low frequencies are generally affected to a greater extent, hearing loss influences all frequencies in the advanced disease, which causes a flat audiogram (9, 10). The diagnosis of MD cannot be established according to the configuration of the audiogram since there is not a specific pathognomonic audiometric pattern (11). In accordance with the AAO HNS CHE guidelines, the mean pure tone air conduction hearing threshold at the frequencies of 0.5, 1.2, and 3 kHz refers the stage of hearing level (8).

Considering diagnostic specificity, it was revealed that 125 kHz and 8 kHz pure tone hearing thresholds could determine 98% of patients without MD and 94% of patients with MD (12). A shift of 10 dB or more in pure tone thresholds is accepted as the fluctuation in MD. With regard to its prognostic value, the presence of fluctuation in the previous attack increases the possibility and severity of the fluctuation in the next one. But no relationship was found between the occurrence of fluctuation and the severity or progress of the hearing loss (10). Rather than low-frequency (125-500 Hz), moderate-frequency (500-2000 Hz) and high-frequency (2000-8000 Hz) hearing loss in the initiation worsen the prognosis of hearing more (13).

3. Speech Audiometry: As a result of hearing deterrioration, the speech discrimination score and speech reception threshold are also impaired in MD. The mean speech discrimination score is 53% or lower in long-term disease (14). It was mentioned that the "roll over" phenomenon was more effective in unilateral MD cases; therefore, the speech discrimination score was found to be worse than the estimated level according to pure tone hearing thresholds (15). However, data obtained from more recent studies have shown that speech discrimination scores and speech reception thresholds of patients whose pure tone hearing thresholds are 40 dB or above are worse compared to MD patients that hear better, but not apparently different from those of non-MD patients having the same hearing thresholds (16).

4. Acoustic Admittance Measurements: Acoustic reflex threshold decreases in cochlear pathologies due to recruitment. In the Metz test based on this principle, the detection of the difference between 0.5,1, and 2 kHz acoustic reflex thresholds and pure tone airway thresholds of 60 dB or below is an objective datum indicating the presence of cochlear pathology. In terms of diagnosis, otoacoustic immittance measurements can also be helpful. In fact, basal otoacoustic immittance values are higher in fluctuating MD cases than non-fluctuating MD cases (or the control group). This difference derives from the diversity of underlying physiopathological mechanisms. With regard to the prediction of reversible and irreversible endolymphatic hydrops (EH), acoustic immittance measurements were shown to have higher sensitivity than conventional audiometric tests (17).

Although the tympanometry configuration is type A in most cases, patients with severe hearing loss in long-term MD usually experience the Eustachian tube dysfunction. Based on patients having benefited from ventilation tube application in treatment, it was hypothesized that EH in MD could be associated with

Eustachian tube dysfunction, and it was claimed that sonotubometry was more sensitive than tympanometry (18).

5. Multi-frequency Tympanometry: It has been demonstrated that the resonance frequency (RF) of MD patients apparently increases during an attack (or just before the attack), decreases in the inter-attack period, and returns to normal values after glycerol intake. Therefore, it is thought that variations in RF may reflect the pressure fluctuations in the inner ear. Multi-frequency tympanometry (MFT), which enables the impedance of the conduction system of the middle ear to be measured in a wide frequency range from 0.2 to 2 kHz, can also be employed for the diagnosis of MD and EH. Using MFT, a conductance range of 2 kHz at a 235 daPa threshold was found to be wider in patients with symptomatic MD compared to control, with a diagnostic sensitivity and specificity 53.6% and 95%, respectively (19). Recent studies show a relationship between the results obtained from MFT and MD, but they reveal that the results are not sufficient for diagnostic accuracy (19). The sensitivity and specificity of MFT in the diagnosis of EH is at a moderate level, which is similar to those of electrocochleography (ECoG) and vestibular-evoked myogenic potential (VEMP) tests. However, it can be considered as a complementary test in the diagnosis of EH based on its rapid and non-invasive nature (20).

6. Otoacoustic Emissions: Otoacoustic emission (OAE) measurement tests (especially distortion product) are more sensitive than pure tone audiometry; therefore, the use of OAE is recommended, particularly during the glycerol test. It was reported that delayed evoked and distortion product OAE amplitudes were lower in the non-affected ears of MD patients than in the healthy control subjects (21). Offering a reliable evaluation on the functional condition of the inner ear, OAE has a validity of 50% in the diagnosis of EH, and is not sufficiently sensitive and specific for MD (22).

7. Brainstem Auditory-Evoked Potentials: The most important objective audiological test routinely used for the differentiation of cochlear pathologies from retrocochlear ones is auditory brainstem response (ABR). Prolonged latency, decreased amplitude or complete disappearance of the wave I, prolonged latencies between waves, or impaired wave morphology are the typical findings observed in cochlear pathologies, but they are valuable for MD only in the differential diagnosis of retrocochlear pathologies (23). For the diagnoses of EH and MD, an ABR technique called "cochlear hydrops analysis masking procedure" (CHAMP) has been introduced (24). The CHAMP test is the measurement of the difference between the wave V latency obtained with a single-click stimulus and the wave V latency obtained in the presence of a masking noise at 0.5 kHz frequency in addition to a click stimulus. In healthy individuals, masking noise prevents the formation of wave V or prolongs wave latency significantly, but in the presence of EH, no difference is observed between wave V latencies obtained in both ways. In the first studies that determined the cut-off value of the delay in the wave V latency to be 0.3 ms, it was stated that healthy controls could be differentiated from MD cases with 100% sensitivity and 100% specificity. Another parameter of this test, in addition to wave V latency, is the complex amplitude ratio (CAR). An abnormal CAR value (CAR value below 0.95) has been suggested to have 95% specificity and 90% sensitivity (24, 25). It is claimed that the CHAMP test can demonstrate not only the presence of active MD but also the progress of the disease in treatment and follow-up periods. For instance, it was proposed that the CHAMP test could be guiding for prognosis in patients with low-frequency hearing loss not accompanied by vertigo (cochlear MD or acute low tone sensorineural hearing loss). The incidence of fluctuant hearing loss and vertigo increased in these patients if the CAR value is 0.975 or below (26). On the other hand, the use of the CHAMP test was reported to be invalid and unreliable in later studies where the sensitivity and specificity were calculated to be 31% and 28%, respectively (27). In conclusion, the CHAMP test presents low sensitivity for the demonstration of EH in MD.

8. ECoG: ECoG is the most valuable electrophysiological diagnostic test that is for EH. It shows cochlear bioelectrical activity that occurs by auditory stimulation of hairy cells. The best recording is obtained with needle electrodes placed on the promontorium through the tympanic membrane (transtympanic) (29). ECoG can also be performed by placing the electrode on the tympanic membrane or in the external auditory canal. Four parameters are recorded and measured in ECoG. These are cochlear microphonics, summating potential (SP), compound action potential (AP) (which occurs with synchronous firing of auditory fibers and shows the activity of the distal afferent fibers of the nerve VIII), and the ratio of these values to each other (SP/AP) (6).

The EH findings in EcoG are an increased ratio of SP/AP (above 0.4), an enlarged SPwave (above 3 ms), and prolonged AP latency (above 0.2 ms) (29). The cut-off value of a normal SP/AP amplitude ratio is 0.50 for the canal electrode, 0.40 for the tympanic membrane electrode, 0.30 for the transtympanic electrode, and 0.34 for the extratympanic electrode (30, 31). The sensitivity and specificity of transtympanic ECoG is higher than those of extratympanic ECoG (32). There are some conditions that negatively affect ECoG measurements, whose sensitivity increases up to 90% in the diagnosis of MD. For instance, if the patient has severe hearing loss, it can be difficult to observe the waves (33). If the patient is not in an acute attack stage, the sensitivity decreases to 60% (34). Because ECoG has low sensitivity in patients with insignificant symptoms, it can lead to some problems in the diagnosis of possible or probable MD (33). Moreover, ECoG is affected by the stage and duration of the disease. While an increased SP/AP ratio is found in 71% of patients in stage 1, it is seen in 82% in stage 2, 85% in stage 3, and 90% in stage 4. While the increased SP/AP ratio is observed in 43% of patients having MD for a time shorter than one year, the rate of this increase is up to 100% in patients having this disease for more than 30 years (29).

To improve the diagnostic sensitivity of the ECoG test, additional parameters are submitted. The SP/AP curve area ratio,

one of these parameters, has a higher sensitivity, particularly in early-stage MD (34). In another parameter, stimulus biasing ratio carries the sensitivity of ECoG up to 85% (35). Combining with another parameter called the graphic angle measurement raises the sensitivity of ECoG to 89% (33).

ECoG may not correlate with the stage of disease, duration of symptoms, patient history, and audiometric findings all the time (6, 36-38). Moreover, even if vertigo attacks disappear completely after treatment, the SP/AP ratio does not recover (38). Besides that, ECoG is an informative test, in prediction of when the disease will be bilateral, decision of treatment choices, or renewal of the treatment method (6, 36, 37). The sensitivity of the ECoG test in the diagnosis of MD variants, vestibular MD (recurrent vestibulopathy) and cochlear MD (acute low tone sensorineural hearing loss), were reported to be 62.5% and 67%, respectively (39).

9. Dehydration Tests: Glycerol test is one of the most common dehydration tests with the highest validity. Following oral intake of glycerol immediately after recording a basal audiogram, second and third audiometric measurements are performed in the 90th minute and 3rd hour. A gain of 10 dB or above in the pure tone hearing thresholds or an increase of 10% or above in the speech discrimination score at two or more frequencies, means a positive test result. The positive test result is diagnostic for EH, and it represents decreased inner ear impedance (40). This test can also be performed by administering other dehydrating agents such as furosemide or urea. The use of glycerol has decreased because of its taste (40).

The sensitivity of dehydration tests is approximately 66%, which is similar to ECoG in this respect (55%). While the sensitivity of the glycerol test is higher at the beginning of symptoms (83.3%), it is lower in the remission inter-attack period (43.1%) (42). Therefore, it is more appropriate to exert this test at an early stage (when fluctuation exists). A positive dehydration test result is an evidence of fluctuating hearing. It denotes that the disease is just in the early stage, and endolymphatic sac surgery works better in these patients. The combination of ECoG and dehydration tests enhance the diagnostic sensitivity in EH, the prognosis of MD variants, and whether they transform into a classical form. Moreover, the reliability of the diagnosis of EH in the contralateral asymptomatic ear also improves by combining these two tests (43, 44).

10. Electronystagmography (ENG): In MD, spontaneous nystagmus is seen in the ipsilateral ear just before vertigo and in the contralateral ear when an attack starts. The most common finding is decreased vestibular response of the affected ear due to EH. The sensitivity of ENG in the diagnosis of MD is approximetely 50% (45).

11. Caloric Test and Head Impulse Test (HIT)/Video HIT: Caloric responses occur due to low-frequency vestibular stimuli, and responses in HIT develop due to high-frequency vestibular stimuli. Because peripheral vestibular dysfunction mostly affects low frequencies in MD, caloric responses deteriorate more than the responses in HIT (46). In caloric tests, directional preponderance in the onset and then canal paresis in the advanced stage are generally observed. However, different results can be obtained from the measurements performed at different times in the same patient (47). In general, while caloric responses report unilateral vestibular hypofunction only in 50 to 67% of cases (46), no caloric response can be encountered in 6 to 11% of patients (14). This is because of the cupula movement, which is limited due to horizontal semicircular canal hydrops in the advanced stage of the disease (48).

HIT is a test that does not change with the stage of the disease but is less sensitive than the caloric test. Compared to the head impulse test (Halmagyi test), in which the clinician directly assesses the vestibule ocular reflex (VOR), the sensitivity of video HIT is higher because covert saccades can be detected and vestibular dysfunction in the affected ear can be documented (49). However, if it is not an acute attack, a clear pathology cannot be seen even through video HIT. While abnormal HIT findings are noticed in only 40% of patients who have abnormal findings in caloric tests, the rate of abnormal HIT findings is 10% in ears with normal caloric responses (46). HIT and video HIT are more specific but less sensitive than caloric tests, but they can provide quite useful information (46, 49). In advanced-stage MD cases, even if caloric responses disappear, high-frequency VOR functions can be protected substantially. To confirm the efficiency of vestibular ablation after intratympanic gentamicin therapy, HIT and video HIT tests are recommended rather than caloric tests (46).

12. VEMP: VEMP is an objective test that measures dynamic otolith functions. Cervical VEMP (cVEMP) gives data about the saccule, and ocular VEMP (oVEMP) gives data about the utricle (48). Because EH is known to involve mostly the cochlea, and then saccule, utricle, and semicircular canals, seriatim VEMP results are considered to correlate with the stage of the disease (48, 50). If the VEMP test is applied within the first 24 h following a Ménière attack, abnormal findings are present in 67% of patients (51). As a result of the saccular membrane rupture due to the saccular hydrops, the amplitudes of cVEMP can reduce and finally disappear. However, increased pressure due to hydrops does not allow a reduction in pressure in the utricle because of the unidirectional nature of the utriculo-endolymphatic valve (Bast's valve).Therefore, a compensatory increase occurs in oVEMP values (50, 51). On the other hand, in cases passing over 48 h, test results return to normal in half of the patients with abnormal findings at the beginning (51). Hence, the oVEMP test can point out a recent Ménière attack. Increased oVEMP and abnormal cVEMP amplitudes are signs of early-stage disease (50).

Another alteration in VEMP occurs in response frequency. Normally, high-amplitude responses are received at 500 Hz and 1000 Hz in the VEMP test. However, the high-amplitude responses in MD are recorded at higher frequencies (altered tuning) (52). In probable MD, this frequency deviation is less

prominent and it is seen only at 1000 Hz. The altered tuning in cVEMP, which is observed in one-third of asymptomatic MD cases is a promising test for silent EH cases. On the other hand, altered tuning in oVEMP comprises a wider frequency spectrum than cVEMP, and this alteration is apparent, particularly at frequencies between 750 and 2000 Hz (53).

The sensitivity and specificity of VEMP in MD is similar to those in caloric tests but lower than those of ECoG. However, because it gives more detailed data and helps mapping the topographic involvement of EH, it contributes a lot to the diagnosis of MD (48, 50-53).

13. Temporal High-Resolution Computed Tomography: According to the results of high-resolution computed tomography (HRCT) in MD cases, usually the vestibular aqueduct cannot be visualized and periaqueductal pneumatization is disappeared. However, the sensitivity of these findings is quite low (27.8%) (54).

14. Magnetic Resonance Imaging with Gadolinium: In MD, hypoplasia in the endolymphatic sac / endolympatic ductus complex, or the loss of radiological visibility of this complex, is pathognomonic. Its sensitivity is higher than the findings obtained through HRCT (60.9%) (54). The presence of EH can be demonstrated in vivo with suppressed or disappeared signal intensity of the perilymphatic space in the Three-Dimensional Fluid Attenuated Inversion Recovery (3D FLAIR) sequences obtained from 3-Tesla MR that is performed 24 hours after intratympanic gadolinium injection. After intratympanic injection of gadolinium, Gd first reaches to the vestibule, passes through the basal turn of the cochlea, travels the semicircular canals, and finally arrives at the apical region of the cochlea (54, 55). In patients with EH, perilymphatic space surrounding the endolymph is collapsed and sometimes invisible due to enlarged endolymphatic space. That's why the contrast agent passing from the tympanic cavity to the perilymph cannot enhance the perilymphatic space as high as the contralateral ear. This method is more sensitive than conventional MRI for EH in the cochlea or in the vestibule because it allows performing quantitative analysis and an objective comparison with the contralateral ear. It is believed that both intratympanic and intravenous application of gadolinium have similar diagnostic utility in viewing EH (55).

It was reported that the degree and location of hydrops that is demonstrated radiologically was compatible with the severity of hearing loss and vestibular dysfunction (56), and MRI findings were correlated with patient's history (audiological and vestibular symptoms), ECoG, and VEMP (57). While the sensitivity of 3T MRI in the diagnosis of MD, performed after intratympanic gadolinium injection, was found to be 95%, the sensitivity of other diagnostic tests was 55% for the glycerol test, 60% for ECoG, and 75% for the combination of ECoG and glycerol tests (57).

15. Blood Tests and Autoimmunity: There is no specific blood test to MD. Congenital or acquired syphilis can sometimes mimic as MD. Therefore, serological control must be done in the case of clinical suspicion (9). Besides that, because autoimmune diseases such as rheumatoid arthritis, ankylosing spondylitis, and systemic lupus erythematosus increase the incidence of MD 3-8 times, autoimmune markers must be analyzed. Moreover, in some patients with MD, many autoantibodies have been found, mostly against HSP 70, HSP 68, myeloperoxidase, and thyroperoxidase. However, a specific and sufficiently sensitive biomarker for MD has not been identified yet (58).

16. Other Tests: In the literature the use of some uncommon techniques including vestibular autorotation test, video-oculography, and traveling wave velocity measurement have also been recommended for the diagnosis of MD. However, because these tests are not used routinely, there is no general consensus on their diagnostic validity and reliability (59).

Conclusion

In spite of many improvements in the techniques used for the diagnosis of MD, there are still some limitations that decrease the validity of diagnostic tests. No specific diagnostic test is available yet and it is impossible to calculate the exact reliability values of routinely used clinical tests. In addition, these tests contribute a few to the decision of the treatment choice because post-treatment results of these tests usually do not ameliorate and do not reflect the clinical relief of a successfully treated symptom-free patient. Nevertheless, especially before ablative surgeries, each patient must be evaluated with an audiological and vestibular diagnostic test battery for revealing residual cochlear and vestibular functions of the affected and contralateral ears.

Among the diagnostic tests, the medical history of the patient takes an important place because the diagnosis of MD is actually a clinical diagnosis apart from audiometric measurements. For this reason, it is very important that the patient must explain his/her history clearly and accurately, and the clinician must be skillful in taking the history. A patient's medical history, although it is subjective, is essential not only in the stage of diagnosis, but also in the follow-up period and the decision of treatment response. The definition and recording of vertigo attacks are highly critical at this point. It should be kept in mind that only one third of patients fully have the diagnostic criteria for MD at admission, and medical histories of patients should be taken carefully and meticulously. Because the contralateral ear is affected in 50% of bilateral MD patients within the first two years, questioning the patient on the symptoms of the contralateral ear while taking the history is important. In the audiovestibular test battery, the test having the highest diagnostic validity and reliability is ECoG (after medical history of the patient). ECoG is highly beneficial in the diagnosis of MD, particularly in the case of insignificant symptoms. However, attention should be paid such that the findings obtained from this test must be supported with the patient's history, symptoms, and audiometric examinations.

In conclusion, audiological, vestibular, and electrophysiological tests are recommended for routine use together as a test battery for

the diagnosis and follow-up of MD. It is anticipated that, in time, with the help of technological improvements, research on diagnostic tools will increase the validity and reliability of these tests.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - E.A.G., A.Ç., B.M.; Design - E.A.G., A.Ç., B.M.; Supervision - E.A.G., A.Ç., B.M.; Resource - E.A.G., A.Ç., B.M.; Materials - E.A.G., A.Ç., B.M.; Data Collection and/or Processing - E.A.G., A.Ç., B.M.; Analysis and/or Interpretation - E.A.G., A.Ç., B.M.; Literature Search - E.A.G., A.Ç., B.M.; Writing - E.A.G., A.Ç., B.M.; Critical Reviews - E.A.G., A.Ç., B.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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