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Review Article

Advances in Eustachian tube function testing

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Abstract Obstructive and patulous Eustachian tube dysfunction provide a significant diagnostic and management challenge. The development of new treatments such as balloon Eustachian tuboplasty has generated renewed interest in measuring Eustachian tube function, as a method of selecting appropriate patients for intervention, and measuring their treatment outcomes.

This review summarises recent findings relating to Eustachian tube function assessment. Increasingly it is recognised that patient reported outcome measures based on symptoms are highly non-specific and non-diagnostic, and clinical assessment alone may not permit the selection of individuals with abnormal Eustachian tube opening. Tests of Eustachian tube opening therefore may represent a practical and objective addition to patient assessment in clinic, allowing the identification of individuals with abnormal (patulous or obstructive) Eustachian tube function. A diagnostic pathway is described on this basis.

More work is required to validate the described Eustachian tube function tests, and there remain individuals, such as those with dysfunction limited to pressure challenges, in whom function tests have yet to fully characterise the disorder.

Introduction

When considering how best to measure Eustachian tube (ET) function, the three primary functions of the ET should be considered: (1) gas transfer and pressure equalisation between the nasopharynx and middle ear (ME); (2) clearance of secretions from the ME through both muscular action and mucociliary transport; and (3) prevention of sound, pathogen and fluid reflux from the nasopharynx.[1,2] The ET is normally closed in a healthy individual, though clearance of some secretions via mucociliary transport still takes

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place in this state.[3] Gas transfer along the ET usually occurs when the cartilaginous portion of the ET opens every 1–2 min with swallowing, yawning or other movements,[4–7] although not all swallows generate an opening.[8,9]

The most important function of the ET is maintenance of an ambient ME air pressure, to facilitate efficient sound transmission to the inner ear, and to maintain mucosal and tympanic membrane (TM) health.[10] ET opening acts as a regulatory valve to maintain semi-stable physiological ME pressure, counteracting the effects of gas absorption by diffusion, and environmental pressure changes.[10]

It is the opening of the ET that forms that basis of the majority of tests of ET function. Active opening of the ET due to paratubal muscle contraction typically lasts 300–600 ms.[6,11,12] Most active opening is involuntary and triggered by a need to swallow, however opening may also be stimulated by an increased pressure differential between baroreceptor or mechanoreceptors in the TM, ME and nasopharyngeal mucosa.[13–15] Passive distension occurs if the nasopharyngeal or ME pressure exceeds the peri-luminal pressures that hold the lumen closed,[10,16] due either to ambient pressure change[17] or patient-generated pressures, such as during a Valsalva (forcibly exhaling with the nose and mouth occluded).[18]

Assessment of Eustachian Tube Function

Clinical assessment

Most clinicians currently rely on the clinical history, patient-reported symptoms, and a basic examination when assessing adult patients suspected of suffering from Eustachian tube dysfunction (ETD).[19] ETD is often described as a syndrome with a constellation of symptoms and signs suggestive of abnormal function of the ET,[19] occurring due to either abnormally prolonged or reduced opening of the ET. The clinical presentation is varied, and many symptoms associated with the disorder are non-specific, such as a blocked ear, hearing loss or tinnitus.[2] In addition, some patients with ETD may not experience symptoms, and there is difficulty distinguishing patulous from obstructive ETD on the basis of history alone, as patients with both disorders experience sensations of aural fullness, blockage or pressure.[20,21]

Given the inability to diagnose ETD reliably based on symptoms alone, there is clearly a role for more objective and direct measures of ET function. Measures of ET function are also required as objective outcome measures for research into treatments forETD. Studies relating to balloon Eustachian tuboplasty (BET) represent a significant proportion of the work published in the last decade to investigate the efficacy of treatments for obstructive ETD, and highlight the current lack of consensus regarding ET function tests. An analysis by the authors of 31 BET studies published prior to August 2018 found 27 different subjective and objective outcome measures had been adopted, excluding variation in the way that symptoms and otoscopy were interpreted. This illustrates the fact that there is currently no widely accepted means by which to assess ET function. The following provides a summary of tests of ET function and new developments within the field.

Patient-reported outcome measures

Patient-reported outcome measures (PROMs) are questionnaire-based tools intended to measure patient-centered outcomes such as symptoms and quality-of-life. If well designed, they are repeatable and quantitative, providing advantages over clinical history-taking. Disease-specific PROMs are particularly useful where a gold standard objective test does not exist,[22] and two have been developed for ETD; the ETDQ-7 and the CETDA. In theory PROMs could be used as a proxy marker of ET function.

The 7-Item ETD Questionnaire (ETDQ-7) has undergone initial validation trials with translation into several languages[23–27] and has gained use as an outcome measure in both clinical and research use. The 10-item Cambridge ETD Assessment (CETDA) was developed and validated more recently.[28] However, both have been found unable to discriminate between patients with obstructive and patulous ETD.[26,28] In addition, when the PROMS were tested in a clinically-relevant mixed population including patients with ETD, hearing loss and Menieres, the ETDQ-7 and CETDA were found to have very poor specificity (33% for both).[28] It appears that through the use of healthy volunteer controls and those with unrelated pathology, earlier assessments of the ETDQ-7 greatly over-estimated its accuracy as a diagnostic tool.

On the basis of clinical trials for BET, the ETDQ-7 appears responsive to changes in ET symptoms, and despite not being useful in making a diagnosis of ETD, both PROMs probably retain an important role in quantifying the presence and severity of ETD-related symptoms, making them of value for assessing change in symptoms of ETD after an intervention.

Other scores such as the 5- and 7-item Eustachian Tube Scores (ETS and ETS-7) combine patient-reported symptoms with the results of more objective measures (including tubomanometry) on a simple scale,[29] although validation and clinical use have been limited.

Indirect measures of ET function

Tympanometry remains the only widely-used objective measure of ET function, albeit acting as an indirect assessment based on a measurement of ME pressure, often at a single point in time. Tympanometry is simple to perform and is repeatable, with a ME pressure below −50daPa highly suggestive of obstructive ETD, and correlating with other more complex ET opening tests.[30] However, tympanometry is limited to use in patients with an intact tympanic membrane and aerated ME, and a measured normal ME pressure does not exclude obstructive or patulous ETD.

Tests of ET opening

Obstructive ETD is the most common presentation of the disorder, due to absent or reduced ET opening, and numerous tests have been devised to assess for it. Most tests of ET opening are based on the transmission of air along the ET with a resultant pressure change in the external auditory canal or ME. A previous review

summarises these tests,[31] some of which measure active ET opening (e.g. with swallowing), while others detect passive ET opening. The simplest tests involve asking the patient to perform a Valsalva or Toynbee manoeuvre, with a ME pressure change due to ET opening detected either by monitoring tympanic membrane movement or asking the patient to subjectively report aural pressure change. Tympanic membrane movements may also be detected via a transmitted change in external auditory canal pressure (known as the TTAG test) or tympanic impedance assessment. The nine-step-test uses repeated tympanometry measures in an assessment of ME pressure equalisation, using a protocol that in part replicates ascent and descent in an aeroplane.

Tubomanometry is a development of TTAG whereby an artificial, metered pressure is generated in the nose in response to swallowing, to produce a mixed active and passiveET opening. As well as detecting those ears where the ET does not open, ET opening can be characterised as early or delayed, with delayed opening reported to indicate obstructive ETD.[32] The tuboimpedance test has also been described as a modification of tubomanometry, whereby ME pressure changes are detected with a tympanic impedance probe.[33]

In those patients with a tympanic membrane perforation or ventilation tube *in situ*, alternativeET opening tests are required, such as the inflation-deflation and forced response tests, the latter of which has been useful in a research setting to measure ET passive opening,[18] but has had less of a role in clinical practice.

ET opening may also be detected using a sound stimulus transmitted from the nose to the ear, via the momentarily patent ET, a test known as sonotubometry. Peaks in the transmitted sound that are synchronous with swallowing are interpreted as ET opening, assessed in terms of amplitude[34,35] or shape.[36] Although usually performed at atmospheric pressure, the nasopharyngeal pressure may be varied,[37] or the procedure performed in a pressure chamber.[38] If performed at atmospheric pressure, sonotubometry is one of the only tests to be able to detect ET opening under physiological pressure conditions in the nasopharynx and ME.

Endoscopy has been described as an assessment tool for ET function, to confirm both ET patency[39,40] and opening,[41–43] with correlation shown with other tests of ET opening.[44,45] It remains largely subjective and highly dependent on operator experience.

Tests of ET closure

To protect the ME from sound, pharyngeal pathogens and changes in nasopharyngeal air pressure, the ET must act as a valve with a passive closed state. Failure of this state results in patulous ETD. As with obstructive ETD, the diagnosis of patulous ETD is largely subjective, with emphasis placed on the clinical history.[20,46] However, there is a distinct subset of tests that assess adequate ET closure, and are therefore specific for patulous ETD. Tests for patulous ETD are more established in clinical practice, although often overlooked beyond more obvious cases featuring autophony, leading to a risk of mis-diagnosis, for example as superior semi-circular canal dehiscence syndrome, or obstructive ETD.

Breathing-synchronous TM movement is considered a specific sign of patulous ETD that may be detected by visual monitoring of the TM,[20] or through the use of continuous (also known as long time-base) impedance recording,[47] TTAG,[48] or sonotubometry. For those patients in whom the ET is not permanently patulous, tubomanometry[32,49] or sonotubometry[35,50] using specific protocols have shown promise in defining the severity of patulous ETD. However, detection of an intermittently patulous ET, or an ET with low acoustic impedance remains difficult, as discussed in the partner review of patulous ETD [*cross reference*].

Correlation between different measures of ET function

A recent large study by the authors demonstrated that the results of a battery of different objective tests of ET opening in a mixed cohort correlated strongly with each other, suggesting that despite the diverse methodology, they all appear to measure ET opening.[30] However, the sensitivity and specificity of these tests varies, and caution should be used when interpreting test results in isolation.[51]

Until recently it had been assumed that patient symptoms, and the clinical diagnoses often based on these, correlated well with the ability of the ET to perform its physiological functions, in particular opening to permit ME pressure. However, it is increasingly recognised that the results of objective tests (tympanometry,[52] tubomanometry[53,54] and ME pressure equilibration tests[55]) may not match patient reported symptoms of ETD. The authors found in a cohort of 116 patients that while a consensus expert diagnosis of ETD correlated well with the results of ETD-specific PROMs, the correlation of both the expert diagnosis of ETD and PROMS with abnormal ET function measured by tests of ET opening for obstructive and patulous ETD was poor.[30] There was also a higher proportion of patients diagnosed with ETD clinically than with the tests of ET opening, either due to over-diagnosis on the basis of symptoms, or inadequate sensitivity of tests of ET opening.

An interesting result of exploring objective tests of ET function has been the discovery that some patients appear to have a predominance of dysfunction in either passive or active ET opening.[18,30,56] The ability to characterise obstructive ETD patients in this way may provide a means to target medical or surgical therapies better to specific causes of ETD.

Use of ET function tests in clinical practice

Clinical assessment, representing patient history (interpreted by an experienced clinician in a manner that the PROMs cannot, ensuring adequate specificity) and examination remain important in the diagnostic process for ETD, but should be supplemented by objective measures of ET function that determine whether or not the ET opens. Current methods of diagnosis based on clinical assessment alone may not select the cohort of patients who would benefit most from medical or surgical interventions, as

these are often designed to aid ET opening for obstructive ETD, or reduce patency for patulous ETD. Patient selection is key to ensure only those with abnormal ET function underlying their symptoms are treated.

Currently tympanometry, sonotubometry and tubomanometry show the greatest potential as tests of ET function for obstructive ETD, and a diagnostic pathway incorporating these has been proposed by the authors previously (Fig. 1).[30] There is however a need for further validation of these instruments.

Interpretation of ET function test results

A continuous spectrum of ET function exists, extending in both directions from normal intermittent opening, towards either permanently open or closed states. Given that even the healthy ET appears not to open with every swallow, and both obstructive and patulous ETD may be intermittent, the clinician must currently decide the point at which a diagnosis of ETD is made, as only a few tests have consistently applied diagnostic thresholds.

Identifying ETD patients on the basis of ET function tests is the first step towards improved patient selection for treatment. Having done this, additional selection on the basis of the specific presentation may be of benefit. Even the most rigorous of systematic reviews has failed to consider the varied manifestations of ETD,[57] and the potential for different treatment effects on these. It is not clear from existing ET function tests why some patients develop tympanic membrane retraction or otitis media with effusion, while others do not, and in particular why baro-challenge induced symptoms (for example pain during air travel) may be present in some individuals with apparently normal ET function, and not in others with tests indicative of a severe disorder.

Practicalities of ET function testing in clinic

Almost all ET function tests are safe and non-invasive, and in most cases do not cause patient discomfort. In the authors practice many tests take only a few minutes, and even the more complex measures can be repeated several times within a 10 min period.[30] There is undoubtedly a learning curve for the test operator, and a dedicated audiologist or specialist nurse may be best placed to undertake the tests routinely in clinics. While tests such as the observed Valsalva do not require specialist equipment, sonotubometry and tubomanometry availability is currently limited, and incurs additional costs.

Future direction of ET function testing

An aim of future work should be to identify if there is superior effectiveness of treatments such as BET in cohorts of patients with particular characteristics, whether these be certain symptoms, otoscopic findings or patterns of results from tests of ET opening (for example demonstrating a predominance of active of passive ET dysfunction). To facilitate this process, studies should recruit clearly defined groups of individuals characterising ET function, and report outcomes in the context of these groups.

While most evidence suggests that the ET opens momentarily along its full length, CT imaging has suggested that both passive and active opening could occur with progressive opening along the length of the tube, permitting the transit of a bolus of air.[58,59] This may explain why

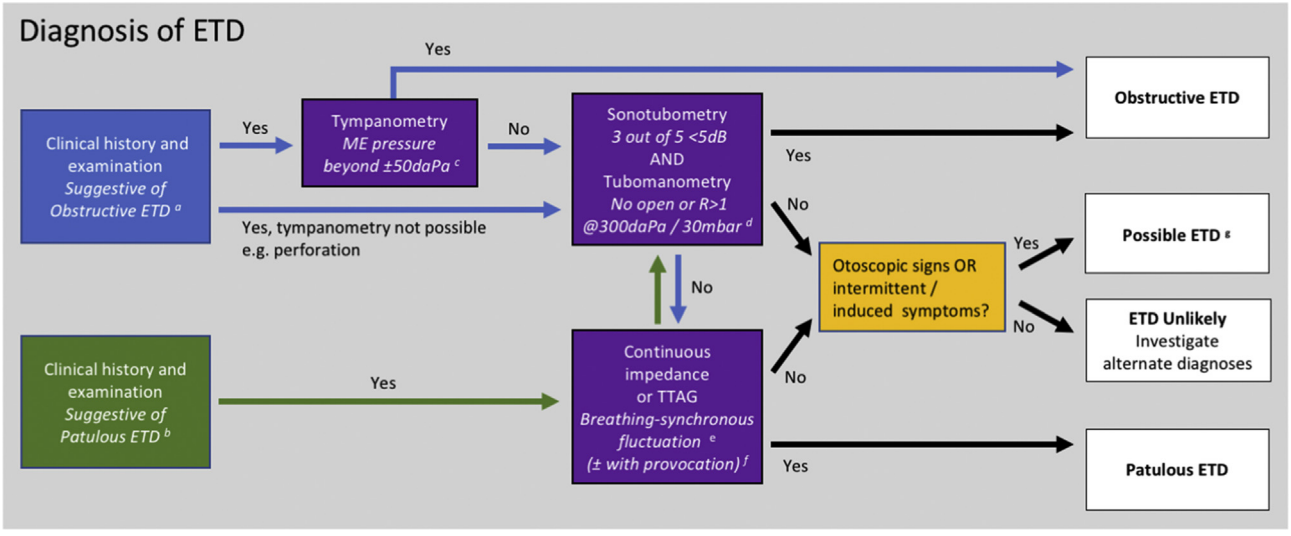

Fig. 1 Proposed diagnostic flow chart for ETD (reproduced from Smith et al. 2018[31]). [a, b]Clinical assessment may not be diagnostic of ETD, but remains a means to identify patients for investigation. [c] Effort should be made during assessment of the clinical history to identify habitual sniffing, as a negative middle ear pressure in these individuals may not indicate obstructive ETD, and further testing should be undertaken. [d] Described diagnostic thresholds may require adjustment based on local test methodology. [e] TTAG is recommended if a tympanic membrane perforation is present. [f] A simple provocation test for use in clinic is asking the patient to exercise prior to testing. [g] Consider repeating tests on a separate occasion to improve sensitivity in patients with variable ET function. Patients with baro-challenge induced obstructive ETD may present in this group.

the ET appears not to open with every swallow, even in healthy individuals. New high resolution rapid-acquisition imaging techniques promise to improve our understanding of ET opening, better defining the nature and duration of this process.

There is particular need for new tests that can indicate if a patient has a tendency to develop obstructive ETD intermittently, even if they are symptom free at the time of testing. The most clinically important presentation of intermittent ETD is baro-challenge induced obstructive ETD. Pressure chambers enable the conditions of baro-challenge to be replicated while testing ET function,[60] but these are not widely available and therefore form an impractical standard for clinical use.

Conclusions

New interventions for ETD such as BET have enhanced the need for robust patient selection and objective outcome assessment, and recent evidence suggests that clinical assessment alone is inadequate to achieve this. Both disease-specific PROMS and ET function tests continue to be designed *de novo* or further refined, and with evidence that measured ET function does not correlate with patient symptoms or examination findings, ET function tests are likely to be increasingly important in selecting patients for treatments designed to modify ET opening.

Conflict of interest

The authors declare no conflict of interest relevant to this report.

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