Testes de função da Trompa de Eustáquio: Avaliação prospetiva da acuidade diagnóstica

Eustachian Tube function tests: Prospective analysis of diagnosis accuracy

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RESUMO

A disfunção da trompa de Eustáquio (DTE) relaciona-se com patologia otológica de gravidade variável. O seu diagnóstico está atualmente assente em sintomas ou achados no exame físico, sendo a acuidade e utilidade diagnóstica dos testes de avaliação da TE indeterminada. No entanto, a seleção de doentes para tratamentos como a dilatação da TE deverá estar assente em exames objetivos e reprodutíveis. O intuito deste trabalho é avaliar a acuidade diagnóstica e correlação entre os diferentes meios atualmente disponíveis.

Método e metodologia: foram criados dois grupos de doentes - uma amostra de conveniência composta por doentes com diagnóstico clínico de DTE obstrutiva (baseado em queixas compatíveis e achados ao exame físico – retração timpânica); e uma amostra de pacientes controlo (sem queixas e/ou achados compatíveis). A amostra com queixas compatíveis com DTE obstrutiva foi validada por 3 médicos ORL, e apenas foram incluídos os pacientes nos quais houve concordância total. Estes doentes foram de seguida prospetivamente submetidos a 3 testes – uma ferramenta de avaliação sintomatológica validada em português – Eustachian Tube Dysfunction Questionnaire-7 (ETDQ7); timpanograma (T); e tubomanometria (TMM). Foi calculada a sensibilidade (S), especificidade (E) e valor preditivo positivo (VPP) e negativo (VPN) de cada um dos testes; foi testada a correlação entre os testes (correlação de Pearson). Foram calculadas curvas receiver operating caractheristic (ROC) para cada um dos testes e determinada a area under the curve (AUC) para comparação entre eles. Foi utilizado o SPSS para macOS, e um p-value < 0,05 para rejeição da hipótese nula.

Resultados: a população em análise era constituída por 36 pacientes com DTE obstrutiva e 27 pacientes sem DTE. O ETDQ7 apresentou uma alta S (94,4%), mas baixa E (40,7%); o contrário foi verificado relativamente ao T (S de 61,1% e E de 92,6%); a TMM mostrou uma S e E altas, de 91,7% e 67,7%, respetivamente. Embora se tenha verificado uma correlação estatisticamente significativa entre os resultados dos três testes utilizados, estas foram fracas, exceto entre o T e a TMM, que foi moderada. A AUC correspondente ao TMM foi a mais elevada das três (de 0,8 ± 0,06), seguida do timpanograma (0,71 ± 0,07).

Discussão e conclusões: os resultados corroboram a literatura mais recente, que significa que isoladamente, nenhum teste ou exame é suficiente. Se, por um lado, todos os testes podem ser úteis, por outro lado, isoladamente, o T é insuficiente, o ETDQ7 sobrestima, sendo a TMM o exame com maior fiabilidade para o diagnóstico.

Palavras-chave: Disfunção da Trompa de Eustáquio; tubomanometria; timpanometria; Eustachian Tube Dysfunction Questionnaire-7

ABSTRACT

Eustachian tube dysfunction (ETD) may relate to otologic disorders of variable severity. Its diagnosis is based on symptoms and signs, being the usefulness of eustachian tube function tests undetermined. However, patients selection to procedures such as ET dilation should be dependent on objective and reproductive exams. The objective of this study is to assess the diagnostic accuracy and correlation between different exams.

Methods and methodology: two groups of patients were selected: one convenience sample of patients with clinical diagnosis compatible with obstructive ETD (based on symptoms and physical exam signs); one convenience sample of control patients (without symptoms or signs). The sample of patients with obstructive ETD was validated by 3 Otorhinolaryngologists, and only the ones who gathered consensus of the three were included. All the patients were prospectively evaluated with 3 tests: a patient-reported

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outcome measure, validated in Portuguese – Eustachian Tube Dysfunction Questionnaire-7 (ETDQ-7), tympanometry T; and tubomanometry (TMM). Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated. Pearson correlation was used to test the correlation between them. Receiver-operating characteristic (ROC) curves were created and the area-under the curve (AUC) was used to compare between them. Statistical analysis was performed with macOS, and a p-value < 0,05 was used to reject the null hypothesis.

Results: the group of obstructive ETD was comprised by 36 patients; the control group by 27 patients. ETDQ-7 had a high Se (94,4%), but low Sp (40,7%); the opposite was verified regarding tympanometry (Se of 61,1% and Es of 92,6%); TMM had a high Se and Sp, of 91,7% and 67,7%, respectively. Despite a statistically significant correlation between the three used tests, they were weak, except for tympanometry and TMM, that was moderate. The AUC of TMM was the highest of the three (0,8 ± 0,06), followed by tympanometry (0,71 ± 0,07).

Discussion and conclusion: our results are compatible with the most recent literature, that means that no test or exam is sufficient when used alone. If, on one hand, all the tests can be useful, when isolated, tympanometry is insufficient, ETDQ-7 may overestimate, and TMM is the most accurate of the three.
Keywords: Eustachian Tube Dysfunction; tubomanometry; tympanometry; Eustachian Tube Dysfunction Questionnaire-7

INTRODUCTION

Eustachian tube (ET) is a tubular structure that connects the nasopharynx to the middle ear (ME).[1,2] The main functions of the ET comprise pressure equalization between ME and the nasopharynx and clearing secretions from the ME when they open, and prevention of the passage of sound, pathogens, and reflux from the nasopharynx when it is closed.[2,3] ET dysfunction (ETD) is thought to be the most important causative factor of ME pathology.[2]

There are two main types of ETD, namely obstructive ETD (OETD) and patulous ETD (PETD), and some authors argue that there is a third type, a subtype of OETD, the baro-challenge induced.[3,4] The former, OETD, refers to the inability to open after a proper stimulus. It may have different etiologies, but inflammation of the mucosa lining ET during episodes of upper respiratory tract infections (URTI) is the most common. The baro-challenge induced ETD happens with a change of pressures (most commonly flying or diving).[2] On the other hand, PETD refers to a persistently patent ET, and its characterized by autophony and aural fullness; it may improve with URTI.

Despite its clinical importance, the best method to establish the diagnosis of ETD is still a matter of great controversy in the literature. In 2015, a consensus statement proposed that the diagnosis of ETD should be defined by clinical evaluation: symptoms, namely aural fullness, popping or discomfort/ pain, in a defined time frame, accompanied by specific signs, such as tympanic membrane (TM) retraction (for OETD) or excursion of the TM induced by breathing (for PETD).[4]

More recently, Smith *et al*. (2019) emphasized the need to objectively evaluate ET function (ETF) given the rise in procedures that address ET, such as balloon dilation tuboplasty, that demands an adequate patient selection.[3]

Patient-reported outcome measures (PROMs) are useful for symptom evaluation, resulting in a score that enables standardization and comparison of the results between patients. There are several used in ETD evaluation, but the most widely-employed is Eustachian Tube Dysfunction Questionnaire-7 (ETDQ7) and the 10-item Cambridge Assessment (CETDA).

On the other hand, regarding other exams that evaluate ETF, they are divided in: indirect measures of ET function, which includes the most used one, the tympanometry; tests that evaluate ET opening, such as evaluation of the TM movement, inflation-deflation tests, tubo-tympano-aerodynamic graph (TTAG) sonotubometry, and tubomanometry (TMM); and tests that evaluate ET closure, such as TTAG, sonotubometry and TMM. They all have different sensitivities, specificities, positive and negative predictive values, but none is considered the gold standard.

OBJECTIVE

This study aims to assess the accuracy of the available methods in a Portuguese tertiary hospital to evaluate ET function considering a standard clinically-based diagnosis. It also aims to verify the correlation between the exams available.

METHODS AND METHODOLOGY

This study was developed in the Department of Otorhinolaryngology of a tertiary hospital after Ethics Committee approval.

Nonconsecutive patients > 18 years-old were selected for two convenience groups from the routine outpatient clinic of Otorhinolaryngology:

- OETD group: One cohort of patients with symptoms (aural fullness or popping, or discomfort/pain) and findings in physical exam (TM retraction and/or retraction pocket) compatible with unilateral OETD. These patients were evaluated by three Otorhinolaryngologists that confirmed the clinical diagnosis according to symptoms and signs in physical examination. Only the ones that gathered total consensus between the three observers were included.
- Control group: One cohort of control patients without symptoms or signs of ETD.

The exclusion criteria included: former ear surgery, TM perforation, ME effusion, and patients who were unable to complete all the evaluation protocol.

Demographic features were collected.

The patients were further evaluated through the following protocol:

- The ETD questionnaire-7, validated in Portuguese, that comprises 7 questions, in which a score > 14.5 is

considered compatible with ETD.5 The patients from the group with ETD were instructed to answer the questionnaire regarding the diseased ear.
- Tympanometry on both ears. It was classified as C type if middle ear (ME) pressure < - 100 daPa. In the group with OETD the result on the affected ear was considered; in the control group the right ear was considered for analysis purposes.
- Tubomanometry (TMM): it was performed at 300daPa, 400daPa, and 500daPa on both sides. It was defined as normal if R < 1 in all the evaluated pressures; compatible with OETD when R > 1 in one of the tested pressures. In the group with OETD the ET on the side of the affected ear was considered; in the control group the right side ET was considered for analysis purposes.

Statistical analysis
Continuous variables without normal distribution were described as median and interquartile range (IQR). Non-parametric Mann-Whitney U Test was used to compare medians of continuous variables without normal distribution. The Pearson Chi-square was used to evaluate the correlation between two categorical variables. The Pearson correlation coefficient was used to assess the strength of a linear association between two categorical variables and was denoted by *r.*
ETDQ7 and objective tests (tympanometry and TMM) were analyzed as index tests, in relation to reference clinical diagnosis, and sensitivity, specificity, PPV, and NPV were calculated for the three. Receiver operating characteristic (ROC) curves were calculated, and area-under the ROC curve (AUC) was used to compare them. SPSS v24.0 for macOS was used for statistical analysis. A p-value < 0.05 was defined to reject the null hypothesis.

RESULTS
A total of 40 patients were initially selected for the cohort of patients with symptoms of OETD. They were further evaluated by three Otorhinolaryngologists: there was complete agreement in the diagnosis of OETD in 36 of them (90%), which comprised the final cohort of the OETD group.
A total of 30 patients were selected to the control group. 3 were excluded for difficulties in completing all the evaluation protocol.

Demographic features
The median age of the patients in the OETD group was 52.5 (IQR = 23.75) years old and 47 (IQR = 24) in the control group, with no significant difference between the two ($p = 0.091$). Both the OETD group and the control group had a female predominance, with no significant difference in what gender concerns ($p = 0.769$).

ETDQ-7 results
We found a significant difference in the score of ETDQ7 between patients from the OETD group and the control group, with a median of 34 (IQR = 8.5) in the former and 15 (IQR = 13) in the latter ($p < 0.001$).
Most patients in the ETD group had a score > 14.5; nonetheless, a high percentage of patients in the control group also had a score compatible with ETD.

Objective tests
We found a significant difference in the results of tympanometry and TMM in both groups (p = 0.001 and $p < 0.001$, respectively).

Correlation between the three tests
Our results showed a moderate correlation between the objective exams used, namely tympanometry and TMM [r (63) = 0.49, $p = 0.001$]; on the other hand, the correlation between ETDQ7 and tympanometry and between ETDQ7 and TMM were weak [r (63) = 0.283, $p = 0.025$ and r (63) = 0.388, $p = 0.002$, respectively].

Sensitivity, specificity, positive and negative predictive value of ETDQ7, tympanometry, and TMM
Using a clinical diagnosis as reference for OETD diagnosis, our results showed that ETDQ7 had the highest sensitivity of the three (94.4%); TMM had also a high sensitivity, of 91.7%; tympanometry was the least sensitive of the three (61.1%). On the other hand, tympanometry had the highest specificity (92.6%), followed by TMM (67.7%) and ETDQ7 (40.7%).
Overall, TMM had a good AUC, of 0.8 ± 0.06, tympanometry a fair AUC (0.71 ± 0.07) and a poor AUC for ETDQ7 (0.68 ± 0.07) (Figure 1).

TABLE 1
Demographic features

	OETD Group	Control Group	*p*-value
Age (Median (IQR))	52.5 (IQR = 23.75)	47 (IQR = 24)	0.091*
Gender			
Female	55.6% (n=20)	59.3% (n=16)	0.769**
Male	44.4% (n=16)	40.7% (n=11)	

*Independent-Samples Mann-Whitney U Test, **Pearson Chi-square

TABLE 2
Results of the ETDQ7

	OETD Group	Control Group	*p*-value
Median (IQR)	34 (IQR = 8.5)	15 (IQR = 13)	< 0.001*
Score			
< 14.5	5.6% (n=2)	40.7% (n=11)	0.001**
> 14.5	94.4% (n=34)	59.3% (n=16)	

*Independent-Samples Mann-Whitney U Test, **Pearson Chi-square

TABLE 3
Results in the objective exams: tympanometry and TMM

	OETD Group	Control Group	*p*-value
Tympanometry			
Type A	38.9% (n=14)	92.6% (n=25)	0.001*
Type C	61.1% (n=22)	7.4% (n=2)	
Tubomanometry			
R < 1	8.3% (n=3)	66.7% (n=18)	< 0.001*
R > 1	91.7% (n=33)	33.3% (n=9)	

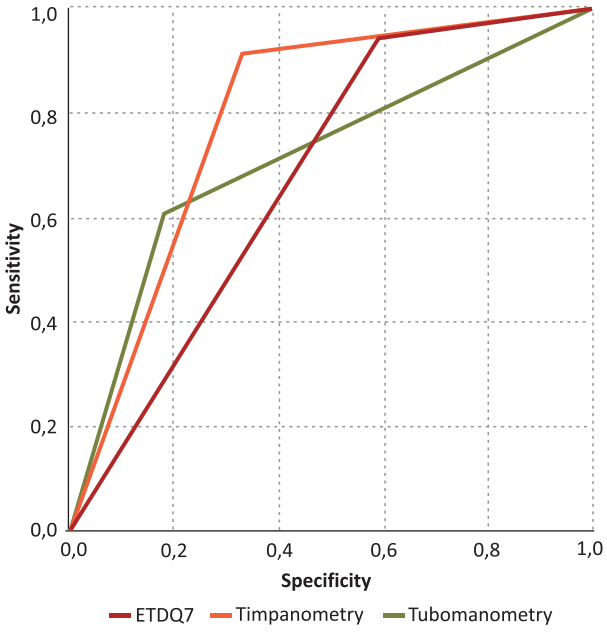
*Pearson Chi-square

TABLE 4
Sensitivity, specificity, positive predictive value, negative predictive value and Area-under the ROC curve of the three exams considering clinical diagnosis the reference

	Sensitivity	Specificity	PPV	NPV	AUC
ETDQ-7	94.4%	40.7%	68%	84.6%	0.68 ± 0.07
Tympanometry	61.1%	92.6%	81.5%	61.1%	0.71 ± 0.07
Tubomanometry	91.7%	67.7%	78.6%	85.7%	0.8 ± 0.06

PPV: positive predictive value; NPV: negative predictive value

FIGURE 1
Receiver operating characteristic (ROC) curve of the ETDQ7, tympanometry, and TMM in relation to the reference clinical diagnosis



DISCUSSION

Despite OETD being a common condition and existing several tests, there is no gold-standard to evaluate ET function.

Several investigators argued that given the absence of widely accepted PROMs, functional tests or scoring systems, the diagnosis of ETD should rely on the clinical evaluation, namely symptoms and signs.[4] Nonetheless, our results showed that there was an important percentage (10%) of the evaluated patients in whom the diagnosis of OETD based on the clinical evaluation was not consistent between the evaluating Otorhinolaryngologists. Other studies had also high rates of disagreement using the same diagnostic criteria, varying from 1.7 to 25%.[6] This emphasizes the need for an objective exam, repeatable, able to standardize findings.

Despite being quantitative, easing the process of clinical history-taking regarding symptoms of ETD, making it repeatable and comparable between patients, the clear disadvantage of ETDQ7 was confirmed by our results, namely the poor specificity. Our study showed good sensitivity and an AUC of 0.68 ± 0.07. Other authors

reported similar results.[6,7] Smith et al (2018) further compared the test accuracy between patients with ETD and healthy patients, but also other otologic disorders, such as Menière's disease, and concluded that its performance to distinguish between ETD and other otologic disorders was poor.[8] According to the previous data, most authors indicate that ETDQ7 is important for the assessment of symptoms and its severity, being useful to evaluate patients before and after certain procedures (such as ET balloon dilation), but not as a sole mean for diagnosis of ETD.

Regarding the ETF evaluating objective tests, the ideal exam should be non-invasive, repeatable, and able to evaluate changes in ETF with time (since there are ETD conditions in which its function varies over time).[2,3,9]

Our data regarding tympanometry showed a good specificity, but a poor sensitivity, with a fair AUC. Smith *et al* (2018) reported an even lower AUC, of 0.66.[6] Its low sensitivity makes it unsuitable to exclude OETD or PETD especially in patients with suspicious symptomatology. Although it remains as the most widely-used one, it has some limitations, namely in patients with perforations of the TM, in whom the pressure in the middle ear does not reflect ETF.[3] The patients with intermittent OETD may also be missed by this exam, especially considering the variability of ME pressure within only a few hours.

TMM, a manometric exam, consists on the application of a pre-defined pressure in the nasopharynx simultaneously instructing the patient to swallow, that should result in ET opening; a rising in ME pressure is recorded by a sealed earpiece.[10,11] Our results showed TMM as the one with the highest AUC between the three evaluated. Despite other studies showing a lower AUC considering clinical diagnosis as the reference, TMM has been shown as one of the exams with the best accuracy for ETD diagnosis.[6] It is a relatively recent exam, that is not widely available. Some authors use different cutoffs for normality, for example, consider ETF normal if the R > 1 in only one of the three evaluated pressures when the other ones have an R < 1, which directly influence sensitivity and specificity. It can be useful to evaluate PETD besides OETD, and it is the only exam available at the moment that is able to quantify ETF.[1,3,12,13]

More recently, Smith et al (2018), and in accordance with the results of our research, proposed a diagnostic algorithm for the different types of ETD that included symptoms, signs, and exam results.[3] Regarding OETD, and in the presence of the proper symptoms and signs constellation, tympanometry should be the first exam to confirm the diagnosis (except if a TM perforation is present); even in the absence of a compatible result, the diagnosis of OETD should not be excluded before TMM or sonotubometry. On the other hand, PETD diagnosis depends on symptomatology and continuous impedance or TTAG breathing-synchronous fluctuation. This will necessarily change the paradigm in these patients evaluation approach, demanding a more thorough assessment to identify the ones with OETD and PETD.

CONCLUSIONS

Although some authors recommend the diagnosis of ETD solely based on symptoms and signs, our results showed that clinical diagnosis alone might be inadequate, given the interobserver discrepancies. This emphasizes the importance of objectively evaluating ETF as complementary to clinical evaluation, which is particularly significant in selecting patients to ET interventions, such as balloon tuboplasty. According to our results, despite ME pressures < 100 daPa in tympanometry being diagnostic of OETD, they might underestimate the true prevalence of ETD. ETDQ7, given its low specificity, is not adequate for the diagnosis of ETD; it has a more important role in the evaluation before and after an intervention. TMM is the most accurate of the three, with high sensitivity, and moderate specificity.

Conflito de Interesses

Os autores declaram que não têm qualquer conflito de interesse relativo a este artigo.

Confidencialidade dos dados

Os autores declaram que seguiram os protocolos do seu trabalho na publicação dos dados de pacientes.

Proteção de pessoas e animais

Os autores declaram que os procedimentos seguidos estão de acordo com os regulamentos estabelecidos pelos diretores da Comissão para Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

Política de privacidade, consentimento informado e Autorização do Comité de Ética

Os autores declaram que têm o consentimento por escrito para o uso de fotografias dos pacientes neste artigo.

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Disponibilidade dos Dados científicos

Não existem conjuntos de dados disponíveis publicamente relacionados com este trabalho.

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