Sensitivity and Specificity of Eustachian Tube Function Tests in Adults

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IMPORTANCE The study demonstrates the utility of eustachian tube (ET) function (ETF) test results for accurately assigning ears to disease state.

OBJECTIVES To determine if ETF tests can identify ears with physician-diagnosed ET dysfunction (ETD) in a mixed population at high sensitivity and specificity and to define the interrelatedness of ETF test parameters.

DESIGN, SETTING, AND PARTICIPANTS Through use of the forced-response, inflation-deflation, Valsalva, and sniffing tests, ETF was evaluated in 15 control ears of adult subjects after unilateral myringotomy (group 1) and in 23 ears of 19 adult subjects with ventilation tubes inserted for ETD (group 2). Data were analyzed using logistic regression including each parameter independently and then a step-down discriminant analysis including all ETF test parameters to predict group assignment. Factor analysis operating over all parameters was used to explore relatedness.

EXPOSURES ETF testing.

MAIN OUTCOMES AND MEASURES ETF parameters for the forced response, inflation-deflation, Valsalva, and sniffing tests measured in 15 control ears of adult subjects after unilateral myringotomy (group 1) and in 23 ears of 19 adult subjects with ventilation tubes inserted for ETD (group 2).

RESULTS The discriminant analysis identified 4 ETF test parameters (Valsalva, ET opening pressure, dilatory efficiency, and percentage of positive pressure equilibrated) that together correctly assigned ears to group 2 at a sensitivity of 95% and a specificity of 83%. Individual parameters representing the efficiency of ET opening during swallowing showed moderately accurate assignments of ears to their respective groups. Three factors captured approximately 98% of the variance among parameters: the first had negative loadings of the ETF structural parameters; the second had positive loadings of the muscle-assisted ET opening parameters; and the third had negative loadings of the muscle-assisted ET opening parameters and positive loadings of the structural parameters.

CONCLUSIONS AND RELEVANCE These results show that ETF tests can correctly assign individual ears to physician-diagnosed ETD with high sensitivity and specificity and that ETF test parameters can be grouped into structural-functional categories.
T he eustachian tube (ET) represents a potential communication between the middle ear (ME) and the nasopharynx. While usually closed, the ET lumen is opened periodically for short periods by contraction of the tensor veli palatini muscle (mTVP) with perhaps the assistance of the levator veli palatini muscle (mLVP). 1 These transient, muscle-assisted ET openings allow for the gradient-driven exchange of gas between the ME and the nasopharynx. 2 Such gas transfers decrease the extant ME-ambient pressure gradient that is constantly being perturbed by changes in atmospheric pressure and by changes in ME pressure secondary to diffusive gas transfer from the ME to mucosal blood. 2 Experiments in monkeys (and other animal species) show that an inability to open the ET causes the successive development of ME underpressures (reference pressure, ambient), ME mucosal inflammation, and effusion accumulation in the normally air-filled ME cavity. 3 This presentation is similar, if not identical, to that for otitis media with effusion (OME), a common disease in infants and children that also occurs in adults. 4,5 When persisting as a chronic condition (COME), OME secondary to ET dysfunction (ETD) is a primary cause of hearing loss in the population and is associated with other complications such as balance disturbances 6 and speech and language delays in children. 7

A large number of tests have been developed to assess ET function (ETF) for purposes of diagnosing ETD and identifying the underlying cause. 8–13 Because the most information-rich tests require a nonintact tympanic membrane (TM), which is uncommon in subjects with “normal” ME function, and all tests require an effusion-free ME, which is uncommon in subjects with ME disease in the absence of a ventilation tube (VT), the results for those tests are usually presented as a distribution for the outcome parameters in the subset of the affected population(s) with functional VTs without reference to an age-matched population with normal ME function. 4,14,15 Alternatively, where tests can be performed in effusion-free ears with and without a history of ME disease, the information is limited to yes/no detections of ET opening during a specified maneuver, and usually, the frequency of positive assignments is compared between affected and control populations or between different test methods in either population. 12,16

These types of comparisons at the population level do not translate well to the clinical setting, where the focus of testing is on the individual patient and, specifically, on a diagnosis of the presence or absence of ETD, an identification of the underlying cause(s) of ETD, and, where possible, the development of a treatment plan to improve ETF and “cure” ETD-related diseases. However, there is little support in the literature that any ETF test is used with regularity in clinical practice or that clinicians base their decision making on those test results, even when available.

In this study, we used a broad test panel to evaluate ETF in a “diseased” group of adults with VTs inserted for physician-diagnosed ETD with or without concurrent OME and in a control group of adults without extant or history of ETD or ME disease after surgical perforation of the TM by myringotomy. We first determined the sensitivity and specificity of the ETF test parameters alone, and in combination, with respect to the correct assignment of ears to the ETD group, and then we explored the general relatedness among the ETF test parameters included in the panel. The study was designed to evaluate the principle that ETF tests can accurately identify affected (and nonaffected) ears with high sensitivity and specificity. This has direct applications to the clinical diagnosis of extant ETD on presentation and to documentation of improved ETF after specific interventions. A more complete understanding of the structural-functional information captured by the ETF test parameters included in our panel may lead to diagnostic methods that can determine the cause of ETD in individual ears and to the development of targeted interventions specifically tailored to a given type of ETD.

Methods

Screening Procedures
Male and female subjects, aged at least 18 years and of any self-assigned race, as is consistent with the rules of the National Institutes of Health, were recruited for study participation by advertisement and by referral from otology practices that treat adults with ETD in the greater Pittsburgh area. All persons presenting as candidates for enrollment signed an informed consent form approved by the institutional review board and then provided general demographic information and were screened by history and physical examination for qualification under the inclusion and exclusion criteria. Their MEs were examined using pneumatic otoscopy and tympanometry to document the presence or absence of a patent VT(s) and to rule out the presence of extant ME effusion and/or otorrhea.

Group Definition
Fifteen subjects with no extant symptoms or diagnoses of ETD or ME disease and without a significant history of those conditions were enrolled as control subjects (Group 1). Five, 3, and 2 of these subjects reported a history of allergic rhinitis, sinusitis, and gastroesophageal reflux disease (GERD), respectively. The average age for this group was 30.0 years (range, 19.3–47.9 years); 8 were male and 7 female; and 9 identified their race as being white, 5 as black, and 1 as Asian. These subjects were further screened for normal hearing by clinical audiometry and for known adverse reactions to lidocaine or epinephrine. The TM(s) of each subject were visualized through a speculum with the aid of an operating microscope, and lidocaine, 4%, with epinephrine was applied topically to 1 TM. After approximately 20 minutes, a 3- to 4-mm radial incision was made in the anterior-inferior quadrant of that TM using a myringotomy knife. 4 After the procedure, a unilateral nonpatent TM was confirmed by pneumatic otoscopy and tympanometry. The myringotomy was performed on the right TM in 12 subjects and on the left TM in 3 subjects, with the sidedness of the procedure chosen by the surgeon based on technical ease and clear visualization of the TM. After the procedure and follow-up testing, these subjects were examined weekly by otoscopy and tympanometry until the incised TM had healed, and then they underwent repeated audiologic testing to confirm no procedure-related change in hearing threshold. All TMs healed with-

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out incident or complications, and none of the ears had a significant change in hearing threshold.

Nineteen screened subjects with extant, functional, bilateral (n = 4) or unilateral VTs (n = 15; 8 in the left ear, 7 in the right) that had been inserted by their otologist to treat diagnosed ETD were enrolled into group 2. The average age for the group was 35.2 years (range, 18.3-60.4) years; 8 were male and 11 female; and 16 identified their race as being white, 2 as black and 1 as Asian. From subject history and medical records (available for 14 subjects) review, the VT was determined to have been inserted into 3 group 2 TMs (all unilateral cases) for an isolated diagnosis of ETD defined by a “hyper-inflated” ME that could not be cleared in 1 case and by symptoms of tinnitus, ME “fullness,” and “muffled” hearing in 2 cases. The VTs had been inserted into the remaining 20 group 2 TMs (4 bilateral, 12 unilaterial) for a combined diagnosis of OME/ME effusion secondary to ETD (unspecified). None of the 3 isolated ETD cases had a history of COME or of acute and/or recurrent acute otitis media, but of the 20 ears with a combined ETD/OME diagnosis, all had a history of COME, and 10 had a history of acute and/or recurrent acute otitis media. Of the 19 group 2 subjects, 11 reported a history of ME disease in childhood (10 with VTs inserted) and 10, 6, and 4 reported a history of allergic rhinitis, sinusitis, and GERD, respectively. There is no evidence in the medical records or by subject history that any of these comorbidities were specifically targeted for treatment in an attempt to resolve the ETD/OME prior to VT insertion. The study protocol was approved by the University of Pittsburgh institutional review board (REN1210013).

ETF Testing Methods

The ETF in the 15 group 1 ears with a TM perforation and in the 23 group 2 ears with functional VTs was evaluated using a panel of 4 test protocols; the forced-response test (FRT), the inflation-deflation test (IDT), the sniffing test, and the Valsalva test. The instrument used for ETF testing was developed by us and consists of an ear-canal probe coupled serially via tubing to an SDX01D4 differential pressure transducer (Honeywell), via a 3-way valve to a flow sensor (Respiratory Flowhead 1L MLT11; AD Instruments), and via a second 3-way valve to a variable-speed, constant-flow pump (Harvard Apparatus Pump 22; Harvard Apparatus) with a controller (Syringe Pump Controller version 1.2; National Instruments); and a nasal probe was coupled via tubing to an SDX01D4 differential pressure transducer. The transducer signals are routed via a PL3504 PowerLab 4/35 data acquisition system to a personal computer running Laboratory Chart software, version 7.3.6 (AD Instruments), for real-time display of waveforms and data storage (See Figure 1A for schematic and Figure 1B for idealized waveforms).

For the FRT, the ear-canal probe was sealed into the test ear. Both valves of the test instrument were opened, and the constant-flow pump delivered an airflow of approximately 11 mL/min to the ME. This increased ME pressure to passively force open the ET lumen (opening pressure [PO]). Continued delivery of the airflow usually resulted in a semistable system pressure (PS), where trans-ET flow (QS) approximated the applied flow rate. At steady state, the subject was instructed
to swallow, which is associated with contraction of the mTVP and mLVP. Activity of those muscles causes a change in ET lumen diameter, reflected as an increased or decreased trans-ET airflow (QA indicates maximum airflow during a swallow). The pump was then turned off, allowing the ET to passively close at a residual ME pressure (PC). This test sequence was then repeated at an applied airflow rate of about 23 mL/min. Throughout the test, system pressure and flow were continuously recorded. These waveforms were analyzed by 2 blinded investigators who identified and recorded PO, PC, PS, QS, and QA and calculated 2 derived parameters: passive ET resistance (RS = PS/QS) and ET dilatory efficiency (DE = QA/QS) for both flow rates. The data were reconciled, and the following parameters were entered into the database for analysis: PO, PC, RS, and DE at each airflow rate and the ratio of the ET resistance at the 11- and 23-mL/min flow rates (RS11/RS23). The PO and PC are measures of the passive forces that act to maintain a closed ET lumen; RS is a measure of the ease of trans-ET airflow; and RS11/RS23 is a measure of ET compliance. Together, these parameters characterize the structural properties of the ET. In contrast, DE is a measure of the functional efficiency of muscle-assisted ET lumen dilation independent of surface adhesive forces, ie, a functional property of the ET.6

For the IDT, the ear-canal probe was sealed into the test ear. Both valves were opened; ME pressure was increased at about 11 mL/min to an overpressure of about 200 daPa (reference pressure, ambient); the valves were closed to reduce system volume; and the subject was asked to swallow repeatedly at a normal rate to a residual pressure (RP) the ME pressure at which further swallowing did not cause an ME pressure change. Then, ME pressure was reduced to ambient by venting the system to the atmosphere, and the procedure was repeated at an applied ME underpressure of about 200 daPa. The parameters for analysis were the percentage differences (%SW+, %SW−) between the applied ME overpressure or underpressure and the respective residual pressures divided by the applied pressure. These 2 parameters are measures of the efficiency of muscle-assisted opening of the closed ET lumen, ie, a functional property of the ET.1

For the sniffing and Valsalva tests, the probe was sealed into the ear canal; ME pressure was set at 0 daPa (reference pressure, ambient); and the valves were closed to reduce system volume. Nasopharyngeal pressure was measured by the pressure sensor connected to a nasal olive held against one na-ris. The subject was asked to perform a forcible sniff, and the pressures in the nasopharynx and ME during the maneuver and any residual ME pressure were recorded. The test was repeated if the minimum nasopharyngeal pressure was greater than −400 daPa. The ME system pressure was reduced to 0 daPa; the upstream valves were closed; and the subject was asked to perform the Valsalva maneuver with both nares blocked, and those parameters were again recorded. The test was repeated if the maximum nasopharyngeal pressure was less than 400 daPa. These tests were scored as positive if the change in ME pressure during the maneuver was at least 10% of the peak pressure (PP), defined as the maximum nasopharyngeal pressure recorded during the Valsalva test (VAL) or at least 10% of the minimum nasal pressure during the sniffing test (SNF). Both of these tests are effort-dependent and susceptible to false-negative results.4,37 A negative Valsalva test may evidence a physical obstruction of the ET lumen and a positive Sniffing test was suggested to evidence ET closing failure.16 We do not assign these parameters ad hoc to a structure or function category.

### Statistical Methods

Table 1 lists the ETF test parameters included in the statistical analyses and, for each, the associated ETF test, a tentative assignment to a category (structural or functional), and a brief description of the measure. First, we defined the subset of parameters whose values were different between the 2 groups. There, the between-group difference for each parameter was evaluated for statistical significance using a t test for continuous variables and the χ² test for binomial variables, both evaluated at α = 0.05. The sensitivity and specificity of each parameter alone to assign test ears to group 2 were determined using logistic regression based on the receiver operating characteristic curve for parameters measured as a continuous variable.

### Table 1. Description and Categorization of ETF Test Parameters

<table>
<thead>
<tr>
<th>Parameter, Units</th>
<th>Test</th>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAL, yes/no</td>
<td>VAL</td>
<td>Unclassified</td>
<td>NP to ME trans-ET gas flow at high NP overpressures</td>
</tr>
<tr>
<td>SNF, yes/no</td>
<td>SNF</td>
<td>Unclassified</td>
<td>ME to NP trans-ET gas flow at high NP underpressures</td>
</tr>
<tr>
<td>PO, da/Pa</td>
<td>FRT</td>
<td>Structural</td>
<td>ME pressure at which a closed ET is forced open</td>
</tr>
<tr>
<td>PC, da/Pa</td>
<td>FRT</td>
<td>Structural</td>
<td>ME pressure at which an open ET passively closes</td>
</tr>
<tr>
<td>RS, daPa/mL/min</td>
<td>FRT</td>
<td>Structural</td>
<td>ET resistance at a specified airflow (intra-ET pressure/ET flow)</td>
</tr>
<tr>
<td>RS23/RS11, none</td>
<td>FRT</td>
<td>Structural</td>
<td>Ratio of ET resistances recorded at 23 and 11 mL/min (ET compliance)</td>
</tr>
<tr>
<td>DE, none</td>
<td>FRT</td>
<td>Functional</td>
<td>Dilatory efficiency of muscle-assisted ET opening</td>
</tr>
<tr>
<td>SW+, %</td>
<td>IDT</td>
<td>Functional</td>
<td>Percentage applied ME overpressure equilibrated by swallowing</td>
</tr>
<tr>
<td>SW−, %</td>
<td>IDT</td>
<td>Functional</td>
<td>Percentage applied ME underpressure equilibrated by swallowing</td>
</tr>
</tbody>
</table>

### Abbreviations:

DE, eustachian tube (ET) dilatory efficiency (calculated by QA/QS); FRT, forced-response test; IDT, inflation-deflation test; ME, middle ear; NP, nasopharynx; PC, residual ME pressure; PO, ME opening pressure; PS, system pressure; QS, trans-ET flow; QA, maximum airflow during a swallow; RP, residual pressure; RS, passive ET resistance (calculated by PS/QS); SNF, sniffing test; SW+, percentage of ME overpressure; SW−, percentage of ME underpressure; VAL, Valsalva test; 11 or 23 at the end of any abbreviation indicates airflow rate at 11 or 23 mL/min, respectively. For a more detailed explanation of the parameters, see the Methods section.

* Value recorded at a specified flow rate (11 or 23 mL/min).
or using a standard 2 × 2 contingency table for parameters measured as a binomial variable. The set of individual parameters that were identified as significant predictors of group assignment in these analyses were entered together into a logistic regression equation to determine if that set had a higher sensitivity and specificity for assignment to group 2 than those for the individual parameters. We also attempted to identify a minimized subset of parameters that maximized between-group discrimination by entering all parameters into a step-down discriminant function analysis. Finally, we used factor analysis with varimax rotation to explore the dimensionality of the set of ETF test parameters and to determine if there are a limited number of factors that group the parameters into meaningful subsets.

The more simple analyses for individual parameter used the total available data set for all tested ears. However, discriminant function analysis and factor analysis require a complete matrix of entries for all ears and parameters. Three group 1 and 4 group 2 tests did not satisfy this criterion and were not included yielding a sample size of 12 group 1 and 19 group 2 ears for those analyses. All analyses were performed using the NCSS, 2007 statistical software package (Kaysville, Utah).

Results
For each parameter, Table 2 lists the mean (SD) values of the measures for the 2 groups, the t or χ2 values and associated probability levels for the between-group comparisons, the percentage variances explained by a logistic regression equation that included each parameter as a predictor of group assignment, and the sensitivity and specificity of each parameter for assigning ears to group 2. The between-group difference was significant for all test parameters classified as functional measures of ETF: the percent applied over-pressure (%SW+) and under-pressure (%SW−) equilibrated by swallowing and the ET DEs recorded at the 2 flowrates (DE11 and DE23); however, the between-group difference was not significant for any parameter classified as a structural measure of the ET. One of the 2 uncategorized parameters, the ability to force open the ET at high nasopharyngeal overpressure (Valsalva), was also significantly different between groups. In all cases, the values associated with a more efficient ETF characterized group 1 ears more than group 2 ears. Individually, the 5 parameters had sensitivities ranging from 55% to 79% and specificities ranging from 58% to 85% for assigning ears to the ETD group. To determine if this combination of parameters was a better predictor of group assignment than any individual parameter, a logistic regression including the 5 parameters as predictors was run. The r2 value of that regression equation was 0.52, and the sensitivity and specificity for assigning ears to the ETD group were 84% and 83%, respectively.

Table 3 lists the minimum set of parameters identified by the step-down discriminant analysis that maximizes the accuracy of the model for assignment of ears to the 2 groups. Four parameters were members of that set: 2 functional measures, the percentage of ME over-pressure equilibrated by swallowing (%SW+) and the DE recorded at an airflow rate of 11 mL/min (DE11); 1 structural measure, the PO at an airflow rate of 11 mL/min (PO11); and 1 other parameter (%PO11/PO23).

### Table 2. Parameters of ETD Testing

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ETD, Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>Value of t or χ2</th>
<th>P Value</th>
<th>r2</th>
<th>SENS, %</th>
<th>SPEC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuous Variables</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>SW+</td>
<td>0.57 (0.36)</td>
<td>0.94 (0.1)</td>
<td>−3.43</td>
<td>.002</td>
<td>0.411</td>
<td>75</td>
<td>65</td>
</tr>
<tr>
<td>SW−</td>
<td>0.33 (0.38)</td>
<td>0.73 (0.23)</td>
<td>−3.35</td>
<td>.002</td>
<td>0.279</td>
<td>73</td>
<td>58</td>
</tr>
<tr>
<td>PO11</td>
<td>323.4 (223.3)</td>
<td>335.1 (90.8)</td>
<td>−0.19</td>
<td>.85</td>
<td>0.001</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>PC11</td>
<td>85.8 (103.4)</td>
<td>81.9 (51.1)</td>
<td>0.13</td>
<td>.90</td>
<td>0.000</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>RS11</td>
<td>15.11 (11.89)</td>
<td>13.36 (3.81)</td>
<td>0.53</td>
<td>.60</td>
<td>0.006</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>DE11</td>
<td>3.16 (3.08)</td>
<td>8.7 (7.4)</td>
<td>−3.07</td>
<td>.004</td>
<td>0.205</td>
<td>79</td>
<td>58</td>
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<tr>
<td>PO23</td>
<td>334.1 (155.2)</td>
<td>297.2 (96.0)</td>
<td>0.8</td>
<td>.43</td>
<td>0.016</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>PC23</td>
<td>69.0 (59.0)</td>
<td>57.6 (30.0)</td>
<td>0.67</td>
<td>.51</td>
<td>0.013</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>RS23</td>
<td>8.76 (5.92)</td>
<td>7.18 (2.57)</td>
<td>0.87</td>
<td>.39</td>
<td>0.013</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>DE23</td>
<td>2.48 (2.25)</td>
<td>4.51 (2.83)</td>
<td>−2.44</td>
<td>.02</td>
<td>0.115</td>
<td>79</td>
<td>58</td>
</tr>
<tr>
<td>RS11/RS23</td>
<td>1.86 (0.66)</td>
<td>1.97 (0.52)</td>
<td>−0.51</td>
<td>.61</td>
<td>0.014</td>
<td>ND</td>
<td>ND</td>
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<td><strong>Binomial Variables</strong></td>
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</tr>
<tr>
<td>VAL</td>
<td>0.38 (0.5)</td>
<td>0.83 (0.39)</td>
<td>6.3</td>
<td>.01</td>
<td>ND</td>
<td>55</td>
<td>85</td>
</tr>
<tr>
<td>SNF</td>
<td>0.19 (0.4)</td>
<td>0.17 (0.39)</td>
<td>0.03</td>
<td>.87</td>
<td>ND</td>
<td>52</td>
<td>51</td>
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</tbody>
</table>

Abbreviations: DE, eustachian tube (ET) dilatory efficiency (calculated by QA/QS); ETD, ET dysfunction; ME, middle ear; PC, residual ME pressure; PO, ME opening pressure; ND, not defined; PS, system pressure; QA, maximum airflow during a swallow; QS, trans-ET flow; RP, residual pressure; RS, passive ET resistance (calculated by PS/QS); SNF, sniffing test; SW+, percentage of ME over-pressure; SW−, percentage of ME under-pressure (SNF); VAL, Valsalva test; 11 or 23 at the end of any abbreviation indicates airflow rate at 11 or 23 mL/min, respectively. For a more detailed explanation of the parameters, see the Methods section.

a Values for t, χ2, and P are listed for the between-group comparisons; r2 values, sensitivities (SENS) and specificities (SPEC) of the logistic regression equations included the parameter as the sole predictor for correct assignment of ears to the ETD group.

b Binomial variables expressed as a frequency and compared using a χ2 test.
11 mL/min (PO11); and 1 unclassified measure, the ability to force open the ET at high nasopharyngeal overpressures (VAL). For this set of parameters, the sensitivity and specificity of the model equation for correct assignment of ears to group 2 were 95% and 83%, respectively (Table 4).

Three primary factors accounted for 98% of the variance among parameters: factor 1 at 56%, factor 2 at 23%, and factor 3 at 20%. Figure 2 shows a bar chart of the absolute loadings of each ETF test parameter on the 3 factors. Examination of factors 1 and 2 suggests an interpretation consistent with expectation. Specifically, most of the test parameters are dichotomized into 2 structural-functional domains. Those parameters believed to be associated with the structural properties of the ET, such as the forced pressures for ET opening (PO11 and PO22), ET closing pressures (PC11 and PC22), ET resistances (RO11 and RO22), and ET compliance (RS11 and RS22), loaded negatively on factor 1, while those parameters believed to be associated with the functional properties of the ET, such as the ET dilatory efficiency (DE11 and DE22) and the percentage of applied ME overpressure (%SW+) and underpressure (%SW−) equilibrated by swallowing loaded positively on factor 2. In contrast, the 2 parameters that are not easily assigned to a given category, the ability of large nasopharyngeal overpressure (VAL) and underpressure (SNF) to change ME pressure did not load on either factor. The structure of factor 3 is more complicated, with a negative loading of most functional measures of the ET and a positive loading of most structural measures of the ET. Our interpretation is that factor 3 represents a negative interaction between the 2 groups of parameters such that the structural properties of the ET constrain the efficiency of the functional measures of the ETF.

Table 3. Minimum Set of Parameters That Maximize Group Discriminationa

<table>
<thead>
<tr>
<th>Parameter</th>
<th>λ Change, %</th>
<th>F Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW+</td>
<td>23.78</td>
<td>9.05</td>
<td>.01</td>
</tr>
<tr>
<td>DE11</td>
<td>16.3</td>
<td>5.26</td>
<td>.03</td>
</tr>
<tr>
<td>PO11</td>
<td>17.25</td>
<td>5.42</td>
<td>.03</td>
</tr>
<tr>
<td>VAL</td>
<td>15.35</td>
<td>5.08</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: DE, eustachian tube (ET) dilatory efficiency (calculated by QA/QS); PO, middle ear (ME) opening pressure; QA, maximum airflow during a swallow; QS, trans-ET flow; SW+, percentage of ME overpressure; VAL, Valsalva test; the number 11 placed at the end of an abbreviation indicates airflow rate at 11 mL/min. For a more detailed explanation of the parameters, see the Methods section.

* Arrived at by a step-down discriminant function analysis and the associated sensitivity and specificity of the model for assignment of ears to the ET dysfunction group.

Table 4. Contingency Analysis for Group Discrimination Using Parameters Identified by Discriminant Analysisa

<table>
<thead>
<tr>
<th>Actual, No.</th>
<th>Predicted, No.</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETD</td>
<td>18</td>
<td>1</td>
<td>95%</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

* Arrived at by a step-down discriminant function analysis and the associated sensitivity and specificity of the model for assignment of ears to the eustachian tube dysfunction (ETD) group.

Discussion

Eustachian tube function refers to the efficiency of ET openings with respect to maintaining an approximate ME-ambient pressure balance while protecting the ME from nasopharyngeal pressures and pathogens. Adequate ETF is a prerequisite for normal hearing and continued ME health. Most evidence suggests that there is a constitutive ETF imposed by the physical composition (eg, distribution of elastic fibers in the periluminal tissues), mechanical properties (eg, compliance and hysteresis of the periluminal tissues), and geometry (eg, mTVP/mLVP-ET vector relationships) of the ET system, ie, the structural properties of the ET. In young children, constitutive ETF improves with growth and development as the ET system matures, and at all ages, constitutive ETF is downgraded during periods with extant comorbid conditions that provoke inflammation in or around the ET, such as viral upper respiratory tract infection, allergic rhinitis, and GERD. Eustachian tube dysfunction occurs when an extant ETF is insufficient to maintain ME pressure greater than the critical underpressure that precipitates disease (eg, OME) and can be either constitutive or secondary (compromised ETF attributable to comorbidities). Eustachian tube dysfunction can be caused by an extrinsic (eg, impinging adenoids, ET lumen obstruction during palatal elevation) or intrinsic (eg, luminal inflammation, high periluminal tissue pressures) mechanical obstruction of the ET lumen or by a functional ET obstruction attributable to inefficient muscle-assisted dilation of the ET lumen (eg, atrophic mTVP, inefficient mTVP-ET vector relationships).

Because of the important role played by ETD in the pathogenesis of common ME diseases such as OME and the low efficacy of standard medical treatments for promoting long-term resolution of these disease conditions, there has long been an interest in developing tests to evaluate ETF for purposes of diagnosing the presence or absence of ETD, identifying the type and cause of diagnosed ETD, and targeting interventions to improve ETF and resolve the consequent ME disease. To date, these efforts have been largely confined to the research setting, with little evidence that any of the available ETF tests has been adopted for use in clinical decision making.

In that regard, a number of ETF tests has been described. Simple, noninvasive tests such as sonotubometry, barotubometry, and the 9-step test can determine if the ET opens during specified maneuvers by detecting the presence or absence of signal transmission through the open ET, but these tests provide no information regarding the underlying cause of any observed ET opening failure. Alternatively, more complex, multiple-protocol tests that require a nonintact TM can assess the efficiency of ET opening via swallowing and other...
maneuvers, rule out certain causes of ETD, and provide information that may relate to the physical and mechanical properties of the ET that constrain constitutive ETF, however, the interrelatedness of the various parameters for these tests has not been well characterized, and existing interpretations of test results are based primarily on theory without strong empirical foundation.

Most work on ETF tests has focused on describing the test protocol, defining test-retest reproducibility, and documenting a difference in the test measure(s) between populations with and without ME disease and/or suspected ETD. While providing evidence that ETD as measured by each test is prevalent in populations at risk for ETD/ME disease, the results of this research cannot be used to support the clinical utility of the test under study, which requires a focus on ETF in the individual patient and ear. Recently, our research group began to explore the clinical utility of the more comprehensive ETF testing protocols that require a nonintact TM. For example, we completed a study wherein we enrolled children aged 3 to 6 years with VTs secondary to COME, repeatedly

Figure 2. Absolute Loading of the Eustachian Tube (ET) Function Test Parameters Onto Each of the 3 Factors Identified by Factor Analysis After Varimax Rotation

Factors are listed in an arbitrary sequence corresponding to those that capture structural measures of the eustachian tube (ET) (factor 1), functional measures of the ET (factor 2), and mixed measures (factor 3). See Table 1 for parameter definitions.
tested the children using an abbreviated FRT while the VTs were functional, and evaluated the MEs for COME recurrence after the VTs became nonfunctional. For the population, there was no evidence of a patterned change in any of the ETF parameters over the period of functional VTs. One FRT parameter, ET DE, when combined with sex, race, and duration of VT functionality, predicted disease recurrence at a sensitivity of 82% and a specificity of 77%. These results support the prognostic capabilities of this test protocol and hold promise for other clinical applications of ETF tests.

In the present study, we continue our research on the clinical utility of ETF testing by determining if a broad panel of ETF test parameters, alone or in combination, can identify individual ears with physician-diagnosed ETD and functional VTs within a mixed population of affected and control subjects. Because the test protocols require a nonintact TM, which is not typical for ears without recent ME disease, a unilateral TM perforation was created in the control subjects by performing a myringotomy. Using standard between-group statistical comparison procedures, measures of the 4 parameters believed to reflect the efficiency of ET opening during swallowing (%SW+, %SW−, DE11, and DE23), but none of those believed to reflect the structural properties of the ET, were significantly different between the 2 groups. Values for each parameter indicative of better ETF characterized the control group. When each of the 4 parameters was entered alone into an accuracy analysis, all had a sensitivity of approximately 75% and a specificity of approximately 60% for ear assignment to the ETD group. The percentage of subjects who could open their ET at high nasopharyngeal overpressures (VAL) was also significantly different between the 2 groups, and that measure had a sensitivity of 55% and a specificity of 85% for ear assignment to the ETD group. When combined, these 5 parameters correctly assigned ears to the ETD group at an 84% sensitivity and an 83% specificity, which are levels comparable to those for other clinical tests and examinations (eg, pneumatic otoscopy, tympanometry) used by otorhinolaryngologic clinicians in their diagnosis of ME diseases.

An ideal diagnostic test would include the minimum number of test parameters (protocols) required to maximize the information needed for group assignment. We explored this issue using a step-down discriminant function algorithm operating on all available data. The resulting model included 4 parameters that together had a sensitivity and specificity for detecting ETD of 95% and 83%, respectively. This set was a subset of the parameters that were independent predictors of group assignment (%SW+, DE11, and VAL) with an additional parameter (PO11). The higher sensitivity and specificity of this maximized discriminatory model compared with the 5-parameter model and the difference in set elements for the 2 models suggest that the individual parameters capture a degree of redundant information and that interactions between parameter subclasses add important information for group discrimination.

From theory, we previously classified the test parameters as either measuring muscle-assisted ET opening efficiency or characterizing ET structure. We used factor analysis to test empirically the validity of those parameter assignments. Consistent with our expectations, we identified 2 independent factors with high loadings of the presumed structural (factor 1) and functional (factor 2) parameters. A third factor was identified that can be interpreted as a negative interaction between the structural and functional parameters such that the structural parameters constrain the efficiency of the functional ones. Of interest, the parameters associated with the Valsalva and sniffing tests did not load on either of the independent factors, though the Valsalva test parameter did load onto the interaction factor. These results support our suggestion that the test protocols used in this study capture redundant information with respect to the efficiency of ET opening, the structure of the ET system, and the interplay between ET structure and function.

The results of the present study establish an empirical classification of the relatedness among the measured ETF test parameters and support our tested proof of principle that certain combinations of ETF test parameters can accurately identify ears with ETD in a mixed population with high sensitivity and specificity. These results have clinical applications for identifying ears with ETD and evaluating the efficacy of selected interventions (medical treatments and/or surgical procedures) with respect to improving ETF. While it is expected that these test protocols can rule out certain causes of ETD such as physical obstruction of the ET lumen, it is not expected that they will be able to distinguish between secondary and constitutive ETD, which would require an intervention with an efficacious medication targeting the suspected comorbidity and then retesting.

There are 2 caveats to our interpretation of the study results. First, the relatively small sample sizes for the 2 groups may have allowed us to develop a discriminant function equation that includes a parameter subset and assigns sensitivity and specificity estimates relevant only to the studied population. Future application of this type of statistical model to larger populations will be required to determine if the model developed here is generalizable or needs to be modified. Second, when assigning specificity and sensitivity to a diagnostic test, an independent gold standard is needed to define the presence or absence of the true disease state. Conceptually, ETD is an extant ETF insufficient to maintain ME pressure greater than the critical underpressure that precipitates disease, but there is no accepted method to diagnose ETD based on a defined set of symptoms and signs without recourse to testing. Here, we used the presence of VTs inserted to treat physician-diagnosed ETD to define a true-state positive finding (ETD) and no history of ME diseases to define a true-state negative finding. For the true-state positive, we assume that practitioners have a shared, unarticulated, experiential conception of ETD that they use in diagnosing the condition. Finally, our ETD group had a diverse ME disease history, which introduces the possibility that ETF in group 2 was not homogeneous but included subsets of ears with different types of ETD and perhaps even with normal ETF. However, the high accuracy of our test protocols to assign ears to the true disease state, combined with the agreement between theory and experiment with respect to which parameters have the greatest discriminatory power, suggests that the possible intragroup heterogeneity was not realized.
Accuracy of Eustachian Tube Function Tests

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Acquisition of data: Swarts, Banks.

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