



Surgical Parameters for Minimally Invasive Trans–Eustachian Tube CSF Leak Repair: A Cadaveric Study and Literature Review

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■ **BACKGROUND:** Cerebrospinal fluid rhinorrhea from a lateral skull base defect refractory to spontaneous healing and/or conservative management is most commonly managed via open surgery. Approach for repair is dictated by location of the defect, which may require surgical exploration. The final common pathway is the eustachian tube (ET). Endoscopic ET obliteration via endonasal and lateral approaches is under development. Whereas ET anatomy has been studied, surgical landmarks have not been previously described or quantified. We aimed to define surgical parameters of specific utility to endoscopic ET obliteration.

■ **METHODS:** A literature review was performed of known ET anatomic parameters. Next, using a combination of endoscopic and open techniques in cadavers, we cannulated the intact ET and dissected its posterior component to define the major curvature position of the ET, defined as the genu, and quantified the relative distances through the ET lumen. The genu was targeted as a major obstacle encountered when cannulating the ET from the nasopharynx.

■ **RESULTS:** Among 10 ETs, we found an average distance of 23 ± 5 mm from the nasopharynx to the ET genu, distance of 24 ± 3 mm from the genu to the anterior aspect of the tympanic membrane and total ET length of 47 ± 4 mm.

■ **CONCLUSIONS:** Although membranous and petrous components of the ET are important to its function, the genu

may be a more useful surgical landmark. Basic surgical parameters for endoscopic ET obliteration are defined.

INTRODUCTION

Cerebrospinal fluid (CSF) leak is a phenomenon that may occur spontaneously, following trauma, or iatrogenically with surgery. Persistent CSF leak creates risk for adverse effects, such as intracranial hypotension and, more importantly, intracranial infection.¹ Thus, resolution of a known CSF leak is critical to a good patient outcome. CSF rhinorrhea may be related to an acquired defect creating a direct communication into the nasopharynx and paranasal sinuses or an indirect communication via CSF passage through a lateral skull base defect into the mastoid air cells and/or the middle ear from which passage through the eustachian tube (ET) occurs.

Despite use of multiple standard surgical techniques to minimize risk of CSF leak, lateral skull base surgery is complicated by CSF leak in >10% of cases.²⁻⁴ At least half of all iatrogenic CSF leaks may be managed conservatively through placement of a lumbar drain combined with bed rest.² However, refractory cases often lead to return to the operating room for open exploration and repair. A minimally invasive approach has the potential advantages of avoiding the well-known risks associated with open re-exploration and decreasing length of hospitalization. Endoscopic eustachian tube obliteration (EETO) has been described by a number of authors to successfully treat refractory CSF rhinorrhea,^{2,4} and techniques to safely cannulate the ET are

Key words

- Cadaver
- Catheter
- Cerebrospinal leak
- Endoscopy
- Eustachian tube

Abbreviations and Acronyms

- aET:** Anterior eustachian tube segment
CSF: Cerebrospinal fluid
EETO: Endoscopic eustachian tube obliteration
ET: Eustachian tube
pET: Posterior eustachian tube segment

tET: Total eustachian tube length

TM: Tympanic membrane

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under development.^{5,6} Reported evidence shows it to be a relatively simple procedure with low morbidity although not widely employed.

EETO represents a range of techniques to occlude the ET; most are permanent, but some are potentially temporary. A recent literature review on this topic⁶ describes limited reports of widely varying, unstandardized techniques. These surgical options may significantly reduce invasiveness in the resolution of refractory CSF rhinorrhea associated with lateral skull base defects. One method of EETO involves ET cannulation.⁵ Although this particular technique has yet to be the subject of a case report, it may represent a promising pathway for standardization of technique and therefore encourage more widespread utilization. Cannulation of the ET from either a lateral skull base or an endonasal approach would allow for delivery of a range of obstructive materials and methods to any point along the ET. Whereas ET anatomy has been studied, direct measurements of surgical landmarks most useful in cannulating the full ET length have not been previously described. To cannulate the ET successfully, one would need to define the minimum diameter, the maximum length, and the point of greatest curvature of the ET to minimize the risk of harm. In this article, we define such specific parameters in the context of ET cannulation.

We undertook a 2-pronged approach to evaluate and define parameters useful in EETO with cannulation. First, we performed a complete literature review of ET anatomic descriptions. Second, informed by the literature review, we performed a cadaveric dissection study involving ET cannulation along with objective measurement of relevant anatomy using a dual endoscopic technique.

MATERIALS AND METHODS

Literature Review

We had a very specific literature review question regarding ET length and related anatomic definitions. We chose an open-ended yet formal and descriptive approach without restriction to controlled studies to maximize the number of reports reviewed in such a specific area of study with few examples in the literature, and therefore this does not constitute a systematic review. An English-language PubMed literature review, unrestricted by year, was undertaken for articles describing ET measurement. Relevant references from identified articles were also included. Search terms included “eustachian tube,” “anatomy,” “cadaver,” and “length.” Two authors approved articles identified independently to enhance validity, with any disagreements settled by a third author. The most common definitions of ET components were agreed on across authors following individual review. For each final article identified, ET length was recorded along with a measurement method summary.

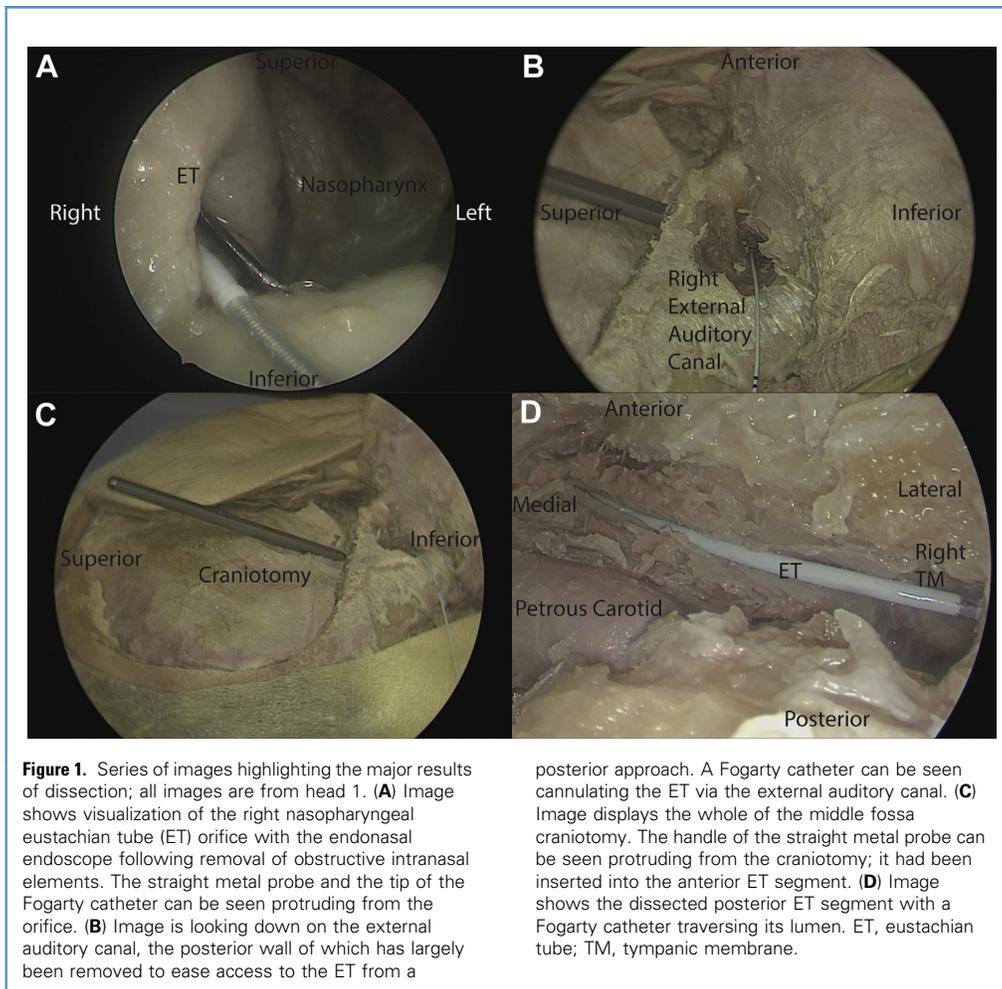
Cadaveric Dissection

We obtained 5 cadaveric heads, 2 female and 3 male, middle-aged to elderly (preserved for at least 1 year) from the institution's body donation program. Dissection proceeded using a combined endoscopic and open dissection approach; endoscopic techniques involved a 0-degree endoscope and exoscope (Karl Storz GmbH, Tuttlingen, Germany), and dissection was aided by standard

neurosurgical drills (DePuy Synthes Power Tools, Palm Beach Gardens, Florida, USA). First, an endoscopic endonasal view of the nasopharyngeal ET orifice was created with any necessary removal of the posterior nasal septum and/or turbinates (Figure 1). Once achieved, a modified middle fossa craniotomy was performed using a wide inverted-U-shaped incision. Scalp and periosteum were carefully dissected away from the skull proceeding inferiorly and involving the auricle to expose the bony external auditory canal without violating the tympanic membrane (TM) (Figure 1). A large middle fossa craniotomy was created via drilling techniques extending the opening inferiorly into the temporal bone just superior to the prominent bony structures surrounding the middle ear (Figure 1). Further temporal bone drilling was performed to remove the posterior wall of the bony external auditory canal, maintaining the TM intact, creating a direct trajectory to the ET for eventual cannulation as well as working space for accurate measurements. At this time, dura mater was separated from the intracranial surface of the temporal bone to expose the region of the petrous carotid, where dehiscence was noted in nearly all samples, which increased ease of locating the nearby ET lumen.

A dual endoscopic technique was used to ensure accuracy. A 0-degree endonasal endoscopic view was secured with a scope holder (Karl Storz GmbH). A second tower was connected to the exoscope when viewing the middle cranial fossa and the 0-degree 4-mm endoscope when visualizing the anterior TM attachment to bone. With all initial exposure completed, the TM was incised circumferentially, noting the position of its anterior attachment, and the tympanic ET orifice was identified. An attempt to cannulate the ET from a posterior approach was made using semirigid 14-gauge microcatheters with a flexible guidewire (Figure 2) and a 2-mm Fogarty catheter. Once cannulation was accomplished, attention was returned to the middle cranial fossa where bony dissection proceeded along the anterolateral aspect of the petrous carotid until the ET was exposed, revealing the catheter within its lumen (Figure 1).

Based on the literature review, a genu of the ET was identified as the major curve within the membranocartilaginous portion (described later in Results). Thus, the portion of ET lumen exposed during dissection was that from the midpoint of the genu to the tympanic orifice, the genu being identified when a straight metal probe could be easily passed from the middle cranial fossa into the nasopharynx via the nasopharyngeal orifice (Figure 3). The ET genu was the transition from the posterior horizontal portion of the ET (posterior eustachian tube segment [pET]) to the more anterior vertical portion (anterior eustachian tube segment [aET]). The pET was measured from the ET genu to the anterior attachment of the TM ridge. Under endoscopic guidance (Figure 4), total eustachian tube length (tET) was measured by first positioning the tip of the catheter at the nasopharyngeal orifice and then identifying the point at which the anterior bony annulus of the TM fell along the catheter. This length was subsequently measured directly on removal of the catheter. These measures were then repeated 1 month later (to blind the operator to the first measurement). For any repeated measurement >5 mm different from the first, a third measurement was obtained. Final measurements represent the numerical average of these 2 (or 3) measurements. The length of



the aET from the nasopharyngeal orifice to the genu was indirectly inferred with subtraction of the pET from tET.

Statistical Analysis

Statistical comparisons were performed using the nonparametric Mann-Whitney U test as implemented in MATLAB 2017a (The MathWorks, Inc., Natick, Massachusetts, USA), with a significance threshold of $P < 0.05$. Data are presented as \pm SD.

RESULTS

Literature Review

The literature review included 15 articles describing adult ET anatomy, including measures of total ET length (Table 1). Generally, the ET is subdivided into a membranocartilaginous, or functional, component and an osseous or petrous component containing the isthmus where the ET reaches its point of minimal luminal diameter. An overall “S” shape is attributed to the ET with a major curve within the membranocartilaginous component and a minor curve within the osseous component; excellent three-dimensional reconstructions can be found in the literature²² for illustration. The major curve of the ET was

identified as an important anatomic landmark for procedural ET cannulation and referred to as the genu. Various techniques have been used to measure ET length (computed tomography–based techniques predominating). With few exceptions, there is widespread use of a straight line from the nasopharyngeal orifice to the tympanic orifice to define total length,^{9,10,13–15,18–20} despite the well-known curvature. Only 2 cadaver-based measurement studies were identified^{8,10}; one is not well described,⁸ and the other involves ET cannulation followed by imaging rather than direct dissection.¹⁰ No studies were found to identify the position of the major ET curvature, or genu. Quoted tET across studies was 30–45.2 mm^{7–16,19–21} for men and women; sufficiently powered studies identified a statistically significant difference in tET length between men and women, largely attributed to larger male head size by the authors.^{17,18}

Cadaveric Dissection

Dissection with bilateral measurements was completed across 5 cadaveric heads, 2 female and 3 male, middle-aged to elderly (10 ET measurements). The ET could be cannulated with a 14-gauge semirigid microcatheter and Fogarty catheter with 2-mm external diameter. All specimens except 1 had dehiscent petrous

carotid arteries bilaterally; the ET was still easily dissected even when the petrous carotid was nondehiscent. An ET genu could be identified in all specimens. Mean length for tET was 47 ± 4 mm, mean length for pET was 24 ± 3 mm, and mean length for aET was 23 ± 5 mm (Table 2). Only 2 measures required a third repeat measurement—the right pET of head 3 and right pET of head 4. A statistically significant difference in average tET between male heads (49 ± 3 mm) and female heads (44 ± 2 mm) was noted ($P = 0.0286$). The same was noted for average aET measurements: 26 ± 4 mm for male heads and 19 ± 2 mm for female heads ($P = 0.0095$). There was no significant difference in pET between male heads and female heads ($P = 0.4286$), between left ear and right ear for any measure (tET, $P = 0.5397$; pET, $P = 0.0556$; and aET, $P = 0.7302$), or between pET and aET ($P = 0.6770$).

DISCUSSION

From the literature review and dissection described, 3 anatomic parameters are critical in ET cannulation: isthmus diameter, ET length, and the major curvature. The petrous carotid is very near to the osseous ET and very often dehiscent; thus, a low perforation risk during cannulation is critical. Manes et al.⁵ have already defined that a 14-gauge or 16-gauge catheter is of appropriate size to navigate the narrowest portion of the ET, the isthmus of the osseous ET, and a semirigid microcatheter with a flexible guidewire as suitable for navigating the major curvature. However, the location of the major curvature, what we refer to as the genu, along the length of the ET has not been previously defined. Lack of accounting for the curvilinear structure of the ET in prior studies has likely led to an overall underestimation of total length. Although estimates may be sufficient for the study of structure and function, more direct and precise measurements are necessary when the prospect of safe ET cannulation in patients is under consideration. Detailed surgical anatomy facilitates development of minimally invasive catheter-based systems to provide ET obliteration at any point along its course. The literature review naturally led toward cadaveric dissection for such direct measurements.

A 14-gauge microcatheter with assistance from a flexible guidewire was used to enable the first dual endoscopic cadaveric ET dissection with direct measurements related to its major curvature, or genu. Cannulation was easy when aided by a flexible guidewire navigating curves. Total ET length was found to range from 42 to 52 mm with an average of 47 mm—a value longer than that identified in prior studies per the literature review. This discrepancy could be attributed to the method of measuring the length of catheter positioned within the lumen, accounting for the full curvilinear ET length. The measurements aET and pET have not been reported previously. The pET segment, which contains the isthmus, is only slightly longer than the aET segment. The data we present provide evidence that the increased tET in men may be attributable to a relatively shorter aET in women, whereas the pET segment did not differ; this finding suggests the known sex difference is not simply due to head size.

In the case of treatment for, or prophylaxis against, refractory CSF rhinorrhea via the ET, we envision an endonasal or lateral approach through the ET with introduction of a 14-gauge or

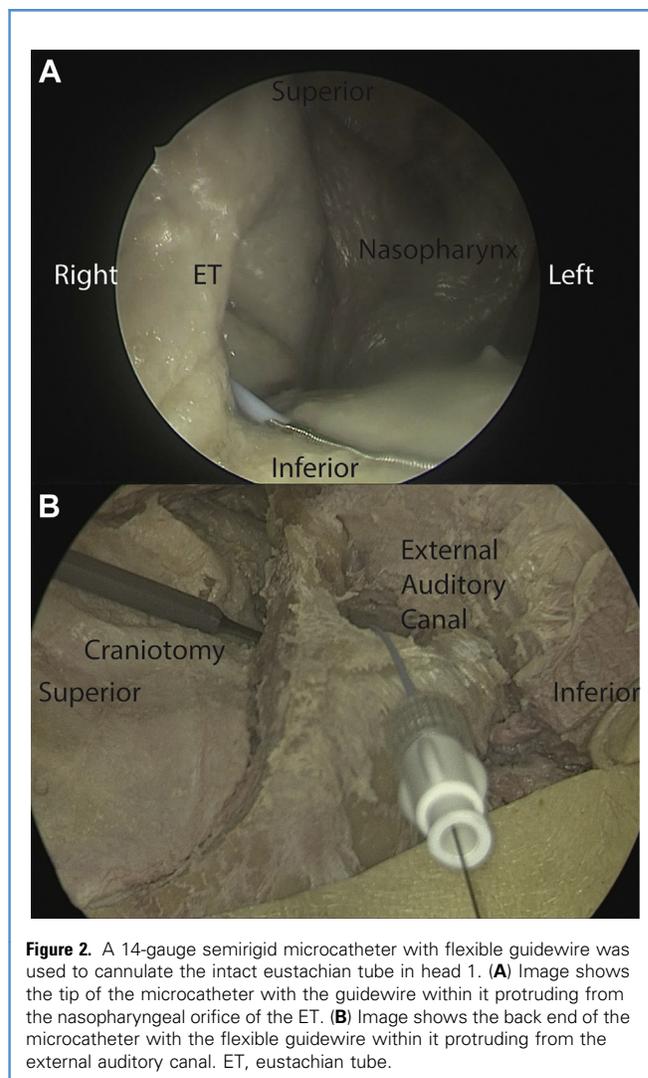
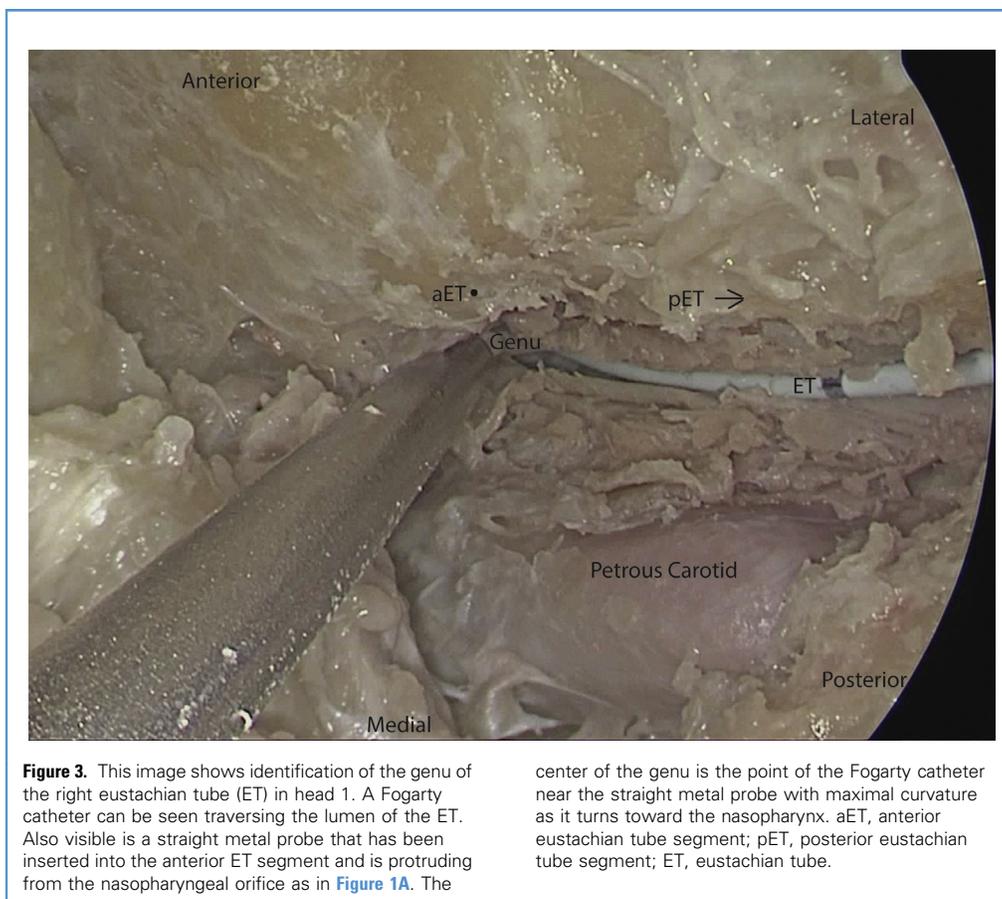


Figure 2. A 14-gauge semirigid microcatheter with flexible guidewire was used to cannulate the intact eustachian tube in head 1. (A) Image shows the tip of the microcatheter with the guidewire within it protruding from the nasopharyngeal orifice of the ET. (B) Image shows the back end of the microcatheter with the flexible guidewire within it protruding from the external auditory canal. ET, eustachian tube.

16-gauge semirigid microcatheter with flexible guidewire to cannulate and then obliterate the lumen from within; techniques for endonasal catheter delivery may build off of similar approaches to dilate the membranocartilaginous segment, such as described by Di Rienzo Businco et al.²³ Such techniques would be useful for both otolaryngologists and neurosurgeons involved in lateral skull-based procedures involving the middle ear, as these practitioners already perform prophylactic middle ear and ET packing as components of these procedures. ET packing in this setting typically involves only obstruction of the tympanic orifice of the ET and destroys structures critical to hearing in the process. Data have suggested that this form of ET and middle ear packing may not achieve the intended benefit of reduced postoperative leak rates.²⁴ It may be that cannulation of the ET for delivery of obstructive material within the lumen, where improved efficacy has been described,²⁵ at the initial surgery could achieve the hoped-for prophylaxis against CSF rhinorrhea with the further benefit of reduced invasiveness. Our findings suggest there would



be approximately 22 mm before encountering the genu from the endonasal approach, possibly shorter by approximately 2 mm for women. Once the genu was successfully navigated, likely requiring aid of the guidewire, there would be at least another 21 mm of length that could be traversed before vulnerable structures of the middle ear might be encountered. The lateral ET approach could see 23 mm until the genu and then another 23 mm to the nasopharyngeal orifice. Once positioned, the catheter could be used to deliver a lumen-filling substance, either artificial or biologic packing material, or cauterizing devices. Further studies are required to develop clinically meaningful tools and techniques for implementation. Questions yet to be explored include whether obstruction is best done with methods that create scar or that deliver packing materials, whether obstructing the entire ET is necessary or obstruction of a particular segment may be sufficient, and how best to avoid injury to critical structures nearby. Definition of surgical parameters is the first step toward standardization.

Study Limitations

Measurements were made by hand, thus introducing human bias and error. An averaging technique was used across 2 measurements separated widely in time, with a third measurement included when the first 2 differed by ≥ 5 mm; it is reassuring that

averaged values across cadavers differed by only ≤ 1.5 mm compared with when the first measurements were used alone.

Measurements presented here were determined in cadavers, which may not entirely recapitulate the *in vivo* ET. The membranocartilaginous segment is well known to be quite flexible, undergoing changes in shape as part of normal function; in a preserved cadaver, this segment is likely far less compliant. As soft tissues tend to contract over time rather than expand during prolonged preservation, we anticipate that the measurements might slightly underestimate the values *in vivo*, although likely on a negligible scale. Similarly, we do not know the precise effects of age on these measurements. It has been shown that the cartilaginous portion of the ET has an increased compliance with age,²⁶ but the small size of this compliance effect is unlikely to influence length measurements. One would not expect the overall shape of a cadaveric ET to be significantly changed. Therefore, as an anatomic and conceptual study, the utility of measurements obtained is not diminished. Further study may include *in vivo* measurements that may be obtained at the time of surgery and in younger subjects (e.g., image-guided safe endoscopic endonasal cannulation of the ET with visualization of the tympanic orifice), or, conversely, during a lateral skull base surgery in a consenting patient without serviceable hearing. Cannulation in this study was from a lateral approach to enable



Figure 4. The setup for dual endoscopic cadaveric dissection involving an endonasal endoscope and lateral exoscope, both fixed in their respective viewing positions, is shown. The viewing monitor on the left shows the exoscope view depicting the Fogarty catheter within the lumen of the left

eustachian tube. The viewing monitor on the right shows the endonasal endoscope view depicting the same Fogarty catheter with the tip protruding into the nasopharynx via the ET orifice.

ease of accurate measurements. The same catheter could be used from a nasopharyngeal approach.

Low sample size ($n = 10$, representing bilateral measurements across only 5 heads) makes statistical comparisons with negative results of poor value. However, even with a small sample size, female heads were noted to have a shorter ET, and it was noted that this difference may be attributed to the segment anterior to the genu, aET, being shorter in female heads. This finding was unanticipated, and as such we did not plan head circumference measurements for comparison before the end of availability of the cadaveric heads. Such a comparison would help to address whether this is due to head circumference alone or to a sex difference; that aET differed by sex but pET did not suggests a sex-related asymmetry in ET shape, which supports the prospect that head circumference may not be the principal cause of sex-related differences in ET length. It is worth noting here again that ET shape was not well accounted for by most prior studies

reporting ET length measures per the literature review. Despite the shortcomings, these data are useful, as they represent the first of their kind directed toward the prospect of EETO. Measurements made relative to the genu have never before been reported, as detailed in the literature review. Further study with expanded sample size and head circumference measurements would be needed to confirm these findings.

We did not combine imaging measurements with our direct cadaveric measurements. However, as detailed earlier, most prior studies describing ET length used computed tomography imaging. As it appears that our direct cadaveric measurement differs from that of prior studies, it would be useful if future work combined direct measurements with measurements from imaging to determine a more accurate, better validated method of ET characterization preoperatively.

This study was not designed to explore the effects of EETO on critical functions of the ear, namely, hearing. It is clear how EETO

Table 1. Literature Review of Eustachian Tube Length Measurement

Author, Year	Number of Subjects	Method	tET (mm)*
Spielberg, 1927 ⁷	Not stated	X-ray; iodized oil injected into ET	30–33
Proctor, 1967 ⁸	Unknown	Gross anatomy; multiply cited values, presumed from cadaver	31–38 (adult)
Todd and Martin, 1988 ⁹	22 adults; 13 right, 9 left	CT; straight line from pharyngeal orifice to ME orifice	38
Robert et al., 1994 ¹⁰	30 cadavers; 6 CT and MRI; 3 MRI only	Catheterize ET for radiographs; on CT/MRI is straight line pharyngeal orifice to TM	35–39 (x-ray); 38 or 39 (CT); 25–30 (MRI)
Sudo et al., 1997 ¹¹	9 adults, 1 side only	30- μ m vertical histology sections virtually reconstructed, pharyngeal orifice to ME orifice	33
Kemaloglu et al., 2000 ¹²	50 adults	Lateral cephalometric radiographs; straight line anterior-inferior ME shadow and inferior point of fissure between pterygoid and maxilla	45.2
Ishijima et al., 2000 ¹³	7 adults, left ET only	Complex histologic method with virtual reconstruction, straight line pharyngeal orifice to TM	37 (left only)
Yoshida et al., 2004 ¹⁴	25 adults (50 ears)	CT MPR; volumetric study of ET components, straight line pharyngeal orifice to TM	36.7
Takasaki et al., 2007 ¹⁵	45 adults (90 ears); 25 children (50 ears)	CT MPR; straight line pharyngeal orifice to TM	42.7 (adults); 37.8 (children)
Tsai et al., 2010 ¹⁶	10 adults, 1 side only	CT with 3D reconstruction; pharyngeal orifice to ME orifice	30.9
Avci et al., 2015 ¹⁷	60 adults (120 ears); 30 M, 30 F	CT in oblique reformat; pharyngeal orifice to TM, cartilaginous part and bony part, junction defined at isthmus, straight line for each	43 (M); 34 (F)
Dinc et al., 2015 ¹⁸	93 adults (124 ears); 46 M (60 ears), 48 F (64 ears)	CT MPR; straight line pharyngeal orifice to TM	40 (M); 38.5 (F)
Yegin et al., 2016 ¹⁹	217 adults (434 ears)	CT MPR; straight line pharyngeal orifice to TM	42.3
Yegin et al., 2017 ²⁰	160 adults 1 side only; 81 F, 79 M	CT MPR; straight line pharyngeal orifice to TM	42.9 (M); 37.6 (F)
Hong et al., 2018 ²¹	8 adults (12 ears)	CT with 3D reconstruction; pharyngeal orifice to TM, cartilaginous part and bony part, junction defined at isthmus, straight line for each	39.3

tET, total eustachian tube length; ET, eustachian tube; ME, middle ear; CT, computed tomography; MRI, magnetic resonance imaging; TM, tympanic membrane; MPR, multiplanar reconstruction; 3D, three-dimensional; M, male; F, female.

*Values are ranges or means.

might be employed with little or no adverse effects in patients without serviceable hearing (i.e., without a level of hearing function useful in daily life even with correction). We recently described such a case in which we performed EETO from an endonasal approach.⁶ However, there remains an important question as to the effects of EETO on patients who otherwise remain with serviceable hearing. This particular topic is not well discussed in related literature to date, but some investigators are optimistic. Orlandi and Shelton²⁷ claim that their iteration of endonasal EETO may have the potential to be reversed at a later date, thus raising the prospect for reversible EETO after the risk of CSF leak has resolved, although a methodology is not described. They endorse that the conductive hearing loss associated with the serous otitis media that may result from ET obstruction could be corrected with a simple hearing aid. This is certainly an area requiring further study. We expect the broad literature on the pathologic condition of ET dysfunction to be quite informative, as EETO in a patient with serviceable hearing

would generate a severe and iatrogenic form of ET dysfunction, a condition that affects many people. It is our expectation that EETO may find utility in patients with serviceable hearing in addition to patients with nonserviceable hearing.

We hope that the work presented here inspires the development of improved techniques for more accurate in vivo ET assessment in individual patients in whom surgical therapy via the ET is being considered. Further studies with larger populations, using either cadavers or in vivo imaging techniques, are recommended.

CONCLUSIONS

This literature review and cadaveric study of the ET suggests that the genu, the major curvature, is an important landmark for safe cannulation. Further research and development are necessary regarding standardization of EETO techniques. The total length of the ET averages 47 mm, and if traversing the lumen from the nasopharyngeal orifice, the genu should be encountered at about

Table 2. Eustachian Tube Length Data

Cadaver	Sex	Ear (side)	tET (mm)	pET (mm)	aET (mm)
1	Female	Right	42	22.5	19.5
1	Female	Left	43	27	16
2	Male	Right	47	23	24
2	Male	Left	53	23.5	29.5
3	Male	Right	49.5	24.7	24.8
3	Male	Left	51.5	24.5	27
4	Female	Right	44.5	24.3	20.2
4	Female	Left	46.5	27	19.5
5	Male	Right	46.5	16.5	30
5	Male	Left	46.5	26	20.5
Average			46.9	23.7	22.7
SD			3.5	3	4.7

tET, total eustachian tube length; pET, posterior eustachian tube segment; aET, anterior eustachian tube segment.

22 mm, although this distance may be shorter in women. Prior studies may have underestimated the length of the ET, and the position of the genu has not been precisely measured previously. These important surgical landmarks will aid further development of EETO procedures. In clinical applications, these surgical parameters will assist surgeons to more accurately and safely perform minimally invasive ET obliteration for prevention and treatment of refractory CSF leak from a lateral skull base source, whether it is performed from an endoscopic endonasal approach or a lateral transtympanic, middle ear, or transmastoid approach. Safe cannulation of the ET may provide an easily standardized approach to expand utilization. This study is also novel in its examination of the ET anatomy from an anterior (endoscopic endonasal) as well as lateral (endoscopic transtympanic) approach.

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