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Prospective Multi-institutional Transnasal Esophagoscopy: Predictors of a Change in Management

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Objectives/Hypothesis: To evaluate clinical indications and endoscopic findings for patients undergoing transnasal esophagoscopy (TNE).

Study Design: Prospective, multi-institutional, observational cohort study at four tertiary centers.

Methods: Demographics, reflux finding score, reflux symptom index, Eating Assessment Tool (EAT-10) scores, clinical indications, and endoscopic findings were compared among patients whose TNE findings resulted in a changes in management (FCIM), defined as a referral, new medication, or surgery recommendation.

Results: Of the 329 patients who were enrolled nine (3%) were unable to complete the exam. In an adjusted regression model, male gender and elevated body mass index were significantly predictive of a positive TNE (P =.013-.045); 51% (n = 162/319) had TNE with FCIM. Common FCIM were esophageal stricture (7.5%), irregular Z-line (27.4%), reflux esophagitis (12.8%), and infectious esophagitis (6.3%) (P <.001-.010). Overall, the average EAT-10 was higher for patients with FCIM (9.7 vs. 5.4) than in those without it (P =.014). Patients with a history of head and neck cancer (HNCA) had FCIM 64% of the time, which rose to 81% if they had both HNCA and dysphagia.

Conclusions: In treatment-seeking patients TNE is predictive of a change in management in males and obese patients. In patients with HNCA and dysphagia, TNE is likely to yield findings that cause a change in management.

Key Words: Transnasal esophagoscopy, esophageal pathology, head and neck cancer, Eating Assessment Tool, odynophagia.

Level of Evidence: 2b.

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INTRODUCTION

In 1994, Shaker published the first report of unsedated transnasal esophagogastroduodenoscopy, which was later adopted by otolaryngology in 1997 by Herrmann and subsequently referred to as transnasal esophagoscopy (TNE).[1,2] Performed under topical anesthesia, TNE is an evaluation of the entire upper aerodigestive tract from the nasal cavities through the gastroesophageal junction without the risks and discomfort of sedating anesthetics.

In 2001, the first small TNE case series evaluated safety and tolerance of office-based endoscopy.[3] Shortly thereafter, Belafsky et al. and Postma et al. demonstrated the ease, high yield results, and further validated safety during in-office TNE to comprehensively evaluate the esophagus in the largest case series worldwide.[4,5] Patients presented for reflux, globus, dysphagia, head and neck cancer screening, biopsy of known lesions, evaluation for esophageal foreign bodies, tracheoscopy, dilation of esophageal stricture, and tracheoesophageal puncture under direct vision. The rate of positive findings on TNE ranged from 43% to 50% in published series.[4–6]

In 2008, the American Broncho-Esophagological Association (ABEA) released a position statement citing evidence for diagnostic accuracy and image quality of TNE when compared with conventional esophagoscopy,

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TABLE I.
Demographic Data.

	Total, N = 319	Change in Management After TNE, N = 162	No Change in Management After TNE, N = 157	*P* Value
Gender, female, n (%)	154 (48.1)	86 (53.1)	58 (43.3)	.081
Age, mean ± SD (range), yr	55.6 ± 15.1 (15–89)	57.1 ± 15.7 (15–89)	53.8 ± 14.3 (23–89)	.052
BMI, mean ± SD (range), kg/m^2	27.8 ± 6.1 (14.7–48.8)	27.3 ± 6.1 (16–48.8)	28.3 ± 6.1 (14.7–45.9)	.148
Race, n (%)				.135
Caucasian	180 (57.3)	95 (60.1)	84 (54.2)	
African American	93 (29.6)	49 (31.0)	44 (28.4)	
Hispanic	29 (9.2)	9 (5.7)	20 (12.9)	
Asian	10 (3.2)	4 (2.5)	6 (3.9)	
Other	2 (0.6)	1 (0.6)	1 (0.7)	
PPI, n (%)				.006
None	90 (28.3)	57 (35.4)	33 (21.2)	
Daily dosing	107 (33.7)	52 (32.3)	55 (35.3)	
Twice-daily dosing	121 (38.0)	52 (32.3)	68(43.6)	
Tobacco use				.059
None	193 (60.9)	89 (56.0)	103 (65.6)	
Current	41 (12.9)	21 (13.2)	20 (12.7)	
Prior	83 (26.2)	49 (30.8)	34 (21.7)	
RFS, mean ± SD (range)	8.2 ± 5.3 (0–35)	7.3 ± 5.1 (0–29)	9.0 ± 5.5 (0–35)	.009
RSI, mean ± SD (range)	17.6 ± 11.4 (0–52)	18.0 ± 11.5 (0–52)	17.3 ± 11.2 (0–47)	.607
EAT-10, mean ± SD (range)	8.7 ± 11.1 (0–40)	9.5 ± 11.4 (0–40)	7.7 ± 10.7 (0–40)	.238
Presenting symptoms, n (%)				
Globus	143 (44.8)	61 (37.7)	82 (52.6)	.007
Sore throat	52 (16.3)	21 (13.0)	31 (19.9)	.142
Cough	97 (30.4)	33 (20.4)	64 (41.0)	<.001
Heartburn	72 (22.6)	35 (21.6)	37 (23.7)	.654
Swallowing trouble	101 (31.7)	67 (41.4)	33 (21.2)	<.001
Throat clearing	118 (37.0	46 (28.4)	72 (46.2)	.001
LPR	74 (23.2)	22 (13.6)	52 (33.3)	<.001
Head and neck CA	65 (20.4)	43 (26.5)	22 (14.1)	.006
Dysphonia	107 (33.5)	41 (25.3)	66 (42.3)	.001
Odynophagia	10 (3.1)	4 (2.5)	6 (3.8)	.483

BMI = body mass index; CA = cancer; EAT-10 = Eating Assessment Tool; LPR = laryngopharyngeal reflux; PPI = proton pump inhibitor; RFS = Reflux Finding Score; RSI = Reflux Symptom Index; SD = standard deviation; TNE = transnasal esophagoscopy.

as well as safety, cost savings, and patient preference and satisfaction supporting the use of in-office TNE.[7]

Over the past decade, TNE has become a widely accepted tool in the otolaryngologist's diagnostic armamentarium, and its use has increased. However, despite this increase, indications for and efficacy of TNE have not been well defined or widely accepted. This is the first multicenter prospective study to be undertaken simultaneously by four institutions across the United States to evaluate the indications and patient population for which TNE has the highest yield, hoping to establish future guidelines for the use of TNE.

MATERIALS AND METHODS

Study Population

We conducted a prospective, multi-institutional study to evaluate the role and indications for in-office TNE at four tertiary referral centers (three academic and one private practice). The study population consisted of adult patients who were undergoing TNE secondary to symptoms of dysphagia, traditional laryngopharyngeal reflux symptoms that have been present for at least 3 months, or patients presenting with head and neck cancer (Table I). Those patients with abdominal pain, nausea, or vomiting were excluded from the study, as they were not candidates for TNE due to the elevated risk of gastric or duodenal pathology. As the patients recruited were presenting for TNE, participation in the study incurred no additional risk to these patients. The risks of TNE included temporary mild nasal and epigastric discomfort, epistaxis, and vasovagal reaction. Institutional review board approval was obtained at each individual institution enrolling patients.

Statistical Analysis

Demographic data were summarized for categorical and continuous measures. Means and ranges are presented for continuous data. Categorical variables are presented as percentages. Continuous data was compared between groups using the

Student t test. Categorical data were compared among more than two groups using the nonparametric Kruskal-Wallis test. Univariable and multivariable regression modeling was carried out with change in management as the primary outcome. P values <.05 were considered significant. All analyses will be performed using Stata 12 (StataCorp, College Station, TX).

RESULTS

From 2012 to 2015, 329 patients were enrolled and nine were excluded due to patient intolerance during the exam. Our outcome measure was defined as findings that resulted in changes in management (FCIM), where a new medication was prescribed, a referral was made, or surgery was recommended.

Demographic characteristics in adults prior to in-office TNE are presented in Table I. Our patients ranged in age from 18 to 89 years, with a median of 55 years of age. Body mass index (BMI) ranged from 14.7 to 48.8 kg/m^2. Our study enrolled almost twice as many Caucasian patients (n = 180) compared to African American patients (n = 93). Characteristics of patients who had a change in management are also presented and compared in Table I. The groups did not differ in gender, age, BMI, race, or tobacco use. When assessing proton pump inhibitor (PPI) use prior to TNE, patients not currently taking a PPI were likely to have a change in management, patients taking a PPI daily were equivalent, and patients on a twice-daily PPI were unlikely to have a change in management (P =.006). Evaluating the data from validated survey instruments (Reflux Symptom Index [RSI] and Eating Assessment Tool [EAT-10]) were higher in patients with a change in management but were not statistically significant. The Reflux Finding Score (RFS) was statistically significant, but paradoxically, it was lower in those with FCIM (P =.009) and therefore unlikely to have clinical significance. Patients presenting with sore throat, heartburn, or odynophagia were all unlikely to have FCIM. However, those with globus (P =.007), cough (P <.001), swallowing trouble (P <.001), throat clearing (P =.001), laryngopharyngeal reflux (LPR) (P <.001), head and neck cancer (P < .001), and dysphonia (P =.001) were likely to have FCIM.

Endoscopic findings during in-office TNE that caused a change in provider management after evaluation are presented in Table II; 51% (n = 162/319) of patients who underwent TNE had FCIM. Common findings causing change in management were esophageal stricture (7.5%), irregular Z-line (27.4%), reflux esophagitis (12.8%), and infectious esophagitis (6.3%) (P < .001-.010). Patients presenting with rings, hiatal hernia, ulcer, varices, or decreased esophageal motility were positive for pathology not associated with FCIM. Stricture (P < .001), infectious esophagitis (P < .001), and tumor (P < .014), however, were all statistically associated with FCIM. Findings of irregular Z-line (P <.001) or reflux esophagitis with severity recorded according to the Los Angeles Classification were more likely to cause a change in management (P < .001).[8]

In an adjusted regression model controlling for gender, age, smoking status, PPI use, and presenting symptoms (as listed in Table I), only male gender and elevated BMI were predictive of a positive TNE with FCIM, whereas patients with odynophagia were unlikely to have FCIM (P =.013-.045). The average EAT-10 was higher for patients with FCIM (9.7 vs. 5.4) than in those without (P = .014). Surprisingly, patients with head and neck cancer (HNCA) were unlikely to have FCIM in the adjusted regression.

In a subset analysis looking at HNCA patients alone (n = 67), 64% (n = 43) had a change in management after in-office TNE. However, 81% of patients with both HNCA and swallowing difficulty (n = 36) had FCIM (n = 29). In patients with HNCA and swallowing difficulty with FCIM, EAT-10 scores were higher that those with HNCA with FCIM alone (20.6 vs. 15.5).

DISCUSSION

The largest worldwide TNE case-series, reported by Postma et al., demonstrated a 50% positive finding rate.[5] Our data are the first multi-institutional, prospective study to not only evaluate findings on TNE but findings that resulted in a change in patient care (FCIM). Our study demonstrated 51% of TNE with FCIM. The third largest case series from the United Kingdom showed a 44% positive rate in outpatient TNE, with a 15% gastrointestinal referral rate compared to our 18.1%.[9]

According to the American Gastroenterological Association (AGA) Medical Position Statement on the Management of Barrett's Esophagus (BE), there remains continued variability in the diagnosis of BE and dysplasia and even more controversy regarding management and surveillance. The annual incidence of esophageal cancer in patients with biopsy proven, intestinal metaplasia or BE, is 0.5% per year. Therefore, according to the AGA in the general population with gastroesophageal reflux disease (GERD), the recommendation is strongly against screening for Barrett's esophagus due to cost-effectiveness, risk of cardiovascular complications from sedation, in addition to the psychological and financial burden on patients themselves. There is a weak recommendation of esophageal screening for patients with multiple risk factors associated with adenocarcinoma of the esophagus: age >50 years, male sex, white race, chronic GERD, hiatal hernia, obesity, and intra-abdominal distribution of body fat.[10] The current study's results show that obesity and male gender are at higher risk for FCIM, which is in concordance with these guidelines.

Furthermore, according to the AGA Medical Position Statement on the Management of Gastroesophageal Reflux Disease, an empiric trial of a twice-daily PPI for GERD and once- or twice-daily PPI for extraesophageal GERD is recommended prior to consideration of endoscopy.[11] LPR was addressed by the American Academy of Otolaryngology–Head and Neck Surgery position statement in 2002 advocating at least a twice-daily PPI.[12] According to the 2015 ABEA survey, otolaryngologists more commonly treat LPR empirically, but dosing of PPI therapy and adjunctive testing remains controversial.[13] One of four providers in our study used negative TNE

TABLE II.
Findings at the Time of TNE for Those Patients Who Did and Did Not Have a Change in Management Based Upon Their TNE Findings.

	Total, N = 319	Change in Management After TNE, N = 162	No Change in Management After TNE, N = 157	*P* Value
TNE findings, n (%)				
Stricture				<.001
None	294 (92.5)	139 (86.3)	155 (98.7)	
Neopharynx	11 (3.5)	11 (6.8)	0 (0)	
Proximal	12 (3.8)	10 (6.2)	2 (1.3)	
Rings				.761
None	288(91.2)	144 (90.6)	144 (91.7)	
Schatzki	25 (7.9)	15 (9.4)	10 (6.4)	
Muscular	2 (0.6)	0 (0)	2 (1.3)	
Irregular Z-line	87 (27.5)	57 (35.8)	30 (19.1)	<.001
LA esophagitis classification				<.001
None	278(87.2)	129 (79.6)	149 (94.9)	
NEE	15 (4.7)	10 (6.2)	5 (3.2)	
Class A	5 (1.6)	3 (1.9)	2 (1.3)	
Class B	10 (3.1)	9 (5.6)	1 (0.6)	
Class C	11 (3.4)	11 (6.8)	0 (0)	
Infectious esophagitis	20 (6.3)	20 (12.6)	0 (0)	<.001
Hiatal hernia	84(26.4)	40 (25.0)	44 (28.0)	.543
Tumor	6 (1.9)	6 (3.8)	0 (0)	.014
Eosinophilic esophagitis	3 (1.0)	3 (1.9)	0 (0)	.084
Ulcer	1 (0.3)	1 (0.6)	0 (0)	.321
Varices	3 (1.0)	1 (0.6)	2 (1.3)	.556
Decreased motility	11 (3.5)	8 (5.0)	3 (1.9)	.131
Diverticuli	0 (0)	0 (0)	0 (0)	NA
Biopsy done	75 (23.8)	41 (25.5)	34 (21.7)	.425
Complications	1 (0.3)	0 (0)	1 (0.6)	.309
Referral, n (%)				<.001
None	247 (77.5)	98 (60.5)	149 (94.9)	
GI	58 (18.1)	50 (30.9)	8 (5.1)	
Allergy	5 (1.6)	5 (3.1)	0 (0)	
Other	8 (2.5)	8 (4.9)	0 (0)	
New medication prescribed, n (%)	59 (18.4)	58 (35.8)	1 (0.8)	<.001
Dilation, n (%)	21 (6.6)	20 (12.5)	1 (0.6)	<.001

GI = gastrointestinal; LA = Los Angeles; TNE = transnasal esophagoscopy; NEE = non-erosive esophagitis.

findings to decrease PPI therapy. However, due to our definition for change in management (addition of medication, referral to specialist, or surgical consultation), this was not delineated in our results. Given this information, however, a negative TNE may have value for de-escalation of therapy, although the efficacy of this has not been established.

In the ABEA position statement on TNE, indications were divided into three categories: esophageal (dysphagia, refractory GERD, abnormal imaging, BE screening); extraesophageal (globus, panendoscopy with biopsy for head and neck cancer, chronic cough, LPR); and procedural (biopsy, esophageal balloon dilation, secondary tracheoesophageal puncture, delivery of flexible lasers, and insertion of wireless pH devices).[7] Our study was designed to evaluate patient demographics and clinical indications with the highest yield for TNE. Univariate regression modeling demonstrated little value in patients presenting with sore throat, heartburn, or odynophagia. However, only 10 patients complained of odynophagia. Globus, cough, swallowing trouble, throat clearing, LPR, head and neck cancer, and dysphonia were more likely to have FCIM. On multivariant regression analysis, however, male gender and obesity were the only two factors (demographics and patient characteristics included) that demonstrated statistical significance. The RSI and EAT-10 were not significant. The RFS did show significance on univariate analysis, though paradoxical, with a lower RFS being associated with a higher likelihood of FCIM, In addition, RFS was not predictive in the regression model. Although inclusion criteria were symptoms of >3 months duration, our

study did not correlate duration of symptoms in relation to positive TNE findings, which may be considered in future studies.

Finally, in the subgroup analysis on head and neck cancer, compared to the overall 51% FCIM, patients with HNCA alone had 64% FCIM. Further evaluating patients who presented with HNCA and swallowing difficulty, 81% demonstrated FCIM. The population of patients treated for HNCA was only 20% of the case cohort, limiting the statistical power for this study. EAT-10 scores increase in patients with HNCA with FCIM and even more in HNCA with swallowing difficulties.

In the United States, Farwell et al. described a prospective TNE cohort in patients at least 3 months after completion of HNCA treatment, with only 13% described as normal, and the most common findings were peptic esophagitis (63%), esophageal stricture (23%), and carcinoma (4%).[14] From Taiwan, metachronous esophageal squamous cell carcinoma (5.1%, 15/398) was detected on TNE in routine cancer surveillance in patients treated with HNCA.[15] In another small case series from Taiwan, among 33 patients with new-onset dysphagia and previous primary HNCA treatment who completed TNE, there was one local recurrence at the primary site, seven newly diagnosed hypopharyngeal cancers, four with isolated esophageal cancer, and one with previous epiglottic cancer who had simultaneous hypopharyngeal and esophageal cancer. The mean interval between completion of treatment and evaluation ranged from 6 months to 240 months, with an average of 36 months.[16] Lin et al. demonstrated synchronous HNSCC and esophageal squamous cell carcinoma in 33% of patients with history of HNCA with swallowing disorders.[17]

Given the paucity in the literature on TNE utilization in the HNCA population worldwide, the subgroup analysis on head and neck cancer patients in our study showed promising data for future directions. TNE in HNCA should be included in future studies.

CONCLUSION

In treatment-seeking patients TNE should be considered in patients with obesity or male gender regardless of presenting symptoms. Physicians should have a high index of suspicion in patients with a history of head and neck cancer and dysphagia, as TNE is likely to yield findings that cause a change in management.

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