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Demographic and clinical characteristics of patients with nonspecific esophageal motility disorder

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ABSTRACT

Aim: Although nonspecific esophageal motility disorder(NEMD) is the most common diagnosis in manometry, unlike other primary esophageal disorders, it is the least known and least studied disorder in the literature. Studies with a small number of patient groups have been reported in the literature. The aim of this study is to share the demographic and clinical characteristics of the single center high-volume NEMD patients we have followed up.

Material and Method: The study was carried out retrospectively by examining the motility records of 391 patients diagnosed with NEMD in the motility laboratory of the gastroenterology clinic of our hospital. 20-year motility laboratory records between 1991 and 2019 were reviewed.

Results: The mean age of 391 patients diagnosed with NEMD was 49.08±14.4 (18-90). 213 (54.5%) of them were female, and 178 (45.5%) of them were male. The primary symptom was reflux in 56.8% (222/391) of the patients, and dysphagia in 43.2% (169/391). While there was no esophagitis in 78.2% of the patients who had endoscopy, esophagitis was found in 21.8% of them. Pathological reflux was detected in 73.5% of the patients whose 24-hour pH was measured. In the repeated manometry results of patients due to increased complaints in their follow-up whose initial manometry findings were compatible with NEMD, 18 patients were diagnosed with achalasia, 5 patients with nutcracker esophagus, and 4 patients with diffuse esophageal spasm (DES).

Conclusion: The majority of patients with NEMD are associated with reflux. Patients with NEMD who do not have endoscopic and radiological organic disorders should be re-evaluated with manometry and further examinations if their complaints persist.

Keywords: Nonspecific esophageal motility disorder, esophageal manometry, gastroesophageal reflux

INTRODUCTION

Motility disorders that are not associated with causes such as esophageal stenosis or cardia tumor and that are not caused by neurological, muscular or other systemic disorders are called primary esophageal motility disorders. In conventional manometry, primary esophageal motility disorders are classified as achalasia, diffuse esophageal spasm (DES), nutcracker esophagus, hypertensive and hypotensive lower esophageal sphincter and nonspecific esophageal motility disorder (NEMD) (1,2). While the diagnostic criteria of primary esophageal motility disorders other than NEMD are certain, those that cannot be classified according to a certain criterion are called NEMD (2,3). Findings in conventional esophageal manometry that cannot be classified in other known primary motility disorder criteria, non-conducted contractions (>20%) in response to wet swallowing, retrograde contractions, repetitive contractions (>2 peaks), low amplitude contractions (<30 mm Hg), prolonged contraction time (>6 secs), high amplitude contractions (>180 mm Hg), spontaneous contractions, incomplete lower esophageal sphincter (LES) relaxation are called NEMD (1-5).

Although NEMD is the most common diagnosis in manometry (1,2), unlike other primary esophageal disorders, it is the least known and least studied disorder in the literature. Studies with a small number of patient groups have been reported in the literature. The aim of this study is to share the demographic and clinical characteristics of the single center high-volume NEMD patients we have followed up.

MATERIAL AND METHOD

Patients

The study was carried out retrospectively by examining the motility records of 391 patients diagnosed with NEMD in the motility laboratory of the gastroenterology clinic of our hospital. After obtaining approval from the

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Ankara Bilkent City Hospital No: 2 Clinical Researches Ethics Committee (Date: 01.03.2023, Decision No: E2-23-3579), the motility laboratory records between 1991 and 2019 were reviewed. Demographic characteristics of the patients, complaints at admission, 24-hour pH meter and esophageal manometry results were evaluated. Those younger than 18 years of age, those with another primary esophageal motility disorder, those with rheumatologic or systemic disorder that may involve the esophagus, patients with organic disorders in the esophagus, and those with a history of esophagus and stomach surgery for any reason were excluded from the study. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Manometry Protocol

After 8 hours of fasting, the manometric catheter was inserted nasally into the stomach. Esophageal motility was assessed using conventional esophageal manometry (Dentsleeve; Dentsleeve International, Mui Scientific, Mississauga, Ontario, Canada). Conventional manometry uses an 8-channel polyvinyl catheter with a Dent sleeve. The catheter is placed in the lower esophageal sphincter (LES) and sensors evaluate LES relaxation and pressure and esophageal contractions. After the sleeve area of the catheter was placed in the lower esophagus, esophageal motor functions were assessed with 10 wet swallows at 20-second intervals and the results were interpreted according to the recommendations of the American Gastroenterological Association (6-8).

pH Monitoring Protocol

Use of medications that could affect the gastric pH of the patient was terminated 7 days before the procedure and 24-h esophageal pH monitoring was performed after 8 hours of fasting. The distal sensor of the PHI15/PHN15 dual pH catheter (Sandhill Scientific Inc., Highlands Ranch, CO, USA) was placed 5 cm above the LES and 20 cm above the proximal sensor. A pH monitor was used to record findings for 24 hours after the catheter was fixed in the nose. The presence of distal and proximal reflux was investigated and the results were interpreted according to the recommendations of the American Gastroenterological Association (7,8).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Among the numerical variables, those with normal distribution are shown as mean±standard deviation, and those with normal distribution are shown as median (min-max). Categorical variables are expressed as numbers and percentages.

RESULTS

The mean age of 391 patients diagnosed with NEMD was 49.08±14.4 (18-90). Of these, 213 (54.5%) were female, and 178 (45.5%) were male. The primary symptom was gastroesophageal reflux in 56.8% (222/391) of the patients, and dysphagia in 43.2% (169/391). While there was no esophagitis in 78.2% of the patients who had endoscopy, esophagitis was found in 21.8% of them. Pathological reflux was detected in 73.5% of the patients whose 24-hour pH was measured. In the repeated manometry results of patients (due to increased complaints in their follow-up) whose initial manometry findings were compatible with NEMD, 18 patients were diagnosed with achalasia, 5 patients with nutcracker esophagus, and 4 patients with DES (**Table 1**).

Table 1. Demographic and characteristics of the patients

Gender	
Female (%)	213 (54.5%)
Male (%)	178 (45.5%)
Mean Age (years)	49.08±14.4 (18-90)
Application complaint	
Dysphagia	43.2% (169/391)
Reflux symptoms, %,n	56.8% (222/391)
Esophagitis	
Endoscopy report could not be reached in 180 patients	
In the endoscopy of 211 patients	
No esophagitis	78.2%
Grade A esophagitis	10.9%
Grade B esophagitis	9.9%
Grade C esophagitis	1%
pH meter	
Reflux was not studied in 195 patients	
Reflux was studied in 196 patients	
Has pathological reflux	73.5% (144/196)
No pathological reflux	26.5% (52/196)
Mean LESP (mmHg)	15.6±11.91
End of follow-up	
Achalasia	18
Nutrcacker esophagus	5
Diffuse esophageal spasm	4

LESP: Lower esophageal sphincter pressure

Evaluating the contractions in the esophageal body in manometry, 71.3% of the patients had normal peristalsis, 28.7% of them had non-peristaltic contractions. In 63.4% (248/319) of them, the contraction amplitude of the esophageal body was low (< 30 mmHg). Some contractions were not transmitted distally in 70 patients and interrupted contractions were detected in 26 patients. In addition, 97 (67.4%) of 144 patients with pathological reflux on a 24-hour pH meter had low esophageal body contraction amplitude (**Table 2**).

Table 2. Evaluation of contraction amplitudes in theesophageal body in manometry.

	Patients, n (%)
Peristaltic contraction	279 (71.4%)
Non-peristaltic contraction rate	112(28.6%)
≤ 30%	48
40-50%	45
≥60	19
Normal amplitüde contraction	138 (35.3%)
Low amplitude contraction	248 (63.5%)
High amplitude contraction	5 (1.2%)
10% contraction	2
20% contraction	2
30% contraction	1
Interruptered contraction	26
≤ 30%	19
40-50%	7
Nontransmitted contraction	70
≤ 30%	52
40-50%	18
Normal contraction duration	380 (97.2%)
Prolonged contraction	11 (2.8%)
Mean contraction duration	10.36±1.53 (8-13.5)
Tripled-peaked contraction	6
Complete LES relaxation	307 (78.6%)
Incomplete LES relaxation	79 (20.2%)
≤ 30%	11
40-50%	25
≥60	43
Noncomplete LES relaxation contraction (only 10% noncomplete relaxation)	5 (1.2%)

LES: Lower esophageal sphincter

The pH meter was studied in 161 of 222 patients whose primary complaint was reflux, and the procedure could not be performed in 61 patients because they did not accept or tolerate the pH meter. In 35 patients, whose primary complaint was dysphagia and who also had reflux symptoms, manometry was performed first, and a pH meter was also performed upon detection of NEMD in manometry. As a result, the pH meter results of a total of 196 patients were examined. Pathological reflux was detected in 144 (73.5%) of the patients whose 24-hour pH values were measured (Pathological reflux was detected in the distal esophagus in 102 patients and in the proximal and distal esophagus in 42 patients). Comparing the demographic characteristics to esophageal manometry findings of patients with and without reflux in patients whose 24-hour pH values were measured, statistically more reflux was found in males than in females. No significant correlation was found between other findings in manometry and reflux (**Table 3**).

Manometry was performed again in 87 patients due to the persistence of their complaints. As a result of repeated manometry, 18 patients were diagnosed with achalasia, 5 patients with nutcrucker esophagus, and 4 patients with diffuse esophageal spasm. 18 patients who were initially diagnosed with NEMD were diagnosed with achalasia after 1 to 4 years of follow-up, and they undergone balloon dilatation therapy. In the initial manometry of the patients diagnosed with achalasia, LESP was greater than 45 mmHg in 5 patients, and LES relaxation was normal in 11 patients; 7 of them had >20% incomplete swallowing relaxation, and >20% of esophageal wet swallows were aperistaltic in 9 of them; 7 of them had contraction amplitudes less than 30 mmHg at >20% swallowing, only 1 patient had contraction amplitudes averaging 240 mmHg in 30% of swallows. Due to the increasing complaints of this patient, type 3 achalasia was diagnosed by repeat manometry performed in the center where high-resolution manometry was performed. (**Table 4**).

Table 3. Manometric and demographic characteristics of patients with reflux studied.

n= 196	Reflux positive (n=144, 73.5%) (n)(%)	Reflux negative (n=52, %26.5) (n),(%)	p
Gender			
Female (n=112)	76 (67.9)	36 (32.1)	0.04
Male (n=84)	68 (81)	16 (19)	
Mean age (years)	46.9±13.02	48.5±14.0	0.52
LESP (mmHg)	14.36±10.65	14.86±12.7	0.78
Non-peristaltic contraction			
Yes (n=48)	38 (79.2)	10 (20.8)	0.3
No (n=148)	106 (71.6)	42 (28.4)	
Incomplete LES sphincter relaxation			
Yes (n=26)	18 (69.2)	8 (30.8)	0.59
No (n=170)	126 (74.1)	44 (25.9)	
Interruptered contraction			
Yes (n=13)	11 (84.6)	2 (15.4)	0.52
No (n=183)	133 (72.7)	50 (27.3)	
Nontransmitted contraction			
Yes (n=40)	32 (80)	8 (20)	0.32
No (n=156)	112 (71.8)	44 (28.2)	

LESP: Lower esophageal sphincter pressure, LES: Lower esophageal sphincter

Table 4. Initial manometry findings of patients diagnosed with achalasia in their follow up.

Gender	
Female, n (%)	12 (66.7%)
Male, n (%)	6 (33.3%)
Mean age (years)	50.44±11.52 (35-80)
Application complaints	
Dysphagia, n(%)	12 (66.7%)
Reflux symptoms, n(%)	6 (33.3%)
The mean time for patients to be diagnosed with achalasia (years)	1.72±0.89 (1 – 4)
Mean LESP (mmHg)	30 ±15.43
Normal (10 – 45 mmHg), n,(%)	13 (72.3%)
High (> 45 mmHg) , n,(%)	5 (27.7%)
LES relaxation	
Normal relaxation, n (%)	11 (61.1%)
Incomplete relaxation, n (%)	7 (38.9%)
Normal peristaltic contraction, n (%)	9 (50%)
Non-peristaltic contraction, n (%)	9 (50%)
Normal amplitude contraction	10 (55.6%)
Low amplitude contraction, n (%)	7 (38.9%)
High amplitude contraction, n (%)	1 (5.5%)

LESP: Lower esophageal sphincter pressure, LES: Lower esophageal sphincter

DISCUSSION

Although NEMD was identified by Sanderson et al. (9) in 1967, few studies have been reported in the literature on its clinical significance or course.

Our study showed that this disorder is mostly seen in middle aged persons, and it is seen a little more in women. Patients mostly present with reflux-like symptoms or dysphagia. In approximately two-thirds of patients, the esophagus is exposed to pathological acid exposure.

GERD-associated motility abnormality has been classified as NEMD in some studies (2, 10). NEMD is mostly named as ineffective esophageal motility (IEM) according to the Chiago classification in high resolution esophageal manometry (2, 11, 12). It is still controversial whether NEMD is a primary esophageal motility disorder or whether the abnormality is secondary to acid-induced pathological damage to the esophagus. It has been shown that disorders in esophageal motility (absent or incomplete contractions, weak contractions) play a role in the pathogenesis of GERD (11, 13). In a study (2), 52.8% of reflux patients had NEMD, 43.8% had normal manometry findings, and 4% had nutcracker esophagus. As seen in this study, NEMD was detected in 94% of GERD patients with abnormal esophageal motility. Again in this study, more severe acid exposure was reported in 24-hour pH meters of patients with NEMD. In our study, we found reflux in approximately three-fourths (73.5%) of NEMD patients whose reflux was studied, and reflux was even higher in males. Considering the prevalence of reflux normally seen in the community, NEMD is largely associated with reflux, as seen in our study.

Contrary to studies (14,15) claiming that abnormal esophageal motility impairs esophageal acid clearance and therefore facilitates the development of mucosal damage in the esophagus, in other studies, no difference was observed in terms of mucosal damage in the esophagus between those with normal or abnormal motility in patients with pathological acid reflux (2, 16, 17). In our study, although we detected reflux in the pH meter in most of the patients, only 21.8% of them had mucosal damage endoscopically.

NEMD is associated with disturbances in the conduction of contractions in the esophageal body and relaxation in the lower esophageal sphincter (1, 2, 18). Müller M et al. (1) reported non-peristaltic contractions in more than half of the patients, prolonged contractions in 22.4%, low-amplitude contractions in 15%, and incomplete LES relaxation in 15.8% of the patients with NEMD. In our study, we found low-amplitude contractions in more than half of the patients, non-peristaltic contractions in 28.6%, and incomplete LES relaxation in 20.2%.

Manometry of the patients diagnosed with NEMD because they do not meet the diagnostic criteria for other primary esophageal motor diseases was repeated due to the continuation or increase of their complaints; 18 of these patients were diagnosed with achalasia, 5 with nutcracker esophagus, and 4 with DES. Müller et al. (1) diagnosed 53.6% of the patients with achalasia as a result of manometry repetitions in the four-year follow-up of the patients with NEMD. In another study, 23% of patients reported progression to achalasia and 14% to DES. (19, 20, 21).In another study, progression to nutcracker esophagus was reported in 14.3% of patients. (8). Unlike our study, these studies reported higher rates. This may be due to the manometry catheter being studied and the different patient populations. In our study, manometry was not performed again on all patients who were initially diagnosed with NEMD during their follow-up, but only on patients who had complaints and applied to us, thus our lower rates. In addition, we found esophageal dysmotility secondary to reflux in the majority of our patients.

The limitations of this study were that the changes in the complaints and motility of the patients could not be evaluated in the long-term follow-up because the study was retrospective, and endoscopy and 24-hour Ph-meter measurement were not performed in all patients. Although our unit is one of the largest motility laboratories in our country, conventional manometric methods are still used for reasons not caused by us. Although the manometry we used had superior Dentsleeve than other conventional manometry, high resolution manometry was not used. We could not performed detailed symptom evaluation because the patients were recorded only to have dysphagia and reflux symptoms in their initial complaints.

CONCLUSION

Patients with NEMD usually admit to the clinic with symptoms of dysphagia or reflux. It should not be forgotten that the majority of patients with NEMD are associated with reflux. Patients with NEMD who do not have endoscopic and radiological organic disorders should be re-evaluated with manometry and, if necessary, with further examinations if their complaints increase.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Bilkent City Hospital No:2 Clinical Researches Ethics Committee (Date: 01.03.2023, Decision No: E2-23-3579).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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