

Manometric findings in patients with isolated distal gastroesophageal reflux

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Abstract

AIM: To analyze manometric abnormalities in patients with isolated distal reflux and compare these findings in patients with erosive and non-erosive disease.

METHODS: Five hundred and fifty patients who presented to the outpatient clinic of Türkiye Yuksek Ihtisas Hospital with gastroesophageal reflux disease-like symptoms were enrolled. Each individual was evaluated with esophageal manometry, 24-h ambulatory pH monitoring, and upper gastrointestinal endoscopy. Manometric findings for the patients with isolated distal reflux were compared to findings in controls who were free of reflux disorders or hypersensitive esophagus. Findings for isolated distal reflux patients with and without erosive reflux disease were also compared.

RESULTS: Of the 550 subjects enrolled, 97 (17.6%, mean age 48 years) had isolated distal reflux and 100 had no abnormalities on ambulatory pH monitoring (control group, mean age 45 years). There were no significant differences between the isolated distal reflux group and control group with respect to age, body mass index, and esophageal body contraction amplitude (EBCA). Mean lower esophageal sphincter pressure was significantly higher in the control group (12.7 ± 10.3 mmHg vs 9.6 ± 7.4 mmHg, $P = 0.01$). Fifty-five (56.7%) of the 97 patients with isolated distal reflux had erosive reflux disease. There were no statistical differences between the erosive reflux disease and non-erosive reflux disease subgroups with respect to mean EBCA, lower esophageal sphincter pressure, or DeMeester score.

However, 13% of patients with gastroesophageal reflux disease had distal wave amplitudes ≤ 30 mmHg, whereas none of the patients with non-erosive reflux disease had distal wave amplitudes in this low category.

CONCLUSION: Patients with erosive and non-erosive disease present with similar manometric abnormalities. The only striking difference is the observation of very low EBCA exclusively in patients with erosive disease.

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Key words: Esophageal motility disorders; Isolated distal reflux; Gastroesophageal reflux disease; Manometry; Esophagitis

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is defined as the pathological retrograde movement of gastric contents into the esophagus. Patients with GERD are typically categorized into one of 3 groups: those without esophagitis [suffering from non-erosive reflux disease (NERD)]; those with esophagitis [suffering from erosive reflux disease (ERD)], and those with complicated forms of GERD^[1].

Non-erosive reflux disease is the most common presentation of GERD^[2]. Peristaltic dysfunction of the esophagus is well documented in cases of GERD^[3,4]. The main esophageal motility disorder in these patients is ineffective esophageal motility (IEM)^[5].

Gastroesophageal reflux can be classified as isolated proximal reflux (IPR), isolated distal reflux (IDR), or both proximal and distal reflux as determined by ambulatory pH monitoring. Whereas increased acid clearance time and IEM are strongly associated with IPR^[6], there are no data

that conclusively link motility disorders with IDR. Our aim in this study was to investigate manometric measurements in patients with IDR and compare the findings in individuals with and without erosive esophagitis.

MATERIALS AND METHODS

Between January 2000 and July 2002, 550 patients with GERD-like symptoms were screened for the study. These individuals had typical GERD symptoms (acid regurgitation and heartburn) or extraesophageal symptoms (hoarseness, asthma-like clinical presentation, nocturnal cough, and nocturnal waking). They were evaluated at the outpatient clinic of Turkiye Yuksek Ihtisas Hospital's Gastroenterology Unit, which is a tertiary referral center. Demographic characteristics and body mass index (BMI) were recorded for each patient.

All subjects were referred to our motility unit for 24-h pH monitoring and manometric studies. Each was assigned to one of 5 groups according to the pH results: (1) those with IDR; (2) those with IPR; (3) those with both proximal and distal reflux; (4) those with hypersensitive esophagus; (5) those with normal findings.

All patients underwent gastrointestinal endoscopy. Individuals with GERD whose esophageal mucosa appeared normal on esophagogastroduodenoscopy were considered to have NERD. Those with varying degrees of esophagitis were considered to have ERD.

Patients were excluded if they had Barrett's esophagus, hiatal hernia, esophageal varices, connective tissue disease, primary esophagus disease, or had undergone endoscopic therapy. Informed consent was obtained from each participant and the study was approved by our hospital's ethics committee. All patients underwent esophagogastroduodenoscopy, esophageal manometry, and ambulatory 24-h pH monitoring as described below.

Esophagogastroduodenoscopy was performed after a 10-h fast using an Olympus GIF XQ endoscope (Tokyo, Japan). Local anesthesia was administered (1% xylocaine) and the esophagus, stomach and duodenum were evaluated. During endoscopy, special attention was paid to the distal esophageal mucosa. Patients with esophagitis were classified according to the Los Angeles classification^[7]: Grade A, mucosal break < 5 mm in length; grade B, mucosal break > 5 mm; grade C, mucosal break continuous between > 2 mucosal folds; grade D, mucosal break > 75% of the esophageal circumference.

Esophageal manometry was carried out using a Medical Measurement Systems (MMS) unit (ver. 8.4i Beta) and an 8-channel Dent-sleeve catheter. Lower esophageal sphincter pressure (LESP) and esophageal body contraction amplitude (EBCA) were recorded. Based on these findings, patients were categorized as normal, hypotensive lower esophageal sphincter, or IEM^[8].

Ambulatory 24-h pH monitoring was performed using a Synetics Digrapper MHIII machine and double-channel, 15 cm antimony catheter. Findings were recorded and analyzed using Microsoft esophagram version 2.04. Based on the results, patients were categorized as normal, IDR, IPR, both proximal and distal reflux, or hypersensitive esophagus^[9-12]. Hypersensitive esophagus

was defined if the symptom index for distal measurements (symptom index = number of symptoms at pH < 4 / total number of symptoms) was $\geq 50\%$ while there was no measurable distal or proximal reflux.

Acid reflux was defined as a fall in esophageal pH below 4. All standard parameters (DeMeester score, percentage of time below pH 4, number of reflux episodes and number of long reflux episodes) were determined throughout the study period^[13].

A control group was established based on the combined results from the above battery of tests. Individuals who were free of abnormal esophageal conditions (distal or proximal esophageal reflux, or hypersensitive esophagus) comprised this group. Subjects were asked not to take antacids, H₂ blockers, prokinetic agents, or proton-pump inhibitors throughout the duration of the study. They were also directed not to consume acidic foods or foods containing bicarbonate during the study. During ambulatory pH monitoring, patients continued their normal daily routines. Throughout the 24 h of monitoring, individuals recorded their meal times, sleep periods and times of onset of heartburn complaints.

Statistical analysis

All values are expressed as mean \pm SD. Comparisons between the study and control groups were made using the χ^2 test. The Student's *t* test was used to compare continuous variables between groups. *P*-values < 0.05 were considered significant.

RESULTS

Of the 550 patients initially screened, 241 (43.8%) had combined proximal and distal esophageal acid reflux, 97 (17.6%) had IDR, 70 (12.7%) had IPR, 42 (7.6%) had hypersensitive esophagus, and 100 (18.2%) were free of these conditions. The latter 100 became the control group, with 42 women and 58 men of mean age 44.9 ± 12.8 years. The 97 patients in the IDR group formed the study group, with 47 women and 50 men of mean age 47.8 ± 13.4 years.

There were no significant differences between the IDR and control group means for age, BMI, and EBCA. However, mean LESP was significantly lower in the IDR group than in the control group (9.6 ± 7.4 mmHg *vs* 12.7 ± 10.3 mmHg, *P* = 0.01) (Table 1).

Of the 97 patients with IDR, 42 (43.3%) had NERD and 55 (56.7%) had ERD. Of the 55 patients with ERD, 20 (36.4%) had grade A esophagitis, 18 (32.7%) had grade B esophagitis, 12 (21.8%) had grade C esophagitis, and 5 (9.1%) had Grade D esophagitis. In the ERD subgroup, mean age was 45 ± 13 years, mean BMI was 26.8 ± 3.4 kg/m², mean DeMeester score was 42.9 ± 27.2 , mean LESP was 9.2 ± 6.5 mmHg, and mean EBCA was 70.9 ± 50.9 mmHg (Table 2).

Patients in the NERD subgroup tended to be older than those in the ERD subgroup (51 ± 13 years *vs* 45 ± 13 years, *P* = 0.03). There was no significant difference between the mean DeMeester scores for these 2 groups (Table 2). All 42 patients with NERD had EBCA > 30 mmHg,

Table 1 Comparison of 24-h pH monitoring and esophageal manometry findings in the IDR group and control group

	IDR group <i>n</i> = 97	Control group <i>n</i> = 100	<i>P</i> -value
Age (yr)	47.8 ± 13.4	44.9 ± 12.8	0.134
Sex (F/M)	47/50	42/58	0.512
BMI (kg/m ²)	26.6 ± 3.8	26.2 ± 3.8	0.437
EBCA (mmHg)	73.6 ± 44.4	77.6 ± 41.0	0.507
LESP (mmHg)	9.6 ± 7.4	12.7 ± 10.3	0.019
DeMeester score	42.6 ± 24.3	6.2 ± 4.8	0.000

IDR: Isolated distal reflux; BMI: Body mass index; EBCA: Esophageal body contraction amplitude; LESP: Lower esophageal sphincter pressure.

whereas 7 (12.7%) of the 55 patients with ERD had EBCA ≤ 30 mmHg. This difference was statistically significant (*P* = 0.01). In all cases where EBCA was less ≤ 30 mmHg, the patient had severe esophagitis (Grade C or D).

DISCUSSION

Gastroesophageal reflux refers to retrograde passage of gastric contents into the esophagus. This movement of material is not considered pathologic until symptoms or mucosal damage occur, but at that stage the condition is termed GERD. The most important mechanisms and phenomena that protect the esophagus from gastric reflux are esophageal peristalsis, salivary pH, and gravity. Several well-characterized abnormalities of LESP and esophageal peristalsis are known to increase gastroesophageal reflux and acid-induced mucosal damage^[14].

The most common esophageal motor disorder in patients with GERD is IEM, and 20%-50% of patients with GERD are affected^[15]. Ineffective esophageal motility is defined as esophageal contractions of amplitude < 30 mmHg and/or a 30% or higher rate of nontransmission of wet swallows to the distal esophagus^[6,8].

IEM is also the most prevalent motility abnormality in patients with IPR and GERD-associated respiratory symptoms^[16]. However, the relationship between IDR and IEM is not clear. In our study, we focused specifically on manometric findings in patients with IDR.

We detected no statistical differences between our IDR group and control group with respect to age, BMI or EBCA. However, we did note significantly lower mean LESP for the IDR patients. This finding is in accordance with other studies that have documented motility abnormalities in patients with GERD^[3,17].

The presence of erosive disease in the esophagus is another factor that is thought to promote esophageal motility disorders in patients with GERD^[18]. Impairment of esophageal body contraction, as manifested by reduced contraction amplitude and aperistalsis, is a frequent finding in patients with ERD. Twenty percent of individuals with moderate esophagitis and 50% of patients with severe esophagitis show aperistalsis and hypotensive contractions^[19].

Somani *et al*^[17] analyzed manometric findings in 47 patients with GERD. They found that distal esophageal contraction amplitude was lower in cases of severe

Table 2 Comparison of parameters for the ERD and NERD subgroups of IDR patients

	ERD (<i>n</i> = 55)	NERD (<i>n</i> = 42)	<i>P</i> -value
Age (yr)	45.2 ± 13.3	51.2 ± 13.0	0.032
Sex (F/M)	25/30	22/20	0.511
BMI (kg/m ²)	26.8 ± 3.4	26.3 ± 4.2	0.485
EBCA (mmHg)	70.9 ± 50.9	77.1 ± 34.5	0.497
LESP (mmHg)	9.2 ± 6.5	10.2 ± 8.6	0.526
DeMeester score	42.9 ± 27.2	42.1 ± 20.1	0.876

ERD: Erosive reflux disease; NERD: Non-erosive reflux disease.

esophagitis than in cases of mild esophagitis (*P* = 0.001). Frazzoni *et al*^[20] analyzed esophageal manometric findings in 88 patients with NERD, 76 with ERD, and 56 with complicated esophagitis. They found that mean EBCA was significantly lower in the complicated esophagitis and ERD groups than in the NERD group, but observed no significant difference between the 3 groups with respect to mean LESP. In contrast with these results, Lemme *et al*^[21] assessed 70 patients with ERD and 40 patients with NERD using esophageal manometry and detected no statistical differences between these groups with respect to mean numbers of low amplitude, non-transmitted, and normal waves. The authors suggested that IEM alone is unlikely to be the major determinant of abnormal esophageal acid exposure, and that it is not a prerequisite for development of esophagitis. Similarly, Martinek *et al*^[22] evaluated 111 patients with NERD, 77 patients with mild to moderate ERD, 33 patients with severe esophagitis, and 92 individuals with no evidence of gastroesophageal reflux using esophageal manometry and pH monitoring. They found no significant differences between NERD and ERD groups with respect to mean LESP or frequency of IEM. Similar proportions of patients in each group had low LESP and hiatus hernia. Martinek *et al*^[22] suggested that a variety of other factors, including genetics, mucosal defense, and acid clearance, may influence patients' susceptibility to developing ERD. Ho *et al*^[5] observed that patients with IEM were no more likely to have endoscopic evidence of esophagitis than individuals with normal manometry findings. They concluded that esophageal injury is not always associated with IEM.

All of the above-mentioned studies included patients with GERD, but IDR and IPR patients were not analyzed as separate groups in these studies. These 2 conditions may feature different manometric characteristics, and this might explain the contradictory results found in these studies. To our knowledge, no study to date has analyzed manometric data from patients with IDR alone. We focused solely on this patient group and detected no significant differences between the ERD and NERD subgroups with respect to mean EBCA or mean LESP. However, 12.7% of our patients with GERD exhibited EBCA ≤ 30 mmHg, whereas none of those with NERD had distal wave amplitudes in this category. In all cases where EBCA was ≤ 30 mmHg, the patient had severe esophagitis.

Various abnormalities of esophageal motor function

are observed in patients with GERD. Our data suggest that, among patients with IDR, those with NERD and those with ERD exhibit similar types and severity of esophageal motility disorders. The only striking difference between these 2 patient subgroups is that individuals with ERD have a significantly higher frequency of very low EBCA, and this is limited to patients with severe esophagitis.

COMMENTS

Background

Gastroesophageal reflux disease (GERD) is defined as the pathological retrograde movement of gastric contents into the esophagus. Various esophageal motility disturbances which may be important in reflux are observed in patients with GERD. The main esophageal motility disorder in these patients is ineffective esophageal motility (IEM). Increased acid clearance time and IEM have been shown to be strongly associated with isolated proximal reflux. However, there are no data that conclusively link motility disorders with isolated distal reflux.

Research frontiers

In the present study, patients with symptoms of GERD were evaluated with esophageal manometry, 24-h ambulatory pH monitoring, and upper gastrointestinal endoscopy. The manometric findings of patients with isolated distal reflux were compared with those who did not have pathological reflux. Among patients with isolated distal reflux, the manometric findings of patients who had erosive disease and non-erosive disease were also compared. There were no significant differences between the isolated distal reflux group and control group with respect to age, body mass index, and esophageal body contraction amplitude. Mean lower esophageal sphincter pressure was significantly higher in the control group. There were no differences between the erosive reflux disease and non-erosive reflux disease subgroups with respect to mean esophageal body contraction amplitude (EBCA), lower esophageal sphincter pressure, or DeMeester score. However, IEM was observed only in patients with erosive reflux disease.

Innovations and breakthroughs

In this study, the authors evaluated the manometric findings in a homogenous group of patients with isolated distal reflux. In this context, it is distinct from other related studies, since manometric findings have not been thoroughly analyzed in this special patient population. They also compared these findings in patients with erosive and non-erosive disease which has not been done previously.

Applications

This study, the authors believe, provides more insight into the pathophysiology of reflux disease. The finding of very low EBCA being observed only in patients with erosive disease might be helpful in identifying these patients.

Terminology

NERD: Patients with this condition exhibit typical reflux symptoms caused by reflux of gastric contents into the esophagus, but have no visible esophageal mucosal injury. ERD: Patients have visible esophageal mucosal injury on endoscopy. IPR: The upper esophageal sphincter localization was determined by manometry and proximal reflux was determined by the proximal probe localization and upper esophageal sphincter. If the proximal probe was localized in the upper esophageal sphincter or above it, a single acid reflux synchronously occurring with distal probe was accepted as pathologic acid reflux; if the probe was localized under the upper esophageal sphincter, acid contact time > 1% of total time was accepted as pathologic in proximal reflux. IDR: De Meester score > 14.72 and acid contact > 4.0% of total time below pH 4 were accepted as pathologic in distal reflux.

Peer review

The study addresses an important question, is well written, clear, and is accompanied by legible and clear tables. In addition, the results are well presented and the limitations of the study appropriately addressed. Appropriate controls were chosen for the study.

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