

## Gender differences in 24-hour pH meter results for gastroesophageal reflux

Gender differences for gastroesophageal reflux

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**Aim:** The pH meter, which records the 24-hour esophageal acidity, is accepted as the best standard method for understanding the physiology of gastroesophageal reflux disease (GERD) and making the diagnosis. In this study, we investigated gender differences in our patients who were diagnosed with GERD using this method.

**Material and Methods:** Outpatient pH monitoring was applied to patients with reflux symptoms. The results were evaluated according to the De-Meester scoring.

**Results:** In our study, we found the rate of GERD as 79.4% (83.3% of women and 70.0% of men). It was found that the number of reflux episodes, total reflux time, and mean values of reflux episodes lasting longer than 5 minutes, which are among the De-Meester criteria indicating GERD were higher in women than in men. Among the GERD parameters, only the mean duration of the longest reflux episode was found to be higher in male cases.

**Discussion:** We found that the 24-hour pH monitoring method was a reliable method for detecting GERD without the need for any other radiological or endoscopic intervention in patients with significant reflux symptoms, and the results differed according to gender.

**Keywords**

Gastroesophageal Reflux; pH Meter; Gender

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## Introduction

Gastroesophageal reflux is defined as the retrograde passage of stomach contents or sometimes duodenal contents into the esophagus [1]. Under standard conditions, although the intragastric pressure is positive and the intraesophageal pressure is negative, gastric contents do not pass into the esophagus, even in a person standing upside down. Although the mechanisms regulating this are not known exactly, it is accepted that lower esophageal sphincter tone is the leading factor that prevents GERD [1].

The data show that gastroesophageal reflux occurs through 3 main mechanisms [2]: First, reflux resulting from temporary lower esophageal sphincter relaxation that is not associated with swallowing (Spontaneous Reflux). Second, stress reflux was caused by the temporary increase in intra-abdominal pressure due to contraction of the abdominal muscles. Third, it is free reflux. Although spontaneous reflux can occur at normal or low lower esophageal sphincter pressures, stress or free reflux always occurs at low or no lower esophageal sphincter pressures. Reflux in normal persons is always due to temporary lower esophageal sphincter relaxation. This mechanism is also valid in 2/3 of the esophagitis. Therefore, the differentiation of gastroesophageal reflux in normals and esophagitis is quantitative rather than qualitative. However, the reflux mechanism prevailing in patients is heterogeneous. In some patients, reflux may be due to only temporary lower esophageal sphincter relaxation, while in others it may be due to stress or free reflux. In some other patients, it may participate equally in all three mechanisms.

In the last 20 years, there has been a consensus that factors such as the effectiveness of the antireflux mechanism, the corrosive potential of the refluxing material and the ability of the stomach to empty, as well as the resistance of the esophageal mucosa and the "clearing" ability of the esophagus play important roles in the development of gastroesophageal reflux disease (GERD) [3]. Since esophagitis may not develop in some cases with lower esophageal sphincter insufficiency and sufficient number of GERD episodes, a disorder that may occur in one or more of the mechanisms for the protection of the esophageal mucosa may cause esophagitis. Therefore, GERD is a multifactorial disease.

Various methods have been used in the diagnosis of GERD. These include the standard acid reflux test [4], acid perfusion test (Bernstein test), mano-metric examination of the lower esophageal sphincter, radiological examination of the esophagus, endoscopy, biopsy and isotope studies. With the development of sensitive devices that record 24-hour esophageal acidity, significant advances have been made in understanding esophageal physiology, and the investigation of the reflux event and the definition of physiological and pathological reflux margins have been achieved. A 24-hour intraesophageal pH meter is currently considered the best standard method for the evaluation of GERD [5].

The ambulatory pH technique was introduced in 1985 because of the limited benefit of esophagography and endoscopy in the diagnosis of GERD disease. This method plays an important role in understanding the pathophysiology of GERD. Although pH monitoring is not required in most patients with GERD,

there are various situations that require this test. Although endoscopy is normal, pH monitoring is helpful in diagnosis in patients with atypical pharyngeal or pulmonary symptoms such as cough, wheezing, asthma and recurrent pneumonia. PH monitoring should be performed in all patients with esophageal spasms even in the absence of GERD symptoms. Ambulatory pH monitoring is the method of choice in patients who have typical GERD symptoms but do not respond to standard medical treatment, when the effectiveness of medical or surgical treatment needs to be followed, and in patients who are considered to undergo anti-reflux surgery and whose diagnosis needs to be confirmed [6].

Ambulatory pH monitoring is applied over a period of 18-24 hours. The use of H<sub>2</sub> receptor blockers and prokinetic agents is discontinued 48 hours before the procedure. Proton pump inhibitors (PPIs) should be stopped 2 weeks in advance. The pH monitoring system consists of three parts as follows: The pH probe placed 5 cm proximal to the lower esophageal sphincter, whose level was previously determined by the manometric method, a reference electrode placed on the skin and a portable data logger that can be carried by wearing a belt or hanging on the shoulder, the pH distal to the esophagus is continuously recorded in a 24-hour period. During pH monitoring, patients are asked to continue their routine daily activities and diets, avoid activities that require great effort, avoid alcohol and smoking, start and end times of meals and sleep periods, and the time of occurrence of reflux symptoms on the device. In addition, the patient is advised to document the relationship between pain or reflux symptoms occurring during the follow-up with the type of food taken, body activity and changes in position [7].

At the end of the recording period, the pH area scale is created as a result of the analysis of the information recorded during the monitoring period. The symptoms recorded by the patient are documented on a radiograph. The parameters obtained from the data are calculated. The specificity and sensitivity of ambulatory pH monitoring, which is the gold standard method in detecting GERD patients, is around 90% and 85%, respectively. There are several factors that limit the use of the method; firstly, this technique is the longest running test among esophagus tests. As a result of discomfort and displacement of the probe with body movements, erroneous results may be obtained. Secondly, bending of the probe in the esophagus or embedding in the mucous fold leads to incorrect data collection. As for the third, acid reflux can vary from day to day. pH monitoring cannot distinguish between weak reflux and reflux reduction caused by the use of drugs that block acid release [3]. With this study, we aimed to show the presence of GERD by applying the 24-hour pH meter monitoring method in patients who presented to our outpatient clinic with reflux complaints, and to evaluate whether these results differ according to gender.

## Material and Methods

Patients with reflux symptoms and suspected GERD were evaluated in the outpatient clinic of the Department of General Surgery of our hospital. Patients with previous endoscopically or radiologically detected gastric ulcer, duodenal ulcer

history, gastric surgery, esophageal surgery history, Nissen fundoplication, pre-intervention H2 receptor blocker or PPI intake were excluded from the study.

Care was taken to keep the monitor on for 24 hours. During this test, patients were asked to continue their daily activities normally during the examination. However, due to the social status of the patients, they remained under observation in the hospital. The use of H2 receptor blockers and prokinetic agents was discontinued 48 hours before the procedure. PPIs were discontinued 2 weeks ago. Flexible probes with a length of 180 cm, a width of 2.1 mm and a distance of 15 cm between two probes were used with a medical measurement system brand monitor (version 7.3). First, the probe was inserted through the nasopharynx to patients who were not hungry. The sensor at the distal end of the probe with two ends was placed in the stomach, and the sensor at the proximal end was placed distal to the esophagus. The location of the catheter (medical measurement system catheter) was confirmed by monitoring the pH of the distal and proximal ends on the monitor. The catheter was fixed to the nasal skin. The patients were called again 24 hours later, the recording was ended, and the catheters were removed. The results were documented using the Medical Measurement System program. The results obtained during the 24-hour ambulatory esophageal pH monitoring were evaluated according to the DeMeester Scoring [8]. Reflux time lasting more than 4% of the total duration, reflux of more than 50, the number of reflux lasting longer than 5 minutes, and reflux lasting longer than 10 minutes were considered significant.

Ethics committee approval and practice approval was obtained from the ethics committee of our university to conduct our study (Decision no: 2005-26 / 06). The study was explained in detail to the patients participating in the study, and their verbal and written informed consent was obtained.

#### Statistical analysis

Statistical analyzes were performed using SPSS Statistics version 24.0 (IBM Corp., Chicago). Numerical variables were given as median (range) and mean  $\pm$  SD. Categorical variables were expressed as numbers and percentages. For the correlation between parameters, the Chi-square test or Fisher's tests was applied by selecting the appropriate one. A value of  $P < 0.05$  was considered statistically significant.

#### Results

Thirty-four evaluated patients were included in the study. Twenty-four (70.6%) of the patients were female and 10 (29.4%) were male. The mean age of all patients was 44.2 (range: 19-73) years. While the mean age of female patients was 40.8 (19-72) years, it was 52.4 (31-74) years for men. According to 24-hour pH measurements; We found the rate of GERD as 79.4% (83.3% of women and 70.0% of men). While the number of reflux episodes and the number of reflux lasting longer than 5 minutes were significantly higher in women, the longest reflux episodes were found to be significantly higher in men (Table 1).

Considering the DeMeester scoring criteria, since the total reflux time in 24 hours was more than 4%, the presence of reflux was detected in 20 (83.3%) women and 7 (70.0%) men. The rate of GERD in the total reflux time in women was

**Table 1.** GERD parameters in women and men

GERD parameters	Women	Men	P
Number of reflux episodes (n)	79,54 $\pm$ 55,63	61,40 $\pm$ 30,80	0,04
Total reflux time (%)	34,87 $\pm$ 24,53	32,70 $\pm$ 34,21	0,66
Number of reflux episodes lasting longer than 5 minutes (n)	12,60 $\pm$ 6,70	8,10 $\pm$ 7,95	0,04
Duration of longest reflux episode (min)	118,50 $\pm$ 124,96	158,30 $\pm$ 224,94	0,03

**Table 2.** Demographic characteristics of patients presenting with dyspeptic complaints, results of 24-hour pH monitoring.

Patient	Age	Gender	Total reflux time (%)	Number of reflux > 5 min (n)	Longest reflux time (min)	Reflux number (n)
1	29	W	88,00	13,00	568,00	38,00
2	56	W	46,00	12,00	132,00	84,00
3	31	M	82,00	13,00	652,00	41,00
4	41	W	53,00	16,00	216,00	79,00
5	31	W	57,00	17,00	247,00	77,00
6	58	M	3,00	1,00	30,00	13,00
7	40	W	1,00	1,00	3,00	4,00
8	38	W	35,00	18,00	47,00	244,00
9	38	W	23,00	16,00	38,00	130,00
10	68	M	43,00	16,00	99,00	73,00
11	48	W	1,00	1,00	3,00	10,00
12	58	W	66,00	25,00	154,00	124,00
13	37	W	29,00	17,00	37,00	158,00
14	25	W	4,00	2,00	7,00	55,00
15	53	W	25,00	13,00	73,00	26,00
16	30	W	75,00	20,00	218,00	65,00
17	41	W	36,00	12,00	136,00	62,00
18	48	W	10,00	9,00	31,00	48,00
19	42	W	25,00	8,00	89,00	69,00
20	51	W	48,00	12,00	156,00	57,00
21	29	W	1,00	2,00	8,00	11,00
22	19	W	61,00	15,00	200,00	45,00
23	72	W	20,00	6,00	118,00	41,00
24	30	W	61,00	24,00	235,00	120,00
25	73	M	32,00	16,00	96,00	72,00
26	46	W	26,00	17,00	56,00	103,00
27	34	M	4,00	2,00	8,00	69,00
28	49	M	1,00	1,00	3,00	32,00
29	38	W	23,00	15,00	45,00	152,00
30	66	M	6,00	1,00	3,00	84,00
31	40	W	23,00	13,00	27,00	107,00
32	44	M	7,00	2,00	7,00	82,00
33	49	M	60,00	22,00	228,00	115,00
34	52	M	89,00	7,00	457,00	33,00

statistically significantly higher than in men ( $p = 0.04$ ).

According to the number of reflux lasting more than 5 minutes, the presence of reflux was detected in 20 (83.3%) of women and 5 (50.0%) of men. According to the number of reflux lasting longer than 5 minutes in women, the rate of GERD was found to be statistically significantly higher than in men ( $p = 0.01$ ). According to whether reflux lasts longer than 10 minutes, GERD was detected in 16 (66.6%) women and 6 (60.0%) men. When the distribution of reflux lasting longer than 10 minutes by gender

was compared, no significant difference was found between the groups ( $p = 0.38$ ). More than 50 refluxes were detected in 15 (62.5%) women and 4 (40.0%) men, and the difference was statistically significant ( $p = 0.03$ ). The age, gender and 24-hour pH monitoring results of the patients are shown in Table 2.

## Discussion

GERD is the retrograde passage of stomach contents or sometimes duodenal contents into the esophagus. Reflux is a physiological situation, but it is named “Reflux disease” when it causes esophageal tissue damage or symptoms [1]. Various methods have been used in the diagnosis of GERD. Methods used to contribute to the diagnosis have not been able to demonstrate the condition of GERD objectively. For example, although the acid perfusion test is 100% positive in reflux cases [9], it only shows the acid sensitivity of the distal esophagus and does not determine endogenous reflux. Although the esophageal manometer is a good method for detecting both lower esophageal sphincter insufficiency and esophageal motility disorders, it is not sensitive in detecting reflux. Likewise, although endoscopic examination is valuable in the diagnosis of esophagitis and its complications, radiological examination is valuable in the diagnosis of hiatus hernia, they are not sensitive in detecting GERD [9]. However, it is certain that a method that will reveal GERD status objectively will make great contributions to the evaluation of GERD.

Over the last 20 years, with the development of sensitive devices that measure intraesophageal pH for 24 hours, it has been possible to detect intraesophageal pH changes in accordance with physiological conditions as much as possible. Thus, the limits of normal and abnormal reflux were determined, the relationship of symptoms with reflux was revealed, thus new dimensions were reached in the diagnosis of GERD.

There have been many studies investigating the reliability of this method and comparing it with other methods. De Meester and Johnson, who contributed greatly to the development of this direction, reported the sensitivity of the test as 90.3% and the specificity as 90% (5,8,10). In their study, the researchers endoscopically evaluated 199 patients with typical reflux symptoms, and found that 96 of the cases were normal and 103 of them have esophagitis. With a 24-hour intra-oesophageal pH meter performed in both groups, GERD was detected in 55% of cases evaluated as endoscopically normal and in 90% of the cases evaluated as esophagitis. At the end of this study, the researchers suggested that endoscopy is not a sensitive method in recognizing GERD, and in cases with typical reflux symptoms, even if the endoscopic examination is evaluated as normal, a 24-hour intraesophageal pH measurement should be performed [11].

Pujol et al., investigated 15 controls and 47 patients with typical reflux symptoms. They determined the sensitivity of the 24-hour intraesophageal pH meter test as 94% and the specificity as 100% [12]. The investigators also found GERD on a 24-hour intraesophageal pH meter test, as in the DeMeester and Johnson's studies, in more than half of the patients with reflux symptoms that were endoscopically normal.

Fuchs et al., found that the results of 24-hour intraesophageal

pH meter had higher sensitivity and specificity compared to standard acid reflux test, manometry and endoscopy results in their study in 45 cases with reflux symptoms and 45 cases of controls [13]. DeVault and Castell reported that the most sensitive and specific test in the diagnosis of GERD is the 24-hour intraesophageal pH meter [14]. In the light of these data, it has been shown that the 24-hour intraesophageal pH meter is the most sensitive and specific method in the diagnosis of GERD, which is the most objective way of presenting GERD.

In our study, we investigated the diagnosis of GERD by 24-hour pH monitoring, which is the gold standard in the diagnosis of GERD. We found the rate of GERD as 79.4% in the patients we evaluated (83.3% of women and 70.0% of men). The high rate of GERD in our study compared to the rates stated in the literature can be explained by the presence of severe GERD symptoms in the patients included in the study. It was observed that the majority of the patients presenting with dyspeptic complaints were women aged 35-45. However, no etiological reason could be found to explain its prevalence in female patients. It was found that the mean values of the number of reflux episodes, total reflux time, and the number of reflux episodes lasting longer than 5 minutes, which are among the DeMeester criteria indicating GERD in female cases, were higher than that of men. Among GERD parameters, only the mean duration of the longest reflux episode was found to be higher in male cases. We can think that the high number of female cases in our study may affect these results. The number of reflux lasting longer than 5 minutes was higher in women. However, reflux lasting longer than 10 minutes did not differ between men and women. In the literature, epidemiological studies on GERD have shown that there is a gender difference depending on geographical location. There was no difference in North America and Europe, while women in South America and Asia had more symptoms [15-18]. However, in a study on the prevalence of GERD, it was reported that male gender is an independent risk factor, especially for erosive reflux disease [19]. Non-erosive GERD is frequently observed in women. It has been suggested that the sex effect may be due to differences in parietal cell mass between men and women, and even female sex hormones may play a protective role.

The small number of patients in our study is a serious limitation. However, considering that 24-hour pH monitoring provides reliable results, this technique is not easy to apply and takes a long time, and we can show this as a reason for the number of patients. In addition, the numbers of men and women were not equal in our study. This is seen as another limitation. We explain this by the fact that the majority of our patients who applied to the polyclinic with reflux complaints are women.

In this study, we thought that the 24-hour pH monitoring method is a reliable method for detecting GERD without the need for any other radiological or endoscopic intervention in patients with significant reflux symptoms. Despite all these limitations, our study is one of the few studies comparing male and female data in the literature. If all the data in the study are discussed with a larger number of randomized groups, it will help explain these gender differences.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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