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Original Article

Manometric assessment of esophageal motor function in patients with primary biliary cirrhosis

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ABSTRACT

Introduction/aim: Primary biliary cirrhosis is associated with other autoimmune diseases including Sjögren's syndrome, and scleroderma. Esophageal dysmotility is well known in scleroderma, and Sjögren's syndrome. The aim of this study is to investigate whether any esophageal motor dysfunction exists in patients with primary biliary cirrhosis.

Method: The study was performed in 37 patients (36 women, mean age: 56.29 ± 10.01 years) who met diagnostic criteria for primary biliary cirrhosis. Thirty-seven functional dyspepsia patients, were also included as a control group. Patients entering the study were asked to complete a symptom questionnaire. Distal esophageal contraction amplitude, and lower esophageal sphincter resting pressure were assessed.

Results: Manometric findings in primary biliary cirrhosis patients vs. controls were as follows: Median lower esophageal sphincter resting pressure (mm Hg): (24 vs 20, $p = 0.033$); median esophageal contraction amplitude (mm Hg): (71 vs 56, $p = 0.050$); mean lower esophageal sphincter relaxation duration (sc, x ± SD): (6.10 ± 1.18 vs 8.29 ± 1.92, $p < 0.001$); and median lower esophageal sphincter relaxation (%) (96 vs 98, $p = 0.019$); respectively. No significant differences were evident in median peak velocity (sc) (3.20 vs 3.02, $p = 0.778$) between patients with primary biliary cirrhosis and the functional dyspepsia patients. Esophageal dysmotility was found in 17 (45.9%) primary biliary cirrhosis patients (non-specific esophageal motor disorder in ten patients, hypomotility of esophagus in five patients, nutcracker esophagus in one patient and hypertensive lower esophageal sphincter in one patient).

Conclusion: Esophageal dysmotility was detected in 45.9% of patients. The study suggests that subclinic esophageal dysmotility is frequent in patients with primary biliary cirrhosis.

1. Introduction

Primary biliary cirrhosis is a chronic, progressive autoimmune liver disease of unknown etiology characterized by inflammatory destruction of septal and interlobular bile ducts that leads to cholestatic chronic liver disease and, eventually, to cirrhosis [1]. Primary biliary cirrhosis is associated with other autoimmune diseases such as Sjögren's syndrome, autoimmune thyroiditis, rheumatoid arthritis, ankylosing spondylitis, polymyositis, scleroderma, and thrombocytopenia [2–8]. Patients with a cholestatic biochemical pattern, positive antimitochondrial autoantibody test, and hepatic histological features compatible with primary biliary cirrhosis would generally be diagnosed as having primary biliary cirrhosis [9,10].

Primary biliary cirrhosis has been shown to be associated with primary Sjögren's syndrome [11]. Indeed, in several studies the most common autoimmune disorder associated with primary biliary cirrhosis is Sjögren's syndrome, with a reported prevalence of Sjögren's syndrome in primary biliary cirrhosis patients ranging from 50% to 81% [12,13]. Esophageal motility abnormalities are well known in progressive systemic sclerosis, Sjögren's syndrome, and some rheumatic diseases with sicca syndrome [14–16]. In a study by Parés et al., it has been demonstrated that esophageal motor disturbances existed in patients with primary biliary cirrhosis who have scleroderma and also in those with Sjögren's syndrome without scleroderma [17]. Therefore, the aims of this study were to investigate whether any esophageal motor abnormalities exist in patients with primary biliary cirrhosis and compare results with age-matched functional dyspepsia patients.

2. Patients and methods

Thirty-seven primary biliary cirrhosis patients were enrolled into the study. Thirty-six of the patients were women, with a mean age of 56.29 ± 10.01 years (range: 34–78 years). The diagnosis of primary

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biliary cirrhosis was made with combination of abnormal serum liver tests (elevation of alkaline phosphatase of liver origin for at least 6 months) and the presence of antimitochondrial autoantibody (P1:40) in serum [18]. A liver biopsy was performed to confirm the diagnosis of primary biliary cirrhosis. Histologic lesions are classically divided into four stages [19]. The presence of heartburn, dysphagia and epigastric pain was queried in patients with primary biliary cirrhosis. Thirty-seven age-matched patients with functional dyspepsia, who were diagnosed according to the Rome II criteria, were also included in the study and served as a control group [20]. None of the patients was on drugs that might alter esophageal motor function during motility testing. All patients had undergone upper gastrointestinal endoscopic examination and esophageal motility testing in two separate days. Endoscopic examinations were performed by one of the investigators using a standard video gastroscope (Fujinon, Tokyo, Japan).

The presence of Sjögren's syndrome was investigated in patients with primary biliary cirrhosis and American–European Consensus Group criteria used for diagnosis of Sjögren's syndrome [21]. Esophageal manometry was performed by using a single catheter containing 8 microperfusion state pressure transducers spaced at 5 cm intervals and attached to an online computer (MMS, Medical Measurement Systems, Netherlands). Patients came to the laboratory after at least 8 h of fasting. The 8-channel catheter was lubricated and passed nasally and advanced into the stomach. A slow station pull-through was performed at 1 cm increments. Once the lower esophageal sphincter was profiled, the distal pressure transducer which included four lumens was placed in the high-pressure zone of the lower esophageal sphincter, so that the proximal pressure transducers were located 5 cm, 10 cm, 15 cm and 20 cm above the lower esophageal sphincter. A series of 10 wet swallows (with 5 mL water bolus) were given at 30 s intervals. Each contraction was recorded and then analyzed by a computerized software system (MMS, Medical Measurement Systems, Netherlands) for amplitude, contraction and velocity. The catheter assembly was then located 5 cm above the lower esophageal sphincter for assessment of the pressures from the distal part (5 cm and 10 cm) of the esophagus. Average lower esophageal sphincter resting pressure (reference 6–25 mm Hg), percentage of wet swallowing over peristaltic waves (reference N: 80%) and average esophagus corpus amplitude (reference 30–160 mm Hg) were determined. Lower esophageal sphincter relaxation and residual pressures were also recorded. The conventional classification of esophageal motility was used for diagnosis of abnormal esophageal function [22]. This classification is summarized below.

Normal

- Normal velocity
- Normal peristaltic amplitude
- ≥7 peristaltic contractions with an intact wave progression (amplitude >30 mm Hg)

Aperistalsis

- Absent or simultaneous contractions (<30 mm Hg)

Ineffective esophageal motility (IEM)

- ≥3 peristaltic contractions with failure of wave progression due to an ineffective distal contraction amplitude (>30 mm Hg) or failed peristalsis over a segment of the distal esophagus

Nutcracker esophagus

- Average peristaltic amplitude >180 mm Hg over pressure sensors 3 and 8 cm above lower esophageal sphincter

Isolated hypertensive lower esophageal sphincter

- Basal LES resting pressure greater than 45 mm Hg (mid-respiratory pressure).

The present study was approved by the Institutional Review Board of Ankara University Medical School and all patients signed informed consent before entering the study. Statistical analysis was performed with SPSS 11.5 for Windows (SPSS Inc., Chicago, IL). Continuous variables were expressed as mean ± standard deviation and median (min–max). Categorical variables were expressed as frequencies and percentages. Shapiro–Wilk test was used to check the normality for each group. A p value of less than 0.05 was considered significant. The differences between two groups were evaluated by Student's t test, and when the data distribution was not normal Mann–Whitney U test was used. Chi-square test and Fisher's exact test were used to evaluate categorical and continuous variables, respectively, where applicable.

3. Results

The mean age of the patients enrolled in the study (n = 37) was 56.29 ± 10.01 years. Median primary biliary cirrhosis disease duration was 74.5 months (range 3–360 months). As for symptoms, there was epigastric pain in 7 (18.9%) patients. Dysphagia in 6 (16.2%) and heartburn in 5 (13.5%) were found. Of the 37 patients who had undergone upper gastrointestinal endoscopy, 4 patients had endoscopic abnormalities which consisted of esophagitis according to the Los Angeles classification (3 grade A, 1 grade B) [23]. The clinical manifestations of primary biliary cirrhosis, and liver functions and gastrointestinal symptoms in our cases are summarized in Table 1.

There was no significant difference between mean age 56.29 ± 10.01 years (range: 34–78 years) vs 44.25 ± 11.35 years (range: 23–73), p = 0.576 in patients with primary biliary cirrhosis compared to the control group. As for manometric findings, median lower esophageal sphincter resting pressure (mm Hg) (24 vs 20, p = 0.033), and median esophagus contraction amplitude (mm Hg) were significantly higher (71 vs 56, p = 0.050); median lower esophageal sphincter relaxation (%) (96 vs 98, p = 0.019), and mean lower esophageal sphincter relaxation duration (sc) were significantly lower (6.10 ± 1.18 vs 8.29 ± 1.92, p < 0.001), in patients with primary biliary cirrhosis compared to functional dyspepsia patients. There were no significant differences between median peak velocity (sc) (3.20 vs 3.02, p = 0.778) in patients with primary biliary cirrhosis compared to functional dyspepsia patients (Table 2). Esophageal dysmotility was detected in 17 of 37 patients (45.9%) with primary biliary cirrhosis, whereas none of the functional dyspepsia patients had any abnormality. Individual analysis of the esophageal motility studies showed different patterns of esophageal dysfunction:

1. Hypertensive lower esophageal sphincter in one patient.
2. Nutcracker esophagus one patient.
3. Hypomotility of esophagus in five patients.
4. Non-specific esophageal motor disorder in ten patients.

Of the 17 patients, 12 of them had at least one of the findings such as dysphagia, heartburn and esophagitis. Esophageal dysmotility was detected in 3 of 6 patients suffering from dysphagia symptoms.

Table 1
The characteristics of primary biliary cirrhosis patients.

	PBC n = 37, (%)	SS (+) n = 21, (%)	SS (−) n = 16, (%)	p
Age (mean ± SD)	56.3 ± 10.0	60.1 ± 8.3	51.3 ± 10.1	0.006[a]
Symptoms				
• Pruritus	19 (51.3%)	12 (57.1%)	7 (43.7%)	0.535[b]
• Weakness	19 (51.3%)	14 (66.7%)	5 (31.3%)	0.048[b]
• Heartburn	5 (13.5%)	5 (23.8%)	0	0.062[c]
• Dysphagia	6 (16.2%)	4 (19.0%)	2 (12.5%)	1.000[c]
• Epigastric pain	7 (18.9%)	7 (33.3%)	0	0.027[c]
• Esophagitis	4 (10.8%)	3 (14.2%)	1 (6.3%)	1.000[c]
• Jaundice	1 (2.7%)	1 (4.8%)	0	1.000[c]

SD: standard deviation.
[a] Student's t test.
[b] Chi-square test.
[c] Fisher's exact test.