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## Original Article

**Combined multichannel intraluminal impedance-pH monitoring to select patients with persistent gastro-oesophageal reflux for laparoscopic Nissen fundoplication**I. Mainie<sup>1</sup>, R. Tutuian<sup>1</sup>, A. Agrawal<sup>1</sup>, D. Adams<sup>2</sup>, D. O. Castell<sup>1\*</sup><sup>1</sup>Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, South Carolina, USA<sup>2</sup>Department of Surgery, Medical University of South Carolina, Charleston, South Carolina, USAemail: D. O. Castell ([castell@musc.edu](mailto:castell@musc.edu))

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**ABSTRACT****Background:**

Combined multichannel intraluminal impedance-pH (MII-pH) monitoring detects gastro-oesophageal reflux and identifies acid and non-acid reflux events. It can be used in patients with persistent symptoms on proton-pump inhibitor (PPI) therapy. The aim of this study was to assess laparoscopic Nissen fundoplication as a treatment for patients with persistent symptoms associated with reflux despite acid suppression documented by MII-pH monitoring.

**Method:**

A prospectively maintained database identified patients with persistent symptoms of gastro-oesophageal reflux disease despite PPI therapy who had undergone MII-pH monitoring and this was cross-referenced with patients who had undergone fundoplication at this institution. Follow-up after fundoplication was by periodic telephone interview and review of clinical records.

**Results:**

Of 200 evaluated patients, 19 (14 female; mean age 40 (range 0.7-78) years) underwent laparoscopic Nissen fundoplication. Before surgery, 18 of 19 patients had a positive symptom index (at least half of symptoms associated with reflux) and one, a negative symptom index. After a mean follow-up of 14 (range 7-25) months, 16 of 17 (94 per cent) patients with a positive symptom index were asymptomatic or markedly improved (one patient was lost to follow-up). Persistent symptoms occurred in the patient with a negative symptom index, and one patient had recurrent symptoms after 9 months.

**Conclusion:**

Patients with a positive symptom index resistant to PPIs with non-acid or acid reflux demonstrated by MII-pH monitoring can be treated successfully by laparoscopic Nissen fundoplication. Copyright © 2006 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd.

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## ARTICLE TEXT

## Introduction



Acid reflux is the primary mechanism responsible for the oesophageal manifestations of gastro-oesophageal reflux disease (GORD). Proton pump inhibitors (PPIs) are potent acid suppressors with healing rates for erosive oesophagitis of up to 93 per cent. Complete symptom control is, however, difficult to achieve, as shown in a large clinical trial in which 35-40 per cent of patients with GORD had persistent symptoms while taking PPIs[1].

The surgical alternative to PPIs is fundoplication[2][3]. Successful outcome after antireflux surgery can be predicted by an abnormal 24-h pH score, typical primary symptoms of GORD and a good response to acid suppression[4]. Combined multichannel intraluminal impedance-pH (MII-pH) monitoring can detect reflux episodes independent of pH. The technique identifies the refluxate by changes in impedance produced by the presence of a bolus in the oesophagus, and this event can be classified as acid or non-acid by concomitant changes in intraluminal pH. Liquid boluses conduct better than the empty oesophagus, leading to a rapid decline in intraluminal impedance when the bolus enters the impedance measuring segment. Impedance returns to baseline once the bolus has exited the segment. Multiple impedance measuring segments mounted on the same catheter allow determination of the direction of bolus movement. Proximal to distal progression of impedance changes is indicative of swallowing, whereas a distal to proximal progression indicates reflux episodes. The pH component of MII-pH monitoring characterizes the chemical content of the refluxate. Impedance-detected reflux episodes during which the pH drops to less than 4.0 are considered acid reflux episodes, whereas episodes during which the pH stays above 4.0 are traditionally considered to be non-acid[5][6]. Symptoms that persist despite acid suppression therapy can be associated with either acid or non-acid gastro-oesophageal reflux, or not related to reflux episodes[7]. There remains, however, a lack of data regarding outcome in patients in whom combined MII-pH monitoring has documented a positive symptom association with either acid or non-acid reflux while taking acid-suppressing agents.

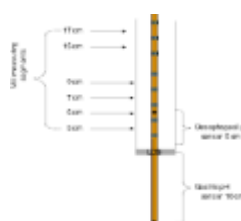
The aim of this study was to evaluate the clinical outcome of patients undergoing laparoscopic Nissen fundoplication for persistent symptoms on acid suppressive therapy, where MII-pH monitoring had shown a positive association between symptoms and reflux.

## Patients and methods



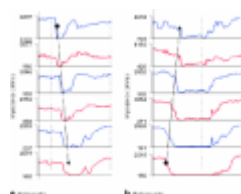
From January 2002, all patients referred to the oesophageal laboratory at the Medical University of South Carolina with persistent symptoms on at least normal twice-daily doses of PPIs (with or without the use of H<sub>2</sub>-receptor antagonists at night) underwent combined MII-pH monitoring.

Patients presented to the laboratory after fasting for at least 4 h. Baseline multichannel intraluminal impedance and oesophageal manometry (MII-EM) was measured in all patients aged over 10 years. The combined MII-pH probe (*Fig. 1*) was placed with reference to the manometrically located proximal border of the lower oesophageal sphincter (LOS) using a station pull-through technique. On completion of manometry, a 2.1-mm MII-pH catheter was inserted transnasally and the oesophageal pH sensor positioned 5 cm above the LOS. In patients younger than 10 years, a formula was used to calculate placement of the catheter using the European Society for Paediatric Gastroenterology and Nutrition guidelines[8]. The configuration of the adult catheter allowed monitoring of changes in intraluminal impedance at 3, 5, 7, 9, 15 and 17 cm above the LOS. After recording for 24 h, data were analysed using dedicated software (Bioview Analysis<sup>TM</sup>; Sandhill Scientific, Highlands Ranch, Colorado, USA). Combined MII-pH data allow differentiation between swallows and reflux episodes (*Fig. 2*), and separation of reflux episodes into acid and non-acid events, depending on whether the lowest oesophageal pH was below or above 4.0 during the impedance-detected reflux changes (*Fig. 3*).



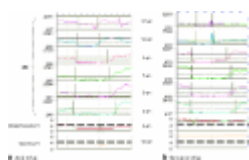
**Figure 1. Multichannel intraluminal impedance (MII)-pH catheter (diameter 2.1 mm) with impedance electrodes (4 mm in length) set in pairs at 2-cm intervals. This allows for six impedance rings and one pH electrode in the oesophagus, and a second pH electrode in the stomach. The oesophageal pH sensor is placed 5 cm above the lower oesophageal sphincter (LOS) and gastric pH sensor 10 cm below the LOS; impedance is measured at six different sites, 3, 5, 7, 9, 15 and 17 cm above the LOS**

[\[Normal View 25K | Magnified View 38K\]](#)



**Figure 2. Impedance changes during a swallowing and b reflux of a bolus, detected by multichannel intraluminal impedance monitoring. Proximal to distal progression of changes in impedance indicates antegrade bolus movement, as seen during swallowing, whereas distal to proximal progression indicates retrograde bolus movement, as seen during reflux (arrows indicate direction of bolus movement)**

[\[Normal View 44K | Magnified View 75K\]](#)



**Figure 3. Tracings from the multichannel intraluminal impedance (MII)-pH study. The six impedance measuring segments and two pH sites are shown on the y-axis. Both tracings demonstrate a drop in impedance (measured in ohms) beginning distally as liquid travels retrogradely up the oesophagus. The dashed lines identify the pH 4 level. a There is continuing gastric acidity and an associated drop in pH to less than 4 in the oesophagus during the reflux episode. The vertical lines correspond to the retrograde reflux event, classifying this episode as acid reflux. b Both gastric and oesophageal pH remain above 4, thereby classifying this episode as non-acid reflux [Normal View 55K | Magnified View 95K]**

Before testing, patients were asked to identify their predominant residual symptom, and this was categorized as being typical of GORD (heartburn, regurgitation, chest pain) or as atypical (cough, wheezing, throat clearing, globus, acid taste). Diaries were provided for patients or their family members (for children aged less than 10 years) to record symptoms during 24-h MII-pH monitoring. A symptom was considered to be associated with reflux if MII detected reflux 5 min before onset of the symptom. The symptom index was calculated as the number of symptoms associated with reflux divided by the total number of symptoms. When the patient recorded different types of symptom, separate indices were determined for each symptom. A positive symptom index was defined as at least 0.5 (at least half of symptoms associated with reflux)[9]. A prospectively maintained database was used to identify patients with persistent symptoms of GORD despite PPI therapy after evaluation with MII-pH monitoring; these patients were cross-referenced with patients who had a fundoplication at the authors' institution. All patients had normal oesophageal motility[10].

Data were collected prospectively every 3 months for all patients who underwent fundoplication after MII-pH testing. Patients were reviewed in the clinic or contacted by telephone. Telephone interviews were limited to assessment of the primary symptom after surgery. Patients were contacted by the same gastroenterologist, who asked, 'Are you experiencing any symptoms (old or new) after the surgery?'. If the patient answered 'yes', they were asked to describe the symptoms and compare them to those experienced before surgery. When the patient was symptomatic, a second question was asked: 'Are you taking any acid suppression therapy?' (with examples of various PPIs and H<sub>2</sub>-receptor antagonists mentioned). The Institutional Review Board at the Medical University of South Carolina approved the follow-up data collection.

## Results



Of 200 patients who experienced persistent symptoms despite receiving PPIs twice daily, 172 (86.0 per cent) had symptoms during 24-h MII-pH monitoring. Sixty-one (35.5 per cent) of these patients had a positive symptom index for non-acid reflux, 13 (7.6 per cent) had a positive index for acid reflux, and 98 (57.0 per cent) had a negative symptom index for any reflux. Nineteen of the 172 patients (18 with positive symptom indices) (14 female patients; mean age 40 (range 0.7-78) years) with normal oesophageal body motor function on standard manometry underwent laparoscopic Nissen fundoplication at the authors' institution.

Ten patients had atypical and nine had typical symptoms. Cough was the most common presenting symptom before surgery, and all seven of these patients had a positive symptom index with non-acid reflux. Six patients had heartburn, three regurgitation, one throat clearing, one hoarseness and one nausea. Before surgery, 18 of the 19 patients were diagnosed with a positive symptom index (14 with non-acid and four with acid reflux) and one patient was diagnosed as having no reflux associated with her symptoms.

After a mean follow-up of 14 (range 7-25) months, 16 of 17 patients with positive symptom indices were asymptomatic and no longer taking any antireflux medication or markedly improved (one patient with a cough was lost to follow-up). Symptoms persisted in the patient with hoarseness (symptoms recurred after 9 months) and in the patient in whom MII-pH monitoring had shown a negative symptom index for heartburn before surgery and continued to complain of heartburn after fundoplication despite reintroduction of PPI therapy.

Seven of the patients, including the patient with recurrent hoarseness, had previously undergone 24-h pH testing that had shown abnormal reflux. Four patients had an upper endoscopy, three of which showed oesophagitis, and the remaining eight had no previous studies documented, including the patient with persistent symptoms.

## Discussion



This study has shown that patients with a positive symptom association for reflux (acid and non-acid) documented by MII-pH monitoring who are taking PPIs benefit from antireflux surgery. Eleven of the 19 patients did have previous documentation of reflux by pH monitoring or upper endoscopy, but eight had undergone no previous studies for reflux. Despite two abnormal studies both on and off acid suppression therapy, the patient with hoarseness had a recurrence of symptoms.

This study used MII to document the association of symptoms with ongoing reflux. This relatively new technique allows

the detection of gastro-oesophageal reflux independent of pH by recording electrical resistance within the oesophagus. As a result of this ability to identify all types of reflux episode, combined MII-pH monitoring seems the ideal technique for evaluating patients with residual symptoms while taking acid-suppressing therapy[1][2].

The authors acknowledge the potential for selection bias. Some patients may have undergone treatment elsewhere, and their outcome is unknown. Those with poor motility were not offered fundoplication at this institution and some patients decided against surgery, opting to continue with medical therapy.

Previous studies have evaluated surgery in PPI-resistant patients. In a cohort of eight patients thought to have chronic cough secondary to ongoing reflux, based on 'fitting a clinical profile', who were followed for more than 1 year, all experienced either complete resolution or marked improvement in the cough[11].

Antireflux surgery has been used to treat extraoesophageal symptoms secondary to GORD, and its efficacy was related to appropriate patient selection[11]. Good predictors of surgical outcome appear to be a history of nocturnal asthma, a history of reflux before the onset of pulmonary symptoms, laryngeal signs and a response to medical therapy[12]. Short- and long-term results of open and laparoscopic antireflux surgery indicate beneficial results in 50-100 per cent of patients with extra-oesophageal symptoms[13-20]. A study by Westcott *et al.*[21] prospectively followed 44 patients with a diagnosis of laryngopharyngeal reflux for up to 14 months after laparoscopic Nissen fundoplication. Patients were evaluated by means of the reflux finding score, reflux symptom index and quality of life questionnaires before and after surgery. A total of 41 patients completed the study, with improvement in 34. One of the reasons suggested for some of the patients failing to improve was exposure of the larynx to pH neutral reflux as PPIs do not eliminate retrograde fluid flow[21].

The present study has several limitations. The number of patients was small and there was no control group. There might have been observational or recall bias by the interviewer, although the absence of acid-suppressing therapy was an objective measure. In addition, the elimination of reflux after laparoscopic Nissen fundoplication was not documented. Although properly designed trials are warranted to address these limitations, the study has indicated that this approach may be clinically appropriate and worthy of wider evaluation.

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