

## Preoperative Multiple Rapid Swallows Examination for Prediction of Dysphagia after Laparoscopic Toupet Fundoplication

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### ABSTRACT

**Background :** Patients with dysphagia are assessed with high-resolution manometry (HRM). Recently, the multiple rapid swallows (MRS) technique has been reported to provide additional details for characterizing esophageal transit, but no study has assessed MRS before laparoscopic Toupet fundoplication (LTF). The aim of the present study was to compare the test characteristics of MRS between patients who had or did not have dysphagia and underwent LTF to treat gastroesophageal reflux disease.

**Methods :** We identified patients who had undergone HRM and before LTF from November 2014 through July 2016. HRM assessed ten single swallows (SS) and MRS. Patients were classified as those having or not having dysphagia. The anatomy-function-pathology (AFP) classification, valve factor, and symptom scores before LTF, HRM variables, and multichannel intraluminal impedance pH variables were compared.

**Results :** Four had dysphagia and 16 did not. The patient groups did not differ significantly in the preoperative pathophysiology or in the symptom scores before LTF. However, both the MRS-distal contractile integral (DCI) and the MRS-DCI/SS-DCI ratio were higher in patients without dysphagia than in patients with dysphagia (MRS-DCI : 831 vs. 43,  $p = 0.002$  ; MRS-DCI/SS-DCI : 0.7 vs. 0.05,  $p = 0.014$ ).

**Conclusions :** With the MRS technique, patients with dysphagia after LTF are characterized by weakness of esophageal body contractions. Therefore, the MRS technique is valuable for preoperative evaluation of the likelihood of a patient having dysphagia after LTF.

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**Key words :** laparoscopic fundoplication, multiple rapid swallows, dysphagia, high-resolution manometry

### INTRODUCTION

Laparoscopic fundoplication (LF) is the standard treatment for advanced gastroesophageal reflux disease (GERD) and has a patient satisfaction rate 10 years later of nearly

90%<sup>1</sup>. However, dysphagia appears early after surgery in some patients and can be chronic. A study by Lundell et al. compared postoperative dysphagia between the Nissen and Toupet methods of fundoplication and dysphagia after Toupet fundoplication is more frequently at 3 months after op-

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eration<sup>2</sup>.

High-resolution manometry (HRM) is an examination performed to evaluate esophageal motor function. HRM is performed single swallows (SS) method and multiple rapid swallows (MRS) method. Therefore, SS is performed before surgery to evaluate the functions of the esophagogastric junction (hypotensive lower esophageal sphincter [LES] pressure or the presence of hiatal hernia or both) and of the esophageal body (fragmented peristalsis, ineffective esophageal motility, or absent contractility).

MRS has recently been introduced to evaluate the contraction reserve and provide additional details for characterizing esophageal transit<sup>3</sup> (Fig. 1). Several studies have examined MRS for predicting dysphagia after fundoplication surgery<sup>4,5</sup>, but no studies have included patients who have undergone Toupet fundoplication. In the present study, we compared the test characteristics of MRS between patients who had or did not have dysphagia and MRS examinations were performed before laparoscopic Toupet fundoplication (LTF) to treat GERD.

## PATIENTS AND METHODS

### Subjects

This study was approved by the Ethics Committee of The Jikei University School of Medicine for Biomedical Research (#30-304 ; 9325). Twenty-five patients with GERD underwent SS and MRS before undergoing LTF from November 2014 through July 2016 at The Jikei University Hospital. Preoperative and postoperative symptoms were assessed via questionnaires. Of these patients, 5 were excluded from the study because they did not complete both the preoperative and postoperative questionnaires and 20 met the study criteria and were included as subjects. The 20 subjects had a mean age of 46 years (range, 30 to 80 years), and 14 subjects (70%) were men.

### Assessment of preoperative clinical condition

The frequency and fluency of the patients' dysphagia, heartburn, regurgitation, vomiting, and chest pain were given scores of 0 to 4. The frequency scores were as follows : 0 = no symptom ; 1 = symptoms 2 to 3 times per month ; 2 = symptoms 2 to 3 times per week ; 3 = symp-

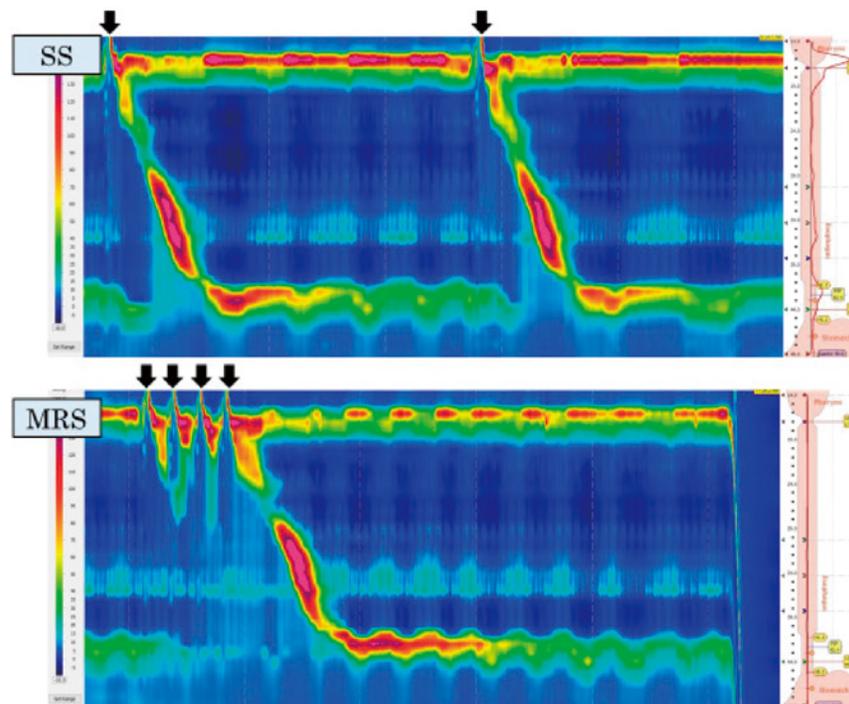


Fig. 1. The upper figure shows single swallows (SS), and the lower figure shows multiple rapid swallows (MRS). Arrows indicate swallows.

The MRS examination was performed with 2-ml water boluses 4 to 6 times at 4-second intervals. Normal MRS does not have failure of contraction after last swallows.

toms every day ; and 4 = symptoms during or after or both of every meal. The fluency scores were as follows : 0 = no symptom ; 1 = mild symptom ; 2 = moderate symptom ; 3 = severe symptom ; and 4 = extremely severe symptom<sup>6</sup>. The product of these scores (frequency score\* fluency score) was designated the “symptom score” (0-16). A symptom score  $\geq 2$  indicated symptomatic dysphagia.

The patients were divided into 2 groups : those with dysphagia and those without dysphagia after undergoing LTF. Of the patients who had symptomatic dysphagia before surgery, none had dysphagia after surgery.

The condition of patients was assessed with the anatomy-function-pathology (AFP) classification system<sup>7</sup>. The factors represented the following conditions : “A,” hiatal hernia ; “F,” acid reflux time, and “P,” reflux esophagitis. The cardiac orifice was assessed with the valve factor<sup>8</sup>. We assessed the AP factor but did not analyze the F factor because the holding time of pH < 4 was assessed. Each AP and valve factor were graded from 0 to 3.

### HRM

The HRM was performed before LTF with a 36-channel probe having circumferential sensors at 1-cm intervals and its results were analyzed via the ManoView software program (Medtronic plc, Minneapolis, MN, USA). The pressure topography of ten SS was analyzed with the Chicago Classification of esophageal motility disorders, v3.0<sup>9</sup>. The MRS examination was performed with 2-ml water boluses swallowed 4 to 6 times at an interval of less than 4 seconds (Fig. 1). The variables assessed were overall LES length, abdominal LES length, LES pressure, integrated relaxation pressure, distal contractile integral (DCI), and MRS-DCI. The MRS-DCI/SS-DCI ratio was then calculated.

### Multichannel intraluminal impedance pH monitoring

Before LTF was performed, all patients underwent multichannel intraluminal impedance pH monitoring (MII-pH). Acid suppression medications (H2 receptor antagonists  $\geq 3$  days or proton-pump inhibitors  $\geq 7$  days before MII-pH) were discontinued in these patients. The catheter-based pH probe (ZAN-BG-44 ; Diversatek Healthcare, Milwaukee, WI, USA) was inserted transnasally and positioned 5 cm above the upper border of the manometrically defined LES. Variables assessed were the pH < 4 holding time, episodes > 5 minutes, the longest event, liquid acid reflux, li-

quid nonacid reflux, total liquid reflux, symptom index, and the symptom association probability.

### Operative method

LTF was performed for all patients with a procedure previously described<sup>10,11</sup>. The standard procedure consisted of the suturing of the esophageal hiatus and of fundoplication. The indications for the use of a mesh to reinforce the hiatus were a A2 or A3 hiatal hernia, patient age  $\geq 75$  years, and a body mass index  $\geq 28$  kg/m<sup>2</sup>.

### Statistical analysis

Characteristics of HRM (SS and MRS) and MII-pH were summarized with median values and an interquartile range (25<sup>th</sup> and 75<sup>th</sup> percentiles). The Mann-Whitney *U* test was performed to compare the medians of the manometric and pH study values between patients with and patients without dysphagia, and the Fisher test was used to compare the percentage of male patients, surgical use of a mesh, AP factors, Valve factor, the symptom index, and symptom association probability. Statistical significance was accepted for *p* values < 0.05. Statistical analysis was performed with the software program IBM® SPSS® Statistics, version 22 (IBM Corp., Armonk, NY, USA).

## RESULTS

### Demographic and clinical characteristics before LTF

Four had dysphagia and 16 did not. Age, sex, and the body mass index did not differ significantly between patients with or without dysphagia before undergoing LTF (Table 1). The percentage of patients in whom the hiatus was reinforced with a mesh also did not differ significantly between these groups (patients without dysphagia, 31% ; patients with dysphagia, 50% ; *p* = 0.59).

### Symptoms before LTF

The symptom scores for heartburn, regurgitation, vomiting, and chest pain before LTF was performed did not differ significantly between the patient groups (Table 2).

### AP values of AFP classification and valve factor before LTF

The endoscopic state (AP value assessment) before LTF did not differ significantly between the patient groups (Table 3).

Table 1. Characteristics of patients with or without dysphagia before fundoplication

	No dysphagia ( <i>n</i> = 16)	Dysphagia ( <i>n</i> = 4)	<i>p</i> value
Age, years [IQR]	45 [40-50]	65 [38-78]	0.17
Male	12 (75%)	2 (50%)	0.55
Body mass index, kg/m <sup>2</sup> [IQR]	24 [21-29]	24 [22-24]	0.96
Duration of symptoms, months [IQR]	46 [12-75]	24 [15-42]	0.35
Mesh reinforcement	5 (31%)	2 (50%)	0.59

IQR : interquartile range

Table 2. Symptom scores of patients with or without dysphagia before fundoplication

	No dysphagia ( <i>n</i> = 16)	Dysphagia ( <i>n</i> = 4)	<i>p</i> value
Heartburn	2 [0-7.5]	8 [1.8-12]	0.12
Regurgitation	4 [0.3-7.5]	6 [0-12]	0.82
Vomiting	0 [0-0]	0 [0-9]	0.55
Chest pain	0 [0-3]	2 [0-10]	0.49

*Assessment of conventional SS and MRS before LTF*

Overall length, abdominal length, LES pressure, integrated relaxation pressure, and DCI did not differ significantly between the patient groups (Table 4). However, both MRS-DCI and the MRS-DCI/SS-DCI ratio were higher in patients without dysphagia than in patients with dysphagia (MRS-DCI : 831 vs. 43, *p* = 0.002 ; MRS-DCI/SS-DCI ratio : 0.7 vs. 0.05, *p* = 0.014).

*Assessment of MII-pH before LTF*

The pH < 4 holding time, episodes > 5 minutes, longest event, liquid acid reflux, liquid nonacid reflux, and total liquid reflux did not differ significantly between the patient groups (Table 5). The incidences of symptom index (≥ 50%) and of symptom association probability (≥ 95%) also did not

Table 3. Anatomy and pathology values of the anatomy-function-pathology classification and valve factor of patients with or without dysphagia before fundoplication

	No dysphagia ( <i>n</i> =16)	Dysphagia ( <i>n</i> =4)	<i>p</i> value
Anatomy			0.63
A0	3 (19%)	0	
A1	8 (56%)	3 (75%)	
A2	4 (25%)	1 (25%)	
A3	0	0	
Valve			0.64
V0	1 (6%)	0	
V1	0	0	
V2	2 (13%)	0	
V3	13 (81%)	4 (100%)	
Pathology			0.40
P0	10 (63%)	1 (25%)	
P1	4 (25%)	2 (50%)	
P2	2 (13%)	1 (25%)	
P3	0	0	

differ between the groups.

**DISCUSSION**

As an established treatment for GERD, LF is extremely useful<sup>1,12-15</sup>. However, a subset of patients are dissatisfied

Table 4. High-resolution manometry and multiple rapid swallow variables of the and dysphagia patients with and without dysphagia before fundoplication

	No dysphagia ( <i>n</i> = 16)	Dysphagia ( <i>n</i> = 4)	<i>p</i> value
Overall LES length, cm	2.8 [1.8-3.4]	2.6 [2.1-2.8]	0.75
Abdominal LES length, cm	1.6 [0-2.2]	0 [0-1.4]	0.25
LES pressure, mm Hg	21 [12-25]	19 [13-23]	0.89
Integrated relaxation pressure, mm Hg	9 [6.5-10.8]	6.9 [2.8-10.7]	0.34
DCI, mm Hg·cm·s	1,706 [767-2,909]	336 [125-1,625]	0.050
MRS-DCI, mm Hg·cm·s	831 [407-1429]	43 [9-56]	0.002
MRS-DCI/SS-DCI ratio	0.7 [0.2-1.1]	0.05 [0.06-0.4]	0.014

LES : lower esophageal sphincter ; MRS : multiple rapid swallows ; DCI : distal contractile integral ; HRM : high-resolution manometry

Table 5. Multichannel intraluminal impedance pH monitoring variables of patients with or without dysphagia before fundoplication

	No dysphagia (n=16)	Dysphagia (n=4)	p value
pH < 4 holding time (%)	1.7 [0.3-3.6]	10 [2.9-41]	0.053
Episodes over 5 min (times/day)	0 [0-1]	5 [3-14]	0.11
Longest event (min)	4 [1-11]	24 [10-166]	0.11
Liquid acid reflux (times/day)	25 [10-42]	19 [7-58]	1
Liquid non-acid reflux (times/day)	17 [9-34]	19 [6-40]	0.96
Total liquid reflux (times/day)	45 [30-71]	53 [17-89]	0.68
Symptom index ( $\geq 50\%$ )	11 (69%)	4 (100%)	0.53
symptom association probability ( $\geq 95\%$ )	9 (56%)	3 (75%)	1

with symptom control and might need to undergo LF again. However, secondary fundoplication is neither as effective nor as safe as primary fundoplication. For example, the risks of intraoperative and postoperative complications are much higher for secondary antireflux surgery than for primary fundoplication<sup>16</sup>. A study by Funch-Jensen et al. has found that after secondary antireflux surgery, complications developed in 16.9% of patients<sup>17</sup>. By predicting postoperative dysphagia, the deterioration of postoperative activities of daily living can be prevented and the need for reoperation can be decreased.

The LES pressure integral is greater after fundoplication than before fundoplication<sup>16</sup>; i.e., both the resistance of the LES and the esophageal body's force of peristalsis required during swallowing is greater after surgery than before surgery.

We had thought that the load on the esophageal body increases more with MRS than with SS. As a result, the resistance to LES also increased relatively. Therefore, MRS might be a useful for predicting conditions after fundoplication. The present study suggests that patients with a weak esophageal body movement (DCI) are not able to cope with the improved LES achieved after LTF.

A study by Shaker et al has found that patients with dysphagia after laparoscopic Nissen fundoplication had a mean MRS-DCI/SS-DCI ratio of 0.73<sup>5</sup>. In contrast, the present study found that patients with dysphagia after LTF had a mean MRS-DCI/SS-DCI ratio of 0.05 (Table 4). We surmise that the difference in the DCI ratio between the previous and the present studies is because of the use of laparoscopic Nissen fundoplication (360°) or LTF (270°). Patients with a lower MRS-DCI/SS-DCI ratio might be effectively treated when 180° wrapped fundoplication was performed.

The LES pressure integral, overall length, and abdominal length values are higher after fundoplication than before fundoplication, but LES pressure values do not significantly change<sup>18</sup>. Importantly, the LES position is maintained below the crural diaphragm<sup>19</sup>. Even with 180° wrapped fundoplication, the length of wrapping helps maintain proper overall length and abdominal length and can maintain the function to prevent gastroesophageal reflux by proper placement of the anchor and shoulder stitches.

In the present study, the percentages of patients with "P" factor, representing reflux esophagitis, of 0 before LTF were 63% in patients without dysphagia and 25% in patients with dysphagia. These results indicate that the majority of patients without dysphagia had endoscopy-negative GERD and that the lower MRS-DCI in patients with dysphagia indicates weaker esophageal clearance.

A limitation of the present study was the small number of patients, especially patients with dysphagia. Therefore, we were not able to determine a cutoff value of MRS-DCI/SS-DCI for predicting dysphagia. Nonetheless, the present results might be useful in future studies for examining surgical formulas for patients who have GERD requiring fundoplication with low DCI in MRS. If we are able, after accumulating more cases, to assume a cutoff value for Toupet (270°), the MRS-DCI value flexibly corresponds to 360°, 270°, or 180° of wrap range from the viewpoint of preventing dysphagia after surgery.

## CONCLUSION

The present study has found that patients with dysphagia after LTF are characterized by weakness of esophageal body contractions during MRS and suggests that the MRS

examination is a valuable adjunct as a preoperative evaluation.

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### DISCLOSURES

Doctors Akimoto, Yano, Omura, Tsuboi, Hoshino, Yamamoto, Masuda, Kashiwagi, and Yanaga have no conflicts of interest or financial ties to disclose.

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