

Laparoscopic Nissen-Rossetti fundoplication is effective to control gastro-oesophageal and pharyngeal reflux detected using 24-hour oesophageal impedance and pH monitoring (MII-pH)

La Nissen-Rossetti laparoscopica è efficace nel contrastare il reflusso gastro-esofageo e faringeo, identificato alla pH-impedenzometria esofagea di 24 ore (MII-pH)

G. DEL GENIO, G. ROSSETTI, L. BRUSCIANO, V. MAFFETTONE, V. NAPOLITANO,
F. PIZZA, S. TOLONE, A. DEL GENIO, M. DI MARTINO
I Division of General and Gastrointestinal Surgery, Second University of Naples, Naples, Italy

Key words

Gastroesophageal reflux • Pharyngeal reflux • Surgical treatment • Nissen fundoplication • MII-pH

Parole chiave

Reflusso gastroesofageo • Reflusso faringeo • Trattamento chirurgico • Fundoplicazio • MII-pH

Summary

The study aims to evaluate, at medium- and long-term follow-up, the efficacy of Nissen-Rossetti fundoplication to control both gastro-oesophageal and pharyngeal reflux, detected with the use of 24-hour pH-multi-channel intra-luminal impedance. Of the 1000 patients who underwent Nissen-Rossetti fundoplication in our Division since 1972, the laparoscopic approach was adopted in 428 consecutive patients with gastro-oesophageal reflux disease. The study population consisted of patients from this group with one-year follow-up. Thirty-one patients had undergone pre-operative evaluation with pH-multi-channel intra-luminal impedance and were classified on the basis of clinical assessment into gastro-oesophageal, or pharyngeal reflux disease group. Pre-operative data are reported. Comparison between gastro-oesophageal reflux and pharyngeal reflux are extrapolated from pH-multi-channel intra-luminal impedance. No conversion to open surgery and no mortality occurred. A major complication occurred in 4 patients (1.1%) and led to a re-intervention in 3. An excellent outcome was reported in 92.9% of the patients at mean follow-up of 83.2 ± 7 months. Instrumental outcomes are discussed. In conclusion, Nissen-Rossetti fundoplication provides excellent protection from gastro-oesophageal and pharyngeal reflux. The use of pH-multi-channel intra-luminal impedance is suitable in patients candidate to anti-reflux surgery to detect non-acid reflux.

Riassunto

Scopo del lavoro è valutare, a medio e a lungo termine, l'efficacia della plastica secondo Nissen-Rossetti nel contrastare il reflusso gastroesofageo e faringeo, individuato attraverso la pH-impedenzometria intraluminal multicanale di 24 ore (MII-pH). Su 1.000 pazienti, sottoposti a fundoplicazio secondo Nissen-Rossetti nella nostra divisione dal 1972, l'approccio laparoscopico è stato adottato in 428 pazienti consecutivi affetti da reflusso gastroesofageo. La popolazione dello studio consiste nei pazienti di tale gruppo con almeno 1 anno di follow-up. Inoltre, trentuno pazienti sono stati valutati con MII-pH e classificati sulla base dei sintomi clinici nel gruppo del reflusso gastroesofageo o faringeo. I dati pre-operatori sono riportati. Il confronto tra reflusso gastroesofageo e faringeo è dedotto dall'attenta analisi di MII-pH. Non è stata osservata alcuna conversione alla chirurgia tradizionale o mortalità. Una complicanza maggiore si è avuta in 4 pazienti (1,1%) ed ha condotto ad un reintervento in 3 di questi. Un risultato eccellente è stato riportato nel 92,9% dei pazienti al follow-up medio di $83,2 \pm 7$ mesi. I risultati strumentali sono riportati e discussi. La fundoplicazio secondo Nissen-Rossetti garantisce una protezione eccellente al reflusso gastroesofageo e faringeo. L'uso della pH-MII è appropriato nei pazienti candidati alla chirurgia per individuare il reflusso non-acido.

Introduction

In the last decade, widespread use of laparoscopy has changed the scenario of anti-reflux surgery. Standardization of the techniques with the parallel improvement in the available technology has led to the minimally invasive access being at least as safe and as effective as its open counterpart¹. At the same time, new, more accurate, diagnostic tools have enhanced

the diagnostic process. In particular, refinement of the indications, recently made possible thanks to 24-hour multichannel intraluminal impedance – pH monitoring (MII-pH), which is currently the most sophisticated diagnostic device to investigate gastro-oesophageal and pharyngeal reflux². MII-pH provides information concerning the direction of the flow (oral or aboral), the physical characteristics of the refluxate (liquid, gas or mixed) and, by means of two

pH sensors located in the catheter, 5 cm above the LES and in the pharynx, assigns a degree of acidity to the single episode of reflux at oesophageal and pharyngeal level.

In this report, personal experience is described with Nissen-Rossetti fundoplication, standardized definitively in 1972, and transposed without modifications to laparoscopy³. This technique was adopted in 1000 cases to eliminate a primary gastro-oesophageal reflux (GERD), hiatal hernia, duodeno-gastro-oesophageal reflux) or to prevent reflux secondary to a surgical procedure (i.e., Heller's myotomy, epiphrenic diverticulectomy, subtotal oesophagectomy with gastric or colic interposition). Particular emphasis is focused on this unmodified surgical technique; long-term outcomes and MII-pH, as a diagnostic instrument, will be discussed.

Patients and methods

Since 1972, more than 1000 Nissen-Rossetti fundoplications have been performed in our institution; starting from September 1992, the laparoscopic approach was adopted and 700 patients underwent this procedure (Fig. 1). Of these, 428 patients (172 male, 256 female, mean age 41.9 years; range 12-80) with a documented GER resistant to medical therapy were operated on, and 380 consecutive patients (153 male, 227 female, mean age 41.8 years; range 12-80) with a minimum follow-up of 12 months were prospectively followed.

Data were analyzed after approval of the local Ethics Committee Review Board. Patients had to have suspended proton pump inhibitors (PPI), prokinetics, or any other drug having an effect on reflux, at least 8 days before 24 hour pH monitoring or MII-pH. Exclusion criteria were: para-oesophageal (Type II), mixed (Type III) or giant hernias (> 5 cm), and previous surgery at oesophago-gastric junction level. Statistical analysis was carried out using SPSS for Windows (version 12.0, SPSS Inc. Chicago, IL). Results are expressed as mean \pm SD unless otherwise indicated. Student t test, the Chi-square test, Fisher's exact test were used as appropriate. A p value < 0.05 was considered statistically significant.

PRE-OPERATIVE EVALUATION

Pre-operatively all patients underwent oesophago-gastro-duodenoscopy (EGDS), X-ray (RX) barium swallow, stationary oesophageal manometry (Dyno 2000[®] – Menfis Biomedical, Bologna, Italy) and 24-hour pH monitoring (Digitrapper Proxima[®] – Synetics Medical, Stockholm, Sweden), as described elsewhere. Starting from September 2005, in 31 consecutive cases, instrumental assessment was completed by MII-pH (Sleuth[™] System[®] – Sandhill Scientific

Inc., Highlands Ranch, CO, USA) instead of the classic 24-hour pH monitoring.

Manometric variables assessed were: 1) pressure of the lower oesophageal sphincter (LES); 2) amplitude and propagation of peristalsis (oesophageal peristalsis was considered impaired when < 30 mmHg). Twenty-four hour oesophageal pH monitoring was carried out with a single or double probe (Digitrapper Proxima[™] - Synetics Medical, Stockholm, Sweden): the distal electrode was placed 5 cm above the proximal margin of the LES, identified by means of stationary manometry; percent time with pH < 4 total, and collected in upright and recumbent position.

24/HOUR pH-MULTICHANNEL INTRA-LUMINAL IMPEDANCE (MII-PH)

A dedicated pH/impedance catheter with six pairs of impedance sensors positioned in the oesophagus 3, 5, 7, 9, 15, and 17 cm above the upper edge of the LES was placed trans-nasally. A catheter with one pH sensor 5 cm above the LES was used in GERD, while a second pH sensor, at the cervical oesophagus, was added in the catheter in PR (Fig. 2). The information was transmitted by the catheter into a software programme included in the device (Sleuth, Sandhill Scientific Inc. Highlands Ranch, Colorado, USA) worn by the patient for 24 hours. Patients were invited, as far as possible, to continue with their normal activity and diet. They were invited to carefully insert, into the device by digital input, and to simultaneously take note on a prescribed paper form, of the meal periods, the time at which, with recumbent/upright position, each symptom occurred. Data were acquired and analyzed with the Bioview GERD Analysis Software (Sandhill Scientific Inc.). All tracings were carefully reviewed to check correspondence between the result of the computer evaluation and the morphology of every single reflux episode. Meal periods and drops in pH, not related to a retrograde movement at the impedance (i.e., swallow of acid drink), were automatically excluded from the analysis to improve accuracy of the pH monitoring.

From September 2005 to December 2005, 31 consecutive patients were investigated by MII-pH. Of these, 24 patients (14 female, 10 male; mean age 41.7 \pm 14 years, range 21-71) with typical reflux symptoms were included in the GERD group, while 7 patients (4 female, 3 male; mean age 38.7 \pm 18 years, range 8-75) with complaints of respiratory symptoms (chronic cough, sleep apnoea, asthma, laryngitis) were defined as pharyngeal reflux (PR) group.

SURGICAL TECHNIQUE

The patient was placed in the lithotomy position with legs abducted, the monitor located at the right shoulder, the endoscope at the left shoulder and the mano-

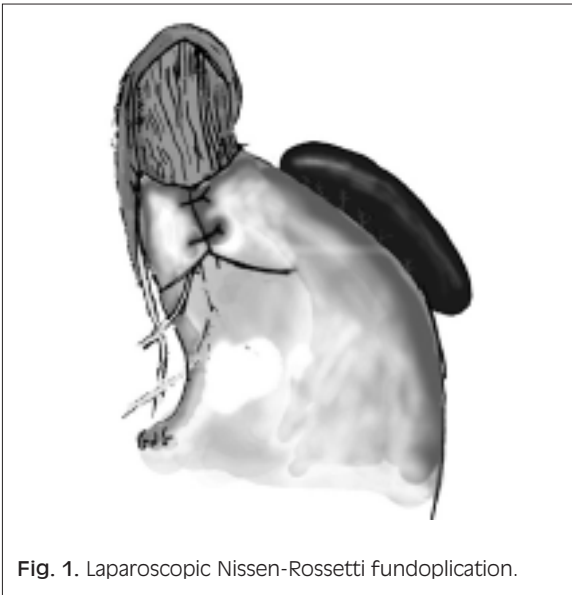


Fig. 1. Laparoscopic Nissen-Rossetti fundoplication.

meter just behind it. The surgeon stands between the patient's legs, the first assistant on the patient's right side and the camera driver on the opposite site. A pneumo-peritoneum was induced at 12 mmHg using a Veress needle. Five trocars (one 10 mm and four 5 mm) were inserted in the classic position for gastro-oesophageal surgery⁴. A steep reverse-Trendelenburg position was adopted.

The aspirator was inserted in the epigastric trocar to retract the left liver. The abdominal portion of the oesophagus and the height of the cardias was localized with the help of the trans-illumination provided by the endoscope. The first step consisted in freeing the oesophagus from the right and then the left crus. To achieve this step, the assistant with a Babcock grasper positioned at the anterior oesophageal fat pad retracted downwards the oesophagus. Recently, dissection was achieved with the 5-mm radiofrequency dissector (Atlas, USSC, Norwalk, CT, USA), which significantly facilitates the procedure. The procedure begins with the section of the anterior peritoneal reflection of the gastro-oesophageal junction, taking care to start the section of the hepato-gastric ligament high enough to avoid accidental cutting of the vagal branch to the liver. Once the anterior vagal nerve has been identified, the gastrophrenic ligament is sectioned; the dissection continues from the right to the left behind the oesophagus until the crura are exposed and Hill's angle is annulated, taking extra care to visualize and avoid injury to the posterior vagus. The oesophageal retractor replaces the Babcock grasper and the posterior window for the wrap is adequately enlarged. With the help provided by the right and left steering of the retrac-

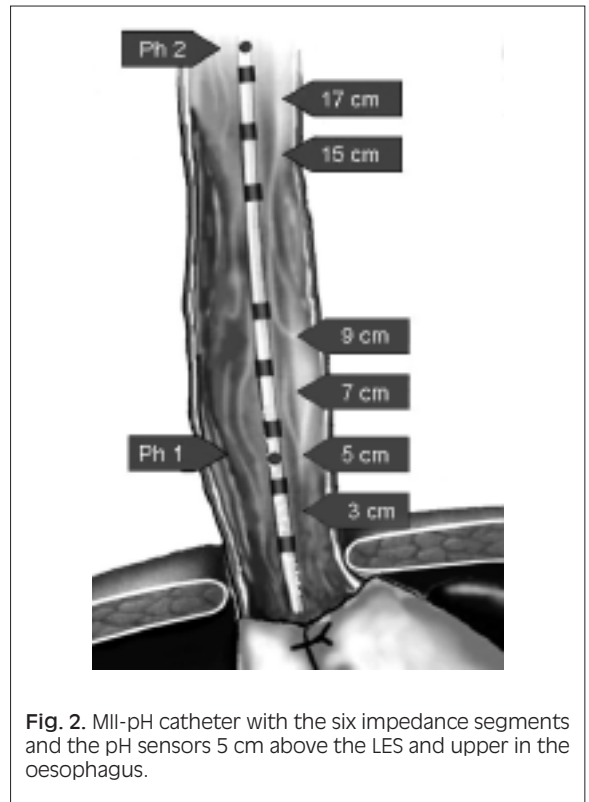


Fig. 2. MII-pH catheter with the six impedance segments and the pH sensors 5 cm above the LES and upper in the oesophagus.

tor and the cautious trans-hiatal exposure of the irrigator, the oesophagus is extensively mobilized in the mediastinal portion until it remains in the abdomen without tension. Cruroplasty is accomplished by one simple extra-corporeal non-absorbable suture, additional sutures may be required only in the case of a larger defect (> 4 cm). The 2 cm-long Nissen-Rossetti wrap is fashioned with the superior-anterior wall of the gastric fundus, passed, whenever possible, between the posterior vagus nerve and the oesophagus. In the present series, the short gastric-vessels have been preserved in all cases. The two gastric hemi-valves are sutured with two stitches which did not incorporate the oesophageal muscular layer. The routine preservation of the short gastric vessels is the most important mechanism of fixation of the gastric fundus, thus the gastro-gastric suture to avoid the slippage or any other expedient to anchor the wrap to the crura or to the oesophagus were considered useless. At the same time, the bougie was never used to avoid accidental oesophageal lesions. Early in the series, the wrap was built around the gastroscope (diameter 9-10 mm) to obtain a hypercalibrated wrap in order to avoid recurrence of long-term reflux. Currently, the wrap is tailored upon the morphology of the patient's fundus, grasping the tissue at the point which leads to the most satisfactory

anti-reflux fundoplication. This technique is safe and a satisfactory wrap within the desired pressure range is achieved (25-35 mmHg) because an intra-operative manometric control was routinely attempted at the end of the procedure. Moreover, the endoscope, at the end of the procedure, verified the correct geometry of the wrap, in particular whether the superior aspect of the gastric fundus was not included into the wrap and the passage of the endoscope through the fundoplication.

Finally, the endoscopic trans-illumination established the height of the wrap with respect of the cardia which, after reduction of the hiatal hernia and hiatoplasty, may have changed level in the abdomen. If the pressure was not within the range or if the endoscopic control was not satisfactory the wrap was partially or totally refashioned.

POST-OPERATIVE EVALUATION

Peri-operative data were collected prospectively. Clinical evaluation consisted in analysis of resolution of the pre-operative symptoms and functional outcomes. Instrumental follow-up was accomplished during the first year after surgery and included Rx barium swallow, EGDS, oesophageal manometry and 24 h pH monitoring.

Results

PRE-OPERATIVE DATA

Mean duration of pre-operative symptoms was 4.9 ± 3.8 years (range 1-22). Table I outlines the incidence of typical and respiratory symptoms. At manometric evaluation, mean LES pressure was 11.0 ± 1.2 mmHg and impaired peristaltic waves of distal oesophageal amplitude (DEA) showed a pressure value lower than 30 mmHg in 37.4% (142/380) of cases. Hiatal hernia, oesophagitis and Barrett's oesophagus were present in 73.9% (281/380), 39.2% (149/380), and 3.9% (15/380) of cases, respectively.

The mean percentage with pH < 4 at 24 h monitoring was 7.8 ± 4 for total time, 9.2 ± 5 and 5.0 ± 3 in upright and recumbent position, respectively.

24 h pH-MULTICHANNEL INTRALUMINAL IMPEDANCE

At MII-pH, mean analysis time was 1246 ± 172 min (GERD) and 1273 ± 61 min (PR). Mean period of time in recumbent position was 583 ± 243 min (GERD) and 748 ± 191 min (PR); pH monitoring obtained with the pH distal catheter is outlined in Table II. Table III shows data obtained at MII-pH.

PERI-OPERATIVE RESULTS

All the procedures were completed under laparoscopy. Mean operative time was 52 ± 14 minutes. No cases of mortality occurred. A major complication was obser-

Table I. Incidence of pre-operative symptoms.

Symptom	GERD (Total no. = 380) no. (%)
Heartburn	315 (82.9)
Acid regurgitation	291 (76.6)
Dysphagia	40 (10.5)
Chest pain	62 (16.3)
Respiratory complications	27 (7.1)

ved in 4/380 patients (1.1%). In one patient (0.3%), an intra-operative mucosal tear occurred; immediate repair was possible performing a suture. In the other 3 patients, post-operative bleeding occurred: the patients were re-operated via the laparoscopic approach, on the first post-operative day and, in one case, splenectomy was necessary. Mean post-operative hospital stay was 2.6 ± 0.9 days. Return to normal activity was achieved in a mean of 8.3 ± 3.4 days.

POST-OPERATIVE RESULTS

Of the 380 patients, 368 (96.8%) were observed at clinical follow-up. Mean follow-up was 83.2 ± 7 months (range 6-141).

An excellent outcome was observed in 92.9% (341/368) of cases. Persistence of post-operative dysphagia, at 6 months, was observed in 13 cases (3.5%): two patients had pre-operatively been found to present impaired peristalsis, the remaining 11 had been classified as normal motility patients. Seven of these patients were submitted to endoscopic dilatation, whereas 6 patients (1.6%) underwent laparoscopic redo-fundoplication with partial resolution of dysphagia. Recurrent heartburn, confirmed at pH monitoring was observed in 14 patients (3.8%); ten patients, needed to return to previous peptic medications; whereas the remaining 4 patients underwent redo-fundoplication with improvement in symptoms control. At Rx barium swallow, a "disrupted wrap" was retrieved in 7 patients, a "herniated wrap" in 4 patients and a "slipped Nissen" in the remaining 3 patients.

Instrumental follow-up at 1 year was possible in 96 out of 380 patients (25.3%). Stationary oesophageal manometry showed a significant improvement in the mean new high pressure zone (28.1 ± 1.2 mmHg); an increase of DEA was observed in 79.1% of patients (76/96).

Discussion

When compared with other antireflux procedures, total fundoplication is the most effective barrier against reflux. Nissen-Rossetti, in particular, achieves this

Table II. Distal pH monitoring at combined MII-pH. Noteworthy, excluding pH drops not associated with retrograde movements detected at impedance.

	GERD (N = 24)	PR (N = 7)	p
(%) pH < 4 total – min			
Mean ± SD	5.2 ± 6	7.35 ± 15	< 0.02
(%) pH < 4 upright – min			
Mean ± SD	3.84 ± 4	6.8 ± 8	NS
(%) pH < 4 recumbent – min			
Mean ± SD	1.4 ± 2	10.5 ± 7.5	< 0.001
No. reflux episodes			
Mean ± SD	25.2 ± 21	35.2 ± 27	NS
DeMeester's score			
Mean ± SD	9.5 ± 10	32.6 ± 24	< 0.005

NS: not significant?

Table III. Mean ± SD of the number of reflux episodes at pH-MII.

	GERD (N = 24)	PR (N = 7)	p
All-reflux total	55.2 ± 38	100.0 ± 65	< 0.05
All-reflux upright	43.7 ± 32	60.8 ± 46	NS
All-reflux recumbent	11.5 ± 11	39.1 ± 37	NS
Acid reflux total	29.1 ± 20	46.6 ± 35	NS
Acid reflux upright	24.4 ± 19	23.8 ± 17	NS
Acid reflux recumbent	4.7 ± 5	22.7 ± 20	< 0.005
Non-acid reflux total	43.7 ± 33	60.8 ± 27	NS
Non-acid reflux upright	19.2 ± 17	36.8 ± 45	NS
Non-acid reflux recumbent	26.0 ± 22	53.2 ± 59	NS

goal without the need to resection the short gastric vessels, thus it consists in a safer procedure than the classic “floppy” Nissen. Avoiding this manoeuvre results in a significant decrease in lesions to the spleen and bleeding from the short gastric vessels which may be difficult to control and, in some cases, may lead to an unavoidable splenectomy.

The primary function of the fundus consists in accepting and storing swallowed food. This reservoir function is based on the incredible ability of the anterior gastric wall to relax with the onset of swallowing of the bolus⁵. This adaptive characteristic allows the subject to store a large amount of food with only a slight increase in intra-gastric pressure and consequently minimal discomfort.

The fundic compliance to food is activated by the intrinsic innervation of the stomach, as demonstrated in a recent study, by intra-gastric perfusion of a small quantity of lipids. It is likely that both the volume and the type of food ingested influence the degree of distention and contraction of the gastric fundus⁶.

As the anterior gastric wall is used to fashion the anti-reflux wrap, its incredibly elastic feature not only

restores the competence of the LES, increasing its basal tone, but also adapts the efficiency of the wrap at the level of gastric fullness achieving the protection when the stomach is distended in the post-prandial periods. In previous studies, we demonstrated the advantages of the Nissen-Rossetti fundoplication by means of intra-operative manometry⁷ and 24-hour manometric monitoring⁸.

In the last decade, laparoscopic Nissen fundoplication has gained widespread popularity and growing numbers of anti-reflux procedures have been performed worldwide. Besides the cosmetic advantages, minimally invasive surgery allows a faster return to daily activities and almost totally avoid the previous wound and respiratory complications. The main advantage of laparoscopy is intrinsic in the possibility of viewing the surgical field through the monitor(s). This, from the surgeon's standpoint, magnifies and improves vision allowing more precise movements, while, at the same time, greatly improving the teaching aspects for the assistants and offering the same view to the first surgeon; moreover, easy recording of the images with current digital cameras, surgical debates are more complete,

thus improving standardization of the techniques. Our data, at long-term post-operative follow-up confirm the validity of this approach – in a large series – in the control both of classic and respiratory symptoms. Recently, the 24-h multichannel intraluminal impedance and pH (MII-pH) have become available. This sophisticated tool has refined the diagnostic process of GER and pharyngeal reflux, by allowing the movement and type of refluxate to be followed along the oesophagus; moreover, by means of two pH sensors which are inserted in the catheter at different levels it is possible to assign a degree of acidity to the single reflux episode. MII-pH investigation, using different models of catheter, may be used to monitor the acidity in the stomach and 5 cm above the LES or 5 cm above the LES and in the cervical oesophagus. In the latter version, MII-pH provides useful data to study the patients with pharyngeal reflux ⁹. Moreover, MII-pH software eliminates the drop in pH to < 4 which do not correspond to a retrograde movement at impedance, thus it enhances the specificity of the pH monitoring by excluding the false acid episodes simply induced by the swallowing of an acidic liquid (Coke, lemon

juice). Using the same technology, a pilot study has indicated that PPI therapy is able to shift the pH composition of refluxate, but does not affect the number or duration of reflux episodes in patients with GERD ¹⁰. Our preliminary data with MII-pH indicate that non-acid reflux is a predominant factor in patients with GERD and PR. Moreover, it accounts for a large portion of the symptoms associated with reflux, with the symptom correlation index for non-acid episodes being higher than its acid counterpart. Overall the number of reflux episodes was statistically higher (< 0.05) in patients with supra-oesophageal symptoms (PR) when compared with GERD patients, especially in the recumbent position (< 0.005) (Table III).

In summary, laparoscopic Nissen-Rossetti is a safe and effective procedure at long-term follow-up to protect against gastro-oesophageal and pharyngeal reflux. The lack of response of non-acid reflux to the currently available medical drugs, predisposes these patients as perfect candidates to Nissen-Rossetti fundoplication. MII-pH is extremely useful in the selection of these cases for surgical treatment.

References

- Catarci M, Gentileschi P, Papi C, Carrara A, Marrese R, Gaspari AL, et al. *Evidence-based appraisal of antireflux fundoplication*. *Ann Surg* 2004;239:325-37.
- Shay S, Tutuian R, Sifrim D, Vela M, Wise J, Balaji N, et al. *Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers*. *Am J Gastroenterol* 2004;99:1037-43.
- Rossetti G, Bruscianno L, Amato G, Maffettone V, Napolitano V, Russo G, et al. *A total fundoplication is not an obstacle to esophageal emptying after heller myotomy for achalasia: results of a long-term follow-up*. *Ann Surg* 2005;241:614-21.
- Del Genio A, Rossetti G, Maffettone V, Renzi A, Bruscianno L, Limongelli P, et al. *Laparoscopic approach in the treatment of epiphrenic diverticula: long-term results*. *Surg Endosc* 2004;18:741-5.
- De Ponti F, Azpiroz F, Malagelada JR. *Relaxatory responses of canine proximal stomach to esophageal and duodenal distension. Importance of vagal pathways*. *Dig Dis Sci* 1989;34:873-81.
- Castro A, Mearin F, Larish J, Malagelada JR. *Gastric fundus relaxation and emetic sequences induced by apomorphine and intragastric lipid infusion in healthy humans*. *Am J Gastroenterol* 2000;95:3404-11.
- Del Genio A, Izzo G, Di Martino N, Maffettone V, Landolfi V, Martella A, et al. *Intraoperative esophageal manometry: our experience*. *Dis Esophagus* 1997;10:253-61.
- Di Martino N, Bortolotti M, Izzo G, Maffettone V, Monaco L, Del Genio A. *24-hour esophageal ambulatory manometry in patients with achalasia of the esophagus*. *Dis Esophagus* 1997;10:121-7.
- Oelschlager BK, Quiroga E, Isch JA, Cuenca-Abente F. *Gastroesophageal and pharyngeal reflux detection using impedance and 24-hour pH monitoring in asymptomatic subjects: defining the normal environment*. *J Gastrointest Surg* 2006;10:54-62.
- Tamhankar AP, Peters JH, Portale G, Hsieh CC, Hagen JA, Bremner CG, et al. *Omeprazole does not reduce gastroesophageal reflux: new insights using multichannel intraluminal impedance technology*. *J Gastrointest Surg* 2004;8:890-7; discussion 897-8.

■ Address for correspondence: Dr. G. del Genio, via Stretto-la a Chiaia 7, 80122 Napoli, Italy. Fax +39 081 5666614. E-mail: gdg@doctor.com