The effects of lung resection on physiological motor activity of the oesophagus†

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Abstract

OBJECTIVES: To assess the modifications of oesophageal function after major lung resection and whether these modifications are correlated with the extent of resection (pneumonectomy vs others).

METHODS: In the last 5 years, 40 consecutive surgical patients with lung cancer were prospectively enrolled and divided in two groups: Group A (n = 20) patients scheduled for elective pneumonectomy and Group B (n = 20) for more limited resections (lobectomy or bilobectomy). In addition to routine evaluations, all patients underwent preoperative (within 5 days) and postoperative (6 months) oesophageal manometry to assess the lower oesophageal sphincter (LES), the oesophageal body and the upper oesophageal sphincter functions. Symptoms scoring questionnaires were recorded for each patient and the oesophageal dislocation assessed by radiological examinations.

RESULTS: Thirty-three (15 of Group A and 18 of Group B) patients completed the study. After operation, we found that LES resting pressure was significantly lower in Group A compared with Group B (P = 0.01); conversely, the relaxing pressure resulted as being higher in Group A than in Group B (P = 0.01). In Group A compared with Group B, a significant reduction of amplitude and that of wave duration of oesophageal contractions were seen at the upper (0.0001 and 0.02, respectively), middle (0.0003 and 0.002, respectively) and lower (0.0001 and 0.0004, respectively) oesophageal body. In addition, 12 of 15 (80%) patients of Group A and 3 of 18 (17%) of Group B presented a lack of regular peristaltic movement (P = 0.001). Despite chest CT scan showing a shift of the oesophagus in 11 of 15 (73%) and 2 of 18 (11.1%) patients of Groups A and B (P = 0.001), the oesophagus dislocation resulted ‘severe’ on barium swallow study in only two patients of Group A. The manometric alterations were subclinical; heartburn was recorded in three patients (two of Group A and one of Group B) and epigastric pain in four (two for each group). No other symptoms were observed.

CONCLUSIONS: Pneumonectomy may cause significant oesophageal motility disorders that are mostly subclinical. Thus, this type of surgery should not be denied to patients if required to treat their cancer.

Keywords: Oesophageal motility · Lung cancer · Resection

INTRODUCTION

Pneumonectomy, first performed with success in 1933 by Graham and Singer [1], is still required in ~15–20% of patients undergoing surgical resection of primary lung cancer when a wedge resection, lobectomy or other lesser resection will not clear the tumour [2].

Pneumonectomy is known, however, to be associated with worse functional outcomes than lesser resections. In the literature, most publications concern the alterations of respiratory and circulatory functions with post-pneumonectomy that accounted for >85% of all complications [3–5].

However, the removal of one entire lung not only reduces the pulmonary vascular bed, but may also change the position of several mediastinal structures including the oesophagus. In 1935, Blalock [6] was the first surgeon who demonstrated in a dog model that the oesophagus shifted after pneumonectomy. Then, an increase in oesophageal dysmotility and delayed gastric emptying after pneumonectomy were described, but, to date, there are limited data on the impact of lung resection on oesophageal function [7].

To further define such an issue, we hereby describe the results of a prospective study designed to assess the modifications of oesophageal function after major lung resection, their correlation with the extension of resection (pneumonectomy vs lobectomy or bilobectomy) and whether such modifications have clinical effects.
MATERIALS AND METHODS

Study design

Consecutive patients with lung cancer suitable for major lung resections were enrolled in this prospective study. They were divided in two groups according to the type of resections: Group A patients were scheduled for elective pneumonectomy and Group B patients underwent more limited resections, i.e. lobectomy or bilobectomy. Exclusion criteria were (i) previous history of systemic disease, (ii) gastrointestinal surgery or other upper gastrointestinal conditions that could influence oesophageal motility, (iii) serious postoperative complications, i.e. bronchopleural fistula, empyema, respiratory failure or acute myocardial infarction, and (iv) lack of patient consent. In addition to routine evaluations, all patients underwent preoperative (within 5 days) and postoperative (6 months) oesophageal manometry to assess the lower oesophageal sphincter (LES), the oesophageal body and the upper oesophageal sphincter (UES) functions. Symptoms scoring questionnaires were recorded for each patient, and the intergroup differences were then statistically evaluated. The present investigation was approved by the Ethics Committee of Second University of Naples, and informed consent was obtained from every subject before being entered in the study.

Patients

In the last 5 years, 44 consecutive patients with pathologically proven lung cancer were assessed for eligibility in the present study. Of these, 21 (Group A) patients were scheduled for pneumonectomy and 23 (Group B) for lobectomy or bilobectomy. All patients underwent a standard preoperative work-up for lung cancer surgery; patients of Group A had an adequate cardiac reserve and predictive postoperative FEV1 of at least 1 L, as assessed by preoperative spirometry and/or ventilation isotopic scan. Oesophageal manometry was performed within 5 days before lung resection and at 6 months after. In addition, patients were asked to complete a symptom questionnaire concerning the presence of heartburn, regurgitation, epigastric pain, nausea, dysphagia and vomiting before and after operation. Histopathological analysis was carried out and the tumours were re-staged using the 7th international edition of TNM staging system for lung cancer.

Oesophageal manometry

Stationary oesophageal manometry was carried out using eight-channel perfusion catheters, four disposed radially and oriented at 90° to each other and four positioned longitudinally at intervals of 5 cm. The catheter was perfused with distilled water using a low-compliance capillary pump at a constant infusion rate of 0.8 ml/min at 1.2 kg/cm². A system of pressure transducers transmitted data to an acquisition device (ACQ1TM-Menfis BioMedica-Bologna, Italy) and from there to a personal computer. A specific software package (Dyno 2000 TM Menfis BioMedica-Bologna, Italy) was used for data acquisition and processing. The catheter assembly was introduced nasally without prior sedation or local anaesthesia and was positioned with all orifices into the stomach. Intragastric end pressure was used as zero reference. A slow station pull-through was performed at 1 cm increments. Once the LES was profiled, the distal pressure transducer that included four lumen was placed in the high-pressure zone of the LES, so that the proximal pressure transducers were located 5, 10, 15 and 20 cm above the LES. Oesophageal peristalsis was assessed with 10 wet swallows (5 ml of room temperature) at 30 s intervals. The manometry catheter was then pulled through the UES using the distal sphincter transducer to record UES pressure.

Data analysis

All traces were analysed visually by observers blinded to the clinical history of subjects. Small differences (≤5%) in manometric values were not taken into account, and the mean values of the two readings were transcribed. When differences >5% were found, the investigators had to reach an agreement.

Lower oesophageal sphincter evaluation

In the area of the LES muscle, measurements were made to check the pressure of the sphincter muscle as well as the length of the muscle in the abdominal cavity and its entire length. The end-expiratory intragastric pressure was the baseline for the manometric measurement. The position at which pressure was >2 mmHg higher than the intragastric baseline pressure was the distal border of the LES. The area that showed the decrease to the end-inspiratory oesophageal baseline pressure was the proximal border. When the intraluminal pressure of the oesophageal sphincter was <6 mmHg, the intra-abdominal length was >1 cm or the entire length >2 cm, it was defined as abnormal [8]. When the LES relaxed at ~5 mmHg lower than the gastric intraluminal pressure and the oesophageal body that had a near border was moving peristaltically, we defined it as normal relaxation and well-established coordination [9].

Oesophageal body evaluation

After the catheter was fixed in the area 3 cm above the distal border of the LES, measurements were taken to check the pressure (measured as mmHg), the contraction period (measured as seconds) and the peristaltic coordination of the oesophageal body. Following wet swallows in the supine position, amplitude was measured as from the mean oesophageal baseline to peak of the contraction. The contraction period or wave duration was measured in seconds from the starting point of the contraction to the point where the pressure dropped to the baseline pressure of the oesophagus. The transmission time of the peristaltic wave was measured in seconds between the maximum contracting points of two consecutive peristaltic waves. The contraction speed was measured in centimetres per second as the difference in the distance of the maximum contracting points, measured from each continuing internal tube and divided by time. If this speed is >20 cm/s, it is defined as a simultaneous contraction (or dysmotility), and this means that the peristaltic movement does not occur in coordination from the proximal part of the oesophageal body to the distal part of the oesophageal body [9].
Upper oesophageal sphincter evaluation

UES pressure was calculated as the highest mean pressure recorded over at least a 2-s period during this station pull-through. Using the technique described by Castell [10], the distal sphincter transducer was placed just proximal to the manometric UES and a series of 10 5-ml wet swallows was recorded. The UES was lifted into the transducer with initiation of swallowing and relaxation was measured as a fall in pressure after this initial rise. The two transducers proximal to the distal sphincter transducers were used to evaluate pharyngeal peristalsis. If the relaxation with the pharyngeal contracting movement overlapped the minimum point of the UES, it was defined as the well-established coordination of the pharynx and the UES.

Radiological evaluation

All patients underwent chest CT scan during the follow up. If a dislocation of the oesophagus was seen on chest CT scan, the patient underwent barium swallow studies to determine the grade of oesophageal displacement. The displacements were defined as severe if a shift of more than the width of a spinal body occurred as previously reported by Kriedemann and Mateev [11].

Statistical analysis

The simple size calculation was based on the values of previous studies concerning the oesophageal alterations after lung resection and clinical judgement (effect size: 4.5). Assuming a standard deviation of 2.25 points, an alpha of 0.05 and a beta of 0.20 (power of 0.80), this analysis indicated that a sample size of at least 14 patients per group was necessary. Results were expressed as number and percentages for categorical variables and as median and range or mean ± SD for scaled variables. The intergroup differences were assessed using Mann-Whitney U-test and χ² test as indicated. A difference between observed variables was considered statistically significant when P < 0.05. Statistical analysis was conducted with the MedCalc test.

RESULTS

Of the 44 patients evaluated, 4 (one for Group A, and three of Group B) were excluded for previous gastrointestinal disease. Two patients of Group A and one of Group B refused to continue the study; one patient of Group A and one of Group B were excluded because their oesophageal motility studies were considered technically inadequate; finally two patients of Group A with nerve phrenic crush during surgery were excluded. That was because the LES and diaphragmatic sphincter are anatomically superimposed on each other, and therefore it is difficult to discern whether the intraluminal pressure is related to LES or diaphragmatic sphincter contraction [12, 13].

Thus, our study population included 33 patients (15 of Group A and 18 of Group B). A study flow diagram is reported in Fig. 1.

Five of 15 patients (33%) of Group A received right pneumonectomy (1 intrapericardial) and 10 of 15 (67%) left pneumonectomy (1 intrapericardial). In Group B, 16 of 18 (89%) patients underwent lobectomy, of which 7 of 16 (44%) were on the right side. In two cases (11%), bilobectomy was performed. Induction chemotherapy with a cisplatinum-based regimen was performed in 2 of 15 (13%) and 1 of 18 (5.5%) patients, respectively, in Groups A and B; 7 of 15 (47%) of Group A and 5 of 18 (28%) among Group B patients received adjuvant therapy. No mortality was observed during the postoperative course. The median length of stay of Group B was shorter than Group A (6 vs 13 days) due to the increased risk of developing complications after pneumonectomy compared with lobectomy or bilobectomy. The clinical features of the study population are shown in Table 1.

Lower oesophageal sphincter findings

The results are listed in Table 2. In LES, the baseline resting pressure of Group A was similar to that of Group B (24 ± 5.4 vs 25.9 ± 6.1, respectively, P = 0.7). After resection, we found that Group A presented a more significant reduction of resting pressure than Group B (18.6 ± 4.8 vs 24.5 ± 5.4, respectively, P = 0.01, Fig. 2A). The baseline values of relaxing pressure were similar in

![Figure 1: Diagram of the study.](https://academic.oup.com/ejcts/article-abstract/44/2/250/439026/figure1.png)
Groups A and B (6.8 ± 1.4 vs 6.8 ± 0.8, respectively, \( P = 0.8 \)); after operation, in Group A, relaxing pressure was significantly higher than in Group B (7.8 ± 1.3 vs 6.9 ± 0.7, \( P = 0.01 \), Fig. 2B). For the rest, similar values of total and abdominal LES lengths before and after resection were registered, irrespective of the surgical resection performed. No alteration of timing wave opening was recorded in 12 of 15 (80%) patients of Group A and 16 of 18 (89%) of Group B before operation; and no significant change was recorded after operation between the two study groups.

### Oesophageal body findings

The results are summarized in Table 3. Both study groups had similar baseline values of amplitude of oesophageal contractions at the upper, middle and lower oesophagus body without significant intergroup difference. After operation, Group A compared with Group B presented a significant reduction of oesophageal contractions at upper \(116 (93–131) \) vs \(155 (130–174) \); \( P < 0.0001 \), middle \(92 (81–125) \) vs \(120 (98–150) \); \( P = 0.0003 \) and lower oesophageal body \(49 (30–75) \) vs \(85 (55–95) \); \( P = 0.0001 \) (Fig. 3A). After operation, Group A compared with Group B presented a significant reduction of wave duration at upper \(3.2 (2.5–4.3) \) vs \(3.6 (2.1–5.1) \); \( P = 0.02 \), middle \(3.1 (2.4–4.1) \) vs \(3.7 (3.3–4.1) \); \( P = 0.002 \) and lower oesophageal body \(3.4 (2.8–4.1) \) vs \(3.9 (3.5–4.5) \); \( P = 0.0004 \) (Fig. 3B). Preoperative oesophageal motility resulted in altered 5 of 15 (33%) patients of Group A and 1 of 18 (6%) of Group B \( (P = 0.07) \). After operation, 12 of 15 (80%) patients of Group A and 3 of 18 (17%) of Group B presented a lack of regular peristaltic movement, with significant statistical difference between the two groups \( (P = 0.001) \).

### Upper oesophageal sphincter findings

The results are listed in Table 4. The baseline value of UES resting pressure of Group A was similar to that of Group B without significant difference. After resection, we found that Group A presented a significant lower resting pressure than Group B \(21 ± 4.3 \) vs \(25.3 ± 6.3 \); \( P = 0.03 \), Fig. 4). No significant difference of UES length before and after operation was found between the two study groups. Before operation, in 2 of 15 (13%) patients of Group A and 1 of 18 (5%) patients of Group B no good coordination of the pharynx and the UES was found. After operation, 4 of 15 (27%) and 2 of 18 (11%) patients of Group A and B, respectively, presented an altered coordination of UES, but these difference did not reach significant difference \( (P = 0.4) \).

### Radiological findings

Chest CT scan showed a shift of the oesophagus in 11 of 15 (73%) and in 2 of 18 (11.1%) patients of Groups A and B \( (P = 0.001) \), respectively. These patients had barium swallow studies as part of their evaluation that showed a severe oesophageal displacement in only 2 of 15 (13%) cases—all after right pneumonectomy. An example is reported in Fig. 4.

### Other data

The manometric alterations were subclinical, and none of the patients complained of dysphagia. The presence of heartburn was recorded in 2 of 15 (13%) patients of Group A and 1 of 18 (5%) of Group B; epigastric pain in 2 of 15 (13%) of Group A and 2 of 18 (11%) of Group B. No other symptoms were observed.
DISCUSSION

The oesophagus maintains an intimate anatomic relationship to the trachea, both main bronchi and both lungs. It has been understood for many years that pneumonectomy is associated with oesophageal dysfunction [7], but sparse data are available in the literature. Vogt-Moykopf et al. [14] and Suen et al. [7] showed an alteration of oesophageal peristalsis after pneumonectomy, but none of the two studies [7, 14] included tests before pneumonectomy. Dougenis et al. [15] evaluated oesophageal motility before and after pneumonectomy. With respect to normal controls, in pneumonectomy patients they found an alteration of swallowing coordination and a significant increase of UES and LES relaxing pressures. However, this study included only patients undergoing pneumonectomy. Olak et al. [16] found that not only patients subjected to pneumonectomy, but even those undergoing more limited lung resections had abnormal preoperative oesophageal function; however, the manometric data were not correlated with the different type of resection.

Thus, the present study is the first that investigated the oesophageal motor function before and after surgical resection in patients with lung cancer and its correlation with the extent of the resection (pneumonectomy vs more limited, i.e. lobectomy and bilobectomy).

First, we found a significant reduction of LES resting pressure in Group A compared with Group B. There are several factors influencing LES resting pressure, which are not completely understood, including (i) gastrointestinal hormones; (ii) the gastro-oesophageal junction (GEJ); and (iii) the autonomic nervous system.

Table 3: Oesophageal body patterns

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Group A (n = 15)</th>
<th>Group B (n = 18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplitude (mmHg), median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper third</td>
<td>Before</td>
<td>164 (145–181)</td>
<td>167 (135–185)</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>116 (93–131)</td>
<td>155 (130–174)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Middle third</td>
<td>Before</td>
<td>130 (95–145)</td>
<td>133 (91–150)</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>92 (81–125)</td>
<td>120 (98–150)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Lower third</td>
<td>Before</td>
<td>79 (59–101)</td>
<td>87 (64–100)</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>49 (30–75)</td>
<td>85 (55–95)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Wave duration (s), median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper third</td>
<td>Before</td>
<td>3.7 (2.9–5.1)</td>
<td>3.7 (1.9–5.1)</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>3.2 (2.5–4.3)</td>
<td>3.6 (2.1–5.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Middle third</td>
<td>Before</td>
<td>3.7 (2.9–4.5)</td>
<td>3.7 (3.1–4.5)</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>3.1 (2.4–4.1)</td>
<td>3.7 (3.3–4.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>Lower third</td>
<td>Before</td>
<td>3.9 (3–4.5)</td>
<td>3.9 (3.3–4.7)</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>3.4 (2.8–4.1)</td>
<td>3.9 (3.5–4.5)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Dysmotility, number of cases (percentage)</td>
<td>Before</td>
<td>5 (33)</td>
<td>1 (5)</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>12 (80)</td>
<td>3 (17)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Mann–Whitney U-test and χ² test were used for statistical analysis.

Table 4: UES patterns

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Group A (n = 15)</th>
<th>Group B (n = 18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting pressure (mmHg)</td>
<td>Before</td>
<td>25 ± 4</td>
<td>26.2 ± 5.2</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>21 ± 4.3</td>
<td>25.3 ± 6.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Total length (cm)</td>
<td>Before</td>
<td>3 ± 0.1</td>
<td>3.1 ± 0.2</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>3 ± 2.5</td>
<td>3.1 ± 3.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Coordination, number of cases (percentage)</td>
<td>Before</td>
<td>13 (87)</td>
<td>17 (99)</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>11 (73)</td>
<td>16 (89)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Mann–Whitney U-test and χ² test were used for statistical analysis.
Many excitatory hormones such as gastrin, histamine, prostaglandins, creatin-phosphokinase, dopamine, glucagon, progesterone, vasoactive intestinal peptide and others may regulate LES pressure. However, there is no evidence in the literature that pneumonectomy rather than lesser resection is associated with any significant alteration in the production of these hormones [15].

Pronounced changes in the position of the stomach may occur after pneumonectomy even to the degree of changing the angle of His. Kriedemann and Mateev [11] showed that severe cephalic after pneumonectomy even to the degree of changing the angle of His and or hiatal hernia, which may have consequences on LES resting pressure [17]. Yet, no significant difference in total length and intra-abdominal length of LES was found between the two groups before and after operation. Thus, the alteration of the autonomous nervous system due to direct or indirect vagal injury during pneumonectomy may probably explain the results of LES resting pressure seen in Group A, since vagotomy in dogs and cats affects LES function variably and may lead to decreased resting tone or spasm [18]. Regarding relaxing pressure, after surgery we found a significant increase of its value in Group A compared with Group B in agreement with the data of Dougenis et al. [15]. Because relaxing pressure is under the control of vagal nervous, our results may be due to the injury of vagal nervous and/or autonomous nervous system, which is more frequent during pneumonectomy rather than lobectomy or bilobectomy.

Second, in the study of the oesophageal body, after pneumonectomy we found a significant reduction of amplitude of contractions, and of wave duration, particularly at the middle and lower parts of the oesophageal body. Yet, a lack of regular peristaltic movement was observed in agreement with other reports [7, 14, 15]. The displacement of the oesophagus towards the site of pneumonectomy may partially explain our results, which are most likely due to an injury of the oesophageal body or its innervations.

In only two cases was the displacement severe; the low incidence of severe mediastinal shift may be due to the brief follow-up period (6 months) of our study. In fact, the oesophageal displacement increases with the time after pneumonectomy; Vogt-Moykopf et al. [14] showed that the alteration of oesophageal motility was more evident in patients who had pneumonectomy performed more than 6 years ago compared with those who had it performed <6 years ago. Conversely, a direct or indirect trauma of the oesophageal body or of its innervations is most likely to occur during pneumonectomy due to several factors: (i) the greater-extension dissection needed for attending pneumonectomy compared with lobectomy or bilobectomy; (ii) pleural cavity after pneumonectomy requiring meticulous haemostasis; (iii) pneumonectomy usually completed with radical dissection of hilar and mediastinal lymph nodes. Thus, extreme caution should be taken during these manoeuvres. Modification of the surgical technique can decrease the risk of vagal or oesophageal injury, thus reducing the risk of oesophageal dismotility; it involves a circumspect use of electrocautery; yet bipolar diathermy or using new devices such as LigaSure may be useful to reduce thermal injury.

Third, in the UES study, the relaxing pressure, the entire length and the coordination showed no significant difference between two study groups before and after surgery. Only resting pressure in Group A showed a significant decrease after operation compared with Group B. The effects of pneumonectomy on UES function are unknown. Choi et al. [9] and Duranceau et al. [19] showed marked derangements in the UES function and the oesophageal body after laryngectomy. The injuries of the pharyngeal branches of the vagus nerve and/or of the superior laryngeal nerves, reported by Duranceau et al. [19] as possible causes of oesophageal dismotility, are very rare during pneumonectomy, as well as the destruction of the pharyngo-oesophageal junction responsible for swallowing. Thus, the exact neuromuscular basis to explain the alteration of UES resting pressure after pneumonectomy is not clear and requires further evaluation.

What is the clinical significance of our results? In patients undergoing lung transplantation, gastro-oesophageal reflux (GER) and derangement of oesophageal body motility are common; the evidence collected to date strongly supports a role for the aspiration of gastric contents as a causative or additive aetiology...
to developing bronchiolitis obliterans syndrome. The pathology behind this process involves progressive fibrosis of the small airways with sclerosis, intimal thickening and destruction of the pulmonary vasculature [20]. Clinically, this is accompanied by a decreased of forced expiratory volume in 1 s (FEV1) and progressive dyspnoea [21]. In theory, a similar phenomenon may occur in pneumonectomy patients with dramatic consequences. Since the modifications of oesophageal motility seen in our pneumonectomy patients may in part alter the antireflux barrier at the GEJ (i) the low resting LES pressure reduces the internal and external sphincter mechanisms favouring gastric reflux and (ii) the motility alteration of the oesophageal body may reduce the clearance of reflux from the oesophagus. Despite everything, in the most of our patients the oesophageal alterations remained subclinical except for four who had epi gastric pain, and three who complained of heartburn, a classic symptom of gastric reflux. In the three patients with heartburn, the presence of GER was confirmed by 24-h pH monitoring. However, we believe that the prevalence of reflux in our population may be underestimated. Sometimes asymptomatic patients may have a GER, and unfortunately all asymptomatic patients did not perform objective measurements as 24-h pH measurement. We were unable to perform it because the patients did not tolerate the nasal catheterization for 24 h, and in our hospital, new devices such as wireless capsules to measure the pH for 24 h were not available. Probably the low compliance of such patients was because of their not understanding of the effective aim of such examinations since they were asymptomatic. It may be of great clinical importance to detect GER-related aspiration in pneumonectomy patients in order to identify the patients who benefit from conservative treatment, considering that GER and aspiration are modifiable. Thus, we are starting to assess such issues in a second phase of our study.

Study limitation
We acknowledge specific limitations of our study.
First, although from our study the modifications of oesophageal activity that occur after pneumonectomy become apparent, the overall simple size is relatively small, rendering a multivariate analysis difficult. Thus, a larger population of patients would be useful to evaluate the potential impact of several variables: including chemotherapy, site of pneumonectomy, etc.
Second, as reported above, we do not perform other tests such as oesophageal pH monitoring in order to identify the presence of GER, which may be an important clinical expression of the oesophageal alterations seen after pneumonectomy.
Third, the follow-up period after lung resection is too short in our study to adequately compare the difference between the two groups correlated with mediastinal displacement.

CONCLUSIONS
Pneumonectomy may cause significant oesophageal motility disorders. Even if they do not show a clear clinical impact, they should not be neglected. However, this type of surgery should not be denied to patients if required to treat their cancer. In closing, future prospective studies should elucidate the frequency of oesophageal dysmotility after lung resection to better understand the clinical basis of such a complication.

ACKNOWLEDGEMENT
We thank Vincenzo Pastore, who stimulated our interest and research in the field of the oesophagus.

Conflict of interest: none declared.

REFERENCES
APPENDIX. CONFERENCE DISCUSSION

Dr R. Berrisford (Plymouth, UK): You have described some interesting changes in the oesophagus after pneumonectomy, which have been described previously, but you have also extended this into lesser resections and showed us how much the extent of resection might be an influence. But you found in 40 patients that there were no real significant symptoms of dysphagia. So can you explain to us why you undertook this study, given the lack of symptoms, in that number of patients and also the lack of symptoms documented in the literature?

Dr Fiorelli: The first question is the lack of pH manometry?

Dr Berrisford: Why did you do this study, because there were very few patients with symptoms?

Dr Fiorelli: In this study we aimed to define the oesophageal alterations after resection and whether they had clinical effects. The results were that no important symptoms were seen after pneumonectomy, only subclinical effects. Probably other clinical effects such as gastric reflux are underestimated, because sometimes asymptomatic patients may be affected by gastro-oesophageal reflux according to data reported for patients undergoing lung transplantation. It is an important point considering that in patients undergoing lung transplantation, gastric reflux may favour microaspiration of gastric juice in the lung, and it may reduce the respiratory function. If this phenomenon occurred in patients undergoing pneumonectomy, obviously it would have more dramatic consequences because such patients only have one lung.

Probably a limitation of this paper is that we did not measure the 24-hour pH in these patients to identify which patients had gastric reflux. In the study design we planned to measure 24-hour pH manometry. However, we were not able to perform it, probably because the patients were asymptomatic. In other words, when we proposed this exam to asymptomatic patients, they replied ‘why do I have to perform it if I don’t have specific oesophago-gastric disease?’

We were able to perform pH manometry in only three patients with heart-burn. Probably the follow-up was too short and the pain consequent on thoracotomy made the nasal catheterization intolerable, or the patients were not very sympathetic to scientific research.

Dr Berrisford: That is an issue. You didn’t measure pH in these patients to see whether the manometric changes are related to pH, and, as you pointed out, that is important for a small group of patients undergoing lung transplant who have very similar manometric changes.

But I still have a concern that you would be doing this, and in fact in your conclusion you are recommending that we do manometry on patients who have oesophageal symptoms before we do a pneumonectomy. But what are you going to do that is different for the patient who may have dysphagia? What is different in your operation to put them through manometry?

Dr Fiorelli: I believe that pneumonectomy is a high-risk operation to produce direct trauma of the oesophagus, or of the vagal nerve or autonomic nervous system, which control oesophageal function. That is because pneumonectomy is different from lesser resection. After pneumonectomy the pleural cavity requires careful haemostasis. In addition, pneumonectomy is usually completed with a radical resection of the hilar and mediastinal lymph nodes. So these surgical manoeuvres have a high risk of oesophageal injury or vagal nerve injuries.

In the light of my small experience of these manoeuvres, we should pay attention and use electrocautery with great care, especially during the haemostasis of the posterior mediastinum or during dissection of mediastinal or hilar lymph nodes. Probably the use of bipolar electrocautery or new devices such as LigaSure may reduce thermal injury.

Postoperatively, I think it is important to identify which patients have gastric reflux and then to start these patients on specific medical therapy. The aim is to avoid the microaspiration of gastric juice which may favour the mechanism of bronchiolitis obliterans syndrome, as seen in lung transplanted patients, which dramatically reduces respiratory function.

Dr S. Bölükbas (Wiesbaden, Germany): I have a statistical issue. You had cited two papers. What was your expected difference between the two groups, and did you have a power analysis for your prospective study to detect any differences? And if you have small sample sizes, it would be useful if you use Bonferroni corrections, or if you do an effect size calculation to detect real differences in this small subset of patients. Can you comment on that?

Dr Fiorelli: As you underlined, the present study included a small number of patients. We divided the patients prospectively into two groups according to the different resections, elective pneumonectomy and lesser resection, and the sample size for each group was 14 patients. Probably it might have been better to perform a logistic regression and analyse whether other factors such as chemotherapy, site of the operation, etcetera, may affect oesophageal function, but the number of patients was too small for this analysis.

Dr E. Lim (London, UK): I will also add that the Bonferroni correction is used to apply for multiple testing. This is only a two-way hypothesis test, so there is no reason to require statistical correction for that.

Dr S. Mattioli (Bologna, Italy): I would not magnify a small clinical problem, this well-known dysmotility, and if you know the pathophysiology of the oesophagus, you understand what is going on.

I think that the core, the most important message of your study is what you have highlighted. If the patient has trouble post-pneumonectomy with cough or digestive symptoms, consider proximal reflux as the possible cause. The real practical message from your paper is only one: if you get those troubles, think to reflux. I would not do any further study before and after. The message is purely clinical.

Dr J. Schirren (Wiesbaden, Germany): You cited our teacher, Ingolf Vogt-Moykopf, in the early years of 1970, and we learned from him that patients postoperatively after each lung resection have a high risk of getting aspiration pneumonia. How high was the rate in your group? I think it does not depend on pneumonectomy. It depends on the dissection of the mediastinum, the effect of the manipulations there. We have a high risk of aspiration pneumonia; how high was the rate in your group?

Dr Fiorelli: Aspiration is the real problem of these patients; the rate is similar between the two groups. Despite the fact that we have a reduction of resting LES pressure in the pneumonectomy group, the LES barrier works against the reflux, yet no alterations of the oesophago-gastric junction or of the angle of His were seen in our patients. The real problem is the vagal injury.

This study has another limit, probably the short follow-up time, because in the study of Vogt-Moykopf in 1970, the patients were evaluated six years after pneumonectomy and the author showed a dramatic dislocation of the oesophagus.