Original research

Outcome of gastro-oesophageal reflux-related respiratory manifestations after laparoscopic fundoplication

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1. Introduction

Gastro-oesophageal reflux disease (GORD) is a known cause of respiratory and intractable extra-oesophageal symptoms such as cough, hoarseness and asthma [4,19,21,24]. It can also exacerbate cough in patients with pre-existing respiratory conditions. Several articles have documented that patients with chronic cough due to reflux disease have improvement of their symptoms after anti-reflux surgery [1–3,6,9,14,16,19,21–24].

The relationship between cough and other symptoms of gastro-oesophageal reflux disease (GORD) and factors which may predict the response of reflux related cough to anti-reflux surgery remain unclear [19,23]. Three mechanisms have been postulated linking GORD with cough and these are the intra-oesophageal reflux, extra-oesophageal reflux and micro-aspiration [4,10]. Each of these mechanisms act by directly stimulating the cough receptors or indirectly causing increased sensitizing to the cough reflex.

Patients with chronic cough due to reflux disease or exacerbation of cough in patients with pre-existing respiratory condition are increasingly referred to Upper Gastrointestinal surgeons in the UK for consideration of laparoscopic fundoplication (LFP) as recommended by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). However there are limited data to support this practice.

The aim of this study was to evaluate the magnitude of the short-term and long-term effect of LFP on improving gastro-oesophageal reflux related respiratory manifestations particularly cough and to identify any predictive factors.

2. Methodology

A retrospective analysis of patients who underwent LFP from January 2005 to January 2012 at a single center was performed. Patients were identified through coding system from Information Technology (IT) department and manual search of consultant’s theatre diary. Data was collected from patient’s notes and electronic clinic letters. Patients who had LFP for oesophageal motility disorder or gastric volvulus were excluded from the study. All patients included in the study were reviewed for symptom presentation which included heartburn, retrosternal/epigastric pain, dysphagia,
regurgitation and cough. Patients with pre-existing respiratory disease such as asthma, bronchiectasis and interstitial lung disease were also collected.

Patients underwent investigations to evaluate the severity of the reflux disease pre-operatively, which included pH studies, oesophageal manometry, oesophagogastroduodenoscopy (OGD) and barium meal.

Patients with intractable cough or respiratory symptoms as primary symptom of reflux disease had pre-operative respiratory assessment by the respiratory physicians prior to referral to the Upper Gastrointestinal Surgeons. This included spirometry, lung function test (LFT) and high resolution CT scan of thorax (HRCT).

All patients had either Laparoscopic Toupetts or Nissens fundoplication performed by 3 experienced upper gastrointestinal surgeons. Patients were followed up at 4–6 weeks (short term) and then 6–12 months (long term) following surgery to check for the improvement of their cough and reflux symptoms. A reduction in the frequency of cough or resolution of cough was considered as improvement of cough symptoms in this study. Complications from surgery and any post-operative investigations (pH studies, oesophageal manometry, barium meal, OGD) were also noted.

3. Statistical analysis

Comparisons between two groups were made using non-parametric continuity corrected chi-square test or a chi squared test was used when more than two groups were analyzed. Fisher exact test was performed for comparison when the numbers were less than 10. Multivariate Cox regression analysis was conducted using a stepwise forward selection approach starting with the most significant variable on univariate analysis including every variable with a P-value of <0.10 sequentially. All analysis was performed using Statview version 5.01 (SAS Institute Inc.). A P-value of <0.05 was considered significant.

4. Results

There were 208 patients identified for the study (51% females) with median of 53 years (range 17–81 years). Of these 208 patients, 73 (35%) patients underwent LFP for cough and or respiratory symptoms due to GORD. Heartburn (84%) was the most common symptom presentation (Table 1) while asthma (14%) was the most prevalent pre-existing respiratory condition (Table 2).

All patients had pre-operative reflux evaluation however, not all results were retrievable. 167 (80%) of patients had documented total reflux time (range 0.6–76.3) while 159 (76%) of patients had documented DeMeester score (range 2.6–317.1) and 189 (90%) of patients had documented oesophageal manometry (96% with hypotonic lower oesophageal sphincter). There were 176 (84%) and 56 (26%) patients who underwent pre-operative OGD and barium swallow respectively. The median length of hospital stay post-operatively was 2 days (range 1–13 days) including the day of surgery.

There were 55 (75%) patients who had improved respiratory symptoms at 4–6 weeks following surgery (Fig. 1) while no short term data was available for 4 patients. In comparison, 190 (91.2%) of 207 patients had GOR symptoms improvement at 4–6 weeks following surgery. The 18 (25%) patients with no improvement of respiratory symptoms at 4–6 weeks following surgery had post-operative investigations to exclude technical failure of fundoplication as a cause of persistent respiratory symptoms (Table 3); all of these patients had post-operative pH studies and oesophageal manometry which showed no evidence of significant gastro-oesophageal reflux disease. Ten (55%) patients had OGD, 3 (17%) patients had barium meal while 5 (28%) patients had both OGD and barium meal post-operatively. All of these investigations ascertained intact fundoplication.

At 6–12 months, 44 (62%) had improved respiratory symptoms of which 7 patients had recurrence of respiratory symptoms, while 4 patients had improved respiratory symptoms which were not apparent in the short-term. There were 17 patients whose long term data were not available. The 7 patients with recurrence of respiratory symptoms had pH studies and oesophageal manometry which showed no evidence of significant gastro-oesophageal reflux disease. Two patients had OGD while 2 other patients had both OGD and barium meal, all of which were normal. We therefore found no evidence of fundoplication failure to explain their recurrence of respiratory symptoms.

No significant predictive factor (gender, age, DeMeester score, total reflux time) for improving respiratory symptoms was identified (P > 0.05) upon regression analysis.

Dysphagia (35%) was a common side effect of LFP. There was no mortality.

5. Discussion

The SAGES 2010 guidelines on the management of GORD suggest that patients with intractable cough or worsening of respiratory conditions thought to be attributed to reflux disease are to be

<table>
<thead>
<tr>
<th>Respiratory condition</th>
<th>Number (%) of patients</th>
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<tbody>
<tr>
<td>Asthma</td>
<td>31 (14)</td>
</tr>
<tr>
<td>COPD/bronchiectasis</td>
<td>12 (5)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>4 (1)</td>
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</tbody>
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Table 2

Number of patients with pre-existing respiratory conditions.

Table 1

Presenting symptoms of patients who had undergone LFP.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number (%) of patients</th>
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<tbody>
<tr>
<td>Heartburn</td>
<td>176 (84)</td>
</tr>
<tr>
<td>Retrosternal/epigastric pain</td>
<td>102 (49)</td>
</tr>
<tr>
<td>Reflux/regurgitation</td>
<td>158 (75)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>51 (24)</td>
</tr>
<tr>
<td>Cough</td>
<td>55 (26)</td>
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</tbody>
</table>

Fig. 1. Summary of outcome of patients with respiratory manifestation following LFP.
referred to the upper gastrointestinal surgeons for consideration of LFP. These groups of patients are increasingly being referred to our center for consideration of LFP after having a respiratory assessment by the respiratory physicians. All patients that were referred to our center had objective confirmation of reflux with pH studies and oesophageal manometry prior to having LFP. Chronic cough was the most common respiratory symptom and reason for referral for consideration of LFP. It should be noted that all patients in the study had a trial of anti-reflux medication with proton pump inhibitors (PPI) prior to being referred for LFP. Studies have documented some benefits in improving respiratory manifestations due to reflux with medical anti-reflux therapy [3,2,10] however anti-reflux surgery is documented to provide better benefits in improving respiratory manifestations due to reflux compared to anti-reflux medication [3,11,12,18,19,21,23,25].

From our study, we identified three groups of patients; patients with cough only, patients with cough plus other respiratory symptoms and patients with other respiratory symptoms only [Fig. 1]. We considered other respiratory symptoms to be asthma, COPD, bronchitis, interstitial lung disease and hoarseness of voice. We observed that patients with cough only had a better improvement of their cough symptoms compared to patients with cough plus respiratory symptoms and respiratory symptoms only in the short and long term (Fig. 1) though the number of patients were small for a meaningful statistical analysis. This trend has also been observed in other studies [13,19,21,23] and the reason for this trend is unknown. Overall response rates were over 70% in the control of respiratory manifestations. This is in keeping with short term improvement ranges in other studies [1,7,8,15,19,21,25].

Patients who did not have improvement of respiratory manifestations or who had recurrence of cough symptoms were subjected to pH studies, oesophageal manometry barium meal or OGD to exclude failure of fundoplication. We found no abnormality from these post-operative investigations to account for the persistence or recurrence of patients' respiratory symptoms following surgery. It is likely that factors other than GORD may be contributing to these patients' cough or recurrence of cough [6,8,10,17,18,19,23,24]. It may be possible that the reflux is due to cough [10]. The cough-reflux mechanism is thought to occur due to rapid rise in pressure in both the thorax and the abdomen during coughing which may be sufficient to overcome the lower oesophageal sphincter thereby causing reflux [16]. Careful selection of patients is paramount to improve the outcome of surgery for resolving respiratory symptoms. However we did not identify any significant predictive factors in this context.

As a quality control measure, 190 (91.2%) of 208 patients had GOR symptoms improvement at short-term follow-up. Our study showed that LFP has better results with typical GOR symptoms compared to atypical symptoms which is similar to other studies [1,4,11,19–23].

\[ \text{Post-operative test} \quad \text{Number (%) of patients (total } = 18) \]

<table>
<thead>
<tr>
<th>Test</th>
<th>Number (%)</th>
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<tbody>
<tr>
<td>pH studies</td>
<td>18 (100)</td>
</tr>
<tr>
<td>Oesophageal manometry</td>
<td>18 (100)</td>
</tr>
<tr>
<td>Barium meal</td>
<td>8 (45)</td>
</tr>
<tr>
<td>OGD</td>
<td>15 (83)</td>
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</table>

6. Conclusion

LFP is a safe procedure with low complication rates and a short hospital stay. We have shown that it is effective with the response

rates of over 70% in the control of respiratory manifestation of GORD, compared to over 90% response rates in the control GOR symptoms alone. It is likely that there are other causative factors to the respiratory symptoms along with GORD. Therefore more research is needed to identify factors to aid patient selection for LFP to improve response rate.

Ethical approval

Ethical approval was not requested as this research was a retrospective study which involved review of patient’s notes.

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Author contribution

1. Mr F. Adaba: Author involved in the study design, data collection, data analysis and writing of manuscript.
2. Mr C.W. Ang (shared first authorship); Author involved in study design, data collection, data analysis and writing of manuscript.
3. Mr A. Perry: Author involved in study design and writing of manuscript.
4. Mr M.S. Wadley: Author involved in study design and writing of manuscript.
5. Mr C.S. Robertson: Author involved in study design and writing of manuscript.

Conflict of interest

There are no conflicts of interest with the manuscript.

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