Lung (2018) 196:491–496
https://doi.org/10.1007/s00408-018-0128-4

PULMONARY ASPIRATION

Gastro-Oesophageal Reflux and Aspiration: Does Laparoscopic Fundoplication Significantly Decrease Pulmonary Aspiration?

Oleksandr Khoma[1,6] · Susanna Elizabeth Falk[2] · Leticia Burton[3] · Hans Van der Wall[3] · Gregory Leighton Falk[3,4,5]

Received: 28 February 2018 / Accepted: 23 May 2018 / Published online: 26 May 2018

Abstract

Purpose Pulmonary aspiration of gastric refluxate is one of the indications for anti-reflux surgery. Effectiveness of surgery in preventing pulmonary aspiration post-operatively has not been previously tested. The aim of this project is to assess effectiveness of anti-reflux surgery on preventing pulmonary aspiration of gastric refluxate.

Methods Retrospective analysis of prospectively populated database of patients with confirmed aspiration of gastric refluxate on scintigraphy. Patients that have undergone anti-reflux surgery between 01/01/2014 and 31/12/2015 and had scintigraphy post-operatively were included. Objective data such as resolution of aspiration, degree of proximal aero-digestive contamination, surgical complications and oesophageal dysmotility as well as patient quality of life data were analysed.

Results Inclusion criteria were satisfied by 39 patients (11 male and 28 female). Pulmonary aspiration was prevented in 24 out of 39 patients (61.5%) post-operatively. Significant reduction of isotope contamination of upper oesophagus supine and upright ($p=0.002$) and pharynx supine and upright ($p=0.027$) was confirmed on scintigraphy post-operatively. Severe oesophageal dysmotility was strongly associated with continued aspiration post-operatively OR 15.3 (95% CI 2.459–95.194; $p=0.02$). Majority (24/31, 77%) of patients were satisfied or very satisfied with surgery, whilst 7/31 (23%) were dissatisfied. Pre-operative GIQLI scores were low (mean 89.77, SD 20.5), modest improvements at 6 months (mean 98.4, SD 21.97) and deterioration at 12 months (mean 88.41, SD 28.07) were not significant ($p=0.07$).

Conclusion Surgery is partially effective in reversing pulmonary aspiration of gastric refluxate on short-term follow-up. Severe oesophageal dysmotility is a predictor of inferior control of aspiration with surgery.

Keywords LPR · GORD · Pulmonary aspiration · Laparoscopic fundoplication · Scintigraphy

Introduction

Pulmonary aspiration of gastric refluxate is a feared complication of gastro-oesophageal reflux disease (GORD). Patients presenting with typical symptoms of GORD and those with symptoms of extraoesophageal reflux are at risk of pulmonary aspiration [1–3]. Scintigraphy is currently the only available test to objectively demonstrate pulmonary aspiration in GORD [2].

Recurrent pulmonary aspiration can result in significant symptoms and cause permanent damage to the lungs (bronchiectasis, recurrent infections, adult onset asthma, pulmonary fibrosis and lung transplant rejection) and laryngeal disease (voice changes, laryngeal stenosis and laryngeal cancer) [3–6]. Laparoscopic anti-reflux surgery (LARS) is a common treatment offered to patients failing medical therapy for GORD [7, 8]. The effectiveness of laparoscopic fundoplication in reducing pulmonary aspiration post-operatively has

✉ Oleksandr Khoma
khoma.a@gmail.com

1 Department of Upper Gastro-Intestinal Surgery, Concord Repatriation General Hospital, Hospital Road, Concord, NSW 2137, Australia

2 Sydney Heartburn Clinic, 29/12-18 Tryon Road, Lindfield, NSW 2070, Australia

3 Concord Nuclear Imaging, Suite 101/5 Bay Dr, Meadowbank, NSW 2114, Australia

4 Concord Repatriation General Hospital, Sydney, Australia

5 University of Sydney, 29/12-18 Tryon Road, Lindfield, NSW 2070, Australia

6 Lindfield, Australia

not been previously tested, although anecdotally utilised for many years [9].

Patients and Methods

A single surgeon prospective cohort study of consecutive patients with a positive pre-operative pulmonary aspiration scan and undergoing 360-degree laparoscopic fundoplication for severe reflux disease is reported. Patient data were acquired between 01/01/2014 and 31/12/2015.

The data were extracted from a prospectively populated database that was approved by the Concord Hospital Ethics Committee (LNR/12 CRGH/248). Inclusion criteria were pulmonary aspiration on pre-operative scintigraphy and follow-up post-operative scintigraphy. Exclusion criteria were failure to attend post-operative scintigraphy, technically inadequate pre-operative scan and loss to follow-up.

All patients were pre-operatively interviewed by an experienced senior upper gastro-intestinal surgeon and were diagnosed as having predominantly gastro-oesophageal (GOR) or predominantly laryngopharyngeal (LPR) symptoms. Patients with massive hiatal hernia (> 30% of stomach above diaphragm) were identified as a separate subgroup (MHH). Patient selection was planned to include dual-channel 24-pH monitoring, multi-channel oesophageal impedance, oesophageal manometry and gastroscopy. Patients were asked to complete gastro-intestinal quality of life index questionnaire (GIQLI), Respiratory Symptoms Index (RSI) before the operation and then at 3, 6, 12 and 24 months after surgery [10, 11].

Patients with ongoing pulmonary symptoms despite maximum medical therapy and evidence of pulmonary aspiration on scintigraphy and symptoms or objective evidence of pulmonary disease were offered surgery. Patients were also operated for typical GORD symptoms.

All operations were 360-degree composite fundoplication with repair of the hiatal pillars. Detailed operative technique was previously described by one of the authors [12].

Reflux aspiration scintigraphy was conducted using validated technique [13]. Scintigraphy was performed after an overnight fast using Hawkeye 4 gamma camera (General Electric, Milwaukee, United States) with stomach, chest and upper airway in the field of view. 40–60 MBq of 99mTc DTPA was administered orally mixed with 150–200 ml of water. Images were obtained for 5 min at 15 s per frame into a 64 × 64 matrix, followed by a 30-min dynamic image whilst supine for 30 s per frame. Aspiration was proven on delayed images at 2 h by the presence of isotope in the lungs (Fig. 1). Isotope time-activity curves (Fig. 2) were recorded for pharynx and upper oesophagus supine and erect and classified as showing no reflux, falling, flat or rising curves (0–3).

Statistical analysis was performed using SPSS Statistics 23 software (IBM, New York, United States). Standard ANOVA statistics, student's *t* test, Fisher's exact test, χ^2 test and Pearson correlation coefficient (2 tails) were used. Result with *p* value of 0.05 or less were considered significant.

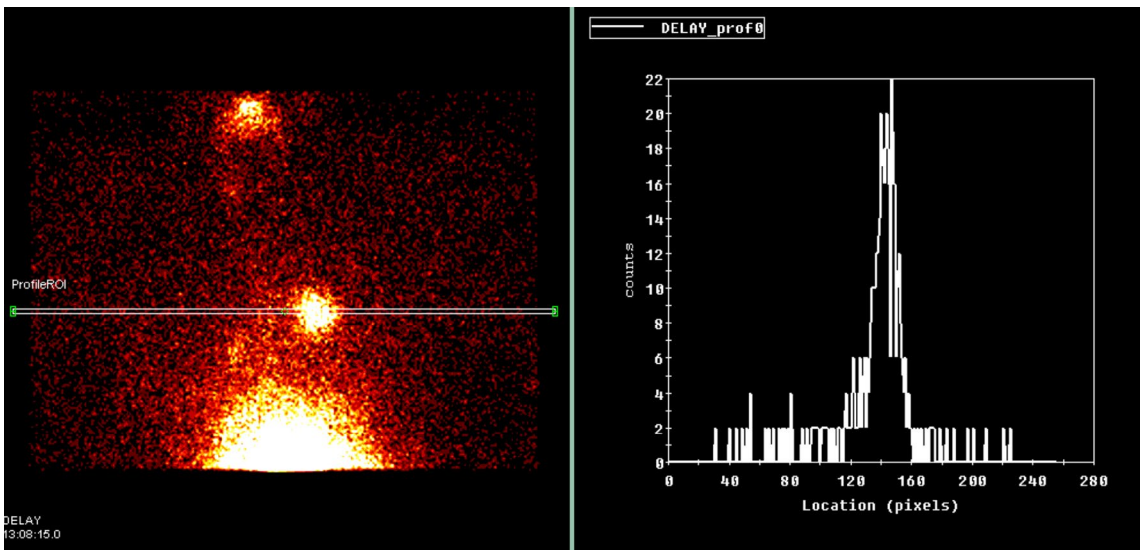

Fig. 1 Delayed study showing aspiration of tracer into left lung and the line profile showing the count profiles through this region. A high-count profile is apparent for the left lung activity

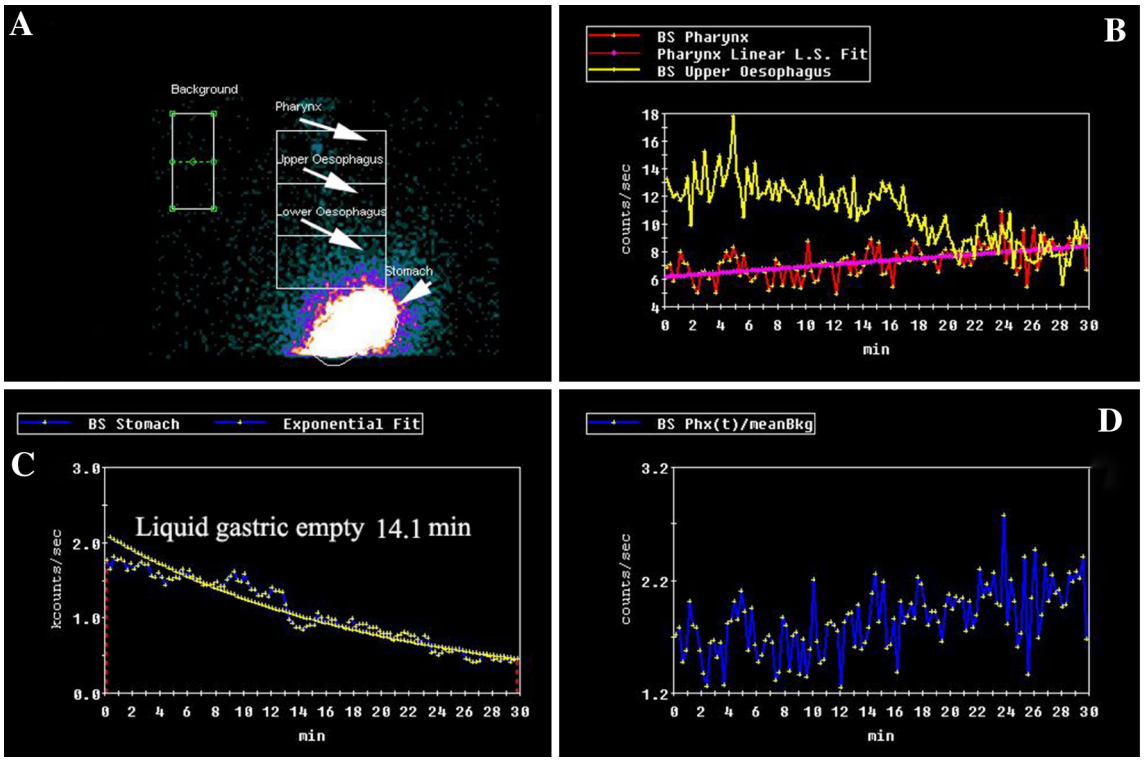

Fig. 2 Typical graphical analysis of the scintigraphic study showing the regions of interest for the pharynx, oesophagus, stomach and background in the top left panel (**a**). Time-activity curves are generated for the pharynx and upper oesophagus, with an exponential fit to the curve for the stomach (**c**). The time to half clearance for liquid contents is determined from this curve (14.1 min). **b** Analysis of the time-activity curves for the pharynx (red curve) with the curve of best fit to the data points (pink curve). The curve for the upper oesophagus is shown in yellow. A rising curve is apparent for the pharynx. **d** Graphical representation of the ratio of pharyngeal to background time-activity curves. This is used for quality assurance and gives an idea of the amplitude of the reflux relative to background

Results

Inclusion criteria were satisfied by 39 patients (11 male and 28 female). Indications for surgery were as follows: massive hiatal hernia (6 patients), predominantly LPR (21 patients) and predominantly GOR (12 patients). Patients had pre- and post-operative scintigraphy aspiration scans within 12 months of surgery. Pre-operative manometry was performed on 33 patients. Quality of life data were available for 26 patients pre-operatively, 18 patients at 6 months and 22 patients at 12 months (Table 1).

All patients had evidence of reflux on pre-operative scintigraphy, including 32 patients with intermittent reflux, five with continuous reflux and two patients with evidence of reflux that was ungraded. Post-operatively, there was no evidence of reflux in four patients, intermittent reflux in 32 and continuous reflux in three patients.

Oesophageal motility was classified using modified classification based on Kahrilas et al. [14]. Patients with 2–3 out of 10 ineffective swallows were labelled as having "mild", 4–5 out of 10 as "moderate" and 6 or more ineffective swallows as "severe" oesophageal dysmotility [14]. Motility was normal in six patients (18.2%), seven patients (21.2%) had mild category, six (18.2%) patients had moderate and 14 (42.4%) patients had severe ineffective oesophageal motility (IOM). Pulmonary aspiration in this group was strongly associated with severe IOM (χ^2, $p = 0.001$).

Table 1 Patients characteristics

Age, years	60.2 (range 31–78)
Gender	Male = 11; female = 28
Symptom profile	
LPR	21
GORD	12
MHH	6
Oesophageal motility	
Normal	18.20%
Mild IOM	21.20%
Moderate IOM	18.20%
Severe IOM	42.40%

Pulmonary aspiration was prevented in 24 out of 39 patients (61.5%) post-operatively as determined by

scintigraphy. Aspiration was best controlled in patients without severe grade oesophageal dysmotility (89.5% resolution of aspiration). Confirmed aspiration was seen in 9 patients (64.3%) with severe oesophageal dysmotility post-operatively (Table 2). Severe oesophageal dysmotility was strongly associated with continued aspiration post-operatively OR 15.3 (95% CI 2.459–95.194; $p=0.02$) (Chart 3).

Analysis of pharyngeal and upper oesophageal isotope curves revealed significant reduction of isotope contamination of upper oesophagus supine and upright ($p=0.002$) and pharynx supine and upright ($p=0.027$) post-operatively.

Scores of overall satisfaction with surgery scores were available for 31 patients. Majority (24/31, 77%) of patients were satisfied or very satisfied with surgery, whilst 7/31 (23%) were dissatisfied. Satisfaction scores were independent of scintigraphy of post-operative aspiration or severe oesophageal dysmotility. Most common post-operative complaints were of dysphagia ($n=8$), mild epigastric or chest pain ($n=4$) and bloating ($n=4$). Endoscopic dilatation was required in four patients to manage post-operative dysphagia.

Quality of life was impaired in most patients which was reflected in pre-operative GIQLI scores (mean 89.77, SD 20.5). Modest improvements at 6 months (mean 98.4, SD 21.97) and deterioration at 12 months (mean 88.41, SD 28.07) were not significant ($p=0.07$). (Table 3).

Discussion

Reflux pulmonary aspiration may cause symptoms and occasionally serious complications. It is uncommon in the general population, however, prevalence in a highly selected group of patients referred for specialist surgical opinion following failure of maximum medical therapy can be as high as 24% [15]. Potential long-term consequences of pulmonary aspiration and pharyngeal contamination by refluxate include bronchiectasis, adult onset asthma, recurrent pneumonia, laryngeal stenosis, voice changes and laryngeal cancer and possibly "idiopathic" pulmonary fibrosis [6, 9, 16].

Evidence of the effectiveness of treatment of extraoesophageal reflux symptomatology is weak [17, 18]. Multiple

Table 2 Resolution of pulmonary aspiration post-operatively in various IOM groups

	Normal motility	Mild IOM	Moderate IOM	Severe IOM
Post-operative aspiration	0/6	1/7	1/6	9/14
% ongoing aspiration	0%	14.3%	16.7%	64.3%

Chart 3 Association between severe IOM and post-operative aspiration

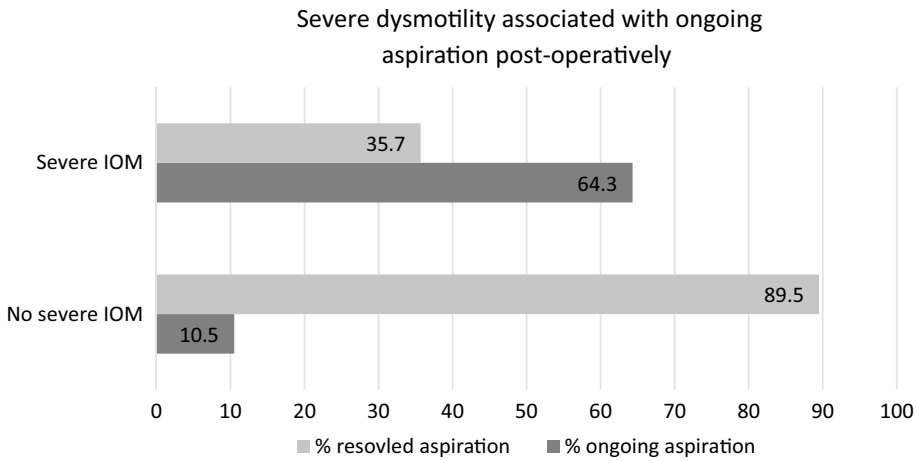

Table 3 Quality of life

Score	Pre-op ($n=26$)	6 months ($n=18$)	12 months ($n=22$)
GIQOL	89.77 (48–117; SD 20.05)	98.4 (43–133; SD 21.97)	88.41 (34–132; SD 28.07)
Visik	3.12 (1–4; SD 1.01)	2.06 (1–4; SD 0.83)	3.05 (2–4; SD 0.97)
Dysphagia	34.14 (15–45; SD 7.74)	33.61 (2.5–45; SD 10.82)	30.57 (5–45; SD 11.67)
Demester	8.42 (0–13; SD 3.2)	7.39 (2–13; SD 3.35)	7.82 (2–12; SD 3)
LPR	22.85 (0–45; SD 13.6)	17.44 (4–43; SD 11.44)	22.27 (1–44; SD 14.34)

studies have evaluated safety and effectiveness of surgical management of severe reflux without specific focus on patients with respiratory symptoms. Although some controversy still exists [19], it is generally accepted that LARS can be offered to patients with reflux disease who have failed medical therapy [7–9, 17].

Proton-pump inhibitors (PPI) are only effective in reducing the acidity of gastric contents and only have minor effect on volume and frequency of reflux as well as reflux of other gastric and pancreatic enzymes and bile that are commonly found in stomach [20, 21]. Association between PPI and community-acquired pneumonia has been previously established [22]. Furthermore, new data from a large US study suggest link between long-term PPI use and significantly increased mortality [23]. Therefore, reducing the amount, frequency and proximal extent of reflux as well as preventing pulmonary aspiration should be goals of treatment in patients with GOR and LPR.

The Society of American Gastrointestinal and Endoscopic Surgeons lists pulmonary aspiration as one of the indications for anti-reflux surgery [24]. Proximal oesophageal acid reflux on 24-h pH monitoring has been associated with pulmonary aspiration, however, this test is limited by inability to detect non-acidic reflux episodes and does not positively diagnose pulmonary aspiration being merely an indicator of probability [15]. Oesophageal impedance has an advantage of detecting non-acid reflux episodes; however, results in the proximal oesophagus are commonly difficult to interpret and clinical relevance of the test has been questioned by some authors [25]. Scintigraphy is currently the only test available to objectively demonstrate pulmonary aspiration [13, 15].

This is the first study demonstrating relative effectiveness of LARS in objective relief of pulmonary aspiration. Significant reduction in pharyngeal and upper oesophageal contamination with refluxate post-operatively further supports the potential benefit of surgery in patients with severe reflux. This reduction in pharyngeal contamination suggests a reduction in pulmonary aspiration severity, which may reduce pulmonary symptoms or damage.

Durability of surgical control of aspiration and symptoms remains unknown. This study focuses on short-term follow-up results. Patient satisfaction and symptom control after LARS for GORD have been previously reported to be sustained at 10 years [26]. Future studies looking at long-term outcomes of surgery in the subgroup of patients with severe reflux with pulmonary aspiration are necessary.

It has been previously established that IOM is associated with increased risk of aspiration in patients with LPR and GOR [15]. This study indicates that severe IOM also predicts worse outcomes of LARS in patients with pulmonary aspiration. Close to 90% of aspiration was relieved in patients with normal motility and mild or moderate IOM, whilst a substantial 64% of patients with severe IOM continued to aspirate to a lesser extent after surgery. Furthermore, in patients with severe IOM curves of pharyngeal and upper oesophageal contamination on scintigraphy did not improve post-operatively. Considering that patient satisfaction with the proposed treatment is determined by their expectations of the treatment effect, it is relevant to identify patients with less favourable prognosis. The presence of severe IOM increases risk of ongoing aspiration despite surgery by at least 2.5-fold (95% CI 2.459–95.194; $p=0.02$). Although many of the patients with ongoing aspiration reported improvement in symptoms after surgery scintigraphy was not predictive. Longer duration studies are required to demonstrate prevention of lung and laryngeal damage.

In patients with massive hiatal hernia, four out of six continued to aspirate post-operatively (66%). This was of no valid statistical assessment due to tiny sample size of the subgroup; however, a more focused study of reversal of aspiration in patients with giant hiatal hernia are warranted and underway.

Quality of life scores were low in this group of patients. Although modest improvement in QoL scores was observed at six and deterioration at 12 months, it is remarkable that mean score remained low and none of the patient's quality of life scores were comparable with healthy subjects. Lack of significant improvement in GIQLI scores may be attributed to a small sample size. GIQLI also may not be an optimal tool for this group of patients as it will neglect improvement in respiratory symptoms whilst being negatively affected by post-operative dysphagia which is a known side-effect of laparoscopic fundoplication [27]. Relevant quality of life tool that includes respiratory and laryngeal symptoms in addition to the gastro-intestinal symptoms is warranted to assess the effect of surgery on other systems affected by extraoesophageal reflux. Leicester cough questionnaire is one of the validated tools that may be more appropriate to reflect an effect of surgery on quality of life of patients with predominant respiratory complications of reflux disease [28].

This study was limited by being a cohort design, having a small sample size and short follow-up period.

Conclusion

Laparoscopic fundoplication may partially alleviate pulmonary aspiration and pharyngeal contamination in patients with severe, treatment-resistant proximal gastro-oesophageal reflux disease.

Oesophageal dysmotility is one of the key risk factors for aspiration in GOR and LPR. Severe IOM is associated with higher risk of persistent aspiration after surgery.

Long-term effect of surgical treatment of pulmonary aspiration on respiratory and laryngeal function is not known.

Compliance with Ethical Standards

Conflict of interest All authors declare no conflict of interest.

References

1. Barry DW, Vaezi MF (2010) Laryngopharyngeal reflux: more questions than answers. Clevel Clin J Med 77(5):327–334. https://doi.org/10.3949/ccjm.77a.09121
2. Falk GL, Beattie J, Ing A, Falk SE, Magee M, Burton L, Van der Wall H (2015) Scintigraphy in laryngopharyngeal and gastroesophageal reflux disease: a definitive diagnostic test? World J Gastroenterol 21(12):3619–3627. https://doi.org/10.3748/wjg.v21.i12.3619
3. Postma GN, Halum SL (2006) Laryngeal and pharyngeal complications of gastroesophageal reflux disease. GI Motil Online. https://doi.org/10.1038/gimo46
4. Koufman JA, Aviv JE, Casiano RR, Shaw GY (2002) Laryngopharyngeal reflux: position statement of the committee on speech, voice, and swallowing disorders of the American Academy of Otolaryngology-Head and Neck Surgery. Otolaryngology 127(1):32–35
5. Blondeau K, Mertens V, Vanaudenaerde BA, Verleden GM, Van Raemdonck DE, Sifrim D, Dupont LJ (2008) Gastro-oesophageal reflux and gastric aspiration in lung transplant patients with or without chronic rejection. Eur Respir J 31(4):707–713. https://doi.org/10.1183/09031936.00064807
6. Lee JS, Collard HR, Raghu G, Sweet MP, Hays SR, Campos GM, Golden JA, King TE (2010) Does chronic microaspiration cause idiopathic pulmonary fibrosis? Am J Med 123(4):304–311. https://doi.org/10.1016/j.amjmed.2009.07.033
7. Vaezi MF (2009) Extraesophageal Reflux. Plural Publishing, San Diego
8. Luketich JD (2014) Master techniques in surgery: esophageal surgery. Wolters Kluwer Health, Philadelphia
9. Martinucci I, de Bortoli N, Savarino E, Nacci A, Romeo SO, Bellini M, Savarino V, Fattori B, Marchi S (2013) Optimal treatment of laryngopharyngeal reflux disease. Ther Adv Chronic Dis 4(6):287–301. https://doi.org/10.1177/2040622313503485
10. Eypasch E, Williams JI, Wood-Dauphinee S, Ure BM, Schmulling C, Neugebauer E, Troidl H (1995) Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. Br J Surg 82(2):216–222
11. Belafsky PC, Postma GN, Koufman JA (2001) The validity and reliability of the reflux finding score (RFS). Laryngoscope 111(8):1313–1317. https://doi.org/10.1097/00005537-200108000-00001
12. Gibson SC, Wong SK, Dixon AC, Falk GL (2013) Laparoscopic repair of giant hiatus hernia: prosthesis is not required for successful outcome. Surg Endosc 27(2):618–623. https://doi.org/10.1007/s00464-012-2501-3
13. Falk M, Van der Wall H, Falk GL (2015) Differences between scintigraphic reflux studies in gastrointestinal reflux disease and laryngopharyngeal reflux disease and correlation with symptoms. Nucl Med Commun 36(6):625–630. https://doi.org/10.1097/mnm.0000000000000289
14. Kahrilas PJ, Dodds WJ, Hogan WJ, Kern M, Arndorfer RC, Reece A (1986) Esophageal peristaltic dysfunction in peptic esophagitis. Gastroenterology 91(4):897–904
15. Khoma O, Burton L, VanderWall H, Falk M, Falk GL (2017) Pathophysiology of laryngopharyngeal reflux disease: association with pulmonary aspiration on scintigraphy and abnormal oesophageal motility disease (**under review**)
16. McShane PJ, Naureckas ET, Tino G, Strek ME (2013) Non-cystic fibrosis bronchiectasis. Am J Respir Crit Care Med 188(6):647–656. https://doi.org/10.1164/rccm.201303-0411CI
17. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R (2006) The montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol 101(8):1900–1920. https://doi.org/10.1111/j.1572-0241.2006.00630.x (**quiz 1943**)
18. Catania RA, Kavic SM, Roth JS, Lee TH, Meyer T, Fantry GT, Castellanos PF, Park A (2007) Laparoscopic Nissen fundoplication effectively relieves symptoms in patients with laryngopharyngeal reflux. J Gastrointest Surg 11(12):1579–1587. https://doi.org/10.1007/s11605-007-0318-5 (**discussion 1587–1578**)
19. Garg SK, Gurusamy KS (2015) Laparoscopic fundoplication surgery versus medical management for gastro-oesophageal reflux disease (GORD) in adults. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD003243.pub3
20. Pearson JP, Parikh S, Orlando RC, Johnston N, Allen J, Tinling SP, Johnston N, Belafsky P, Arevalo LF, Sharma N, Castell DO, Fox M, Harding SM, Morice AH, Watson MG, Shields MD, Bateman N, McCallion WA, van Wijk MP, Wenzl TG, Karkos PD, Belafsky PC (2011) Review article: reflux and its consequences–the laryngeal, pulmonary and oesophageal manifestations. Conference held in conjunction with the 9th International Symposium on Human Pepsin (ISHP) Kingston-upon-Hull, UK, 21–23 April 2010. Aliment Pharmacol Ther 33(Suppl 1):1–71. https://doi.org/10.1111/j.1365-2036.2011.04581.x
21. Ludemann JP, Manoukian J, Shaw K, Bernard C, Davis M, al-Jubab A (1998) Effects of simulated gastroesophageal reflux on the untraumatized rabbit larynx. J Otolaryngol 27(3):127–131
22. Giuliano C, Wilhelm SM, Kale-Pradhan PB (2012) Are proton pump inhibitors associated with the development of community-acquired pneumonia? A meta-analysis. Expert Rev Clin Pharmacol 5(3):337–344. https://doi.org/10.1586/ecp.12.20
23. Xie Y, Bowe B, Li T, Xian H, Yan Y, Al-Aly Z (2017) Risk of death among users of proton pump inhibitors: a longitudinal observational cohort study of United States veterans. BMJ Open. https://doi.org/10.1136/bmjopen-2016-015735
24. Jobe BA, Richter JE, Hoppo T, Peters JH, Bell R, Dengler WC, DeVault K, Fass R, Gyawali CP, Kahrilas PJ, Lacy BE, Pandolfino JE, Patti MG, Swanstrom LL, Kurian AA, Vela MF, Vaezi M, DeMeester TR (2013) Preoperative diagnostic workup before antireflux surgery: an evidence and experience-based consensus of the Esophageal Diagnostic Advisory Panel. J Am Coll Surg 217(4):586–597. https://doi.org/10.1016/j.jamcollsurg.2013.05.023
25. Ravi K, Katzka DA (2016) Esophageal Impedance Monitoring: Clinical Pearls and Pitfalls. Am J Gastroenterol 111(9):1245–1256. https://doi.org/10.1038/ajg.2016.256
26. Cowgill SM, Gillman R, Kraemer E, Al-Saadi S, Villadolid D, Rosemurgy A (2007) Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. Am Surg 73(8):748–752 (**discussion 752–743**)
27. Fumagalli U, Bona S, Battafarano F, Zago M, Barbera R, Rosati R (2008) Persistent dysphagia after laparoscopic fundoplication for gastro-esophageal reflux disease. Dis Esophagus 21(3):257–261. https://doi.org/10.1111/j.1442-2050.2007.00773.x
28. Birring SS, Prudon B, Carr AJ, Singh SJ, Morgan MD, Pavord ID (2003) Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). Thorax 58(4):339–343