

Idiopathic Pulmonary Fibrosis and Gastroesophageal Reflux. Implications for Treatment

Marco E. Allaix · Piero M. Fisichella · Imre Noth ·
Fernando A. Herbella · Bernardo Borraez Segura ·
Marco G. Patti

Received: 4 April 2013 / Accepted: 20 August 2013 / Published online: 4 September 2013
© 2013 The Society for Surgery of the Alimentary Tract

Abstract

Background Even though the pathogenesis of idiopathic pulmonary fibrosis (IPF) is unknown, there is mounting evidence that abnormal reflux (GERD) and aspiration of gastric contents may play a role in the pathogenesis of this disease.

Aims The aims of this study were to determine in patients with GERD and IPF: (a) the clinical presentation, (b) the esophageal function, and (c) the reflux profile.

Methods We compared the clinical presentation, the esophageal function (as defined by high-resolution manometry), and the reflux profile (by dual sensor pH monitoring) in 80 patients with GERD (group A) and in 22 patients with GERD and IPF (group B).

Results Heartburn was present in less than 60 % of patients with GERD and IPF. Lower esophageal sphincter pressure and peristalsis were normal in both groups, while the upper esophageal sphincter (UES) was more frequently hypotensive in IPF patients ($p=0.008$). In patients with GERD and IPF, the proximal esophageal acid exposure was higher ($p=0.047$) and the supine acid clearance was slower as compared with patients with GERD only ($p<0.001$).

Conclusions The results of this study show that in patients with GERD and IPF: (a) reflux is frequently silent, (b) with the exception of a weaker UES, the esophageal function is preserved, and (c) proximal reflux is more common, and in the supine position, it is coupled with a slower acid clearance. Because these factors predisposing IPF patients to the risk of aspiration, antireflux surgery should be considered early after the diagnosis of IPF and GERD is established.

Keywords Idiopathic pulmonary fibrosis · Gastroesophageal reflux disease · Heartburn · Esophageal manometry · Ambulatory 24 h pH monitoring

Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive form of usual interstitial pneumonia of unknown origin which leads to lung fibrosis. IPF affects approximately 38,000 individuals every year in the USA, and it is an irreversible disease.^{1,2} Median survival after the diagnosis is established is between 3 and 5 years, with approximately 80 % of all deaths secondary to respiratory failure.² Because pharmacological therapy is mostly ineffective, lung transplantation offers the only chance for increased survival.³ Unfortunately, the number of available organs is limited, and in about 50 % of patients, a double lung transplant is performed. In addition, the 5-year survival of patients after lung transplantation is much lower than the survival after other organ transplants such as heart and kidneys, being close to only 50 %.

Today, there is increasing evidence that gastroesophageal reflux (GERD) may play a role in the pathogenesis of IPF.

This study is presented at the Plenary Session III, 54th SSAT Annual Meeting on May 19, 2013, Orlando, FL.

M. E. Allaix · F. A. Herbella · B. Borraez Segura · M. G. Patti (✉)
Center for Esophageal Diseases, Department of Surgery, University
of Chicago Pritzker School of Medicine, 5841 S. Maryland Ave, MC
5031, Room G-207, Chicago, IL 60637, USA
e-mail: mpatti@surgery.bsd.uchicago.edu

P. M. Fisichella
Swallowing Center and Department of Surgery, Loyola University
Chicago, Stritch School of Medicine, Chicago, IL, USA

I. Noth
Department of Medicine, University of Chicago Pritzker School of
Medicine, Chicago, IL, USA

Recent studies have, in fact, suggested that this disease might not be as idiopathic as previously thought and that GERD, by inducing microaspiration, might be one of the causative factors.^{4–6} In addition, other studies support the use of fundoplication in the management of patients with IPF and GERD, as they have shown that by controlling reflux and avoiding aspiration, a fundoplication can stop the progression of this disease.^{7–9}

Thus, even in the absence of a prospective and randomized trial confirming the positive impact of antireflux surgery in patients with IPF and GERD, it has become a common practice in most lung transplant centers to perform a fundoplication in IPF patients when GERD is demonstrated.^{7–9} It is not clear, however, on what type of preoperative work-up is necessary and what is the motility and reflux profile in patients in whom microaspiration is thought to be the original lung insult that leads to fibrosis.

The aims of this study were to compare in a group of patients with GERD and a group of patients with GERD and IPF: (a) the clinical presentation, (b) the esophageal function as defined by high-resolution manometry, and (c) the reflux profile by dual sensor pH monitoring.

Materials and Methods

This is a retrospective review of a prospectively set institutional review board-approved database of patients referred to the Center for Esophageal Diseases of the University of Chicago Medical Center between October 2008 and October 2012. Patients with prior antireflux or gastric surgery and patients with pulmonary disorders other than IPF were excluded from the study. Overall, 102 patients with GERD proven by pH monitoring were included in the analysis. Of these, 80 patients had a diagnosis of GERD but no respiratory symptoms (group A) and 22 had both GERD and IPF (as established by lung biopsy) (group B). There were 44 (43 %) men and 58 (57 %) women, whose mean age was 57 ± 14 years (range, 27–86 years). In these two groups, we compared (a) the clinical presentation, (b) the esophageal function, and (c) the reflux profile.

Clinical Presentation Patients were questioned regarding the presence of typical (heartburn, regurgitation, dysphagia) and atypical symptoms (hoarseness, cough, chest pain) of GERD.

Esophageal Function High-resolution manometry was performed in all patients after an overnight fast using a solid-state catheter with 36 circumferential sensors spaced at 1-cm intervals. The probe was inserted transnasally and positioned in order to record from the pharynx to the stomach. Pressure, length, and relaxation of the lower esophageal sphincter (LES), as well as the pressure of the upper esophageal sphincter (UES), were measured. Esophageal body motility was

assessed starting with a basal period without swallowing, followed by ten wet swallows of 5 ml of water at 30-s intervals. Amplitude, duration, and velocity of the peristaltic waves were recorded. Peristalsis was considered normal if the distal esophageal amplitude (DEA) was greater than 40 mmHg. Ineffective esophageal motility (IEM) was defined by DEA less than 30 mmHg or by presence of simultaneous waves following more than 30 % of the wet swallows.¹⁰ A nonspecific esophageal motility disorder (NSEMD) was defined as the presence of abnormal esophageal peristalsis without meeting the criteria for IEM. The data were analyzed using a commercially available computer software.

Reflux Profile All patients underwent ambulatory catheter-based 24-h pH monitoring. Acid-suppressing medications were discontinued 10 days (proton pump inhibitors (PPIs)) or 3 days (histamine-2 receptor antagonists) before the study. The pH probe was calibrated in a buffer solution at pH 7 and 1 before and after the monitoring. The test was performed by placing transnasally the dual-channel pH catheter with two sensors located 15 cm apart so that the distal and the proximal sensors were positioned, respectively, 5 and 20 cm above the upper border of the manometrically determined LES. Patients were encouraged to consume an unrestricted diet during the study, but to avoid snacks and carbonated beverages in between meals.

Gastroesophageal reflux was evaluated in terms of (1) number of reflux episodes, (2) number of episodes longer than 5 min, (3) duration of the longest reflux episode, (4) acid exposure (percentage of time with pH less than 4), and (5) esophageal acid clearance (mean duration of a reflux episode) in total, in the distal and proximal esophagus, in the supine and upright position. Data were integrated into the DeMeester score, with a value greater than 14.7 set as abnormal.¹¹

Barium Swallow and Upper Endoscopy In the majority of patients, these tests were performed in outside hospitals and only the report was available.

Statistical Analysis Statistical analysis was performed using SPSS version 19 (Copyright © SPSS Inc., 2000). The data were collected in an Excel spreadsheet. Quantitative data are given as mean and Standard Deviation (SD). Proportions were compared using the χ^2 test or the Fisher exact test where appropriate. Student's *t* test was used to compare normally distributed variables. A level of 5 % was set as the criterion for statistical significance.

Results

Table 1 summarizes the results in the two groups of patients: group A, 80 patients with GERD, and group B, 22 patients

Table 1 Demographic, manometry, and pH monitoring results

	GERD (80 patients)	GERD+IPF (22 patients)	P value
Age (years)	55.7±15	61.3±8.9	0.098
Gender (male), N (%)	31 (38.8)	13 (59.1)	0.143
Heartburn, N (%)	67 (83.8)	13 (59.1)	0.028
LES pressure (mmHg)	19.9±9.7	20.5±11.9	0.807
Normal peristalsis, N (%)	51 (63.8)	14 (63.6)	0.810
Hypotensive UES, N (%)	6 (7.5)	7 (31.8)	0.008
% time <4 total			
Distal	9.7±6.6	12.7±13.6	0.149
Proximal	0.9±1.1	2.5±6.9	0.047
Acid clearance total (s)			
Distal	85.3±65.2	137.5±112.4	0.006
Proximal	42.4±67.1	169.9±406.8	0.008
% time <4 supine			
Distal	10.5±12.8	8.6±17.1	0.569
Proximal	0.5±1.2	2.9±7.6	0.007
Acid clearance supine (s)			
Distal	181.1±270.1	171.5±259.9	0.882
Proximal	47.6±72.3	899.1±1668.1	<0.001

with GERD and IPF. No differences were observed between the two groups in terms of age and gender.

Clinical Presentation Heartburn was present less frequently in group B than in group A patients (59 vs. 84 %, $p=0.028$), while the prevalence of regurgitation was similar between the two groups. Extra-esophageal manifestations of GERD were significantly more common among group B patients. Duration of symptoms was 138 ± 128 months in group A patients and 86 ± 49 months in group B patients ($p=0.375$). Four IPF patients (18 %) recently underwent a laparoscopic total fundoplication, but the follow-up is too short to draw any conclusions.

Esophageal Function An average of 16 ± 19 months had passed between the time the diagnosis of IPF was established and the performance of the esophageal function tests. There was no difference between the two groups in terms of LES pressure and presence of abnormal peristalsis. Amplitude of peristalsis in the proximal and distal esophagus was similar in both groups, while proximal and distal wave duration was significantly shorter among group B patients (3.9 ± 0.9 vs. 3.2 ± 0.7 mmHg, $p=0.001$ and 3.4 ± 0.8 vs. 3.0 ± 0.8 mmHg, $p=0.040$). A higher percentage of group B patients had a hypotensive UES (31.8 vs. 7.5 %, $p=0.008$).

Reflux Profile Mean DeMeester score was similar in the two groups (39.5 ± 24.9 vs. 39.1 ± 36.3 , $p=0.952$). Table 1 summarizes the esophageal acid exposure and esophageal

clearance for the proximal and distal esophagus in the upright and supine position in the two groups of patients.

Distal Esophagus There was no difference between the two groups with regard to the total and the supine acid exposure. Group B patients had a greater esophageal acid exposure in the upright position.

Total and upright acid clearances were significantly slower in group B, while acid clearance in supine position was similar in the two groups.

Proximal Esophagus Total acid exposure was significantly higher in group B patients. This difference was mainly observed in the supine position, while the acid exposure in the upright position was similar between the two groups. We did not find a correlation between the degree of reflux and the extent of pulmonary damage.

Total and supine acid clearances were significantly slower in group B patients, while no significant differences were observed in the upright position.

Barium Swallow and Upper Endoscopy The barium swallow results were available in 75 patients in group A and 16 patients in group B. A hiatal hernia was present in 52 and 38 % of patients, respectively ($p=0.437$). No information was available about the size of the hernia.

An upper endoscopy was performed in 45 patients in group A and in 4 in group B. Esophagitis was present in 40 and 50 % of patients, respectively ($p=0.888$). No information was available about the degree of esophagitis.

Discussion

The results of this study showed that in patients with GERD and IPF: (a) reflux was often asymptomatic, as heartburn was present in less than 60 % of patients; (b) with the exception of a weaker UES, the esophageal function was preserved; and (c) proximal reflux was more common, and in the supine position it was coupled with a slower acid clearance.

IPF and Reflux Symptoms

While heartburn was experienced by most patients with GERD, it was present in less than 60 % of patients with GERD and IPF. In other words, in approximately 40 % of patients with IPF, the abnormal reflux was silent and it was only identified because all patients were screened by ambulatory pH monitoring. Our observation confirms the findings of other studies that have shown that typical symptoms of GERD are frequently absent in patients with lung disease.^{12–15} For instance, Sweet et al. studied the prevalence of reflux

symptoms among patients awaiting lung transplantation for end-stage lung disease and found that typical symptoms of GERD had low sensitivity (67 %) and specificity (26 %), and could not distinguish between patients with and without abnormal reflux.¹⁴ The positive predictive and the negative predictive values were 64 and 28 %, respectively. Based on these findings, we feel that all patients in whom a diagnosis of IPF is established should be screened by esophageal manometry and ambulatory pH monitoring with a dual probe to determine if abnormal reflux is present and if it extends all the way to the proximal esophagus.

IPF and Esophageal Motility

The LES pressure was normal in both groups, suggesting that transient LES relaxations (TLESR) rather than a mechanically defective LES caused the abnormal reflux. Peristalsis was also normal and similar in the two groups. This is somewhat surprising as IEM is frequently found in patients with respiratory disorders other than IPF.¹⁰ The UES pressure was lower in group B patients, and this could theoretically increase the risk of aspiration. The esophageal function is however different in patients with other types of end-stage lung disease who might need a lung transplant. For instance, Gasper et al. found that among 26 patients with connective tissue disorders and end-stage lung disease awaiting lung transplant, peristalsis was either impaired or absent in 78 %. In 60 % of patients who underwent a fundoplication, a partial rather than a total wrap was performed because of the absence of peristalsis and the fear of causing severe postoperative dysphagia.¹⁶ Because of the finding of normal peristalsis in our patients with IPF, a total (360°) fundoplication was either performed or planned. This is particularly important as in the USA, contrary to the results obtained in European centers; a total fundoplication has been found to have better long-term control of reflux as compared to a partial fundoplication.^{17–22} In addition, a total fundoplication has been shown to normalize the esophageal motility profile as it increases LES pressure and decreases TLESR, while improves esophageal peristalsis.^{23–25}

IPF and Reflux Profile

The reflux score was similar in the two groups. However, the total esophageal acid exposure in the proximal esophagus was significantly higher in group B patients. This difference was mainly observed in the supine position, while the acid exposure in the upright position was similar between the two groups. In addition, total and supine acid clearances were significantly slower in group B patients while no significant differences were observed in the upright position. Even though we did not prove that patients with proximal reflux had aspiration by measuring pepsin or bile acids in the bronchoalveolar lavage fluid (BALF), we think that this reflux

profile creates a potential milieu for aspiration. Other studies have in fact shown that proximal acid reflux is associated with high levels of pepsin in the BALF.^{1,5} The realization that in these patients micro-aspiration occurs has important therapeutic implications. It has been shown that acid is just one component of the refluxate and that duodenal contents (containing bile salts and pancreatic enzymes) play an important role in the genesis of reflux symptoms. Kauer and colleagues were the first to clearly show the mixed nature of the refluxate.²⁶ They studied simultaneously acid reflux (by conventional pH monitoring) and duodenal juice reflux (by a sensor for bilirubin) in 53 patients with GERD and found that about 2/3 of patients had a mixed form of reflux. These findings explain why some patients have only partial control of symptoms when treated with proton pump inhibitors (PPIs) as they only decrease the acid production by the parietal cells. Furthermore, different studies using intraluminal impedance technology have shown that PPIs just change the pH of the gastric refluxate because of the reduced production of acid, but indeed, reflux persists due to the incompetence of the LES.²⁷ Ambulatory impedance pH monitoring clearly identifies the relationship between typical and atypical symptoms and reflux episodes, both acid and non-acid.²⁸ And when non-acid episodes of reflux are thought to be the cause of symptoms, a fundoplication is more effective than PPIs, as it is able to restore the competence of the gastroesophageal junction, therefore blocking any type of reflux.²⁹

Conclusions

We do acknowledge that this study has some limitations. Firstly, the number of IPF patients was small. However, it is important to remember that this is a rare disease and that even institutions with established IPF Centers have a limited number of patients.

Secondly, a barium swallow and upper endoscopy were performed in outside hospitals in few patients only, and we did not have data regarding the size of hiatal hernia and the degree of esophagitis.

We feel, however, that even with these limitations, this study contributes to the management of IPF patients as it shows the importance of screening routinely all patients with manometry and pH monitoring. IPF patients should not be offered a fundoplication based on the presence or absence of reflux symptoms only, but they should rather have a proper work-up to document the presence and the extent of reflux.³⁰ Overall, a definitive answer about the role of reflux control by a laparoscopic fundoplication can only be given by a prospective and randomized trial comparing survival in IPF patients with GERD treated by either a laparoscopic fundoplication or no therapy. Until then, a fundoplication should only be performed in selected IPF patients whose functional status

does not preclude general anesthesia and in centers where a skilled laparoscopic foregut surgeon is part of an experienced multidisciplinary team.³¹

References

- Lee JS, Collard HR, Raghu G, Sweet MP, Hays SR, Campos GM, Golden JA, King TE Jr. Does chronic microaspiration cause idiopathic pulmonary fibrosis? *Am J Med* 2010;123:304–311.
- Raghu G, Weycker D, Edelsberg J, Bradford WZ, Oster G. Incidence and prevalence of idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2006;174:810–816.
- Raghu G, Brown KK, Bradford WZ, Starko K, Noble PW, Schwartz DA, King TE Jr; Idiopathic Pulmonary Fibrosis Study Group. A placebo-controlled trial of interferon gamma-1b in patients with idiopathic pulmonary fibrosis. *N Engl J Med* 2004; 350:125–133.
- Patti MG, Tedesco P, Golden J, Hays S, Hoopes C, Meneghetti A, Damani T, Way LW. Idiopathic pulmonary fibrosis: how often is it really idiopathic? *J Gastrointest Surg* 2005;9:1053–1056.
- Sweet MP, Patti MG, Leard LE, Golden JA, Hays SR, Hoopes C, Theodore PR. Gastroesophageal reflux in patients with idiopathic pulmonary fibrosis referred for lung transplantation. *J Thorac Cardiovasc Surg* 2007;133:1078–1084.
- Raghu G, Meyer KC. Silent gastro-oesophageal reflux and microaspiration in IPF: mounting evidence for anti-reflux therapy? *Eur. Respir J* 2012;39:242–245.
- Linden PA, Gilbert RJ, Yeap BY, Boyle K, Deykin A, Jaklitsch MT, Sugarbaker DJ, Bueno R. Laparoscopic fundoplication in patients with end-stage lung disease awaiting transplantation. *J Thorac Cardiovasc Surg* 2006;131:438–446.
- Hoppo T, Jarido V, Pennathur A, Morrell M, Crespo M, Shigemura N, Bermudez C, Hunter JG, Toyoda Y, Pilewski J, Luketich JD, Jobe BA. Antireflux surgery preserves lung function in patients with gastroesophageal reflux disease and end-stage lung disease before and after lung transplantation. *Arch Surg* 2011;146:1041–1047.
- Lee JS, Ryu JH, Elicker BM, Lydell CP, Jones KD, Wolters PJ, King TE Jr, Collard HR. Gastroesophageal reflux therapy is associated with longer survival in patients with idiopathic pulmonary fibrosis. *Am. J Respir Crit Care Med* 2011;184:1390–1394.
- Fouad YM, Katz PO, Hatlebakk JG, Castell DO. Ineffective esophageal motility: the most common motility abnormality in patients with GERD-associated respiratory symptoms. *Am J Gastroenterol* 1999;94:1464–1467.
- Jamieson JR, Stein HJ, DeMeester TR, Bonavina L, Schwizer W, Hinder RA, Albertucci M. Ambulatory 24-h esophageal pH monitoring: normal values, optimal thresholds, specificity, sensitivity and reproducibility. *Am J Gastroenterol* 1992;87:1102–1111.
- Patti MG, Debas HT, Pellegrini CA. Clinical and functional characterization of high gastroesophageal reflux. *Am J Surg* 1993;165:163–168.
- Raghu G, Freudenberg TD, Yang S, Curtis JR, Spada C, Hayes J, Sillery JK, Pope CE 2nd, Pellegrini CA. High prevalence of abnormal acid gastroesophageal reflux in idiopathic pulmonary fibrosis. *Eur Respir J* 2006;27:136–142.
- Sweet MP, Herbella FA, Leard L, Hoopes C, Golden J, Hays S, Patti MG. The prevalence of distal and proximal gastroesophageal reflux in patients awaiting lung transplantation. *Ann Surg* 2006;244:491–497.
- Salvioli B, Belmonte G, Stanghellini V, Baldi E, Fasano L, Pacilli AM, De Giorgio R, Barbara G, Bini L, Cogliandro R, Fabbri M, Corinaldesi R. Gastro-oesophageal reflux and interstitial lung disease. *Dig Liver Dis.* 2006;38:879–884.
- Gasper WJ, Sweet MP, Golden JA, Hoopes C, Leard LE, Kleinhenz ME, Hays SR, Patti MG. Lung transplantation in patients with connective tissue disorders and esophageal dysmotility. *Dis Esophagus* 2008;21:650–655.
- Horvath KD, Jobe BA, Herron DM, Swanstrom LL. Laparoscopic Toupet fundoplication is an inadequate procedure for patients with severe reflux disease. *J Gastrointest Surg* 1999;3:583–591.
- Oleynikov D, Eubanks TR, Oelschlager BK, Pellegrini CA. Total fundoplication is the operation of choice for patients with gastro-oesophageal reflux and defective peristalsis. *Surg Endosc* 2002;16:909–913.
- Patti MG, Robinson T, Galvani C, Gorodner MV, Fisichella PM, Way LW. Total fundoplication is superior to partial fundoplication even when esophageal peristalsis is weak. *J Am Coll Surg* 2004;198:863–869.
- Dallemagne B, Weerts J, Markiewicz S, Dewandre JM, Wahlen C, Monami B, Jehaes C. Clinical results of laparoscopic fundoplication at ten years after surgery. *Surg Endosc* 2006; 20: 159–165.
- Booth MI, Stratford J, Jones L, Dehn TC. Randomized clinical trial of laparoscopic total (Nissen) versus posterior partial (Toupet) fundoplication for gastro-oesophageal reflux disease based on preoperative oesophageal manometry. *Br J Surg* 2008;95:57–63.
- Broeders JAJL, Mauritz FA, Ahmed Ali U, Draaisma WA, Ruurda JP, Gooszen HG, Smout AJ, Broeders IA, Hazebroek EJ. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br J Surg* 2010;97:1318–1330.
- Herbella FAM, Tedesco P, Nipomnick I, Fisichella PM, Patti MG. Effect of partial and total laparoscopic fundoplication on esophageal body motility. *Surg. Endosc* 2007;21:285–288.
- Heider TR, Behrns KE, Koruda MJ, Shaheen NJ, Lucktong TA, Bradshaw B, Farrell TM. Fundoplication improves disordered esophageal motility. *J Gastrointest Surg* 2003;7:159–163.
- Bahmeriz F, Dutta S, Allen CJ, Pottruff CG, Anvari M. Does laparoscopic antireflux surgery prevent the occurrence of transient lower esophageal sphincter relaxation? *Surg Endosc* 2003;17:1050–1054.
- Kauer WK, Peters JH, DeMeester TR, Ireland AP, Bremner CG, Hagen JA. Mixed reflux of gastric and duodenal juices is more harmful to the esophagus than gastric juice alone. *Ann Surg* 1995;22:525–533.
- Tamhankar AP, Peters JH, Portale G, Hsieh CC, Hagen JA, Bremner CG, DeMeester TR. Omeprazole does not reduce gastroesophageal reflux: new insights using multichannel intraluminal impedance technology. *J Gastrointest Surg* 2004;8:888–896.
- Mainie I, Tutuian R, Shay S, Vela M, Zhang X, Sifrim D, Castell DO. Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicenter study using combined ambulatory impedance-pH monitoring. *Gut* 2006;55:1398–1402.
- Mainie I, Tutuian R, Agrawal A, Adams D, Castell DO. Combined multichannel intraluminal impedance-pH monitoring to select patients with persistent gastro-oesophageal reflux for laparoscopic Nissen fundoplication. *Br J Surg* 2006; 93:1483–1487.
- Bello B, Zoccali M, Gullo R, Allaix ME, Herbella FA, Gasparaitis A, Patti MG. Gastroesophageal reflux disease and antireflux surgery—what is the proper preoperative work-up? *J Gastrointest Surg.* 2013; 17:14–20 discussion p. 20
- Gasper WJ, Sweet MP, Hoopes C, Leard LE, Kleinhenz ME, Hays SR, Golden JA, Patti MG. Antireflux surgery for patients with end-stage lung disease before and after lung transplantation. *Surg Endosc* 2008;22:495–500.

Discussant

Dr. John Hunter (Portland, Oregon): This is a descriptive paper, demonstrating the similarities and differences in reflux pattern and esophageal function in patients with GERD and idiopathic pulmonary fibrosis (IPF). From the outset, we must be careful not to read too much into these

data, as the indication for evaluation creates an intrinsic selection bias. The first sentence in the results section says that heartburn was less common in IPF patients than GERD controls. Well, of course, in GERD patients, the indication for study is most commonly heartburn, so you would expect them to report primarily typical reflux symptoms such as heartburn. In IPF, the indication for evaluation is most commonly IPF, so you would expect more pulmonary symptoms and less heartburn. If the authors want to learn whether the percentage of “silent” reflux is higher than expected in IPF patients, you would need to define a suitable control population, such as a cohort of patients with another chronic disease, such as diabetes or kidney failure, and perform pH studies on them, then determine the frequency of heartburn in the pH-positive patients. In such a control population stratified for the presence of GERD, I suspect you would find that at least 40 % denied heartburn symptoms.

So what can we learn from this paper?: While most parameters of esophageal function are not different between GERD and GERD+IPF, there appear to be differences in esophageal function between these groups. IPF patients are more likely to have lower UES pressures, more proximal reflux, especially supine, and diminished esophageal clearance of acid. As the authors point out, this is a set-up for microaspiration, one of the more plausible explanations for IPF. Two questions:

1. Your group B is GERD+IPF. As the indication for testing was IPF, I cannot help but wonder how many IPF patients referred to you proved to

have normal pH studies. Said another way, what proportion of the IPF population that you screened did not have GERD, by pH criteria?

2. Are your observations a “chicken or the egg” phenomenon? Could chronic pulmonary disease, with all the physiologic consequences (greater work of breathing, tachypnea, more negative inspiratory pressures) partially or completely explain your observations? Did the IPF create the differences in observed physiology or did proximal GERD, poor clearance, and a weak UES lead to IPF?

Closing Discussant

Dr. Marco Allaix: I want to thank Dr. Hunter for his comments.

In response to his first question, abnormal reflux was found by pH monitoring in 61 % of IPF patients referred for evaluation. Interestingly, however, heartburn was experienced by some IPF patients who had a normal pH monitoring study. This observation stresses again the low sensitivity and specificity of symptoms for the diagnosis of GERD.

Is GERD causing IPF or vice versa? This is a great question, but the answer is not known. We do know however that stopping reflux in IPF patients by a fundoplication can halt the progression of the disease. We also know that stopping reflux after lung transplantation may avoid the development of the bronchiolitis obliterans syndrome (BOS).