J Gastrointest Surg (2016) 20:104–110
DOI 10.1007/s11605-015-2955-4

2015 SSAT PLENARY PRESENTATION

Pathophysiology of Gastroesophageal Reflux in Patients with Chronic Pulmonary Obstructive Disease Is Linked to an Increased Transdiaphragmatic Pressure Gradient and not to a Defective Esophagogastric Barrier

Leonardo M. Del Grande[1] · Fernando A. M. Herbella[1] · Amilcar M. Bigatao[2] · Henrique Abrao[1] · Jose R. Jardim[2] · Marco G. Patti[3]

Received: 7 April 2015 / Accepted: 14 September 2015 / Published online: 24 September 2015

Keywords Gastroesophageal reflux · Chronic obstructive pulmonary disease · High-resolution esophageal manometry · Esophageal pH monitoring

Introduction

The association of gastroesophageal reflux disease (GERD) and pulmonary diseases is well known.[1] Early studies showed that gastroduodenal contents may reflux up to the proximal esophagus[2] and cause aspiration.[3] Other studies showed a higher incidence of GERD in patients with asthma,[4] interstitial fibrosis,[5] chronic cough,[6] and chronic obstructive pulmonary disease (COPD).[7–10]

Esophageal (or typical) GERD symptoms (heartburn, regurgitation, and dysphagia) are not always present in these patients, and even when they are reported, they yield a low accuracy for GERD diagnosis.[11] Extra-esophageal symptoms such as cough are common and thus represent a confounding factor. As a consequence, clinical questionnaires are insufficient and objective determination of GERD is mandatory for the correct management of these patients.

COPD is attributed to tobacco smoking in the majority of cases, different from adult asthma and pulmonary fibrosis that, although still considered idiopathic, have GERD as a putative etiologic factor. However, a great number of smokers will never develop COPD leading to the suggestion that tobacco alone is not responsible for the disease in every patient and that aspiration of gastroduodenal contents may play a contributory role. In addition, COPD disrupts the ventilatory dynamics, and this may promote abnormal reflux. COPD is probably the main pulmonary disease that lacks a satisfactory number of studies dealing with objective evaluation of esophageal motility and acid exposure by esophageal function tests. We believe that the study of the incidence of GERD, esophageal motility, and ventilatory dynamics by esophageal manometry and ambulatory pH monitoring may shed some light on the association between COPD and GERD.

This study aims to evaluate in patients with COPD (1) the incidence and profile of GERD, (2) esophageal motility, and (3) the transdiaphragmatic pressure gradient.

Patients and Methods

Population

We studied 48 consecutive patients (56 % females, mean age 66.2±9.6 years) with COPD diagnosed by spirometry, over 40 years of age, treated at the Lung Rehabilitation Center of the Federal University of São Paulo. Patients that could not understand or comply with the protocol and those who refused to sign the informed consent were excluded. Patients with

Plenary presentation at the SSAT 56th Annual Meeting, Washington, DC, May, 2015

✉ Fernando A. M. Herbella
herbella.dcir@epm.br

[1] Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Rua Diogo de Faria 1087 cj 301, Sao Paulo, SP 04037-003, Brazil

[2] Department of Medicine, Respiratory Division, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, Brazil

[3] Department of Surgery, Pritzker School of Medicine, University of Chicago, Chicago, USA

previous foregut surgery or primary esophageal motility disorders were also excluded from the study.

Esophageal Function Tests

High-resolution esophageal manometry (HRM) was performed in all patients. Medications that interfere with esophageal and gastric motility were discontinued 3 days before the study. HRM data of all volunteers were acquired using a solid-state HRM assembly with 36 sensors spaced at 1-cm intervals (Given Imaging, Los Angeles, CA). All studies were performed with patients in sitting position, after a minimum fasting period of 8 h.

Position, pressure (defined as the mid-respiratory pressure), relaxation, and length of the lower esophageal sphincter (LES) were recorded. Esophageal body function was assessed by giving 10 wet swallows of 5-ml water boluses at 30-s intervals when amplitude, duration, and propagation of the peristaltic waves were assessed at 3 and 7 cm above the LES. Upper esophageal sphincter (UES) pressure was also measured.

The transdiaphragmatic gradient was calculated subtracting the thoracic pressure measured at 2 cm above the upper border of the LES considering its respiratory excursion and the abdominal pressure at 2 cm below the lower border of the LES considering its respiratory excursion. Both pressures were calculated based on the average pressure in a 30-s period encompassing all phases of the respiration (mid-respiratory measurement). LES retention pressure was calculated subtracting the transdiaphragmatic gradient from the mid-respiratory LES basal pressure. All measurements were obtained at the beginning of the test in the same time window.

The normal values considered in this study were LES length >2.7 cm, LES basal pressure 13–43 mmHg, LES residual pressure <15 mmHg, distal esophageal amplitude (DEA) (sensor located 3 cm above the upper border of the LES) 41–168 mmHg, and proximal esophageal amplitude (PEA) (sensor located 7 cm above the upper border of the LES) 37–166 mmHg. Distal contractile integral (DCI) defined esophageal contractions as ineffective (failed+weak) if <800 mmHg.s.cm or hypercontractile if >8000 mmHg.s.cm, and distal latency (s) <4.5 s defined a premature contraction.[12] Crural and LES dissociation was classified according to Pandolfino et al. [13]

Esophageal pH monitoring was performed in all patients. Acid-suppressing medications were discontinued 14 days before the study. During the study, the patients consumed an unrestricted diet. A dual pH probe catheter (sensor at 5 and 15 cm above the upper border of the manometric determined lower esophageal sphincter) was used. The data were incorporated into a composite score (DeMeester score). A score greater than 14.7 was set as abnormal.[14] Patients were grouped according to abnormal pH monitoring in GERD+ or GERD−.

COPD

All patients underwent spirometry (performed no more than 6 months prior to the esophageal tests). COPD was defined as a forced expiratory volume in the first second over forced volume capacity (FEV_1/FVC) ratio below 88 % of predicted after bronchodilator use and no response to bronchodilator. All patients were free of exacerbations at least 4 weeks previous to the esophageal tests.

Patients' distribution according to COPD severity was 8 stage I (FEV>80 %), 16 stage II (FEV_1 50–80 %), 17 stage III (FEV_1 30–50 %), and 7 stage IV (FEV_1<30 %). All patients but one had chronic use of inhaled beta agonists and 26 (54 %) were under the use of inhaled anticholinergics. All patients were past smokers but not active for at least 1 year.

Statistical Analysis

Data were presented as mean±SD. Student's *t*, Pearson correlation, and Fisher tests were used when appropriate. A p value <0.05 was considered statistically significant.

Ethics

The study protocol was approved by the local ethics committee (#1960/11) and written informed consent was obtained from each subject. No financial compensation was provided to the individuals.

The authors had no conflict of interest. All authors contributed sufficiently to be named as authors and are responsible for the manuscript. No professional or ghost writer was hired.

Results

Demographic data are shown in Table 1. GERD+ and GERD− groups did not differ in regard to gender, age, body mass index, and COPD severity (p=0.9).

Esophageal symptoms (heartburn or regurgitation) were referred by 10 (48 %) patients GERD+ and 14 (52 %) patients GERD− (p=1). Respiratory symptoms were referred by 17 (81 %) patients GERD+ and 24 (89 %) patients GERD− (p=0.7).

Manometric data are shown in Table 2. The incidence of distal hypocontractility and UES basal pressure was different between groups. Thoracic pressure was lower in GERD+ patients with a higher transdiaphragmatic pressure gradient and

Table 1 Patients demographics according to the presence or absence of gastroesophageal reflux disease (GERD)

n (%)	GERD+ 21 (44 %)	GERD− 27 (56 %)	*p*
Females (%)	43	67	0.1
Age (mean±standard deviation years)	67.42±9.37	65.33±9.91	0.5
Body mass index (kg/m^2)	25.91±4.82	26.34±5.24	0.8

GERD gastroesophageal reflux disease

lower LES retention pressure (LES basal pressure-transdiaphragmatic gradient) in this group. A positive correlation is noticed between the transdiaphragmatic gradient and the DeMeester score (p=0.00253) (Fig. 1).

pH monitoring data are depicted in Table 3. As expected, group GERD+ had higher values compared to group GERD− patients for both proximal and distal reflux. Abnormal supine reflux (>3.5 %) and upright reflux (>8.4 %) were present in 52 and 5 % of the GERD+patients, respectively.

Proximal reflux (episodes of reflux >0 at the proximal sensor) was present in 20 (95 %) of patients GERD+ and in 21 (78 %) of patients GERD− (p=0.2).

Discussion

Our results show that (1) almost half of COPD patients have GERD on pH monitoring, (2) esophageal motility is not

Table 2 Manometric data in patients with chronic pulmonary obstructive disease (COPD) and presence or absence of gastroesophageal reflux disease (GERD)

Manometric parameter	GERD+ (n=21)	GERD− (n=27)	*p*
LES length (cm)	3.58±0.92	3.86±1.31	0.412
Abnormal	4 (19 %)	5 (18 %)	1
LES abdominal length (cm)	1.83±1.06	2.34±1.42	0.183
LES basal pressure (mmHg)	20.44±10.35	22.35±10.9	0.541
Hypotonic	4 (19 %)	6 (22 %)	1
Hypertonic	0	0	1
Mean wave amplitude at 3 cm (mmHg)	62.40±42.94	69.72±29.75	0.489
Hypocontractility	10 (48 %)	3 (11 %)	0.008*
Hypercontractility	0	0	1
Mean wave amplitude at 7 cm (mmHg)	67.47±38.8	77.84±38.19	0.359
Hypocontractility	3 (14 %)	4 (15 %)	1
Hypercontractility	1 (5 %)	1 (4 %)	1
Peristalsis (%)	87.23±10	79.48±27.81	0.230
Distal contractile integral (mmHg.s.cm)	1919±1834	1838±1338	0.860
Ineffective hypercontractility	7 (33 %)	2 (7 %)	0.0306*
Ineffective hypercontractility	0	0	
Distal latency (s)	5.8±2.6	5.8±1.9	1.000
Premature	5 (24 %)	6 (22 %)	1.000
UES basal pressure (mmHg)	48.13±38.82	82.71±54.93	0.018*
Abdominal pressure (mmHg)	11±5	10±4	0.6
Thoracic pressure (mmHg)	0.8±6	5±6	0.02*
Transdiaphragmatic gradient (abdominal pressure-thoracic pressure)	10±7	5±4	0.001*
LES retention pressure (LES basal pressure-transdiaphragmatic gradient)	10±10	18±11	0.01*
Crural-LES dissociation			
Type I	9 (43 %)	17 (63 %)	0.244
Type II	6 (29 %)	3 (11 %)	0.153
Type III	6 (29 %)	7 (26 %)	1.000

LES lower esophageal sphincter, *UES* upper esophageal sphincter

*Statistical significance

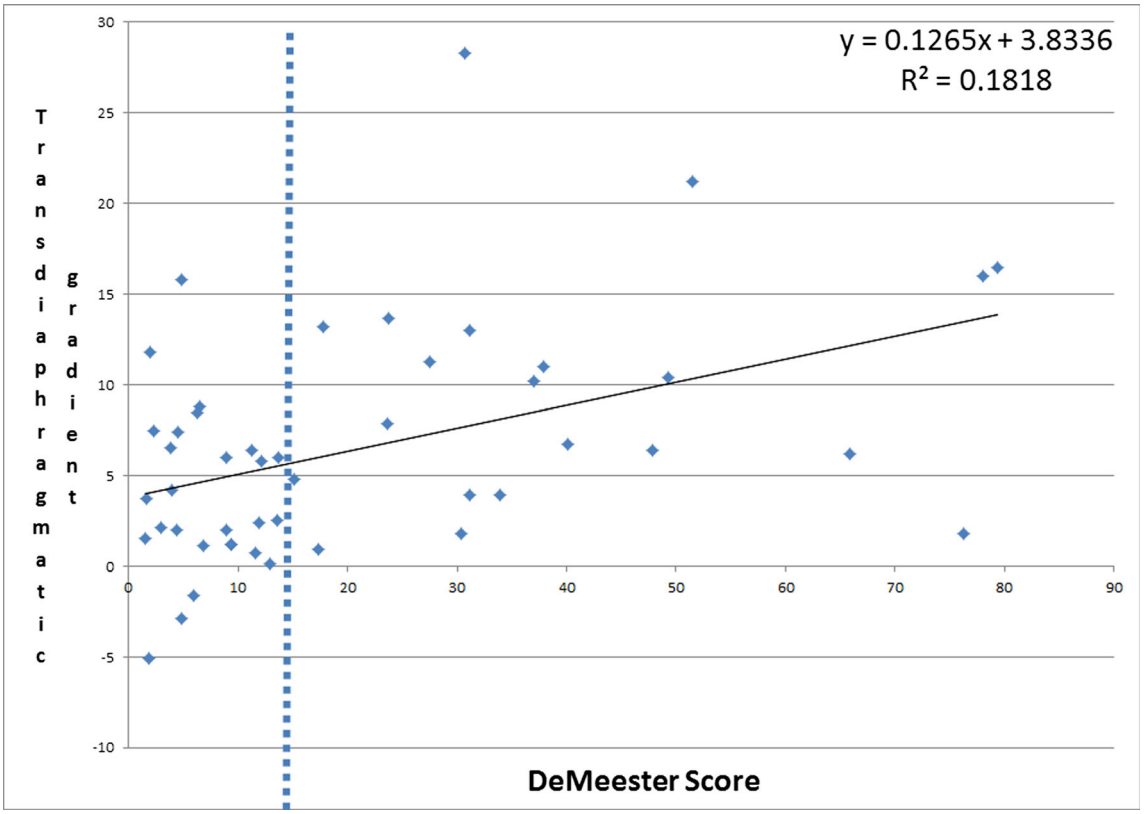

Fig. 1 Correlation between transdiaphragmatic gradient and DeMeester score

different in COPD GERD+ and COPD GERD−, and (3) GERD+ patients have a higher transdiaphragmatic pressure gradient and lower LES retention pressure

Association Between GERD and COPD

The association of GERD in COPD varies from 17 to 62 %.[10,15] This variability may be explained by different definitions for COPD (spirometry criteria for the diagnosis, degrees of severity, selection by cause, inclusion of active smokers, etc.) and different definitions for GERD (symptomatic evaluation by distinct questionnaires, pH monitoring, multichannel intraluminal impedance, detection of gastroduodenal contents in the bronchi, etc.). We included in our study a group of patients with a wide range of COPD severity and opted for an objective diagnosis of GERD based on pH monitoring. The standardized GOLD criteria for COPD definition of FEV1/FVC <0.70 are for epidemiological studies, and it is well known that underdiagnose COPD in smoking and symptomatic young patients but overdiagnose COPD in persons over 65 years old (due to a normal reduction in lung elastic recoil). The use of FEV1/FVC <88 % predicted for COPD diagnosis makes our sample more robust as it takes in consideration the individual age, sex, and height. As our sample included several patients over 65 years old, the use of a ratio <0.70 for the COPD diagnosis could by chance include patients that did not have COPD.

We found an intermediate prevalence of GERD in COPD patients in comparison to current literature data. Regardless, the association between the diseases is higher than the prevalence in normal population to be considered only a coincidence

The normal limit for proximal reflux is a very controversial topic. Although higher degrees of acid exposure were noted in patients GERD+, any amount of proximal reflux was noted in the majority of patients from both groups; however, we believe this is not a pathologic finding since proximal reflux is not a guarantee that the refluxate will be aspirated and it is found even in healthy volunteers.[16] If the threshold of >1 % total time pH <4[17] is adopted, 57 % of GERD+ patients had pathologic proximal reflux, while only 4 % of the GERD− patients had pathologic proximal reflux. This finding is in accordance with previous studies.[11]

Esophageal Motility in COPD

Our results show that the majority of patients with COPD have normal esophageal motility and that the differences between GERD+ and GERD− patients are subtle.

The LES was abnormal in only 20 % of our patients with COPD. Previous studies have shown that LES pressure may not discriminate patients with normal versus abnormal acid

exposure in patients without COPD;[18] however, a hypotonic LES is frequently found in up to 75 % of GERD+ patients.[19] Even though most reports focused only on pH monitoring and omitted results for esophageal manometry, previous studies also showed a majority of normal LES in COPD patients[20] and no difference between GERD+ and GERD−.[9]

Although mean distal wave amplitudes are similar between groups, a higher percentage of patients in group GERD+ had the amplitudes below normal values. The same is true if a more sophisticated metric, DCI, is compared between groups. This may be secondary to reflux.

UES pressure was found to be hypotonic in GERD patients. This may predispose to the risk for aspiration. A similar finding was noticed in patients with idiopathic pulmonary fibrosis.[5]

Pathophysiology of GERD and COPD

It is questionable whether the association of GERD and COPD is primary or secondary. COPD is usually credited to smoking in over 75 % of the cases;[21] however, the most pessimist analysis showed that no more than 50 % of the smokers will develop COPD.[22] This leads to the assumption that genetic factors may be involved.[23]

GERD has a multifactorial pathophysiology.[24] Manometric findings in patients with COPD and GERD did not show a defective esophagogastric barrier neither an important panesophageal dysmotility, different from other pulmonary diseases such as idiopathic pulmonary fibrosis that occurs in the presence of a hypotensive LES and abnormal esophageal peristalsis.[25,26] Crural-LES dissociation was not different in patients with or without GERD.

These findings lead to the hypothesis that GERD has a different pathophysiology in patients with COPD. GERD is probably secondary to COPD, and it has its pathophysiology based on increased transdiaphragmatic pressure gradient caused by COPD due to frequent cough, a flattened diaphragm, and increased respiratory effort. GERD may contribute to COPD genesis as an adjuvant to tobacco but certainly plays a part in COPD aggravation as the presence of GERD has been imputed as a predictor for COPD gravity and clinical exacerbations by previous studies[27] and in this series of patients (data reported in a separate paper focused on the pulmonary and symptomatic side of the association) and GERD therapy leads to improvement in COPD symptoms.[28,29]

Study Limitations

Our study has some limitations. First, although the number of studied patients matches other similar studies, it is small since the esophageal function tests are still not part of their care and they volunteered to the study irrespective of symptoms. Second, upper digestive endoscopy and barium esophagram were not performed in the patients; thus, no information on the presence of hiatal hernia was available. Third, non-acid reflux was not studied by impedance pH monitoring; however, we believe that non-acid reflux parallels acid reflux and impedance series still show controversial results and lack clinical implication regarding prognosis, therapeutic decisions, or postoperative evaluation.[30]

Conclusions

COPD patients have a high incidence of GERD whose physiopathology is linked to an increased transdiaphragmatic pressure gradient and not to a defective esophagogastric barrier.

Table 3 pH monitoring data in patients with chronic pulmonary obstructive disease (COPD) and presence or absence of gastroesophageal reflux disease (GERD)

pH monitoring parameter	GERD+ (n=21)	GERD− (n=27)	p
Distal sensor			
Number of reflux episodes	35±11.4	10.22±8.17	0.000*
Number of reflux episodes ≥5 min	5.52±3.91	0.85±1.19	0.000*
Longest reflux episode (min)	1839±2212	398±542	0.002*
Percent total time pH<4	12.1±12.46	1.59±1.25	0.000*
Percent Upright time pH<4	3.7±2.1	1.6±2.1	0.001*
Percent supine time pH<4	9.6±11.5	0.9±0.9	0.000*
DeMeester score	40.3±20,0	6.8±3.9	0.000*
Proximal sensor			
Number of reflux episodes	10.1±10.16	3.19±4.64	*0.003**
Number of reflux episodes ≥5 min	0.52±1.03	0.11±0.32	*0.05**
Longest reflux episode (min)	394±635	232±635	0.385
Percent total time pH<4	1.55±1.65	0.28±0.32	*0.000**
Percent Upright time pH<4	1.7±2.2	0.5±0.6	*0.009**
Percent Supine time pH<4	1.3±3.0	0.04±0.1	*0.03**

*Statistical significance

GERD should be aggressively investigated and treated in these patients since other series showed that GERD is associated to COPD worsening.

Acknowledgments We are indebted to Ms. Vanessa Horich Tuxen for her invaluable assistance with the esophageal tests.

Authors' contribution LMDG participated in the analysis and interpretation of data as well as final approval of the version to be published

FAMH participated in the conception and design, acquisition of data, analysis and interpretation of data, drafting the article, and final approval of the version to be published

AMB participated in the acquisition of data, analysis and interpretation of data, and final approval of the version to be published

HA participated in the analysis and interpretation of data, final approval of the version to be published

JRJ reviewed the manuscript for intellectual content and for final approval of the version to be published

MGP participated in the conception and design, analysis and interpretation of data, review for intellectual content, and final approval of the version to be published

Ethics The study protocol was approved by the local ethics committee (#1960/11) and written informed consent was obtained from each subject. No financial compensation was provided to the individuals.

References

1. Allaix ME, Fisichella PM, Noth I, Mendez BM, Patti MG. The pulmonary side of reflux disease: from heartburn to lung fibrosis. J Gastrointest Surg. 2013 Aug;17(8):1526–35.
2. Pellegrini CA, DeMeester TR., Johnson, LF, Skinner DB. Gastroesophageal reflux and pulmonary aspiration: incidence, functional abnormality, and results of surgical therapy. Surgery 1979;86:110–118.
3. Sweet MP, Patti MG, Hoopes C, Hays SR, Golden JA. Gastro-oesophageal reflux and aspiration in patients with advanced lung disease. Thorax. 2009 Feb;64(2):167–73
4. Harding SM. Recent clinical investigations examining the association of asthma and gastroesophageal reflux. Am J Med. 2003 Aug 18;115 Suppl 3A:39S-44S.
5. Allaix ME, Fisichella PM, Noth I, Herbella FA, Borraez Segura B, Patti MG. Idiopathic pulmonary fibrosis and gastroesophageal reflux. Implications for treatment. J Gastrointest Surg. 2014 Jan;18(1):100–5.
6. Kahrilas PJ, Smith JA, Dicpinigaitis PV. A Causal Relationship Between Cough and Gastroesophageal Reflux Disease (GERD) has been Established: A Pro/Con Debate. Lung. 2014 Feb;192(1): 39–46.
7. Gadel AA, Mostafa M, Younis A, Haleem M. Esophageal motility pattern and gastro-esophageal reflux in chronic obstructive pulmonary disease. Hepatogastroenterology. 2012 Nov-Dec;59(120): 2498–502.
8. Kamble NL, Khan NA, Kumar N, Nayak HK, Daga MK. Study of gastro-oesophageal reflux disease in patients with mild-to-moderate chronic obstructive pulmonary disease in India. Respirology. 2013 Apr;18(3):463–7.
9. Kempainen RR, Savik K, Whelan TP, Dunitz JM, Herrington CS, Billings JL. High prevalence of proximal and distal gastroesophageal reflux disease in advanced COPD. Chest. 2007 Jun;131(6): 1666–71.
10. Casanova C, Baudet JS, del Valle Velasco M, Martin JM, Aguirre-Jaime A, de Torres JP, Celli BR. Increased gastro-oesophageal reflux disease in patients with severe COPD. Eur Respir J. 2004 Jun;23(6):841–5.
11. 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 Oct;244(4):491–7.
12. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJ, Pandolfino JE; International High Resolution Manometry Working Group. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015 Feb;27(2):160–74. doi: 10.1111/nmo.12477. **Epub 2014 Dec 3**.
13. Pandolfino JE, Kim H, Ghosh SK, Clarke JO, Zhang Q, Kahrilas PJ. High-resolution manometry of the EGJ: an analysis of crural diaphragm function in GERD. Am J Gastroenterol. 2007 May;102(5):1056–63. **Epub 2007 Feb 23**.
14. Johnson LF, Demeester TR. Twenty-four-hour pH monitoring of the distal esophagus. A quantitative measure of gastroesophageal reflux. Am J Gastroenterol. 1974 Oct;62(4):325–32.
15. Lindberg A, Larsson LG, Rönmark E, Lundbäck B. Co-morbidity in mild-to-moderate COPD: comparison to normal and restrictive lung function. COPD. 2011 Dec;8(6):421–8.
16. Neto SC, Herbella FA, Silva LC, Patti MG. Ratio Between Proximal/Distal Gastroesophageal Reflux Does Not Discriminate Abnormal Proximal Reflux. World J Surg. 2014 Apr. 38(4):890–896.
17. Dobhan R, Castell DO. Normal and abnormal proximal esophageal acid exposure: results of ambulatory dual-probe pH monitoring. Am J Gastroenterol. 1993;88:25–29.
18. 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 Jan;17(1):14–20: **discussion p. 20.**
19. Riedl O, Gadenstätter M, Lechner W, Schwab G, Marker M, Ciovica R. Preoperative lower esophageal sphincter manometry data neither impact manifestations of GERD nor outcome after laparoscopic Nissen fundoplication. J Gastrointest Surg. 2009 Jul;13(7):1189–97.
20. Orr WC, Shamma-Othman Z, Allen M, Robinson MG. Esophageal function and gastroesophageal reflux during sleep and waking in patients with chronic obstructive pulmonary disease. Chest. 1992 Jun;101(6):1521–5.
21. Lindberg A, Bjerg A, Rönmark E, Larsson LG, Lundbäck B. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking Report from the Obstructive Lung Disease in Northern Sweden Studies. Respir Med. 2006 Feb;100(2):264–72.
22. Lundbäck B, Lindberg A, Lindström M, Rönmark E, Jonsson AC, Jönsson E, Larsson LG, Andersson S, Sandström T, Larsson K; Obstructive Lung Disease in Northern Sweden Studies. Not 15 but 50 % of smokers develop COPD?–Report from the Obstructive Lung Disease in Northern Sweden Studies. Respir Med. 2003 Feb;97(2):115–22.
23. Salvi S. Tobacco Smoking and Environmental Risk Factors for Chronic Obstructive Pulmonary Disease. Clin Chest Med. 2014 Mar;35(1):17–27.
24. Herbella FA, Patti MG. Gastroesophageal reflux disease: From pathophysiology to treatment. World J Gastroenterol. 2010 Aug 14;16(30):3745–9.
25. 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 Nov;9(8):1053–6; **discussion 1056–8**.
26. Hoppo T, Komatsu Y, Jobe BA. Gastroesophageal reflux disease and patterns of reflux in patients with idiopathic pulmonary fibrosis

using hypopharyngeal multichannel intraluminal impedance. Dis Esophagus. 2012 Oct 26.
27. Hurst JR, Vestbo J, Anzueto A, et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. New Engl J Med 2010;363:1128–38.
28. Sasaki T, Nakayama K, Yasuda H, Yoshida M, Asamura T, Ohrui T, Arai H, Araya J, Kuwano K, Yamaya M. A randomized, single-blind study of lansoprazole for the prevention of exacerbations of chronic obstructive pulmonary disease in older patients. J Am Geriatr Soc. 2009 Aug;57(8):1453–7.
29. Eryuksel E, Dogan M, Olgun S, Kocak I, Celikel T. Incidence and treatment results of laryngopharyngeal reflux in chronic obstructive pulmonary disease. Eur Arch Otorhinolaryngol. 2009 Aug;266(8):1267–71.
30. Herbella FA. Critical analysis of esophageal multichannel intraluminal impedance monitoring 20 years later. ISRN Gastroenterol. 2012;2012:903240.

Primary Discussant

Dr. Mario Costantini, M.D. (Padua, Italy): In this paper, the authors suggest an interesting hypothesis on the cause of the increased frequency of GERD detected in patients with chronic obstructive pulmonary disease.

Their study has several limitations the authors have already acknowledged (recruitment of the patients on a voluntary basis, the lack of impedance data….); that lessened the strength of their findings and their conclusions.

I would not like to discuss them again.

I have, however, some further enquiries, and I would like to know the opinion of the authors on them.

1. Duration of symptoms: If GERD in these patients is secondary to chronic cough and respiratory distress, I should expect a longer duration of respiratory symptoms in patients with abnormal acid reflux.

2. Reflux or reflex: Several papers report that respiratory symptoms in GERD patients may be due to a vagal reflex more than to a gastroesophageal reflux.

3. Therapy: The authors do not discuss GERD symptoms present in these patients and how they eventually respond to PPI therapy.

Partial or absent symptomatic response may happen (for example, for the association with weakly acidic reflux). Do the authors have any experience in treating these patients with fundoplication, i.e., is the rate of recurrence or wrap disruption higher than usual?

I appreciated reading and discussing this paper, with the new insights it suggests on the fascinating relationship between GERD and respiratory symptoms. However, I think further studies are necessary in order to confirm the findings and the hypothesis of the authors.

Closing Discussant

Dr. Herbella: Thank you for your thoughtful comments.

Our report has indeed limitations, and further studies are necessary to better understand the pathophysiology of the association of gastroesophageal reflux disease (GERD) and chronic pulmonary obstructive disease (COPD).

In regard to the duration of the respiratory symptoms, both groups had a similar average—5.8 years for the GERD− group versus 5.5 for the GERD+ group; however, it is hard to tell if the respiratory symptoms were originally related to the lung disease, GERD, or both.

Answering your second question: We firmly believe that reflux, i.e., aspiration, is contributory to COPD genesis in some patients, but we do acknowledge that reflex, i.e., bronchoconstriction, may be contributory to COPD severity and the onset of clinical exacerbations.

Finally, all patients on antirreflux medication had a good response controlling esophageal symptoms but a poor response to respiratory symptoms. We are still discussing with the pulmonologists how the patients with GERD should be treated. To this point, we have not operated any patients from this series.