

INTERSTITIAL LUNG DISEASE AND GASTROESOPHAGEAL REFLUX DISEASE: key role of esophageal function tests in the diagnosis and treatment

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ABSTRACT – *Context* - Gastroesophageal reflux disease (GERD) is common in patients with respiratory disorders and interstitial lung fibrosis from diverse disease processes. However, a cause-effect relationship has not been well demonstrated. It is hypothesized that there might be more than a coincidental association between GERD and interstitial lung damage. There is still confusion about the diagnostic steps necessary to confirm the presence of GERD, and about the role of effective control of GERD in the natural history of these respiratory disorders. *Objectives* - To determine the prevalence of GERD in patients with respiratory disorders and lung involvement; the sensitivity of symptoms in the diagnosis of GERD; and the role of esophageal function tests (manometry and 24-hour pH monitoring) in the diagnosis and treatment of these patients. *Methods* - Prospective study based on a database of 44 patients (29 females) with respiratory disorders: 16 patients had idiopathic pulmonary fibrosis, 11 patients had systemic sclerosis associated interstitial lung disease, 2 patients had polymyositis associated interstitial lung disease, 2 patients had Sjögren associated interstitial lung disease, 2 patients had rheumatoid arthritis associated interstitial lung disease, 1 patient had undifferentiated connective tissue diseases associated interstitial lung disease and 10 patients had sarcoidosis. The average forced vital capacity (% predicted) was 64.3%. All patients had esophageal function tests. *Results* - Thirty patients (68%) had pathologic reflux (average DeMeester score: 45, normal <14.7). The average number of reflux episodes recorded 20 cm above the lower esophageal sphincter was 24. Sensitivity and specificity of heartburn were 70% and 57%, of regurgitation 43% and 57%, and of dysphagia 33% and 64%. Twelve patients with GERD underwent a laparoscopic fundoplication which was tailored to the manometric profile: three patients in which peristalsis was normal had a total fundoplication (360°) and nine patients in which the peristalsis was absent had a partial anterior fundoplication (180°). *Conclusions* - The results of our study show that: (a) abnormal reflux was present in about 2/3 of patients with respiratory disorders (idiopathic pulmonary fibrosis, connective tissue disorders and sarcoidosis), and it extended to the upper esophagus in most patients; (b) the sensitivity and specificity of reflux symptoms was very low; and (c) esophageal function tests were essential to establish the diagnosis of abnormal reflux, to characterize the esophageal function and guide therapy. Long term follow-up will be necessary to determine if control of reflux alters the natural history of these respiratory disorders.

HEADINGS – Gastroesophageal reflux. Lung diseases, interstitial. Esophageal pH monitoring. Manometry.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF), connective tissue disorders (CTD) associated lung diseases and pulmonary sarcoidosis are a heterogeneous group of restrictive respiratory disorders that have in common inflammation and/or fibrosis of the pulmonary interstitium, with consequent dyspnea on exertion⁽²⁾.

Idiopathic interstitial pneumonias – IPF and idiopathic non-specific fibrotic interstitial pneumonias are diseases of unknown association. These diseases cause progressive dyspnea with eventual oxygen dependence. In both disorders the lung seems to be the only organ

affected. A high prevalence of gastroesophageal reflux disease (GERD) in patients with IPF has been documented in a number of studies^(9, 16, 19, 22, 29).

CTD (systemic sclerosis, polymyositis, Sjögren syndrome and rheumatoid arthritis) are multi-organ disorders with auto-immune basis in which the lung interstitium may be involved with variable frequency and severity. In these patients, abnormal motility of the esophagus has been associated with worsened pulmonary function and more severe GERD.

Sarcoidosis affects the lung in 85%-90% of patients. The diagnosis is made by clinical and radiological characteristic findings and supported by a surgical

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biopsy demonstrating non-caseous granulomas in an affected organ. No studies to date have been done in the prevalence of GERD in sarcoidosis.

In this study, we hypothesized that: (a) abnormal gastroesophageal reflux is highly prevalent in patients with interstitial lung diseases related to CTD, sarcoidosis and IPF; (b) presence of gastroesophageal reflux symptoms cannot reliably predict abnormal gastroesophageal reflux; and (c) esophageal function tests are essential for the diagnosis of abnormal reflux and for management.

METHODS

Patients with interstitial lung disease (ILD) from diverse causes were prospectively collected from the referrals for esophageal function tests in the Swallowing Center of the University of Chicago, Ill, USA from October 1, 2008 to September 30, 2009. Forty-four patients were included. They were evaluated by the rheumatology and pulmonary clinic for IPF, CTD and sarcoidosis and referred for esophageal function tests at the attending physician discretion. All patients had esophageal function tests (esophageal manometry and 24-hour pH monitoring). Forty-three patients had pulmonary function tests (PFT). Sixteen patients had IPF, 18 patients had CTD and ILD (scleroderma ILD- 11, polymyositis ILD- 1, dermatomyositis 1, Sjögren syndrome -ILD- 2, rheumatoid arthritis ILD-2, undetermined CTD ILD- 1), 10 patients had sarcoidosis.

Consecutive patients with a confirmed diagnosis of IPF, CTD or sarcoidosis with lung involvement according previously published American Thoracic Society/ European Respiratory Society criteria⁽²⁾ for ILD, who also had a successful completion of esophageal function testing comprised the study cohort.

Symptomatic evaluation

All patients referred for esophageal function tests answered a standardized questionnaire that included presence or absence of symptoms (heartburn, regurgitation, difficulty swallowing, chest pain, hoarseness and cough). Each patient was discussed with the referring physicians (pulmonologist and rheumatologist) regarding the presence of a respiratory condition and/or rheumatologic condition. Current use of acid reducing medications was also documented.

Esophageal manometry

Patients stopped medications that interfere with esophageal motility at least 48 hours before the procedure. After an overnight fast, esophageal manometry was performed using a solid state catheter with 5 circumferential pressure sensors (Sandhill Scientific, Highlands Ranch, CO, USA). Lower esophageal sphincter (LES) pressure and length were determined using the station pull-through technique, with 0.5 cm increments between stations. Esophageal peristalsis was measured then with 10 swallows of 5 mL of water given at 30-s intervals. Peristaltic wave amplitude, duration and velocity were recorded at 3, 8, 13, 18 cm above the manometrically determined LES. Peristaltic wave amplitude was then independently calculated for the distal esophagus (3 cm and 8 cm above the LES, distal esophageal amplitude) and for the proximal esophagus (13 cm

and 18 cm above the LES, proximal esophageal amplitude). Final manometric reporting was done using the Spechler and Castell criteria⁽²⁶⁾.

Ambulatory pH monitoring

Acid reducing medications were stopped 3 days for histamine H₂-receptors antagonists and 10 days for proton pump inhibitors before the test. A dual sensor pH probe in which the lower sensor was placed 5 cm above the superior border of the manometrically determined LES and the proximal sensor was placed 15 cm above the distal sensor was used. Four patients had a pH with impedance (for these patients, only calculations on the pH probe located 5 cm above the LES were performed). Patients were instructed to eat an unrestricted diet and avoid acid suppressing medications during the study. Patients were given a diary to describe symptoms and events. Based on the collected data, a composite reflux score (DeMeester score) was calculated for the distal esophagus. The data were analyzed using a commercial software program (BioView, Sandhill Scientific, Highlands Ranch, CO, USA). Meal periods were excluded from analysis. A DeMeester score above 14.7 was considered abnormal⁽¹¹⁾. These patients were referred as GERD+ group (pathologic gastroesophageal reflux). Patients with DeMeester score less than 14.7 were called GERD- (normal esophageal acid exposure). Patients were considered to have abnormal proximal reflux if the acid exposure was above 1%⁽⁵⁾ 20 cm above the LES. In the proximal channel, pseudoreflux (gradual decrease in pH to less than 4 in the proximal channel without an accompanying drop in the distal channel, with rapid recovery, usually occurring in the recumbent position), and artifacts due to acidic foods or drinks (an abrupt drop in the pH identical in the two electrode sites) were excluded from analysis⁽¹⁴⁾. For the patients that had pH with impedance testing, the threshold for abnormal reflux was 73 episodes (both acid and non-acid)⁽²⁵⁾.

Pulmonary function tests

Spirometry, diffusion capacity for carbon monoxide, and lung volumes by plethysmography were obtained per American Thoracic Society guidelines^(12, 17, 30).

Surgical technique

A total fundoplication (360°) was the preferred technique for patients with normal esophageal peristalsis. In patients with absent peristalsis, a partial anterior (180°) fundoplication was performed. The initial steps were similar for both operations. They included: (1) mobilization of the esophagus in the posterior mediastinum; (2) transection of the short gastric vessels; (3) approximation of the right and left pillars of the crus behind the esophagus; and (4) creation of a wrap. The total fundoplication was constructed over a 56 F bougie.

RESULTS

Forty-four patients were included. The average age was 54 years (range 28-76). Twenty-nine patients were female and 15 were male. Twelve patients were in the lung transplant list. Demographic characteristics in each group of patients and the results of the PFT are outlined in Table 1.

Symptom evaluation

The prevalence of symptoms of GERD, sensitivity, specificity, positive predictive value and negative predictive value of each symptom for the diagnosis of GERD were determined (Table 2). Table 3 shows the difference in prevalence of the typical reflux symptoms in patients with (GERD+) and without abnormal esophageal acid exposure (GERD-).

Manometric profile

Esophageal peristalsis was abnormal in 28 patients (64%). In 14 patients (32%), peristalsis in response to wet swallows was absent (Table 4). In patients with absent peristalsis, the median DeMeester score was 37.3, compared to 19.9 in patients with normal peristalsis ($P = 0.024$)

Ambulatory 24h pH monitoring

Abnormal DeMeester score was diagnosed in 30 of the 44 patients (68%). The mean score in this population was 45.2 (normal <14.7). In 8 patients (20%), the acid exposure in the proximal channel (20 cm above the LES) was abnormal. In 7 of these, the acid exposure in both proximal and distal channels were abnormal.

Four patients had pH with impedance testing. The DeMeester score was abnormal in two (average 22.5), and normal in two (average 3.6). In all four patients, the number of reflux episodes detected by impedance was within normal limits.

Surgical treatment

Twelve patients with abnormal reflux score DeMeester (score >14.72) had a laparoscopic fundoplication. There

TABLE 1. Demographic characteristics and pulmonary function tests

	IPF/NISP (n = 16)	CTD (n = 18)	Sarcoidosis (n=10)	Total
Age (average)	61	51	50	54
Female sex	5	15	9	29
BMI (kg/m ² , average)	29	27	33	28
DLCO (average, % predicted)	49	51	72	55
FEV1 (average, % predicted)	75	71	73	73
FVC (average, % predicted)	63	63	68	64
Race	15 C 1AA	11C 7 AA	2 C 8 AA	28 C 16AA

IPF – idiopathic pulmonary fibrosis; NISP – idiopathic non-specific fibrotic interstitial pneumonias; CTD – connective disorders; BMI – body mass index; DLCO- diffusion capacity of carbon monoxide; FEV1- forced expiratory volume in 1 second; FVC- forced vital capacity; C - Caucasian race; AA - African-American race.

TABLE 2. Prevalence of reflux symptoms in 44 patients with ILD, sensitivity, specificity, positive predictive value, negative predictive value

Symptom	Prevalence (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Heartburn	61	70	57	77	47.5
Regurgitation	43	43	57	68	31
Dysphagia	34	33	64	67	31
Any typical reflux symptom	77	83	29	71	40

PPV: positive predictive value. NPV: negative predictive value

TABLE 3. Prevalence of symptoms in patients with and without GERD

	GERD+ (%)	GERD- (%)	P-value
Heartburn	70	42.8	0.53
Regurgitation	43.3	42.8	0.89
Dysphagia	30	35.7	0.83

TABLE 4. Esophageal manometry

	Aperistalsis	IEM	NEMD	NE	Normal
CTD	10 (55.6%)	2 (11.8%)	3 (11.8)	0	3 (17.6%)
IPF/NISP	3 (18.8%)	4 (25%)	1 (6.25%)	1(6.25%)	7(43.45%)
Sarcoid	1(10%)	2 (20%)	1(10%)	0	6 (60%)
Total	14 (32%)	8 (19%)	5 (11%)	1(2%)	16 (36%)

IEM- ineffective esophageal motility disorder; NEMD - non-specific esophageal dismotility; NE - Nutcracker esophagus. IPF- Idiopathic pulmonary fibrosis; NISP- idiopathic non-specific fibrotic interstitial pneumonias

were no intra-operative complications. Of these, nine had a partial fundoplication (six scleroderma, two IPF, one sarcoidosis) and three had a total fundoplication (three sarcoidosis). At a mean follow-up of 10 months, two patients who had preoperative dysphagia (both with scleroderma and diffuse gastrointestinal involvement) had worsening of this symptom. Because the dysphagia persisted despite dilation, they both required total parenteral nutrition while taking only liquids by mouth. One patient with sarcoidosis developed post-operative dysphagia that improved after one dilation done 6 months after the operation.

DISCUSSION

The results of our study show that: (a) pathologic distal gastroesophageal reflux is present in more than two-thirds of patients with ILD, and abnormal proximal gastroesophageal reflux is present in 20%; (b) typical reflux symptoms are a poor predictor of pathological reflux; and (c) esophageal function tests are essential for establishing the correct diagnosis and for the treatment of these patients.

Prevalence of GERD in ILD

Idiopathic pulmonary fibrosis

A link between abnormal reflux and pulmonary fibrosis have been suggested since Pearson et al.⁽²¹⁾ and latter Mays et al.⁽¹⁶⁾ reported that a hiatal hernia seen in a barium swallow was more common IPF patients when compared with controls. In a large Veteran's study, patients with erosive esophagitis had a 1.36 odds ratio for IPF⁽⁷⁾.

Abnormal 24-hour pH-monitoring in patients with IPF have been reported to be as high as 94%⁽²⁹⁾. In other articles, the prevalence of abnormal reflux varied from 87% to 67%^(19, 22, 23), but in a recent report only 35% of an IPF cohort had pathological reflux⁽³⁾.

In our study, 56% of patients with IPF had abnormal distal reflux and 23% had abnormal proximal reflux. The reasons for this relatively low prevalence of GERD in this IPF cohort are unclear. Abnormal motor function of the esophagus was seen in 56% of the patients, similar of that of a previous report by our group⁽¹⁹⁾. The most prevalent abnormal finding on esophageal manometry was ineffective esophageal motility disorder.

Connective tissue disorders

The prevalence of ILD in patients with connective tissue disorders is high^(1, 4). In a study with high-resolution computed tomography, 81% of CTD patients had signs of ILD⁽¹⁾. GERD is also frequent in patients with CTD. Studies with 24-hour pH with and without impedance monitoring demonstrated abnormal reflux in 83% to 50%^(8, 9, 24) of patients. A negative impact of abnormal reflux in the pulmonary function has been demonstrated.

For example, Johnson et al.⁽¹⁰⁾ studied 13 patients with systemic sclerosis with 24-hour pH monitoring and PFT. This author did a multiple regression analysis and the impairment in the diffusion capacity of carbon monoxide (DLCO) correlated with proximal and distal reflux. The fact that ILD and GERD frequently coexist in patients with CTD, and that CTD patients with lung involvement may have a higher incidence of pathologic reflux reinforce the hypothesis that GERD may play a role in the natural history of the interstitial lung fibrosis in patients with connective tissue disorders.

In our study, 78% of patients with CTD had abnormal reflux score. In the scleroderma group, abnormal reflux was found in 91%. Nevertheless, the 57% of patients with CTD other than scleroderma had also abnormal reflux. Esophageal dysmotility was present in 15 out of 18 patients (82%). In 10 patients (55.6%) peristalsis was absent.

Sarcoidosis

Little is known about the prevalence of reflux in patients with sarcoidosis and if GERD plays a role in the natural history of this disease. In our study, 70% of patients with sarcoidosis had an abnormal DeMeester score. While this percentage seems very high, one must acknowledge that the reason for referring patient for EFT in this population was a little different compared to the other patients of the study. While patients with IPF and patient with CTD are systematically send to be screened for reflux, in patient with sarcoidosis, only when clinical suspicion of GERD arises the patient are screened for reflux by EFT (8/10 patients had typical reflux symptoms and 1/10 patient had EFT as part of lung transplant protocol). The majority of the patients in this group had preserved peristalsis.

Does impairment in the esophageal motility have influence on prevalence and severity of ILD?

In the present study, abnormal motility was diagnosed in 64% of our patients. Approximately one third of the patients had complete absence of peristalsis. Impairment of the motor function of the esophagus has been linked to more severe reflux and possible recurrent episodes of micro aspiration and lung damage. For example, Marie et al.⁽¹⁵⁾ studied 43 patients with scleroderma. These authors divided the patients in three groups according to the degree of esophageal dysmotility. Patients with absent peristalsis had significant lower DLCO compared with patients that had preserved peristalsis. The degree of mucosal damage diagnosed by endoscopy was also worse in patients with aperistalsis. In our study, absence of peristalsis was also linked to more severe reflux. Fagundes et al.⁽⁸⁾ studied 50 patients with mixed connective tissue disease and correlated esophageal dilation seen on high resolution CT scan with the presence of ILD. The prevalence of ILD in patients with esophageal dilation was 92%, compared with 45% in patients without esophageal dilation. Patti et al.⁽²⁰⁾ compared

the esophageal motility pattern in patients with connective tissue disorders with or without pulmonary involvement. Forty-six percent of the patients with CTD and pulmonary involvement had no peristalsis. Peristalsis was present in all patients who had CTD but no pulmonary involvement.

Can the presence of GERD symptoms reliably predict GERD?

This study confirms that the clinical history, even using a standardized questionnaire, cannot distinguish between patients with and without abnormal reflux. Neither the presence nor the severity of symptoms predicted the presence of abnormal reflux, which is consistent with other reports^(6, 27). For example, among 822 patients with a clinical diagnosis of GERD, manometry and pH monitoring showed that only 575 patients (70%) actually had abnormal reflux⁽¹⁸⁾.

Others have documented low sensitivity and specificity between reflux symptoms and a positive DeMeester score in patients with IPF as well as in patients with ILD associated with CTD. For instance, Raghu et al.⁽²²⁾ reported 87% of abnormal reflux in 65 patients with IPF. However, only 47% had heartburn more than once a month. Patti et al.⁽¹⁹⁾ reported the symptom profile in 16 patients with IPF. No difference was demonstrated in the prevalence of heartburn and regurgitation between the 10 patients in whom the 24 hour pH was abnormal and the remaining 6 patients that had a normal reflux score. Gasper et al.⁽⁹⁾ studied 26 patients with CTD and ILD listed for lung transplant. In this study, the sensitivity of having one or more typical reflux symptoms was 74%, and specificity was 75%.

Is surgical treatment effective and does it alter the natural history of these diseases?

Our study shows that in patients with CTD and lung disease a pan esophageal motility disorder are often present, characterized by a hypotensive LES and weak or absent esophageal peristalsis. In addition, reflux often extends all the way to the pharynx. It is reasonable to suggest that the esophageal dysmotility can cause or contribute to the development of pulmonary complications through repeated episodes of micro aspiration. For instance, in a prospective study of patients with systemic sclerosis, Marie et al.⁽¹⁵⁾ identified a correlation between the degree of esophageal dysmotility (as shown by manometry) and evidence of ILD both by pulmonary function tests and high resolution computed tomography. In addition, at 2 year follow-up, patients with severe esophageal dysmotility had a faster deterioration of lung function and a higher frequency of ILD on high resolution computed tomography scans, suggesting that GERD may be one of the contributing factors of ILD in patients with systemic sclerosis. Proton pump inhibitors do not stop reflux but they only change

the pH of the gastric refluxate⁽²⁸⁾, while a fundoplication restores the competence of the gastroesophageal junction, blocking acid and nonacid reflux. This observation is very important because aspiration of nonacid reflux can also cause respiratory symptoms. For instance, Mainie et al.⁽¹³⁾ were able to identify by pH impedance monitoring patients with cough due to nonacid reflux while treated by proton pump inhibitors. A laparoscopic Nissen fundoplication improved or resolved the symptoms in 13 of 14 such patients (93%). In our study, symptoms were improved suggesting control of abnormal reflux, although we do not have post operative pH testing. Some patients with absent esophageal peristalsis and dysphagia had worsening of this symptom requiring total parenteral nutrition. Even a partial fundoplication aggravated the emptying of food from the esophagus into the stomach. For this reason it would be important to treat patients with CTD and GERD at an early stage, when peristalsis is still preserved. Long term follow-up will determine if control of reflux improves the respiratory status and prognosis of these patients.

Our study has deficiencies. A referral bias may have occurred, since the patients were sent to the Swallowing Center of the University of Chicago at the referring physician discretion. Even with that, we were able to demonstrate that typical reflux symptoms are not reliable for the diagnosis of abnormal reflux. Besides, the small number of patients limited the statistical power of the study. Increased severity of reflux did not correlate with worsened pulmonary function (DLCO or FVC). Also, changes in trans-diaphragmatic pressures and respiratory mechanics may predispose patients with pulmonary diseases to abnormal reflux, without a cause-effect relationship. Our study cannot contribute to answer this question. Finally, the study is not able to prove if adequate control of reflux changes the natural history of ILD. However, we do have the merit to demonstrate that it is important to screen patients with interstitial damage for reflux, even if asymptomatic. Furthermore, our study has shown that in several different pulmonary disease processes, abnormal motility of the esophagus is often present and linked to more severe reflux.

CONCLUSION

In summary, correct diagnosis and adequate control of reflux are particularly challenging in this group of patients. Pathological distal and proximal abnormal reflux are highly prevalent. Spillage of gastric juice into the lungs may play a role in this heterogeneous group of pulmonary diseases. While typical reflux symptoms are not enough to reliably predict abnormal reflux, importance of the 24-hour pH monitoring cannot be overemphasized. Furthermore, esophageal manometry is crucial to tailor surgical therapy in these patients, since a considerable proportion will have absent peristalsis.

Soares RV, Forsythe A, Hogarth K, Sweiss NJ, Noth I, Patti MG. Papel-chave dos testes de fisiologia do esôfago no diagnóstico e tratamento da doença do refluxo gastroesofágico em pacientes com doença intersticial pulmonar. *Arq Gastroenterol.* 2011;48(2):91-7.

RESUMO – Contexto - A doença do refluxo gastroesofágico (DRGE) é comum em pacientes com lesões intersticiais pulmonares. Todavia, a relação de causa e efeito não foi claramente demonstrada. Tem sido formulada a hipótese de que a frequente coexistência de DRGE e dano pulmonar intersticial não seja meramente uma coincidência. Ainda existe controvérsia em relação a melhor forma de se confirmar o diagnóstico de DRGE e se o controle efetivo do refluxo tem influência na história natural destas enfermidades respiratórias. **Objetivo** - Determinar: (a) a prevalência da DRGE em pacientes com doenças respiratórias e envolvimento pulmonar intersticial; (b) a sensibilidade dos sintomas típicos de DRGE para o diagnóstico; (c) o papel dos exames de fisiologia do esôfago (manometria esofágica e pHmetria de 24 horas) no diagnóstico e manejo destes pacientes. **Métodos** - Estudo prospectivo de 44 pacientes (29 sexo feminino) com doenças respiratórias: 16 pacientes com fibrose pulmonar idiopática, 11 com doença intersticial pulmonar associada à esclerose sistêmica, 2 com doença intersticial pulmonar associada à polimiosite, 2 com doença intersticial pulmonar relacionada à síndrome de Sjögren, 2 com doença intersticial pulmonar associada à artrite reumatóide, 1 com doença intersticial pulmonar associada à doença indiferenciada do tecido conjuntivo e 10 pacientes com sarcoidose e acometimento pulmonar. A capacidade vital forçada média (% predito) foi de 64,3%. Todos os pacientes fizeram manometria esofágica e pHmetria de 24 horas. **Resultados** - Trinta pacientes (68%) tiveram refluxo patológico (média do escore de DeMeester de 45; normal <14.7). A média de episódios de refluxo detectados 20 cm acima do esfíncter inferior do esôfago foi de 24. A sensibilidade e especificidade de queimação retroesternal foi de 70% e 57%, de regurgitação de 43% e 57% e de disfagia de 33% e 64%. Doze pacientes com DRGE foram levados à fundoplicatura videolaparoscópica guiada pelo perfil manométrico: em três pacientes com peristalse normal foi realizada uma fundoplicatura à Nissen e em nove pacientes com peristalse ausente foi realizada fundoplicatura à Dor. **Conclusões** - Os resultados do estudo demonstraram que: (a) refluxo anormal esteve presente em 2/3 dos pacientes com doenças respiratórias e comprometimento intersticial; (b) a sensibilidade e especificidade dos sintomas de refluxo foi baixa; (c) provas de fisiologia do esôfago foram essenciais para o diagnóstico de refluxo anormal, para caracterizar a função esofágica e guiar o manejo. Seguimento de longo prazo vai ser importante para determinar se o controle do refluxo tem influência na história natural destas doenças respiratórias.

DESCRITORES – Refluxo gastroesofágico. Doenças pulmonares intersticiais. Monitoramento do pH esofágico. Manometria.

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