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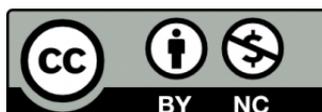
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SHORT LENGTH OF THE ESOPHAGUS AND DISTAL REFLUX ARE RISK FACTORS FOR PROXIMAL ESOPHAGEAL REFLUX?

Short length of the esophagus and distal reflux are risk factors for proximal esophageal reflux?

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ABSTRACT – Background - It is not clear whether patients suffering from distal esophageal reflux also present high risk to proximal esophageal reflux. Common sense suggests that reflux would more easily reach the pharynx in patients who have a smaller distance between the lower esophageal sphincter and the upper one and, thus, short esophagus. **Aim** - To Investigate if short esophageal length and presence of esophageal distal reflux are risk factors for proximal reflux among patients presenting respiratory symptoms. **Methods** – A hundred and seven patients were evaluated prospectively by interview, esophagoscopy, manometry and 24-hour esophageal pH monitoring. Student's t test (two-sided), Spearman's rank correlation, Chi-square and odds ratio were used in the statistical analysis. Significance level was set at 0.05. **Results** - Respiratory symptoms that motivated the search for gastroesophageal reflux disease were cough 43 (40.2%); throat irritation 25 (23.4%), pharyngeal globe 23 (21.5%) and hoarseness 16 (14.9 %). By esophagoscopy, 22 (27.2%) presented some degree of esophagitis. A hiatal hernia was observed in 14 (17.5%) patients. According to manometry, 11 (10.8%) had lower esophageal sphincter hypotonia. The average esophageal body length was 24.3 (\pm 1.9) cm, ranging from 20 to 30 cm. The esophageal length was not associated with the presence of proximal esophageal reflux. As indicated by pH monitoring, 23 (21.5%) presented pathologic distal reflux and 12 (11.2%) had proximal reflux. **Conclusion** - The esophageal length was not associated with the presence of proximal esophageal reflux. Patients who had pathological distal esophageal reflux, independent of the esophageal length, were 4.6 times more likely to have proximal esophageal reflux.

HEADINGS – Gastroesophageal reflux. Manometry. Esophageal pH monitorings.

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DESCRITORES - Refluxo gastroesofágico, Manometria, Monitoramento do pH esofágico.

RESUMO – Racional - Não está claro se pacientes que apresentam refluxo gastroesofágico distal têm maior risco de apresentar também refluxo proximal. O senso comum sugere que um episódio de refluxo poderia chegar mais facilmente à faringe em pacientes que tivessem menor distância a percorrer entre o esfíncter inferior do esôfago e o superior. **Objetivo** - Investigar se o esôfago curto e a presença de refluxo esofágico distal são fatores de risco para refluxo proximal nos pacientes com sintomas respiratórios. **Método** – Cento e sete pacientes foram avaliados prospectivamente por meio de entrevista, esofagoscopia, manometria e pHmetria. Utilizaram-se o teste t de Student, o de correlação de Spearman, o do Qui-quadrado e odds-ratio. O nível de significância foi 0,05. **Resultados** - Os sintomas que motivaram a investigação da doença do refluxo gastroesofágico foram: tosse 43 (40,2%); pigarro 25 (23,4%), globo faríngeo 23 (21,5%) e rouquidão 16 (14,9%). No estudo endoscópico 22 apresentaram esofagite e 14 hérnia de hiato. Na avaliação manométrica 11 (10,8)% apresentaram hipotonia do esfíncter inferior. A média do comprimento do esôfago foi 24,3 (\pm 1,9) cm, variando de 20 a 30 cm. Na avaliação pHmétrica 23 (21,5%) apresentaram refluxo distal patológico e 12 (11,2%) refluxo proximal. **Conclusões** - O comprimento do esôfago não esteve associado com a presença de refluxo proximal. Pacientes que apresentaram refluxo gastroesofágico distal, independente do comprimento do esôfago, tiveram risco aumentado de 4,6 vezes para apresentarem refluxo proximal.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is considered one of the most prevalent digestive diseases in Western countries¹². It occurs as a result of exposure of esophageal or supra-esophageal mucosa to the intragastric content, containing harmful agents such as hydrochloric acid, pepsin, bile salts and pancreatic enzymes¹¹.

GERD has long been recognized as a potential cause of many laryngeal and respiratory symptoms. Although cough, hoarseness, wheezing, and other airway symptoms may be caused by several etiologic factors, recent emphasis has been placed on the role of gastroesophageal reflux as the culprit¹³.

Although several tests have been reported to help determine whether reflux in a given patient is the cause of respiratory symptoms, none is perfect. A "gold standard" for diagnosis has been 24-hour esophageal pH monitoring using a 2-channel pH-probe¹³. Because direct monitoring of laryngeal pH is impractical, the placement of a probe in the pharynx or in the upper esophageal sphincter has been employed to detect extraesophageal acid reflux⁹.

Manometry is important to locate the lower esophageal sphincter (LES) and the upper esophageal sphincter (UES), to study the motor characteristics of the esophageal body and to determine its length.

The average length of the esophagus in adults varies from 20 to 35 cm³. In vivo measurement of esophageal length can be accomplished through endoscopic visualization of the gastroesophageal junction¹⁵ and manometric analysis⁸.

It is not clear whether patients suffering from distal esophageal reflux also presented high risk of proximal esophageal reflux. Common sense suggests that reflux would more easily reach the pharynx of patients who have a smaller distance between the LES and UES and thus, short esophagus.

Thus, the aim of this study is to look for an association between esophageal length and presence of proximal esophageal reflux, and to investigate whether those presenting distal reflux were at increased risk of presenting proximal reflux among patients presenting respiratory symptoms.

METHODS

A hundred and seven patients of both genders were evaluated prospectively, with 81 (75.7%) being females and 26 (24.3%) males. The mean age was 43.1 (\pm 13.4) years, ranging from 20 to 77. All were referred by outpatient clinics of pneumology, otorhinolaryngology and gastroenterology who presented with pulmonary or laryngeal symptoms, whose symptoms were suspected to be caused by gastroesophageal reflux, from January 2005 to June 2010. It was a convenience sample,

selected from a group of patients who presented the features of interest to the study.

Were included only patients who had respiratory symptoms, with suspected GERD, at least during two months, and nonsmokers. Were excluded all patients younger than 18 years.

Symptoms

An interview was performed by the same health professional with all patients before esophageal function testing, regarding the presence or absence of typical or atypical gastroesophageal reflux symptoms (aphtha, apnea, asthma, heartburn, bitter mouth, globus, dysphagia for liquids and solids, abdominal pain, chest pain, choking, belching, halitosis, acid tongue, nausea, odynophagia, throat irritation, bloating, regurgitation, hoarseness, hiccoughing, suffocation, coughing and vomiting).

Esophagoscopy

An upper gastrointestinal esophagoscopy was performed to detect erosive esophagitis (according to Savary-Miller's classification) and hiatal hernia, diagnosed if >2 cm of gastric mucosa appeared above the diaphragm during endoscopy.

Manometry

A solid-state manometry catheter, inserted transnasally into the stomach with the patient in a sitting position, after six hours of fasting, was used to exclude motor disorders and to accurately identify the location of the upper and lower esophageal sphincter. The design combines three sensors, each separated by 5 cm. A station pull-through measurement of the LES pressure determined the characteristics of the sphincter. The LES pressure was averaged over a series of three respiratory cycles. The peristaltic pump of the esophageal body was assessed over a minimum of 10 episodes of deglutition with 5 mL aliquots of normal saline at 30-second intervals. Each swallow evaluated the speed, duration, amplitude, and propagation of the peristaltic wave through the esophagus. Esophageal length was defined as the distance between the lower border of the lower esophageal sphincter and the lower border of the upper esophageal sphincter. UES location, pressure, and relaxation were measured before completion of the procedure.

Ph monitoring

After the manometric study, 24-hour esophageal pH monitoring was performed using a 2-channel pH-probe with 18 cm spacing between sensors, connected to a continuous pH-recording device (Alacer Biomédica, São Paulo, Brasil). Before the examination patients were instructed to stop proton pump inhibitors for seven days and H₂-blocking agents for 48 hours. The study was carried out only if the gastric pH was lower than 4. The probe was positioned with the sensors 5 and 23 cm above the LES. Continuous pH recordings

were obtained for 24 hours. Patients were asked to maintain normal activity and diet, avoid acidic foods and alcoholic drinks. They were instructed to record episodes of symptoms, time and duration of meals, and time and duration of supine and upright position.

The patients kept a diary of their symptoms. The recordings and diary information were entered into a software program, which reported events (number and duration of reflux episodes) and calculated acid exposure times over the course of the study. Patients were considered to have pathological gastroesophageal reflux when the fraction of total time with pH below 4 was higher than 3.0% of the total time of examination, i.e. more than 45 minutes, recorded by the distal sensor.

All tracings were individually reviewed, rather than relying only on the computer interpretation, to determine episodes of proximal reflux (the pH in the proximal sensor had to fall below 4, had to drop more than one point from its previous baseline, and had to be accompanied by a simultaneous drop in esophageal pH to below 4 in all distal sensors). One or more episodes of proximal reflux recorded in proximal sensor were regarded as abnormal.

Statistical analysis

Differences in mean esophageal length in patients with and without proximal reflux were tested by the Student's t test (two-sided). Spearman's rank correlation between esophageal length and LES pressures was estimated. Chi-square was used to compare prevalence of proximal reflux according to presence of distal reflux. The odds-ratio for proximal reflux was calculated comparing those presenting distal reflux to those without distal reflux. Significance level was set at 0.05.

Ethics

This project was approved by the Ethics Committee of the University Hospital of the UFMA (Federal University of Maranhão), Brazil, under number 33104-0451/2007.

RESULTS

Symptoms

Respiratory symptoms that motivated the search for GERD, reported in those interviews, were: cough 43 (40.2%); hoarseness 25 (23.4%), pharyngeal globe 23 (21.5%) and hoarseness 16 (14.9 %).

Esophagoscopy

Eighty-one patients underwent esophagoscopies with 59 (72.8%) having normal results, while 22 (27.2%) presented some degree of esophagitis. Hiatal hernia was observed in 14 (14.75) patients.

Manometry

Patients underwent manometry, and 11 (10.8%) had LES pressure below 10 mmHg (hypotonia). The

average length of the sphincter was 3.6 (\pm 0.8), ranging from 1 to 6 cm. The average body length of the esophagus was 24.3 (\pm 1.9) cm, ranging from 20 to 30 cm.

TABLE 1 – Mean esophageal length in patients presenting respiratory symptoms with and without proximal reflux

Proximal reflux	N	Mean (cm)	95% Confidence Interval
No	95	24,23	23,83 to 24,64
Yes	12	24,83	24,08 to 25,59

Student's t test = 0.15

Table 1 shows that there was no statistical significant difference between the mean esophageal length in patients with and without proximal reflux and respiratory symptoms ($p=0.15$).

Ph monitoring

All patients underwent continuous esophageal pH monitoring for 24 hours. Twenty three (21.5%) had pathological distal reflux and 12 (11.2%) had proximal reflux.

Table 2 shows that patients with distal reflux were 4.59 times more likely to present proximal reflux ($p=0,01$; OR=4.59 – 95% CI 1.32-15.97). A nonsignificant correlation was found between esophageal length and LES pressure (Spearman $r=0,12$ and $p=0,20$).

TABELA 2 – Prevalence of proximal reflux according to the presence of distal reflux among patients with respiratory symptoms

Distal reflux	Proximal reflux		Total
	Yes	No	
Yes	6 (26,1%)	17(73,9%)	23(100%)
No	6(7,1%)	78 (92,9%)	84(100%)
Total	12(11,2%)	95 (88,8%)	107(100%)

p value for the Chi-square test=0.01

DISCUSSION

The mechanisms involved in the genesis of proximal esophageal reflux have not been fully elucidated yet. Some causes have been proposed, such as the incompetence of the LES¹⁴, the transient lower esophageal sphincter relaxation^{4,5,10} and the deficiency of the esophageal body motility⁷.

In general they are considered as major changes when the pressure of the LES is lower than 6 mmHg, total length lower than 2 cm and intra-abdominal length of lower than 1 cm². This study found that 10.8% of patients had lower esophageal sphincter hypotonia (pressure <10 mmHg). One patient had total LES length

lower than 2 cm. Spearman correlation showed an association between LES hypotonia and the presence of pathological reflux in the distal canal ($p=0.02$).

Ineffective esophageal motility, the motor disorder more prevalent in GERD, has been found in patients with respiratory symptoms and proven reflux⁶. In this study, motor disorders were not associated neither with distal esophageal reflux nor with proximal esophageal reflux. Spearman correlation between variables that measured the esophageal body motor function (amplitude of the distal esophagus, peristaltic waves and waves that were not transmitted) with the presence of distal esophageal reflux and proximal esophageal reflux did not show a statistically significant association.

The authors wished to determine if there was a relationship between esophageal length and distal reflux with proximal esophageal reflux. In this study, Spearman correlation coefficient showed that proximal esophageal reflux was not significantly related to esophageal length. Also, t test revealed that there was no statistically significant difference between the mean of the esophageal length in patients presenting respiratory symptoms with and those without proximal reflux. However, presence of distal esophageal reflux increased the risk of suffering from proximal esophageal reflux (OR=4.6 $p=0,017$).

The esophagus begins in the neck at the cricoid cartilage and passes through the thorax within the posterior mediastinum and extends for a few centimeters past the diaphragm to its junction with the stomach³. The ideal method for measuring esophageal length is controversial. It was measured esophageal length manometrically and its mean was 24.3 (± 1.9) cm, ranging from 20 to 30 cm, in accordance to what has been found by others^{3,13,15}.

Awad, et al.¹ performed a retrospective study to test the relationship between esophageal length in normal control subjects, patients with esophageal disorders (achalasia, diffuse esophageal spasm, stricture, nutcracker esophagus), patients with GERD diagnosed by positive 24-hour pH monitoring, possible GERD but negative 24-hour pH monitoring. They found that patients with GERD (positive 24-hour pH monitoring) and patients with GERD-related stricture had a shorter than normal esophagus. In this study, the authors found that mean esophageal length did not differ between patients with and without proximal esophageal reflux, probably because none of these patients presented stricture GERD-related.

CONCLUSION

The esophageal length was not associated with presence of proximal esophageal reflux. Patients who presented pathological distal esophageal reflux, independent of the esophageal length, were 4.6 times more likely to have proximal esophageal reflux.

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