CHEST

Original Research

SIGNS AND SYMPTOMS OF CHEST DISEASE

Comparison of Gastroesophageal Reflux Disease Questionnaire and Multichannel Intraluminal Impedance pH Monitoring in Identifying Patients With Chronic Cough Responsive to Antireflux Therapy

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Background: **Empirical therapy has been recommended as an initial clinical approach for treating gastroesophageal reflux-induced chronic cough (GERC). This study compared the predictive accuracy of the Gastroesophageal Reflux Disease Questionnaire (GerdQ) with the accuracy of multichannel intraluminal impedance pH monitoring (MII-pH) for GERC.**

Methods: **A total of 126 consecutive patients with potential GERC were recruited to undergo MII-pH and complete the GerdQ. A final diagnosis of GERC was made after favorable response to consequent medicinal antireflux therapy, regardless of laboratory findings. The predictive accuracy of the GerdQ for GERC was assessed and compared with that of MII-pH.**

Results: **GERC was confirmed in 102 of 126 patients (81.0%); cough was due to acid reflux in 55 (53.9%) and nonacid reflux in 47 (46.1%). The optimal cutoff point of the GerdQ for predicting GERC was defined as 8.0 according to the highest Youden index of 0.584, with a sensitivity of 66.7%, specificity of 91.7%, positive predictive value of 97.1%, and negative predictive value of 42.9%. A subanalysis for only acid GERC showed further improvement in the predictive accuracy of the GerdQ, corresponding to a sensitivity of 90.9%, specificity of 78.6%, positive predictive value of 71.4%, and negative predictive value of 96.4%. However, a meaningful GerdQ cutoff point for prediction of nonacid GERC could not be determined. In general, MII-pH was superior to the GerdQ for predicting GERC and acid GERC.**

Conclusions: **The GerdQ can be used for predicting acid GERC but not nonacid GERC and is inferior to MII-pH.**

Trial registry: **Chinese Clinical Trial Registry; No.: ChiCTR-ODT-12001899; URL: www.chictr.org**

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Abbreviations: GERC = gastroesophageal reflux-induced chronic cough; GERD = gastroesophageal reflux disease; GerdQ = Gastroesophageal Reflux Disease Questionnaire; MII-pH = multichannel intraluminal impedance pH monitoring; SAP = symptom association probability

Gastroesophageal reflux is a common cause of chronic cough.[1,2] Based on pH values of refluxate in the esophagus, gastroesophageal reflux-induced chronic cough (GERC) can be classified as acid or nonacid.[3]

Multichannel intraluminal impedance pH monitoring (MII-pH) can detect both acid and nonacid reflux[4] and is the most sensitive and specific test for diagnosing GERC. Unfortunately, MII-pH has not been extensively used clinically because of its invasiveness and limited availability. Alternatively, empirical therapy has been advocated as an initial approach for treating GERC.[1,5,6] Because empirical trials frequently fail to relieve patients' cough,[7] screening patients with potential GERC prior to antireflux treatment may improve therapeutic gains.

The Gastroesophageal Reflux Disease Questionnaire (GerdQ) is a patient-centered and self-reported diagnostic instrument for gastroesophageal reflux disease (GERD)[8] and can achieve an overall diagnostic accuracy similar to that made by a gastroenterologist, with a sensitivity of 64.6% and a specificity of 71.4%.[8,9] However, to our knowledge the usefulness of the GerdQ in

GERC diagnosis has never been addressed. Therefore, we conducted a prospective study to compare the predictive accuracies of the GerdQ and MII-pH for GERC.

Materials and Methods

Patients

Consecutive patients referred to our respiratory clinic for potential GERC between January 2011 and March 2013 were recruited for this study. Requirements for participation included any one of the following: (1) presence of chronic cough and typical reflux-related symptoms, (2) GERC considered when previous laboratory workups failed to identify other possible causes of chronic cough,[10] and (3) coexisting GERC suspected when the treatment of current etiologies failed to completely resolve a cough. Patients refusing to undergo or who were intolerant of MII-pH were excluded. The study protocol was approved by the ethics committee of Tongji Hospital [No. LL(H)-11-13] and registered with the Chinese Clinical Trials Register. Written informed consent was obtained from all subjects before enrollment.

Study Design

This was a single-center observational study. Initial patient assessments included a medical history, physical examination, plain chest radiography, lung function tests, and evaluation of cough severity as determined by validated cough symptom scores that rate a cough using six incremental scales (0 = no cough, 5 = worst cough)[11] (e-Appendix 1). Additionally, patients were evaluated with the previously validated Chinese version of the GerdQ[12,13] (e-Appendix 2).

The GerdQ comprises six symptom-related items consisting of four reflux-related items positively related to GERD and two items negatively related to GERD. Patients were asked to recall how often they experienced the events described in the questionnaire during the preceding week and to score their answers on a four-point scale ranging from 0 to 3 for positive predictors and from 3 to 0 for negative predictors. The total scores represented a GerdQ score ranging from 0 to 18. A higher score signifies a greater possibility of GERD.[8]

MII-pH was performed as previously described[3] after the patients had stopped taking acid-suppressing medication for at least 1 week. Briefly, a combined MII-pH catheter was inserted transnasally into the patient's esophagus, with six impedance channel sensors (K6011-E10632; Unisensor AG) located 3, 5, 7, 9, 15, and 17 cm above the lower esophageal sphincter and an antimony pH electrode (819100; Medical Measurement System BV) positioned 5 cm above the proximal border of the lower esophageal sphincter. A connected portable data logger (Ohmega; Medical Measurement System BV) stored data from all seven channels over 24 h. Reflux episodes recorded on the tracings of MII-pH were manually characterized by their impedance value as liquid, gas, or mixed liquid-gas reflux or characterized using a pH meter as acidic (pH < 4.0), weakly acidic (pH 4.0-7.0), or weakly alkaline (pH > 7.0) reflux, with the latter two collectively referred to as nonacid reflux. The DeMeester score was calculated as a global measure of esophageal acid exposure. Symptom association probability (SAP) was used to represent the temporal association between cough recorded by patients on diary cards and reflux that had occurred during the preceding 2-min period.[3,14] Abnormal acid reflux was defined as a DeMeester score ≥ 14.72, SAP for acid reflux ≥ 95%, or both. These scores were used for diagnosing acid GERC, whereas abnormal nonacid reflux was defined as an SAP for nonacid reflux ≥ 95%, which was used for diagnosing nonacid GERC.[3]

Regardless of MII-pH findings, all patients received an 8-week course of standard antireflux therapy consisting of omeprazole 20 mg bid and domperidone 10 mg tid. If the initial treatment failed and MII-pH revealed abnormal reflux, patients received an augmented antireflux trial by doubling the dose of omeprazole to 80 mg/d or replacing domperidone with baclofen 20 mg tid.[15] All study patients and investigators were blinded to GerdQ scores throughout treatment. GERC was finally diagnosed only when a cough disappeared (resolved completely) or improved (combined daytime and nighttime cough symptom score decreased by ≥ 2 points)[3] as recommended by American College of Chest Physicians guidelines.[1] The predictive accuracies of the GerdQ and MII-pH for GERC were analyzed and compared (Fig 1).

Statistical Analysis

Data with normal distributions are expressed as mean ± SD, whereas data with skewed distributions are expressed as median

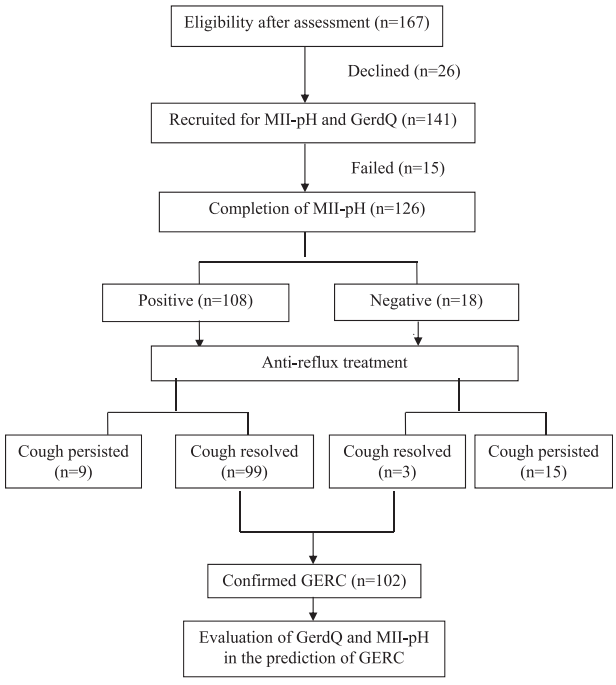

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flow diagram of the study and algorithm for GERC. GERC = gastroesophageal reflux-induced chronic cough; GerdQ = Gastroesophageal Reflux Disease Questionnaire; MII-pH = multichannel intraluminal impedance pH monitoring.

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