



Abstract

Background and aim: Post-reflux swallow-induced peristaltic wave (PSPW) index and mean nocturnal baseline impedance (MNBI) are associated with proton pump inhibitor (PPI) response in GERD patients. Few data concerning these variables in patients with reflux hypersensitivity (RH) are available. This study aimed to assess, in RH patients, the prevalence of PPI responders and nonresponders, and investigate the role of the predictive value of impedance-pH variables, including PSPW and MNBI for PPI response.

Introduction

Currently, because of their profound and prolonged acid suppression effects, proton pump inhibitors (PPIs) are the main therapeutic options for GERD. These therapeutic options have revolutionized the management of patients with reflux-related symptoms. However, persistent reflux-related symptoms have been reported in up to 10%-45% of GERD patients administered with a standard-dose of PPI once daily. Therapeutic PPI failures have been associated with missed diagnoses of functional esophageal disorders (FEDs). The most recent Rome IV criteria defines 2 distinct FEDs based on GERD-related symptoms (heartburn and/or chest pain) and normal endoscopy findings: reflux hypersensitivity (RH) characterized by normal esophageal acid exposure but positive symptom reflux association and functional heartburn (FH) characterized by normal esophageal acid exposure and negative symptom reflux association. In a previous study, based on Rome II definition, an estimated 50% of RH patients responded to a standard-dose of PPIs. Besides, in the Rome III criteria, the RH group was removed from the clinical definition of FH. Therefore, using this criteria, only 35% or lower of patients exhibited symptomatic relief after standard-dose PPI administration.

Methods and Materials

A total of 108 patients RH patients who met ROME IV criteria were prospectively recruited from June 2018 to May 2021. The prevalence of PPI responders/nonresponders was calculated, and impedance-pH variables were compared between the response and non-response groups. Multiple logistic regression was used to investigate predictors for PPI response.

Table 1. Demographic and clinical characteristics in responder and non-responder patients.

	Responders(n=60)	Non-Responders(n=48)	P value
Gender (female,n)	33	24	0.605
Age (years; mean±SE)	45.08±13.07	47.30±12.75	0.648
BMI (kg/m2; mean±SE)	21.19±2.54	22.14±2.35	0.314
Duration of symptoms (months; mean ± SE)	41.27 ± 7.59	40.46 ± 6.83	0.409
Presence of typical symptoms(n)	51	24	<0.001
Gender (female,n)	33	24	0.605

Results

In a total of 108 patients with RH, 60 patients (55.56%) were the PPI responders, and 48 (44.44%) were the nonresponders. When compared with the nonresponders, the PPI responders had a lower PSPW index (54.55±14.78 vs. 60.56±13.00, P=0.032) and a decreased value of MNBI (2391.36±337.44 vs. 2595.32±361.14, P=0.017). Multivariate logistic regression revealed that only pathologic PSPW index (OR: 2.064) and MNBI (OR: 1.800) exerted a significant influence on PPI response.

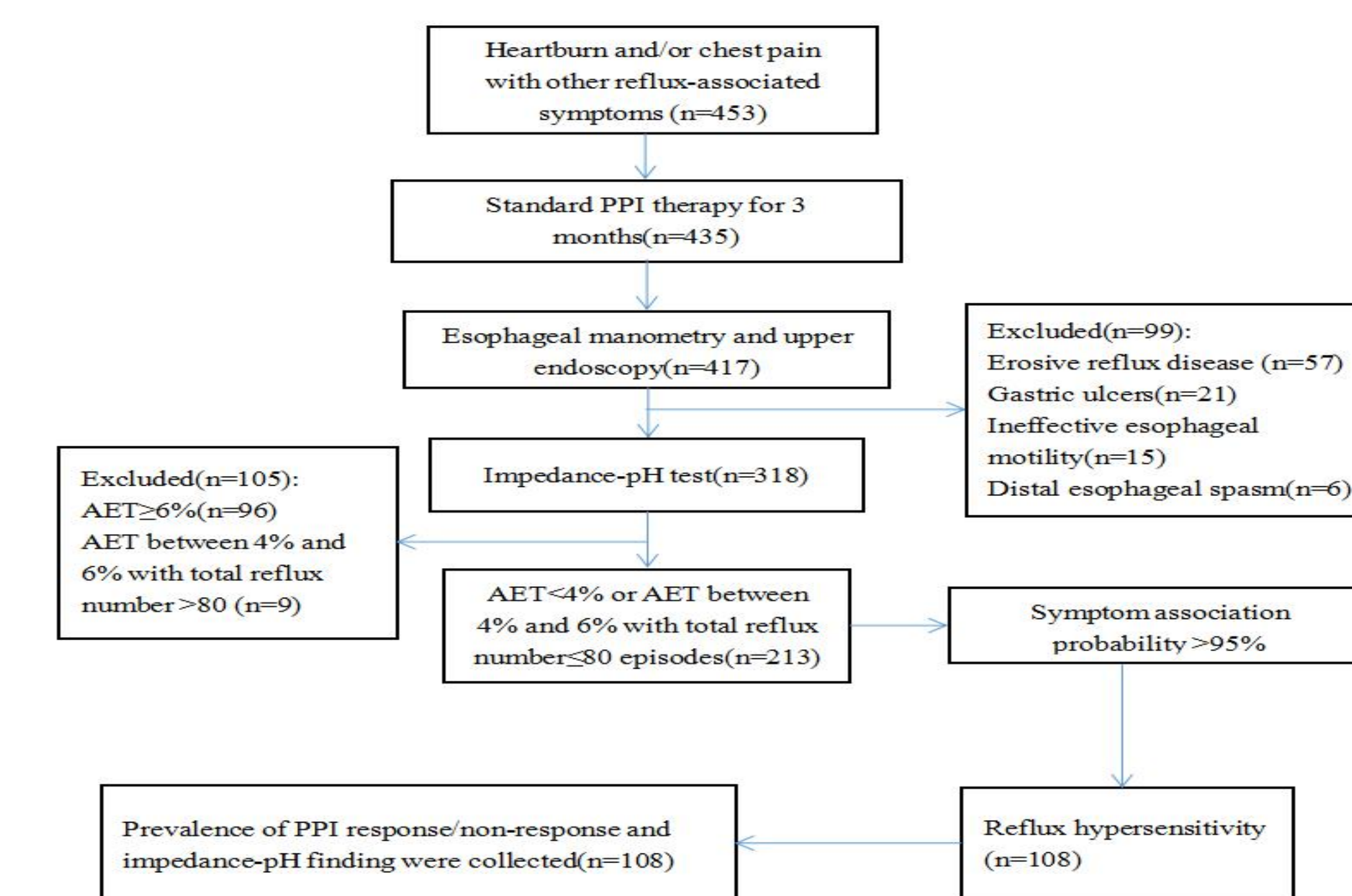


Chart 1. Flow chart of study participation.

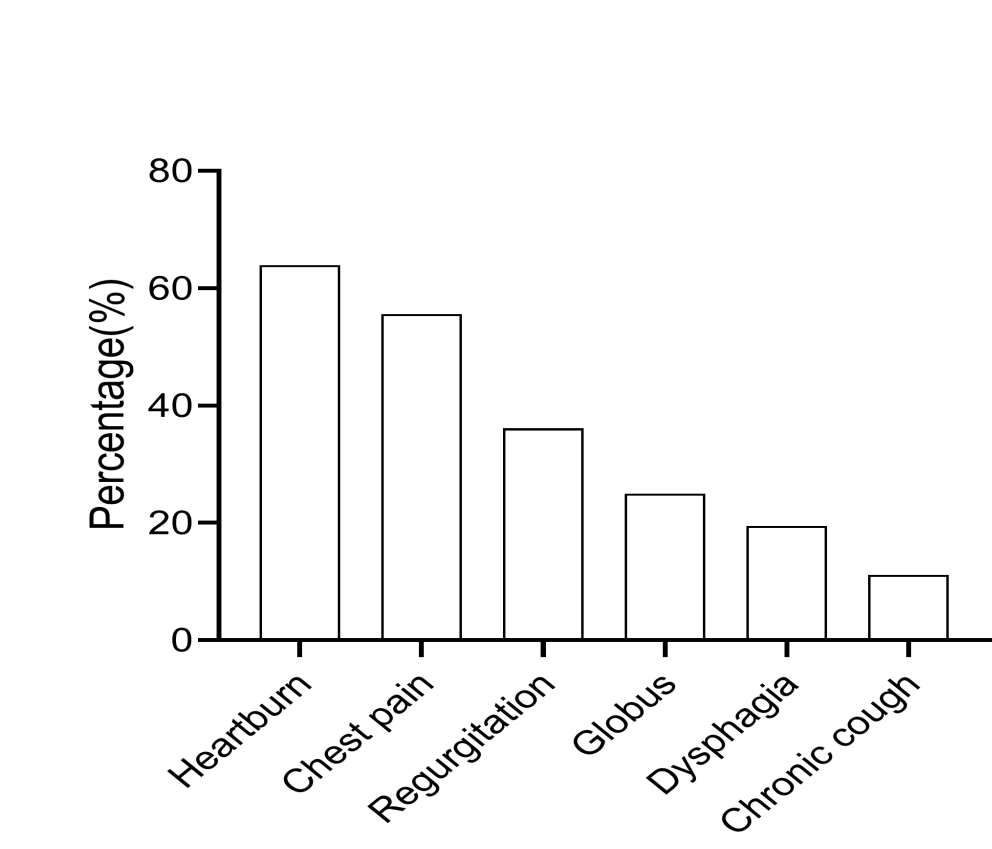


Figure 1. Frequency of each RH in the studied population.

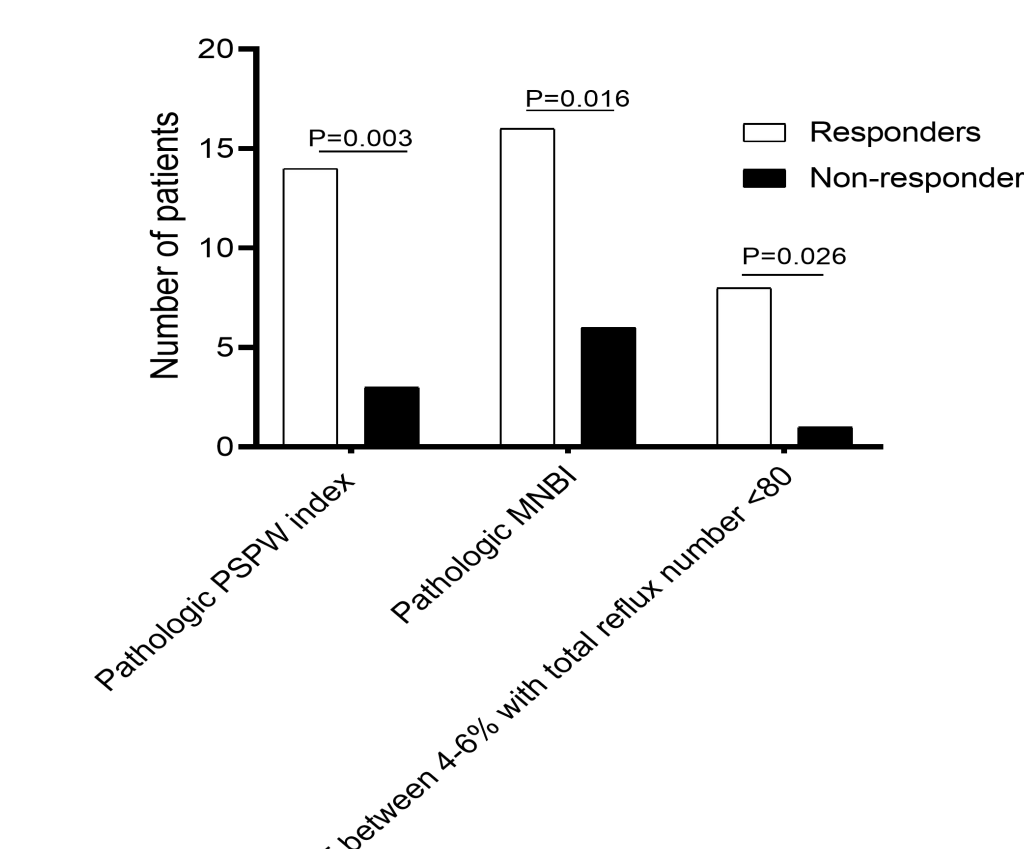


Figure 2. The comparison of the pathologic PSPW index, pathologic MNBI, AET

Discussion

A marked reduction in patients quality of life and a loss of considerable healthcare resources are associated with these disorders. Approximately 50% of FH patients have been shown to respond to a standard-dose of PPIs. However, to the best of our knowledge, this is the first study to evaluate the prevalence of PPI non-responses in RH patients whose identification was based on the Rome IV criteria. In this study, 48 (44.44%) of 108 RH patients exhibited unsatisfactory responses to PPIs, in agreement with findings from a previous study. Moreover, this is the first study to compare pH-impedance parameters between PPI responsive versus PPI non-responsive RH patients. In this study, the number of acid reflux events in responders was significantly high when compared to the PPI non-responsive group. The PPI response group also had a lower PSPW index and MNBI when compared to the PPI non-response group. The pathologic PSPW index and pathologic MNBI were significantly and independently associated with PPI responses in RH patients, highlighting the importance of impedance-pH tests for RH patients.

Conclusions

A big proportion of RH patients exhibited unsatisfactory responses to PPIs. Our findings show that acid reflux episodes, the pathologic PSPW index and pathologic MNBI are significantly and independently associated with PPI responses in RH patients, highlighting the importance of performing impedance-pH tests for RH patients.