Predictors of Gastroesophageal Reflux Disease Evidence in Noncardiac Chest Pain: A New Management Algorithm

Background: In noncardiac chest pain (NCCP) patients, proton pump inhibitor (PPI) therapy is only superior to placebo at improving chest pain when there is objective evidence of gastroesophageal reflux disease (GERD) on endoscopy or pH monitoring. The current guidelines recommend referring patients for confirmatory testing prior to starting treatment.

Aims: We aimed to identify clinical factors in NCCP patients that predict the presence of GERD.

Methods: Medical records from all patients admitted to Albert Einstein Medical Center with NCCP confirmed by stress test who had undergone an endoscopy within 3 years of discharge were included and grouped in accordance to their endoscopic results. Demographics, past medical history, outpatient medication list and details from their hospital course were evaluated to determine independent predictors.

Results: Analysis of over 20 variables in 86 patients identified two positive predictors of GERD evidence on endoscopy: older age (OR 3.12; 95% CI 1.07 - 8.36) and prior disease evidence on endoscopy (OR 5.40; 95% CI 1.02 - 28.52). One negative predictor, history of coronary artery disease (OR 0.54; 95% CI 0.17 - 0.74), was also identified. With these three predictors, a scoring system was created that divided patients into indeterminate and high risk categories. High risk patients on PPI had a decrease in repeat emergency room visits and hospital readmissions compared to those not on therapies.

Conclusions: Based on these results we propose NCCP management algorithm, which, if utilized, would standardize care and optimize endoscopy and PPI allocation.

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INTRODUCTION

Noncardiac chest pain (NCCP) affects 25% of all adults and accounts for 2-5% of all emergency room (ER) visits. Gastroesophageal reflux disease (GERD) is the most common finding. An empiric trial of a proton pump inhibitor (PPI) is the standard of practice; however, a recent systematic review demonstrated that PPIs were not superior to placebo in reducing chest pain in patients without objective evidence of GERD (i.e. esophagitis on endoscopy or positive pH testing). Furthermore, the broad use of PPI therapy leads to unnecessary, costly long-term treatment and may increase the risk of Clostridium difficile infections and osteoporotic bone fractures. The latest GERD guidelines recommend that suspected GERD-related NCCP be considered for diagnostic evaluation with esophagogastroduodenoscopy (EGD) or pH monitoring before initiating a PPI trial. Yet, less than one third of NCCP patients are referred to a gastroenterologist.

The current management of NCCP patients needs to be addressed due not only to the unpredictable response to PPI therapy but also to the high healthcare utilization and cost incurred by this population. It has been estimated that the cost to the healthcare system is approximately $315 million yearly due to frequent physician visits, hospital admissions, and use of medications and procedures, which is ongoing for many years. The only factors shown to lower readmissions in this population despite their persistent symptoms is appropriate gastrointestinal (GI) diagnostic studies (i.e. pH monitoring, EGD, barium swallow and manometry) and patient reassurance. However, it seems impractical to assign all patients to diagnostic testing given the prevalence of the disease.

In order to identify a cost-effective, organized approach to managing NCCP, we aimed to identify clinical predictors of objective evidence of GERD on endoscopy in order to stratify patient risk and optimize utilization of EGDs and PPI trials in this population.

METHODS

Study Population

This retrospective, case-control study was approved by the Institutional Review Board at Albert Einstein Medical Center and exempt from patient consent. The medical records of all patients who were admitted to the Cardiology/Telemetry service at Albert Einstein Medical Center (a tertiary teaching and referral hospital) between January 1, 2006 and January 1, 2008 were reviewed. Patients were included in the study if they were (1) admitted for chest pain or an equivalent diagnosis, (2) had a negative cardiac evaluation during that admission, and (3) had a subsequent EGD within 3 years. For the purposes of this study, chest pain equivalent diagnoses included: angina (413.x, 411.1), tachycardia (427.x, 785.x), acute coronary syndrome (411.x), chest pain (786.5x), heartburn (787.1), elevated troponin (790.6), shortness of breath (786.05), myocardial infarction (410.x, 861.01) and chest tightness/pressure/discomfort (786.59). A negative cardiac evaluation was defined as documentation of low risk for acute coronary syndrome and a negative stress test. Patients were excluded if they underwent percutaneous coronary intervention (i.e. cardiac catheterization) regardless of the findings due to their high pretest probability for significant coronary artery disease.

DATA COLLECTION

Demographics, past medical history, outpatient medication list and details from the hospital admission were collected from the Albert Einstein Medical Center electronic medical record. In the case of multiple admissions during the above defined time period, only the first admission was included. The frequency of repeat ER visits and readmissions to Einstein Medical Center for chest pain were also recorded. EGD reports were reviewed and noted to be positive for objective signs of GERD if they reported esophagitis, Barrett’s esophagus, and/or hiatal hernia. In the event of multiple EGDs, the findings of the EGD closest to the discharge date were included. All data was entered into an electronic database and was reviewed by two individuals to ensure accuracy.

Statistical Analysis

Patients were divided into two groups based on objective findings of GERD on EGD, and odds ratios with 95% confidence intervals were calculated for all demographic, prior medical history, outpatient medication and hospital course data. Those with significant odds ratios were analyzed using a multivariate logistical regression to confirm they were independent predictors. A scoring system based on the three validated clinical predictors (indeterminate risk <2, high risk ≥ 2) was created and evaluated with descriptive statistics including
RESULTS

Few patients diagnosed with NCCP get appropriate GI work-up.

During the study period, over 1,400 patients were admitted for chest pain or an equivalent diagnosis and underwent a stress test and cardiac evaluation. Subsequently, approximately 60% were found to have a noncardiac etiology. Only 86 patients (less than 10%) were referred to a GI specialist and subsequently underwent an EGD.

Age, history of coronary artery disease and prior GERD-positive EGD are independent predictors of objective evidence of GERD in NCCP.

To identify which NCCP patients were most likely to benefit from PPI therapy, we analyzed the clinical characteristics of the 86 patients who underwent subsequent EGD. 48.8% of patients had EGD consistent with objective evidence of GERD (i.e. (+) EGD). When the clinical characteristics of the (+) EGD and (-) EGD group were compared, three factors were significantly associated with objective findings on EGD (Figure 1). Age greater than or equal to 65 (OR 3.12; 95% CI 1.07 - 8.36) and (+) EGD in the past (OR 5.40; 95% CI 1.02 - 28.52) were both positively associated with (+) EGD while prior history of coronary artery disease (CAD) (OR 0.54; 95% CI 0.17 - 0.74) was negatively associated. Multivariate logistical regression confirmed age, history of CAD, and prior (+) EGD as independent predictors of objective evidence of GERD in NCCP.

Patients at high risk for objective evidence of GERD had fewer return ER visits and readmissions when discharged with PPI.

After establishing age, history of CAD and prior (+) EGD as independent predictors of objective evidence of GERD, we created a scoring system to divide patients into risk categories. Patients were given 1 point each for age greater or equal to 65, no prior history of CAD and prior (+) EGD such that the score ranged from 0 to 3. Using the scoring system, patients were divided into indeterminate risk (score 0-1, n=30) and high risk (score 2-3, n=56). This scoring system predicted evidence of GERD more robustly than any of the individual

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components alone (OR 2.31; 95% CI 1.50 - 10.06). Furthermore, it had high specificity (79.5%) and positive predictive value (70.0%) but limited sensitivity (50.0%) and negative predictive value (62.5%). The risk categories had similar rates of PPI usage at discharge (37.5% vs 50.0%, p = 0.263) and number of return ER visits and readmissions for chest pain (2.23±3.38 vs 2.17±2.87 respectively, p = 0.928). Interestingly, high risk patients on a PPI had a significantly lower number of return ER visits and readmissions when compared to those not on a PPI (Figure 2). Meanwhile in indeterminate risk individuals, PPI therapy did not affect repeat presentations for chest pain.

DISCUSSION
NCCP is a common clinical problem that is without a standardized, cost-effective and streamlined management algorithm. Our study established age greater than or equal to 65, past medical history of CAD and prior (+) EGD as independent predictors of objective evidence of GERD in NCCP patients. Using these three predictors we developed a scoring system to divide patients into indeterminate (score 0-1) or high risk (score 2-3) categories and proposed a NCCP management algorithm.

We identified age greater than or equal to 65 and prior (+) EGD as positive predictors of a (+) EGD in patients with NCCP. GERD and its complications (i.e. erosive esophagitis, Barrett esophagus and esophageal malignancy) are more common in the elderly so the presence of advanced age as a risk factor for GERD-related NCCP is not surprising. Furthermore, elderly patients often have atypical presentations of GERD and tend to reach advanced stages of disease before seeking treatment. However, increased cardiovascular risk is also associated with age, and patients should be thoroughly evaluated for cardiac etiology before GERD-related NCCP is considered as a cause. The discovery that prior (+) EGD is an independent predictor for GERD is novel but intuitive. Unlike the reflux symptoms of GERD, GERD-induced chest pain responds modestly to PPI therapy; therefore, patients are more likely to discontinue prescribed PPI therapy and not have resolution of their disease.

We also identified a history of CAD as a negative predictor. In this study, we used a negative stress test as evidence to lack of cardiac disease. One limitation of stress testing is that it may not be sensitive enough to detect some cardiac etiologies of chest pain (i.e. moderate luminal obstruction and vasospasm not resulting in ischemia). Patients with known history of CAD are at much higher risk of this inaccuracy. The use of the history of CAD as a negative predictor may not have held true if more sensitive diagnostic modalities, such as cardiac catheterization or coronary computed tomography angiography, were utilized. This again highlights the need for a thorough cardiac evaluation prior to GI work-up.

Using the above three independent clinical predictors we developed a scoring system which divides patients into indeterminate and high risk for objective GERD findings. Given the limited sensitivity and negative predictive value of this metric, an indeterminate score of 0-1 is not sufficient to exclude the possibility of GERD. Therefore, further work-up is indicated, including EGD. In contrast, high risk patients (score 2-3) are very likely to have objective evidence of GERD. PPI therapy was associated with a 63.8% decrease in repeat hospital admissions and therefore we recommend an empiric PPI trial for this population. EGD should be reserved for those with alarm features or poor treatment response. While this algorithm is promising, this study is retrospective and single-center with a relatively small sample size; therefore larger prospective multi-center studies are needed to confirm its efficacy.

Figure 2. High risk patients on PPI therapy have few repeat visits for chest pain.
Patients were stratified by risk category and PPI usage. High risk patients on a PPI had 62% fewer return emergency room visits and readmissions when compared to those not on a PPI. Meanwhile in indeterminate risk individuals, PPI therapy did not affect repeat presentations for chest pain.

PPI: proton pump inhibitor
studies are needed for validation. Once validated this algorithm will standardize the physician’s approach to NCCP and optimize EGD and PPI allocation.

References