



ESOPHAGEAL MANOMETRY COMBINED WITH PROTON PUMP INHIBITOR TEST APPLIED IN THE DIAGNOSIS OF NON-CARDIAC CHEST PAIN ASSOCIATED WITH GASTRO-ESOPHAGEAL REFLUX DISEASE.

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Abstract

Background: Esophageal manometry (EM) and proton pump inhibitor (PPI) tests are used to see how well they could diagnose GERD-related chest pain that are not caused by the heart diseases.

Methods: Randomly, 21 cases of GERD-related NCCP and 8 cases of non-GERD-related NCCP were assigned into two groups of total 29 patients with NCCP. General information, esophageal dynamic indices, and the diagnostic effectiveness of PPI in patients from various groups were observed and documented.

Results: The lower esophageal sphincter (LES) pressure at rest was found to be significantly lower in patients with non-cardiac chest pain (NCCP) caused by GERD than in patients with NCCP not caused by GERD. The mean LES resting pressure and mean residual pressure were also lower in the GERD-related NCCP group. Additionally, the maximum residual pressure was lower in the GERD-related NCCP group. These differences between the two groups were statistically significant, with a p-value less than 0.05. The PPI test yielded a sensitivity of 78.95%, a specificity of 83.33%, a positive predictive value (PPV) of 93.75%, and a negative predictive value (NPV) of 55.56% in relation to non-cardiac chest pain (NCCP) associated with gastro esophageal reflux disease (GERD).

Conclusion: In summary, the utilization of high-resolution esophageal manometry (EM) has demonstrated significant diagnostic utility in the context of non-cardiac chest pain (NCCP). The strategic use of antispasmodic medications has the potential to alleviate symptoms experienced by individuals with non-cardiac chest pain (NCCP) and enhance their overall quality of life (QOL). Also, the proton pump inhibitor (PPI) test is widely thought to be the best way to diagnose non-cardiac chest pain (NCCP) caused by gastro-esophageal reflux disease (GERD) in a clinical setting.

Keywords: high resolution esophageal manometry; proton pump inhibitor; non-cardiac chest pain; gastro esophageal reflux disease; diagnostic efficacy; antispasmodic drugs.

1. Introduction

Non-cardiogenic chest pain (NCCP) is a term for chest pain that is persistent and does not originate in the heart. It usually comes from the esophagus or is thought to be caused by the esophagus [1]. Chest discomfort symptoms may be present in cases of esophageal dyskinesia, including diffuse esophageal spasm and non-union, as described in the National Center for Complementary and Integrative Health (NCCIH) publication [2]. Esophageal motility abnormalities that are often seen in non-cardiac chest pain (NCCP) include esophageal clamps, non-specific esophageal motility disorders, LES hypoxia, widespread esophageal spasm, and atypical hyperplasia [3]. Gastro esophageal reflux disease (GERD) is identified as the predominant etiology for non-cardiac chest pain (NCCP), constituting a significant proportion of 40%-60 % among the overall patient's population [4]. According to the study conducted by T Frieling [5], individuals experiencing typical symptoms of reflux exhibit a greater prevalence of non-cardiac chest discomfort. According to a study, a notable proportion of individuals experiencing frequent heartburn (occurring at least once a week) were found to have non-cardiac chest pain syndrome (NCCPS), with a prevalence of 37%. In contrast, only 7.9 % of individuals without any symptoms of reflux were found to have NCCPS [6]. Gastro-esophageal reflux disease (GERD) is a prevalent medical condition characterized by the occurrence of heartburn and acid reflux as its most prominent symptoms. The typical gastrointestinal tract possesses a defensive mechanism primarily characterized by the presence of a sphincter located in the lower esophagus that contracts to prevent reflux, along with coordinated movements of the esophagus for evacuation. If these protective mechanisms sustain damage and experience impairment in their functionality, their capacity to provide protection will be diminished [7]. Lower esophageal sphincter dysfunction refers to a condition where the lower esophageal sphincter exhibits relaxation, leading to the reflux of stomach acid and bile into the esophagus. This occurrence heightens the vulnerability to potential harm. Additionally, there exist anomalous peristaltic contractions of the esophagus, with only a limited number exhibiting extrinsic mechanical compression [8]. When these different things work together, they might weaken the anti-reflux system. This could make the underlying damage worse and lead to the development of gastro-esophageal reflux disease (GERD). Under typical conditions, individuals may also experience gastro-esophageal reflux disease (GERD). However, this occurrence is classified as physiological reflux and does not elicit the symptoms commonly associated with acid reflux-induced heartburn [9]. In the event of an escalation in reflux and exacerbation of damage, individuals may experience typical symptoms of acid reflux-induced heartburn, necessitating the implementation of appropriate therapeutic interventions. Gastro-esophageal reflux disease (GERD) encompasses three distinct conditions: reflux esophagitis (RE),

non-erosive reflux disease (NERD), and Barrett's esophagus. It is worth noting that Barrett's esophagus has the potential to progress into a malignant state [10,11]. The proton pump inhibitor (PPI) is a pharmaceutical agent that effectively suppresses the production of gastric acid [12]. It is currently recognized as the most potent family of medications for suppressing stomach acid secretion. This therapeutic intervention is mostly employed for the management of peptic ulcers, gastritis, esophageal reflux, gastrointestinal hemorrhage, and various other medical conditions [13]. The class of medicines commonly used in clinical settings includes omeprazole, lansoprazole, pantoprazole, and esomeprazole [14,15]. The mechanism of action of these medications involves the inactivation of pump molecules, resulting in the inhibition of gastric acid secretion. Regardless of the underlying causes of excessive stomach acid secretion, pharmaceutical interventions have been shown to effectively reduce the release of gastric acid [16]. The measurement of esophageal pressure is employed to assess the motor function of the upper and lower esophageal sphincters, as well as the esophageal body. This is achieved by recording the baseline state of the esophagus and the subsequent pressure alterations in different regions following the act of swallowing, utilizing specialized equipment. This technique is primarily employed for the purpose of diagnosing esophageal dynamic abnormalities. Additionally, it can be utilized to aid in the diagnosis of systemic diseases that are accompanied by esophageal movement disorders such as scleroderma and dermatomyositis [17]. Furthermore, it can be employed to assess the impact of specific surgical procedures, such as esophageal dilatation for achalasia of the esophagus or diffuse esophageal spasm, lower esophageal sphincterotomy, or surgical fundoplication for reflux esophagitis [18]. Most of the research done in the past thought that finding erosive esophagitis with endoscopy or confirming pathological acid reflux with 24-hour esophageal pH monitoring was the best way to diagnose non-cardiac chest pain (NCCP) caused by gastro-esophageal reflux disease (GERD). These studies have subsequently assessed the efficacy of alternative diagnostic approaches in light of this gold standard. Nevertheless, it should be noted that this standard has certain limitations. According to prior research [20], one of the drawbacks is its inability to remove non-acid-related non-cardiac chest pain and its low sensitivity. Hence this study integrated esophageal manometry (EM) and proton pump inhibitor (PPI) trials to detect non-cardiac chest pain (NCCP) associated with gastro-esophageal reflux disease (GERD) and investigate its diagnostic effectiveness.

Consequently, it offers a valuable framework for the clinical diagnosis of this ailment.

2. Materials and Methods

2.1 Research subjects: A total of 29 individuals diagnosed with non-cardiac chest pain (NCCP) were chosen for this study. The sample consisted of 12 male and 17 female patients who were admitted to XX hospital between the years 20XX and 20XX. Among these patients, 19 had NCCP due to gastroesophageal reflux disease (GERD), while the remaining 6 had NCCP un-related to GERD. The experiment receive approval from the XXX medical ethics committee, and participants and their families were duly informed and provided their consent by signing the appropriate informed consent form. The inclusion criteria for the patients were as follows: Patients who did not have ischemic heart disease as confirmed by coronary angiography; patient whose electrocardiogram (ECG) did not indicate myocardial insufficiency; patients whose primary symptom was posterior sternal pain; patients with complete clinical data available; and patients who are 18 years of age or older. Patients with gastric and duodenal ulcers, which could be seen with an endoscope; patients with tumors in the upper digestive tract or a history of surgery of the upper digestive tract; pregnant or nursing woman; people who were addicted to drugs or had allergies to the experimental drugs; and people who could not finish the whole research protocol were not allowed to take part in the study.

2.2 Methods of research: The patients who underwent coronary angiography were systematically evaluated based on exclusion criteria and follow-up examination findings. Ultimately, a total of 29 subjects were selected for the study, comprising 21 individuals with GERD-related non-cardiac chest

pain (NCCP) and 8 individuals no-GERD-related NCCP. The clinical data of both patients' groups was subjective to statistical analysis. Within a period of 7 days following coronary angiography, gastrointestinal endoscopy was performed, along with simultaneous monitoring of esophageal pH and bile for duration of 24 hours. A preliminary evolution of symptoms was conducted over a period of 7 days before initiating treatment. This was followed by a 14 days of proton pump inhibitor (PPI) treatment, during which patients documented the intensity and frequency of chest pain and other symptoms on a daily basis using a journal card.

2.3 High- resolution esophageal manometry (EM) imaging: The Synectic's Digi trapper MKIII dynamic pH monitor and Synectic's PW esophageal reflux analysis software were utilized to monitor esophageal pH throughout a 24- hour period. The utilization of a single crystal antimony electrode was employed for the purpose of pH measurement. Prior to usage, the electrodes underwent calibration in pH 7.0 and pH 1.07 buffer solutions. It is recommended to refrain from consuming solid or liquid meals for a minimum of six hours prior to the examination to mitigate the risk of vomiting or aspiration, as well as to prevent the potential neutralization of gastric contents. It is recommended to discontinue the use of proton pump inhibitors (PPIs) after duration of 14 days and to cease the administration of motility medications after a period of 72 hours. The healthcare professional elucidates the process to the patient and secures their collaboration to alleviate worry and minimize discomfort during the intubation procedure. A catheter was introduced into the nasal cavity, and the electrodes were positioned using the pH gradient method and/ or esophageal manometry (EM) approach. The positioning of the esophageal pH electrode was performed at 5 centimeters above the upper boundary of the lower esophageal sphincter. Additionally, the reference electrode on the chest wall was securely affixed to the smooth surface of the thoracic area.

2.4 PPI test: It refers to a specific assessment or measurement tool used in academic or research settings. The medication in question was esomeprazole, specifically the brand NeXium, which is produced by Astrazeneca Pharmaceutical Co, Ltd. This company has its origins in Sweden, and the medication is Sub-packaged in Wuxi, China. The medication was administered orally, with a frequency of 2 times a day before the consumption of breakfast and dinner. The dosage for each administration was 40mg. The duration of the therapy regimen spanned a period of 14 days.

2.5 Indices of Observation: The collected data encompassed demographic variables such as gender, age, and body mass index (BMI) as well as clinical factors including the length of chest pain, presence of heartburn, acid reflux, heartburn combined with acid reflux, GERDQ score, and the rate of GERDQ diagnosis. The parameters used to measure esophageal dynamics were the lowest lower esophageal sphincter (LES) resting pressure (LRP), mean average residual pressure (RP), maximum RP, relaxation rate, average wave duration, and velocity at the front of contraction. The indices utilized for assessing the diagnostic effectiveness were sensitivity, specificity and positive predictive value (PPV). The formulae for calculating sensitivity, specificity, and positive predictive value (PPV) are denoted as formulae (1), (2) and (3) respectively. The variables A, TPR, TNR, TP, FP, TN, and FN represent accuracy, sensitivity, specificity, true positive, false positive, true negative, and false negative, respectively, within the context of the equations.

2.6 Statistical methodologies: The data was processed using SPSS 20.0 and the count data was represented as percentages for analysis using the X^2 test. A normality test was conducted on the measurement data. To depict the test results in a manner compatible with the normal distribution, the mean plus or minus the standard deviation was utilized, along with the t-test. In instances where the test results deviate from the normal distribution, the median (interquartile) was employed as a statistical measure, along with the t-test. A p-value less than 0.05 is indicative of a statistically significant difference.

3. Results

3.1 Overview of Data: Patients with GERD-related non-cardiac pain (NCCP) and those without GERD-related NCCP did not differ in terms of gender, age, body mass index (BMI), duration of chest pain, presence of heartburn, acid reflux, heartburn combined with acid reflux, GERD questionnaire (GERDQ) score, and rate of GERDQ diagnosis, with a p-value greater than 0.05. The information was presented in Table 1.

The calculation equations of sensitivity, specificity, and PPV were shown in Equations (1), (2), and (3), respectively. In the equations, A, TPR, TNR, TP, FP, TN, and FN referred to accuracy, sensitivity, specificity, true positive, false positive, true negative, and false negative respectively.

$$TPR = \frac{TP}{TP + FN} \quad (1)$$

$$TNR = \frac{TN}{TN + FP} \quad (2)$$

$$PPV = \frac{TP}{TP + FP} \quad (3)$$

Table 1: Comparison of general data of patients from the GERD-related and non-GERD-related NCCP groups

Index	GERD group (21 cases)	non-GERD group (8 cases)	t/x2	p
Gender				
Males	9 (43.11%)	3 (34.33%)	0.348	0.456
Females	12 (58.89%)	5 (67.67%)		
Age (years old)	58.63 ± 7.49	59.14 ± 7.81	0.076	0.935
BMI (kg/m ²)	22.54 ± 3.14	21.50 ± 3.26	1.421	0.083
Duration of chest pain (months)	31	20	0.874	0.411
Heartburn	9 (43.11%)	1	/	0.653
Acid reflux	12 (58.89%)	1	/	0.127
Heartburn + acid reflux	13 (74.6%)	2	/	0.623
GERDQ score	7.12 ± 2.45	6.38 ± 2.14	0.869	0.426
Diagnosis rate of GERDQ	17	2	/	0.947

3.2 A Comparative Analysis of Esophageal Dynamics in Gastroesophageal Reflux Disease (GERD) and Non-GERD-related Non-Cardiac Chest Pain (NCCP)

The study examined several parameters in patients with GERD-related NCCP, including the minimum LRP, mean KRP, mean RP, maximum RP, relaxation rate, mean wavelength, and contraction front velocity. These results showed that the minimum LRP was -2.31 ± 7.46 , the mean LRP was 5.30 ± 8.46 , the mean RP was 1.51 ± 4.55 , the maximum RP was 4.86 ± 5.32 , the relaxation rate was 82.16 ± 18.41 , the mean wave duration was 2.84 ± 0.53 and the contraction front velocity was 4.81 ± 1.28 . The study observed several parameters in patients with non-GERD-related non-cardiac chest pain (NCCP). These parameters included the minimum lower esophageal sphincter relaxation pressure (LRP). Mean LRP, mean residual pressure (RP), maximum RP, relaxation rate, mean wave duration, and contraction front velocity. The values obtained for these parameters were as follows: The minimum LRP was 0.09 ± 8.97 , the mean LRP was 9.47 ± 9.68 , the mean RP was 3.87 ± 4.58 , the maximum RP was 6.88 ± 5.46 , the relaxation rate was 73.95 ± 18.73 , the mean wave duration was

2.84 ± 0.51, and the contraction front velocity was 4.66 ± 1.14.

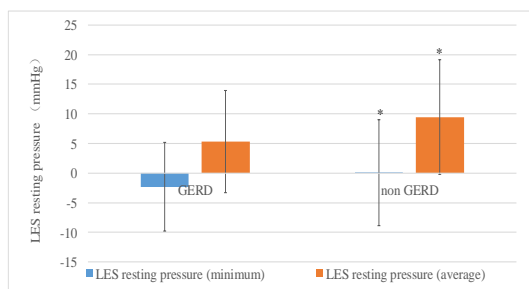


Figure. 1 Comparison of minimum LRP and mean LRP in GERD and non-GERD-related NCCP patients. Note: "*" indicated p<0.05 compared with the values of GERD-related NCCP patients.

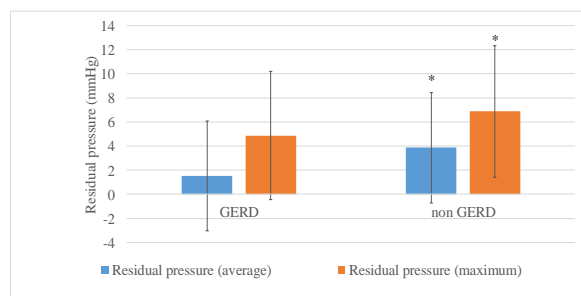


Figure. 2 Comparison of minimum RP and mean RP in GERD and non-GERD-related NCCP patients. Note: "*" indicated p<0.05 compared with the values of GERD-related NCCP patients.

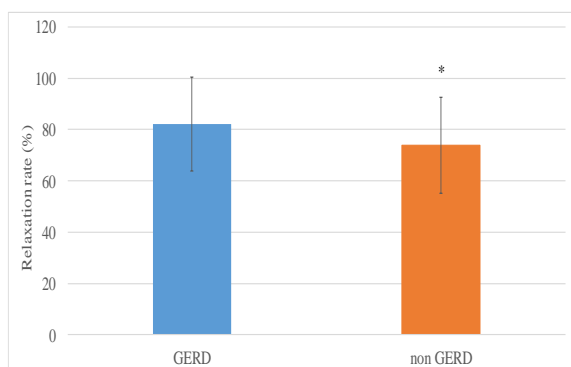


Figure. 3 Comparison of relaxation rate in GERD and non-GERD-related NCCP patients. Note: "*" indicated p<0.05 compared with the values of GERD-related NCCP patients.

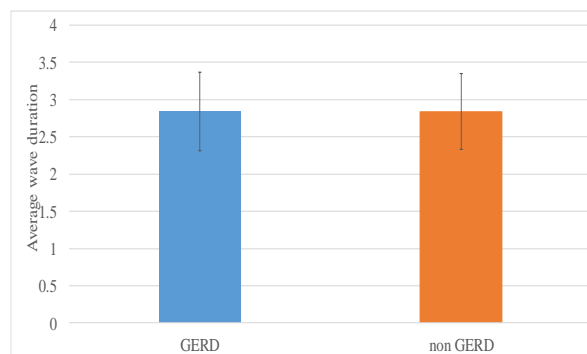


Figure. 4 Comparison of mean wave duration in GERD and non-GERD-related NCCP patients. Note: "*" indicated p<0.05 compared with the values of GERD-related NCCP patients.

The study found that patients with GERD-related non-cardiac chest pain (NCCP) had lower values for minimum lower esophageal sphincter relaxation pressure (LRP), mean LRP, mean residual pressure (RP), and maximum RP compared to patients with non-GERD-related NCCP. Additionally, the relaxation rate was higher in the GERD-related NCCP group. These observed differences between the two groups were statistically significant, with a p-value of less than 0.05. There were no significant variations found in the mean duration of waves or the velocity of the contraction front (p> 0.05). The specifics were illustrated in Figures 1 through 5.

Table 2: Comparison of diagnosis results of PPI test

GERD group	non-GERD group		Total
	Positive	Negative	
Positive	16	2	18
Negative	5	6	11
Total	21	8	29

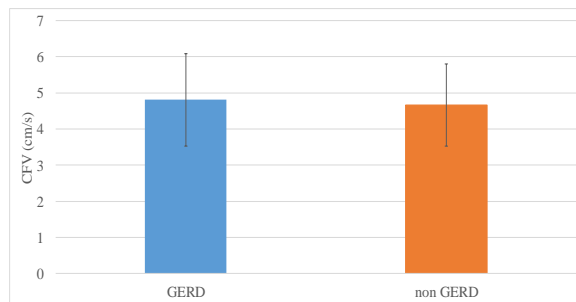


Figure. 5 Comparison of contraction front velocity in GERD and non-GERD-related NCCP patients. Note: "*" indicated $p < 0.05$ compared with the values of GERD-related NCCP patients.

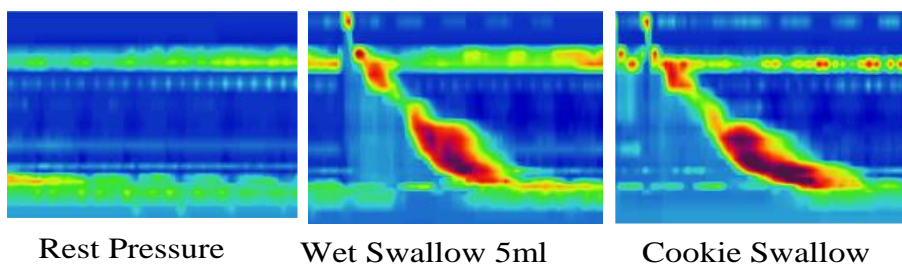


Figure. 6 The high-resolution dynamic image of the esophagus of patient 1.

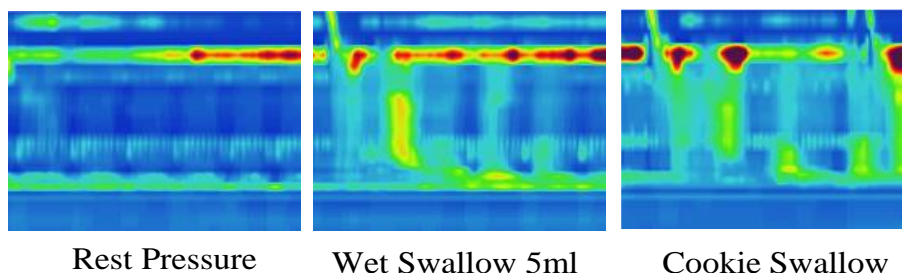


Figure. 7 The high-resolution dynamic image of esophagus of patient 2.

The PPI test also known as the Proton Pump Inhibitor test, is a widely used diagnostic and therapeutic tool in the field of gastrology. Out of the total sample size of 29 patients diagnosed with non-cardiac chest pain (NCCP), 21 cases (72%) were identified as NCCP associated with gastro-esophageal reflux disease (GERD). These cases met at least one of the following three criteria: (1) presence of erosive esophagitis (EE) and / or pathological acid reflux (pH++), (2) positive symptom index (SI+), or (3) pathological bile reflux +. Out of the total of 21 cases, 9 instances, which represent 42.8% of the sample, satisfied the established criteria (1) for GERD-related NCCPS, as per the conventional definition. Within the sample population, a solitary instance of erosive esophagitis (grade B) was identified, constituting 4.76% of the total cases. Notably, this case did not exhibit any pathological evidence of acid reflux. Additionally, one case of Barrett esophagus was pathologically confirmed, and it was accompanied by pathological evidence of acid reflux. A total of 11 cases were found to meet the criteria outlined in item (2), representing 52.38% of the total. A total of 14 cases met the criteria outlined in item (3) representing 66.66 % of the sample. A total of 8 cases satisfied both criteria concurrently, and 38.09% of the total. 19.04% of the total instances satisfied the three specified requirements, for a total of 4 cases meeting these conditions. A total of 16 patients diagnosed with GERD-related non-cardiac chest pain (NCCP) exhibited positive results on the proton pump inhibitor (PPI) test, representing 76.19% of the sample. Conversely, just two patients with non-GERD-related NCCP, comprising 25% of the sample, demonstrated positive results on the PPI test. The observed

distinction between the two groups was statistically significant at a significance level of $p < 0.05$. In proton pump inhibitor (PPI) testing, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of non-cardiac chest pain (NCCP) caused by gastro esophageal reflux disease (GERD) were found to be 76.19%, 75.00 %, 88.89% and 54.55% respectively. The specific information was presented in Table 2.

3.4 Illustrative Instances: Two common signs of hyper dynamic esophagus are non-cardiogenic chest pain and chest pain that does not come from the heart. This type of chest pain lasts for a long time and comes and goes. The presence of chest pain resulting from cardiopulmonary disease was ruled out through the utilization of pulmonary CT, ECG, myocardial enzyme spectrum, and coronary angiography. First, the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines were looked at. Then, a gastroscopy and a barium meal exam were done, but they did not show any major problems. Subsequently, a high- resolution esophageal manmetry test was contemplated. The individual was diagnosed with distal esophageal spasm, experiencing chest pain because of a hyperkinetic esophageal disorder. Subsequently they were administered the antispasmodic medication otilonium bromide by oral route. The patient experienced relief from chest pain due to improvements in esophageal spasm and reductions in visceral hypersensitivity. Figure 6 and 7 presented patient's high-resolution dynamic images depicting the esophagus.

Discussion

The term NCCP, or non-cardiac chest pain, is used to describe instances of chest pain that are not associated with coronary artery disease. Instead, these cases are attributed to various conditions such as lung illness, pleural disease, chest wall disease, intercostals nerve disease, esophageal disease, thoracic spinal cord disease, and upper abdominal disease [21]. The primary manifestation of this condition is the experience of pain in the chest, thoracic region, and underarm region. This pain may occasionally radiate to the shoulder and back, and it can be either intermittent or persistent in nature. The pain is characterized by sensations such as squeezing, burning, needling, chest tightness, and swelling. Notably there is no palpitation or difficulty breathing while sitting. Additionally, individuals may also experience a dry cough and fever [22]. Gastro-esophageal reflux disease (GERD) is a medical condition characterized by impaired esophageal closure following the passage of food from the esophagus to the stomach, resulting from a variety of underlying factors. Inadequate closure of esophagus can result in the regurgitation of food into the esophagus or oral cavity, leading to symptoms such as heartburn, acid reflux, coughing, and asthma. This condition, commonly known as GERD (gastro-esophageal reflux disease), is recognized in the medical field [23]. Gastro-esophageal reflux disease (GERD) is frequently observed in individuals who are obese or pregnant, as well as those who engage in long-term alcohol consumption, smoking and overeating. Additionally, the prevalence of GERD may progressively rise with advancing age [24]. Long term gastro-esophageal reflux disease (GERD) can cause burning and pain posterior to the sternum, frequently in conjunction with acid reflux, discomfort when swallowing, a sore throat, and various sensations experienced while eating. This phenomenon has the potential to impact the sleep quality, mental health, and emotional well-being of patients, thereby influencing their overall work performance and quality of life. Reflux has the potential to result in severe esophagitis, gastrointestinal bleeding, and potentially life-threatening consequences (25). Prolonged esophageal reflux can lead to the development of esophageal stenosis and may also increase the risk of cancer. Furthermore, reflux may manifest as symptoms beyond the digestive system, including a sore throat, cough and even asthma (26). Differentiating between gastro-esophageal reflux disease (GERD)- associated non-cardiac chest pain syndrome (NCCPS) and non-GERD-associated NCCPS poses a significant challenge. Previous research has commonly utilized endoscopy to identify erosive esophagitis and 24-hour pH monitoring to confirm pathological acid reflux as the primary criteria for diagnosis non-cardiac chest pain (NCCP) related to gastro esophageal reflux disease (GERD). Subsequently the value of alternative diagnostic approaches has been assessed in relation to this gold standard. However, it is important to

acknowledge that this diagnostic method possesses certain limitations [27]. This study was undertaken based on the aforementioned information. The results of this study show that patients with GERD-related NCCP had lower minimum LRP, mean LRP, mean RP, and maximum RP values than patients with NCCP that was not caused by GERD. The relaxation rate exhibited a statistically significant increase in patients with non-GERD-associated NCCP compared to those without this condition ($p < 0.05$). The LRP (lower esophageal sphincter relaxation pressure) has a significant influence on the incidence of gastro-esophageal reflux disease GERD [28]. This study provided evidence indicating that individuals with non-cardiac chest pain (NCCP) associated with gastro esophageal reflux disease (GERD) exhibited reduced esophageal motility compared to those with NCCP not associated with GERD. This finding further strengthens the diagnostic association between these two conditions. PPI therapy tests have been extensively employed in the clinical assessment of gastro-esophageal reflux disease (GERD) for a significant duration. The findings of a particular investigation demonstrated that the utilization of a 24-hour esophageal pH monitoring method effectively established pathological acid reflux as the benchmark norm. The test's sensitivity and specificity for diagnosing GERD were reported as 78% and 54%, respectively, according to reference [29]. In this study, 16 patients with non-cardiac chest pain (NCCP) caused by gastro-esophageal reflux disease (GERD) who tested positive for proton pump inhibitors (PPIs) made up 76.19% of the sample. Additionally, there were two patients with non-GERD-related NCCP, accounting for 25% of the sample. These findings demonstrate statistically significant differences with a p-value of less than 0.05. In the proton pump inhibitor (PPI) test, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of non-cardiac chest pain (NCCP) caused by gastro-esophageal reflux disease (GERD) were found to be 76.19%, 75.00%, 88.89% and 54.55%, respectively. The results of this study suggest that using esophageal manometry (EM) along with proton pump inhibitor (PPI) testing can help identify non-cardiac chest pain (NCCP) that is caused by gastro-esophageal reflux disease (GERD). Furthermore, the patients received oral administration of otilonium bromide, an antispasmodic medication. This intervention resulted in the amelioration of esophageal spasm as well as a reduction in visceral hypersensitivity, thereby alleviating the patient's chest pain.

Conclusion: The utilization of high-resolution esophageal manometry (EM) has demonstrated significant diagnostic utility in situations of non-cardiac chest pain (NCCP). The strategic administration of antispasmodic medications has the potential to mitigate symptoms and enhance the overall well-being of individuals. The PPI test has been widely utilized as the primary diagnostic method for GERD-associated non-cardiac chest pain (NCCP) in clinical settings. To address the limitations of this study, it is imperative to broaden the research scope in future studies. This expansion will serve as a crucial reference point for the clinical diagnosis of non-cardiac chest pain (NCCP) associated with gastro esophageal reflux disease (GERD).

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