



Original Article

Esophageal Manometry in Patients with Non-Cardiac Chest Pain

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ABSTRACT

Background: Non-cardiac chest pain is a heterogeneous syndrome in which gastroesophageal reflux, esophageal motor dysfunction, and functional mechanisms frequently overlap. Esophageal manometry can identify clinically actionable motor disorders, but the reported diagnostic spectrum varies according to referral patterns, equipment, testing protocol, and classification system.

Aim: To determine the overall spectrum and diagnostic yield of esophageal manometric abnormalities among adults with non-cardiac chest pain after negative cardiac evaluation.

Methods: This single-center cross-sectional study included 100 adults referred to a tertiary gastroenterology service after cardiac causes of chest pain had been excluded. Participants underwent clinical assessment, upper gastrointestinal endoscopy, and 16-channel water-perfused esophageal manometry; 24-hour pH monitoring was performed selectively. Manometric findings were reconstructed from the individual participant-level dataset. Categorical outcomes are reported as frequencies, percentages, and exact binomial 95% confidence intervals; continuous manometric variables are reported using mean, standard deviation, median, interquartile range, and range.

Results: The mean age was 46.97 ± 13.06 years, and 55% were male. An abnormal manometric finding was recorded in 69 patients (69.0%; 95% confidence interval, 59.0%-77.9%). The most frequent abnormality was an isolated hypotensive lower esophageal sphincter pattern in 38 patients (38.0%; 28.5%-48.3%), while 31 patients had normal manometry (31.0%; 22.1%-41.0%). Achalasia was identified in 15 patients: type I in 10, type II in two, and type III in three. Distal esophageal spasm, ineffective esophageal motility, and a legacy nutcracker-esophagus pattern were each recorded in five patients; hypercontractile esophagus was recorded in one. A motor disorder beyond isolated lower esophageal sphincter hypotension was present in 31 patients (31.0%; 22.1%-41.0%), and achalasia or a spastic/hypercontractile pattern was present in 26 (26.0%; 17.7%-35.7%).

Conclusions: Esophageal manometry demonstrated a broad spectrum of findings in adults with non-cardiac chest pain. Although any recorded abnormality was common, much of this yield consisted of isolated lower esophageal sphincter hypotension, which is not a stand-alone Chicago Classification version 4.0 diagnosis. Nevertheless, achalasia and spastic or hypercontractile patterns occurred in a clinically important minority. Standardized protocols, equipment- and posture-specific normative values, and contemporary diagnostic adjudication are essential when interpreting manometric yield.

Keywords: Achalasia; distal esophageal spasm; esophageal manometry; esophageal motility disorders; non-cardiac chest pain; water-perfused manometry.

INTRODUCTION

Non-cardiac chest pain (NCCP) is recurrent retrosternal pain that resembles ischemic cardiac pain but persists after an appropriate cardiac evaluation has excluded a cardiac cause [1-3]. The condition is common, frequently chronic, and associated with repeated healthcare use, impaired quality of life, work absenteeism, and continuing concern about occult heart disease despite a generally favorable cardiac prognosis [1-3]. Because cardiac and esophageal afferent pathways overlap, symptom characteristics alone often cannot reliably distinguish cardiac from esophageal pain.

The esophageal causes of NCCP include gastroesophageal reflux disease (GERD), major and minor esophageal motor disorders, reflux hypersensitivity, and functional chest pain [2-4]. Gastroesophageal reflux is the most frequent esophageal mechanism in many cohorts; however, manometry has a distinct role because it can identify achalasia, esophagogastric junction outflow obstruction (EGJO), distal esophageal spasm (DES), hypercontractile esophagus, absent contractility, and ineffective esophageal motility (IEM) [4-6]. These diagnoses can alter management by directing patients toward disease-specific medical, endoscopic, or surgical treatment rather than repeated empiric therapy.

High-resolution manometry and esophageal pressure topography have improved the standardization of motor diagnosis. Chicago Classification version 4.0 (CCv4.0) organizes disorders hierarchically into disorders of esophagogastric junction outflow and disorders of peristalsis, incorporates clinically relevant symptoms into selected diagnoses, and recommends assessment in both supine and upright positions with provocative maneuvers when appropriate [5-7]. It also emphasizes that diagnostic thresholds are system- and posture-dependent. These considerations are particularly important for water-perfused systems, for which locally validated normative values may differ from those derived using solid-state catheters [8].

The apparent “diagnostic yield” of manometry depends on how abnormalities are defined. An isolated low basal lower esophageal sphincter (LES) pressure may be clinically relevant to antireflux-barrier function but is not a stand-alone CCv4.0 motor diagnosis. Similarly, the term “nutcracker esophagus” belongs to an older classification framework and should not be equated automatically with contemporary hypercontractile esophagus without swallow-level re-adjudication [5-7]. Failure to distinguish physiological findings, legacy patterns, and formal motor disorders can inflate estimates of clinically actionable dysmotility.

Indian data describing the complete manometric spectrum in a cohort selected specifically for NCCP remain limited. Most regional studies have included mixed indications such as dysphagia, reflux symptoms, and preoperative assessment [9,10]. The present study therefore aimed to describe the overall distribution of manometric findings in 100 adults with NCCP referred after negative cardiac evaluation, quantify diagnostic yield with exact confidence intervals, and interpret the recorded findings within the context of contemporary classification.

Materials and Methods

Study design and setting

This was a single-center cross-sectional observational study conducted in the Department of Medical Gastroenterology, Gandhi Medical College and Gandhi Hospital, Secunderabad, Telangana, India. Participants were enrolled over 18 months, from July 2023 to January 2025. The manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [14].

Ethics

The Institutional Ethics Committee of Gandhi Medical College approved the study. Written informed consent was obtained from all participants before study procedures. The present analysis used de-identified participant-level records.

Participants

Adults aged 18 years or older were eligible when they had recurrent chest pain or chest discomfort and had been referred from Cardiology or General Medicine after cardiac chest pain was excluded. The cardiac evaluation specified in the study protocol included clinical assessment, 12-lead electrocardiography, two-dimensional echocardiography, and treadmill testing, with additional evaluation determined by the treating cardiology team. Exclusion criteria were age younger than 18 years, confirmed cardiac chest pain, a mechanical cause of dysphagia, and a postoperative state.

The planned study sample was 100 participants. All 100 participants in the individual-level study dataset were included in this analysis, and no records were excluded for missing manometric outcomes.

Clinical and adjunctive evaluation

Baseline variables included age, sex, heartburn, dysphagia, weight loss, and selected comorbidities. All participants underwent upper gastrointestinal endoscopy to evaluate mucosal and structural disease and to exclude a mechanical explanation for dysphagia. Complete blood picture, liver function tests, and renal function tests were recorded. Ambulatory 24-hour pH monitoring was performed when clinically indicated rather than systematically in the entire

cohort; consequently, pH results were reported descriptively and were not used to define the primary manometric outcome.

Esophageal manometry equipment and procedure

Esophageal manometry was performed after an overnight fast using a 16-channel water-perfused high-resolution manometry system (KangarooJeff, RMH Australia). Pressure acquisition and analysis were performed using Trace software, version 1.3.3 (G. S. Hebbard, Australia). The catheter was passed transnasally and positioned to record pressures from the hypopharynx through the esophageal body, LES, and proximal stomach. A standard sequence of ten 5-mL water swallows was recorded after baseline stabilization. Basal LES pressure, integrated relaxation pressure (IRP), distal contractile integral (DCI), and distal latency (DL) were documented for analysis.

Diagnostic framework and outcome definitions

The parent study stated that manometric interpretation used the Chicago Classification framework. Contemporary CCv4.0 criteria were used to contextualize the recorded diagnoses [5-7]. Achalasia was recorded as type I, II, or III. Distal esophageal spasm (DES), hypercontractile esophagus, and ineffective esophageal motility (IEM) were treated as disorders of peristalsis.

“Hypotensive LES” was retained as an isolated LES pressure pattern rather than treated as a formal CCv4.0 diagnosis. “Nutmacker esophagus” was retained explicitly as a legacy recorded pattern and was not automatically relabeled as hypercontractile esophagus. The primary outcome was the frequency and distribution of all recorded manometric patterns. Secondary descriptive outcomes were: (1) any recorded abnormality; (2) a motor disorder beyond isolated LES hypotension; and (3) achalasia or a spastic/hypercontractile pattern. This manuscript was restricted to descriptive phenotypic distribution and did not include symptom-prediction modeling.

Data validation and statistical analysis

All frequencies and summary statistics were recalculated directly from the individual participant-level table. Continuous variables were summarized as mean $\pm$ standard deviation, median with interquartile range, and minimum-maximum range. Categorical variables were summarized as number and percentage. Exact two-sided 95% confidence intervals for proportions were calculated using the Clopper-Pearson method. The proportion and its confidence interval were treated as the principal effect estimate.

No goodness-of-fit test was applied to the distribution of diagnoses because equal expected frequencies would have no clinical justification. Inferential comparisons of IRP, DCI, distal latency, or LES pressure across diagnostic categories were also deliberately avoided because those measurements contribute directly to the diagnoses, making such comparisons partly tautological. There were no missing values for the variables used in the primary analysis. Statistical analysis was performed using Python version 3.13.5 (Python Software Foundation, Wilmington, Delaware, United States), pandas version 2.2.3, SciPy version 1.17.0, and statsmodels version 0.14.6. All reported confidence intervals are two-sided.

RESULTS

All 100 participants had complete manometric diagnoses and were included. Their mean age was 46.97 ± 13.06 years, and 55 were male. Heartburn was present in 67%, dysphagia in 32%, and weight loss in 28%. Upper gastrointestinal endoscopy was normal in 62 patients, showed Los Angeles (LA) grade B-D reflux esophagitis in 25, and showed a dilated esophagus in 13. Ambulatory pH monitoring was performed in 43 participants and was positive in four (9.3% of those tested). The baseline clinical and adjunctive-test profile is summarized in Table 1.

Table 1. Baseline clinical characteristics and adjunctive diagnostic evaluation

Characteristic	Result
Age, years	46.97 $\pm$ 13.06; median 47 (interquartile range 36-58); range 18-73
Male	55 (55.0%)
Female	45 (45.0%)
Heartburn	67 (67.0%)
Dysphagia	32 (32.0%)
Weight loss	28 (28.0%)
Normal UGI endoscopy	62 (62.0%)

Characteristic	Result
LA - B esophagitis	4 (4.0%)
LA - C esophagitis	9 (9.0%)
LA - D esophagitis	12 (12.0%)
Dilated esophagus on endoscopy	13 (13.0%)
24-hour pH monitoring performed	43 (43.0%)
Positive pH monitoring among those tested	4/43 (9.3%)
Negative pH monitoring among those tested	39/43 (90.7%)

Values are mean $\pm$ standard deviation, median (interquartile range), range, number (percentage), or number/denominator (percentage), as specified. Los Angeles grade refers to the Los Angeles classification of reflux esophagitis. Percentages for pH-monitoring results among those tested use 43 as the denominator. UGI: upper gastrointestinal, LA: Los Angeles

The overall mean basal LES pressure was 23.32 ± 10.23 mmHg, mean IRP was 16.09 ± 12.93 mmHg, mean DCI was 3731.02 ± 2310.58 mmHg·s·cm, and mean distal latency was 5.04 ± 1.04 seconds. Because the distributions were broad and included disease-specific extremes, medians, interquartile ranges, and full ranges are also provided in Table 2.

Table 2. Distribution of recorded esophageal manometric variables

Manometric variable	Mean $\pm$ standard deviation	Median (interquartile range)	Range
LESP, mmHg	23.32 ± 10.23	28 (17-30)	5-35
IRP, mmHg	16.09 ± 12.93	12 (10-13)	7-58
DCI, mmHg·s·cm	3731.02 ± 2310.58	4050 (3075-4900)	40-12,000
DL, seconds	5.04 ± 1.04	5.10 (4.78-5.70)	1.9-6.9

All variables were available for 100 participants. LESP: Basal lower esophageal sphincter pressure, IRP: Integrated relaxation pressure, DCI: Distal contractile integral, DL: Distal latency

An abnormal manometric finding was recorded in 69 patients (69.0%; exact 95% confidence interval [CI], 59.0%-77.9%), while 31 had normal manometry (31.0%; 95% CI, 22.1%-41.0%). The most frequent abnormality was an isolated hypotensive LES pattern, recorded in 38 patients (38.0%; 95% CI, 28.5%-48.3%). The detailed distribution of individual recorded patterns is presented in Table 3.

Achalasia was recorded in 15 patients (15.0%; 95% CI, 8.6%-23.5%). Among patients with achalasia, type I accounted for 10 of 15 (66.7%), type II for two of 15 (13.3%), and type III for three of 15 (20.0%). Distal esophageal spasm, ineffective esophageal motility, and a legacy nutcracker-esophagus pattern were each recorded in five patients; hypercontractile esophagus was recorded in one.

Table 3. Detailed spectrum of recorded esophageal manometric patterns

Recorded manometric pattern	Number	Percentage	Exact 95% confidence interval	Contemporary interpretive context
Normal manometry	31	31.0%	22.1%-41.0%	No motor abnormality recorded
Isolated hypotensive LES	38	38.0%	28.5%-48.3%	LES pressure finding; not a stand-alone CCv4.0 diagnosis
Achalasia type I	10	10.0%	4.9%-17.6%	Major esophagogastric junction outflow disorder
Achalasia type II	2	2.0%	0.2%-7.0%	Major esophagogastric junction outflow disorder

Recorded manometric pattern	Number	Percentage	Exact 95% confidence interval	Contemporary interpretive context
Achalasia type III	3	3.0%	0.6%-8.5%	Major spastic esophagogastric junction outflow disorder
DES	5	5.0%	1.6%-11.3%	Disorder of peristalsis
IEM	5	5.0%	1.6%-11.3%	Hypomotility disorder of peristalsis
Nutcracker esophagus	5	5.0%	1.6%-11.3%	Legacy pattern; not automatically equivalent to CCv4.0 hypercontractile esophagus
Hypercontractile esophagus	1	1.0%	0.0%-5.4%	Disorder of peristalsis

Confidence intervals are exact two-sided Clopper-Pearson 95% confidence intervals. CCv4.0 indicates Chicago Classification version 4.0; The legacy nutcracker category was retained exactly as recorded because swallow-level tracings were unavailable for contemporary re-adjudication. LES: lower esophageal sphincter, DES: Distal esophageal spasm, IEM: Ineffective esophageal motility

When isolated LES hypotension was separated from formal or legacy motor diagnoses, 31 patients had a motor disorder beyond isolated LES hypotension (31.0%; 95% CI, 22.1%-41.0%). Achalasia or a spastic/hypercontractile pattern was recorded in 26 patients (26.0%; 95% CI, 17.7%-35.7%). The clinically interpretable grouped diagnostic yields are shown in Table 4.

Table 4. Clinically interpretable grouped diagnostic yield

Grouped outcome	Number	Percentage	Exact 95% confidence interval	Clinical interpretation
Any recorded manometric abnormality	69	69.0%	59.0%-77.9%	Includes isolated hypotensive LES and all recorded motor disorders
Isolated hypotensive LES pattern	38	38.0%	28.5%-48.3%	Physiological LES pressure abnormality; not a formal stand-alone CCv4.0 diagnosis
Motor disorder beyond isolated LES hypotension	31	31.0%	22.1%-41.0%	Achalasia, spastic/hypercontractile patterns, or ineffective esophageal motility
Achalasia	15	15.0%	8.6%-23.5%	Types I-III combined
Spastic or hypercontractile pattern	11	11.0%	5.6%-18.8%	Distal esophageal spasm, legacy nutcracker pattern, or hypercontractile esophagus
Achalasia or spastic/hypercontractile pattern	26	26.0%	17.7%-35.7%	Potentially treatment-relevant major or spastic motor physiology
Ineffective esophageal motility	5	5.0%	1.6%-11.3%	Recorded hypomotility disorder

Rows are intentionally overlapping and should not be added together. Confidence intervals are exact two-sided Clopper-Pearson 95% confidence intervals. LES indicates lower esophageal sphincter.

DISCUSSION

This NCCP-focused cohort demonstrated a broad manometric spectrum. A recorded abnormality was present in 69% of participants, but the composition of that yield is more informative than the headline percentage: 38% had an isolated hypotensive LES pattern, 31% had a motor disorder beyond isolated LES hypotension, and 26% had achalasia or a spastic/hypercontractile pattern. Thus, the study supports a meaningful role for esophageal manometry after negative cardiac evaluation while also illustrating why all abnormal pressure findings should not be presented as equally actionable diagnoses.

The predominance of isolated hypotensive LES requires careful interpretation. Basal LES pressure can contribute to assessment of the antireflux barrier, but CCv4.0 does not recognize “hypotensive LES” as an independent motor disorder [5-7]. Moreover, manometry alone cannot establish gastroesophageal reflux disease; contemporary reflux frameworks rely on endoscopic evidence and/or ambulatory reflux monitoring when objective confirmation is needed [4,15,16]. Accordingly, the 69% overall abnormality rate should not be interpreted as a 69% prevalence of formal esophageal motility disorders. The more conservative estimate of a motor disorder beyond isolated LES hypotension was 31%.

Achalasia was the most important major disorder and was found in 15% of the full cohort. Type I predominated, followed by type III and type II. This proportion is high for a general NCCP population and probably reflects tertiary referral and the inclusion of patients with associated dysphagia or weight loss. Achalasia can produce chest pain through impaired esophageal emptying, distension, pressurization, and spastic activity, and chest pain may precede or coexist with prominent dysphagia. Identification is clinically important because subtype influences therapeutic planning and expected response to pneumatic dilation, laparoscopic Heller myotomy, or peroral endoscopic myotomy [5,6].

Spastic or hypercontractile patterns accounted for 11% when distal esophageal spasm, the legacy nutcracker category, and hypercontractile esophagus were considered together. CCv4.0 requires clinically relevant symptoms for distal esophageal spasm and hypercontractile esophagus and uses stricter swallow-level criteria than older schemes [5-7]. The five records labelled “nutcracker esophagus” therefore cannot be assumed to represent contemporary hypercontractile esophagus. Retaining the original label, rather than retrospectively converting it from a single summary DCI value, avoids diagnostic overstatement.

The observed spectrum differs from several modern cohorts. In an Indian study of patients referred for mixed indications, Goyal and colleagues found a broad distribution dominated by achalasia and ineffective motility, highlighting the influence of referral indication [9]. Assadian and colleagues likewise reported a high prevalence of achalasia in a specialist manometry population rather than an NCCP-only cohort [10]. In a 2025 NCCP series from Abu Dhabi, normal motility was reported in approximately 45% and ineffective esophageal motility was the most frequent abnormality, while achalasia and esophagogastric junction outflow obstruction were uncommon [11]. Differences in case selection, sex distribution, classification version, catheter system, posture, and inclusion of isolated LES findings can plausibly explain much of the between-study variability.

Ineffective esophageal motility was recorded in 5% of this cohort, lower than in several recent series [10,11]. CCv4.0 uses more stringent criteria for ineffective esophageal motility than earlier classification versions, requiring more than 70% ineffective swallows or at least 50% failed peristalsis for a conclusive diagnosis [5,6]. Because the complete swallow-level data were unavailable, it was not possible to determine whether every recorded case would remain conclusive under CCv4.0. Conversely, additional borderline cases might have been categorized differently if contractile reserve had been assessed with multiple rapid swallows.

Normal manometry in 31% of patients does not imply that the chest pain was unexplained or non-esophageal. Standard short-duration manometry is designed primarily to classify motor function and does not exclude gastroesophageal reflux, reflux hypersensitivity, functional chest pain, or intermittent motor events. In the present cohort, pH monitoring was selective and positive in four of 43 tested patients, so the study cannot estimate the prevalence of reflux-mediated NCCP. Barret and colleagues showed that ambulatory pH-impedance and prolonged manometry can identify mechanisms not captured by standard HRM [12]. More recent 24-hour high-resolution manometry data suggest that prolonged recording may markedly increase detection of intermittent spastic or hypercontractile events, although the clinical consequences of this additional yield require further study [13].

Technical standardization is central to interpretation. CCv4.0 recommends a structured protocol incorporating supine and upright swallows and provocative maneuvers, and it emphasizes the need for catheter- and posture-specific normative values [5-8]. Water-perfused systems are clinically valuable and more accessible in many resource-limited settings, but metrics should not be interpreted using uncritical extrapolation from solid-state systems. Indian normative work with a 16-channel water-perfused system has demonstrated clinically relevant postural differences in IRP, DCI, and distal latency [8].

The clinical implication is not that every patient with NCCP requires manometry immediately. Cardiac disease must first be excluded, and endoscopy and reflux evaluation should be selected according to symptoms, alarm features, and pre-test probability [2-4,15,16]. Manometry is especially important when dysphagia or another obstructive symptom persists after mechanical disease has been excluded, before invasive antireflux therapy, and when chest pain remains unexplained after appropriate reflux assessment [4]. In this cohort, one in four patients had achalasia or a spastic/hypercontractile pattern, supporting a low threshold for physiologic testing in appropriately selected tertiary-care referrals.

The principal strengths of this study are its NCCP-specific design, complete manometric outcome data for 100 participants, reconstruction of results from individual-level records rather than reliance on aggregate tables, and reporting of exact confidence intervals. The analysis also distinguishes an isolated LES pressure finding from formal or legacy motor disorders, providing a more clinically honest estimate of diagnostic yield.

Limitations

1. Study was conducted at a single tertiary referral center, and selection and spectrum bias probably increased the prevalence of achalasia and other major disorders relative to unselected NCCP populations.
2. The study used the final diagnoses recorded in the parent dataset. Original swallow-level pressure topography plots were unavailable for blinded re-adjudication, and the recorded labels could not be reassessed fully under CCv4.0. This is particularly important for “hypotensive LES,” “nutcracker esophagus,” ineffective esophageal motility, and clinically relevant spastic disorders.
3. The archived dataset did not preserve the application of provocative maneuvers for each study. These omissions limit reproducibility and prevent confirmation that the complete CCv4.0 protocol was followed.
4. Ambulatory reflux monitoring was performed selectively in 43% of participants, and pH-impedance monitoring was not systematically available. The study therefore cannot determine the proportion of NCCP attributable to acid reflux, non-acid reflux, reflux hypersensitivity, or functional chest pain.
5. Symptom severity, duration, temporal correlation between chest pain and motor events, validated quality-of-life measures, psychological comorbidity, treatment, and longitudinal outcomes were not captured consistently. The findings describe the manometric spectrum but do not establish that every recorded abnormality caused the presenting chest pain.

CONCLUSIONS

In this tertiary-care cohort of adults with NCCP after negative cardiac evaluation, esophageal manometry identified a wide range of abnormalities. Any recorded abnormality was present in 69%, but 38% of the cohort had an isolated hypotensive LES pattern rather than a formal CCv4.0 motor diagnosis. A motor disorder beyond isolated LES hypotension was present in 31%, and achalasia or a spastic/hypercontractile pattern was present in 26%. These findings support manometry as an important component of targeted NCCP evaluation while emphasizing that diagnostic yield must be interpreted according to contemporary definitions, standardized acquisition protocols, and equipment- and posture-specific normative values.

Declarations

Ethics approval and consent to participate: The study was approved by the Institutional Ethics Committee of Gandhi Medical College. Written informed consent was obtained from all participants.

Consent for publication: Not applicable; no identifiable individual patient information is presented.

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