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Original Article

Ineffective Motility Revisited Through High-Resolution Manometry After Chicago Classification v4.0

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ABSTRACT

Objectives: "Ineffective motility" (IM) is a motility disorder characterised by weakened and uncoordinated muscle contractions in the oesophagus, leading to regurgitation and swallowing difficulties. This study aims to redefine cases previously labelled as IM using CCv3.0 and redefine such cases in high-resolution manometry (HRM) in CCv4.0.

Material and Methods: A retrospective study on 366 dysphagia patients was conducted at Holy Family Hospital, Rawalpindi, Pakistan, from December 2015 to October 2023. Based on CCv3.0, 71 cases were evaluated. They were reanalysed using Solar™ GI HRM, Laborie, to compare with CCv4.0. Analysis was performed using statistical package for the social sciences (SPSS) 25.0.

Results: Upon re-evaluation using CCv4.0, 90% of initially identified IM cases remained, reducing the estimated prevalence from 19.4% to 17.5%. Mean LES pressure and mean IRP were inversely correlated with the percentage of absent swallows. In contrast, mean IRP showed a positive correlation with the rate of ineffective contractions. Demographics and baseline characteristics showed no significant differences between the two groups.

Conclusion: This study strongly supports the efficacy of CCv4.0 in better categorising IM once deemed minor. It calls for prospective research focusing on clinical endpoints and diagnostic criteria refinement. The diverse IM spectrum suggests further studies for subgroup classification enhancement.

Keywords: Chicago classification v3.0, Chicago classification v4.0, Ineffective motility, Motility diseases, Pakistan

INTRODUCTION

Ineffective Motility (IM), also known as "Ineffective Esophageal Motility (IEM)," "ineffective motility disorder," or "non-obstructive dysphagia," is a condition where oesophageal muscles lose their ability to contract correctly and are often weak and uncoordinated.[1] IEM can be diagnostically assessed by high-resolution oesophageal manometry (HRM) to evaluate these abnormalities. HRM is considered a particular and sensitive test for diagnosing oesophageal motility disorders like achalasia, oesophageal spasm, gastroesophageal reflux disorder (GERD), etc., holding some advantages over other diagnostic tests like barium swallow and endoscopy as it can identify additional abnormalities that are not well assessed by conventional diagnostic tests.[2] While prevalence or data estimates of patients undergoing HRM are not well established, considering that it is specifically reserved for patients with suspected or known oesophageal disorders that are relatively uncommon and affect a small proportion of the population, literature shows high prevalence among specific populations.[2,3]

With the latest advancements, the definition of HRM has progressed well, while the Chicago classification system in which Chicago classification version 3.0 (CCv3.0) remains the standardised update for categorising and diagnosing motility disorders of the oesophagus based on HRM findings. It divides motility disorders into four groups: Esophagogastric junction (EGJ) relaxation disorders (achalasia and EGJ outflow obstruction), major disorders (absent contractility, hypercontractile oesophagus & distal oesophageal spasm), minor disorders (IEM and fragmented peristalsis), & normal.[4] CCv3.0 suggested that patients were susceptible to IEM when around 50% of swallows were non-effective. It also recommended distal contractile integral (DCI) to be <450 mm-Hg-sec-cm^{-1} with normal integrated relaxation pressure (IRP)[5] but failed to give evidence of esophagogastric junction outflow obstruction (EGJOO). While with overlapping

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similarities between EGJOO and IEM, CCv3.0 was non-significant in differentiating IEM from motility disorders, and questions to the context were raised related to inadequacies leading to the establishment of more advanced criteria, i.e., CCv4.0 that tells 70% ineffective swallows (DCI ≥100 mm-Hg-sec-cm^{-1} and <450 mm-Hg-sec-cm^{-1}) or at least 50% failed peristalsis (DCI <100 mm-Hg-sec-cm^{-1}) to diagnose better and differentiate IEM.[6] Also, the CCv4.0 has divided motility disorders into three groups, i.e., EGJ disorders (achalasia and EGJ outflow obstruction), peristaltic disorders (absent contractility, hypercontractile oesophagus, distal oesophageal spasm, and IEM), & normal.[7]

As in CCv3.0, over 50% of ineffective swallows were the cut-off mark for IEM and considered a minor disorder. Nevertheless, with the advent of CCv4.0, IEM is no longer reflected as a minor motility disorder; instead, with a more stringent definition, there is no possibility for minor disorders in the proposed new classification system. If a patient fulfils the criteria of > 70% ineffective or >50% absent swallows, they will be considered as having a significant motility disorder. Moreover, CCv4.0 also incorporates the large peristaltic beaks of >5 cm in an otherwise strong peristaltic wave with a DCI of > 450 mm-Hg-sec-cm^{-1}. For this purpose, we aim to differentiate the practicality of CCv3.0 and CCv4.0 to assess, in a real-world setting, how many patients may be eliminated from the category of IEM once they are evaluated considering CCv4.0. The study also redefines patients previously labelled as IEM in terms of their primary and secondary (additional) diagnosis based on CCv4.0.

MATERIAL AND METHODS

A retrospective study with all patients presented with dysphagia with normal upper GI endoscopies at the Centre for Liver and Digestive Diseases, Holy Family Hospital, Rawalpindi, from December 2015 to October 2023 was conducted. Patients were identified from the health records by searching for "oesophageal manometry." Duplicate records were deleted. Utilizing the SolarTM GI HRM, Laborie manometry studies were evaluated for the percentage of weak and failed contractions. DCI values between 100 and 449 mm-Hg-sec-cm-1 were used to define weak contractions, while DCI values below 100 mm-Hg-sec-cm-1 were used to describe failed contractions. Weak and unsuccessful contractions add up to ineffective contractions. The lower oesophageal sphincter (LES) pressure, IRP, and intrabolus pressure were additional manometric variables examined. A thorough manual review of the charts of all recognised manometries was conducted to determine the reading physician's diagnosis for each identified manometry. The following criteria were used to ensure that all probable and possible cases of IEM were identified: the interpreting physician had to have diagnosed IEM, and at least 50% of the swallows had to be weak (DCI 450 mm-Hg-sec-cm-1) in the absence of any other oesophageal disorders. Age, gender, body mass index (BMI), and Eckardt score[8] were baseline characteristics. The HRM results were re-analysed per Chicago classification v4.0 to compare the two classification systems.

According to the mean distribution of the data, continuous data were reported as mean ± standard deviation (SD) and compared using a 2-tailed Student's t-test. Chi-squared was used for comparison when categorical data were presented as frequencies (proportions). When necessary, nonparametric Wilcoxon rank-sum tests and parametric two-sample t-tests, or Fisher exact tests, were used to compare the two groups statistically. P-values and Spearman correlation coefficients (r) were reported for all groups to examine the bivariate associations between quantitative measures. Curve estimation, which applied a linear regression model, was also assessed to find the associations. $P \leq 0.05$ was used to determine whether a statistical difference was significant or not. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 25.0 (SPSS Inc, IBM, USA).

RESULTS

A total of 366 HRMs were reviewed for potential IEM cases, from which 71 confirmed cases were identified and included in the study, according to CCv3.0. These 71 cases were re-analysed through CCv4.0, and 64 cases remain IEM by CCv4.0 criteria [Figure 1], with no case fulfilling the requirements of inconclusive IEM.

Out of 71 patients diagnosed with IEM as per the CCv3.0 protocol, 57 (80.3%) showed concordance for the diagnosis of IEM for CCv3.0 as well as v4.0 [Figure 2], whereas 7 (9.9%) patients no longer qualified for the IEM criteria as per CCv4.0 and hence were not considered motility disorders.

Table 1 categorises the demographics intended for patients from CCv3.0 and CCv4.0, including age, gender, and average BMI, which did not vary significantly. There was no statistically significant change in the Eckardt score, a combined score for dysphagia, retrosternal discomfort regurgitation, and weight loss, which is greater than 5, suggesting a patient with a motility disorder.

Regarding manometric findings, both groups had similar IRP, LES pressure, and bolus clearance measurements, as shown in Table 2. A statistically significant difference was observed for weak and ineffective contractions between the two groups, with no comparison between absent contractions of the two. As expected, based on the definition, DCI was lower in the CCv4.0 than in the CCv3.0.

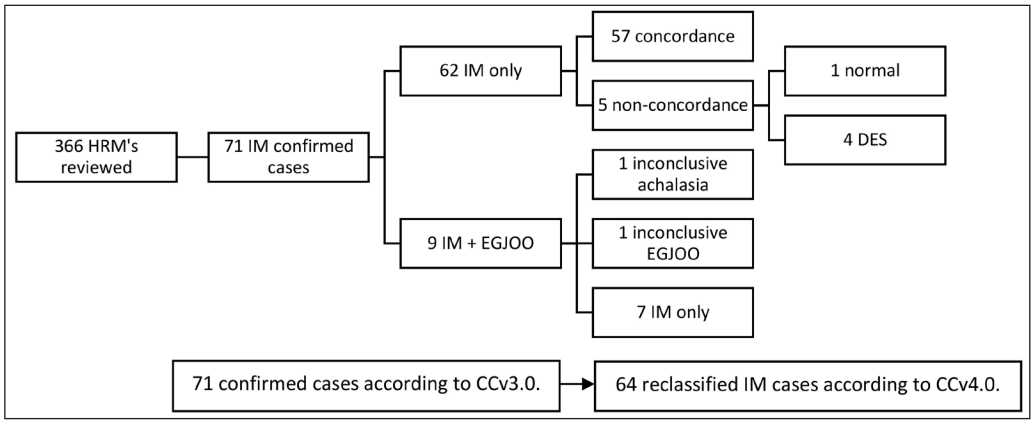

Figure 1: Flowchart demonstrating patients with IM according to Chicago Classification version 3.0 and 4.0; HRM: High-resolution manometry, IM: Ineffective motility, EGJOO: Esophagogastric junction outflow obstruction, DES: Distal esophageal spasm, CCv4.0: Chicago classification verison 4.0.

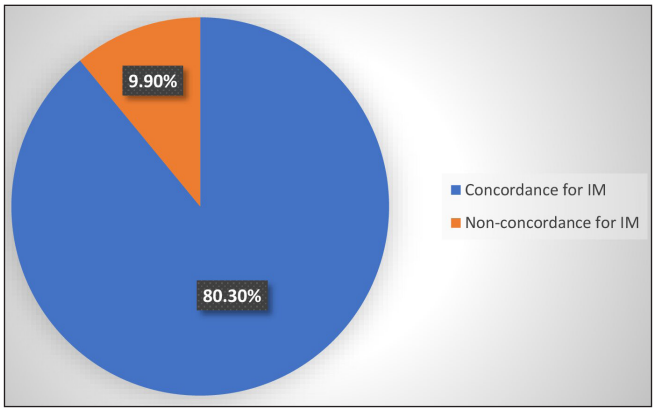

Figure 2: Frequency distribution of concordance of diagnosis according to criteria fulfilled for IM as per CCv4.0; IM: Ineffective motility, CCv4.0: Chicago classification verison 4.0.

Table 1: Baseline clinical characteristics

	CCv3.0 IM (n=71)	CCv4.0 IM (n=64)	P-value
Age (y), mean±SD	40.55 ± 17.60	40.69 ± 18.01	0.31
Gender (male), n (%)	28 (41.8)	26 (40.6)	0.801
Duration of Dysphagia (months), mean±SD	24.25 ± 40.091	25.11 ± 39.01	0.263
BMI (kg/m^2), mean±SD	21.61 ± 2.9	22.10 ± 2.8	0.529
Eckardt Score, mean±SD	5.94 ± 2.56	5.60 ± 2.47	0.4108

BMI, Body mass index, IM: Ineffective motility, CCv3.0: Chicago classification verison 3.0, CCv4.0: Chicago classification verison 4.0, SD: Standard deviation; Data are presented as mean ± SD or n (%).

Table 2: Average manometric findings among CCv3.0 and CCv4.0 patients for IM

Average manometric findings (mean ± SD)	CCv3.0 IM (n=71)	CCv4.0 IM (n=64)	P-value
Absent contractions (%)	36.27 ± 16.05%	41.26 ± 12.88%	0.552
Weak contractions (%)	43.21 ± 21.36%	67.3 ± 14.97%	<0.001*
Ineffective contractions (%)	72.46 ± 14.21%	87.75 ± 11.53%	0.018*
LES Pressure (mmHg)	18.19 ± 9.18	15.27 ± 9.64	0.621
IRP (mmHg)	10.04 ± 4.22	9.41 ± 3.74	0.338
DCI (mm-Hg-sec-cm^{-1})	375 ± 84.101	252.5 ± 91	0.04*
Swallows followed by cleared bolus (%)	16.34 ± 9.83 %	11.25 ± 8.77 %	0.864

*Significant as p ≤ 0.05
LES: Lower oesophageal sphincter, IRP: Integrated relaxation pressure, DCI: Distal contractile integral, IM: Ineffective motility, CCv3.0: Chicago classification version 3.0, CCv4.0: Chicago classification version 4.0, SD: Standard deviation; Data are presented as mean ± SD or n (%).

In the CCv4.0 group, there was no statistically significant variation between the mean LES pressure and the percentage of failed or absent swallows (DCI > 100 mm-Hg-sec-cm-1) (r = -0.108, p = 0.01) [Table 3]. Between CCv3.0 and CCv4.0, no additional associations were found in any additional contraction group in any observed IEM patients as illustrated in Figures 3a-3f. The IRP metric evaluates how well the LES has relaxed at the oesophagogastric junction. In both the CCv3.0 and CCv4.0 groups, the mean IRP was positively associated with the percentage of ineffective contractions with values such as r = 0.061 and p = 0.026 [Table 3] and r = 0.035, p = 0.04 [Table 3]. In the CCv3.0 group, the mean IRP was negatively correlated with the percentage of failed

Table 3: Correlation of mean LES pressure and mean IRP with percent of absent, weak, and ineffective contractions among CCv4.0 and CCv3.0 patients for IM

	CCv3.0 IM (n=71)	CCv4.0 IM (n=64)
Mean LES Pressure		
Absent contractions (%)	r = -0.026, p = 0.11	r = -0.108, p = 0.01*
Weak contractions (%)	r = 0.04, p = 0.387	r = 0.012, p = 0.534
Ineffective contractions (%)	r = -0.117, p = 0.971	r = -0.013, p = 0.703
Mean IRP		
Absent contractions (%)	r = -0.47, p = 0.041*	r = -0.17, p = 0.28
Weak contractions (%)	r = 0.15, p = 0.924	r = -0.041, p = 0.65
Ineffective contractions (%)	r = 0.061, p = 0.026*	r = 0.035, p = 0.04*

*Significant as p ≤ 0.05
CCv3.0: Chicago classification version 3.0, CCv4.0: Chicago classification version 4.0, LES: Lower oesophageal sphincter, IRP: Integrated relaxation pressure, IM: Ineffective motility.

contractions (r = -0.47, p = 0.041; [Table 3]), but not in the CCv4.0 group. A complete picture can be observed in Figures 4a-4f.

DISCUSSION

Ineffective motility of the oesophageal body is a diverse motility disorder that can occur in asymptomatic healthy people and is not always accompanied by symptoms or any gastrointestinal disorder.[4] As in CCv3.0, IEM is a minor motility disorder that only requires 50% unsuccessful swallows; however, with CCv4.0, the distinction between significant and minor motility disorders has been eliminated, and IEM is now classified as an oesophageal peristalsis disorder that requires >70% unsuccessful swallows or at least 50% failed swallows.[1,9] For this reason, we have studied how many patients may be eliminated from the category of ineffective motility once they are assessed in light of CCv4.0.

The main findings of this study are that when 71 patients being diagnosed confirmed as having IEM according to CCv3.0 were re-analysed on CCv4.0, only 64 patients who met the criterion of IEM and retained the same diagnosis. According to CCv4.0 criteria, the remaining cases would not qualify for

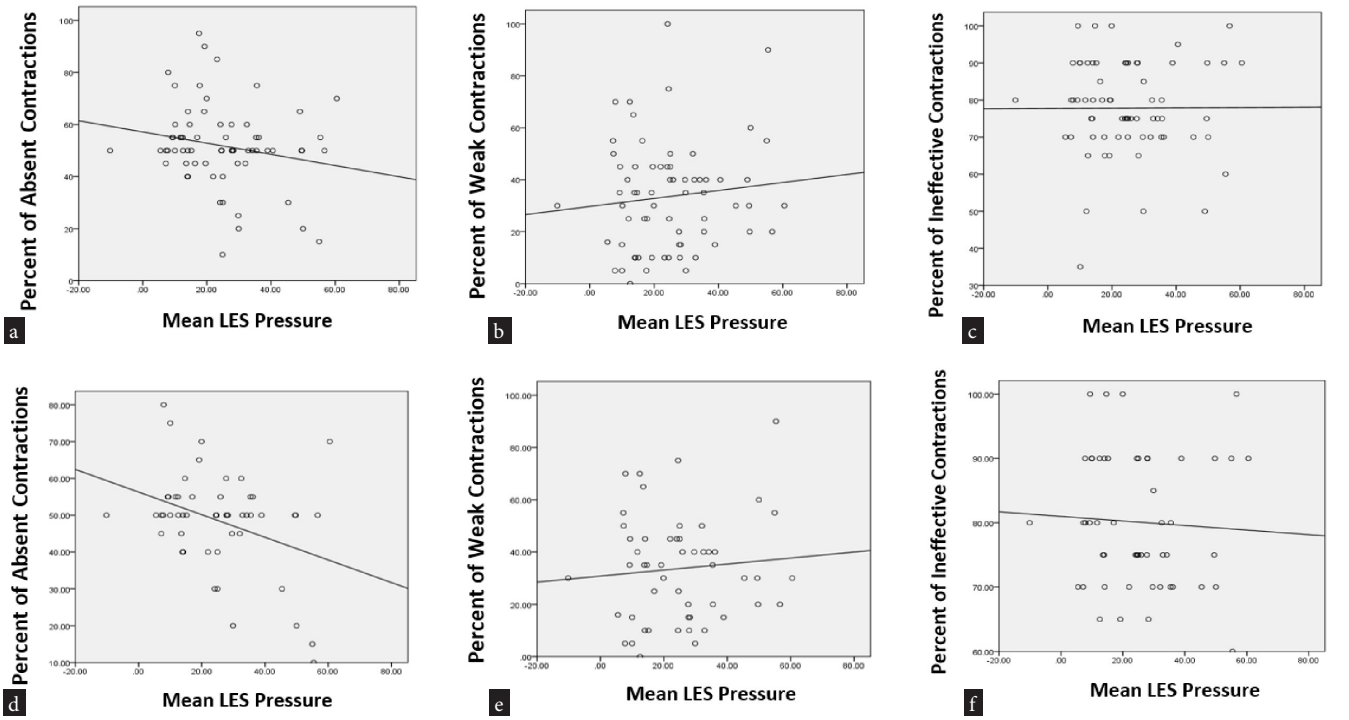

Figure 3: Correlation of mean LES pressure with: (a) Percent of absent contractions among CCv3.0 IM patients (n = 71) (r = -0.026, p = 0.11), (b) Percent of weak contractions among CCv3.0 IM patients (n = 71) (r = 0.04, p = 0.387), (c) Percent of ineffective contractions among CCv3.0 IM patients (n = 71) (r = -0.117, p = 0.971), (d) Percent of absent contractions among CCv4.0 IM patients (n = 64) (r = -0.108, p = 0.01), (e) Percent of weak contractions among CCv4.0 IM patients (n = 64) (r = 0.012, p = 0.534), (f) Percent of ineffective contractions among CCv4.0 IM patients (n = 64) (r = -0.013, p = 0.703); LES: Lower Oesophageal sphincter, IM: Ineffective motility. CCv3.0: Chicago classification version 3.0, CCv4.0: Chicago classification version 4.0; The points in a correlation plot are called data points and represents a pair of values (X, Y) corresponding to two variables being compared.

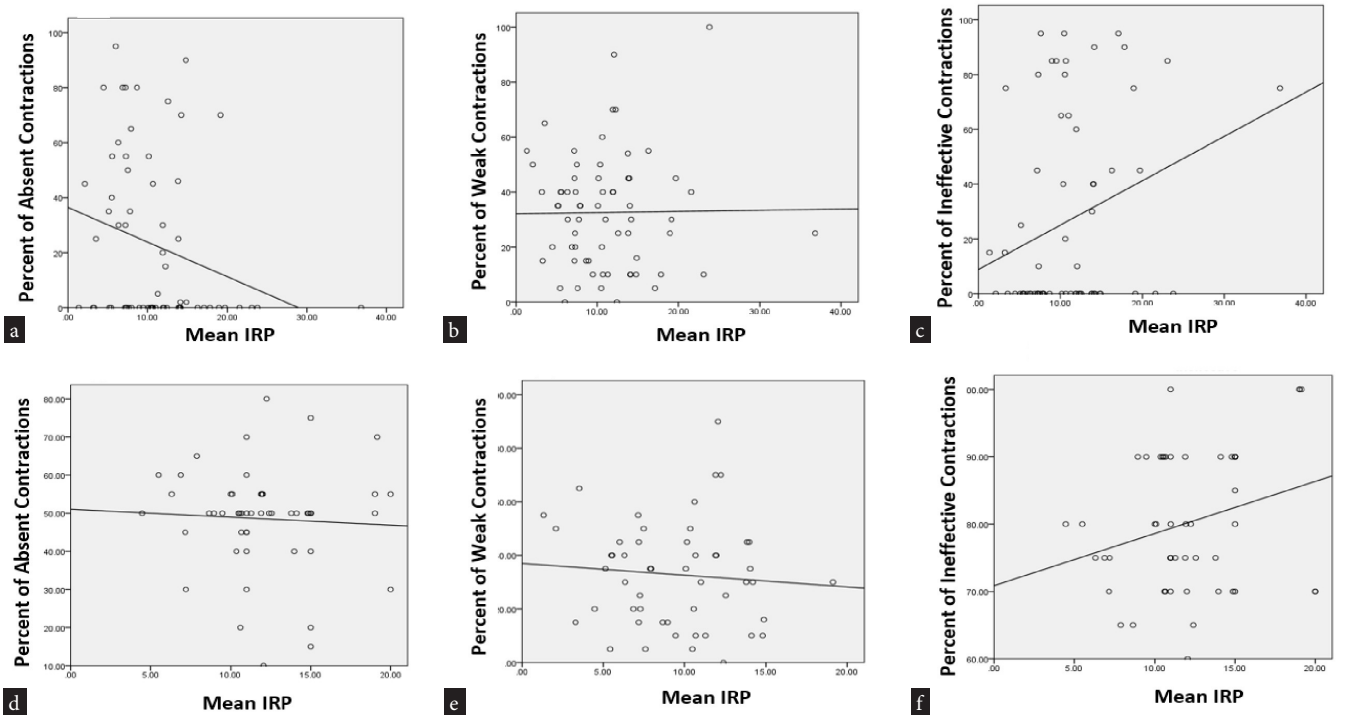

Figure 4: Correlation of mean IRP with: (a) Percent of absent contractions among CCv3.0 IM patients (n = 71) (-0.47, p = 0.041), (b) Percent of weak contractions among CCv3.0 IM patients (n = 71) (r = 0.15, p = 0.924), (c) Percent of ineffective contractions among CCv3.0 IM patients (n = 71) (r = 0.061, p = 0.026), (d) Percent of absent contractions among CCv4.0 IM patients (n = 64) (r = -0.17, p = 0.28), (e) Percent of weak contractions among CCv4.0 IM patients (n = 64) (r = -0.041, p = 0.65), (f) Percent of ineffective contractions among CCv4.0 IM patients (n = 64) (r = 0.035, p = 0.04); IRP: Integrated relaxation pressure, IM: Ineffective motility, CCv3.0: Chicago classification version 3.0, CCv4.0: Chicago classification version 4.0; The points in a correlation plot are called data points and represents a pair of values (X, Y) corresponding to two variables being compared.

motility disorder. So, the overall prevalence rate of 19.4% confirmed IM by CCv3.0 changed to 17.5% when observed on CCv4.0. Even though there hasn't been much research in this area recently, a recent study found that IEM was less familiar with CCv4.0 than CCv3.0, which is something to be envisioned given the new criteria,[10] like our findings. There was no statistical difference between the two groups for demographic and baseline characteristics, including age, gender, duration of symptoms of dysphagia, and BMI. BMI was in the category of underweight, i.e., not in favour of the previous study.[11] This may be due to low socio-economic and health status given with a lack of nutrients in low-middle-income countries like Pakistan.

There are gaps in the literature regarding the indications and presentation of IEM. The most frequent symptom mentioned in medical history or initial presentation of the individuals in both groups was dysphagia, which is still required to be classified as having a motility disorder. In our study, both groups had an equal prevalence of dysphagia symptoms. Chugh *et al*. (n = 33) discovered no differences in symptom severity for dysphagia according to the Eckardt symptom score,[12] which was not seen in our study, between patients with IEM based on CCv3.0 criteria and those with regular manometry studies. In our retrospective study, our team was not able to determine any association between dysphagia and bolus clearance score among IEM patients due to the non-presence of dysphagia characteristics in the selected individuals. The most recent publications also did not report a difference in Eckardt scores among IM patients established by the CCv4.0 or CCv3.0 guidelines.

The severity of oesophageal function, as determined by peristaltic contractions, was linked to a CCv4.0 IEM diagnosis.[9] A negative correlation between the percentage of failed contractions and that of weak contractions was observed because the rate of ineffective contractions ranges between 70% and 100% in both groups. These oesophageal dysfunction findings are consistent with the CCv4.0 update for IEM's ability to identify more scientifically significant cases.[12] Our findings do not include routine barium radiography to confirm an IEM identification. Although they are probably only accessible at specialised centres, radiographic studies should be carried out according to o standards and interpretations that might correlate better.

In the CCv4.0 group, mean LES pressure correlated with a higher percentage of absent contractions but not with failed or ineffective ones in either group; mean LES pressure and IRP were related to higher percentages of ineffective contractions in both groups. Similar significant results were found between declining median IRP and rising rate of unsuccessful or ineffective contractions among the groups. Significant correlations between median IRP, mean LES pressure and motility findings on manometry may indicate an underlying smooth muscle pathology for IEM and call for additional research. When LES pressure is less than intragastric pressure, it is thought that this contributes to the pathophysiology of GERD, which was not under this study's scope.

Healthcare professionals generally follow the standard procedure of 10 supine wet swallows, consistent with the development of CCv3.0.[13] That protocol, however, is frequently not enough to establish a conclusive motility diagnosis that demonstrates symptoms and directs therapy, putting motility disorders, particularly EGJOO, at risk of misdiagnosis and improper treatment. This clinical difficulty with creating a standardised HRM protocol was addressed in CCv4.0. The protocol, as suggested for the CCv4.0, entails a baseline period of 30 seconds (exclusive of swallowing) in the recumbent position, followed by ten 5-mL swallows & 2 sequences of multiple rapid swallows (MRS), which consist of five 2-mL swallows spaced no more than 2 seconds apart. The participant's position then is shifted to a seated position, and five 5-mL swallows are administered, followed by a rapid drink challenge (RDC) test, which involves ingesting 200 mL of water as fast as possible.[14]

As the total number of swallows increased, the average of DCI and IRP changed, leading to a change in diagnosis. Also, normal oesophageal peristaltic pressurisation and LES pressure are influenced by body position.[15] Positioning oneself upright may also lessen the effects of structural elements that affect peristalsis, such as vascular bands that are more obvious when one is lying flat. In contrast to the impact of the oesophageal body, IRP seems to be better elicited in an upright posture than in a supine. Thus, the change in diagnosis prevails in all oesophageal motility disorders due to the impact of posture; therefore, ineffective motility is better diagnosed.

Limitations of study

Provocative manoeuvres during oesophageal HRM, such as multiple rapid swallows, solid swallows, and the standardised test meal lacking from this study, can further characterise ineffective motility. Since no specific treatment can reverse the motor pattern, management strategies that improve patient symptoms, particularly those connected to reflux, are required for research. Future studies may benefit from using novel testing techniques, such as functional lumen imaging probes and baseline impedance measurements, to define IM's pathophysiology further and separate its phenotypes.

CONCLUSION

Our study concludes that CCv4.0 has made the nomenclature more stringent, especially IEM, which was previously considered a minor disorder. About 22% of individuals previously labelled as having motility disorder, and those with IEM are now regarded as having major motility disorder. The correlation between mean LES pressure and mean IRP and the percentage of ineffective contractions points to compromised contractile functioning. We need to conduct more prospective research on the effect on clinical outcomes and, possibly, further improving diagnostic criteria. However, IEM is a vast spectrum, and more data and studies will further help classify this sub-group with better segregation.

Ethical approval: The research/study approved by the Institutional Review Board at Institutional Ethical Review Board and Bio-Ethical Committee (BEC) of Quaid-I-Azam University, Islamabad, number BEC-FBS-QAU2022-381, dated 25th April 2022.

Declaration of patient consent: Patient's consent not required as patients identity is not disclosed or compromised.

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