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Jackhammer Esophagus: Assessing the balance between pre-peak and post-peak contractile integral

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Abstract

Background: We hypothesized that symptoms in Jackhammer esophagus (JH) are associated with an imbalance between the pre-peak and post-peak phases of contraction. Thus, we developed a method to distinguish the contractile integral components of pre-peak and post-peak phase contractile activity to determine the contribution of each phase and their association with dysphagia.

Methods: Patients diagnosed with JH were enrolled and compared to controls. The first 5 intact swallows during manometry were analyzed. A single swallow was divided into a pre-peak and post-peak phase. The contractile integral of each phase and its corresponding time-controlled integral were computed. All metrics were compared between controls and JH patients subcategorized by the Impaction Dysphagia Question (IDQ) score with cut-off of 6.

Key Results: 38 JH patients and 71 controls were included. Twelve JH patients had IDQ ≤ 6 and 26 with IDQ > 6 . JH patients had higher contractile integral in both phases, and a higher ratio between post-peak to pre-peak contractile integral independent of duration. Similarly, JH patients with an IDQ > 6 had higher contractile metrics than those with IDQ ≤ 6 . There was a correlation between the IDQ score and the ratio within the post-peak to pre-peak contractile integral ($r=0.375$).

Conclusions: Abnormalities in contractile integral of the post-peak phase are more significant in JH with higher dysphagia scores. Although the total post-peak contractile integral was higher in symptomatic patients, this was associated with longer duration of post-peak activity suggesting that dysphagia patients with JH have a defect in the post-peak phase of peristalsis.

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Keywords

Jackhammer esophagus; contractile integral; swallow

Introduction

Jackhammer is a motility disorder defined by at least 2 hypercontractile swallows (Distal Contractile Integral (DCI) >8000 mmHg●cm●s) among the total 10 supine liquid swallows in the Chicago classification 3.0(1). Chest pain and dysphagia are the two major symptoms associated with jackhammer esophagus and these symptoms are believed to be derived from over-contraction in the distal esophagus. However, there is a poor correlation between contractile activity and symptoms noted on both conventional and HRM (2–3). Additionally, some patients with jackhammer esophagus are discovered incidentally during an evaluation of GERD suggesting that this motor pattern has a more heterogeneous presentation. Thus, symptom genesis in jackhammer may not be related to hypercontractility alone and further study should focus on a more detailed description of the contractile pattern in jackhammer esophagus.

The current paradigm of analysis of peristaltic function focuses on the contractile vigor of the propagating wave, and the swallow is classified into categories based on hypo- and hyper-contraction using a threshold of 30mmHg or 180mmHg in the contraction amplitude in conventional line tracing manometry (4). This approach was continued in the paradigm of high-resolution manometry where the distal contractile integral (DCI) replaced peristaltic amplitudes on line tracings, albeit using a much more robust measure that incorporated contraction duration and length of the contractile segment (1). However, both measurements have combined the up-slope and down slope of a contraction into a singular measurement. This approach may mask abnormalities that were more apparent when a more qualitative approach was used that described multiple peaks and prolonged contraction.

We hypothesized that the Jackhammer esophagus might be associated with abnormalities in the post-peak phases of contraction instead of the “over-contraction” in the pre-peak phase. We recently developed a novel measurement tool which separated the up- and down- slope of the peristalsis to provide a more detailed quantitative measurement for each phase of contraction. In the current study, we aimed to apply this novel measurement to jackhammer esophagus patients to determine whether patients with dysphagia have abnormalities in both the pre and post-peak phases of contraction.

Materials and Methods

Subjects

Patients with jackhammer esophagus were retrospectively identified using a query of the Esophageal Center at Northwestern (ECN) Motility Laboratory Registry, which includes English-speaking patients aged 18–85 that were evaluated at the ECN for esophageal symptoms with HRM. Patients evaluated between August, 2008 and August, 2015 were included if they had 1) an HRM with at least two supine swallow with DCI > 8,000

mmHg●s●cm and 2) and completed the Impact Dysphagia Questionnaire (IDQ). Patients were excluded if they had previous surgery in the upper gastrointestinal tract. The Impaction Dysphagia Question (IDQ) was obtained on the same day of manometry in all Jackhammer esophagus patients. These patients were further categorized into IDQ>6 and IDQ ≤ 6 (5).

Another group of volunteers were recruited for comparison. Volunteers were recruited by advertisement or word of mouth and had no history of esophageal symptoms (heartburn, regurgitation, dysphagia), previous gastrointestinal surgery, or significant medical conditions. These subjects have been previously described [6]. Thus a total of 75 healthy controls were recruited (age range 19–48 yrs) and 4 subjects were excluded due to insufficient analyzable swallows leaving 71 analyzable studies.

The study protocols were approved by the Northwestern University Institutional Review Board.

HRM Study protocol

HRM studies were done in a supine position after at least a 6-hr fast. The HRM catheter was 4.2 mm outer diameter solid-state assemblies with 36 circumferential sensors at 1-cm intervals (Given Imaging, Los Angeles, CA). Transducers were calibrated at 0 and 300 mmHg using externally applied pressure. The manometry assembly was placed transnasally and positioned to record from the hypopharynx to the stomach with about 3 intra-gastric sensors. The study protocol included at least 30-s baseline recording and ten, 5-ml water swallows in the supine position.

Esophageal pressure topography (EPT) analysis

EPT data were analyzed using ManoView™ analysis software (Given Imaging, Los Angeles, CA), as well as a customized MATLAB (The Math Works, Natick, MA) program. The first 5 intact swallows in the supine positions were analyzed. For each swallow, the distal contractile integral (DCI) was measured in the traditional method [1]. Then, components of the DCI were measured using a novel analysis paradigm using the MatLab program: the DCI of each swallow was divided into a pre-peak phase and post-peak phase by plotting the trajectory of the pressure wave peaks at 1 cm intervals from the transition zone to the proximal aspect of the EGJ (Figure 1). The contractile integral, i.e. pressure amplitude × duration × axial length (mmHg●s●cm), was then computed for both phases: the pre-peak contractile integral (PREP-CI) and post-peak contractile integral (POSP-CI) (Figure 2). Thus, the sum of the PREP-CI and POSP-CI equaled the traditional DCI of a single swallow.

To account for the contribution of contraction-phase durations to the contractile integrals, time-controlled (tc) metrics, i.e. pressure amplitude × axial length, were also obtained. To generate the tc metrics, the duration in seconds of each phase was measured for each 1-cm axial segment; the 1-cm segment contractile integral was then divided by the segment duration to generate the tc-measure in mmHg●cm. The PREP-CI-tc and POSP-CI-tc were then calculated as the sum of all the time-controlled axial segments for the PREP and POSP phases, respectively. The DCI-tc was calculated similarly for the total pressure-wave durations, and therefore equaled the sum of the PREP-CI-tc and POSP-CI-tc.

All the jackhammer swallows were selected for further analysis. These swallows were divided into swallows with single peak and multiple peaks defined by Clouse et al (7), the criteria for multi-peak contractions were defined as the following; (i) at least 2 peaks are present, (ii) pressure trough between the peaks is greater than zero, (iii) the peak of least amplitude is at least 10 mm Hg greater than the inter-peak trough, and (iv) the pressure peaks are separated by at least 1 second. When there were multiple peaks in the Jackhammer swallows, the phase from the beginning of the contraction to the first peak was defined as pre-peak phase, otherwise the post-peak phase represented all of the activity beyond this first peak (Figure 1b and Figure 3).

Statistical analysis

To maintain independence of variables, the median values of the five analyzed swallows and the single swallow with the greatest DCI from each subject were subjected to statistical analysis. All the data including the PREP-CI, POSP-CI, POSP-CI/PREP-CI ratio, DCI, PREP-CI-tc, POSP-CI-tc, POSP-CI-tc/PREP-CI-tc ratio, DCI-tc were presented as median (inter-quartile range, IQR). Statistical comparisons were performed using the Wilcoxon-signed rank test. The correlation between the IDQ score and the POSP-CI/PREP-CI-tc was performed using pearson correlation. A $p < 0.05$ was considered significant. The statistical analysis was done by using the IBM SPSS 20.0 (IBM, Chicago, USA).

Results:

The contractile EPT metrics for the first 5 eligible swallows in the supine positions for both jackhammer esophagus patients and healthy controls

Altogether 38 patients (age range 43–70 years, females:male 19:19) met the inclusion criteria and were included. Among them, 26 patients were categorized into $IDQ > 6$ and 12 into $IDQ \leq 6$. The PREP-CI, POSP-CI, POSP-CI/PREP-CI, DCI, PREP-CI-tc, POSP-CI-tc, DCI-tc and POSP-CI/PREP-CI-tc for the first 5 intact swallows in the supine position were presented in Table 1. The composite DCI measurement in jackhammer esophagus patients was significantly greater than healthy controls and this appears to be weighted towards a slightly higher contractile integral during post-peak phase. When the integral was controlled by time (POSP-CI-tc/PREP-CI-tc), the difference between controls and jackhammer patients was still significant, but significantly reduced. Among the Jackhammer esophagus patients, those with $IDQ > 6$ had higher POSP-CI compared to those with an $IDQ \leq 6$ (Table 1)(Figure 3).

The contractile EPT metrics for supine swallows with greatest DCI in both jackhammer esophagus patients and healthy controls

The measurements in the swallows with the maximal DCI in the supine position are presented in Table 2. Again the composite DCI measurement in jackhammer esophagus patients appears to be weighted towards a slightly higher contractile integral during post-peak phase based on POSP-CI/PREP-CI ratio. And this effect was independent of the contraction duration because the difference was still present when these parameters were controlled by the contraction duration (Table 2).

Among the Jackhammer esophagus patients, those with an IDQ>6 had a higher value on all of the parameters independent of the duration of time compared with the patients with IDQ ≤ 6 (Table 2).

The correlation between the IDQ score and the POSP-CI/PREP-CI-tc among Jackhammer patients

A correlation between the IDQ score and the POSP-CI-tc/PREP-CI-tc among Jackhammer patients was calculated. There was a positive correlation between the IDQ score and the POSP-CI-tc/PREP-CI-tc with a $r=0.375$ ($p=0.019$).

Clinical profile

The therapy for the Jackhammer patients was reviewed. The predominant symptoms of all patients were dysphagia ($n=22$), reflux ($n=12$) and chest pain ($n=4$). None of the patients were on nitrates, 5 of them were on calcium channel blockers, 5 were on opiates and another 5 were on pain modulators including venlafaxine, escitalopram and imipramine. The comparison between the patients on medication and patients with no medication showed no significant difference, which indicated the therapy did not affect the result. There were 25 patients who were on PPI, but only 12 patients had classic reflux symptoms.

Discussion

Our data supports that Jackhammer esophagus is primarily a disorder of increased contractile activity during the post-peak phase of peristalsis. Although both the pre- and post-peak phases are increased compared to controls, the post-peak phase contractile integral was substantially larger than the pre-peak phase. Additionally, the ratio of the post-peak and pre-peak contractile integral was significantly greater in jackhammer esophagus and this was related to a longer duration of contractile activity. This also extended to our findings within the jackhammer population as patients with higher IDQ scores also had a higher ratio and the IDQ score was positively correlated with the ratio when controlled for time. These findings support that dysphagia symptoms are more common in patients with abnormalities in the post-peak phase.

It has long been believed that chest pain and dysphagia in nutcracker esophagus and hypercontractile disorders of the esophagus was related to excessive contractile effort during peristalsis. However, observational data supports that this premise may not be true. Studies suggest that there is a poor correlation between contractile vigor and symptoms during individual swallows (2–3) and that hypercontractility can be seen in patients presenting with GERD (8–10). A study from Sweden investigated 45 nutcracker esophagus patients with 24-hour reflux monitoring, and it turned out that 70% of patients had acid-related esophageal dysfunction suggesting that reflux may play a role in the development of symptoms in nutcracker esophagus (8). The study from our center also indicated that 10% of hypercontractile esophagus patients had evidence of reflux disease (10). However, a randomized controlled study failed to confirm the role of acid reflux in nutcracker esophagus (9).

The pathophysiology of Jackhammer esophagus is complex and incompletely understood, but there may be overlap with findings associated with spasm and simultaneous contractions (11). A recent publication by Bredenoord et al confirmed that the chest pain in Jackhammer esophagus was not related to the value of DCI, however, dysphagia did show a correlation with DCI and an elevated intrabolar pressure (12). In our study, the parameters evaluated among the first 5 intact swallows and the swallow with the maximal DCI revealed higher POSP-CI-tc/PREP-CI-tc in patients with IDQ 6 than those 6. This indicated that abnormalities associated with an augmented POSP-CI would lead to more severe symptoms, and this was also confirmed by the evidence of a correlation between the IDQ and the POSP-CI-tc/PREP-CI-tc.

Given our findings, we speculate that patients with a hypercontractile esophageal motor disorder could be separated into different phenotypes based on the relative contribution of each phase to overall contractile state. For instance, the contractile pattern in patients with higher contractile effort during the pre-peak phase may be influenced by higher cholinergic tone or a heightened sensitivity to acetylcholine. In contrast, the motor dysfunction in patients with prolonged post-peak phase may be related to preferential defects in ion channels that retard return to resting membrane potential or potentially to resistance to the inhibitory influence of neurotransmitters, such as nitric oxide. These findings could have clinical implications as therapies could target the imbalance of these neurogenic influences and also potentially identify the variant of jackhammer that is due to obstruction at the EGJ.

There were some limitations in the current study. The number of the patients with Jackhammer esophagus was limited, which restricted our analysis of the relationship between symptom severity and the POSP-CI-tc/PREP-CI-tc. In addition, our study design did not allow for a thorough analysis of the factors that would lead to augmentation of the post-peak contraction. Systematic studies involving pharmacologic control of the cholinergic and inhibitory influences as well as challenges of multiple rapid swallows and distensibility studies of the esophageal body and EGJ could help further explain what is driving the augmented post-peak contractile response in jackhammer esophagus. The ultimate goal of developing this novel measurement is to provide the measurement paradigm to better understand the contribution of contraction and relaxation phase to symptom genesis, and these measurements could be useful in these translational and animal models.

In conclusion, abnormalities in contractile integral of post-peak phase are more significant in Jackhammer patients with higher dysphagia scores. Although the total post-peak contractile integral was higher in symptomatic patients, this was associated with a longer duration of post-peak activity suggesting that dysphagia patients have a defect in the post-peak phase of peristalsis. Future studies should focus on determining the physiology behind this abnormal finding and this may lead to therapies that can target these abnormalities.

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Abbreviations:

JH	Jackhammer esophagus
IDQ	Impaction Dysphagia Question
DCI	Distal Contractile Integral
ECN	Esophageal Center at Northwestern
EPT	Esophageal pressure topography
PREP-CI	pre-peak contractile integral
POSP-CI	post-peak contractile integral
tc	time-controlled
IQR	inter-quartile range

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Key points:

1. We have developed a novel measurement separating the pre- and post-peak components of the contractile activity during swallowing.
2. Using the pre- and post-peak contractile integral measurements in Jackhammer patients revealed that the contractile integral of the post-peak phase is significantly elevated in patients with higher dysphagia scores.
3. Although the total post-peak contractile integral was higher in symptomatic patients, this was associated with longer duration of post-peak activity suggesting dysphagia patients with Jackhammer esophagus have a defect in the post-peak phase.

Figure 1.

The separation of pre-peak phase and post-peak phase in the peristalsis wave.

Legend: A: single-peak swallow; B multiple-peak swallow, the phase from the beginning of the contraction to the first peak was defined as pre-peak phase, otherwise the post-peak phase represented all of the activity beyond this first peak.

Figure 2.

The schematic diagram of the novel measurement in the esophageal pressure topography (EPT)

Legend: A single swallow was divided into a pre-peak contractile integral (PREP-CI) and a post-peak contractile integral (POSP-CI) phase by plotting the trajectory of the pressure wave peaks at 1-cm intervals. The contractile integral (mmHg●s●cm) at each 1 cm interval before (PREP-CI) and after (POSP-CI) the peak were measured from the transition zone to the proximal aspect of the EGJ. In the swallow displayed, the PREP-CI was 894 mmHg●cm●s and the POSP-CI was 1285 mmHg●cm●s, which made the composite DCI into 2179 mmHg●cm●s.

Figure 3.

Examples of two Jackhammer swallows.

Legend: A) A single-peak jackhammer swallow with normalized POSP-CI (composite DCI=15237 mmHg●cm●s), the POSP-CI/PREP-CI ratio was 1.56. The POSP-CI-tc/PREP-CI-tc was 0.85 after controlled by the phase duration. B) A multiple-peak jackhammer swallow with prolonged POSP-CI (composite DCI=16502 mmHg●cm●s), the POSP-CI/PREP-CI ratio was 2.93. The POSP-CI/PREP-CI-tc was 1.11 after controlled by the phase duration.

Table 1
The metrics of the first 5 swallows in the supine position among groups (median(IQR))

Groups	Healthy control (n=71)	Jackhammer esophagus (n=38)	Jackhammer esophagus (IDQ 6)(n=12)	Jackhammer esophagus (IDQ>6)(n=26)
IRP (mmHg)	7.8(5.8–9.6) ^{##&}	11.5(6.9–15.6)	8.8(6.9–14.6)	11.6(7.1–15.0)
DL (seconds)	6.9(6.1–7.4) ^{##&}	7.1(6.3–8.1)	7.1(6.3–7.5)	7.0(6.2–8.4)
DCI (mmHg●cm●s)	1519(1092–2089) ^{##&}	8357(4829–11943)	7538(1461–8946)	7730(3926–14081)
PREP-CI (mmHg●cm●s)	641(470–891) ^{##&}	2582(1853–4368)	2690(1951–3391)	2665(1730–4887)
POSP-CI (mmHg●cm●s)	843(601–1256) ^{##&}	4941(2903–9332)	4370(2734–5695)	5571(3095–11778)
POSP-CI/PREP-CI	1.50(1.41–1.51) ^{*&}	1.71(1.54–1.97)	1.51(1.28–1.85) [^]	1.80(1.56–2.04)
Pre-peak phase duration (seconds)	1.0(1.0–1.1) ^{##&}	1.5(1.3–2.0)	1.7(1.4–2.2)	1.5(1.3–2.0)
Post-peak phase duration (seconds)	1.6(1.4–1.9) ^{##&}	3.7(3.1–4.8)	3.7(2.7–4.3)	4.1(3.7–5.7)
Swallow duration (seconds)	2.6(2.3–3.1) ^{##&}	5.7(4.8–7.0)	5.3(4.9–5.9)	6.3(5.0–9.5)
DCI-tc (mmHg●cm)	515(407–685) ^{##&}	1226(933–1522)	1086(957–1344)	1006(748–1213)
PREP-CI-tc (mmHg●cm)	557(428–757) ^{##&}	1256(1036–1652)	1126(905–1585)	949(629–1195)
POSP-CI-tc (mmHg●cm)	496(399–650) ^{##&}	1079(923–1491)	1079(923–1332)	954(727–1356)
POSP-CI-tc/PREP-CI-tc	0.92(0.86–0.97)	0.92(0.85–0.97)	0.85(0.78–0.94) [^]	1.02(0.84–1.11)

IRP: integrated relaxation pressure; DL: distal latency; DCI: distal contractile integral; PREP-CI: pre-peak contractile integral; POSP-CI: post-peak contractile integral; POSP-CI/PREP-CI: ratio between PREP-CI to POSP-CI; DCI-tc: distal contractile integral controlled by swallow duration; PREP-CI-tc: PREP-CI controlled by phase duration; POSP-CI-tc: POSP-CI controlled by phase duration; POSP-CI-tc/PREP-CI-tc: ratio between PREP-CI-tc to POSP-CI-tc;

^{*}: p<0.05 vs Jackhammer
[#]: p<0.05 vs Jackhammer IDQ 6
[&]: p<0.05 vs Jackhammer IDQ>6
[^]: p<0.05 vs Jackhammer IDQ>6

Table 2

The metrics of the swallows with the greatest DCI in the supine position among groups (median(IQR))

Groups	Healthy control (n=71)	Jackhammer (n=38)	Jackhammer (IDQ 6)(n=12)	Jackhammer (IDQ>6)(n=26)
IRP (mmHg)	7.8(5.8–9.6) ^{##&}	11.5(6.9–15.6)	9.1(6.9–14.2)	12.4(7.0–15.7)
DL (seconds)	6.9(6.1–7.4) ^{##&}	7.3(6.4–8.4)	7.3(6.8–8.6)	7.1(6.3–8.2)
DCI (mmHg●cm●s)	1755(1301–2453) ^{##&}	13430(9932–25799)	11751(9231–14257) [^]	17847(10722–27296)
PREP-CI (mmHg●cm●s)	759(561–1082) ^{##&}	3810(2767–5465)	3757(3294–4858)	4031(2753–8504)
POSP-CI (mmHg●cm●s)	969(717–1389) ^{##&}	9301(6178–18073)	6474(5720–9224) [^]	15904(6931–21112)
POSP-CI/PREP-CI	1.50(1.39–1.63) ^{*&}	1.98(1.53–4.32)	1.70(1.51–2.17) [^]	2.37(1.53–7.32)
Pre-peak phase duration (seconds)	1.1(1.0–1.2) ^{##&}	1.9(1.6–2.4)	2.2(1.8–4.4)	1.8(1.6–2.3)
Post-peak phase duration (seconds)	1.7(1.5–2.1) ^{##&}	5.0(4.2–8.1)	4.3(4.1–4.8) [^]	6.5(4.5–9.7)
Swallow duration (seconds)	2.8(2.5–3.3) ^{##&}	8.2(6.4–11.2)	6.7(5.9–7.0) [^]	9.7(6.6–13.3)
DCI-ic (mmHg●cm)	594(484–760) ^{##&}	1609(1300–1982)	1347(1169–1704) [^]	1801(1354–2240)
PREP-CI-ic (mmHg●cm)	609(518–824) ^{##&}	1585(1323–1897)	1566(1380–1719)	1586(1326–2122)
POSP-CI-ic (mmHg●cm)	572(459–718) ^{##&}	1508(1313–2068)	1360(1267–1523) [^]	1751(1364–2245)
POSP-CI-ic/PREP-CI-ic	0.90(0.83–0.96) ^{*&}	0.99(0.89–1.14)	0.90(0.83–1.00) [^]	1.02(0.92–1.23)

IRP: integrated relaxation pressure; DL: distal latency; DCI: distal contractile integral; PREP-CI: pre-peak contractile integral; POSP-CI: post-peak contractile integral; POSP-CI/PREP-CI: ratio between PREP-CI to POSP-CI; DCI-ic: distal contractile integral controlled by swallow duration; PREP-CI-ic: PREP-CI controlled by phase duration; POSP-CI-ic: POSP-CI controlled by phase duration; POSP-CI-ic/PREP-CI-ic: ratio between PREP-CI-ic to POSP-CI-ic;

^{*,#}: p<0.05 vs Jackhammer

^{##}: p<0.05 vs Jackhammer IDQ 6

[&]: p<0.05 vs Jackhammer IDQ>6

[^]: p<0.05 vs Jackhammer IDQ>6