Published in final edited form as:

Neurogastroenterol Motil. 2020 January ; 32(1): e13725. doi:10.1111/nmo.13725.

Chaotic Peak Propagation in Patients with Jackhammer esophagus

Yinglian Xiao¹, Dustin A. Carlson², Zhiyue Lin², John E. Pandolfino²

¹Department of Gastroenterology and Hepatology, the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

²Department of Medicine, the Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Abstract

Aims: The contractile activity of Jackhammer esophagus (JE) is heterogeneous and abnormalities in the balance of pre- and post-peak contractile activity has been reported. We observed that the progression of the peak contraction is disordered in JE patients, which reflect underlying abnormalities in the inhibitory and excitatory influence in esophageal contraction. In order to better define this abnormality, we developed novel time metrics to define trajectory of the pressure wave peak and assessed it in healthy controls and JE patients.

Methods: 38 patients with JE (ages 43–70, 19 females) and 71 asymptomatic controls (ages 19–48; 33 females) were retrospectively evaluated. High resolution manometry was performed in all subjects with 10 supine liquid swallows. The first 5 intact supine swallows and supine swallow with the greatest DCI were analyzed using ManoView™ software and customized MATLAB program. The **time distance**, **negative time distance sum** and **chaotic ratio** were calculated. JE patients were subcategorized by the Brief Esophageal Dysphagia Questionnaire (BEDQ) with cut-off of 6.

Results: Jackhammer patients had longer time distance, longer negative time distance, and higher chaotic ratio than controls ($p < 0.001$). The distribution of the number of negative time distances differed between JE patients with BEDQ > 6 and BEDQ ≤ 6.

Conclusions: The trajectory of the pressure wave peak propagation commonly occurred in an unordered fashion in JE, but rarely in controls. Additionally, differences in pressure propagation trajectory was associated with higher symptom scores, thus trajectory of the pressure wave peak may be an important marker of abnormal esophageal motor function.

Correspondence: Yinglian Xiao, MD & Ph.D, Department of Gastroenterology and Hepatology, The First Affiliated Hospital, Sun Yat-sen University, 58 Zhongshan Road 2, Guangzhou, China, 510080, Fax: 86-20-87332916, yinglian.xiao@gmail.com.

Author contribution: Yinglian Xiao and Dustin A Carlson: study concept and design; acquisition of data; analysis and interpretation of data; drafting and finalizing the manuscript; Zhiyue Lin: analysis and interpretation of data, reviewing and editing the manuscript; John E. Pandolfino: study concept and design; finalizing the manuscript and guarantee of the study.

Conflict of interest: John E. Pandolfino [Metronic (consulting, educational), Sandhill Scientific Inc. (Consulting)].

Dustin A Carlson: Medtronic (speaking; consulting)

No other conflicts for remaining authors

Keywords

Jackhammer esophagus; peak pressure; chaotic; high resolution manometry

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). Hypercontraction associated with excessive excitatory activity has been regarded as the primary mechanism for this abnormality, however, there is evidence to suggest that a purely excitatory phenomenon may not be the only defect associated with this abnormal pattern of hypercontractile motor disorder. In addition, there is very little evidence to support that the underlying DCI value or peristaltic amplitude are strongly correlated with symptom severity or abnormal bolus transport (2–3). Therefore, other defects in motor function may play a more dominant role in the pathogenesis of hypercontractile disorders defined by DCI alone and these defects may further define distinct phenotypes within this group of disorders.

Recently, we assessed the pre- and post-peak contractile activity in a group of jackhammer patients and asymptomatic controls and found that increased post-peak contractile activity was associated with dysphagia symptom severity and that this was mostly related to prolonged post-peak contraction and not an overt difference in contraction strength measured by DCI. These findings suggest that although this motor pattern is primarily considered to be a hypercontractile motor disorder, there are also abnormalities in propagation and post-peak return of the muscle fibers to their low-tension state and length (4–5). We theorized that this could be related to an imbalance in the excitatory and inhibitory activity related to defects in the intrinsic myogenic contractile apparatus or a defect in the input from the enteric and central nervous system. Quader et al used provocative testing to induce deglutitive inhibition and found that a subgroup of Hypercontractile patients exhibited abnormal deglutitive inhibition during multiple rapid swallows and rapid drink challenges (6). Thus, hypercontractile disorders may reflect a reduction in inhibition or relaxation as opposed to an augmented contraction.

While we were assessing the pre- and post-peak contractions, we also noted that there was a disruption in the sequenced propagation of the peak of the contraction suggesting that the esophageal body was not coordinated during the isometric phase of contraction. We speculated that this could be another marker of defective inhibition in the esophagus as the smooth muscle esophagus should relax distal to a contraction to promote antegrade bolus transit(7). In order to determine if this phenomenon was important, we developed new metrics to assess the trajectory of the peak pressure wave and the goal of this study was to assess whether differences in peak pressure trajectory occurred between jackhammer patients and asymptomatic controls.

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 Brief Esophageal Dysphagia Questionnaire (BEDQ) (8). Patients were excluded if they had previous surgery in the upper gastrointestinal tract.

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 (9). 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.

Brief Esophageal Dysphagia Questionnaire

The BEDQ was obtained on the same day of manometry in all Jackhammer esophagus patients. The BEDQ consisted of eight 6-point Likert scale questions (scored 0–5) that assess frequency of symptoms and severity of symptoms over the preceding 30 days and 2 open-ended questions regarding frequency of food impactions and related emergency room visits. (8) The BEDQ was previously termed the impaction dysphagia questionnaire and was updated after the validation study by Taft et al. in 2016 (8). BEDQ scores range from 0 (asymptomatic) to 50. Patients in this study were further categorized into BEDQ > 6 (greater dysphagia severity) and BEDQ ≤ 6 (lesser dysphagia severity).

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 (Medtronic Minnesota) 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 (Medtronic Minnesota), as well as a customized MATLAB (The Math Works, Natick, MA) program. The first 5 intact swallows in the supine and the supine swallow with the greatest DCI were analyzed. For each swallow, the trajectory of the pressure wave peaks at 1 cm intervals from the transition zone to the proximal aspect of the EGJ was plotted. The *time distance* was calculated as the

sum of time interval between pressure wave peaks for each 1-cm axial interval (Figure 1 and 2). For each swallow, the number of *negative* times distance was noted and the time values were summed to calculate the ***negative time distance sum*** (Figure 2). The ratio between the ***negative time distance sum*** and *time distance* was defined as the ***chaotic ratio***, indicating the extent of the reverse propagation of the pressure wave peak during the swallow.

The Jackhammer swallows were divided into swallows with single peak and multiple peaks defined by Clouse et al (10), 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 first peak was selected to depict the peak propagation.

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 were presented as median (inter-quartile range, IQR). Statistical comparisons were performed using the Wilcoxon-signed rank test. A $p < 0.05$ was considered significant. The statistical analysis was done by using the IBM SPSS 20.0 (IBM, Chicago, USA).

Results

Altogether 38 patients (age range 43–70 years, 19 females) met the inclusion criteria and were included. Among them, 26 patients were categorized into $BEDQ > 6$ and 12 into $BEDQ \leq 6$. Another 71 asymptomatic controls (ages 19–48; 33 females) were retrospectively evaluated. The distribution of pressure peak in Jackhammer esophagus and normal controls is depicted in Figure 2.

The comparison of the time metrics within all supine swallows between Jackhammer patients and healthy control was shown in Table 1. The patients with Jackhammer esophagus had significantly longer time distance than healthy volunteers ($p < 0.05$). In addition, the healthy controls had very rare instances of negative time distance and the jackhammer patients had statistically significant longer negative time distance sum and events when compared to normal controls ($p < 0.05$). The chaotic ratio was also higher in Jackhammer patients than that in the healthy controls. The comparison of the time metrics of the supine greatest DCI swallows between Jackhammer patients and healthy control was shown in Table 2. Similarly, the patients with Jackhammer esophagus had significantly longer time distance and negative time interval sum than healthy volunteers ($p < 0.05$). The chaotic ratio was again higher in Jackhammer patients than that in the healthy controls.

The time metrics of the first 5 supine swallows and the supine greatest DCI swallows in patients with Jackhammer esophagus were compared based on symptoms scores with $BEDQ > 6$ and $BEDQ \leq 6$ (Tables 3 and 4). The Jackhammer patients with $BEDQ > 6$ had longer negative time distance in the first 5 supine swallows. For the supine greatest DCI swallows,

patients with BEDQ > 6 had longer negative time distance sum, more number of negative time distance events, and higher chaotic ratio when compared with the those patients of BEDQ ≤ 6 . In the first 5 supine swallows 25/38 (65.8%) Jackhammer patients had 2 negative time distance events per swallow compared with only 3/71 (4.2%) controls; $p < 0.001$. In the swallow with greatest DCI, 33/38 (86.8%) Jackhammer patients had 2 negative time distances compared with only 2/71 controls (2.0%); $p < 0.001$.

Clinical profile

The clinical profile was reviewed among all the Jackhammer patients. And 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. There were 25 patients who were on PPI, but only 12 patients had classic reflux symptoms.

Discussion

This study provides evidence that jackhammer esophagus is associated with abnormal propagation of the pressure wave peak despite the fact that jackhammer esophagus is associated with a normal latency interval. We developed novel metrics to determine whether the trajectory of the pressure wave peak is propagating in an ordered time dependent pattern during primary peristalsis. Using the trajectory of the peak along the time axis we were able to show that these events could be quantified by determining the number of negative time events and measuring the sum of these negative time events during the deglutitive window. Our results support that the first peak of the primary peristaltic pressure wave in asymptomatic volunteers is almost always associated with a trajectory that has a positive antegrade axial distance across the time domain. In contrast, we were able to describe abnormal pressure wave peak propagation in jackhammer patients to illustrate disordered contractions within segments 2 and 3 of the peristaltic wavefront by documenting and measuring negative time events. We theorize that jackhammer patients with abnormal pressure wave peak contractions may represent a distinct phenotype of jackhammer more akin to achalasia and distal esophageal spasm.

Normal primary peristalsis is a complicated process that has both central and peripheral control that act independently to control and balance excitatory and inhibitory contractile activity in the esophagus. Peristalsis produces a lumen occluding contraction that propagates down the esophagus at a rate of anywhere from 2.5 to 5 cm per second dependent on location long the esophagus and the velocity and direction of this activity is dependent on coordination of contraction and relaxation. The duration and vigor of the contraction is also mediated by this delicate dual control of contraction and inhibition and velocity and vigor can be altered by a number of other factors ranging from bolus size, temperature and viscosity to position of the patient. Elegant and meticulous studies in both human and animal models have described a model of peristalsis that supports a balance of inhibitory and excitatory activity in peristalsis that is mediated by both central and peripheral neuromuscular control (7,11–13). Although there is still debate regarding the mechanisms that control and modulate this delicate balance, the current pathologic description of

esophageal motor disorders segments patients into those with abnormalities of inhibition, excitation or a combination.

Jackhammer esophagus is a hypercontractile disorder within the Chicago Classification 3.0 based largely on a new metric, the DCI, which measures contractile activity as a function of an integral of the pressure measured across the space time domain of the 2nd and 3rd segments of the contraction wavefront during primary peristalsis. Unfortunately, the classification of abnormal was dependent on an arbitrary cut-off and this measurement largely ignores details of function that may reside deep within the hypercontractile segment. Although the DCI does capture multiple peaks based on its time dependent component, the propagation of the peaks and the varying degrees of post-peak activity have been largely ignored. Recently, we reported that Jackhammer patients have excessive post-peak contractile activity and that symptom severity was associated with more contractile activity in the post-peak phase of contraction (5). We theorized that this was a marker of a defect in the process of post-peak relaxation phase as the muscle should be returning to its relaxed low tension state if no other stimulation, such as swallowing or distention, were occurring during the post-peak phase. Thus, the prolonged post-peak phase could be related to a hyperactive myogenic response related to calcium sensitivity or some unknown or exaggerated trigger that could elicit contraction during the relaxation phase.

The concept that jackhammer esophagus may represent a defect in inhibition despite the prerequisite of having a normal latency interval and LES relaxation is supported by recent investigations of defective deglutitive inhibition in jackhammer. Recently Mauro et al performed an assessment of the response to multiple rapid swallows in jackhammer patients and controls (6). Their results support that abnormal inhibition during MRS was more common in jackhammer patients than controls, but it was not present in all patients. This varying response likely reflects the underlying heterogeneity of this patient group, but it could also support that the defect in inhibition is more peripheral and localized to the enteric nervous system or elicited by the muscle itself. Deglutitive inhibition related to MRS is mediated primarily by a central inhibitory phenomenon and this vagally discharged process is likely intact in many Jackhammer patients as a prerequisite for diagnosis is a normal latency interval.

Our results reporting uncoordinated propagation of the pressure wave peak within the propagating contraction in jackhammer patients suggests that a defect in inhibition may be occurring beyond the latency interval and may be a peripheral defect in the myogenic response. The esophagus responds to distention by contracting above the distending bolus/balloon while relaxing distally to the bolus in order to promote antegrade emptying. This process is facilitated by deglutitive inhibition which allows the bolus to fill the esophagus in a relaxed state, but there is evidence that a second hyperpolarization occurs distinct from the first hyperpolarization associated with swallowing or distention (14). This secondary hyperpolarization is believed to be related to descending inhibitory neurons that are activated by proximal contraction or distention. Many patients with jackhammer have borderline normal latency intervals and a defect in descending inhibitory neurons may present with borderline normal latency and relative deficiencies may account for this uncoordinated response.

Another interesting hypothesis regarding jackhammer esophagus has revolved around the concept that this disease is associated with distorted smooth muscle architecture/hypertrophy or eosinophilic infiltration. It is possible that the uncoordinated activity we have described could be related to regional areas with higher levels of hypercontractile stimuli related to eosinophils and mast cells or potentially a destruction of muscle tissue with regional areas of defective contraction. The esophagus is also responsive to obstruction and it is possible that hypertrophy or altered mechanics of the submucosa and mucosa could elicit a hypercontractile response.

Our study does have limitations in terms of its generalizability and clinic significance. The methodology is relegated to advanced motility centers with expertise in programming beyond the current commercial based software packages and thus, the chaotic ratio and negative time calculation cannot currently be used as a clinical measure. Additionally, we do not fully understand the clinical and pathophysiologic relevance of uncoordinated peak propagation. Much of what we have discussed above is purely speculative and further studies will be required that attempt to interrogate the neurophysiology and molecular basis of this motor disorder.

In conclusion, the trajectory of the pressure wave peak commonly occurred in an uncoordinated fashion, as quantified with the chaotic ratio, in patients with Jackhammer esophagus, but rarely among controls. Furthermore, differences in pressure wave peak propagation was associated with symptom scores among the Jackhammer patients. Jackhammer esophagus is a motor pattern that is not seen in asymptomatic volunteers and is a very heterogeneous disorder that can be found in patients with GERD and a small hernia or stricture, eosinophilic esophagitis, infiltrative disorders and a presentation consistent with a primary motor disorder similar to achalasia and DES. Although these new metrics are helpful in establishing abnormal function, further research will be needed to determine whether uncoordinated peak propagation is clinically relevant and associated with a primary motor issue or an epiphenomenon related to a potential cause.

Acknowledgement

Funding: This work was supported by P01 DK117824 (JEP) from the Public Health service.

Reference

1. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJ, Pandolfino JE; International High Resolution Manometry Working Group. The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterol Motil.* 2015;27(2):160–74. [PubMed: 25469569]
2. Agrawal A, Hila A, Tutuian R, Mainie I, Castell DO. Clinical relevance of the nutcracker esophagus: suggested revision of criteria for diagnosis. *J Clin Gastroenterol.* 2006 7;40(6):504–9. [PubMed: 16825932]
3. Richter JE, Bradley LA, Castell DO. Esophageal chest pain: current controversies in pathogenesis, diagnosis, and therapy. *Ann Intern Med.* 1989; 110:66–78 [PubMed: 2642283]
4. Xiao Y, Carlson DA, Lin Z, Rinella N, Sifrim D, Pandolfino JE. Assessing the pre- and postpeak phases in a swallow using esophageal pressure topography. *Neurogastroenterol Motil.* 2017 9;29(9).
5. Xiao Y, Carlson DA, Lin Z, Alhalel N, Pandolfino JE. Jackhammer esophagus: Assessing the balance between prepeak and postpeak contractile integral. *Neurogastroenterol Motil.* 2018 5;30(5):e13262. [PubMed: 29193439]

6. Mauro A, Quader F, Tolone S, et al. Provocative testing in patients with jackhammer esophagus: evidence for altered neural control. *Am J Physiol Gastrointest Liver Physiol*. 2019 316(3):G397–G403. [PubMed: 30543463]
7. Mittal RK et al. Regulation and dysregulation of esophageal peristalsis by the integrated function of circular and longitudinal muscle layers in health and disease. *Am J Physiol Gastrointest Liver Physiol*. 2016 9 1;311(3):G431–43. [PubMed: 27445346]
8. Taft TH, Riehl M, Sodikoff JB, et al. Development and validation of the brief esophageal dysphagia questionnaire. *Neurogastroenterol Motil*. 2016 12;28(12):1854–1860. [PubMed: 27380834]
9. Ghosh SK, Pandolfino JE, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying esophageal peristalsis with high-resolution manometry: a study of 75 asymptomatic volunteers. *Am J Physiol Gastrointest Liver Physiol*. 2006;290(5):G988–97. [PubMed: 16410365]
10. Clouse RE, Staiano A, Alrakawi A. Topographic analysis of esophageal double-peaked waves. *Gastroenterology*. 2000 ;118(3):469–76. [PubMed: 10702197]
11. Weisbrodt NW, Christensen J. Gradients of contractions in the opossum esophagus. *Gastroenterology* 1972;62(6):1159–1166. [PubMed: 5050313]
12. Mukhopadhyay AK, Weisbrodt NW. Neural organization of esophageal peristalsis: role of vagus nerve. *Gastroenterology* 1975;68(3):444–447. [PubMed: 1120563]
13. Dodds WJ, Christensen J, Dent J, Wood JD, Arndorfer RC. Esophageal contractions induced by vagal stimulation in the opossum. *Am J Physiol* 1978;235(4):E392–E401. [PubMed: 696860]
14. Rattan S, Gidda JS, Goyal RK. Membrane potential and mechanical responses of the opossum esophagus to vagal stimulation and swallowing. *Gastroenterology* 1983;85:922–928. [PubMed: 6884715]

Figure 1: A schematic diagram of the measurement of time distance and negative-time distance. The time distance was calculated as the sum of time interval between pressure wave peaks for each 1-cm axial interval. In swallow A, there is no negative time-value indicating consistent antegrade propagation interval; the negative time distance was 0 seconds and the number of negative time distances was 0 negative. In swallow B, there is a negative time-value (Δt_2) indicating retrograde propagation interval. The negative time distance equaled t_2 and the number of negative time distances was 1.

Figure 2:

The distribution of pressure peak in a Jackhammer swallow with chaotic time distance (A) , a Jackhammer swallow without chaotic time distance (B), a normal swallow (C) and a type III achalasia swallow with $DL < 4.5s$ (D).

Figure 3.

Figure 4.

Table 1

Comparison of esophageal propagation time metrics of median values derived from the first 5 supine swallows between Jackhammer patients and healthy controls. Values represent group median (inter-quartile range)

Group	Jackhammer esophagus	Healthy controls	P-value
Time distance (s)	8.68(7.22–10.41)	5.75(5.01–6.35)	0.000
Negative Time distance (s)	0.18(0.04–0.60)	0.00(0.00–0.05)	0.000
Number of negative time distance	2(1–3)	0(0–1)	0.000
DCI [*] (mmHg●cm●s)	8356(4799–11943)	1526(1066–2120)	0.000
Chaotic ratio	0.10(0.01–0.31)	0.00(0.00–0.00)	0.000

^{*}
DCI: Distal Contractile Integral

Table 2

The comparison of the time metrics of the supine swallow with greatest DCI from each subject between Jackhammer patients and healthy control. Values represent group median (inter-quartile range).

Group	Jackhammer esophagus	Healthy controls	P-value
Time distance (s)	9.07(6.86–13.38)	5.83(5.20–6.71)	0.000
Negative Time distance (s)	0.86(0.15–3.24)	0.00(0.00–.01)	0.000
Number of negative time distance	3(2–4)	0(0–1)	0.000
DCI (mmHg●cm●s)	13766(9745–25997)	1779(1327–2566)	0.000
Chaotic ratio	0.04(0.01–0.09)	0.00(0.00–0.00)	0.000

* DCI: Distal Contractile Integral

Table 3

Comparison of esophageal propagation time metrics of median values derived from the first 5 supine swallows within Jackhammer patients based on symptom score. Values represent group median (inter-quartile range).

Group	Jackhammer BEDQ > 6 (n=26) ¹	Jackhammer BEDQ ≤ 6 (n=12) ¹	P-value
Time distance (s)	9.20(7.23–12.55)	7.87(6.51–9.04)	0.207
Negative Time distance (s)	0.48(0.18–1.09)	0.22(0.00–0.59)	0.049
Number of negative time distance	3(1–4)	2(0–3)	0.093
DCI [*] (mmHg●cm●s)	9470(4896–15796)	7398(4600–9140)	0.114
Chaotic ratio	0.05(0.02–0.13)	0.02(0.00–0.09)	0.155

* DCI: Distal Contractile Integral

Table 4

Comparison of esophageal propagation time metrics of the swallow with greatest DCI from each Jackhammer patient based on symptom score. Values represent group median (inter-quartile range)

Group	Jackhammer BEDQ > 6 (n=26) ¹	Jackhammer BEDQ ≤ 6 (n=12) ¹	P-value
Time distance (s)	8.72(6.69–14.91)	9.36(7.35–10.84)	1.000
Negative Time distance (s)	1.70(0.29–3.51)	0.44(0.07–1.23)	0.028
Number of negative time distance	3(2–5)	3(2–3)	0.146
DCI [*] (mmHg●cm●s)	23323(10565–27285)	10254(9470–13000)	0.004
Chaotic ratio	0.18(0.04–0.45)	0.07(0.00–0.11)	0.045

* DCI: Distal Contractile Integral