J Gastroenterol (2019) 54:1078–1082
https://doi.org/10.1007/s00535-019-01608-3

The Japanese Society of Gastroenterology

ORIGINAL ARTICLE—ALIMENTARY TRACT

Clinical impact of different cut-off values in high-resolution manometry systems on diagnosing esophageal motility disorders

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Received: 11 February 2019 / Accepted: 31 July 2019 / Published online: 6 August 2019

Abstract

Background The values of the parameters in the Chicago classification measured by a high-resolution manometry (HRM) system with the Unisensor catheter (Starlet) are significantly different from those measured by the ManoScan. The contraction vigor is categorized by values of the distal contractile integral (DCI) in the Chicago classification v3.0; however, reference values of the DCI in the Starlet and the clinical impact of the different reference values in the Starlet and ManoScan on diagnosing esophageal motility disorders are not known.

Methods We evaluated data from a previous report in which ManoScan and Starlet were compared in the same subjects. The DCI values in each system were compared and reference DCI values were calculated. Moreover, diagnoses assessed by Starlet using reference values in ManoScan were compared with those using calculated reference values and those assessed by ManoScan.

Results There was a significant positive correlation between the DCI values measured by ManoScan and those measured by Starlet ($r = 0.80$, $p < 0.01$). Based on a linear functional relationship considering measurement errors, the reference DCI values for diagnosing failed, weak and hypercontractile contraction vigor were calculated as 590.6, 1011.3 and 10,085.8 mmHg-s-cm, respectively, in the Starlet. Therefore, the proposed reference values in the Starlet were 500, 1000 and 10,000 mmHg-s-cm, respectively. When the reference values in the ManoScan were used in the Starlet data, approximately 30% of subjects were diagnosed inappropriately. This issue was resolved using the proposed reference values in the Starlet.

Conclusion Recognizing systemic differences in HRM systems is important.

Keywords High-resolution manometry · ManoScan · Starlet · Chicago classification · Reference values

Introduction

High-resolution manometry (HRM) allows us to evaluate esophageal motility more precisely and easier than with conventional manometry. The Chicago classification, which is a systematic classification of esophageal motility disorders, is defined by HRM data [1, 2]. The Chicago classification v3.0 is the latest version and it is widely used to diagnose esophageal motility disorders [3]. In this version, weak peristalsis is defined by values of the distal contractile integral (DCI), while it was defined by the sizes of peristaltic breaks in the previous one (v2.0) [2].

It is known that the values of parameters measured by HRM systems with the Unisensor are significantly different from those measured by the ManoScan [4–6]. We reported

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previously that an HRM system with the Unisensor "Starlet" can assess esophageal motility precisely and as well as the assessment by ManoScan [7]. In that study, values measured by Starlet were also significantly different from those measured by ManoScan, similar to findings in other HRM systems measured with the Unisensor catheter.

However, the reference values of the DCI for diagnosing failed or weak contraction, which have been proposed as 100 and 450 mmHg-s-cm, respectively, in the ManoScan, are not known in the Starlet system. In addition, the reference value for diagnosing hypercontractile contraction in the Starlet also is not known. These reference values are clinically important when esophageal motility disorders are diagnosed using the Chicago classification. Since both ManoScan and Starlet were used for esophageal manometry in the same subjects in the previous study, these data should allow us to calculate these reference values.

Thus, the aims of the present study were to calculate the reference values of the DCI in Starlet to diagnose esophageal motility disorders with this instrument and to reveal a potential clinical impact of using improper reference values when using ManoScan or Starlet to diagnose esophageal motility disorders.

Materials and methods

Subjects

A total of 103 volunteers were recruited for the study [7]. None of the subjects had gastrointestinal disease or a history of surgery in the gastrointestinal tract. Symptoms were evaluated using FSSG [8]. The study was conducted in accordance with the amended Declaration of Helsinki and the protocol was approved by the Ethics Committee of the National Hospital Organization Numata National Hospital, Gunma University Hospital and Nippon Medical School Chiba Hokusou Hospital. Written consents were obtained from all subjects. This study was registered at the University hospital Medical Information Network (UMIN) center. The registration identification number is UMIN000011464.

Esophageal manometry

ManoScan (Medtronic, Minneapolis, MN, USA) and Starlet (Star Medical, Inc., Tokyo, Japan) were used for esophageal manometry. Before the recording, the transducers were calibrated by the manufacturers. The nasal passage was anesthetized with 2% lidocaine jelly. The manometric assembly was passed trans-nasally and positioned to record from the hypopharynx to the stomach. After catheters were positioned, 10 5-ml water swallows were performed.

Study protocol

Esophageal manometry was performed on all study subjects, except one, using both ManoScan and Starlet. Esophageal manometry was performed on one half of the subjects using ManoScan, and then it was repeated using Starlet with one-hour intervals. On the other half of the subjects, Starlet was used prior to ManoScan. The order of performance of the two esophageal manometry studies was random.

Data analysis

Manometric data obtained by ManoScan were analyzed using ManoView version 3.0 (Medtronic, Minneapolis, MN, USA). First, data were corrected for the thermal sensitivity of the pressure-sensing elements using the thermal compensation function of ManoView. The esophago-gastric junction (EGJ) pressure was outlined with the eSleeve tool, which selects among sensors within a rectangle and drives a sleeve-type tracing of maximal pressure.

Manometric data obtained by Starlet were analyzed using special software (Star Medical, Inc., Tokyo, Japan). The software has a function that is similar to the eSleeve function. In addition, the software is able to calculate parameters defined by the Chicago classification. The latest version of the software was used which can calculate the DCI appropriately.

Diagnoses using the Chicago classification

EGJ pressures were referenced to gastric pressure whereas esophageal contraction parameters were referenced to atmospheric pressure. Distal latency (DL) was defined as the interval between upper esophageal sphincter (UES) relaxation and the contractile deceleration point (CDP), which is the inflection point along the 30 mmHg isobaric contour where propagation velocity slows, demarcating the tubular esophagus from the phrenic ampulla. The distal contractile integral (DCI) was calculated by multiplying the length of the smooth muscle esophagus by the duration of propagation of the contractile wave front and the mean pressure in the entire box excluding pressures below 20 mmHg. Integrated relaxation pressure (IRP) was measured at the lowest 4-s cumulative pressure values that occurred during a 10-s postdeglutition time window in the electronically generated e-sleeve signal through the anatomic zone defining the EGJ. All parameters were calculated by both analysis programs automatically and all study data were checked manually by the principal investigator (SK).

Esophageal motility was diagnosed according to the Chicago classification v3.0 [3]. The cut-off values proposed in the Chicago classification v3.0 were defined by the ManoScan data. To clarify the clinical importance of differences in cut-off values between ManoScan and Starlet the cut-off values with ManoScan were used to diagnose esophageal motility in the Starlet, and then the cut-off values calculated in the present study were used to re-diagnose esophageal motility.

Statistical analysis

The mean DCI value of ten water swallows was calculated in each study. The relationship between the DCI values of ManoScan and Starlet was analyzed by regression analysis. In addition, the cut-off values for the DCI in the Starlet were calculated by a linear structural relationship analysis considering measurement errors. Differences were regarded as statistically significant at $p < 0.05$. The statistical analyses in the study were performed using SigmaPlot 12.5 (Systat Software Inc., San Jose, CA, USA) and JMP (SAS Institute Japan Ltd., Tokyo, Japan).

Results

One patient could tolerate the esophageal manometry using Starlet, but she preferred not to undergo the second manometry. Two patients were excluded from the analyses because the esophageal manometry with ManoScan was finished before the catheter was removed, which did not allow us to apply thermal compensation. Three subjects had reflux symptoms assessed by FSSG and these subjects were excluded from analyses. Thus, data from 97 subjects [four females with a median (interquartile range) age of 43 (32–50) years] were used in the present study.

Reference values in parameters defined by the Chicago classification

There was a significant positive correlation between the DCI values measured by ManoScan and those measured by Starlet ($r = 0.80$, $p < 0.01$, Fig. 1). Since there was a proportional bias according to the Bland–Altman plot [7], cut-off values of the DCI in the Starlet were calculated with a linear functional relationship analysis considering measurement error in the present study. The reference DCI values in the Chicago classification for diagnosing failed, weak and hypercontractile contraction vigor (100, 450 and 8000 mmHg-s-cm, respectively) were calculated as 590.6, 1011.3 and 10,085.8 mmHg-s-cm, respectively, in the Starlet (Fig. 1). Therefore, the reference values of DCI in the Starlet were proposed as 500, 1,000 and 10,000 mmHg-s-cm, respectively.

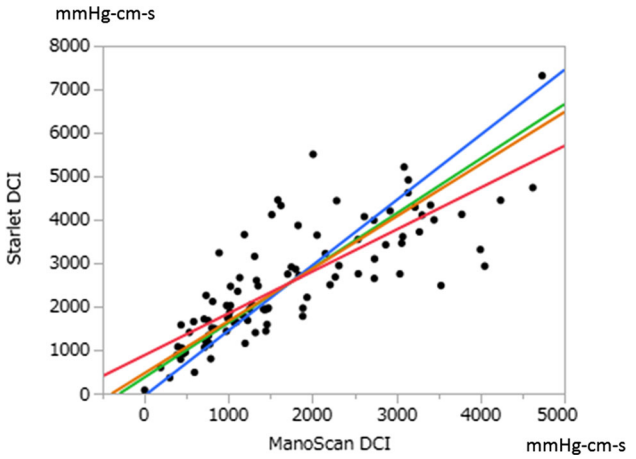

Fig. 1 Correlation between DCI values measured by ManoScan and those measured by Starlet. There was a linear correlation between the DCI values in ManoScan and Starlet. The blue line represents predicted values of ManoScan based on those from Starlet. The red line represents predicted values of Starlet based on those from ManoScan. Since there was a proportional bias between the two value sets, the blue line was not consistent with the red line. The green line represents a linear functional relationship, if the variances of the two value sets were equal. The yellow line represents a linear functional relationship considering measurement errors

The normal value of the IRP was reported previously, and the proposed cut-off value was 26 mmHg. Although DL was also significantly different between ManoScan and Starlet in the previous study, the values were similar. Therefore, the cut-off value of the DL in the Starlet could be the same value as that in the ManoScan. The value of DCI for evaluating small peristaltic breaks was proposed as 25 mmHg in the previous study. The proposed reference values in the Starlet are shown in Table 1.

Clinical impact of different cut-off values in diagnosing esophageal motility disorders

The diagnoses of esophageal motility in 97 subjects assessed by ManoScan are shown in Table 2. When esophageal motility measured by Starlet was diagnosed using the cut-off values for ManoScan, many subjects were diagnosed as esophago-gastric junction (EGJ) outflow obstruction. Moreover, 50% of subjects with ineffective esophageal motility (IEM) were not diagnosed as IEM due to higher DCI values in Starlet than those in ManoScan. When esophageal motility measured by Starlet was diagnosed using the proposed reference values, diagnoses of esophageal motility in Starlet were much more consistent with those measured in ManoScan.

Table 1 Proposed reference values of parameters in Starlet

	ManoScan	Starlet
Contraction vigor		
Failed	DCI < 100 mmHg-s-cm	DCI < 500 mmHg-s-cm
Weak	DCI > 100 mmHg-s-cm, but < 450 mmHg-s-cm	DCI > 500 mmHg-s-cm, but < 1000 mmHg-s-cm
Normal	DCI > 450 mmHg-s-cm, but < 8000 mmHg-s-cm	DCI > 1000 mmHg-s-cm, but < 10,000 mmHg-s-cm
Hypercontractile	DCI ≥ 8000 mmHg-s-cm	DCI ≥ 10,000 mmHg-s-cm
Contraction pattern		
Premature	DL < 4.5 s	DL < 4.5 s
Fragmented	Large break in the 20 mmHg isobaric contour with DCI > 450 mmHg-s-cm	Large break in the 25 mmHg isobaric contour with DCI > 1000 mmHg-s-cm

DCI distal contractile integral, *DL* distal latency

Table 2 Diagnoses of esophageal motility based on different cut-off values

Diagnosis	ManoScan	Starlet	
	Using reference values in the ManoScan	Using reference values in the ManoScan	Using proposed reference values in this study
EGJ outflow obstruction	9	32	4
Absent contractility	1	0	1
DES	2	0	0
IEM	6	3	9
Fragmented peristalsis	0	0	0
Normal esophageal motility	79	62	83

EGJ esophago-gastric junction, *IEM* ineffective esophageal motility

Discussion

The present study shows the importance of using the appropriate reference values in each HRM system. If a wrong cut-off value is used, it could lead to a wrong diagnosis and treatment. When the cut-off values in ManoScan were used in Starlet, approximately 30% of the subjects were diagnosed incorrectly. This problem could be solved using the proposed reference values for the Starlet.

It is clinically important to reveal the cut-off values for the parameters used in the Chicago classification. Normal values of each parameter were shown, but cut-off values for the DCI were not shown in the previous study. Since weak or hypercontractile esophageal contractions are defined by the DCI values in the latest version of the Chicago classification, the cut-off values for the DCI are very important. ManoScan and Starlet were used in the same subjects to evaluate their esophageal motility in our previous study, which allowed us to estimate these values by a statistical calculation. Thus, based on the findings in the present study, Starlet can be used to evaluate esophageal motility with the latest version of the Chicago classification when the proper DCI values are used.

The methods for measuring pressure in these two systems are different. These differences between the two systems may produce differences in the DCI values. We performed a bench test to confirm the accuracy of pressure sensors in each system. When the catheter was placed in a pressure chamber without touching the wall of the chamber and pressure was applied to the chamber, these two systems showed the same pressure. Therefore, differences in the pressure measuring methods are not a major cause of different measured values. The reference values for IRP in systems with the Unisensor catheter are similar and are significantly higher than the reference value for IRP in ManoScan. Thus, we speculate that the difference in pressure values is caused by the differences of catheters. For example, differences in stiffness or diameter of catheter may be responsible for the different values.

There were several limitations in the study. First of all, the study subjects were asymptomatic subjects. There were only six subjects with IEM and only one subject with

absent contractility, when ManoScan was used. Although there were 46 weak and 26 failed swallows evaluated by ManoScan, the number of subjects with IEM or absent contractility may not be sufficient to confirm the proposed cut-off values. In addition, there was no subject with a Jackhammer esophagus. A further study in which many patients with IEM or Jackhammer esophagus are enrolled is necessary to confirm that these cut-off values are appropriate. There is a similar limitation in evaluating the reference value of the DL. Although there was not a proportional bias in the DL analysis in the previous report, there were quite a few premature contractions in the ManoScan data. Therefore, the cut-off value of the DL should be confirmed in a future study in which many patients with distal esophageal spasm are enrolled. Second, diagnoses of esophageal motility evaluated by the Starlet were not completely matched to those by the ManoScan. It is known that some patients with EGJ outflow obstruction do not have impaired EGJ relaxation, which means apparent high IRP values. Since the study subjects in the present study were asymptomatic, some subjects with EGJ outflow obstruction diagnosed by ManoScan may have normal esophageal motility. Finally, these reference values should be confirmed by evaluating patients' symptoms as well as esophageal motility.

Conclusions

It is important to recognize differences in reference values between HRM systems. Appropriate reference values in each HRM system should be used to diagnose esophageal motility disorders using the Chicago classification. The proposed reference values of the DCI in starlet are relevant.

Acknowledgements The English language was reviewed by a native English speaker (NAI Inc., Tokyo, Japan).

Author contributions SK was responsible for study concept and design, revision and drafting the manuscript, acquisition of data at the National Hospital Organization Numata National Hospital and at the Gunma University Hospital, analysis and interpretation of data, and statistical analysis. KI was responsible for acquisition of data at the Nippon Medical School Chiba Hokusoh Hospital, revision of the manuscript. AK, HH and YS were responsible for acquisition of data at the Gunma University Hospital. NK, SH and NT were responsible for acquisition of data at the Nippon Medical School Chiba Hokusoh Hospital. OK and TU were responsible for advising on the study concept and design. MK was responsible for organizing the study team, study concept and design, revision of the manuscript.

Funding There was no financial support for this study. The data from the previous study, which was supported by Star Medical Inc., were used in the present study.

Compliance with ethical standards

Conflicts of interest In the previous study, the HRM systems were provided by Star Medical Inc. All authors declare that they have no conflict of interest.

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