J Neurogastroenterol Motil, Vol. 26 No. 1 January, 2020
pISSN: 2093-0879 eISSN: 2093-0887
https://doi.org/10.5056/jnm19082
Journal of Neurogastroenterology and Motility

Original Article

Normative Values for Esophageal Motility Assessed in the Physiological Seated Position for 16-Channel Water Perfused High-resolution Esophageal Manometry System and Postural Variations in Healthy Volunteers

Melpakkam Srinivas,[1]* Mayank Jain,[1] Piyush Bawane,[1] and Venkataraman Jayanthi[1,2]

[1]GI Motility Unit, Gleneagles Global Health City, Chennai, India; and [2]Sri Ramachandra Institute of Higher Education and Research, Chennai, India

Background/Aims
Consensus guidelines for performance and analysis of high-resolution esophageal manometry (HREM) recommend use of equipment, population and posture specific normative values. To provide normative values for Chicago classification (CC) metrics in the physiological seated position for a 16-channel water perfused system (Dentsleeve HREM catheter, Advanced Manometry Systems, Melbourne, Australia) widely used in India and other countries with limited access to solid-state equipment. The results are compared with published CC metrics in supine position done using the same system and volunteers.

Methods
HREM tracings of ten 5 mL water swallows in sitting posture were acquired in healthy volunteers and normative values for CC version 3.0 metrics calculated. Individual swallows were paired with previously reported supine swallows for postural variations (Wilcoxon sign rank test) and concordance of CC diagnoses (Pearson coefficient).

Results
Analysis of 530 sitting posture water swallows (53 subjects) and comparison with their supine data revealed significantly higher integrated relaxation pressure (IRP; median 6.7 mmHg vs 6.1 mmHg) but lower distal latency (DL; mean 6.3 seconds vs 6.8 seconds) and distal contractile integral (DCI; mean 1224 mmHg·sec·cm vs 1456 mmHg·sec·cm). Sitting posture normal was defined as: IRP < 13.9, DL > 4.5, and DCI = 115-4500 (absent contractility: DCI < 30). CC diagnoses concordance using posture-specific cut-offs was moderate (k = 0.47).

Conclusions
This paper provides normative values for the Advanced Manometry Systems 16-channel water perfused system in the physiological seated position for CC metrics. Our findings of higher IRP and lower DCI in sitting posture than previously reported supine CC cut-offs, confirm the need to use posture-specific cut-offs for reporting HREM tracings.
(J Neurogastroenterol Motil 2020;26:61-66)

Key Words
Healthy volunteers; India; Normal values; Posture; Water perfused manometry

Received: April 15, 2019 Revised: August 4, 2019 Accepted: September 20, 2019

*Correspondence: Melpakkam Srinivas, MRCP(UK)
GI Motility Unit, Gleneagles Global Health City, Chennai 600100, India
Tel: +91-8056069164, E-mail: drsrinivasm@hotmail.com

Introduction

High-resolution esophageal manometry (HREM) is conventionally performed in the supine position to assess esophageal motility. The tracings are interpreted using objective metrics (integrated relaxation pressure [IRP], distal contractile integral [DCI], distal latency [DL], and peristaltic break size) to derive an algorithmic diagnosis called Chicago classification (CC), currently in its third iteration.[1] These metrics have been validated against independent physiological measurement (eg, contrast swallow) and revised by comparison with data from patients with achalasia, spasm, and other defined motility disorders. The "normal" values for the above metrics are based on data from Western populations in supine posture using solid state catheters. We have recently reported CC metric cut-offs for supine posture in Indian volunteers using a 16-channel water perfused HREM system[2] (Dentsleeve HREM catheter, Advanced Manometry Systems [AMS], Melbourne, Australia) that is widely used in India and other countries with limited access to solid-state equipment.

Although the test is routinely performed in the supine posture, patients are more likely to eat and drink in the physiological, upright seated position. The esophagus and adjacent structures such as the crural diaphragm are influenced by the change in body position.[3] It is known that the raised intragastric pressure in Trendelenburg and supine positions is countered by increase in lower esophageal sphincter (LES) pressure to prevent reflux of gastric contents.[4] The workload necessary to transport the bolus decreases in the upright position due to gravitational influence, resulting in lesser esophageal contraction amplitude in the sitting than the supine posture.[3,5,6] Further, artifacts caused by cardiac compression may be less frequent in the upright position.[7]

Based on these, consensus guidelines[1,8] for the performance and analysis of HREM recommend that normative values specific for manometry equipment and posture should be applied.

The present study aims to determine the normative CC metric values for evaluating esophageal motility in the sitting posture using CC metrics algorithm, with the 16-channel water perfused HREM AMS system. We also compared the previously reported supine swallows with the sitting swallows performed in the same volunteers using the same system for postural variations.

Materials and Methods

This prospective study done in a specialist referral center in Chennai (South India) consisted of healthy volunteers recruited by word of mouth from amongst hospital employees and non-hospital volunteers. Health was based on vetting by history of symptoms and medication use.

Only those aged between 18 years and 60 years with no other illnesses, gastrointestinal symptoms, or regular medications were included after obtaining informed consent for study participation and undergoing the test. Baseline information on age, gender, and body mass index (BMI) was collected. The same volunteers had also done the test in the supine posture, based on which supine normative values were previously reported by us.[2]

High-resolution Esophageal Manometry

A 16-channel 3.5 mm diameter silicone Dentsleeve HREM catheter with the lower 8 sensors placed 1 cm apart and the rest 3 cm apart covering a total length of 31 cm was used for all studies. This was water perfused at 0.15 mL/minute/channel using the AMS system. Transpac IV transducer and Trace 1.3.3 software developed and supplied by Geoff Hebbard of AMS systems were used to acquire and report the studies.

As applied in previous upright posture studies,[9,10] zero calibration was done in water and with the catheter lifted vertically before placement in the subject's esophagus via the right nostril in the sitting posture. After ensuring that at least one channel was below the LES, the baseline was set again to correct for hydrostatic pressure artifacts in the upright position and the catheter secured at the nose with adhesive tape. The perfusion system and patient's thorax were at the same level throughout the study.

All studies were performed after volunteers fasted for at least 6 hours (majority had an overnight fast). A standard protocol of 10 × 5 mL water swallows in the sitting posture (90° angle) was followed for all studies. When artifacts occurred, additional swallows were performed until a minimum of 10 reportable swallows were recorded for each subject. All tracings were manually marked by either of the first two investigators (M.S. or M.J.), interpreted using software Trace 1.3.3 and reported as per CC version 3.0 diagnoses. The reading protocol had been standardized between the 2 readers to achieve > 90% concordance as part of clinical governance standards in routine clinical care.

The basal LES pressure in inspiration and expiration, HREM metrics namely IRP, DCI, DL, and peristaltic break divided as proximal (break of any size involving Segment 1 [S1]) and distal (break of any size involving either or both Segments 2 and 3 [S2 and S3]; but not Segment 1) were recorded in an Excel worksheet.

The sitting posture data was analyzed to identify the various

percentiles (5, 10, 25, 50, 75, 95, and 99) and ranges for all CC metrics. Normative cut-off values in the sitting posture were derived by the same method used by us to report supine normative values as follows: IRP (less than 95th percentile), DL (Minimum value), DCI (10th-100th percentile: normal; > 100th percentile jackhammer esophagus; 5th-10th percentile: ineffective esophageal motility [IEM]; and < 5th percentile: absent contractility), and peristaltic break (≤ 5 cm and > 5 cm by segment: proximal or distal). The value reported in the supine posture was retained as normative cut-off in the sitting posture, if the difference between the two was < 5%.

We also studied the relationship between the peristaltic pattern (break size) and contractile vigor (DCI) to test if DCI is a surrogate of break size. The breaks were categorized as ≤ 5 cm and > 5 cm using DCI cut-offs for normal, IEM, and absent contractility.

Postural comparison of all the HREM metrics for individual swallows in all 53 volunteers (previously reported supine versus present study's sitting data) and CC diagnoses by posture-specific cut-offs for concordance were also studied.

Statistical Methods

Age and BMI were reported as mean, standard deviation, and range. Gender was expressed as numbers. Influence of these parameters on IRP, DCI, and DL was evaluated using Pearson coefficient test. Percentiles were reported for all the CC metrics as described above. Comparison of supine and sitting posture swallows was done using Wilcoxon sign rank test or Mann Whitney *U* test as appropriate ($P < 0.05$ deemed significant). Kappa coefficient was used to test for concordance between CC diagnoses using specific cut-offs by posture.

Institutional Ethics Committee approved the study (IRB No. HR/2015/MS/004).

Results

Fifty-three volunteers who underwent the procedure in the sitting posture were included for analysis (530 swallows). None had any procedure related complications.

The cohort included 31 men and the mean age and BMI were 30 years (SD, 6.7; range, 21-51) and 24.2 kg/m^2 (SD, 3.6; range, 17.2-32.8) respectively. Gender, age and BMI had weak or no correlation with IRP, DCI or DL (Pearson correlation coefficient ranging from −0.28 to +0.24).

Normative Values in Sitting Posture

The percentiles of the various HREM metrics in sitting posture are as reported in Table 1. Peristaltic breaks were more common in the proximal segment than distal (41% versus 28%). Only 16% proximal breaks and 9% distal breaks were > 5 cm size with proximal breaks being larger than distal ones (maximum size 21 cm versus 15 cm).

The cut-offs for CC parameters in the sitting posture for normal and abnormal CC diagnoses using the percentiles described in Methods are as shown in Table 2. Since the minimum DL and maximum DCI values were within 5% of corresponding normative values in the supine posture,[2] the supine DL and upper limit of DCI were retained as normal values in the sitting posture (4.5 seconds and 4500 mmHg·sec·cm, respectively). Peristaltic break size cut-off was retained at 5 cm as > 90% sitting posture swallows had breaks ≤ 5 cm.

Contraction vigor (DCI) and pattern (breaks) showed good correlation with larger breaks strongly associated with lower DCI. DCI < 30 was associated with 100% large breaks (> 5 cm); in-

Table 1. Percentiles for High-resolution Esophageal Manometry Parameters in 530 Swallows of 53 Healthy Volunteers in Sitting Posture

Metric	Median	Range	Percentile					
			5	10	25	75	95	99
Basal LES pressure (mmHg)								
Inspiration	35	8-83	15.2	18.4	25.0	46.0	68.8	79.4
Expiration	13	0-45	5.6	7.0	10.0	18.0	30.4	37.7
4s-IRP (mmHg)	6.7	0-20.6	2.1	2.9	4.6	9.5	13.9	16.8
DL (sec)	6.2	4.4-12.4	4.9	5.1	5.5	7.0	8.2	9.7
DCI (mmHg·sec·cm)	999	0-4600	31	115	468	1729	3140	4454
Breaks (cm)								
Proximal	0	0-21	0.0	0.0	0.0	2.5	15.5	17.0
Distal	0	0-15	0.0	0.0	0.0	1.0	8.0	12.7

LES, lower esophageal sphincter; 4s-IRP, 4-second integrated relaxation pressure; DL, distal latency; DCI, distal contractile integral.

volving the proximal segment in majority (85%). In IEM (DCI 30-115), 27 (93%) had large breaks with 63% of them occurring in the proximal segment. With normal DCI (115-4500), almost 90% breaks were < 5 cm. Large breaks were almost equally distributed between the 2 segments (10% and 7%).

Postural Variations in Chicago Classification Metrics

Although normative cut-offs for CC metrics in the sitting posture needed changes only in IRP (higher) and DCI (lower for lower limit of normal), the 3 CC metrics (ie, IRP, DL, and DCI) varied significantly by posture on comparing individual swallows (Table 3). While DL ($P < 0.001$) and DCI ($P < 0.001$) were higher in supine swallows, the IRP was higher ($P < 0.001$) in the sitting posture. Distal peristaltic breaks tended to be larger during sitting with no significant difference between the postures for proximal breaks and basal LES pressure.

Applying the sitting posture cut-offs reported in this study to the HREM tracings of the healthy volunteers, 41 were normal, 5 IEM, 6 failed peristalsis, and 1 esophagogastric junction outflow obstruction. Comparison with the supine study diagnoses using posture-specific cut-offs in the same 53 volunteers revealed only moderate concordance between postures for CC diagnoses (Table 4), suggesting the need to use separate cut-offs for reporting supine and sitting swallows. More volunteers were categorized as normal in the supine posture compared to sitting (44 versus 41).

Discussion

This study provides normal metrics for the Dentsleeve HREM catheter and 16-channel AMS water perfused system in the physiological seated position. The findings indicate higher IRP and lower DCI in the upright compared to the supine position. This confirms that measurements should be reported using posture-specific cut-off values.

As previously done in our report on normative values in supine posture,[2] we defined normal DCI from 10th-100th percentile and applied the entire 10 percentiles for the diagnoses in the hypoperistaltic end. This arbitrary change was done due to CC version 3.0 making 100th percentile the upper limit of normal (from 95th percentile) and increasing the number of peristaltic disorders at the hypoperistaltic end (IEM, fragmented peristalsis and absent contractility). This is vindicated by evidence of good demarcation

Table 2. Suggested Cut-offs for Chicago Classification Metrics in Sitting—Normal and Abnormal

CC parameter (10 swallows)	Normal	Esophageal motility disorders (CC v3.0)
IRP (median, mmHg)	< 13.9	Achalasia/EGJOO> 13.9
DL (sec)	< 4.5	DES < 4.5 (≥ 20% swallows)
DCI (mmHg·sec·cm)	115-4500	IEM < 115 (≥ 50% swallows)
		Absent contractility < 30 (100% swallows)
		Jackhammer > 4500 (≥ 20% swallows)
Peristaltic break (cm)	≤ 5	Fragmented peristalsis > 5 (≥ 50% swallows)

CC v3.0, Chicago classification version 3.0; DL, distal latency; DCI, distal contractile integral; EGJOO, esophagogastric junction outlet obstruction; DES, diffuse esophageal spasm; IEM, ineffective esophageal motility.

Table 3. Comparison of Swallows in Healthy Volunteers by Posture

No. of swallows (530 each)	Supine[2]	Sitting	*P*-value
Basal LES pressure (median [5th-95th percentile])			
Inspiration	36 (13.6-74.8)	35 (15.2-68.8)	0.950
Expiration	13 (4.4-37.6)	13 (5.6-30.4)	0.530
IRP (median [range])	6.1 (0.0-23.9)	6.7 (0.0-20.6)	< 0.001
DL (mean ± SD [SEM])	6.8 ± 1.0 (0.04)	6.3 ± 1.1 (0.06)	< 0.001
DCI (mean ± SD [SEM])	1456 ± 975 (42)	1224 ± 1026 (44)	< 0.001
Peristaltic break size (< 95th percentile)			
Proximal	< 14.0 cm	< 15.5 cm	0.420
Distal	< 5.0 cm	< 8.0 cm	< 0.001

LES, lower esophageal sphincter; IRP, integrated relaxation pressure; DL, distal latency; DCI, distal contractile integral.

of large peristaltic breaks between the 3 DCI categories ie, normal (17%), ineffective motility (93%), and absent contractility (100%).

Postural Variations in Chicago Classification Metrics in Healthy Volunteers Using Different High-resolution Esophageal Manometry Systems (See Table 5)

Studies on normative values and postural variations in HREM metrics using water perfused systems do not exist in the literature. A study on the effects of tegaserod on esophageal function in healthy volunteers provides some data on supine and sitting metrics using a 32-channel water perfused catheter.[10] Similar to our study, in the 17 subjects studied, they reported no postural variations in LES pressure but a reduction in DCI in the sitting compared to supine positions. However, no data on any of the other currently used HREM metrics were provided.

Previous studies using solid state systems in healthy volunteers have reported lower DCI (and therefore larger breaks, where reported) in the sitting posture; however, there are conflicting reports of postural variations in IRP and DL (Table 5). Xiao et al[11] studied 75 healthy volunteers with 120 patients in the upright and supine positions and reported that in the sitting posture IRP and DCI decreased but DL slightly increased in both groups. However, the sitting swallow data was based on only 5 water swallows per volunteer and the sitting angle ranged between 75 to 90 degrees. A recent Thailand study using a similar catheter reported a similar change to IRP but the DL was unaffected by posture.[12] Similar to our study, they reported no effect of age, gender, and BMI on the metrics.

In routine clinical practice, motility units use sitting posture swallows only as an adjunct to the standard supine test. However, studies done so far in healthy volunteers and patients suggest significant variations in HREM metrics between supine and sitting, irrespective of the system used. This confirms that supine cut-offs cannot be applied without adjustment to report sitting posture studies; hence the need to apply specific CC cut-offs for sitting posture.

All previous healthy volunteer studies in the sitting posture have only reported generic values like median, inter-quartile range, 5th-95th percentile without attempting to give specific cut-offs for various CC diagnoses. We have taken small steps in this direction by pragmatically deriving CC diagnoses-specific cut-offs for sitting posture, extrapolating the initial extensive work done correlating HREM metrics with conventional pressure tracing values to establish the supine normal percentile definitions. We hope that further studies on healthy volunteers and patient populations will follow to validate or modify these cut-offs.

The limitations of our study include lack of subjects in extremes of age and the inability to test our cut-offs relative to a gold standard (like the CC values developed for supine using solid state systems).

Table 4. Concordance Between Supine and Sitting Chicago Classification Diagnosis Using Posture-specific Cut-offs

Supine CC	N	Sitting CC				
		Normal	IEM	FP	EGJOO	Kappa
Normal	44	38	1	4	1	0.47 (moderate)
IEM	2	1	1	-	-	
FP	6	1	3	2	-	
EGJOO	1	1	-	-	-	

CC, Chicago classification; IEM, ineffective esophageal motility; FP, fragmented peristalsis; EGJOO, esophagogastric junction outlet obstruction.

Water Perfused High-resolution Esophageal Manometry and Sitting Posture Study

Comment is required regarding the impact of hydrostatic ef-

Table 5. Comparison Between Studies on Postural Variations in High-resolution Esophageal Manometry

Country	System	n	Sitting vs Supine				
			Basal	IRP	DCI	DL	Breaks
UK[10]	36-ch wp	17	Same	-	Lower	-	-
UK[6]	36-ch ss	23	-	Higher	Lower	-	Larger
USA[11]	36-ch ss	75	-	Lower	Lower	Higher	-
Thailand[12]	36-ch ss	41	Lower	Lower	Lower	Same	Larger (TZ)
India[a]	16-ch wp	53	Same	Higher	Lower	Lower	Larger (proximal)

[a]The present study.

IRP, integrated relaxation pressure; DCI, distal contractile integral; DL, distal latency; UK, United Kingdom; USA, United States of America; 36-ch wp, 32-channel water perfused; 36-ch ss, 32-channel solid state; TZ, transition zone.

fects on calibration and measurement in the seated position using the water perfused HREM system. In this study, baseline "zero" calibration was performed prior to insertion with the catheter suspended vertically. Alternatively, if this is not done, a software correction for hydrostatic pressure effects can be applied in the AMS analysis program.[9] Both approaches have been applied successfully in previous studies using water perfused technology (Personal communication, Mark Fox a co-author of the Chicago classification). It remains important to maintain the patient in a constant position, ideally with the patient's thorax level with the perfusion system as was done in this study.

In conclusion, we report normative data in the sitting posture and cut-off values for major and minor CC diagnoses for a 16-channel water perfused HREM system. Compared to measurements acquired in the supine position from the same volunteers, the IRP was higher and lower limit of DCI lower in the sitting posture. Application of appropriate cut-offs results in only moderate concordance for CC diagnoses, especially ineffective motility, between the 2 postures in healthy volunteers. This highlights the need to use system and posture-specific cut-offs when reporting HREM. Further validation of these cut-offs is required in patient populations.

Acknowledgements: We thank Mr. Tom Michael, Research Assistant for help with data entry and Prof. Mark Fox for critical review and valuable suggestions provided prior to submission of the manuscript. We are most grateful and appreciative of all the healthy volunteers who made this study possible.

Financial support: We are extremely grateful to the Tamilnadu Gastroenterologist Trust for supporting us with a research grant (TGT/001).

Conflicts of interest: None.

Author contributions: Melpakkam Srinivas and Venkataraman Jayanthi: study concept and design; Melpakkam Srinivas, Mayank Jain, Piyush Bawane, and Venkataraman Jayanthi: study performance; and Melpakkam Srinivas, Mayank Jain, and Piyush Bawane: manuscript drafting and review.

References

1. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27:160-174.
2. Srinivas M, Jain M, Bawane P, Jayanthi V. Chicago classification normative metrics in a healthy Indian cohort for a 16-channel water-perfused high-resolution esophageal manometry system. Neurogastroenterol Motil 2018;30:e13386.
3. Roman S, Damon H, Pellissier PE, Mion F. Does body position modify the results of oesophageal high resolution manometry? Neurogastroenterol Motil 2010;22:271-275.
4. de Leon A, Thörn SE, Ottosson J, Wattwil M. Body positions and esophageal sphincter pressures in obese patients during anesthesia. Acta Anaesthesiol Scand 2010;54:458-463.
5. Bernhard A, Pohl D, Fried M, Castell DO, Tutuian R. Influence of bolus consistency and position on esophageal high-resolution manometry findings. Dig Dis Sci 2008;53:1198-1205.
6. Sweis R, Anggiansah A, Wong T, Kaufman E, Obrecht S, Fox M. Normative values and interobserver agreement for liquid and solid bolus swallows in upright and supine positions as assessed by esophageal high-resolution manometry. Neurogastroenterol Motil 2011;23:509-e198.
7. Babaei A, Mittal RK. Cardiovascular compression of the esophagus and spread of gastro-esophageal reflux. Neurogastroenterol Motil 2011;23:45-51, e3.
8. Fox MR, Bredenoord AJ. Oesophageal high-resolution manometry: moving from research into clinical practice. Gut 2008;57:405-423.
9. Fox M, Hebbard G, Janiak P, et al. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. Neurogastroenterol Motil 2004;16:533-542.
10. Fox M, Menne D, Stutz B, Fried M, Schwizer W. The effects of tegaserod on oesophageal function and bolus transport in healthy volunteers: studies using concurrent high-resolution manometry and videofluoroscopy. Aliment Pharmacol Ther 2006;24:1017-1027.
11. Xiao Y, Read A, Nicodème F, Roman S, Kahrilas PJ, Pandolfino JE. The effect of a sitting vs supine posture on normative esophageal pressure topography metrics and Chicago classification diagnosis of esophageal motility disorders. Neurogastroenterol Motil 2012;24:e509-e516.
12. Hiranyatheb P, Chakkaphak S, Chirnaksorn S, Lekhaka P, Petsrikun K, Somboonpun K. Normal values of high-resolution manometry in supine and upright positions in a Thai population. Dig Dis Sci 2018;63:173-183.