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The effects of different postures and provocative swallow materials on the normative Chicago 3.0 metrics in a healthy Asian population

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Key words

Asian, body position, Chicago classification, high-resolution esophageal manometry, Malay, solid, viscous.

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Author contribution: MRMS performed the esophageal manometry tests, analyzed the manometric data, and drafted the manuscript. YYL, NCS, and WZ were involved with study design, analyzed the manometric data, supervised the study, and drafted and revised the manuscript. RAR and RARA provided intellectual contributions. The final version of the article was approved by all authors.

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Introduction

Study of esophageal function has greatly evolved since high-resolution multichannel solid-state manometry and impedance were introduced approximately three decades ago.¹ The real-time pressure topography in combination with bolus impedance allows a detailed assessment of sphincters, peristalsis, and bolus characteristics. Esophageal manometry is considered the

Abstract

Background and Aim: Variations in the Chicago 3.0 normative metrics may exist with different postures and with different provocative swallow materials in a healthy Asian population.

Method: Eligible healthy Malay volunteers were invited to undergo the high-resolution esophageal manometry (inSIGHT Ultima, Diversatek Healthcare, Milwaukee, WI, USA). In recumbent and standing positions, test swallows were performed using liquid, viscous, and solid materials. Metrics including integrated relaxation pressure 4 s (IRP-4 s, mmHg), distal contractile integral (DCI, mmHg s cm), distal latency (DL, s), and peristaltic break (PB, cm) were reported in median and 95th percentile.

Results: Fifty of 57 screened participants were recruited, and 586 saline, 265 viscous, and 261 solid swallows were analyzed. Per-patient wise, in the recumbent position, 95th percentile for IRP-4 s, DCI, DL, and PB were 16.5 mmHg, 2431 mmHg s cm, 8.5 s, and 7.2 cm, respectively. We observed that with each posture, the use of viscous swallows led to changes in DL, but the use of solid swallows led to more changes in the metrics including DCI and length of PB. Compared with a recumbent posture, an upright posture led to lower IRP-4 s and DCI values. Both per-patient analysis and per-swallow analyses yielded almost similar results when comparing the different postures and types of swallows. No major motility disorders were observed in this cohort of asymptomatic population. However, more motility disorders were reported in the upright position.

Conclusions: Variations in metrics can be observed in different postures and with different provocative swallow materials in a healthy population. The normative Chicago 3.0 metrics are also determined for the Malay population.

gold standard test for the evaluation of nonstructural dysphagia when endoscopy and imaging studies did not reveal any causative pathology.¹

Liquid swallows with saline are commonly used in esophageal manometric studies to evaluate for peristaltic abnormalities; however, it seldom reproduces the symptoms unlike the more viscous or solid materials.² Evidence indicates that apple sauce may unmask more motor disorders, making viscous or other solid

materials a more preferable challenge as compared with saline in the evaluation of dysphagia.^{3,4} A more recent study using 200-g warm soft boiled rice as the solid meal challenge in healthy and patients with motility disorders has reached a similar conclusion.⁵ The same argument applies for body postures as recumbent position is not exactly the ideal position because normally, patients eat while on a sitting position or even during standing.^{6–9} Likewise, a recent study revealed only a moderate diagnostic agreement for single water swallows in the supine and upright positions, and findings were often discordant for ineffective motility and outlet obstruction.¹⁰ Obviously, the clinical effects of different types of provocative swallow materials in different postures are still limited in literatures and therefore required further validation.^{5,10}

Variations in the normative Chicago metrics exist between the Asian and Western populations possibly due to anatomical and physiological differences. Malaysia, a country situated in the Southeast Asia with a population similar to Canada and Australia of approximately 35 million, is a multicultural nation with a diverse ethnicity. The Malays represent the Malaysia's largest ethnic group followed by the Chinese and Indians.¹¹ In addition, the ethnic Malays are natives to the Indonesian archipelago, the fourth most populous in the world. Variations of metrics may also exist because of technical differences observed between different manufacturers.^{12–15} For example, the type of catheter (either water perfused or solid state) and diameter of catheter may affect the Chicago parameters.^{16–19} More importantly, these inconsistencies or variations may affect the diagnosis of motility disorders. As such, it is fundamental for each motility lab to have their own normative data for their population.

Therefore, we aimed to determine the effects of different provocative swallow materials (liquid, viscous, and solid) on the normative Chicago 3.0 metrics in the two different postures (recumbent and standing) in a healthy Asian population.

Methods

Study participants. Healthy Malay participants of more than 18 years old were recruited through advertisements placed within the *Hospital Canselor Tuanku Muhriz* (HCTM), Kuala Lumpur, Malaysia. In addition to the absence of significant present and past medical history (including neurological and psychiatric disorders), participants with recent history of upper gastrointestinal (GI) symptoms and the Malay version of Gastro-Esophageal Reflux Questionnaire (GERDQ-M)²⁰ score above 8 were excluded. Other exclusion criteria were any prior surgery of the upper GI tract, any allergies to applesauce, wheat and gluten, or taking any regular medications that might affect the upper GI tract such as prokinetic agents, proton-pump inhibitor, or H₂-receptor antagonist drug. During screening visit, for eligible participants, informed consent was obtained, and a validated GERDQ-M questionnaire²⁰ was administered in addition to measurements of weight (kg), height (cm), and waist circumference (cm). Obesity is defined as body mass index (BMI) more than or equal to 30 kg/m².²¹ Subsequently, high-resolution esophageal manometry was performed in all consented participants.

Ethical approval was attained from the Ethics and Research Committee of HCTM (reference number of FF-2015-306).

High-resolution esophageal manometry. A solid-state 4.0-mm diameter probe that consists of 32 pressure channels and 8 impedance sensors (Diversatek Healthcare, Milwaukee, WI, USA) was used for this study. Once calibrated according to the manufacturer's instruction, the probe was inserted nasally while in recumbent position, and its depth was adjusted based on identified high-pressure zone in the distal esophagus, that is, the lower esophageal sphincter (LES). Upon completion of all test swallows, the probe was then removed.

Provocative swallows and postures. After the insertion of probe and after a period of rest in the recumbent position, 10 water swallows of 5 mL each were given first, and this was followed by three apple sauce swallows, also 5 mL each. Subsequently, three pieces from a slice of bread that was cut into squares of 3 × 3 cm were given, and between each swallow, there was a rest interval of approximately 30 s. Once the recumbent position was completed, participants were instructed to assume the standing position. After accustomed to the new posture and after recording the rest period in the standing position, the test swallows were repeated in the same sequence, that is, three water swallows 5 mL each, three apple sauce swallows 5 mL, each and three pieces (3 × 3 cm) of bread swallows with one piece each time at an interval of approximately 30 s.

Data and statistical analysis. Based on a true difference that exist between swallows and postures of 0.8 (based on the metric IRP-4 s from previous studies^{14,15}), type I error of 0.05, standard deviation of 1.2, and power of 0.9, the calculated sample size was 48 normal subjects. All data acquisition was performed using the inSIGHT Ultima system (Diversatek Healthcare) and saved at the end of recording. Data were obtained and subsequently analyzed with the manufacturer's analytical software, BIOVIEW 29.10. After the analysis was verified by an experienced investigator (NCS), all extracted data would be entered into the Statistical Package for Social Science Version 23.0 (SPSS Inc., Chicago, IL, US).

The measured Chicago pressure metrics v3.0 in the current study consisted of integrated relaxation pressure (IRP), distal contractile integral (DCI), and distal latency (DL).¹¹ IRP-4 s (mmHg) is defined as the mean of 4 s of maximal deglutitive relaxation in a 10 s postdeglutition time period beginning at the upper esophageal sphincter (UES) relaxation.^{11,17} DCI (mmHg s cm) is obtained by multiplying amplitude with the duration and length of distal esophagus contraction with value not exceeding 21 mmHg for the Diversatek system.¹¹ DL (s) is the interval between UES relaxation and contractile deceleration point¹¹; contractile deceleration point is the inflection point along the 30-mmHg isobaric contour at which swallow progression velocity slows and demarcates the tubular esophagus peristalsis from phrenic ampulla emptying.^{11,17} In addition to the above metrics, peristaltic breaks (PBs), defined as the length of breaks in 20 mmHg isobaric contour, were evaluated.²

Analysis was per patient, but per-swallow analysis was also performed for comparison purpose. Chicago metric is based on an average of 10 swallows per patient. However, inconsistency¹⁰ and occurrence of "failed peristalsis" of approximately 39% have been reported, and this may potentially skew the per-swallow analysis,

hence the reason for comparison.²² Continuous data were expressed in mean (standard deviation, *SD*) or median, *Median* (range or interquartile range, *IQR*), where applicable. Comparison between peristalsis and bolus characteristics of test swallows and postures would be tested with the Mann–Whitney *U* test, and all test results were considered significant if $P < 0.05$.

Results

Of 57 screened participants, 50 (30 female; *Median* age 23.7 years, range 21 to 37 years old) completed the study. Five participants were excluded because of exclusion criteria (including three with GERDQ-M scores above 8), and two withdrew because of intolerance to the manometry procedure. The mean height, weight, and BMI of study participants were 159.7 (*SD* = 7.2) cm, 61.3 (*SD* = 15) kg and 23.7 (*SD* = 4.4) kg/m², respectively. A total of 586 saline swallows, 265 viscous swallows, and 261 solid swallows were included for per-swallow analysis while others were excluded because of double swallows or belching during the procedure (Fig. 1). Based on the Chicago classification, seven participants (14%) were diagnosed with ineffective esophageal motility (IEM) in the recumbent position; however, in the upright position, in addition to more IEMs, the diagnoses of EGJOO and DES have been observed (Fig. 2).

Sex and body mass index differences in normative metrics. Sex differences in normative Chicago metrics are shown in Table 1. Demographic wise, the median age was almost similar for male *versus* female patients (*Median* = 24 *vs* 23, $P = 0.6$), but BMI was greater in male *versus* female patients (*Median* = 26.3 *vs* 21.6 kg/m², $P < 0.01$) and likewise waist circumference (*Median* 32 *vs* 28 cm, $P < 0.01$). Metrics wise, a significantly lower IRP-4 s was observed in male *versus* female patients for the recumbent (*Median* 7.9 *vs* 10.7 mmHg, $P < 0.05$) posture. In addition, a significantly increased PB was

observed in obese *versus* nonobese participants (*Median* 2.5 *vs* 4.3 mmHg, $P < 0.05$), but not with other metrics (Table 2).

Comparing metrics in standing versus recumbent position.

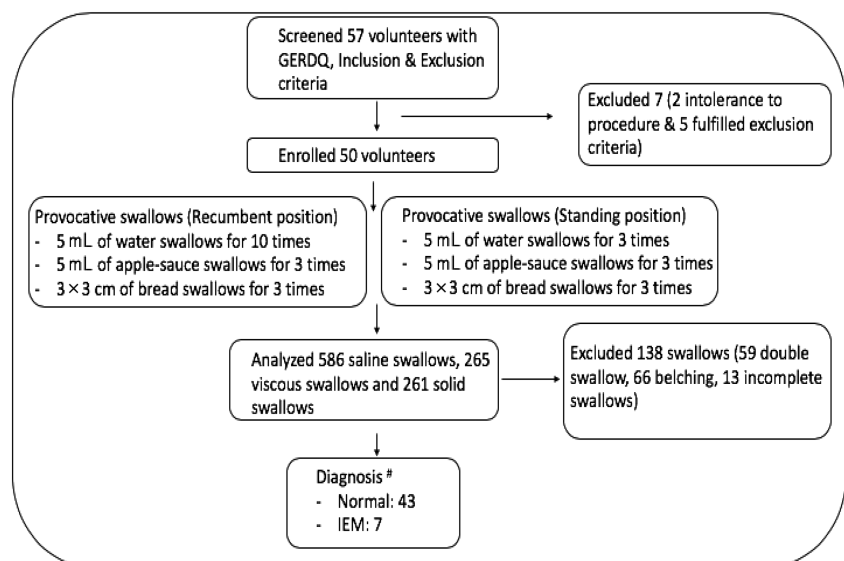
Differences in metrics for the two different postures are shown in Table 1. For liquid swallows, a change in position from recumbent to standing led to a lower IRP-4 s (*Median* 10.1 *vs* 8.7 mmHg, $P < 0.05$). The change in position from recumbent to standing also resulted in a lower DCI with viscous (*Median* 938 *vs* 772 mmHg s cm, $P = 0.03$).

Normative metrics in the recumbent position.

Reported normative metrics for recumbent position is shown in Table 3 (3B). For liquid swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 16.5 mmHg, 2431 mmHg s cm, 8.4 s, and 7.2 cm, respectively. For apple sauce (viscous) swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 15.7 mmHg, 2483 mmHg s cm, 10.3 s, and 8.8 cm respectively. Provocative swallows with viscous *versus* liquid swallows led to a significant increment of DL (*Median* 7.6 *vs* 6.4 s, $P < 0.01$) but not of IRP-4 s (*Median* 10.3 *vs* 10.1 mmHg, $P = 0.6$), DCI (*Median* 938 *vs* 870 mmHg s cm, $P = 0.9$) and PB (*Median* 2.7 *vs* 2.6 cm, $P = 0.7$).

For bread (solid) swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 14.8 mmHg, 3194 mmHg s cm, 12.1 s, and 5.7 cm, respectively. Provocative swallows with solid *vs* liquid swallows led to an increment of DCI (*Median* 1245 *vs* 870 mmHg s cm, $P < 0.05$), a lengthier DL (*Median* 8.5 *vs* 6.4 s, $P < 0.01$), and a shorter PB (*Median* 1 *vs* 2.6 cm, $P < 0.01$). Besides, similar characteristics were observed when comparing solid *versus* viscous swallows including significant increase of DCI (*Median* 1245 *vs* 938 mmHg s cm, $P < 0.05$) and DL (*Median* 8.5 *vs* 7.6 s, $P < 0.01$) but a decrement in PB (*Median* 1 *vs* 2.7 cm, $P < 0.01$).

Figure 1 Flow diagram of volunteers' recruitment and swallow protocols. #, diagnosis made during liquid swallows in recumbent position; IEM, ineffective esophageal motility; GERDQ, Gastro-Esophageal Reflux Questionnaire.



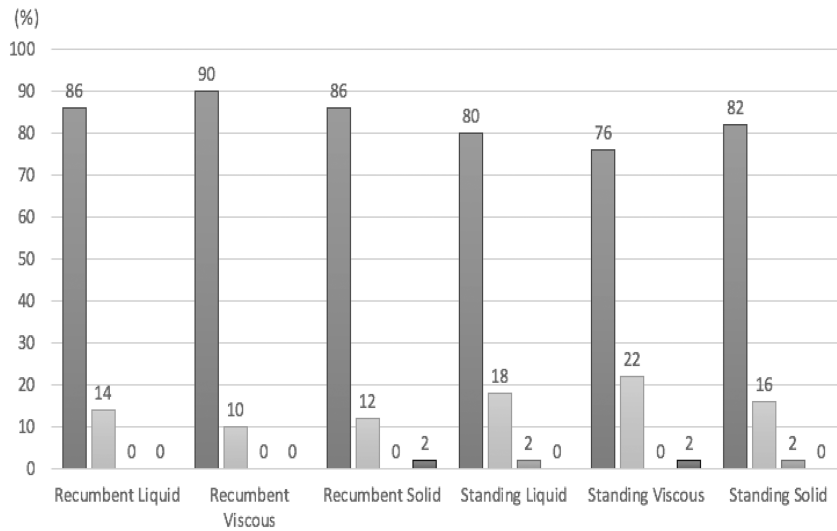


Figure 2 Motility diagnosis in different types of swallows and positions. DES, distal esophageal spasm; EGJOO, esophagogastric junction outflow obstruction; IEM, ineffective esophageal motility. ■, Normal; ■, IEM; ■, EGJOO; ■, DES.

Table 1 Differences between sexes in the characteristics of Chicago metrics v3.0 (CC v3.0) for liquid swallows and comparison of test swallows between recumbent and standing positions

Demographics	Male (n = 20)	Female (n = 30)	P value
Age, years, median (range)	24 (22–37)	23 (21–28)	0.6
BMI, kg/m ² , median (range)	26.3 (22.7–27.1)	21.6 (19.7–23.4)	<0.01
Waist circumference, cm, median (range)	32 (28–33)	28 (27–29)	<0.01
Recumbent	Median (IQR)	Median (IQR)	P value
IRP-4 s	7.9 (5.8–10.6)	10.7 (7.9–13)	0.04
DCI	860 (494–3354)	880 (510–1494)	0.9
DL	6.4 (6–7.5)	6.3 (6–7.4)	0.7
PB	2.6 (1.9–4.3)	2.7 (1.9–7.2)	0.6
Standing	Median (IQR)	Median (IQR)	P value
IRP-4 s	7.9 (5.1–11.7)	9.7 (7–11.9)	0.2
DCI	591 (413–1205)	947 (585–1613)	0.2
DL	6.7 (5.8–8.2)	6.9 (6–7.2)	0.8
PB	3 (2–4.3)	2 (1–3.3)	0.05
	Recumbent Median (IQR)	Standing Median (IQR)	P value
Liquid swallows			
IRP-4 s	10.1 (6.9–12)	8.7 (6.5–11.9)	0.04
DCI	870 (510–1389)	781 (465–1424)	0.7
DL	6.4 (6–7.4)	6.7 (5.9–7.3)	0.3
PB	2.6 (2.0–3.6)	2.5 (1.4–4)	0.6
Viscous swallows			
IRP-4 s	10.3 (6.2–13.7)	9.5 (6–13.7)	0.7
DCI	938 (544–1336)	772 (444–1279)	0.03
DL	7.6 (6.7–8.8)	7.3 (6.7–8.4)	0.3
PB	2.2 (1–4)	2 (1–3.7)	0.7
Solid swallows			
IRP-4 s	10.3 (6.3–13)	9 (5.7–11.6)	0.2
DCI	1245 (611–1846)	944 (500–1479)	0.5
DL	8.5 (7.3–9.8)	8.4 (7.3–9.4)	0.9
PB	1 (0–2.5)	1 (0–3.2)	0.6

BMI, body mass index; DCI, distal contractile integral; DL, distal latency; IQR, interquartile range; IRP, integrated relaxation pressure; PB, peristaltic break.

Table 2 Differences between obesity states in characteristics of the Chicago pressure metrics v3.0 for liquid swallows in the recumbent position

Chicago Classification (CC v3.0)	BMI < 30 (<i>n</i> = 45) Median (IQR)	BMI ≥ 30 (<i>n</i> = 5) Median (IQR)	<i>P</i> value
IRP-4 s	10.4 (7.5–12)	6.8 (4.9–11.8)	0.2
95th percentiles	16.7	12	
DCI	887 (503–1401)	607 (350–913)	0.3
95th percentiles	2317	1534	
DL	6.4 (6–7.5)	6.4 (5.5–7)	0.6
95th percentiles	8.5	7.2	
PB	2.5 (1.8–3.3)	4.3 (2.8–5.8)	0.04
95th percentiles	7.2	5.8	

BMI, body mass index; DCI, distal contractile integral; DL, distal latency; IQR, interquartile range; IRP, integrated relaxation pressure; PB, peristaltic break.

Table 3 Normative metrics for liquid swallow in comparison to viscous and solid provocative swallows (per-patient analysis)

3A	Liquid recumbent		Viscous recumbent			Solid recumbent			
	Median (IQR)	95th percentiles	Median (IQR)	95th percentiles	<i>P</i> value [†]	Median (IQR)	95th percentiles	<i>P</i> value [‡]	<i>P</i> value [§]
IRP-4 s	10.1 (6.9–12)	16.5	10.3 (6.2–13.7)	15.7	0.6	10.3 (6.3–13)	14.8	0.9	0.6
DCI	870 (510–1389)	2431	938 (544–1336)	2483	0.9	1245 (611–1846)	3194	0.04	0.04
DL	6.4 (6.0–7.4)	8.4	7.6 (6.7–8.8)	10.3	<0.01	8.5 (7.3–9.8)	12.1	<0.01	<0.01
PB	2.6 (2–3.6)	7.2	2.7 (1–4)	8.8	0.7	1 (0–2.5)	5.7	<0.01	<0.01
3B	Liquid standing		Viscous standing			Solid standing			
	Median (IQR)	95th percentiles	Median (IQR)	95th percentiles	<i>P</i> value [¶]	Median (IQR)	95th percentiles	<i>P</i> value ^{**}	<i>P</i> value ^{**}
IRP-4 s	8.7 (6.5–11.9)	17.9	9.5 (6–13.7)	17.3	0.5	9 (5.7–11.6)	16.3	0.5	0.2
DCI	781 (465–1424)	2523	772 (444–1279)	2291	0.7	944 (500–1479)	2682	0.5	0.2
DL	6.7 (5.9–7.3)	11.9	7.3 (6.7–8.4)	10.2	<0.01	8.4 (7.3–9.4)	12.6	<0.01	<0.01
PB	2.5 (1.4–4)	7.2	2 (1–3.7)	7.1	0.6	1 (0–3.2)	5.3	<0.01	<0.01

All significant *P* values <0.05.

[†]Comparing viscous *versus* liquid in recumbent position.

[‡]Comparing solid *versus* liquid in recumbent position.

[§]Comparing viscous *versus* solid in recumbent position.

[¶]Comparing viscous *versus* liquid in standing position.

^{**}Comparing solid *versus* liquid in standing position.

^{**}Comparing viscous *versus* solid in standing position.

DCI, distal contractile integral; DL, distal latency; IQR, interquartile range; IRP, integrated relaxation pressure; PB, peristaltic break.

Normative metrics in the standing position. Reported normative metrics for the standing position are shown in Table 3 (3B). For water swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 17.9 mmHg, 3523 mmHg s cm, 11.9 s, and 7.2 cm, respectively. For apple sauce (viscous) swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 17.3 mmHg, 2291 mmHg s cm, 10.1 s, and 7.1 cm, respectively. Provocative swallows with viscous *versus* liquid resulted in a longer DL (*Median* 7.3 vs 6.5 s, *P* < 0.01) but no difference in other metrics (all *P* > 0.1).

For bread (solid) swallows, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 16.5 mmHg, 2682 mmHg s cm, 12.6 s, and 5.3 cm, respectively. Provocative swallows with solid *vs* liquid resulted in a longer DL (*Median* 8.4 vs 6.7 s, *P* < 0.01) and a shorter PB (*Median* 1 vs 2.5 cm, *P* < 0.01). Moreover, with solid *versus* viscous swallows, we observed an increase of DL

(*Median* 8.4 vs 7.3 s, *P* < 0.01) but a decrement of PB (*Median* 1 vs 2 cm, *P* < 0.01).

Similarities and differences between per-patient and per-swallow analysis. Results of per-patient and per-swallow analyses in the recumbent and standing positions are shown in Table 4 (4A and 4B), respectively. Per swallow, in the recumbent position, the 95th percentile values for IRP-4 s, DCI, DL, and PB were 17 mmHg, 2654 mmHg s cm, 8.5 s, and 7 cm, respectively, for liquid swallows. Provocative swallows with viscous *versus* liquid resulted in increment of DL for both types of analyses. Similar increment for both forms of analyses was observed when comparing solid *versus* liquid swallows for DCI and DL and likewise a shorter PB for both analyses. In the standing position, for both per-patient and per-swallow analysis,

Table 4 Normative metrics for liquid swallow in comparison to viscous and solid provocative swallows with both per-patient and per-swallow analysis

4A	Liquid recumbent		Viscous recumbent			Solid recumbent			
	Per-patient Median (IQR)	Per-swallow Median (IQR)	Per-patient Median (IQR)	Per-swallow Median (IQR)	<i>P</i> value [†]	Per-patient Median (IQR)	Per-swallow Median (IQR)	<i>P</i> value [‡]	<i>P</i> value [§]
IRP-4 s	10.1 (6.9–12)	9 (7–12)	10.3 (6.2–13.7)	10 (6.5–14)	0.2	10.3 (6.3–13)	9 (6–13)	0.9	0.3
DCI	870 (510–1389)	869 (506–1529)	938 (544–1336)	877 (503–1401)	0.8	1245 (611–1846)	1137 (653–1908)	0.01	0.01
DL	6.4 (6.0–7.4)	6.3 (5.7–7.3)	7.6 (6.7–8.8)	7.5 (6.7–8.6)	<0.01	8.5 (7.3–9.8)	8.2 (7.2–9.8)	<0.01	<0.01
PB	2.6 (2–3.6)	2 (0–3)	2.7 (1–4)	1 (0–3)	0.7	1 (0–2.5)	0 (0–1)	<0.01	<0.01
4B	Liquid standing		Viscous standing			Solid standing			
	Per-patient Median (IQR)	Per-swallow 95th percentiles	Per-patient Median (IQR)	Per-swallow 95th percentiles	<i>P</i> value [¶]	Per-patient Median (IQR)	Per-swallow 95th percentiles	<i>P</i> value	<i>P</i> value
IRP-4 s	8.7 (6.5–11.9)	7 (6–13)	9.5 (6–13.7)	10 (5–13)	0.3	9 (5.7–11.6)	8 (5–12)	0.9	0.3
DCI	781 (465–1424)	799 (653–1908)	772 (444–1279)	767 (363–1235)	0.1	944 (500–1479)	951 (479–1522)	0.3	0.01
DL	6.7 (5.9–7.3)	6.5 (5.8–9.8)	7.3 (6.7–8.4)	7.2 (6.5–8.6)	<0.01	8.4 (7.3–9.4)	8.0 (6.8–9.3)	<0.01	<0.01
PB	2.5 (1.4–4)	2 (0–3)	2 (1–3.7)	1 (0–3)	0.5	1 (0–3.2)	1.2 (0–3)	<0.01	<0.01

All significant *P* values <0.05.

[†]Comparing viscous *versus* liquid in recumbent position with per-swallow analysis.

[‡]Comparing solid *versus* liquid in recumbent position with per-swallow analysis.

[§]Comparing viscous *versus* solid in recumbent position with per-swallow analysis.

[¶]Comparing viscous *versus* liquid in standing position with per-swallow analysis.

^{||}Comparing solid *versus* liquid in standing position with per-swallow analysis.

^{||}Comparing viscous *versus* solid in standing position with per-swallow analysis.

DCI, distal contractile integral; DL, distal latency; IQR, interquartile range; IRP, integrated relaxation pressure; PB, peristaltic break.

provocative swallows with viscous *versus* liquid and solid *versus* liquid resulted in similar increment of DL and decreased length of PB. Overall, we have observed lower values in all metrics for per-swallow *versus* per-patient analysis.

Discussion

As a summary, in the current study, first, we have reported normative metrics in both recumbent and standing postures using saline, viscous, and solid swallows for the Malay population. Second, we observed that with each posture, use of viscous swallows led to changes in DL, but use of solid swallows led to more changes in the metrics including DCI and length of PB. Third, compared with a recumbent posture, standing led to lower IRP and DCI values. Fourth, both per-patient analysis and per-swallow analysis yielded almost similar results comparing the different postures and

swallows. Fifth, no major motility disorders were observed in this cohort of asymptomatic population. Lastly, being male and having an obese state also affected metrics including IRP and DCI.

Of the Chicago metrics, IRP-4 s is probably the most important, where it determines a diagnosis of achalasia.²³ However, the metric is known to be affected by the type of probe, of which 19 mmHg is the acceptable IRP-4 s threshold for the Diversatek inSIGHT Ultima HRM system.^{2,11} Our reported upper 95th percentile threshold value of IRP-4 s was relatively similar across all swallow types and positions, indicating that a normative threshold of 18 mmHg is probably appropriate and that the accepted threshold of 19 mmHg of the Diversatek system is very close to our established norm.^{13,15} In contrast to Shi *et al.* (Table 5) and Gao *et al.*, who had used similar system, their reported IRP-4 s values were much higher.^{15,24} We postulated that age might have partly contributed to the above discrepancies. Our participants were

Table 5 Comparison of Chicago metrics in 95th percentiles among the Western, Chinese, and the Malay healthy cohorts

Metric	Chicago ^{28–30}	Classification	Europeancohort ²²	Chinese cohort ¹⁵		Malay cohort		
	Liquid swallow		Liquid swallow	Liquid swallow	Viscous swallow	Liquid swallow	Viscous swallow	Solid swallow
IRP-4 s (mmHg)	15		15.5	20.5	23.2	16.5 (17 [†])	16 (17 [†])	15 (16 [†])
DCI (mmHg s cm)	5000		2828	3195	3198	2431 (2654 [†])	2483 (2514 [†])	3194 (3622 [†])
DL (s)	7.6		8.5	7.1	7.5	8.4 (8.5 [†])	10.3 (10.8 [†])	12.1 (12.1 [†])
PB (cm)	<3		8.2	n.a.	n.a.	7.2 (7.0 [†])	8.8 (7.0 [†])	5.7 (5.0 [†])

[†]Parameters performed with per-swallow analysis.

n.a., not available.

younger at a mean age of 23.7 compared with 38.9 years in the study by Shi *et al.*¹⁴ Jung *et al.* have previously reported a higher IRP-4 s with increasing age.²⁵ Aging has been shown to be associated with an impaired peristalsis, an incomplete UES relaxation, and a lesser degree of LES relaxation.²⁵

In addition to age, being male patients also have lower IRP-4 s compared with female patients, similarly reported by Jung *et al.*²⁵ However, this variation between sexes is not consistent in other literatures.²⁶ The low IRP-4 s may be linked to lower LES pressure observed in male patients or may be due to the effect of raised gastroesophageal gradient from obesity because we observed the same effects in obese state, but the exact reason is unknown.^{25,26} At this juncture, whether to have different thresholds for men or women is unclear, and neither does Chicago classification v3.0 discriminate between the two, but future larger population-based studies may be able to address the gender differences and to inform future classifications.

More conflicting is the effect of postures on IRP-4 s. A standing position from recumbent led to a lower median IRP-4 s value but a higher 95th percentile value of 17.9 mmHg. While our data corroborate with that of Xiao *et al.*⁶ and Misselwitz *et al.*¹⁰ but Sweis *et al.*⁷ reported a higher IRP value instead. It is unlikely that the type of system was the culprit because the same ManoScan HRM system was used in Xiao *et al.*⁶ and Sweis *et al.*⁷ The likely reason may be due to differences in the study methodology, but the possibility of type I error cannot be ruled out. Our protocol involved provocative swallows from liquid to viscous and then to solid in a recumbent position before proceeding to a standing position. Such a methodology perhaps contributed to a higher variation in the IRP-4 s.¹⁴ Furthermore, the position may affect the function of the gastroesophageal junction, for example, in the Roman *et al.* study, the prevalence of hiatus hernia was reportedly higher in the supine position.²⁷ Possibly the intragastric pressure that serves as the reference baseline in HRM may have been altered from supine to standing or that its value approaches to that of the gastroesophageal barrier.¹⁰

The second important metric is the DCI, a measure of distal esophageal contractility or strength.³⁰ We observed an almost comparable value of DCI in our population with the European population (Table 5). This might be related to a similarity in the BMIs of the two populations, that is, 23.4 kg/m² in the European cohort and 23.7 kg/m² in our cohort.²² Weijenberg *et al.* explained that a higher distal esophageal contractility²² is associated with a higher BMI, probably in response to a higher gastroesophageal gradient associated with obesity, but this explanation is limited by evidence.^{17,22} We have also observed that viscous and solid swallows were associated with a higher DCI, similarly reported by Shi *et al.*¹⁵ It is possible that viscous and solid materials generate greater intrabolus pressure and therefore require greater esophageal contractility (higher DCI) to clear the bolus.^{7,15,21} Besides, a similar increment with viscous swallow was observed with DL, and perhaps, the greater intrabolus pressure from viscous materials causes a delay in distal esophageal clearance.¹⁵ It is worthy to note that although the 95th percentile value of DL reported by the Chicago classification was 7.6 s,^{30,31} ours and the European population found that 8.5 s may be an acceptable threshold.²⁶ Provocative swallows with solids like bread may have been a better challenge than liquid swallows with the intention to unmask underlying motor diseases.³ Similar with Sweis *et al.*, we found a similar increase

in DCI and but a shorter PB.⁷ We have no explanation for a shorter PB with solids, but perhaps, solids trigger greater contractility response and therefore close the “gap.”³ This “normal” contractility response may be lost in ineffective motility and perhaps merit further studies.

Although there were no major motility disorders, IEM was present in 14% of our study population (Fig. 2).¹² The prevalence of IEM in the healthy population remained uncertain, but previous literatures have estimated between 20% and 30%.^{32,33} A greater occurrence of IEM was observed during the upright position in our study, similarly reported in the literature,^{8,34,35} and this may be due to alleviation of the gravity effect in an upright position.³⁵ In addition, we have observed diagnoses of EGJOO and DES in the upright position (Fig. 2). For reasons not exactly known, upright position seems to enhance diagnoses of EGJOO,^{36,37} and a lower IRP-4 s or fewer artifacts observed in the upright position might have played a role.^{36,38} Likewise, changes in DL that are observed during standing position might have enhanced the sensitivity for diagnoses of DES.³⁴

There are a few limitations to our study. First, we have excluded 138 swallows (approximately 20%) from analysis, because of incomplete procedure, double swallows, or belching during a swallow.³¹ Other studies have similarly reported about 20% of technically imperfect topography that can be attributed to miscellaneous artifacts, sensor malfunction, or failure to intubate the EGJ. However, Roman *et al.*²³ explained that despite the technical limitation, the sensitivity and specificity in the diagnosis of esophageal motility disorder remained unaffected.³¹ Furthermore, our derived normative metrics are more precise and accurate after elimination of “imperfect” swallows. Second, only three swallows of apple sauce and breads were used, but this limited protocol was necessary to enhance tolerability among participants because these swallows were repeated in various positions. Other provocative maneuvers including rapid drink challenge and solid test meal^{9,10} were not performed in the current study, which is a limitation; however, these maneuvers have not been included in the Chicago classification v3.0. Third, our Asian participants were of single ethnicity and relatively young, and male participants were more obese. However, because of our population characteristics, we were able to reduce baseline confounders and could explain some incongruities observed for certain metrics especially IRP-4 s. For example, older age population may be confounded by incompetent peristalsis,²⁵ and a single ethnicity would reduce heterogeneity that may exist because of anatomy or bodily builds. However, it will be beneficial in future studies to include outcome data of patients with motility disorders based on the newly established normative data. For the same reason, the upper 95% confidence interval of IRP-4 s should not be taken as the diagnostic threshold for achalasia as our data only represented healthy cohort. Although we have observed EGJOO and DES in the upright position, these conditions may have been underdiagnosed owing to a higher IRP-4 s threshold of the manufacturer’s probe.

In conclusion, during provocative swallows with liquid, viscous, and solid materials, we found significant variations in the normative pressure metrics, which can be attributed to the bolus materials, age, sex, and the presence of obesity. We also reported the normative Chicago v3.0 metrics for the healthy Malay cohort in the recumbent and standing postures.

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