Original Article

Global and Regional Gastric Emptying Parameters: Establishment of Reference Values and Comparison of Different Camera View Methods

Abstract

Purpose of the Study: The purpose of the study is to establish the reference values of global and regional gastric emptying parameters (GEPs) using a standard vegetarian meal acceptable to the Indian population and compare the values derived on different camera view methods. **Materials and Methods:** Thirty-six consecutive healthy subjects with age ≥18 years underwent gastric emptying scintigraphy using anterior, posterior, and left anterior oblique (LAO) views. GEP was derived based on decay corrected counts in regions of interest defined on the whole and proximal stomach. Counts in the anterior and posterior view images were used to derive GEP based on geometric mean (GM) method. Comparison of GEP among different camera view methods was done with Friedman test and *post hoc* Wilcoxon signed-rank test after Bonferroni correction. Reference values were derived based on percentiles. **Results:** Rapid gastric emptying based on GM method was defined as percent retention <20% at 1 h while delayed emptying as percent retention >40% and >5% at 2 h and 4 h, respectively. The reference range of half-time of gastric emptying was 23–109 min. The reference value of intragastric meal distribution at time $t = 0$ was >64%, while the reference range of retention index was 0.7–1.3. Although the overall distribution of GEP derived on different camera view methods could be statistically significant ($P < 1.00$), the small differences in the derived reference values are likely to be of no clinical significance. **Conclusion:** The reference values of GEPs established in this study can be generalized for the Indian population and may be applied to aid in clinical decision making. We recommend the GM method as the preferred method, although single view method (LAO preferred over anterior) can also be an acceptable alternative.

Keywords: *Different camera views, fundic accommodation, gastric emptying scintigraphy, global gastric emptying, normal values, radiolabeled meal, reference values, regional gastric emptying*

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Introduction

Gastric emptying scintigraphy (GES) is considered as the reference standard for assessment of gastric emptying as it is noninvasive, physiological, quantitative and is associated with low radiation dose to the patients.[1-3] However, since its first introduction by Griffith *et al.*[4] in 1966, there has been a wide variation in various aspects of the methodology, including the types of meal, protocols, and reported quantitative parameters followed in different centers around the globe. The reference values for some of the described protocols have not been conclusively established, thereby limiting the wider clinical acceptance of the test.[1,2] The lack of standardization has hampered inter-center comparison, reliability, and participation in international clinical trials. Subsequently, in 2008, a consensus recommendation was made by the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine addressing those aspects of GES which needed immediate standardization, namely the meal, frequency of imaging, duration of the test, and normative data. However, the consensus recommendation did acknowledge the aspects that still needed further research including the establishment of reference values for meals with composition different from that of the standard egg-based meal.[1] This could be relevant to populations with different food habits or to those who cannot tolerate eggs are allergic to egg proteins or are gluten sensitive. It may also be noted that even if a particular meal is used for GES in different centers, gastric emptying parameters (GEPs) may vary based on the quantity of the meal, imaging protocol (such as supine vs. standing,

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dynamic vs. static imaging, different camera views, etc.,), and presence of slight variations in the meal composition.

Not all patients with symptoms of gastroparesis or functional dyspepsia have abnormal global GEP. Delayed global gastric emptying has been seen in 29%–59% of patients with functional dyspepsia and in up to 40% of gastroesophageal reflux disease.[5] The symptoms of gastroparesis or functional dyspepsia correlate, although weakly, with delayed global gastric emptying, and no symptom has been consistently correlated with abnormal global gastric emptying; thus, implying that the pathophysiology might involve multiple factors localized to more specific regions of the stomach.[6-9] Subsequently, there has been a growing interest on assessing regional GEP that might be responsible for the patients' symptoms and might guide therapeutic approaches that target these regional abnormalities for better patient management. The consensus recommendation also acknowledged analysis of regional GEP as a future area of research.[1]

Based on this overall background, the current study was conducted to establish the reference values of global and regional GEP using a gluten-free standard vegetarian meal acceptable to the Indian population while complying with the imaging frequency and test duration as suggested by the consensus recommendation. The study also aimed to compare the GEP derived on different camera views methods.

Materials and Methods

After obtaining approval from the Institute Ethics Committee (IECPG-94/February 27, 2020), healthy subjects were prospectively enrolled over a 1-year period commencing from April 2020. Prior informed written consent was obtained from all the subjects. The study had a prospective noninterventional analytic cross-sectional design.

Healthy subjects

Thirty-six consecutive healthy subjects with age ≥18 years were prospectively enrolled in the study. Exclusion criteria included the presence of diabetes or any other conditions that might affect gastric emptying (e.g., gastrointestinal illness/surgery, neurological illness), pregnancy or lactating mothers, subjects taking medications that might affect gastric emptying, premenopausal women >10 days of menstrual cycle, refusal to give informed written consent, noncompliance to the protocol (no fasting for at least 6 h, vomiting during meal intake, incomplete meal intake, inability to complete meal within 10 min), and subjects allergic to the meal.

Standard meal

Eighty gram of rice *Idli* powder (rice and lentils) was mixed with 90 ml of potable water, and the mixture was stirred well until a desired viscosity and quality of *Idli* batter were obtained. 2–2.5 mCi (74–92.5 MBq) of Tc-99 m sulfur colloid was then added to the *Idli* batter and mixed properly. The radiopharmaceutical mixed *Idli* batter was then put in *Idli* molds and steamed in a sterilized *Idli* cooker for 10–15 min on medium to high temperature using an induction stove. In total, 5 pieces of *Idli* (savory cake) were prepared each containing approximately 0.4–0.5 mCi of Tc-99 m sulfur colloid. The standard radiolabeled meal consists of 2 pieces of *Idli*, each weighing approximately 32–35 g, and 100 ml of water. The meals were freshly prepared just before the beginning of the study following strict sterilization and radiation safety precautions. The packaged *Idli* powder is shown in Figure 1. The nutritional value and characteristics of the standard meal are given in Table 1.

Gastric emptying scintigraphy protocol

All subjects were fasted for at least 6 h before undergoing the procedure. After consuming the standard meal within 10 min, subjects were allowed to lie supine with arms extended over the head on the scanner table of a single head Brivo NM 615 GE Gamma Camera mounted with parallel-hole, low energy high-resolution collimators. One-min static images were acquired immediately (time, $t = 0$) and then at 1 h, 2 h, and 4 h. At each time point, anterior, posterior, and left anterior oblique (LAO) views were acquired. A zoom factor of 1 was used and images were acquired using a 140 keV Tc-99 m photopeak with a 20% energy window (140 keV ± 10%) and a matrix size of 128 × 128.

Image analysis

Image processing and analysis were done on a dedicated Xeleris 4 DR workstation using a vendor-specified GES analysis protocol. The anterior images from each time point were selected and fed as input to the software for processing, and region of interest (ROI) was drawn manually on the anterior image at time $t = 0$ using polygonal ROI tool to outline the stomach. Before placing the ROI, all the images at different time points (0, 1, 2, 4 h) were visually assessed to ensure

Figure 1: Packaged *Idli* powder

Table 1: Nutritional value and characteristics of standard meal

Nutritional value of packaged rice *Idli* powder		
Content	**Per 1 g**	**Per 40 g**
Energy (kcal)	3.4	136
Protein (g)	0.13	5.2
Carbohydrate (g)	0.67	26.8
Added sugar (g)	0	0
Dietary fiber (g)	0.065	2.6
Total fat (g)	0.0225	0.9
Saturated fat (g)	0.01	0.4
MUFA (g)	0.0075	0.3
PUFA (g)	0.005	0.2
Trans fat (g)	0	0
Cholesterol (mg)	0	0
Sodium (mg)	9	360
Calcium (mg)	0.6	24
Characteristics of standard radiolabeled meal		
Dry weight of *Idli* powder (g)	80	
Water (ml)	90	
Activity (mCi)	2-2.5	
Total weight of *Idli* batter (g)	170	
Diameter of 1 *Idli* piece (inches)	2.7	
Weight of 1 *Idli* piece (g)	32-35	
Total number of *Idli* pieces	5	
Activity in 1 *Idli* piece (mCi)	0.4-0.5	

MUFA: Monounsaturated fatty acid, PUFA: Polyunsaturated fatty acid

proper ROI placing. The total gastric ROI included the whole of stomach with particular attention to avoid any loops of small bowel in close proximity to the stomach. In exceptional cases, when the subjects had small bowel activity on the first image, then the entire field of view was taken in the ROI (for the first image) so that the image at time $t = 0$ included all activity ingested, as entire ingested activity was used to represent ingested meal at time $t = 0$. Next, the ROI drawn on the anterior image at time $t = 0$ was fitted to other anterior images (1, 2, 4 h images) avoiding bowel loop activity, if present. For regional gastric emptying analysis, we adopted the general concept of dividing the stomach into proximal and distal halves as suggested by Piessevaux *et al*.[10] which was later improvised by Orthey *et al*.[6,7] All the images at different time points (0, 1, 2, 4 h) were visually assessed to delineate the ROI and divide the stomach into proximal and distal halves by a line perpendicular to a curvilinear line representing the longitudinal axis of the stomach. After placing the ROIs on all the anterior images, global and regional GEP were generated. The same process was repeated for LAO images. For geometric mean (GM) analysis, anterior and posterior images were used as input images and ROIs were placed on the respective images of each time point [Figures 2 and 3].

GEP generated from the processed images include:

Global gastric emptying parameters

a. Percent retention at 1, 2, and 4 h for anterior, GM, and LAO images
b. Half time (T1/2) of gastric emptying for anterior, GM, and LAO images.

Regional gastric emptying parameters

a. Intragastric meal distribution at time $t = 0$ (IMD_0) for anterior, GM, and LAO images
b. Retention index (RI) for anterior, GM, and LAO images.

IMD_0 is defined as the ratio of kilocounts of proximal stomach to that of the whole stomach, both at time ($t = 0$). RI is defined as the ratio of T1/2 of proximal stomach emptying to T1/2 of whole stomach emptying. These two parameters represent regional GEP depicting the relationship between proximal and distal stomach functions.

Statistical analysis

Categorical variables were described as frequency (percentage). Continuous variables were described with mean ± standard deviation, median (minimum–maximum), and percentiles (2.5th, 5th, 95th, and 97.5th percentiles). Continuous variables were tested for normality with Shapiro–Wilk test. Comparison of GEP among different camera view methods was done with Friedman test. *Post hoc* Wilcoxon signed-rank test was used for pair-wise comparison of GEP between different camera view methods after Bonferroni correction. Comparison of GEP between females and males was done with Mann–Whitney U test. Spearman's rank correlation was performed between IMD_0 and RI, and between age and various GEP. Scatter plots were used to describe relationship between IMD_0 and RI. Reference values for percent retention were derived using the 5th and 95th percentile values and that of IMD_0 was derived using the 5th percentile value while reference ranges for T1/2 and RI were derived using the 2.5th and 97.5th percentile values. A two-tailed $P < 0.05$ was considered significant. For *post hoc* analysis with Bonferroni correction, the new P value was set at < 0.016. Statistical packages IBM SPSS 26.0.0.0 (IBM Corp., Somers, New York, USA), MedCalc 19.6.4 (MedCalc Software, Ostend, Belgium), and XLSTAT 2020.5 (Addinsoft Inc., New York, USA) were used for the statistical analyses.

Results

A total of 41 healthy subjects were initially recruited of which 36 subjects' data were included for the final analysis. Remaining 5 studies were excluded due to technical and methodological factors such as delayed image acquisition well past the designated time points (4 studies) and noninclusion of whole stomach in the imaging field of view (1 study). There were 22 males and 14 females. The mean age of the studied subjects was 30 ± 9 years with a median of 28 years (range: 18–52 years). For each subject,

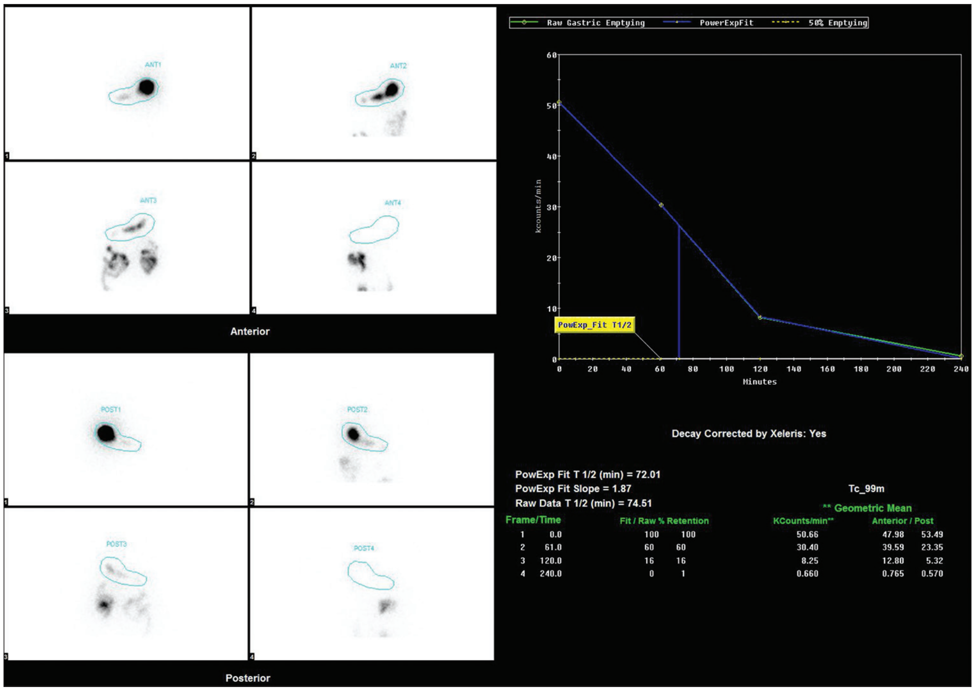

Figure 2: Gastric emptying scintigraphy image analysis by geometric mean method for global gastric emptying parameters in a 23-year-old healthy male subject

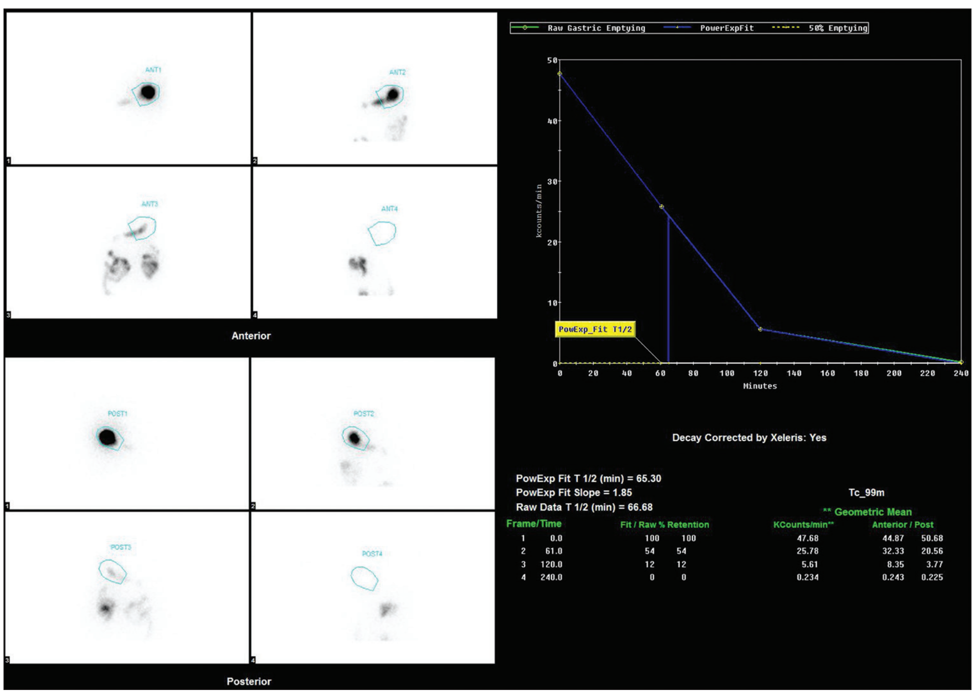

Figure 3: Gastric emptying scintigraphy image analysis by geometric mean method for proximal gastric emptying parameters in a 23-year-old healthy male subject

a total of 12 images were acquired. In total, 432 images of 36 subjects were processed and analyzed.

Global gastric emptying parameters

Percent retention

The median percent retention was 52% (18%–94%; anterior), 39% (17%–80%; GM), and 43% (18%–91%; LAO) at 1 h; 22% (1%–56%; anterior), 15% (2%–52%; GM), and 17% (1%–57%; LAO) at 2 h; and 1% (0%–9%; anterior), 1% (0%–8%; GM), and 1% (0%–9%; LAO) at 4 h, respectively. Descriptive statistics of GEP are shown in Table 2. At 1 h, there was statistically significant difference in the percent retention derived on different camera view methods ($P < 0.001$) which remained statistically significant

Table 2: Descriptive statistics of gastric emptying parameters

Parameter	Mean±SD	Median (range)	Skewness	Kurtosis	Probability of normality	2.5th percentile	5th percentile	95th percentile	97.5th percentile
Anterior view method									
Percent retention (%)									
1 h									
Global	52±21	52 (18-94)	0.369	-0.830	0.174	20	22	90	92
Proximal	45±20	44 (17-91)	0.551	-0.438	0.103	17	17	87	89
2 h									
Global	22±14	22 (1-56)	0.376	-0.392	0.424	1	2	48	52
Proximal	18±14	17 (1-70)	1.400	3.636	0.002	1	1	44	58
4 h									
Global	2±2	1 (0-9)	2.690	9.577	<0.001	0	0	6	7
Proximal	1±1	1 (0-7)	2.512	7.740	<0.001	0	0	4	6
T1/2 (min)									
Global	67±28	68 (28-132)	0.606	-0.337	0.091	28	28	129	130
Proximal	58±28	53 (21-145)	1.169	1.482	0.009	22	23	121	134
IMD_0 (%)	85±12	88 (54-97)	-1.084	0.278	0.001	57	60	97	97
RI	0.9±0.2	0.8 (0.5-1.3)	0.478	0.257	0.119	0.5	0.6	1.2	1.2
Geometric mean method									
Percent retention (%)									
1 h									
Global	41±18	39 (17-80)	0.561	-0.748	0.013	18	20	77	79
Proximal	36±19	36 (12-86)	0.754	0.018	0.023	13	15	75	81
2 h									
Global	17±12	15 (2-52)	0.915	0.580	0.016	2	2	40	46
Proximal	15±13	12 (1-65)	1.928	5.365	<0.001	1	1	42	54
4 h									
Global	2±1	1 (0-8)	2.588	9.955	<0.001	0	0	5	6
Proximal	1±1	1 (0-6)	2.378	6.544	<0.001	0	0	4	5
T1/2 (min)									
Global	53±25	49 (23-119)	0.811	-0.146	0.005	23	23	97	109
Proximal	48±26	43 (17-139)	1.465	3.007	0.001	18	20	100	121
IMD_0 (%)	87±10	90 (62-98)	-0.959	-0.245	0.001	63	64	98	98
RI	0.9±0.1	0.9 (0.7-1.3)	0.946	1.076	0.030	0.7	0.7	1.2	1.3
Left anterior oblique view method									
Percent retention (%)									
1 h									
Global	46±21	43 (18-91)	0.571	-0.705	0.022	18	18	88	89
Proximal	39±21	37 (13-97)	0.813	0.199	0.014	13	14	84	91
2 h									
Global	18±13	17 (1-57)	0.983	0.913	0.011	1	2	45	51
Proximal	15±13	13 (1-65)	1.775	4.284	<0.001	1	1	42	54
4 h									
Global	2±2	1 (0-9)	2.851	10.575	<0.001	0	0	6	7
Proximal	1±1	1 (0-5)	2.044	5.790	<0.001	0	0	3	4
T1/2 (min)									
Global	58±28	52 (23-129)	0.880	0.109	0.011	23	24	123	126
Proximal	51±28	47 (19-136)	1.252	1.522	0.001	20	21	117	127
IMD_0 (%)	86±10	89 (58-97)	-0.915	0.185	0.003	60	63	97	97
RI	0.9±0.2	0.8 (0.6-1.2)	0.596	0.037	0.235	0.6	0.6	1.2	1.2

Global: Whole stomach, Proximal: Proximal stomach, T1/2: Half-time of gastric emptying, IMD_0: Intragastric meal distribution at time t=0, RI: Retention index, SD: Standard deviation

even on *post hoc* pairwise comparison (P < 0.001; Bonferroni corrected significant, P < 0.016). At 2 h, although there was overall statistically significant difference in the percent retention values among the three gamma camera view methods (P < 0.001), on *post hoc* pairwise comparison, there was no significant difference between

GM and LAO ($P = 0.038$; Bonferroni corrected significant, $P < 0.016$). At 4 h, there was no statistically significant difference among the percent retention values derived on different camera view methods ($P = 0.544$). Comparison of GEP among different camera view methods is shown in Table 3. No statistically significant difference was noted in the percent retention at each time point between males and females ($P \geq 0.133$) as shown in Table 4. As shown in Table 5, there was a weak but insignificant negative correlation trend between percent retention and age except at 4 h with LAO method which showed significant but weak negative correlation ($\rho = -0.385$, P value, 0.020).

Half-time of gastric emptying

The median T1/2 of gastric emptying was 68 min (28–132 min; anterior), 49 min (23–119 min; GM), and 52 min (23–129 min; LAO), respectively, as shown in Table 2. There was statistically significant difference in the T1/2 of gastric emptying derived on different camera view methods ($P < 0.001$) which remained statistically significant even on *post hoc* pairwise comparison ($P < 0.001$; Bonferroni corrected significant $P < 0.016$). There was no significant difference between the T1/2 values of males and females ($P \geq 0.227$) as shown in Table 4. No significant correlation was seen between T1/2 and age [Table 5].

Regional gastric emptying parameters

Intragastric meal distribution

The median IMD_0 was 88% (54%–97%; anterior), 90% (62%–98%; GM), and 89% (58%–97%; LAO), respectively. There was statistically significant difference in the IMD_0 derived on different camera view methods ($P < 0.001$); on *post hoc* pairwise comparison, there was no significant difference between GM and LAO ($P = 0.451$; Bonferroni corrected significant, $P < 0.016$). No significant difference was found in the IMD_0 values between males and females [$P \geq 0.296$; Table 4]. No significant correlation was seen between IMD_0 and age [Table 5].

Retention index

The median RI was 0.8 (0.5–1.3; anterior), 0.9 (0.7–1.3; GM), and 0.8 (0.6–1.2; LAO), respectively. There was statistically significant difference in the RI derived on different camera view methods ($P = 0.001$); on *post hoc* pairwise comparison, there was no significant difference between GM and LAO and between anterior and LAO ($P = 0.025$ and 0.625, respectively; Bonferroni corrected significant, $P < 0.016$). There was no significant difference in RI between males and females [$P \geq 0.170$; Table 4]. No significant correlation was seen between RI and age [Table 5]. However, a moderate negative correlation was found between IMD_0 and RI in all the camera view methods ($\rho = -0.627$, $P < 0.001$ for anterior; $\rho = -0.498$, $P = 0.002$ for GM; $\rho = -0.430$, $P = 0.009$ for LAO, respectively). Scatter plots showing the relationship between IMD_0 and RI are shown in Figure 4.

Reference values of gastric emptying parameters

Due to the advantage of attenuation and depth correction, the study established the reference values of GEP based on GM method. In the present study, percent retention at 1 h was used to assess rapid gastric emptying while percent

Table 3: Comparison of gastric emptying parameters

Parameter[#]	Anterior	GM	LAO	Friedman test		*Post hoc* Wilcoxon signed-rank test					
				χ^2	P	Anterior versus GM		GM versus LAO		Anterior versus LAO	
						Z	P	Z	P	Z	P
Percent retention (%)											
1 h											
Global	52 (18-94)	39 (17-80)	43 (18-91)	41.757	<0.001*	-5.040	<0.001**	-3.796	<0.001**	-4.837	<0.001**
Proximal	44 (17-91)	36 (12-86)	37 (13-97)	30.237	<0.001*	-4.682	<0.001**	-2.185	0.028	-4.045	<0.001**
2 h											
Global	22 (1-56)	15 (2-52)	17 (1-57)	38.884	<0.001*	-4.893	<0.001**	-2.068	0.038	-4.666	<0.001**
Proximal	17 (1-70)	12 (1-65)	13 (1-65)	33.431	<0.001*	-4.713	<0.001**	-0.766	0.455	-4.133	<0.001**
4 h											
Global	1 (0-9)	1 (0-8)	1 (0-9)	1.345	0.544	-0.688	0.651	-0.832	0.581	0.000	1.000
Proximal	1 (0-7)	1 (0-6)	1 (0-5)	2.150	0.374	-1.155	0.398	-0.707	0.727	-1.513	0.186
T1/2 (min)											
Global	68 (28-132)	49 (23-119)	52 (23-129)	45.056	<0.001*	-5.122	<0.001**	-3.566	<0.001**	-4.933	<0.001**
Proximal	53 (21-145)	43 (17-139)	47 (19-136)	31.500	<0.001*	-4.878	<0.001**	-1.430	0.157	-4.242	<0.001**
IMD_0 (%)	88 (54-97)	90 (62-98)	89 (58-97)	15.722	<0.001*	-2.891	0.003**	-0.770	0.451	-2.859	0.003**
RI	0.8 (0.5-1.3)	0.9 (0.7-1.3)	0.8 (0.6-1.2)	13.389	0.001*	-3.676	<0.001**	-2.231	0.025	-0.503	0.625

[#]Parameters are depicted as median (range), *Significant at $P<0.05$, **Significant at Bonferroni corrected $P<0.016$. Global: Whole stomach, Proximal: Proximal stomach, T1/2: Half time of gastric emptying, IMD_0: Intragastric meal distribution at time $t=0$, RI: Retention index, Anterior: Anterior view method, GM: Geometric mean method, LAO: Left anterior oblique view method

Table 4: Comparison of gastric emptying parameters between females and males

Parameter	Female		Male		*P**
	Mean±SD	Median (range)	Mean±SD	Median (range)	
Anterior view method					
Percent retention (%)					
1 h					
Global	52±24	48 (18-89)	52±20	53 (24-94)	0.994
Proximal	46±22	42 (17-91)	44±20	44 (17-86)	0.892
2 h					
Global	21±16	18 (2-56)	23±13	26 (1-44)	0.417
Proximal	18±17	15 (1-70)	18±12	19 (1-40)	0.436
4 h					
Global	1±1	1 (1-4)	2±2	1 (0-9)	0.538
Proximal	1±1	1 (0-4)	1±2	1 (0-7)	0.969
T1/2 (min)					
Global	69±32	60 (28-128)	67±27	68 (28-132)	1.000
Proximal	62±32	53 (27-145)	55±25	52 (21-117)	0.597
IMD_0 (%)	82±14	83 (54-97)	86±10	90 (60-97)	0.597
RI	0.9±0.2	0.9 (0.7-1.2)	0.8±0.2	0.8 (0.5-1.3)	0.227
Geometric mean method					
Percent retention (%)					
1 h					
Global	43±20	39 (17-80)	40±18	41 (21-77)	0.804
Proximal	39±21	33 (12-86)	35±17	38 (15-68)	0.569
2 h					
Global	17±14	12 (2-52)	17±11	16 (2-38)	0.602
Proximal	15±17	10 (1-65)	14±11	12 (1-38)	0.829
4 h					
Global	1±1	1 (1-3)	2±2	1 (0-8)	0.865
Proximal	1±1	1 (0-4)	1±2	0 (0–6)	0.133
T1/2 (min)					
Global	58±29	46 (23-119)	50±23	52 (24–94)	0.532
Proximal	55±31	43 (20-139)	44±21	42 (17-85)	0.311
IMD_0 (%)	83±13	88 (62-99)	89±8	91 (70-98)	0.296
RI	1.0±0.1	0.9 (0.8-1.3)	0.9±0.1	0.9 (0.7-1.2)	0.170
Left anterior oblique view method					
Percent retention (%)					
1 h					
Global	49±24	46 (20-91)	44±20	42 (18-87)	0.591
Proximal	43±23	39 (14-97)	36±20	37 (13-82)	0.315
2 h					
Global	18±15	16 (2-57)	18±13	17 (1-43)	0.625
Proximal	16±16	13 (1-65)	15±12	13 (1-38)	0.994
4 h					
Global	1±1	1 (0-4)	2±2	1 (0-9)	0.980
Proximal	1±1	1 (0-3)	1±1	1 (0-5)	0.464
T1/2 (min)					
Global	63±31	55 (26-129)	55±26	52 (23-122)	0.490
Proximal	58±31	51 (19-136)	46±25	41 (22-114)	0.227
IMD_0 (%)	86±12	86 (58-97)	86±9	89 (63-97)	0.713
RI	0.9±0.2	0.9 (0.6-1.2)	0.8±0.1	0.8 (0.6-1.2)	0.191

**P* value based on Mann-Whitney U-test. SD: Standard deviation, Global: Whole stomach, Proximal: Proximal stomach, T1/2: Half time of gastric emptying, IMD_0: Intragastric meal distribution at time t=0, RI: Retention index

retentions at 2 and 4 h were used for assessing delayed gastric emptying. Consequently, the 5th percentile value at 1 h and 95th percentile values at 2 and 4 h, respectively, were used for deriving the reference values. For IMD_0,

Table 5: Spearman's rank correlation between age and gastric emptying parameters

Parameter	Age	
	Spearman's ρ	*P*
Anterior view method		
Percent retention (%)		
1 h		
Global	-0.242	0.154
Proximal	-0.256	0.132
2 h		
Global	-0.260	0.126
Proximal	-0.319	0.058
4 h		
Global	-0.307	0.069
Proximal	-0.307	0.608
T1/2 (min)		
Global	-0.191	0.264
Proximal	-0.233	0.172
IMD_0 (%)	-0.044	0.799
RI	-0.097	0.572
Geometric mean method		
Percent retention (%)		
1 h		
Global	-0.282	0.096
Proximal	-0.317	0.060
2 h		
Global	-0.298	0.077
Proximal	-0.332	0.048*
4 h		
Global	-0.317	0.060
Proximal	-0.191	0.264
T1/2 (min)		
Global	-0.245	0.150
Proximal	-0.284	0.094
IMD_0 (%)	-0.059	0.731
RI	-0.118	0.492
Left anterior oblique view method		
Percent retention (%)		
1 h		
Global	-0.225	0.186
Proximal	-0.274	0.105
2 h		
Global	-0.309	0.066
Proximal	-0.240	0.159
4 h		
Global	-0.385	0.020*
Proximal	-0.259	0.127
T1/2 (min)		
Global	-0.254	0.136
Proximal	-0.286	0.091
IMD_0 (%)	-0.003	0.985
RI	-0.283	0.094

*Significant at $P<0.05$. Global: Whole stomach, Proximal: Proximal stomach, T1/2: Half time of gastric emptying, IMD_0: Intragastric meal distribution at time $t=0$, RI: Retention index

5th percentile value was chosen for defining the reference cutoff. For T1/2 and RI, the respective reference ranges were derived based on 2.5th and 97.5th percentile values. The proposed reference values of GEP based on GM method are given in Table 6.

Discussion

The purpose of the present study was to determine reference values of GEP for the diagnosis of abnormal gastric motility through scintigraphic methods. The reference values of percent retention proposed by our study differ from those suggested by the consensus recommendation based on the study by Tougas *et al.* using a standard egg-based meal.[1,11] The difference is expected due to the different meal used in our study. The corresponding values established by Somasundaram *et al.*[12] were percent retention <30% at 1 h, >30% at 2 h, and >6% at 4 h, respectively. The slight differences in the 1 h and 2 h parameters from our study may be due to the differences in the quantity of the meals used and slight variations in the meal compositions, although both studies used similar gluten-free meals (*Idli*). Furthermore, in the present study, subjects were imaged in supine position while Somasundaram *et al.* imaged the subjects in standing position. However, we believe that positioning at imaging should not affect GEP significantly as the imaging duration is short (1 min) and most of the gastric emptying occurs in between the imaging sessions. The reference value for diagnosing delayed gastric emptying at 4 h in the present study (>5%) is in agreement with that of Somasundaram *et al*., (>6%). This finding re-emphasizes the need for 4 h imaging to reliably diagnose delayed gastric emptying as suggested by the consensus recommendation and Farrell.[1,13]

The mean T1/2 of gastric emptying in the present study differs from that of literature, probably due to differences in the meals and imaging protocols.[14-16] The previous studies did not mention the reference range of T1/2 of gastric emptying based on 95% confidence intervals, as done in the present study. However, we suggest using this parameter only as an adjunct to percent retention since the former is more prone to inaccuracies due to limited time point imaging (four time points only) and the need for extrapolation using mathematical assumptions.[1] This is also supported by the finding that there were significant differences in the distributions and in 2.5th and 97.5th percentile values (more specifically, 97.5th percentile) of this parameter derived on different camera view methods [Tables 2 and 3].

Additional assessment of regional GEP may reliably unmask the causes for symptoms in selected patients and improve patient management. Regional gastric dysmotility has been found to correlate with multiple symptoms including vomiting, nausea, early satiety, abdominal distension, and acid regurgitation.[5,6,17-19] IMD_0 is one such parameter which

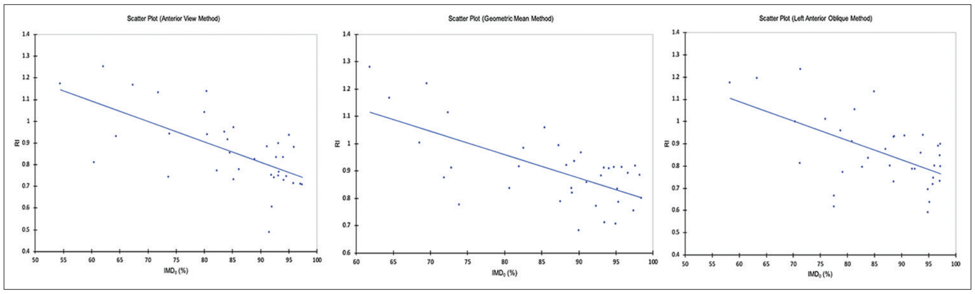

Figure 4: Scatter plots between intragastric meal distribution at time *t* = 0 (IMD0) and retention index in different camera view methods

Table 6: Proposed reference values of gastric emptying parameters based on geometric mean method

Time	Global parameters		Regional parameters	
	Rapid emptying	Delayed emptying		
	Percent retention		IMD_0	RI
1 h	<20%	-	>64%	0.7-1.3
2 h	-	>40%		
4 h	-	>5%		
	Half-time of emptying			
	<23 min	>109 min		

IMD_0: Intragastric meal distribution at time t=0, RI: Retention index

indirectly assesses fundic accommodation (a proxy of proximal gastric function) and has been shown to correlate with measurements by gastric barostat.[6,7,20] RI, initially developed by Spandorfer *et al.*,[8,9] is another regional GEP that might have implications related to therapy planning such as gastric peroral endoscopic myotomy. For IMD_0, we adopted the definition of Orthey *et al.*[6,7] using proximal half of the stomach for the proximal stomach counts. Similarly, we adopted the definition of Spandorfer *et al.*[8,9] for RI with a little modification (i.e. using proximal half of stomach for deriving T1/2 of proximal stomach emptying rather than taking incisura as the landmark to define proximal and distal portions of the stomach as followed by Spandorfer *et al*.). This is because defining incisura on GES is technically demanding in several scans.

The mean IMD_0 (85% ± 12%; anterior view method and 87% ± 10%; GM method) derived in the present study differs from that of Orthey *et al.* (75% ± 15%; anterior view method).[7] The slight difference from our study might be explained due to different meals, protocols, sample sizes, and methodological differences of ROI placing (Orthey *et al.* used semiautomated MatLab (MathWorks) software to automatically derive threshold-based gastric borders to outline the gastric ROI and divide the stomach into two equal parts). However, the mean of IMD_0 derived by Orthey *et al.* in the same study based on a more sophisticated approach using dynamic antral contraction scintigraphy Fourier analysis data was 85% ± 14% (anterior view method), which is similar to our study result. This suggests that simple visual division of the stomach into proximal and distal halves based on a line perpendicular to the longitudinal axis of the stomach correlates well with the functional division of the stomach by Fourier analysis. This is of interest since the former method is easy, quick, and technically less demanding to perform. Orthey *et al.*, in another study on a larger number of patients with gastroparesis and healthy individuals, established a lower limit of 56.8% for IMD_0 to differentiate normal fundic accommodation from impaired fundic accommodation with a sensitivity of 86.7% and specificity of 91.7%.[6] The reference value of IMD_0 (>64%) established in our study based on the 5th percentile value is roughly in agreement with that study although our study included only healthy subjects, and a similar differentiating cutoff could not be derived. A low IMD_0 implies impaired fundic accommodation; the true clinical utility of this parameter remains to be established in large prospective studies.

The reference range of RI established in our study based on GM method was 0.7–1.3. To the best of our knowledge, reference range of this regional GEP has not been previously defined in the literature. A high RI might imply relative proximal gastric retention while a low RI might signify relative distal gastric retention. However, since this parameter is a ratio, interventions that alter the T1/2 of gastric emptying might also alter the RI as seen by Spandorfer *et al.,*[9] and hence, the true clinical implications of this parameter vis-à-vis the clinical profiles of the patients and associated interventional procedures need to be established in large prospective studies. In the present study, there was moderate negative correlation between IMD_0 and RI. This might imply that those who have high or normal fundic accommodation tend to have relatively rapid emptying of food from the proximal stomach and those with low fundic accommodation might have relatively delayed proximal gastric emptying. As this study was done in healthy subjects, a definite conclusion could not be made; larger prospective studies are suggested to understand the interplay between IMD_0 and RI.

Although there were statistically significant differences among majority of the GEP derived on different camera views [Table 3], the clinical significance of these differences needs to be ascertained by critically analyzing the data. From Table 2, we see that the differences in the mean or median values of percent retention derived on different camera view methods become smaller from 1 h to 4 h data. Similarly, the differences in the mean or median values of IMD_0 and RI are small. This becomes more evident and clinically relevant when we derive the reference values of these parameters on each camera view method based on percentiles [Table 2]. These small differences in the reference values or ranges derived on different camera view methods are most likely to be of no clinical significance although the overall distribution of these parameters might have shown statistically significant differences. However, T1/2 of gastric emptying followed a wider range (specifically, the upper reference limit) on anterior view and LAO methods [Table 2]. Based on this finding and due to the advantage of attenuation and depth correction in the GM method, we propose this method to be employed as the standard. However, in very busy departments with high patient throughput where one single-head gamma camera is used for multiple studies, either LAO method or anterior method may be employed especially when 1 h and 4 h percent retention data are used for assessing rapid and delayed gastric emptying, respectively. Furthermore, any camera view method can be employed for regional gastric emptying assessment. However, in general, we prefer LAO over anterior view method due to the lesser overall differences in the distribution of the parameters and the reference percentile values from those derived from GM method.

There are a few studies which compared different camera view methods for GES with varied results and inferences.[15,16,21-24] However, none of these studies critically analyzed the data of GEP (despite being different in different camera view methods) from a clinical significance point of view by assessing the reference values or ranges in a control group or healthy individuals based on percentiles or 95% confidence intervals. As we have shown above, although the majority of the parameters could be differently distributed on different camera view methods, there is little clinical significance as the reference values or ranges derived based on percentiles had little variations.

The present study is not free from limitations. First, the sample size of the study was small, and only subjects who were ≥18 years of age were included; and hence, the proposed reference values might not be applicable to children and adolescents <18 years of age. Second, we used subjective visual analysis of the images to define gastric ROI and proximal stomach instead of more objective approaches such as threshold-based computerized method on summed images, semiautomatic MatLab (MathWorks) software or a more sophisticated dynamic antral contractility scintigraphy-based Fourier analysis method. However, the later approaches are more complex, time consuming, and the involved technology is not available widely. Finally, we derived the intragastric meal distribution at time $t = 0$ (IMD_0) only. The intragastric meal distributions at other time points (1, 2, 4 h) were not derived; these parameters might also provide valuable information.

Conclusion

The study established the reference values of global and regional GEPs, based on an easy to prepare standard vegetarian Indian meal, which may be generalized for the Indian population. The study recommends GM method as the methodology of choice with percent retention as the major parameter while half-time of gastric emptying to be used only as a corroborative parameter. However, single view method (LAO preferred over anterior view) may be followed as an alternative, provided 1 h and 4 h percent retention data are used to define rapid and delayed gastric emptying, respectively. Further studies are suggested to define the clinical utility of regional GEPs.

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Conflicts of interest

There are no conflicts of interest.

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