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## Gastric Emptying Scintigraphy Results in Children are Affected by Age, Anthropometric Factors, and Study Duration

Gregory K. Wong, MD<sup>1,2</sup>, Robert J. Shulman, MD<sup>1,2,3</sup>, and Bruno P. Chumpitazi, MD, MPH<sup>1,2</sup>

<sup>1</sup>Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA

<sup>2</sup>Texas Children's Hospital, Houston, TX, USA

<sup>3</sup>ARS/USDA Children's Nutrition Research Center, Houston, TX, USA

### Abstract

**Background**—A standardized 4-hour adult-based gastric emptying scintigraphy (GES) protocol is increasingly being used in children to evaluate for gastroparesis. We sought to determine the effect of age, anthropometrics, and study duration on GES results using this protocol in children.

**Methods**—Retrospective review of children who underwent a 4-hour solid-meal GES study at a tertiary care center. GES results and anthropometric data (e.g., weight, stature, body surface area) were systematically captured.

**Key Results**—Of 216 children, 188 (87%) were able to complete the study meal. Children unable to complete the meal were younger and smaller. In multivariate analysis, only increasing body surface area (BSA) was identified as being positively associated with ability to complete the meal (odds ratio: 19.7;  $P < 0.001$ ). Of those completing the meal, 48 (26%) had delayed emptying (4-hour retention value  $> 10\%$ ). These children were significantly younger and smaller than those with normal emptying. In multivariate analysis of those completing the meal, only increasing BSA (odds ratio: 0.26;  $P = 0.006$ ) was identified as being negatively associated with delayed emptying. There was a progressive increase in the positive predictive value for identification of delayed gastric emptying as the duration of the study increased (0.25, 0.60, and 0.71 at 1, 2, and 3 hr, respectively) using the 4-hr value as a comparator.

**Conclusions and Inferences**—Young children have more difficulty completing the GES meal. Childhood gastric retention is affected by age and anthropometric factors, primarily BSA. The standardized 4-hr GES protocol may need to take these factors into account in children.

### Keywords

Children; Gastric Emptying; Gastroparesis; Nuclear Medicine; Motility; Dyspepsia

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Correspondence: Bruno P. Chumpitazi, M.D., M.P.H., Texas Children's Hospital, 6701 Fannin Street, CCC 1010.03, Houston, TX, USA 77030, Phone: 832-822-3131, Fax: 832-825-3633, chumpita@bcm.edu.

#### CONFLICTS OF INTEREST

The authors do not have conflicts of interest to report.

#### AUTHOR CONTRIBUTION

GKW, RJS, and BPC designed the research study, analyzed the data and wrote the paper. GKW collected the data. All authors have read, edited, and approved the submitted version of the manuscript.

## INTRODUCTION

Gastroparesis is a gastrointestinal (GI) motility disorder in which the emptying of the stomach is abnormally delayed in the absence of an anatomical obstruction. Estimates of the prevalence of gastroparesis in the adult population range widely, from 0.2 – 4% (1, 2). Females are more affected than males (3, 4). Prevalence rates of gastroparesis in the pediatric population are unknown.

Normal GI motility depends on the integrity of the “gut-brain axis” which is composed of the central, autonomic, and enteric nervous systems, along with the interstitial cells of Cajal and smooth muscle cells of the GI tract (5). Compromise of any of these components can potentially alter GI motility, causing such disorders as gastroparesis, intestinal pseudoobstruction, and intractable constipation (6–8). In the adult population, diabetes, postsurgical complications and Parkinson’s disease are common causes of gastroparesis, though idiopathic gastroparesis is the most common (35.6%) (4). In children, most cases (70%) are believed to be idiopathic (9). However, many so-called idiopathic cases of gastroparesis, in both adults and children, are thought to be postinfectious in nature (9, 10).

Gastric emptying scintigraphy (GES) provides an objective measure of gastric emptying (11). Until recently, the radiolabeled meal utilized for a GES study often differed between institutions. Currently, a low fat solid meal of 2 scrambled eggs (or egg substitute equivalent), 2 pieces of white toast, jam, and 120 mL of water is recommended as the standard meal for GES studies by both the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine (12). Meal standardization has allowed the development of normal adult values for gastric emptying as measured by GES in 123 healthy volunteers (13).

The use of the standardized meal and a 4-hour study has been validated for use in adults but there are few data regarding the utility of these test conditions in children. Although ethical concerns preclude carrying out studies with radiolabels in healthy children, it recently has been reported that the standard solid meal and adult normative values can be used for GES studies in children and that extending the GES study to 4 hours (as opposed to 2 hours) allows for increased sensitivity in detecting gastroparesis in children (14). However, the study population was small (n=71) and not all evaluated participants finished the meal. Other factors potentially affecting GES results were not evaluated.

We therefore sought to determine in children if age and anthropometric measures (weight, stature, body mass index, and/or body surface area) affect GES results. We anticipated that because the same size meal is used for all ages, younger, smaller children would have a more difficult time with meal completion and have slower gastric emptying than would older, larger children. We also aimed to determine in a larger group of patients than in the earlier study if extending the GES study to 4 hr alters the proportion of children identified with delayed gastric emptying and consequently, the predictive value of a gastric retention value obtained prior to the standard time of 4 hours (14). However, unlike the previous investigation, we only studied children able to ingest the entire meal as recommended (14).

## METHODS

### Study Design

We conducted a retrospective review of the electronic medical records of 216 children ranging from 4 – 18 years of age undergoing a GES study as part of their evaluation of upper GI symptoms at the nuclear medicine facility of Texas Children's Hospital over an 18-month time period (February 2012 – July 2013). These evaluations were ordered at the discretion of the treating physician as part of routine clinical practice. The majority of children had dyspepsia (e.g., nausea) of a chronic nature for which the clinician was considering delayed gastric emptying as a potential etiology. Children with a known history of abdominal surgery (e.g., pyloric surgery, bowel resection, fundoplication, etc.) or any known organic GI disease (e.g., inflammatory bowel disease, celiac disease, H. pylori infection, etc.) were excluded. Patients who required a modification of the standard solid meal for GES (see below) were not included. Patient demographics, anthropometric data (height, weight, body mass index, and body surface area) and GES results were collected during the chart review process. The study was approved by the Baylor College of Medicine Institutional Review Board.

### Gastric Emptying Scintigraphy

All GES studies utilized the recommended standard solid meal consisting of 2 pieces of white toast, 120 mL of scrambled egg substitute (equivalent of 2 large eggs), a 15 g packet of jelly, and 120 mL of water (13). Technetium-99-labeled sulfur colloid was utilized for all studies and was mixed in the egg substitute prior to cooking. Meals were consumed within a 10-minute period, after which a baseline scintigraphic image was obtained. Anterior and posterior images were acquired concurrently and a geometric mean value was calculated (12). Subsequent images were taken at 1-hour intervals over a 4-hour period. If a child was unable to consume the entire meal within a 10-minute period or if they vomited within the 4-hour duration of the GES study, he/she was excluded from the primary data analysis and labeled as "unable to complete GES." Children who required a modification of the meal (e.g., gluten-free bread) were not included. GES results were reported as gastric retention values at the 1, 2, 3 and 4-hour time points of the study. Delayed gastric emptying was defined as a gastric retention value greater than 90%, 60%, 30%, and 10% at the respective 1-, 2-, 3-, and 4-hour time points of the GES study (12).

### Data Analysis

Student t-test was used to compare mean age and anthropometric measures between children with and without abnormal GES studies, and between children with and without delayed gastric emptying based upon the recommended 4-hour time point. Age and anthropometric-based groups were created by dividing the range into quartiles. A binary logistic backward stepwise regression was completed to evaluate which anthropometric factors were most strongly associated with ability complete the meal and with the identification of delayed gastric emptying. Due to high correlation between anthropometric variables, only age, body mass index (BMI) and body surface area (BSA) were included in the regression models as independent variables. IBM statistical Package for the Social Sciences (Armonk, New York)

version 19 was used for all statistical analysis. Unless otherwise specified, data are presented as mean  $\pm$  standard deviation.

## RESULTS

Over the 18-month study period, 216 children (135 females; mean age  $12.0 \pm 3.9$  yrs., range 4.2–18.2 yrs.) were enrolled. 28 (13%) children were unable to complete the study (unable to consume or vomited the GES meal). Children unable to complete the study ( $n=28$ ) were significantly younger and smaller in weight, stature, and BSA than those who were able to consume and tolerate the meal ( $n=188$ ) (Table 1). BMI percentile (which takes into account normative values for age) did not differ between groups (Table 1). In multivariable analysis, only BSA remained in the final backward stepwise model suggesting larger children were more likely to complete the meal (Table 2).

Of the 188 children who ate and tolerated the meal and underwent GES, 48 (26%) had delayed gastric emptying based upon the 4-hour time point (Table 3). Children with delayed gastric emptying were significantly younger, with lower body weight, height, and BSA than those with normal gastric emptying (Table 3). BMI percentile did not differ between groups (Table 3). Gender was not associated with an increased likelihood of having delayed gastric emptying (Table 3). In multivariable analysis, only BSA remained in the final backward stepwise model and was negatively associated with having delayed gastric emptying suggesting larger children were less likely to be identified with gastroparesis (Table 4).

In order to evaluate further the relationship between gastric emptying vs age and anthropometric factors, we compared gastric retention values to these variables with the population broken down by quartile groups to facilitate visualization (Figure). In all cases the group with the lowest quartile value had increased gastric retention, particularly noted from the 2-hour time point onward.

Increasing the duration of the GES study improved the positive predictive value of the test as compared to the 4-hour time point (Table 5). In contrast, the negative predictive value did not change significantly as a function of study duration (Table 5).

## DISCUSSION

GES is the gold standard utilized in evaluating gastric retention and making the diagnosis of delayed gastric emptying. The current recommendations for GES require patients to consume a standard meal within a relatively short period of time. Although it has been suggested that the standard GES protocol used in adults can be adopted for use in the pediatric population, our results suggest age and anthropometric factors should be taken into account (14). First, a sizable proportion of children (13%) who tended to be younger, could not consume or tolerate (i.e., vomited) the standard meal within the required time. This could compromise study results. Second, of the children who were able to complete the GES study, those with delayed gastric emptying were found to be significantly younger and smaller than those without delayed gastric emptying. Future studies may help elucidate better standards for children while taking into account age and anthropometric factors.

We questioned whether there was a time by age and/or anthropometry effect on the GES results. We divided the entire population into quartiles based on age and anthropometric factors. In order to evaluate the effect of these variables on gastric residual values over time. The youngest children had higher gastric retention values when compared to the other age groups (Figure). Not surprisingly, because age, weight, stature, body mass index, and body surface area are highly correlated, generally parallel results were seen when dividing the cohort into quartiles according to anthropometric factors (Figure). These findings suggest that younger and smaller children are likely to have increased gastric retention values as compared to older children using the standard 4-hour GES protocol. We note however, that the differences were most pronounced beginning at the 2-hour time point. Drubach et al. compared gastric retention values at 1 hour in children < 8 yrs. of age vs older children (n=65) and in those < 30 kg vs > 30 kg (n=65) and found no differences between groups (15). Although the meal differed between their study and ours in that only labeled eggs or labeled cheese was used in the Drubach study, our findings fit with theirs in that differences among quartiles in our study were not apparent at the 1-hour time point (Figure).

In adults it has been identified that gender plays a role in gastric emptying with women having more gastric retention compared to men as measured by half-time gastric emptying (16). However, in our study a gender difference was not seen when examining the amount of gastric retention at 4 hours. Future prospective studies evaluating the role of gender in children undergoing GES are needed to confirm our findings.

Gastric weight (and presumably size) increases linearly in relationship to age from approximately 3 months of age until adulthood (17). The same linear relationship can be found to anthropometric measures such as BMI with other visceral organs such as the liver through adulthood (18, 19). However in adults, gastric size based on mucosal surface area does not appear to be related to age, weight, or height (20). Some children in the youngest age group have a gastric size less than one third the size of an adult (17). Therefore, we hypothesize that the increased gastric retention in the young children may be related more to the ratio of meal size to gastric size than abnormal gastric emptying per se. The fact that 13% of younger children could not tolerate the GES meal and that increasing BSA was negatively associated with delayed gastric emptying in those who could complete the meal supports this speculation. Given the nature of our study, we can only show an association and as such, it is possible that children with delayed gastric emptying or dyspepsia may have secondary effects on their anthropometric measures (e.g., weight) due to the underlying pathologic process. Nevertheless our results, combined with previous work evaluating gastric size and visceral organ size correlations with body surface area lead us to believe that the currently recommended meal for GES studies in adults may not be appropriate for all children, particularly in those less than ten years of age given the current normal gastric retention values.

Alternatively, normal gastric retention values would need to be defined for young children vs older children if the same meal was used for all groups. Future studies might employ simultaneous use of single photon emission computed tomography (SPECT) and GES. SPECT has been utilized to measure gastric capacity during fasting and during the postprandial state and can be performed in tandem with GES (21, 22). However, SPECT

radiation exposure may limit its feasibility in children. In an attempt to minimize radiation exposure,  $^{13}\text{C}$  gastric emptying breath testing using various meal sizes may be used (23) as can ultrasound evaluations of liquid gastric emptying (24). In addition, satiety testing in normal children and those with dyspepsia may provide insight into appropriate meal sizes (25). Data from such studies may help adjust meal size to gastric size in children. Additionally, it may afford the possibility of assessing the presence of gastric fundus accommodation dysfunction as well as delayed gastric emptying as an etiology of symptoms (21, 22).

Our data also suggest that the positive predictive value of GES increases with a longer duration of study, using the 4-hour time point as a reference (Table 5). Similar findings have been reported in adults (12). However, our results differ from those of Chogle et al. who studied a smaller number of children ( $n=71$ ) and found a higher positive predictive value at 2 hours of 0.89 using the value at 4 hours as a comparator (14). This may be due in part to the fact that in their study children who finished 25% of the meal were included. Additionally, the studied population may have differed between our two studies given the frequency of delayed gastric emptying was much greater in their study than in ours (66% vs 28%, respectively based on the gastric residual value at the 4-hour time point) (14). Our data suggest that, although the positive predictive value increases with time, the negative predictive value at 1, 2, and 3 hours is high and remains relatively stable (0.92, 0.87, and 0.93, respectively) (Table 5).

There are some limitations of our study. First the study was retrospective, though we note that all captured measures were objective and readily available in the electronic medical record and as such, a prospective design would be unlikely to demonstrate significantly different results. Second, the study was conducted at a single center, and therefore the results may not be generalizable to all centers.

Our study has several strengths. First, to our knowledge, it is the largest study to date to evaluate GES in children. Second, the results are clinically relevant and potentially more generalizable to other pediatric practices given that all studies were completed as part of routine clinical practice. Third, the population studied was diverse in nature with a wide range of ages and body sizes represented. Finally, the results were standardized with the data regarding gastric residual values being based only on children who consumed and tolerated the entire meal.

In conclusion, in children, GES results following a standardized 4-hour protocol can be affected by patient age, anthropometric factors such as height and body mass index, and study duration. Extending the duration of GES beyond one hour appears to accentuate the effects of anthropometric factors while increasing the positive predictive value of results at time points prior to 4 hours. Further studies are needed to establish an appropriate meal size and/or normative GES values for use in pediatric patients, particularly young children.

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## Abbreviations

GES      gastric emptying scintigraphy

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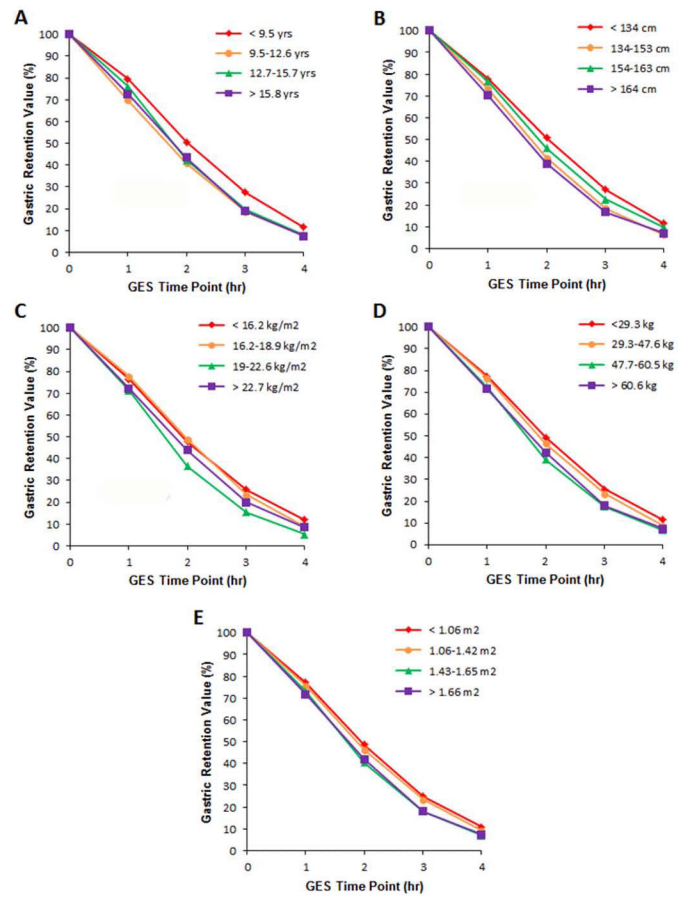
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**KEY MESSAGES**

- We determined the effect of age, anthropometrics, and study duration on gastric emptying as measured by up to 4 hours of gastric emptying scintigraphy (GES) in 188 children in a retrospective study.
- Age, weight, height, and body surface area were less in those who were unable to finish the GES meal compared with those who ingested all of the meal.
- In those children who ate all of the meal, younger age and lower weight, height, and body surface area were associated with slower gastric emptying. The differences were magnified by increasing duration of the GES.



**FIGURE. Gastric Retention Values over Time between Age- and Anthropometric-based Groups**  
 Gastric retention values over time between children (n=188) when divided into quartiles by  
 (A) age, (B) height, (C) body mass index, (D) weight, and (E) body surface area.

**Table 1**

Demographic and Anthropometric Measures of Children Able vs Unable to Complete the GES Study

	Completed GES (n=188)	Unable to Complete GES* (n=28)	P-value
Gender	120 F (64%)	15 F (54%)	0.296
Age (yrs.)	12.5 ± 3.7	8.6 ± 4.2	< 0.001
Weight (kg)	46.4 ± 18.7	29.7 ± 19.6	< 0.001
Height (cm)	149.2 ± 19.2	126.5 ± 23.6	< 0.001
BMI <sup>#</sup> (kg/m <sup>2</sup> )	20.0 ± 4.7	16.8 ± 3.8	0.001
BMI (percentile)	56.4 ± 32.1	45.3 ± 35.1	0.11
BSA <sup>^</sup> (m <sup>2</sup> )	1.4 ± 0.4	1.0 ± 0.4	< 0.001

\* Refused to eat standard meal, ate eggs only, or vomited during the study. Data presented as Mean ± SD.

<sup>#</sup> BMI = Body Mass Index

<sup>^</sup> BSA = Body Surface Area

**Table 2**  
 Backward stepwise logistic regression multivariate analysis of factors associated with ability to complete the meal

Model 1		Model 2		Final Model							
Factor	OR	95% CI	P- Value	Factor	OR	95% CI	P- value	Factor	OR	95% CI	P- value
BMI*	0.97	0.77 – 1.2	0.81	Age	1.15	0.89 – 1.49	0.29	BSA	19.7	5.1 – 75.7	<0.001
Age	1.13	0.83 – 1.5	0.44	BSA	4.97	0.3 – 82.0	0.26				
BSA#	7.88	0.08 – 815.3	0.38								

\* BMI = Body Mass Index

# BSA = Body Surface Area

Each step of the analysis is shown with the final model only including BSA after both BMI and age have been removed.

**Table 3**  
Demographic and Anthropometric Measures of Children with Normal versus Delayed Gastric Emptying

	Normal Emptying (n=140)	Delayed Gastric Emptying (n=48)	P-value
Gender	86 F (61%)	34 F (71%)	0.242
Age (yrs.)	12.9 ± 3.5	11.3 ± 3.8	0.011
Weight (kg)	48.5 ± 18.4	40.4 ± 18.8	0.010
Height (cm)	151.6 ± 18.3	142.2 ± 20.2	0.003
BMI* (kg/m <sup>2</sup> )	20.3 ± 4.7	18.8 ± 4.7	0.066
BMI (percentile)	58.6 ± 31.4	50.0 ± 33.6	0.135
BSA# (m <sup>2</sup> )	1.41 ± 0.35	1.25 ± 0.37	0.005

Mean ± SD

\* BMI = Body Mass Index

# BSA = Body Surface Area

**Table 4**  
 Backward stepwise logistic regression multivariate analysis of factors associated with identification of delayed gastric emptying

Model 1		Model 2		Final Model			
Factor	OR	95% CI	P-Value	Factor	OR	95% CI	P-value
BMI*	1.0	0.91 – 1.2	0.5	BMI	1.0	0.92 – 1.2	0.5
Age	1.0	0.83 – 1.2	0.89	BSA	0.17	0.03 – 0.85	0.03
BSA#	0.14	0.01 – 2.59	0.19				

\* BMI = Body Mass Index

# BSA = Body Surface Area

Each step of the analysis is shown with the final model only including BSA after both BMI and age have been removed.

**Table 5**

Number of Gastric Emptying Scintigraphy Studies Demonstrating Normal or Delayed Emptying at 1, 2, and 3 hr vs Results of the 4-hr Study

	1 hr		2 hrs.		3 hrs.	
	Normal	Delayed	Normal	Delayed	Normal	Delayed
Normal at 4 hrs.	129	11	122	18	130	10
Delayed at 4 hrs.	36	12	19	29	14	34
Positive predictive value	0.25		0.60		0.71	
Negative predictive value	0.92		0.87		0.93	