

Pediatric Solid Gastric Emptying Scintigraphy: Normative Value Guidelines and Nonstandard Meal Alternatives

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INTRODUCTION: Adult standards for gastric emptying scintigraphy, including the type of meal and range of normative values for percent gastric emptying, are routinely used in pediatric practice, but to date have not been validated. The purpose of this study is to determine whether the use of adult criteria for gastric emptying scintigraphy is valid for children and whether alternative nonstandard meals can also be offered based on these criteria.

METHODS: This retrospective study analyzed patients (n = 1,151 total) who underwent solid-phase gastric emptying scintigraphy. Patients were stratified into normal and delayed gastric emptying cohorts based on adult criteria, i.e., with normal gastric emptying defined as $\leq 10\%$ gastric retention at 4 hours. Patients were further stratified based on the type of meal, namely complete or partial adult standard meals or alternative cheese-based meals. Percent gastric retention values at 1, 2, 3, and 4 hours were compared.

RESULTS: The median (95% upper reference limit) percentage gastric retention values for the complete standard meal were 72% (93%) at 1 hour, 39% (65%) at 2 hours, 15% (33%) at 3 hours, and 6% (10%) at 4 hours. By comparison, the values for cheese-based meals were 60% (87%) at 1 hour, 29% (61%) at 2 hours, 10% (30%) at 3 hours, and 5% (10%) at 4 hours. Consumption of at least 50% of the standard meal yielded similar retention percentages; 68% (89%) at 1 hour, 32% (57%) at 2 hours, 10% (29%) at 3 hours, and 5% (10%) at 4 hours. There were no significant age- or sex-specific differences using the adult criteria.

DISCUSSION: The adult normative standards for gastric emptying scintigraphy are applicable for use in the pediatric population. These same standards can be also be applied to nonstandard meal options, including cheese-based alternative meals and partial standard meals.

SUPPLEMENTARY MATERIAL accompanies this paper at <http://links.lww.com/AJG/B627>, <http://links.lww.com/AJG/B628>, <http://links.lww.com/AJG/B629>, <http://links.lww.com/AJG/B630>, <http://links.lww.com/AJG/B631>

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INTRODUCTION

Gastrointestinal motility disorders are common in children and can be associated with severe consequences if not appropriately diagnosed and managed (1–5). Gastric emptying scintigraphy is an important, noninvasive technique used to directly assess gastric motility in the pediatric population (5–8) and provides a physiologic, noninvasive, and quantitative means of measuring gastric emptying. Extensive work has been performed to develop consensus guidelines for standardizing the protocols used for gastric emptying scintigraphy in adults (9), including optimizing image acquisition techniques (7,10), determining the administered dose of radiopharmaceutical (7), identifying appropriate image acquisition time

points (11,12), and establishing normal criteria for study interpretation (13). For ethical and pragmatic reasons, the establishment of normative values and the development of standardized protocols have been challenging in the pediatric population, and there remains a continued need to both optimize and harmonize the gastric emptying scintigraphy protocols used in children.

One important component of the gastric emptying study that has received particular attention has been standardization of the type of meal that is being administered (14). Differences in gastric emptying between liquid and solid meals have been demonstrated (15). Furthermore, the caloric content of the meal (16) and the need for stable binding between the radiotracer being imaged and the

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solid component of the meal (17–19) are additional considerations that can significantly impact study results. In the United States, consensus guidelines for gastric emptying scintigraphy in adults have been published, with recommendations for a standard meal to consist of 118 mL liquid egg whites (equivalent to 2 large eggs), 2 slices of toasted white bread with 30 g jelly, and 120 mL of water (7). The development of practice guidelines with criteria outlining the components of a standard meal is useful, particularly for repeat examinations, intra- and inter-patient comparison, and to enable practitioners to reliably interpret and compare studies performed at other institutions. Nonetheless, it can be challenging to rigorously adhere to the adult standards in pediatric practice. Furthermore, the suitability and validity of applying the adult standards to children have not been established.

Children often have a variable tolerance for the standard meal prescribed in the adult consensus guidelines. This may be based on patient age, behavioral issues, dietary sensitivities, or aversion to certain types of food. In fact, a recent study suggests that less than a third of pediatric patients can consume the entire standard adult meal, especially so in younger patients (20). Other considerations including allergies, cultural sensitivities, and patient preference may also preclude consumption of the entire standard meal. These factors, among others, have motivated the development of alternatives to the adult standard meal, including consumption of a partial standard meal, along with studies to validate the performance of these alternatives in the pediatric population.

We have previously demonstrated the suitability of cheese-based meals as an alternative meal option for pediatric gastric emptying scintigraphy. The binding of radiotracer to cheese was shown to be stable throughout the imaging study duration and was comparable to egg whites used for standard solid-phase gastric emptying (17). As a result, we have routinely used cheddar cheese, added to macaroni or as a topping on pizza, as an alternative to radiotracer-labeled eggs when the children cannot tolerate the standardized meal. Based on these considerations, the purpose of the current study is 2-fold. First, in this retrospective analysis of data obtained from over 1,000 pediatric subjects, we will assess the performance of the standard adult meal in pediatric gastric emptying scintigraphy and to determine whether the standard adult normative ranges for percent gastric retention could be applied for children. Second, using these normative value ranges, we will compare the performance of the standard adult meal with nonstandard meals, namely partial standard meals and cheese-based alternative meals. We hypothesize that the adult normative values can be applied to children, irrespective of age and sex, and that nonstandard meals can have comparable diagnostic performance to the standard adult meal for assessment of delayed gastric emptying. These results provide much needed guidelines for pediatric gastric emptying scintigraphy and in addition validate the use of alternative meal options in children, when either the standard adult meal is poorly tolerated or contraindicated or when a full standard meal cannot be consumed.

METHODS

Subject selection

The institutional review board of our institution approved this retrospective analysis, and the requirement for written informed consent was waived. The reports for 1,151 consecutive gastric emptying scintigraphy studies performed between September 2013

and September 2019 were identified by MONTAGE software (Montage Healthcare Solutions, Philadelphia, Pennsylvania) using the search term gastric motility and filtered for only nuclear medicine studies. The reports were analyzed and sorted as shown in Figure 1. In our clinical practice, infants and young children (aged <6 years) are assessed with a different protocol compared with older children (5,21) and were excluded from further analysis. Patients who were unable to complete the study ($n = 50$), for example, due to vomiting, were also excluded to enable direct comparison with previously reported adult normal gastric emptying ranges (9). Table 1 summarizes the definitions of the meals examined in this study. The standard meal was defined as consisting of 2 eggs, 2 pieces of toast, and 4–8 oz of water. The presence of jelly was considered optional, based on prior studies, which defined standard meals as both including and excluding jelly (7,20,22). Partial standard meals were separated into 4 different cohorts for analysis: $\geq 75\%$, $< 75\%$, $\geq 50\%$, and $< 50\%$ of total meal ingestion, as defined in Table 1, and were further analyzed for this study. The different types of cheese-based alternative meals are defined in Table 1 and were analyzed as a single cohort.

Gastric emptying protocol

Patients are asked to fast for a period of at least 4 hours. Blood sugars were not routinely checked at the time of each examination. The decision to stop or continue medications that may interfere with gastric motility was left to the discretion of the ordering provider in coordination with the patient's family, as often the purpose of the study is to evaluate gastric emptying with medications in place. Studies are performed by mixing ^{99m}Tc -sulfur colloid (0.55 MBq/kg, minimum 7.4 MBq, maximum 24 MBq) with the meal to be administered. Although current North American consensus guidelines and American College of Radiology/Society of Pediatric Radiology practice standards for gastric emptying scintigraphy do not recommend weight-based administered doses of radiopharmaceutical, given the retrospective nature of this study, the range of actual administered doses used in our practice has been reported (23). These doses fall well within the recommended dose ranges in the consensus guidelines (8). Both the standard and alternative solid-phase meals were prepared as previously described, with cheddar cheese being used for the alternative meals (7,17). Sulfur colloid was added during the cooking of eggs on the frying pan or in the case of cheese-based meals while the cheese was melted on the frying pan, in both cases to insure adequate binding of radiopharmaceutical to the protein matrix in the solid-phase meal. The meals were administered orally over 10 minutes under the supervision of a nuclear medicine technologist. Completion of the meal was documented by the technologist. Static upright images were acquired for 30 seconds in anterior and posterior projections using an ultra-high-resolution collimator. Imaging was performed immediately postingestion ($t = 0$) and then hourly for up to 4 hours postmeal ingestion. Regions of interests were drawn manually about the stomach by the technologist at each time point and confirmed by the attending nuclear medicine physician. The geometric mean of counts adjusted for physical decay (square root of the product of the anterior and posterior counts) was determined at each imaging time. The percent gastric residual was calculated by taking the ratio of counts remaining in the stomach at each time point relative to the total gastric counts at $t = 0$ and expressed as a percentage. If the gastric residual became $\leq 10\%$ at any time point from 2 to 4 hours, the study was considered normal and ended.

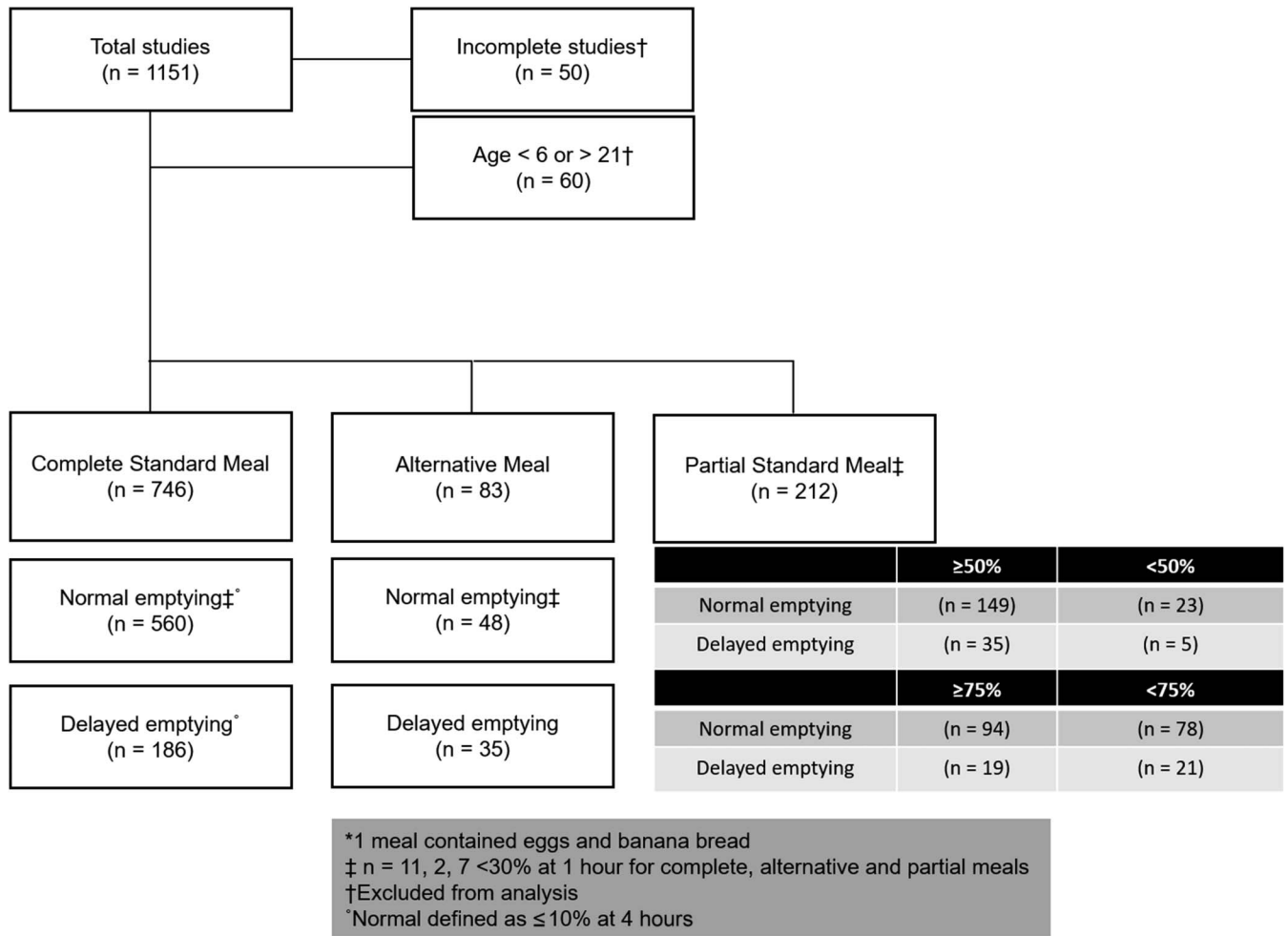


Figure 1. Study schematic.

Assessment of normal and delayed gastric emptying definitions in pediatric subjects

None of the subjects studied here were part of a normal control group because all subjects were undergoing gastric emptying scintigraphy as part of their symptomatic gastroparesis/nausea/gastric dysmotility evaluation. Thus, an independent verification of their normal vs delayed status was not possible. We therefore used data-driven cluster analysis to ascertain the validity of using the adult criteria for children. Gastric retention percentages for each type of meal were subjected to a k-means clustering algorithm using a squared Euclidean distance metric.

Given that we applied the adult literature criteria stating that retention values $\leq 10\%$ at or before 4 hours constituted normal gastric emptying, whereas $>10\%$ at 4 hours constituted delayed emptying (7), studies can potentially have less than 4 values of percent gastric retention reported if subjects achieve retention values of $\leq 10\%$ earlier than 4 hours. For simplicity, in those few cases where the study was completed sooner than the 4-hour time point, the remaining gastric retention values were conservatively estimated as being the last retention value recorded for the study. Physiologic model-based estimation (8) of these values was not performed, given the insufficient temporal resolution of the data for adequate fitting. The subjects were clustered into 2 separate groups for each meal. Clustering via the k-means algorithm was

then compared with the designations determined by using the adult criteria for normal emptying ($\leq 10\%$ at 4 hours). These analyses were performed using MATLAB and GraphPad Prism.

Statistical considerations

Descriptive statistics were calculated for gastric retention values. The upper limit of normality (defined as the reference values) was estimated using the right-sided 90% and 95% reference range, based on the normal distribution method and nonparametric percentile robust bootstrap method (using 5,000 repetitions) (24). All distributions were tested for normality using the Shapiro-Wilk test. Unless otherwise stated, nonparametric tests were performed, namely the Mann-Whitney test and Kruskal-Wallis test with Dunn correction for multiple comparisons. The chi-square test was used where appropriate. Comparison of different age groups was performed using previously defined age ranges (25). A *P* value of 0.05 or less was considered statistically significant. Analyses were performed using MATLAB, GraphPad Prism, and Excel.

RESULTS

Subject demographics and indications for obtaining the examination are presented in Table 2. No significant differences in age were noted between subjects consuming different types of meals. More

Table 1. Meals administered

	Kcal	Weight (g)	Fat (g)
Complete standard meal			
2 scrambled eggs, 2 pieces of toast (with/without jelly), and 8 oz water	180–255	~240	4–5
Partial standard meal ^a			
75%: any one of:			
1 scrambled egg and 2 pieces of toast			
2 scrambled eggs and 1 piece of toast			
1.5 scrambled eggs and 1.5 pieces of toast along with 8 oz water (with/without jelly)			
50%: any one of			
1 scrambled egg and 1 piece of toast			
2 scrambled eggs along with 8 oz of water (with/without jelly)			
Alternative meal (must contain cheese, administered with 8 oz water) ^b			
Macroni and cheese (0.5–1 cup, with 1–2 tablespoons of cheddar cheese)	215–430	110–220	15–30
Pizza (0.5–1 slice, with 1–2 tablespoons of cheddar cheese)	230–460	100–200	13–26
Grilled cheese sandwich (1–2 slices of toast with 1–2 tablespoons of cheddar cheese) ^c	~235	80	8
Egg with banana bread (n = 1)	N/A	N/A	N/A
N/A, not available.			
^a Common reasons for meal incompleteness include aversion to the meal content, satiety before finishing the meal, nausea, and vomiting. This information was not recorded on a per-subject basis at the time of the procedure.			
^b Common reasons for choosing the alternative meal include aversion and allergy (usually egg) to components of the standard meal. This information was not recorded on a per-subject basis at the time of the procedure. The choice of the type of meal was made by the parents.			
^c https://mobile.fatsecret.co.za .			

female subjects underwent gastric emptying studies (851 compared with 442 males), a finding observed with each type of meal (complete standard: 67.2% [502/746]; partial standard: 64% [162/252]; alternative: 56.6% [47/83]). A higher proportion of females consuming the complete standard meal and <50% of the standard meal showed delayed gastric emptying ($P < 0.0001$ and $P = 0.04$, respectively) compared with their male counterparts; otherwise, the proportions were not significantly different between the different meals or between normal vs delayed subjects ($P = 0.1–0.94$). Not unexpectedly, for subjects receiving the partial standard and alternative cheese-based meals, a very small but statistically significant decrease in administered dose was noted compared with the complete standard meal. However, most meals included in this analysis were within 20% of the consensus-recommended administered activity of 18.5 MBq (7). Moreover, all images analyzed for this study demonstrated sufficient activity for image acquisition and interpretation, and all percent gastric retention values were determined relative to total counts present at $t = 0$.

Nonstandard meals show similar gastric emptying performance by 4 hours postingestion

Comparisons between normal and delayed gastric retention values across different time points and with different meal choices are shown in Figure 2. There was no statistical difference between the $\geq 50\%$ and the $\geq 75\%$ partial standard meals (Figure 1, see Table, Supplemental Digital Content 1, <http://links.lww.com/AJG/B627>). As such, partial standard meals is subsequently defined as either <50% of the complete standard meal or $\geq 50\%$ of the complete standard meal (Table 2). Descriptive statistics are provided in Supplemental Digital Content 1, <http://links.lww.com/AJG/B627>. No distributions exhibited normality; hence, median and

percentile-based values are reported. A significant decrease in retention was noted at 1–2 hours for the alternative and partial standard meals compared with the complete standard meal, with the difference most pronounced in subjects consuming <50% of the standard meal. However, no differences in percent gastric retention were observed by 4 hours. Despite these differences, the 95th percentile normative values for both partial meals and alternative meals remained within 6% of the 95th percentile value for the complete meal throughout the 4 hours. Delayed values remained well above the 10% threshold criteria for all meals evaluated (Figure 2b). Taken together, these results support the use of a 4-hour time interval for determination of delayed gastric emptying.

Given the wide age range and sex differences in our cohort, we sought to determine whether any significant age (Figure 3, see Figure, Supplemental Digital Content 2, <http://links.lww.com/AJG/B628>) or sex (Figure 4, see Figure, Supplemental Digital Content 3, <http://links.lww.com/AJG/B629>) dependent differences in either normal or delayed gastric emptying could be seen. No significant differences across the different age ranges were observed, irrespective of which meal was consumed, except for the 13–14 and 15–17 age ranges at the 3-hour time point after ingestion of $\geq 50\%$ partial meal. For all cohorts examined, delayed gastric emptying values were unequivocal, with delayed median gastric retention values being well above the 10% criteria at 4 hours for all ages and both sexes at all time points (Figure 3d–f, Figure 4d–f), reinforcing the use of the 4-hour time point for determining normal vs delayed gastric emptying.

These results were then compared with previously published adult and pediatric studies in normal subjects (Figure 5). Both the standard, partial standard, and alternative meals in this study showed comparable gastric emptying characteristics to other

Table 2. Subject demographics

	Age			Normal	Delayed	P value		
	All, median (5%, 95%)							
Complete standard meal	15 (8, 20)			15 (8, 20)	16 (7.4, 20)	0.99		
Partial standard meal	14 (7, 20)			14 (7, 19)	14 (6.1, 20)	0.99		
Partial standard meal \geq 50%	14 (7, 20)			14 (7, 20)	14 (6, 20)	0.99		
Partial standard meal < 50%	12 (7, 17)			11 (7, 17)	12 (7, 17)	0.99		
Alternative meal	13 (7, 20)			12 (6.5, 18)	15 (8.6, 21)	0.30		
	Sex						χ^2	P value
	Normal			Delayed				
	Male	Female	Total subjects	Male	Female	Total subjects		
Complete standard meal	206	354	560	38	148	186	16.97	<0.0001
Partial standard meal	72	140	212	18	22	40	1.79	0.18
Partial standard meal \geq 50%	47	102	149	14	21	35	0.91	0.34
Partial standard meal < 50%	7	16	23	4	1	5	4.23	0.04
Alternative meal	21	27	48	15	20	35	0.01	0.94
	Activity (MBq), mean \pm SD		P value compared to complete standard meal					
Complete standard meal	18.9 \pm 7.4							
Partial standard meal	17.7 \pm 3.0		<0.001					
Alternative meal	18.2 \pm 1.9		0.02					
Reason for examination ^a	Total (% , n = 1,041)	Total (%)						
Gastroparesis	97 (9)	Diabetic subjects 30 (3)						
Early satiety/feeding intolerance	176 (17)							
Nausea/vomiting	615 (59)							
Abdominal pain	288 (28)							
Weight loss	52 (5)							
Reflux	85 (8)							
Presurgical evaluation	28 (3)							
Symptoms related to surgery	19 (2)							
Other	110 (11)							

^aEach subject can have multiple indications.

studies using the standard meal in healthy adults (13,24), with all reaching the 10% threshold by 4 hours postmeal ingestion, although the values reported by Malik et al., (26) using a vegetarian meal in healthy pediatric subjects, showed overall slower gastric emptying rates.

Adult definition of normal gastric emptying is applicable to the pediatric population

Because all gastric emptying studies included in our analysis were performed in subjects with clinical symptoms, an independent verification of their normal vs delayed status was not possible. We therefore used a data-driven k-means clustering analysis to independently assess the suitability of applying the adult definition for normal and delayed gastric emptying in children. Subjects defined as normal vs delayed based either on the adult criteria or by k-means clustering are shown in Figure 6a,b, respectively. This was performed for subjects consuming the complete standard, partial

standard, and alternative meals based on the comparable gastric emptying characteristics observed with the different meals as presented above. Given that the clustering was performed over 4 dimensions, principal component analysis was performed, and the clusters were plotted along the first 2 principal components. Overall, there was good concordance between the 2 methods, with 80% (597/746), 88% (162/184), and 86% (71/83) of subjects being assigned the same cluster for standard, \geq 50% of the standard and alternative meals, respectively.

A subgroup analysis of the small percentage of discordant subjects, who clustered outside the normal vs delayed groups, showed intermediate percentage gastric retention values. Those defined as delayed by both methods had significantly increased gastric retention values compared with those considered normal by both methods, independent of the imputation method used (see Figure, Supplemental Digital Content 4, <http://links.lww.com/AJG/B630>; see Table, Supplemental Digital Content

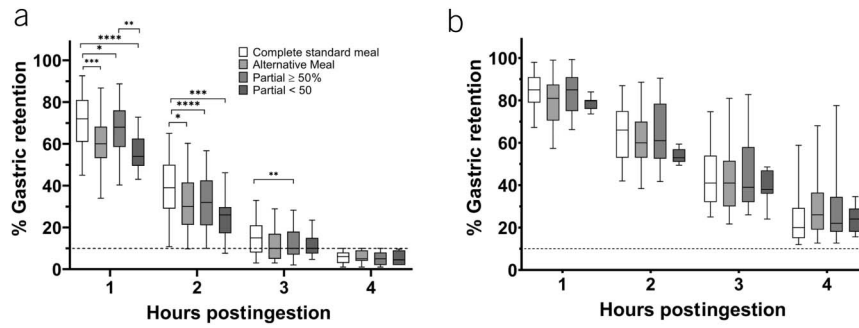


Figure 2. Comparison of normal (a) and delayed (b) gastric retention for different meals. Whiskers denote 5% and 95% percentile values. Boxes denote 25%, 50%, and 75% values. Comparisons between meals for normal and delayed retention were performed with the Kruskal-Wallis test (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, and **** $P < 0.0001$).

5, <http://links.lww.com/AJG/B631>). Taken together, these results affirm, by using a data-driven approach, that the adult guideline criteria, which recommend using $\leq 10\%$ as the upper normal limit for gastric retention at 4 hours, can be extended to children and provide a reasonable definition for identifying children with both normal and delayed gastric emptying.

DISCUSSION

The use of gastric emptying scintigraphy plays an important role in the diagnosis and management of gastric dysmotility in children. Establishment of normative values for gastric emptying scintigraphy in children has been hampered by small sample sizes, wide variability in age and sex, and the practical challenges of evaluating normal subjects to establish benchmark data for reference. A recent report sought to define normative values for milk-based liquid emptying studies for children younger than 5 years (27) but direct

assessment of pediatric solid-phase gastric emptying has been limited. As such, the adult gastric emptying criteria, which designate percent gastric retention values of $\leq 10\%$ at 4 hours as normal, have been adopted in pediatric solid-phase gastric emptying studies (7). We found here that the use of this definition is reasonable and supported by our data, in which more than 1,000 pediatric subjects were evaluated, the largest pediatric cohort to date. In our study, >500 subjects were considered normal by the adult standard (which is based on 123 adult volunteers (13)) and showed 95th percentile values within 5% of the defined adult standard at all time points. This is in keeping with prior reports suggesting similar gastric emptying rates between children and adults (28). Our results also support the use of the longer 4-hour gastric emptying protocol as opposed to a shorter duration examination (22,29,30). For instance, 12% (70/562) of subjects with normal percent gastric retention values at 2 hours ultimately had abnormal delayed values

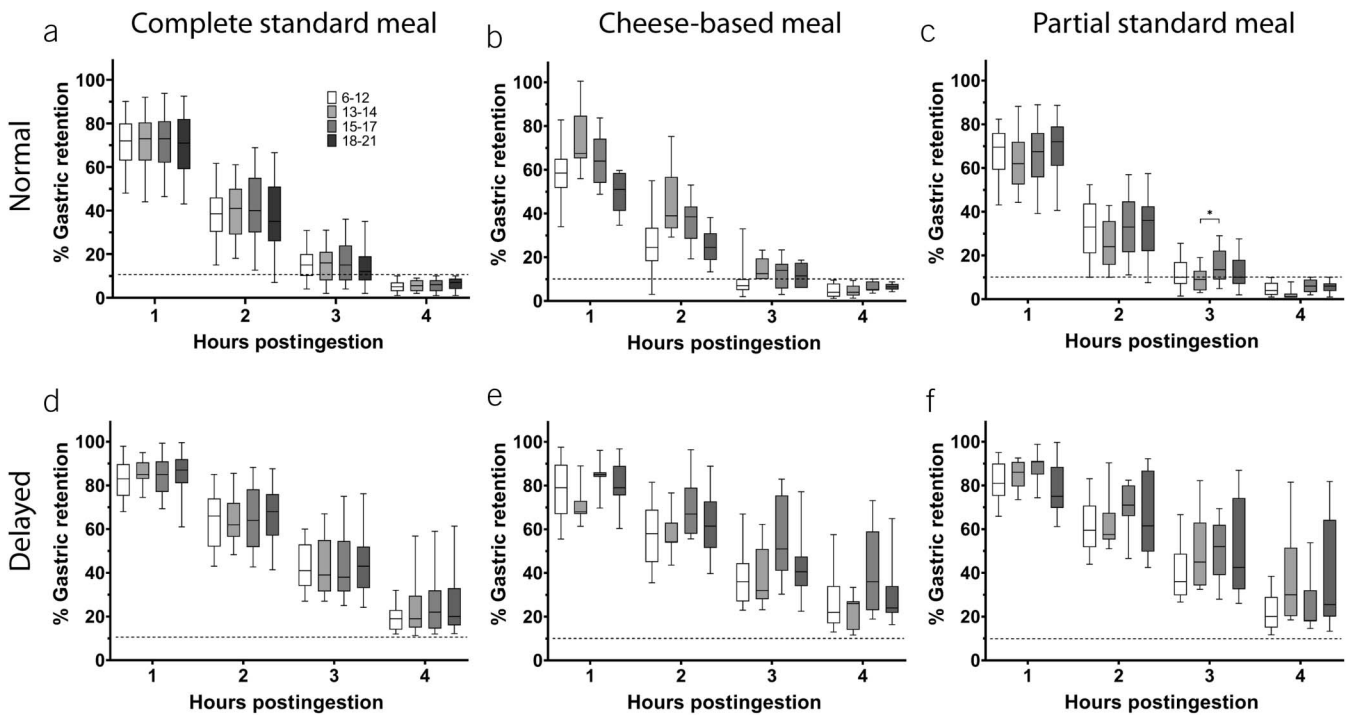


Figure 3. Comparison for across pediatric ages presenting with normal (a-c) and delayed (d-f) gastric emptying for each meal type. (a, d) Complete standard meal, (b, e) alternative meal, and (c, f) $\geq 50\%$ standard meal. Whiskers denote 5% and 95% percentile values. Box denotes 25%, 50%, and 75% values. Comparisons across ages for normal and delayed retention were performed with the Kruskal-Wallis test (* $P < 0.03$).

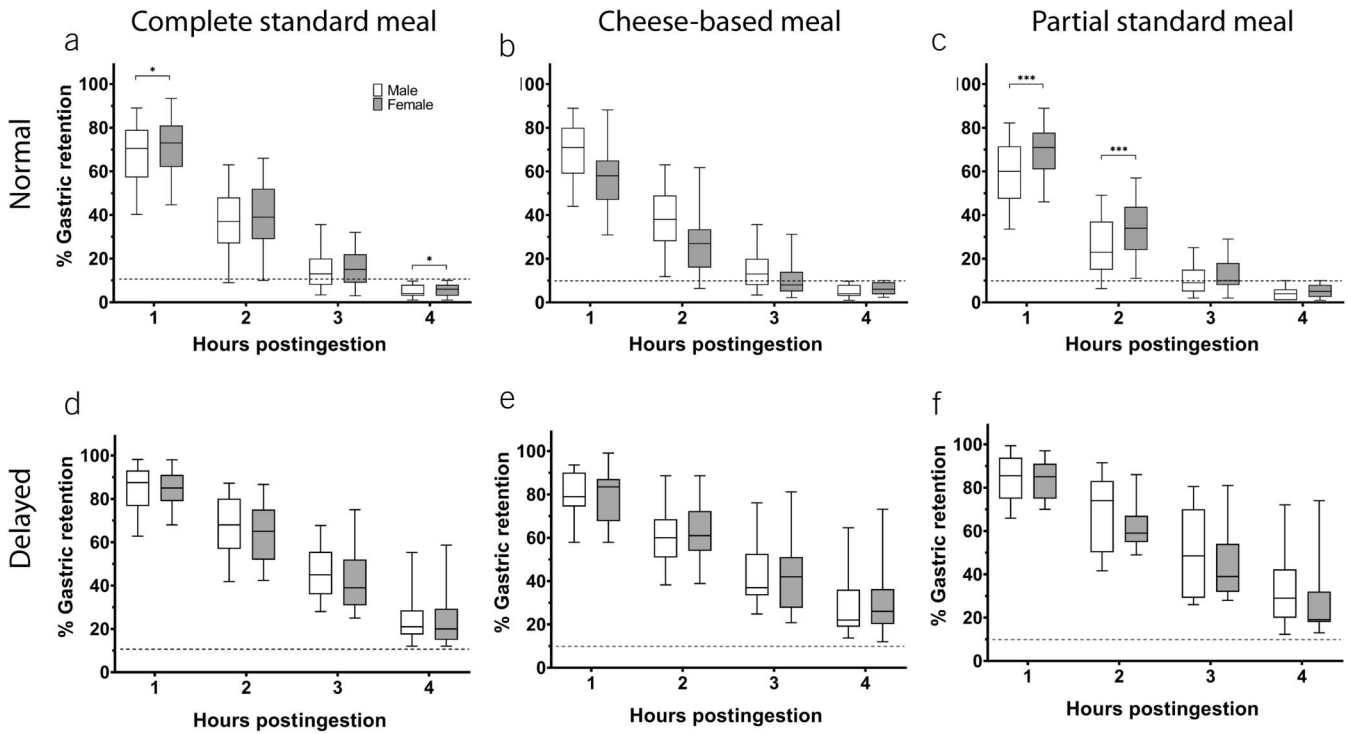


Figure 4. Comparison for between sexes presenting with normal (a–c) and delayed (d–f) gastric emptying for each meal type. (a, d) Complete standard meal, (b, e) alternative meal, and (c, f) $\geq 50\%$ standard meal. Whiskers denote 5% and 95% percentile values. Box denotes 25%, 50%, and 75% values. Comparisons between sexes for normal and delayed retention were performed with the Mann-Whitney test at each time point (* $P < 0.02$ and *** $P < 0.01$).

at 4 hours, consistent with prior reports in both adults and children emphasizing the superiority of the 4 hours study in detecting delayed gastric emptying, while allowing for the assessment of rapid gastric motility at earlier time points.

Because all our subjects were referred with symptoms and clinical concern for gastroparesis, an independent confirmation of normal or delayed gastric emptying for these subjects was not possible. It would also be neither ethical nor practical to perform gastric emptying scintigraphy on normal volunteer pediatric

subjects spanning both sexes and the range of ages encountered in pediatric practice. We therefore used a data-driven approach to further support the use of the adult criteria in our pediatric cohorts. As seen in Figure 6, most studies clustered similarly with either method. Reassuringly, the few discordantly clustered subjects also showed intermediate gastric retention values, as expected. Together, these findings support the use of the $\leq 10\%$ gastric retention value at 4-hour criteria in the pediatric population.

It is well recognized that differences in meal composition can influence gastric emptying. Solid-phase meals can empty more slowly than liquids, while differences in caloric content, fat content, and volume of the ingested meal affect gastric emptying. Several different meals have been examined for use in gastric emptying studies (15,24,31–33), including in children (17,20,22,26,34). However, most of these meal choices exhibit distinctly different gastric emptying properties, which precludes rigorous inter- and intra-subject comparisons between different studies. This is especially problematic in the pediatric population, where the subject numbers at each individual institution are often small. Extension of the adult consensus recommendations for gastric emptying scintigraphy to children has been an attempt to address this situation. However, there are many instances, whether due to allergies, aversion to particular foods, dietary intolerance, or specific dietary restrictions, whereby children either cannot or will not tolerate the standard meal recommended in the consensus guidelines, potentially affecting the interpretability of gastric emptying studies in children. Interestingly, the age of subjects who tolerated the complete standard meal in our study was slightly older than the other 2 cohorts, which was also observed in prior reports (20,35). Ideally, a unique set of normative values should be derived for each type of meal administered, but this is neither ethical nor practical. The

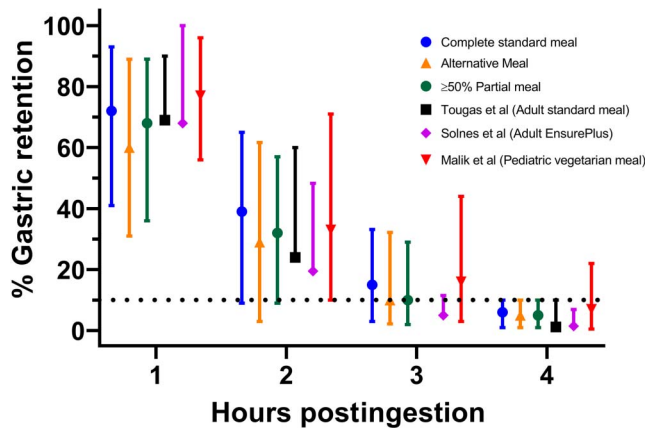


Figure 5. Comparison of gastric retention values from this study with reported normal values from healthy adults using standard meals (Tougas et al. (13), Solnes et al. (24)), and pediatric values from healthy subjects using a vegetarian meal (Malik et al. (26)). Median values are plotted with error bars depicting 5% and 95% percentile values where available.

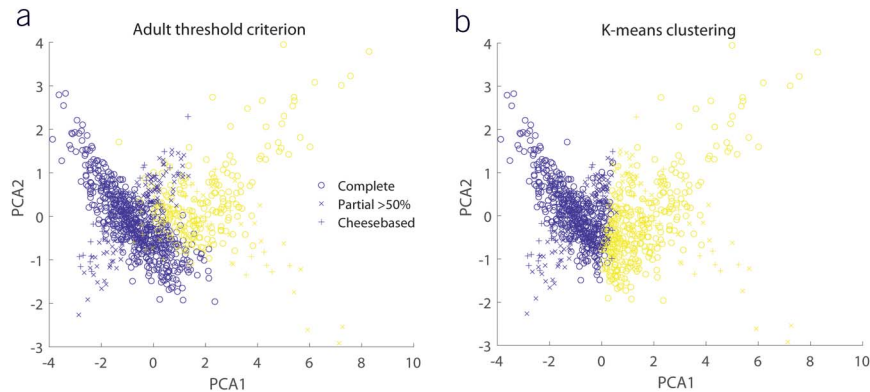


Figure 6. Adult definition of normal gastric emptying is applicable to the pediatric population. Gastric emptying values clustered into normal and delayed studies as defined by the adult standard definition ($\leq 10\%$ gastric retention at 4 hours is normal, **(a)**, and by a k-means clustering algorithm **(b)**. Both methods stratified similar studies across all meal types tested, suggesting that the normal and delayed definition is reasonable for pediatric use. Clusters are plotted along the 2 main principal component axes as derived from the 1–4-hour gastric emptying values (if the study was ended early, the final recorded value was used for the remaining time points to enable clustering).

above considerations thus highlight the need to offer alternatives to the adult standard meal that are still compatible with standard normative gastric emptying criteria, particularly for young children who may not tolerate the complete standard meal.

At our institution, the ingestion of cheese-based alternative meals and the partial ingestion of at least 50% of the standard meal both showed overall comparable gastric emptying properties to the complete standard meal in both normal and delayed subject. Both partial and alternative meals demonstrated slightly faster emptying in normal subjects at 1–3 hours, which is to be expected given the lower mass of these meals compared with the complete standard meal, but the 95th percentile at these time points remained above the 10% threshold range, and by the 4-hour time point, percentage gastric retention values were comparable to standard meals. These alternative meals also showed good emptying characteristics compared with another standard meal alternative, which has been considered acceptable in adults, for example, Ensure Plus (24,32). No overall age or sex differences were noted between the standard meal and partial or alternative meals, whether for normal or delayed emptying subjects, again supporting the use of these meals as potential alternatives to the complete standard meal.

As has been suggested by others (9), a comprehensive gastric emptying scintigraphy protocol should be able to identify both rapid and slow gastric emptying. Although our data support the use of the 4-hour time point for determining delayed gastric emptying, both for standard and nonstandard meals, we acknowledge that including the earlier standard time points (e.g., 1, 2, 3, and 4 hours) has the potential to identify both delayed and rapid emptying. There is certainly opportunity to further optimize the time points necessary for providing a comprehensive and accurate examination; however, at present, our data support the use of the adult consensus guidelines, which recommend that the examination include, at a minimum, images at baseline, 1, 2, and 4 hours.

Although gastric emptying scintigraphy remains the gold standard for motility assessment in adults and children, non-radioactive gastric emptying breath tests exist that would be quite attractive for use in the pediatric population (36–39). One variant, using ^{13}C -Spirulina, was recently Federal Drug Administration approved for use in adult subjects with results showing good correlation with scintigraphic techniques (38). Given that the nonradioactive agent also needs to be mixed into a solid meal

before ingestion, our results would likely be applicable for use with ^{13}C gastric emptying techniques.

There were some limitations in this study. The retrospective nature of this study precluded fine control of all the variables. In particular, the choice of alternative meal was not completely standardized, reflecting the unique challenges we face in developing rigorous and universally applicable standards for pediatric practice. However, each study was performed according to the standard operating procedure at our institution and quality controlled by the interpreting physician on the day of the study. Because of the inherent variability in our pediatric population, there were limits to the degree to which standardization of the cheese-based meals could be accomplished, with a range of caloric, mass, and fat content consumed. Nevertheless, cheese-based meals performed well compared with the complete standard meal, highlighting the robustness of the cheese-based meal alternative. Going forward, improved constancy of the amount and size of the alternative meal will likely improve the fidelity of the results. Future studies assessing the viability of these alternative meals across institutions should also be performed to determine the generalizability of these findings.

We did not routinely check the blood sugars at the time of each examination, as recommended in guidelines (23). This should be pursued in future examinations. The lack of this information is mitigated by the fact that our subjects are followed by our gastroenterologist colleagues who monitor blood glucose levels closely. Furthermore, the small number of diabetic subjects in our study ($<3\%$), and in the pediatric population in general, is much less than in the adult population undergoing this examination (40), thereby reducing the likelihood of hyperglycemia as a confounding variable.

Ethical concerns limit prospective studies to be performed in the normal pediatric population. As noted earlier, all our subjects were referred for assessment of gastroparesis; hence, we cannot fully ascertain whether the normal subjects do indeed have normal gastric emptying in the absence of an independent reference standard. However, the fact that our 95% values from $>1,000$ subjects correspond closely with prior studies in healthy subjects (13,24), along with our data-driven clustering verification, lends support to this assertion.

In summary, using gastric emptying data from $>1,000$ subjects, we present evidence showing that adult normative gastric emptying scintigraphy criteria can be applied to the pediatric

population. Furthermore, for children who cannot tolerate the full standard adult meal, we demonstrate that ingestion of a partial standard meal (at least 50% of the standard meal) as well as cheese-based meals provides excellent alternatives to the complete standard adult meal with comparable gastric emptying characteristics.

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CONFLICTS OF INTEREST

Guarantor of the article: Stephan D. Voss, MD, PhD.

Specific author contributions: The study was conceived by T.N. and S.V. T.N. and S.V. designed the study. T.N. and N.P. performed the study. T.N., N.P., and S.V. analyzed the data with input from all authors. T.N. wrote the manuscript with input from all authors. All authors have seen and approved the final content of the manuscript.

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Study Highlights

WHAT IS KNOWN

- ✓ Pediatric gastric emptying scintigraphy is often evaluated using the complete adult standard meal and using the adult normative criteria.
- ✓ Applicability of the adult normative criteria has not been assessed in the pediatric population.
- ✓ Many children cannot tolerate the complete adult standard meal.

WHAT IS NEW HERE

- ✓ We confirm the applicability of the gastric emptying adult normative criteria for use in the pediatric population, based on review of >1,000 subjects.
- ✓ Nonstandard meals, including partial adult standard meals and alternative cheese-based meals, can be given to children and assessed using the same normative criteria.

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