

Gastroparesis in Children: The Benefit of Conducting 4-hour Scintigraphic Gastric-Emptying Studies

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ABSTRACT

Background and Aim: Scintigraphic gastric emptying study (GES) is the criterion standard for diagnosis of gastroparesis. Adult studies demonstrated that extending GES to 4 hours increases its ability to diagnose delayed gastric emptying. Most pediatric centers assess GES up to 2 hours postmeal. The aim of the present study was to assess the effect of extending GES from 2 to 4 hours in evaluation of children with suspected gastroparesis.

Methods: We conducted a chart review of all children who had a 4-hour GES with standard radiolabeled solid meal in 2009–2010. Results of GES at 1, 2, and 4 hours were compared. Patients were diagnosed as having gastroparesis using adult criteria: if gastric retention of meal was >90%, 60%, and 10% at 1, 2 and 4 hours, respectively. A telephone survey assessed GES time at top 20 pediatric gastroenterology centers in the United States. Cost of evaluation of patients diagnosed as having gastroparesis was estimated. Full-time equivalents of nuclear medicine technicians and number of nuclear medicine studies done at Ann & Robert H. Lurie Children's Hospital of Chicago from 2007 to 2010 were examined.

Results: A total of 71 patients (32 boys, average age 10.8 years) were studied. Sixty-two percent (n = 44) children had abnormal GES; 23% (8/35) of them who had normal values at 2 hours had abnormal GES at 4 hours ($P < 0.0001$). Twenty-eight percent of patients had delayed GES at 1 hour: all persisted to have abnormal GES at 2 and 4 hours. Cost of evaluation of a child for gastroparesis was \$9014. Only 5 of the top 20 pediatric gastroenterology centers in the United States conducted 4-hour GES. Transitioning from 2 hours to 4 hours only required scheduling adjustments and did not result in limitation in the number of scheduled patients.

Conclusions: Extending GES to 4 hours results in a considerable increase in diagnosis of gastroparesis.

Key Words: cost, gastroparesis, pediatric, scintigraphic gastric emptying scan

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Gastroparesis is a common motility disorder in children characterized by delayed gastric emptying in the absence of mechanical outlet obstruction. Clinical presentation of gastroparesis is variable and often nonspecific, which precludes limiting

the diagnosis to patient's symptoms. Various confirmatory diagnostic testing strategies have been studied. Some of these strategies are operator-dependent, cumbersome, or rarely used (1). Scintigraphic gastric emptying study (GES) is now considered the criterion standard for the diagnosis of gastroparesis. GES provides a noninvasive, physiologic, quantitative measurement of gastric emptying (2). The present study is based on the patient's ingestion of a standardized meal that is labeled with nuclear material and the sequential determination of scintigraphic activity in the stomach and small bowel at various times. Although the use of GES has increased over the years, the interpretation and comparison of results among sites have been hampered by the wide range of institutional protocol variations. To maximize the diagnostic confidence and to reduce variation among different test sites, the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine have issued consensus recommendations on conducting gastric emptying scintigraphy, including the composition of the meal and the timing of image acquisition. Adult studies have demonstrated the benefit of performing a 4-hour GES (3–6). Based on these data, the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine consensus statement have recommended a standardized GES protocol with 4-hour testing (7). To date, there have been no studies to support the decision to prolong the duration of GES to 4 hours in children. The combination of lack of pediatric data, the need for longer technician time, and higher resource usage has resulted in most pediatric centers conducting either 1 or 2 hours or using $T_{1/2}$ (time for 50% gastric emptying) with only a handful of centers adopting the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine recommendations. The primary aims of the present study were to determine whether there is clinical benefit of conducting a 4-hour GES and to assess whether extending the GES to 4 hours affected the productivity and costs of the Nuclear Medicine Department. The secondary aims were to evaluate the financial costs and effect of evaluation of children with suspected gastroparesis and to assess the common practice of conducting GES in the United States. We hypothesized that extending GES from 2 hours to 4 hours will increase the number of symptomatic children diagnosed as having gastroparesis.

METHODS

Primary Aims

1. To determine whether there is any clinical benefit of conducting a 4-hour GES: Ann & Robert H. Lurie Children's Hospital of Chicago adopted a 4-hour GES protocol in 2009. Retrospective chart review of all children who underwent GES with a standard solid meal labeled with Tc99m sulfur colloid (2009–10) at Ann & Robert H. Lurie Children's Hospital of Chicago was conducted. The medical records and results of GES were

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abstracted from the electronic medical record system at Ann & Robert H. Lurie Children's Hospital of Chicago. The records were reviewed for results of the laboratory, radiological, and endoscopic tests ordered by the consulting gastroenterology physician.

Protocol for GES—On the day of GES, patients were fasting for at least 6 hours. Prokinetic and other drugs (eg, hyoscyamine, amitriptyline, opiate medications), which could affect gastric motility, were discontinued for at least 3 days before testing. The standard meal for GES consisted of 4 oz Egg Beaters, which is the equivalent of 2 large eggs (60 kcal with zero calories from fat), 2 slices of toast (180 kcal), and 8 oz of water. Patients were given 10 minutes to consume this meal. Subjects with small percentage of meal consumed (<25% of the meal) or prolonged consumption time (>10 minutes) were excluded. This meal was tagged with Tc99m sulfur colloid 0.05 mCi/kg (minimum 0.5 mCi, maximum 1 mCi). A gamma camera with a low-energy high-resolution collimator was used for acquisition of anterior and posterior static images of the stomach with 60-second exposures with a matrix of 128 × 128 at 0-, 15-, 30-, 45-, 60-, 90-, 120-, and 240-minute intervals after meal ingestion. Percentage of gastric retention at 15, 30, 60, 90, 120, and 240 minutes was calculated. The results of GES at 1, 2, and 4 hours were compared. Patients were categorized as having delayed GES using the adult consensus statement established by American Motility and Nuclear Medicine Society: if retention of meal in stomach was >90% at 1 hour, >60% at 2 hours, and >10% at 4 hours according to normative guidelines (7). Rapid gastric emptying was defined as gastric retention <30% at 1 hour (8). Differences in proportions were determined using the χ^2 test, $P < 0.05$ significance.

- Assessed if extending the GES to 4 hours affected the Nuclear Medicine Department: The full-time equivalents of nuclear medicine technicians and number of nuclear medicine studies done at Ann & Robert H. Lurie Children's Hospital of Chicago during 2007–2010 were examined.

Secondary Aims

- To determine the cost of evaluation and financial effect of conducting a 4-hour GES: Total cost of evaluation of patients who were suspected to have gastroparesis was estimated. All children included in the study had undergone at least 1 diagnostic investigation to rule out inflammatory bowel disease, celiac disease, and other inflammatory or infectious conditions. Costs for each diagnostic test were estimated using the amounts charged by the hospital to the payer in 2010. Costs of endoscopies included operating and recovery room charges, medications and supplies, anesthesia, and physician procedure fees. Per patient costs estimates included charges for the initial pediatric gastrointestinal consultation visit only.
- Assessment of common practice of GES in other pediatric centers in the United States: To better characterize the common practices in the United States, we contacted the nuclear medicine department of the 20 highest ranked pediatric gastroenterology centers via a phone survey and inquired about the duration and time intervals of GES at their institution (9).

The study was approved by the institutional review board of Ann & Robert H. Lurie Children's Hospital of Chicago in Chicago, IL.

RESULTS

- Clinical effect of extending GES:** Seventy-seven patients had undergone a 4-hour GES since 2009. Six patients were excluded for inadequate meal consumption and prolonged mealtime. The remaining 71 patients (32 boys, 39 girls, mean age 11.3 years, range 3–21 years) were studied. No significant differences in mean age ($P = 0.15$) and sex ($P = 0.64$) were found between groups with and without gastroparesis. Based on adult GES diagnostic guidelines for gastroparesis, 62% ($n = 44$) children had gastroparesis at 1, 2, or 4 hours. Twenty-three percent (8/35) of patients who had normal gastric emptying at 2 hours were found to have delayed gastric emptying at 4 hours (Table 1; $P < 0.0001$). Eleven percent of patients (4 of 36) who had delayed gastric emptying at 2 hours had normal gastric emptying times at 4 hours. Twenty-eight percent of patients had delayed gastric emptying at 1 hour (20/71), all of whom persisted to have an abnormal GES at 2 and 4 hours. Of the patients with normal GES at 1 hour, 13 had delayed GES at 2 hours and 16 had delayed GES at 4 hours. Rapid gastric emptying was not found in any of the patients. Documented presumptive etiologies for gastroparesis were idiopathic ($n = 36$, 82%), autoimmune ($n = 6$, 13.5%), and diabetes ($n = 2$, 4.5%). Patients with an idiopathic etiology had a history of acute infectious illness before the onset of gastroparesis symptoms in 44% ($n = 14$) cases.
- Effect of 4-hour GES on the Nuclear Medicine Department productivity and costs:** Review of number of personnel and procedures performed in the Nuclear Medicine Department and interview of director of the department revealed that no additional technician had to be hired to extend the GES from 2 to 4 hours with only minor logistic modifications to accommodate the increased number of imaging times. The number of nuclear medicine technologists during 2007–2010 was 3.0 full-time equivalents each year. The average number of nuclear medicine studies done in 2007–2008 was 1018 and in 2009–2010 it was 1100.
- Financial costs of evaluation of gastroparesis:** Total cost of evaluation of all patients suspected to have gastroparesis was USD 640,000. Average cost incurred per child evaluated for gastroparesis was USD 9014. The total cost of evaluation for the 44 children diagnosed as having gastroparesis was USD 360,519 (Table 2).

TABLE 1. Comparison of GES results at 2 and 4 hours

	Abnormal GES at 2 h	Normal GES at 2 h	
Abnormal GES at 4 h	32	8 (23%)	
Normal GES at 4 h	4 (11%)	27	
Individual data for GES comparison			
2 h	2 h	4 h	4 h
Normal	Delayed	Normal	Delayed
35 (49%)	36 (51%)	31 (44%)	40 (56%)
Cumulative data for GES comparison			
2 h	2 h	4 h	4 h
Normal	Delayed	Normal	Delayed
35 (49%)	36 (51%)	27 (38%)	44 (62%)

TABLE 2. Cost of investigations and consultations in patients with gastroparesis

Tests	Subjects (n)	Charge per unit (\$)	Total charges (\$)
CBC	44	157	6908
ESR	25	81	2025
CRP	23	34	782
Amylase	26	133	3458
Lipase	26	138	3588
IgA	33	143	4719
Celiac antibodies	33	531	17,523
Complete metabolic profile	44	307	13,508
Urine analysis	19	96	1824
EGD	19	6460	122,740
Abdominal x-ray	28	339	9492
Abdominal ultrasound	10	889	8890
Abdominal CT scan	4	2841	11,364
Upper GI-small bowel follow-through	14	937	13,118
Gastric emptying scan	44	2300	101,200
Consultations	44	895	39,380
Total charges			360,519

CBC = complete blood count; CRP = C-reactive protein; CT = computed tomography; EGD = esophagogastroduodenoscopy; ESR = erythrocyte sedimentation rate; GI = gastrointestinal; IgA = immunoglobulin A.

4. Duration of GES at pediatric gastroenterology centers in the United States: In our survey of the 20 highest ranked pediatric gastroenterology centers in the United States, only 5 centers conducted 4-hour GES. The rest of the centers conducted GES with protocols varying from 1 to 2 hours.

DISCUSSION

This is the first pediatric study to assess the diagnostic value of 4-hour GES in children. The present American Neurogastroenterology and Motility Society and Society of Nuclear Medicine guidelines for performance of 4-hour GES are based on adult data (3). A recent adult study showed that patients with a 4-hour gastric retention value >10% were 5 times more likely to have gastroparesis than those with ≤10% (10). Pediatric gastric emptying scintigraphy studies are frequently performed for only 1 or 2 hours. Based on our telephone survey of the top 20 pediatric gastroenterology centers in the United States (*US News and World Report* rankings 2011–2012), only 5 hospitals followed a 4-hour GES protocol. There was a wide variation in the time points of imaging in these centers. The remaining 15 centers conducted GES ranging from 1 to 2 hours. This also seems to be true in adult centers despite the existence of the consensus statement for past several years (7,11). It is unclear whether pediatric and adult radiologists used the same cutoff values as the consensus statement for interpreting the gastric emptying times (7,11). Many centers have been reluctant to perform a 4-hour procedure because reimbursement is not commensurate with the time and effort needed. There is also paucity of pediatric data to justify extending the present protocols. To justify extending the study beyond 2 hours, the 4-hour GES has to demonstrate that additional children are diagnosed as having gastroparesis while using longer testing times. We had to use adult standards for diagnosing gastroparesis in children because of absence of standardized pediatric values. Our study supports the performance of the 4-hour GES in children based on the presently available adult criteria and demonstrates the advantages of conducting an extended GES. The study demonstrates that extending the study period from 2 to 4 hours increases the diagnostic yield of the GES without additional costs to the Nuclear Medicine

Department. We found a 23% increase in yield of diagnosis of gastroparesis, which would have otherwise been missed. Our numbers are consistent with the results of a large adult study in which they reviewed 1500 patients and found that a 1-hour study missed 36% patients, a 2-hour study missed 25% patients, and a 3-hour study missed 15% patients when compared with 4-hour studies (12).

Accurate and early diagnosis of gastroparesis could benefit patients and families by instituting early treatment and faster recovery, limiting their suffering and distress. A diagnosis of gastroparesis provides objective evidence to use prokinetic therapies such as metoclopramide or erythromycin. Extending GES to 4 hours using adult consensus normal values will increase the number of patients who qualify for such therapy. In addition, characterization of gastric emptying could provide valuable prognostic information in children with gastroparesis. Adult patients with mild (11%–20% retention) to moderate (21%–35% retention) delay in gastric emptying respond better to medical therapy than patients with severe gastroparesis (>35% retention) (13). A study in the pediatric population determining the influence of the degree of gastroparesis on therapy is a worthy undertaking.

The comparison of 1-hour results with subsequent time points raises an interesting question that should be further investigated. We noted that all patients who had delayed gastric emptying at 1 hour using the adult criteria for gastroparesis persisted to have delayed gastric emptying at 2 and 4 hours. Whether the GES should be terminated at 1 hour if the gastric retention is >90% should be the subject of future studies on larger samples. We consider these results provocative but not sufficient to suggest any deviation from present consensus protocol. Of the patients with normal GES at 1 hour, 25% and 31% patients had delayed GES at 2 and 4 hours, respectively, indicating that just a 1-hour GES is an inadequate test.

There is a subgroup of patients who have abnormal gastric emptying at 2 hours, but their values normalize by the fourth hour. The importance of this pattern of emptying is unclear in terms of clinical presentation or management. It will be interesting to see whether these patients can be categorized into a particular phenotype of gastroparesis as new data emerge from future studies.

The investigation of pediatric GES using liquids and solids and their correlation with symptoms may help better understand our findings.

Our study suggests that the costs related to evaluating children with gastroparesis in the United States are substantial. The total cost of evaluating all the children in our study was USD 640,000 (average cost per child \$9014). This exceeds the annual per capita health care expenditure in the United States for 2009 (\$8086 per capita) (14). The total cost of the workup of those children who were ultimately diagnosed as having gastroparesis was approximately USD 360,519. Limiting the GES to 2 hours would have missed the diagnosis of gastroparesis in 8 children that would account for approximately USD 72,000 of possible wasted expenses (based on average of \$9014 cost per child). The results of our study underestimate the actual costs of evaluating a child with gastroparesis by limiting our cost estimate to some hospital-based charges. Costs of hospitalizations, earlier investigations, repeated physician visits, medications, parental forgone earnings to care for a sick child, and extra child care expenses were not considered in our estimates.

In view of the ongoing drive of curbing health care costs nationwide, it is desirable to optimize limited resources. On examining financial and administrative data from the Department of Radiology, transitioning from 2-hour to 4-hour studies did not result in reduced number of nuclear medicine procedures or additional hiring of personnel. Only minor scheduling adjustments were required. Based on the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine recommendations, ours and other protocols can be simplified by reducing GES imaging to 4 time points (0, 60, 120, and 240 minutes). An abbreviated protocol can help scheduling and permit more efficient use of imaging equipment, allowing multiple GES to be performed on 1 camera in a single day if the starting times are staggered (4,15). The radiation exposure associated with the gastric emptying scintigraphy study is extremely low (0.006–0.012 mSv) and is comparable with that from natural background radiation exposure in 1 month. The gamma camera does not emit any radiation, so increasing the duration of the study from 2 to 4 hours will not result in additional radiation exposure to the patient.

A major limitation of our study is the absence of pediatric norms for interpretation of GES because of which we have used the adult cutoffs to analyze data from children. Other limitations include the study being conducted in a single tertiary care center, its retrospective nature, the lack of correlation of clinical symptoms with GES results, and the partial assessment of evaluation costs that was limited to those incurred in our center. Additional pediatric studies to establish the norms for GES in children and to correlate the results of the GES with outcomes are urgently needed.

CONCLUSIONS

Our study showed that extending GES to 4 hours increases the diagnostic value of the test without increasing costs or reducing the number of tests performed by the Nuclear Medicine Department. Hence, we propose extending the GES to 4 hours in all pediatric centers. Extending GES to 4 hours will result in a

significant increase in diagnosis of gastroparesis based on adult criteria. The savings from avoiding wasteful expenditure on missed diagnoses will offset the time invested in minor scheduling adjustments for conducting a 4-hour GES.

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