Scintigraphy Versus pH Probe for Quantification of Pediatric Gastroesophageal Reflux: A Study Using Concurrent Multiplexed Data and Acid Feedings

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We performed 12 simultaneous scintigraphic and pH probe studies in children being evaluated for reflux to determine the ability of scintigraphic images in comparison to pH probe data to guantify gastroesophageal reflux in children and to identify an optimal scintigraphic framing interval. We used a multiplexor to synchronize exactly the scintigraphy and pH probe and an acid meal to avoid missing postprandial episodes with the pH probe. We reformatted the studies in both 60-sec and 10-sec images to compare the two framing intervals. The 60-sec images produced better agreement between pH probe and scintigraphy than the 10-sec images for both the number of reflux episodes and the duration of reflux. Of the 64 reflux episodes detected by either method at this coarser framing interval, scintigraphy detected 80%, the pH probe detected 63% and both methods concurrently detected 42%. Of the 681 60-sec images aggregated across patients, scintigraphy detected 55% of those with intraesophageal refluxate, the pH probe detected 96% and both tests concurrently detected 51%. Within patients, the number of positive scintigraphic images in the postprandial hour correlated with the number of images with pH < 4 during the same hour (p = 0.008, and p < 0.0001 if two patients with very rapid gastric emptying are excluded), but not with the results of the 24-hr pH probe study. A 1-hr scintigraphic study formatted in 60-sec frames provides a quantitative representation of postprandial gastroesophageal reflux for children, particularly if they do not have rapid gastric emptying.

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Although the 24-hr pH probe test is generally considered to be the "gold standard" for quantifying gastroesophageal reflux, it has two important disadvantages. First, postprandial reflux cannot be reliably detected following physiologic feedings, especially following milk formula feedings to infants in whom intragastric pH often remains above 4 for an hour or two (1-3), but in whom postprandial reflux may produce morbidity, including aspiration, apnea and malnutrition (4-7). Second, when acid reflux does occur, the pH probe is unable to detect reliably subsequent reflux episodes that occur prior to the neutralization of residual acid by saliva (8-10).

Gastroesophageal scintigraphy using ^{99m}Tc sulfur colloid is also used to measure gastroesophageal reflux. In addition to detecting postprandial reflux and identifying repetitive reflux episodes prior to neutralization (8), scintigraphy quantifies refluxate volume, measures gastric emptying, reveals swallowing function and demonstrates aspiration (11).

Most studies comparing the two tests in the same patients have simply attempted to ascertain whether an abnormal quantity of reflux diagnosed by pH probe would also be diagnosed by scintigraphy (12-17). Such studies have varied as to the techniques of both tests and as to the definitions of positive tests. Only rarely have simultaneous pH probes and scintigraphic studies been evaluated (11,18,19). Even these have targeted the positivity of the test as a whole rather than focussing on the ability of the two methods to detect individual reflux episodes by synchronizing them. Recently, three studies of simultaneous esophageal pH monitoring and scintigraphy (two in adults and one in a child) addressed the issue of the relative sensitivities of the two methods to detect individual reflux episodes and found that only a minority of reflux episodes (23%-25%) in the adults, <5% in the children) were detected by both methods (8-10). The authors of these studies surmised, but could not demonstrate, that some of the scintigraphic events were missed by pH probe because of the postprandial buffering of gastric contents.

We performed 12 simultaneous scintigraphic and pH probe studies during the postprandial period in 11 children being evaluated for gastroesophageal reflux disease to determine the sensitivity of scintigraphy in comparison to the pH probe for detecting individual reflux episodes in children. To provide exact synchronization of the scintigraphic and pH probe data, we used a multiplexor that we have previously described and validated (20). We used acid

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TABLE 1Patient Characteristics

	Symptoms			Diagnostic testing					
Age (mo)	Regurgi- tation	Weight deficit	Respi- ratory	24-hr pH probe (%)	Esoph. biopsy	Esopha- gram	GE30 (%)	Dose	
3	+	-	L	11	+	n.d.	23	L	
11	-	-	L,U	23	+	_	29	L(asp)	
87	-	+	L	27	n.d.	n.d.	38*	H	
12	_	-	L	34	+	n.d.	9	L	
71	+	+	_	6 s	+	+	34	н	
56	-	_	L,U	9 c	+	n.d.	16	н	
30	-	-	L	5	n.d.	-	21	н	
1	+	_	LU	16	+	n.d.	22	н	
5 ¥	+	-	L	35	+	+	7	L(asp)	
13 ¥	-	-	L	13 m	n.d.	n.d.	15	H	
5	_	-	L	8 m	+	n.d.	24	L	
1	+	_	Α	30	-	n.d.	42*	L	

X = sequential studies on the same patient 8 mo apart; Symptoms: + = present; - = absent; L = lower (recurrent pneumonia, chronic cough, congestion, wheezing); U = upper (choking, stridor, hoarseness); A = apnea.

Diagnostic testing: + = a positive test; - = a negative test; n.d. = not done; 24-hr pH probe (percentage of the total time that pH was <4); s = small meals; c = cough followed reflux episodes; m = receiving metoclopramide.

Esophageal biopsy: + = papillae >53%, basal layer >25% (of epithelial height), or epithelial eosinophils or neutrophils.

Esophagram: + = read by the radiologist as showing reflux (None showed structural abnormalities).

GE 30: percentage of the meal emptied from the stomach by 30 min; * = "outliers" with rapid gastric emptying (>1 standard deviation above the mean).

Dose (⁹⁹Tc sulfur colloid): H = high (300 μ Ci); L = low (150 μ Ci); and asp = aspiration documented by the scintigraphic study.

feedings to allow detection of postprandial reflux episodes with the pH probe.

To determine the relative sensitivity of two different scintigraphic imaging durations, we reformatted the data for analysis in 60- and 10-sec images.

METHODS

Patients

Twelve simultaneous 1-hr scintigraphy-pH probe studies were performed on 11 children between October 1986 and November 1987 after parental consent of the protocol, which had been approved by the Human Rights Committee of Children's Hospital of Pittsburgh. The children were 2 wk to 7 yr of age (median 12 mo). They were referred for evaluation for reflux and were selected to some extent by clinical utility of identifying aspiration or quantifying gastric emptying via scintigraphy. Table 1 lists their characteristics and results of testing. All but one patient had esophagitis (21), esophageal acidification during more than 10% of a pH probe study or both.

pH Probe

The esophageal pH probe (Microelectrodes MI-506, Londonderry, NH) was calibrated to pH 2 and 7 and inserted transnasally to the level of the fluoroscopic mid right atrium (22). The probe and the reference electrode, applied to the shoulder, were connected to the pH meter (Accumet 810, Fisher Scientific, Springfield, NJ), which was linked to the strip chart recorder (Linseis L600, Princeton, NJ or Anspec 1202, Ann Arbor, MI at 10 cm/hr). The latency of response of the probe when placed from a solution of pH 7 to a solution of pH 2 was 1 sec to reach pH 4, and 4 sec for 90% of the response amplitude.

The pH probe test continued for about 24 hr, during which

meals of apple juice (pH \sim 4) or apple juice alternating with milk formula were given to the six children under 1 yr of age, and age-appropriate meals with apple juice as the liquid were given to the seven older children. Mealtimes were eliminated from analysis. The simultaneous scintigraphic-pH probe study took place during the ongoing pH probe test.

Simultaneous Scintigraphy and pH Probe

After fasting at least 3 hr, generally overnight, the patient came to the nuclear medicine department for the study with the pH probe still in place.

By a method we have previously described and validated (20), the output from the pH probe was multiplexed into the Siemens/ CDA nuclear medicine workstation (Siemens Medical Systems, Inc., Hoffman Estates, IL) to occupy an unused side of the image during the 1-hr simultaneous study so that the pH probe data and scintigraphic data could be analyzed for synchronous events with exact simultaneity assured. The workstation was calibrated with a second identical pH probe to define the vertical location of signals for pH 2, 4 and 7 prior to data acquisition.

The volume of apple juice fed was 2 ml/cm of the patient's height. After removal of 5 ml of "cold chaser" to be used to clear the radionuclide from the esophagus, the remaining volume was mixed with ^{99m}Tc sulfur colloid (150 μ Ci [5.55 MBq] for the first six studies, 300 μ Ci [11.1 MBq] thereafter). A 15-sec image of the patient was obtained with a radioactive marker at the cricoid both before the feeding and after the hour of imaging. The child was fed within 30 min (range 5–28 min, median 16 min), all orally if possible or by nasogastric tube (three patients) if not. The cold chaser was then used to rinse the radioactivity from the mouth and esophagus. Following feeding, the child was burped if appropriate and placed supine on the gamma camera. Swaddling was used if necessary for immobilization. Absorbent pads used to

capture regurgitated material were replaced after each soiling and later counted scintigraphically to estimate volume by reference to a 2-ml aliquot saved from the test meal. Regurgitation, less than 5 ml, occurred during feeding in three patients. Only one child regurgitated during the imaging, an amount less than 1 ml.

A posterior field of view including esophagus and stomach was imaged continuously for ~ 60 min. Image data were acquired by a Raytheon Step 1/Step 2 large field-of-view gamma camera with a parallel-hole, general-purpose collimator. The camera was calibrated for 140 keV. A 20% energy window was used for acquisition. Data from the gamma camera and the pH probe were acquired simultaneously in list mode by the Siemens/CDA nuclear medicine workstation (List mode enables specification of any duration for image reformatting). After the 1-hr study, the child returned to the Clinical Research Center to complete the 24-hr pH probe monitoring.

Four to 6 hr after the study, the child returned to the nuclear medicine department for anterior and posterior 5-min images for aspiration using radioactive cricoid and xyphoid markers to define anatomic boundaries and lead abdominal shielding to maximize detection of aspiration. Gastric emptying was quantified as the fraction of radioactive material emptied from the stomach in 30 min following feeding; we used 30 rather than 60 min to reduce the artifact of an overlying duodenum, which we and others (23) have noted.

Analysis

Scintigraphy Scoring. Each patient's study was formatted from beginning to end in approximately 60 60-sec images and also in approximately 360 10-sec images. The resulting 4713 images from the 12 studies were reviewed on the computer screen and scored as positive or negative for reflux (HAK) without knowledge of the pH probe data. The computer screen (compared to film) facilitated the examination of a large number of images and allowed control of image intensity to permit detection of faint but unequivocal reflux. Equivocal images were scored as negative.

pH Probe Scoring. The pH probe data were graphed by the nuclear medicine computer with time on the x-axis and pH on the y-axis, as previously described (18). For each patient's study, graphs were generated at two different time scales corresponding to the two imaging intervals used for the scintigraphic data. Thus, for a particular study, each one of the set of 60 60-sec scintigraphic images corresponds in the graphic pH display to a single point that represents the average pH during the same 60-sec interval. Likewise, each of the 360 10-sec scintigraphic images corresponds in the pH display to a graphic point representing the average pH during that 10-sec interval. Whereas the first pH display with its rather coarse time scale could be captured for analysis on a single photograph, the finer time scale of the other pH display required six sequential photographs for clear identification of the pH at each point. Each of the 4713 points of the resulting photographs, incorporating only the pH data but with exact temporal identification for later comparison with scintigraphic data, was blindly analyzed for pH below 4 (SRO). Notation was also made of abrupt pH drops of \geq 1.0 unit which occurred when the pH was already below 4. There were no 1.0 unit pH drops from above 4 which did not go below 4.

The 24-hr pH probe study was scored by calculating the "reflux index," the proportion of the total non-meal time during which the esophageal pH was <4.

Sensitivity of Scintigraphy and Its Relationship to pH Probe Scores. Three aspects of scintigraphic images were evaluated: (1) their sensitivity to detect the onset of a reflux episode; (2) their sensitivity to detect refluxate in the esophagus; and (3) the degree to which a quantitative representation of reflux derived from one postprandial hour of scintigraphic images was comparable to a pH probe score from the same hour or from a 24-hr period.

The studies were aggregated across subjects for evaluation of sensitivity for detecting reflux episodes and refluxate in the esophagus. For analysis of the sensitivity of scintigraphy for detecting reflux episodes (*reflux frequency*), a reflux episode was defined by scintigraphy as a positive image following a negative one, and by pH probe as a drop from above 4 to below 4. A secondary definition of pH probe reflux episodes also included pH drops of greater than 1.0 unit which occurred when the pH was already below 4. Because scintigraphy and pH probes have been shown to be complementary in detecting reflux episodes (8-10), all reflux episodes detected by either modality were defined as comprising the total number of reflux episodes. At both the 60-sec and 10-sec imaging frequency, an episode detected simultaneously by the two techniques was one which was detected in concurrent or adjacent images.

For analysis of the sensitivity of scintigraphy for detecting refluxate in the esophagus (*reflux duration*), the "population" being tested was defined as all the time intervals at each imaging frequency: 681 at the 60-sec frequency and 4032 at the 10-sec frequency. Again, refluxate was defined as being present in the esophagus if the pH was below 4, the scintigraphic image was positive or both. Thus, the sensitivity of scintigraphy for the determination of reflux duration was the number of scintigraphically positive intervals divided by the number of intervals which were positive by either or both tests.

For analysis of the relationship between the 1-hr scintigraphic study and both the 1-hr and the 24-hr pH probe study, Spearman's correlation was used. Regression equations were derived without a constant, thus constraining them to intersect the origin.

RESULTS

A composite photograph shows concurrent scintigraphic images at both framing frequencies accompanied by the pH probe computer output at the finer (10 sec per point) framing frequency (Fig. 1). This composite shows relationships between the two types of data and the two framing frequencies.

Reflux Frequency: Sensitivity of Scintigraphic Images

More reflux episodes were detected simultaneously by the two techniques when the studies were analyzed in the 60-sec than in the 10-sec frames (Table 2). Of the 64 episodes detected by either method at the coarser (60-sec) framing intervals, scintigraphy detected 80%, pH probe detected 63% and both methods simultaneously detected 42% of the episodes. Seven more episodes were detected by pH probe when the additional criterion of 1-unit pH drop was used (including four already detected by scintigraphy); the resulting sensitivities were 76% (scintigraphy), 70% (pH probe) and 46% (both simultaneously). Of the 51 episodes detected by scintigraphy at this coarser framing rate, 20 occurred without a coincident drop of pH (either to <4 or of 1 pH unit): 9 of them during periods of sustained low pH and 11 while the pH was >4.

Of the 212 episodes detected by either method with the

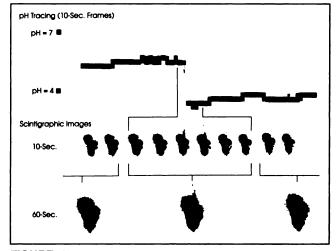


FIGURE 1. Example of scintigraphic and pH probe data. The broken line at the top shows ~10-min of the digitized pH probe data. formatted at 10-sec imaging intervals: each small square represents the average pH during a 10-sec interval. The level for pH 7 and 4 are indicated at the left margin. The first row of scintigraphic images are 10 sequential 10-sec images which correspond to the central portion of the pH probe tracing; the brackets show the central six images (a single minute of data) which correspond exactly to the six points indicated on the pH probe tracing above. The bottom row of images are three sequential 60-sec scintigraphic images, each of which represents the same data as six 10-sec images, but reformatted in the coarser image intervals. The brackets indicate that the central 60-sec image in the bottom row represents the same data displayed by the central six 10-sec images above and by the central six pH probe points. A spontaneous reflux episode is shown. The acid is not quite cleared to above pH 4 by several minutes later. Clearance of refluxate volume, however, occurs within three 10-sec frames (30 sec) and within a single 60-sec image.

finer framing, scintigraphy detected 92%, pH probe detected 24% and both methods detected only 16% of the episodes concurrently. Five more episodes were detected with the additional pH probe criterion (including two detected scintigraphically); the resulting sensitivities were 91% (scintigraphy), 26% (pH probe) and 17% (both simultaneously). Of the 195 episodes detected by scintigraphy at this finer framing rate, 159 occurred without a simultaneous pH drop: 132 of them during sustained low pH and 27 while the esophageal pH was >4.

Of the reflux episodes documented by pH probe, scintigraphy identified about two-thirds at either framing frequency.

Reflux Duration

Sensitivity of Scintigraphic Images. The 60-sec framing also showed more agreement between scintigraphy and pH probe than the 10-sec framing in documenting reflux duration. Of the 681 60-sec images aggregated across patients, 362 were positive by either or both techniques. Scintigraphy's sensitivity was 55%, the pH probe's sensitivity was 96% and both tests concurred on 51% of reflux-positive images (Table 2).

Of the 4032 10-sec images, 2016 of them (336 min) were positive by either or both of the techniques. At this more rapid framing rate, scintigraphy had a sensitivity of only 29%, even though the pH probe remained sensitive to 97%. Thus, both tests concurred on only 26% of reflux-positive images.

Correlation of One-Hour Scintigraphic and pH Probe Scores Within Patients. Despite the limited overlap between pH probe-positivity and scintigraphic-positivity for individual images, within patients the number of positive scintigraphic images correlated well with the number of images with pH < 4 (p = 0.008 and p = 0.03, for the coarse and fine images, respectively). The relationship was closer to identity for the 60-sec images than for the 10-sec images. Exclusion of the two patients with the most rapid gastric emptying (42%) and 38% at 30 min), improved p to <0.0001 for the coarse images and to 0.001 for the fine images (Fig. 2).

Correlation of One-Hour Scintigraphic Score with 24-Hour pH Probe Score Within Patients. We also attempted to determine whether the proportion of positive scintigraphic frames during the 1-hr study correlated with the proportion of time during the entire 24-hr pH probe study that the esophageal pH was below 4. The scintigraphic study did not correlate significantly with the 24-hr pH probe study at either imaging frequency, although the

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	Scintigraphy*	Probe*	Both at once*	Either (total)*			
Reflux episodes (frequency)							
60-sec (coarse) framing	0.80 (51)	0.63 (40)	0.42 (27)	1.00 (64)			
Including 1-unit pH drops	0.76 (51)	0.70 (47)	0.46 (31)	1.00 (67)			
10-sec (fine) framing	0.92 (195)	0.24 (51)	0.16 (34)	1.00 (212)			
Including 1-unit pH drops	0.91 (195)	0.26 (56)	0.17 (36)	1.00 (215)			
Intraesophageal refluxate (duration)							
60-sec (coarse) framing	0.55 (200)	0.96 (346)	0.51 (184)	1.00 (362)			
10-sec (fine) framing	0.29 (96)	0.97 (327)	0.26 (87)	1.00 (336)			

*Numbers in parentheses following the sensitivity are the actual number of episodes of reflux (first four lines) or minutes which were positive for reflux (last two lines).

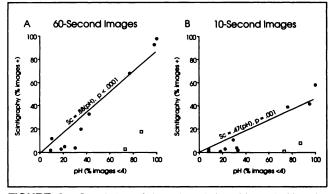


FIGURE 2. Correlation of the 1-hr scintigraphic and pH probe scores within patients at 60-sec image frequency (A) and 10-sec image frequency (B). Each point represents a single patient's study. The x-axis is the percentage of the 1-hr period positive for reflux by pH probe; the y-axis is the percentage of the same 1-hr period positive for reflux by scintigraphic images. The two patients in each graph, represented by open squares, are those with very rapid gastric emptying; their data are not used in the determination of the regression lines shown.

p-value was lower with the coarser imaging frequency. The differing rates of gastric emptying and doses of radionuclide probably contributed to this lack of correlation between 1-hr scintigraphy and 24-hr pH probe, but statistical significance of the correlation was not reached in this small number of patients by consideration of these two factors (Fig. 3).

DISCUSSION

The pH probe is generally considered the gold standard for identifying pathologic reflux in children and adults. However, the test is time-consuming; insensitive for postprandial reflux unless unphysiologic acid feedings are used; insensitive for sequential reflux episodes prior to acid clearance; and uninformative regarding gastric emptying, pulmonary aspiration, refluxate volume and swallowing function. If a scintigraphic method which overcomes these limitations could also quantify reflux comparably to the pH probe, it would be an important tool for both clinical and investigative use. Our results indicate the degree to which image-based scintigraphy approaches the pH probe for reflux quantification in children. They also suggest important aspects of framing, dose and gastric emptying which may affect this quantification.

Reflux Episodes

Our data using acid feedings confirm that some of the previously identified disparity between scintigraphic reflux episodes and pH probe reflux episodes (8-10) is due to the postprandial buffering of gastric acid by the radiolabeled meal. Whether due to the liquid milk meals or to slower gastric emptying in children, this buffering effect seems more pronounced in pediatric patients than in adult patients. In pediatric patients, the result of this buffering is an exaggeration of the disparity between scintigraphic and pH probe quantification of reflux episodes. Thus, the prior pediatric study comparing the sensitivity of scintigraphy

and pH probe for reflux episodes found only a 5% concordance (10), as contrasted with approximately 25% concordance in prior adult studies (8,9). Our relatively high concordance of 46% in detecting reflux episodes at the coarse framing rate while using acid feedings supports the concept that an important number of postprandial reflux episodes are missed by pH probe when using nonacid feedings, particularly in children, and that this represents greater sensitivity of scintigraphy, compared to pH probe, for reflux episodes in the early postprandial period following nonacid feedings.

The small increase in concordance (from 41% to 46% of reflux episodes) obtained by scoring 1-unit pH drops as reflux episodes if the initial pH is below 4 indicates that although some of the disparity between pH probe and scintigraphy may be due to new episodes occurring prior to acid clearance, this effect may be less prominent in children than in adults (8–10).

Despite acid feedings, the 11 reflux episodes (16%) detected on the scintigraphic images without esophageal pH below 4 may represent false-positive scintigraphic images or false-negative pH probe data (due to the borderline pH of the apple juice feedings, to gastric hypochlorhydria or to duodenogastric reflux preceding gastroesophageal reflux). The present study does not clearly distinguish between these possible explanations.

We compared the coarser framing frequency (60-sec images) to the finer framing frequency (10-sec images) because of our previous impression that some reflux episodes, perhaps regurgitant ones in particular, remained in the esophagus too briefly for detection by a 60-sec framing frequency (24, 25). However, the disadvantages of the finer framing frequency—less difference between esophageal and background counts and much more tedious scoring far outweighed any benefits. Furthermore, regurgitant reflux episodes were easily quantified by the attending tech-

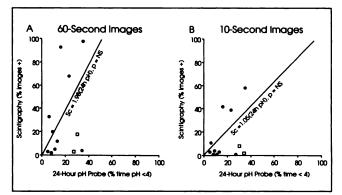


FIGURE 3. Correlation of the 1-hr scintigraphic score and the 24-hr pH probe score within patients at 60-sec image frequency (A) and 10-sec image frequency (B). Each point represents a single patient's study. The x-axis is the percentage of the 24-hr study positive for reflux by pH probe (the "reflux index") and the y-axis is the percentage of the 1-hr study period positive for reflux by scintigraphic images. The two patients in each graph, represented by open squares, are those with very rapid gastric emptying; their data are not used in the determination of the regression lines shown.

nician and were so infrequent, even in these refluxing children, that missing them would have had little impact on any score.

Intraesophageal Refluxate

Our finding of a greater sensitivity for detecting intraesophageal refluxate by pH probe than by scintigraphy is easily understood: bulk clearance, which scintigraphy detects, occurs before acid neutralization, which the pH probe detects (26). Therefore, the disparity and the resulting lower "sensitivity" of scintigraphy at either framing frequency should not be interpreted as a defect of scintigraphy, but as an indication of a fundamental difference between pH probe and scintigraphy. The 60-sec imaging frequency minimizes the disparity by allowing both volume and acid to be scored as present in a single, relatively long, imaging interval even though the volume may actually be present for only a short portion of the interval, as is demonstrated in Figure 1. In a study of normal adults, volume was essentially cleared by the first swallow, whereas acid clearance required nine or ten swallows (26).

Correlation of One-Hour Scintigraphic Score with pH Probe Scores

Although scintigraphy only detects refluxate in the esophagus half of the time that the pH probe does at the 60-sec framing rate, and a quarter of the time at the 10-sec framing rate, the good correlation between scintigraphy and pH probe for quantifying intraesophageal refluxate suggests the utility of using scintigraphic images scored in this way to quantify postprandial gastroesophageal reflux. The number of positive 60-sec scintigraphic images correlates best with the percent of time the pH is below 4 for a particular postprandial hour if the gastric emptying is less than 35% at 30 min; with more rapid gastric emptying, the test becomes less sensitive. Since many children with pathologic gastroesophageal reflux have delayed gastric emptying (27-29), this quantitative use of scintigraphic images may be most reliable in exactly those children most likely to have a truly positive test.

The simplest and most widely-used score for the pH probe is the proportion of the time during a 24-hr period that the esophageal pH is below 4, i.e., "the reflux index" (30). The proportion of positive scintigraphic frames during the 1-hr postprandial study did not correlate well with the 24-hr "reflux index;" thus, the 1-hr scintigraphic study cannot be extrapolated to predict or replace a 24-hr pH probe study. This finding is put in perspective by the inadequacy of an abbreviated pH probe study to represent the 24-hr pH probe study (31) and the threefold or greater day-to-day variability of the 24-hr pH probe score itself (30, 32), probably due, among other things, to variation in position (33, 34), meal size and frequency (35, 36) and meal content (1, 3, 37).

Techniques of the Study

Scintigraphic time-activity curves, as used by Shay et al. (8,9), are simpler to use and more objective than the im-

ages; the analysis can be computerized once the region of interest (ROI) is selected. The review of 60 scintigraphic images takes somewhat more time. However, the use of the curves is potentially inaccurate in infants and children who are difficult to keep still for an hour. The ROI may require re-drawing for each movement of the patient and even careful swaddling cannot prevent such movements. Therefore, despite the subjectivity of the image scores, images are probably more appropriate than curves to use in the case of young children since their scoring does not require an immobile ROI.

The use of two different doses of technetium added a variable to the study. Although the higher dose is likely to increase the sensitivity of the scintigraphic study and is apt to be associated with a greater ratio of scintigraphic score to 24-hr pH probe score, our small number of patients did not provide the power to demonstrate a significant difference in this ratio.

CONCLUSIONS

For many children suspected of having pathologic gastroesophageal reflux, scintigraphy may be the best initial study because of the benefits of demonstrating aspiration, quantifying gastric emptying, revealing swallowing function and detecting postprandial reflux. When gastroesophageal scintigraphy for reflux is to be performed in a young child, our study suggests that a quantitative representation of postprandial reflux may be obtained by continuous formatting of a 60-min study in 60-sec images and scoring the study as the proportion of the 60 images positive for reflux. Slower gastric emptying and higher doses of technetium improve the reliability.

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REFERENCES

 Tolia V, Kauffman RE. Comparison of evaluation of gastroesophageal reflux in infants using different feedings during intraesophageal pH monitoring. J Pediatr Gastroenterol Nutr 1990;10:426-429.

- Jolley SG, Herbst JJ, Johnson DG, Matlak ME, Book LS, Pena A. Postcibal gastroesophageal reflux in children. J Pediatr Surg 1981;16:487–490.
- Sutphen JL, Dillard VL. pH-adjusted formula and gastroesophageal reflux. J Pediatr Gastroenterol Nutr 1991;12:48-51.
- Williams HE, Freeman M. Milk inhalation pneumonia: the significance of fat filled macrophages in tracheal secretions. *Aust Paediatr J* 1973;9:286– 288.
- Moran JR, Block SM, Lyerty AD, Brooks LE, Dillard RG. Lipid-laden alveolar macrophage and lactose assay as markers of aspiration in neonates with lung disease. J Pediatr 1988;112:643-645.
- Spitzer AR, Boyle JT, Tuchman DN, Fox WW. Awake apnea associated with gastroesophageal reflux: a specific clinical syndrome. J Pediatr 1984; 104:200-205.
- Orenstein SR. Gastroesophageal reflux and apnea. *Pediatrics* 1983;72:913– 914.
- Shay S, Eggli D, Johnson L. Simultaneous esophageal pH monitoring and scintigraphy during the postprandial period in patients with severe reflux esophagitis. *Dig Dis Sci* 1991;36:558–564.
- Shay S, Abreu S, Tsuchida A. Scintigraphy in gastroesophageal reflux disease: a comparison to endoscopy, LESp, and 24-hr pH score, as well as to simultaneous pH monitoring. Am J Gastroenterol 1992;87:1094-1101.
- Vandenplas Y, Derde M, Piepsz A. Evaluation of reflux episodes during simultaneous esophageal pH monitoring and gastroesophageal reflux scintigraphy in children. J Pediatr Gastroenterol Nutr 1992;14:256-260.
- Heyman S. Pediatric nuclear gastroenterology: evaluation of gastroesophageal reflux and gastrointestinal bleeding. In: Freeman L, Weissmann H, eds. Nuclear Medicine Annual 1985. New York: Raven Press; 1985:133– 169.
- Kjellen G, Brudin L, Hakansson H-O. Is scintigraphy of value in the diagnosis of gastro-oesophageal reflux disease? *Scand J Gastroenterol* 1991; 26:425-30.
- Tolia V, Calhoun JA, Kuhns LR, Kauffman RE. Lack of correlation between extended pH monitoring and scintigraphy in the evaluation of infants with gastroesophageal reflux. J Lab Clin Med 1990;115:559-563.
- Kaul B, Petersen H, Grette K, Erichsen H, Myrvold HE. Scintigraphy, pH measurement, and radiography in the evaluation of gastroesophageal reflux. Scand J Gastroenterol 1985;20:289-294.
- Arasu TS, Wyllie R, Fitzgerald JF, et al. Gastroesophageal reflux in infants and children: comparative accuracy of diagnostic methods. *J Pediatr* 1980; 96:798-803.
- Hoffman GC, Vansant JH. The gastroesophageal scintiscan: comparison of methods to demonstrate gastroesophageal reflux. Arch Surg 1979;114:727– 728.
- Fisher RS, Malmud SL, Roberts GS, Lobis IF. Gastroesophageal (GE) scintiscanning to detect and quantitate GE reflux. *Gastroenterology* 1976; 70:301-308.
- Martins JCR, Isaacs PET, Sladen GE, Maisey MN, Edwards S. Gastrooesophageal reflux scintigraphy compared with pH probe monitoring. *Nucl Med Commun* 1984;205:201-204.

- Seibert JJ, Byrne WJ, Euler AR, Latture T, Leach M, Campbell M. Gastroesophageal reflux—the acid test: scintigraphy or pH probe? *AJR* 1983; 140:1087-1090.
- Rosenthal MS, Klein HA, Orenstein SR. Simultaneous acquisition of physiological data and nuclear medicine images. J Nucl Med 1988;29:1848–1852.
- Black DD, Haggitt RC, Orenstein SR, Whitington PF. Esophagitis in infants: morphometric histologic diagnosis and correlation with measures of gastroesophageal reflux. *Gastroenterology* 1990;98:1408–1414.
- Putnam PE, Orenstein SR. Determining esophageal length from crownrump length. J Pediatr Gastroenterol Nutr 1991;13:354-359.
- Seibert JJ, Byrne WJ, Euler AR. Gastric emptying in children: unusual patterns detected by scintigraphy. *Am J Roentgenol* 1983;141:49-51.
- Paton JY, Nanayakkhara CS, Simpson H. Vomiting and gastro-oesophageal reflux. Arch Dis Child 1988;63:837–838.
- Orenstein SR, Magill HL, Brooks P. Thickening of infant feedings for therapy of gastroesophageal reflux. J Pediatr 1987;110:181-186.
- Helm JF, Dodds WJ, Pelc LR, Palmer DW, Hogan WJ, Teeter BC. Effect of esophageal emptying and saliva on clearance of acid from the esophagus. N Engl J Med 1984;310:284-288.
- DiLorenzo C, Piepsz A, Ham H, Cadranel S. Gastric emptying with gastrooesophageal reflux. Arch Dis Child 1987;62:449-453.
- Guillet J, Wynchank S, Christophe E, Basse CB, Ducassou D, Blanquet P. Gastro-oesophageal reflux and gastric emptying of liquids in paediatric patients. *Int J Nucl Med Biol* 1984;11:254-258.
- Hillemeier AC, Lange R, McCallum R, Seashore J, Gryboski J. Delayed gastric emptying in infants with gastroesophageal reflux. *J Pediatr* 1981;98: 190–193.
- Hampton FJ, MacFadyen UM, Simpson H. Reproducibility of 24 hour oesophageal pH studies in infants. Arch Dis Child 1990;65:1249-1254.
- Jolley SG, Tunell WP, Carson JA, Smith EI, Grunow J. The accuracy of abbreviated esophageal pH monitoring in children. *J Pediatr Surg* 1984;19: 848-854.
- 32. Wiener GJ, Morgan TM, Copper JB, et al. Ambulatory 24-hour esophageal pH monitoring: reproducibility and variability of pH parameters. *Dig Dis Sci* 1988;33:1127–1133.
- Orenstein SR, Whitington PF, Orenstein DM. The infant seat as treatment for gastroesophageal reflux. N Engl J Med 1983;309:760-763.
- Orenstein SR, Whitington PF. Positioning for prevention of infant gastroesophageal reflux. J Pediatr 1983;103:534-537.
- Sutphen JL, Dillard VL. Effect of feeding volume on early postcibal gastroesophageal reflux in infants. J Pediatr Gastroenterol Nutr 1988;7:185– 188.
- Kerkering KW, Cobb AD, Anderson K, Gutcher GR. Influence of feeding interval on detection of gastroesophageal reflux in preterm infants [Abstract]. *Pediatr Res* 1989;25:220A.
- Sutphen JL, Dillard VL. Dietary caloric density and osmolality influence gastroesophageal reflux in infants. *Gastroenterology* 1989;97:601-604.