

Usefulness of gastroesophageal reflux scintigraphy using the knee-chest position for the diagnosis of gastroesophageal reflux disease

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Objectives: The aim of this study is to evaluate the usefulness of gastroesophageal reflux (GER) scintigraphy using the knee-chest (KC) position for the diagnosis of gastroesophageal reflux disease (GERD). **Methods:** The study subjects were 37 patients with GERD and 8 healthy volunteers (control group). Endoscopically observed esophageal mucosal breaks were evaluated with the Los Angeles classification. For GER scintigraphy, the subjects ingested liquid yogurt labeled with ^{99m}Tc -diethylene triamine pentaacetic acid (^{99m}Tc -DTPA) and water. Imaging was performed in the supine and KC position, and GER was graded as 1–4 according to the extent of GER assessed by scintigraphy. **Results:** GER scintigraphy revealed no reflux in the control group (specificity: 100%). In the supine position, gastroesophageal reflux was observed in 49% of the patients with GERD, compared to 76% in the KC position. 21 of 23 (91%) patients with erosive esophagitis were shown to have GER with scintigraphy. GER scintigraphy revealed severe reflux (grade 3 or 4) (83%, 10/12) in the patients who had severe mucosal breaks (LA grade C or D). GER scintigraphy detected grade 1 or 2 reflux in 7 of the 14 patients who were endoscopically negative. There was a correlation between the endoscopically determined severity of mucosa and the reflux grade which was determined with GER scintigraphy. **Conclusion:** GER scintigraphy can detect gastroesophageal reflux with a high sensitivity in the KC position and might be a useful method in the screening and assessment of the severity of this disease. This method would be useful for the diagnosis of GERD in endoscopically negative patients.

Key words: gastroesophageal reflux scintigraphy, gastroesophageal reflux disease (GERD), KC position

INTRODUCTION

GASTROESOPHAGEAL REFLUX DISEASE (GERD) is a general term for diseases which are caused by reflux of gastric acid and gastric contents into the esophagus. In Japan, the number of patients with GERD is increasing due to population aging, westernized dietary habits, advancement of diagnostic techniques and a decreased *Helicobacter pylori* infection rate in young people.¹

Received November 1, 2004, revision accepted March 16, 2005.

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Upper gastrointestinal endoscopy is the first choice for the diagnosis of GERD. However, endoscopy cannot detect esophagitis in more than half of patients with GERD.^{2,3} Twenty-four-hour esophageal pH monitoring is considered as the gold standard for the diagnosis of GERD, because it has a high sensitivity, and it is possible to perform quantitative observation.⁴ However, this technique is troublesome for patients because a pH sensor is transnasally inserted under fluoroscopic guidance, and they are monitored for 24 hours.

In contrast, gastroesophageal reflux (GER) scintigraphy enables gastroesophageal reflux to be physiologically observed without invasiveness. However, conventional scintigraphic imaging performed with the patient lying in the supine position does not have a high sensitivity for the diagnosis of GERD.⁵ In 1999, Akbunar et al. reported that the knee-chest (KC) position increased the diagnostic

efficiency of GER scintigraphy.⁶ However, detailed examination using this technique on patients with or without esophagitis has not been done. We performed GER scintigraphy using the KC position in patients with GERD including nonerosive reflux disease. To evaluate the usefulness of GER scintigraphy for the diagnosis of GERD, we compared the severity of esophagitis and the grade of GER scintigraphy.

MATERIALS AND METHODS

We studied 37 patients with GERD (15 males, 22 females; mean age 56 ± 11) and 8 healthy volunteers (8 males; mean age 36 ± 2). Twenty-one of 37 patients with GERD had hiatus hernia. Six patients were complicated with scleroderma. Patients who met any of the following 3 criteria were diagnosed as having GERD.

- 1) Endoscopy reveals esophageal mucosal breaks.
- 2) A score of six or more points in the questionnaire for the diagnosis of reflux disease (QUEST).⁷
- 3) Twenty-four-hour esophageal pH monitoring reveals that pH is 4 or less for more than 5% of the total monitoring time.

Endoscopic classification: The Los Angeles (LA) classification was used.^{8,9} Grade 0: Endoscopy reveals no mucosal break. Grade A: One or more mucosal breaks no longer than 5 mm, none of which extends between the tops of the mucosal folds. Grade B: One or more mucosal breaks more than 5 mm long, none of which extends between the tops of two mucosal folds. Grade C: Mucosal breaks that extend between the tops of two or more mucosal folds, but which involve less than 75% of the esophageal circumference. Grade D: Mucosal breaks which involve at least 75% of the esophageal circumference.

QUEST: For interviewing patients, we used QUEST, which was developed by Carlsson et al.⁷ In QUEST, each question is scored based on the existence of GERD-specific symptoms, causes of these symptoms, the occurrence and disappearance patterns of these symptoms, etc. GERD was diagnosed by using the total of these scores.

Twenty-four-hour esophageal pH monitoring: A pH sensor was transnasally inserted under fluoroscopic guidance. This pH sensor was placed about 5 cm above the lower esophageal sphincter.¹⁰ Any medication that could influence gastric acid secretion was stopped 7 days before pH measurement.

Gastroesophageal reflux scintigraphy

Patients fasted for 4 hours or more before this examination. GER scintigraphy was performed after esophageal scintigraphy using liquefied yogurt to evaluate esophageal motility, as we previously reported. Patients ingested 40 ml of liquid yogurt which was mixed with ^{99m}Tc-diethylene triamine pentaacetic acid (^{99m}Tc-DTPA) 111 MBq to assess esophageal motility.¹¹ After this



Fig. 1 Knee-chest position.⁶

Table 1 The results of GER scintigraphy in patient with GERD

Knee-chest position	Supine position		
	GER+	GER-	
GER+	18	10	28 (76%)
GER-	0	9	9 (24%)
	18 (49%)	19 (51%)	

Significantly different between two positions at $p < 0.01$ (Fischer's exact text)

Table 2 The results of GER scintigraphy in patients diagnosed with GERD by twenty-four-hour esophageal pH monitoring

year/sex	Endoscopic classification	pH < 4 (%)	GER scintigraphic grading
45/M	B	13	3
70/M	0	14	2
53/M	0	15	0
41/F	0	13	0
59/F	0	23	1

scintigraphy, patients ingested 500 ml of water within 10 minutes for GER scintigraphy.

A wide-field, low-energy, high-resolution gamma camera (SNC-510R, Shimadzu Co. Ltd., Kyoto, Japan) with a parallel-hole collimator was used. The 20% energy window was centered at 140 keV. Static imaging was performed for 1 minute in the sitting position (pre-image), dynamic imaging for 8 minutes in the supine position and for 8 minutes in the KC position (256 × 256 matrix, 60 seconds per frame). All imagings were performed with the gamma camera adjusted parallel to the patient's back (Fig. 1).

The evaluation of GER was visually determined from a comparison with the pre-image. The following grading was used. Grade 0: gastroesophageal radioactivity reflux is observed in neither the supine nor the KC position. Grade 1: reflux is observed only in the KC position. Grade

2: slight reflux is observed in the supine position. Grade 3: evident reflux is observed in the supine position. Grade 4: reflux extends into the proximal esophagus, that is, reflux radioactivity detected throughout the esophageal body in the supine position. Any medication that could influence gastrointestinal motility was stopped 3 days before scintigraphy. Verbal or written informed consent was obtained from all patients. All examinations were performed within 4 weeks.

Statistical analysis

Statistical analysis was based on Fisher's exact test and Spearman rank correlation test. $P < 0.05$ was considered statistically significant.

RESULTS

Endoscopic findings

The breakdown according to the LA classification was: 14 patients were determined as having grade 0, 5 patients as

grade A, 6 patients as grade B, 8 patients as grade C, and 4 patients as grade D. Three of 14 patients with negative endoscopic findings were diagnosed by pH monitoring. Other 11 cases were diagnosed by QUEST.

Gastroesophageal reflux scintigraphy

GER scintigraphy revealed no reflux in the control group. Therefore, the specificity of this method was 100%. In 37 patients with GERD, this scintigraphy could detect GER in only 49% in the conventional supine position. In the KC position, this scintigraphy could detect GER in 10 more patients. There was a statistically significant difference ($p < 0.01$) between the two positions in detecting GER. In total, GER scintigraphy could detect GER in 28 patients (76%). No patient had reflux in the supine position but in the KC position (Table 1). The results of GER scintigraphy in 5 patients diagnosed as GERD by twenty-four-hour esophageal pH monitoring are shown in Table 2. Grade 1 to 3 reflux with scintigraphy was observed in 3 of the 5 patients. The score of QUEST was not related to the GER scintigraphic grade.

Correlation between endoscopic and scintigraphic findings

Twenty-one of 23 (91%) patients with erosive esophagitis were shown to have GER with scintigraphy. Severe reflux (grade 3 or 4) was observed in 10 of the 12 (83%) patients who were endoscopically diagnosed with severe esophagitis (LA classification: grade C or D). Additionally, mild GER was detected in 7 of the 14 (50%) patients who were endoscopically classified as grade 0. Table 3 shows the correlation between the grades used in endoscopy and GER scintigraphy, which was statistically significant ($p < 0.001$).

Table 3 Correlation between endoscopic and scintigraphic findings

Grade of GER scintigraphy	Endoscopic classification			Total
	Negative (0)	Mild (A + B)	Severe (C + D)	
0	7	2	0	9
1	7	5	0	10
2	2	1	2	5
3	0	3	4	7
4	0	0	6	6
	14	11	12	

Significantly different between endoscopic and scintigraphic findings at $p < 0.001$ (Spearman rank correlation test)

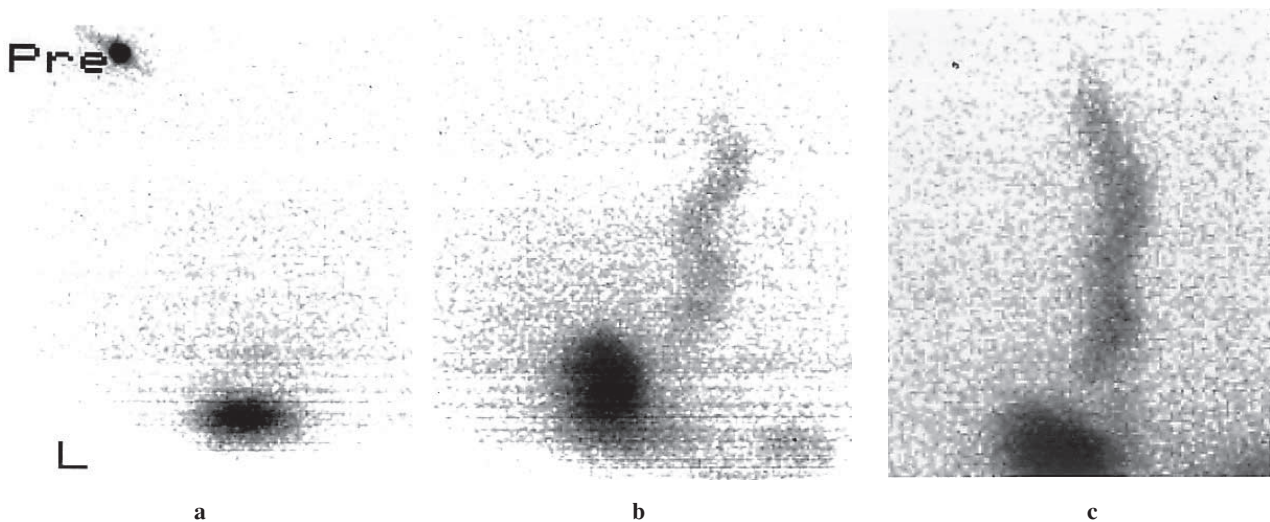


Fig. 2 Case 1: GER scintigraphy detected reflux extending into the proximal esophagus in the supine position, which was classified as grade 4. (a: sitting position, b: supine position, c: KC position)

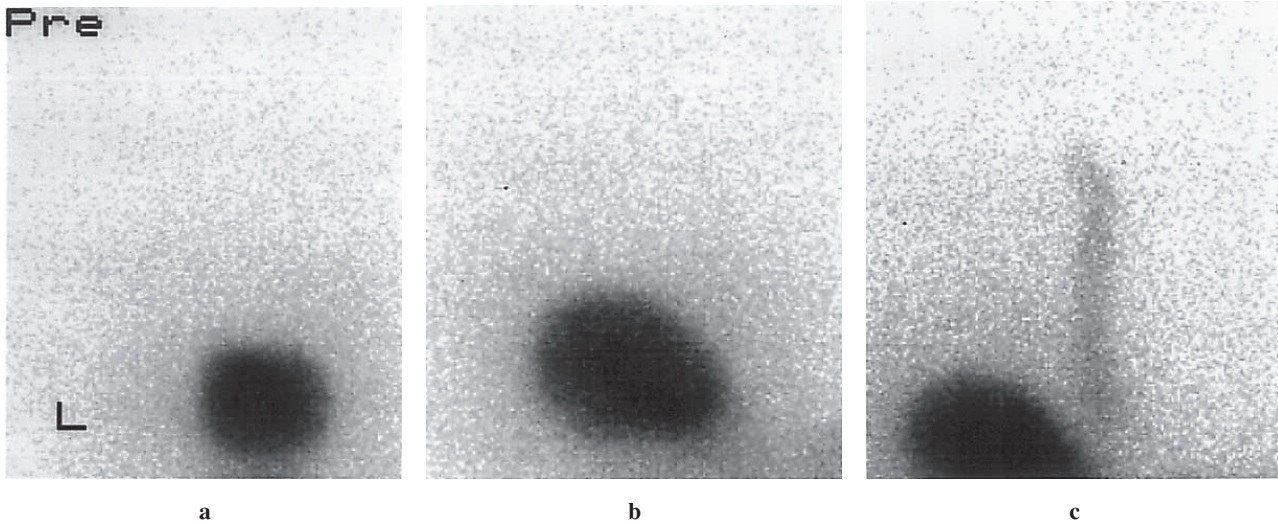


Fig. 3 Case 2: Reflux was not observed in the supine position, but was observed in the KC position (grade 1). (a: sitting position, b: supine position, c: KC position)

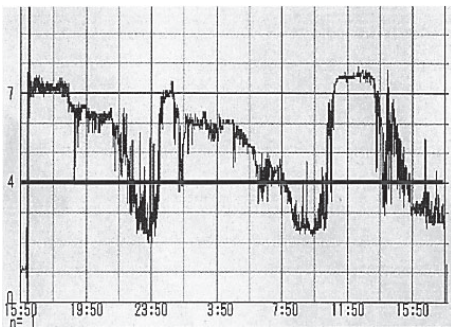
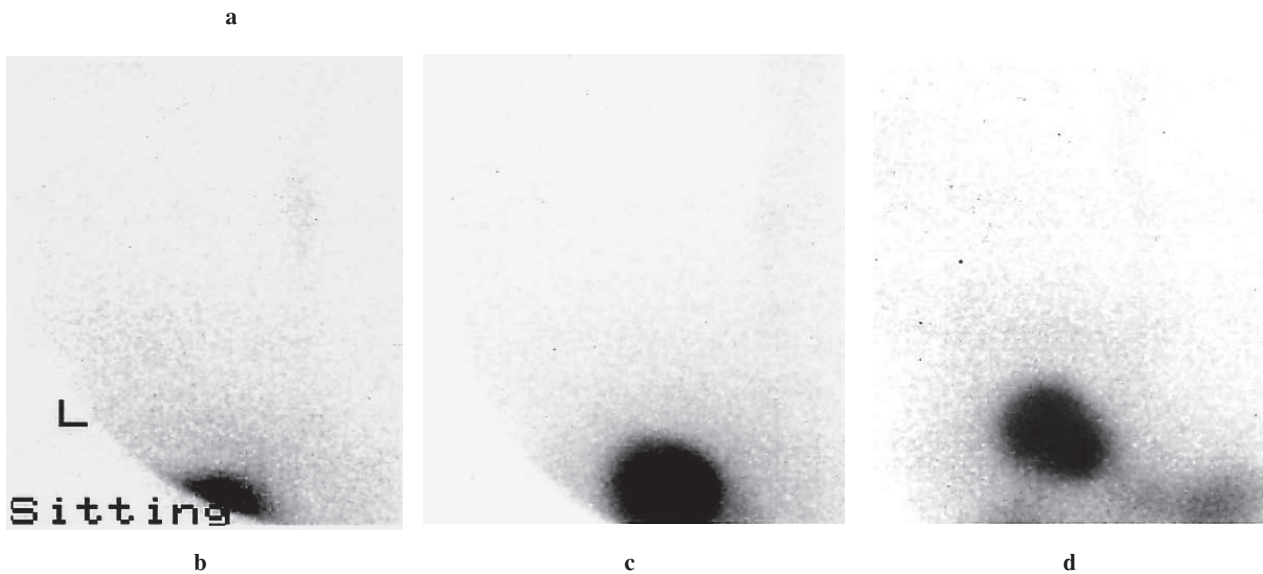


Fig. 4 Case 3: a: Twenty four-hour esophageal pH monitoring revealed that the pH was 4 or less for 15% of the total monitoring time. No reflux was detected with GER scintigraphy (grade 0). (b: sitting position, c: supine position, d: KC position)



Cases

Case 1: A 61-year-old female who complained of heartburn. The QUEST score was 16 points. Endoscopy revealed severe mucosal breaks which were classified as grade C. GER scintigraphy detected reflux extending into

the proximal esophagus in the supine position, which was classified as grade 4 (Fig. 2).

Case 2: A 62-year-old female who complained of heartburn. Although endoscopy revealed no abnormality, the

QUEST score was 18 points. Reflux was not observed in the supine position, but was observed in the KC position (grade 1) (Fig. 3).

Case 3: A 53-year-old male. He had had non-cardiac chest pain. The QUEST score was 0 points. Endoscopy revealed no mucosal break. Twenty-four-hour esophageal pH monitoring revealed that the pH < 4 was 15% of the total monitoring time, and so he was diagnosed with GERD. However, no reflux was detected with GER scintigraphy (grade 0) (Fig. 4).

DISCUSSION

The diagnosis of GERD is usually made by symptoms, such as heart burn and acid regurgitation, confirmed by upper-gastrointestinal endoscopy. Proton pump inhibitor (PPI) test is a simple and non-invasive method for the diagnosis of GERD.¹²⁻¹⁴ In this test, patients are given PPI in order to decrease gastric acid secretion. GERD is diagnosed as a result of disappearance of subjective symptoms, but the placebo effect may cause misdiagnoses. PH monitoring can directly detect reflux of gastric acid into the esophagus.⁴ In this study, only 60% of the patients with GERD diagnosed by twenty-four-hour esophageal pH monitoring were shown to have GER with scintigraphy. However, the examinees suffer because a pH sensor is transnasally inserted and placed for 24 hours. Moreover, for this test, it is necessary to stop the administration of acid reducers for a certain period of time. Additionally, the condition, in which a pH sensor is transnasally inserted, is not physiological. Although it is possible to observe GER using X-ray fluoroscopy, radiation exposure becomes problematic when continuous fluoroscopy is performed for a long period of time.

Conventionally, GER scintigraphy is performed in the supine position, because current gamma camera designs do not allow changes to the angle of the patient table.⁶ Therefore, the sensitivity for detecting GER is considered to be poor. Akbunar et al. performed GER scintigraphy on 27 patients with reflux esophagitis and reported that GER scintigraphy revealed GER in 74% of these patients in the KC position, while in the supine position, it revealed GER only in 33%.⁶ In their report, the specificity of GER scintigraphy using the KC position was not evaluated. Furthermore, they did not evaluate the relation with the severity of esophagitis. We performed GER scintigraphy in 8 normal subjects and observed no reflux in the KC position.

In the KC position, it is considered that GER is induced by the following factors: 1) movement of gastric contents to the cardiac region of the stomach, 2) intragastric pressure increased by a flexed abdomen, and 3) gravity.⁶ It has been reported that in healthy persons, increased lower esophageal sphincter pressure prevents GER when intra-abdominal pressure increases, or when they are in

the Trendelenburg position.^{15,16} It is assumed that in patients with GERD, a defective lower esophageal sphincter induces GER in the KC position.

In the present study, GER scintigraphy using the KC position detected GER in 76% of the patients with GERD and in 91% of the patients with endoscopic positive GERD. There was a correlation between the severity of esophagitis and the grade of GER observed on GER scintigraphy. GER scintigraphy detected GER in only 50% of the patients with endoscopic negative GERD. However, considering that endoscopy could not reveal any abnormality in these cases, this positive ratio is not so low. It has been reported that more than half of patients with GERD are endoscopically negative.^{2,3} Therefore, for these cases, a simple and objective method to evaluate GER is necessary. GER scintigraphy, which is non-invasive and can visualize GER objectively, is likely to be useful for the diagnosis of endoscopic negative GERD. Moreover, GER scintigraphy could be a technique which can detect severe esophagitis without endoscopy. We also consider that this technique is highly useful for determining the effect of drugs which may improve GER, and for examining the effects of endoscopic therapy and surgery on GERD.¹⁷⁻²⁰ Further studies are needed to define the sensitivity of GER scintigraphy for the diagnosis of endoscopic negative GERD.

In conclusion, GER scintigraphy in the KC position can detect gastroesophageal reflux with a high sensitivity. Additionally, this method would be useful for the diagnosis of GERD in patients whose endoscopic results are negative.

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