

Gastric Emptying in Migraine: A Comparison With Functional Dyspepsia

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Background/Aims

Gastric stasis in migraineurs remains controversial. The aim of this study is to investigate gastric emptying (GE) time, and any associations between GE parameters and dyspeptic symptoms among patients with functional dyspepsia (FD) and migraine without any gastrointestinal symptoms during the interictal period.

Methods

We enrolled 27 migraine patients, 32 FD patients and 12 healthy people as controls, and performed GE scintigraphy as gastric function test. Gastrointestinal symptoms were evaluated in the FD and migraine.

Results

The age-adjusted mean gastric half-emptying time in FD (125.51 ± 52.55 minutes) patients was longer than in migraineurs (100.82 ± 23.94 minutes, $P = 0.035$) and controls (95.25 ± 23.29 minutes, $P = 0.021$). The percentage of gastric retention was higher in FD than in migraine. However, migraineurs did not show an obvious delayed gastric emptying or an increase of gastric retention when compared to the normal controls. The association between each dyspeptic symptom and GE parameters was not significant, but postprandial fullness and early satiety showed a tendency of delayed GE. In migraineurs, GE time did not show significant association with nausea and vomiting during interictal periods.

Conclusions

Delayed GE does not appear to be a mechanism that patients with FD and migraine have in common. Migraineurs without dyspepsia during interictal period had normal GE, and further study for association with FD should be investigated.

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Key Words

Dyspepsia; Migraine disorders; Gastric emptying; Radionuclide imaging

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Introduction

Functional dyspepsia (FD), defined as discomfort or pain in the upper part of the abdomen in the absence of organic disease but often linked to a motility disorder, occurs very commonly in the general population.¹⁻³ Several pathophysiologic mechanisms, such as gastric acid secretion, gastroduodenal motility, *Helicobacter pylori* infection, psychosocial factors, and stress may play a role in the pathogenesis of FD.⁴⁻¹⁵ Among them, delayed gastric emptying (GE) is traditionally considered a major pathophysiologic mechanism in FD, and delayed GE has been identified in 29%-59% of patients with FD.⁴⁻¹⁵ Although several methods have been used for evaluating gastroduodenal motility, gastric scintigraphy has been known as the gold standard for measuring GE since it is noninvasive, reproducible, simple to perform, accurate and quantitative.^{16,17}

In clinical practice, migraine and symptoms of upper gastrointestinal distress are among the most frequent complaints seen by clinicians. Also, dyspeptic symptoms are often seen to be accompanied by migraines. In fact, a survey on irritable bowel syndrome showed that headache was present in more than 30% of patients suffering from this condition.¹⁸ In another previous study that used the Bowel Disease Questionnaire to compare the upper abdominal symptoms in 99 patients with migraine and 488 apparently healthy subjects without migraine, 60% of the migraine patients reported frequent dyspepsia while 23% of the subjects without migraine reported dyspepsia.¹⁹ Although FD and migraine were often co-occurred among the general population, the pathophysiological link between the 2 conditions remains unclear.

Some of the patients with migraines have been associated with gastric stasis, such as FD. Recently, a study utilizing gastric scintigraphy reported that migraine patients had an abnormal gastric transit time compared to controls.²⁰ In addition, migraine patients during the interictal period, had delayed gastric stasis compared with during the ictal period.²¹ However, previous studies had the limitation of not evaluating gastrointestinal symptoms during the interictal period and thus showed controversial results.²⁰⁻²² Therefore, in our study we enrolled subjects with migraine without gastrointestinal symptoms during the interictal period in order to eliminate the group that overlaps with FD.

We investigated whether delayed GE plays a pathogenic role in FD patients or migraineurs without any gastrointestinal symptoms during the interictal periods. We also examined whether

several parameters of GE time were associated with dyspeptic symptoms in those patients.

Materials and Methods

Study Subjects

Twenty-seven migraine patients between 18 to 50 years old were included from November 2008 to May 2010. Diagnosis of migraine was made according to the International Headache Society criteria for episodic migraine, and we excluded patients with any dyspeptic symptoms (epigastric pain, epigastric discomfort, postprandial fullness, early satiety, nausea, vomiting and abdominal bloating etc) during the interictal period. Chronic migraine patients were also excluded. Patients were excluded if they had been using daily centrally acting medications, were allergic to eggs, or had any condition known to affect gastric motility, ie, diabetes, thyroid disease, gastric surgery, anorexia, psychiatric disorders or head injury. The migraine patients underwent gastric emptying scintigraphy to measure gastric emptying time during the interictal period.

We included 12 healthy controls without other underlying disease, concurrent medication, or a clinical history of dyspeptic symptoms (epigastric pain, epigastric discomfort, postprandial fullness, early satiety, nausea, vomiting and abdominal bloating etc) and performed gastric scintigraphy. Sample size of patients with migraine and control group were calculated using Gpower sample size calculation program.

Of the patients who visited the Division of Gastroenterology of Eulji Hospital from 2004 to 2010, those who underwent gastric emptying scintigraphy were enrolled. Thirty-two FD patients were included in the study, who were selected to match the age and gender of the migraine and control groups.

Those with other organic diseases (diagnosed on upper endoscopy) were excluded. The FD patients were invited to complete the Rome II dyspepsia module questionnaire. The symptoms assessed by questionnaire included postprandial fullness, early satiety, epigastric pain, nausea and vomiting. All the subjects underwent gastric scintigraphy.

All of the FD patients, migraine patients and normal controls underwent gastroscopy and so we excluded patients with any organic diseases to induce symptoms, such as peptic ulcer, gastroesophageal reflux disease and malignancy.

This study was approved by the Ethics Committee of Eulji University School of Medicine.

Gastric Emptying Scintigraphy

GE scintigraphy was performed in the morning after an overnight fast. Patients had to stop smoking and drinking alcohol at least 24 hours before the study. Drugs known to affect gastrointestinal motility were discontinued at least 48 hours before the study.

A test meal (282 kcal) consisting of a ^{99m}Tc technetium sulphur colloid (500 μCi)-labeled scrambled egg sandwich (2 eggs with 2 pieces of white toast) and 300 mL of water was employed. All subjects were obtained in the anterior and posterior projection immediately, and at 30, 60, 90 and 120 minutes after meal ingestion while the patient was standing. Scintigraphic images were obtained with a large field of view of the gamma camera using a low energy all-purpose collimator with a 20% energy window setting centered at 140 keV. Patients were allowed to sit in a chair between the standing image acquisitions.

GE was graded according to gastric half-emptying times ($T_{1/2}$): normal (< 70 minutes), mildly delayed (70-100 minutes) and delayed (> 100 minutes).¹⁷ The GE parameters used were gastric $T_{1/2}$ and percentage of radioactive material remaining in the stomach (% RMR) at 0, 30, 60, 90 and 120 minutes.

Statistical Methods

The data in the groups are expressed as mean values \pm SD. FD and migraine, FD and controls or migraine and controls were compared using the Student's *t* test. Categorical variables were compared using the Chi-squared test. In FD, an association between dyspeptic symptoms and GE parameters were analyzed using ANOVA. In migraineurs, an association between dyspeptic symptoms and GE parameters were analyzed using Student's *t* test.

Data were analyzed using SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA). Differences were judged as statistically significant if the *P*-value was less than 0.05.

Results

Patient Characteristics

We enrolled 27 migraine patients without any gastrointestinal symptoms during the interictal period, 32 FD patients diagnosed by Rome II criteria, and 12 healthy people as controls. The mean migraine period was 9.25 (\pm 7.02) years. Among 32 FD patients, 12 patients (36.4%) reported postprandial fullness; 15 patients (45.5%) early satiety; 5 patients (15.2%) epigastric

Table 1. Baseline Characteristics of the Enrolled Patients

	FD	Migraine	Controls	<i>P</i> -value
Sex (M:F)	9:23	9:18	5:7	0.345
Age (mean \pm SD, yr)	31.8 \pm 7.8	31.7 \pm 8.1	31.5 \pm 5.9	0.760

FD, functional dyspepsia.

pain, and 5 patients (15.2%) nausea or vomiting. When classifying them into subgroups according to the Rome II criteria, 15.2% had ulcer-like type and 82.9% had dysmotility-like type.

Table 1 shows the patients' characteristics. The mean age and sex of the patients with FD, migraine and controls were not significantly different. The proportion of females with FD and migraine was larger than that of the control group, and FD and migraine did not show significant difference.

Gastric Emptying Times

Age-adjusted gastric $T_{1/2}$ are shown in Figure 1. FD patients (125.51 \pm 52.55 minutes) showed more delayed gastric $T_{1/2}$ compared with migraine patients (100.82 \pm 23.94 minutes, *P* = 0.035) or controls (95.23 \pm 23.29 minutes, *P* = 0.021). However, gastric $T_{1/2}$ in migraine patients showed no significant difference compared with that in the controls (*P* = 0.501).

The proportions of FD, migraine and control groups according to grade of delayed GE are shown in Figure 2. The proportion of patients with mildly delayed GE time was 24.1% in the FD group, 29.6% in the migraine group and 25.0% in the controls, and that with delayed GE time was 58.6% in the FD group, 48.1% in the migraine group and 33.3% in the controls. However, the differences in the proportions among the three groups were not statistically significant (*P* = 0.363).

Percentage of Radioactive Material Remaining in the Stomach

The mean gastric retention over time is shown in Figure 3. FD group showed no significant difference in the early phase compared to migraine group, yet significant gastric stasis was noted at 90 and 120 minutes (61.21% \pm 13.90% vs 53.63% \pm 12.92%, *P* = 0.049 at 90 minutes respectively; 47.15% \pm 17.32% vs 38.05% \pm 14.63%, *P* = 0.045 at 120 minutes respectively). In addition, FD group showed gastric stasis in the delayed phase compared to controls although it was not statistically significant (61.21% \pm 13.90% vs 53.28% \pm 11.50%, *P* = 0.097; 47.15% \pm 17.32% vs 38.05% \pm 14.63%, *P* = 0.086). On

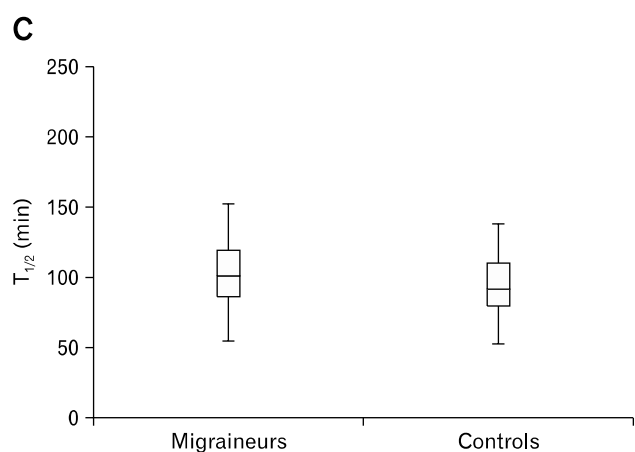
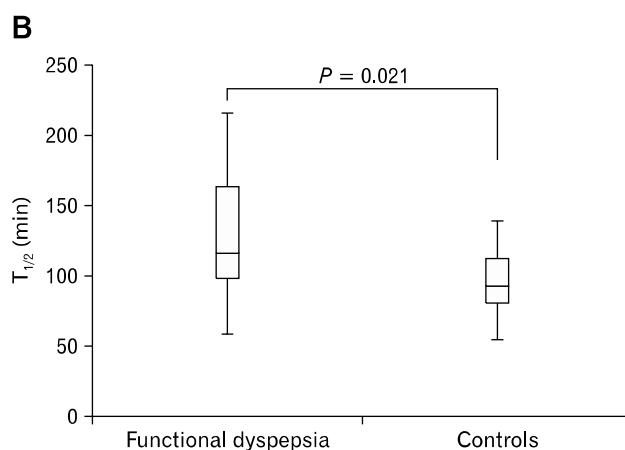
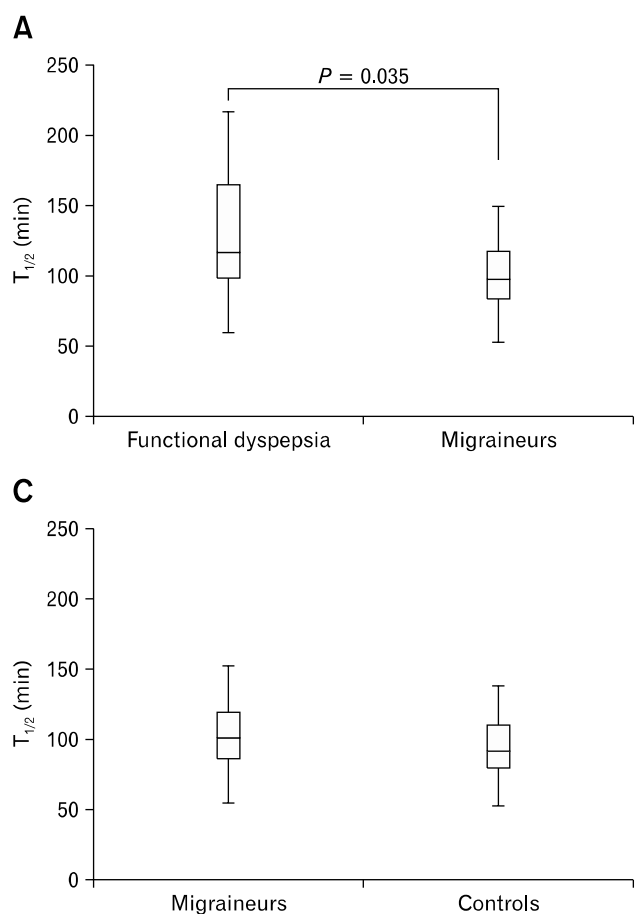


Figure 1. Age-adjusted gastric half-emptying time ($T_{1/2}$) in patients with functional dyspepsia (FD) compared with migraineurs and controls. The range, median, and 25th-75th percentiles are represented by error bars, bold line and box, respectively. Gastric $T_{1/2}$ was 125.51 ± 52.55 minutes in FD patients, 100.8 ± 23.9 minutes in migraineurs and 95.2 ± 23.2 minutes in controls (A: FD vs migraineurs, $P = 0.035$; B: FD vs controls, $P = 0.021$). (C) However, it did not differ significantly between the migraineurs and controls.

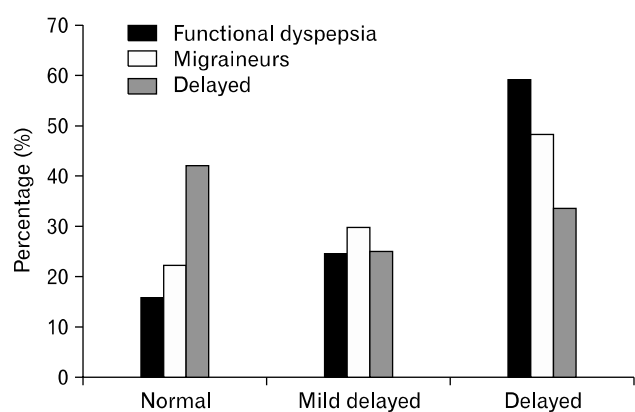


Figure 2. Proportion of the patients with functional dyspepsia (FD), migraine and controls according to grade of delayed gastric emptying. The proportion of patients with mildly delayed gastric emptying time was 24.1% in FD, 29.6% in migraineurs and 25.0% in controls, and that of delayed gastric emptying time was 58.6% in FD, 48.1% in migraineurs, and 33.3% in controls ($P = 0.363$).

the other hand, migraineurs did not show a significant difference from controls.

Association Between Gastrointestinal Symptoms and Gastric Emptying Parameters

In patients with FD, an association was identified between dyspeptic symptoms and GE parameters, as shown in Table 2. Each GE parameter in accordance with dyspeptic symptoms did not show statistically significant differences, yet in the FD group with postprandial fullness and early satiety, GE time was more sluggish than patients with epigastric pain ($P = 0.052$). In particular, this tendency was observed significantly in gastric $T_{1/2}$.

Among the symptoms complained of during ictal period in migraineurs, nausea or vomiting did not show a significant difference in GE parameters (Table 3).

Discussion

We investigated whether delayed GE may play a pathogenic

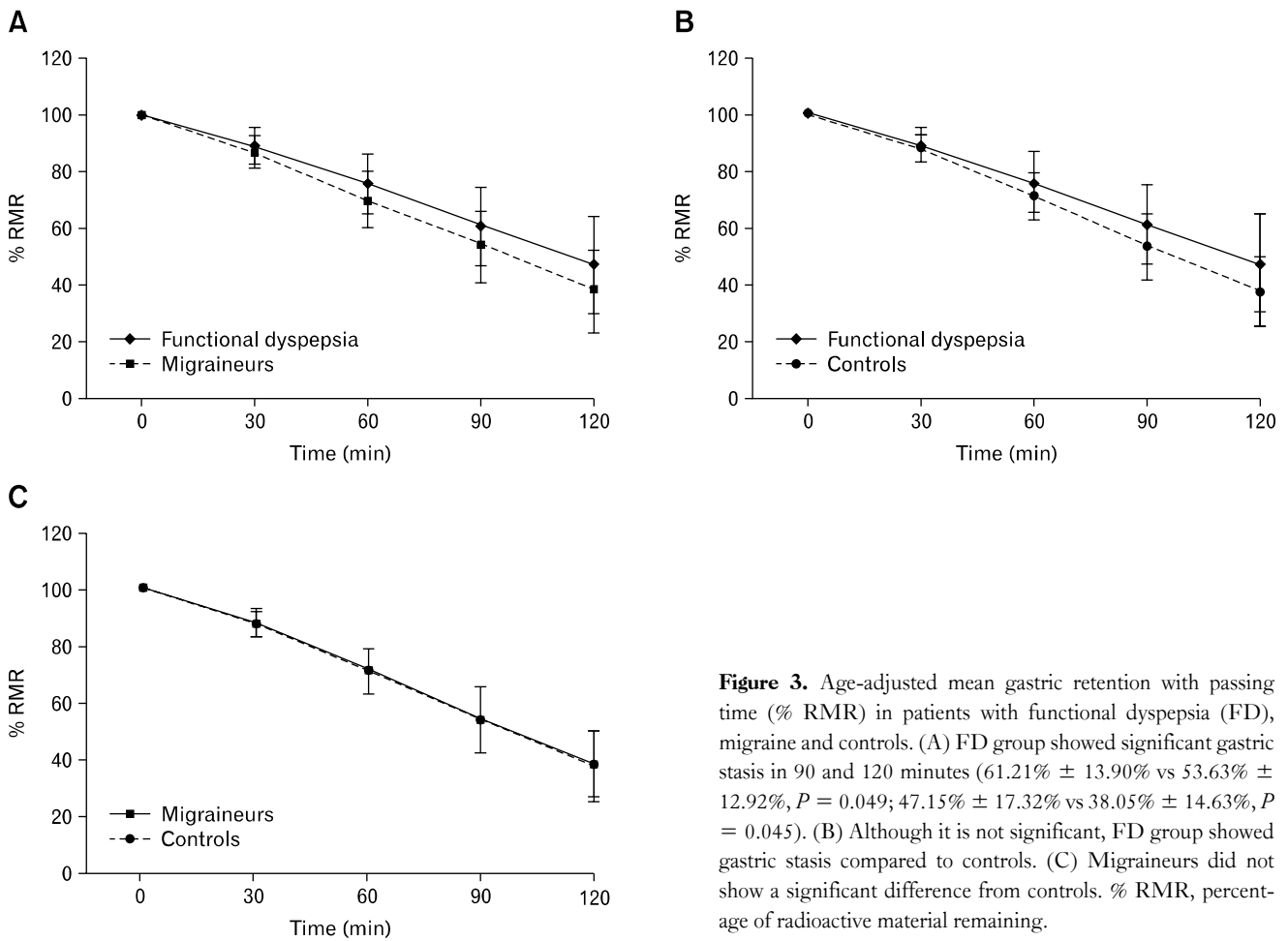


Figure 3. Age-adjusted mean gastric retention with passing time (% RMR) in patients with functional dyspepsia (FD), migraine and controls. (A) FD group showed significant gastric stasis in 90 and 120 minutes (61.21% ± 13.90% vs 53.63% ± 12.92%, *P* = 0.049; 47.15% ± 17.32% vs 38.05% ± 14.63%, *P* = 0.045). (B) Although it is not significant, FD group showed gastric stasis compared to controls. (C) Migraineurs did not show a significant difference from controls. % RMR, percentage of radioactive material remaining.

Table 2. Association Between Main Dyspeptic Symptoms and Gastric Emptying Parameters in Functional Dyspepsia Group (n = 32)

	Postprandial fullness (n = 12)	Early satiety (n = 15)	Epigastric pain (n = 5)	<i>P</i> -value
T _{1/2} (mean ± SD, min)	125.07 ± 34.09	127.16 ± 34.09	98.41 ± 2.58	0.052
30 min % RMR	90.67 ± 6.41	89.91 ± 6.73	84.96 ± 7.07	0.372
60 min % RMR	77.98 ± 11.08	77.62 ± 10.17	68.88 ± 7.38	0.211
90 min % RMR	63.03 ± 13.77	63.79 ± 11.3	53.74 ± 5.90	0.111
120 min % RMR	48.15 ± 17.66	49.95 ± 14.27	40.58 ± 6.62	0.096

T_{1/2}, half-emptying time; % RMR, percentage of radioactive material remaining.

Table 3. Association Between Nausea and Vomiting During the Ictal Period and Gastric Emptying in Migraineurs (n = 27)

	T _{1/2} (min)	<i>P</i> -value	30 min % RMR	<i>P</i> -value	60 min % RMR	<i>P</i> -value	90 min % RMR	<i>P</i> -value	120 min % RMR	<i>P</i> -value
Vomiting (mean ± SD)										
With (n = 13)	98.1 ± 22.8	0.280	87.6 ± 4.6	0.507	69.9 ± 8.0	0.135	51.0 ± 12.8	0.154	35.0 ± 14.5	0.162
Without (n = 14)	103.5 ± 24.7		87.4 ± 6.5		71.3 ± 10.9		55.6 ± 12.9		40.8 ± 13.4	
Nausea (mean ± SD)										
With (n = 7)	103.8 ± 22.1	0.819	88.3 ± 4.5	0.387	72.3 ± 8.0	0.295	55.1 ± 11.7	0.533	39.7 ± 13.1	0.656
Without (n = 20)	95.0 ± 29.9		84.5 ± 9.0		65.0 ± 14.3		51.0 ± 16.8		36.5 ± 16.3	

% RMR, percentage of radioactive material remaining.

role in the generation of gastrointestinal symptoms in patients with FD and migraine, and investigated whether several parameters of GE may be associated with dyspeptic symptoms in the patients with FD or migraine. This study showed that patients with FD had significantly more delayed GE than the migraineurs and controls. This finding may support the previous studies in which the delayed GE was considered as a major pathophysiologic mechanism in FD.^{4,15} In particular, gastric stasis appeared to be more significant in the delayed phase than in the early phase. On the other hand, there was no significant difference in GE between migraine patients and controls. This finding may be contrary to the results of prior studies in which the patients in the migraine groups showed delayed GE.^{12,13,19-21} We believe this result was caused by our selection of subjects. Migraine patients frequently complain of dyspeptic symptoms during interictal periods.²³ Previous studies^{12,13,19,20} did not assess gastrointestinal symptoms during the interictal period. Therefore, in our study, we excluded migraine patients who had dyspeptic symptoms during the interictal periods, lowering the possibility of intermingling FD within migraine compared to the previous studies. In fact, some studies showed GE similar to the control in migraineurs during the interictal period.²²

In our study, the group complaining of postprandial fullness and early satiety showed relatively delayed GE. A recent study on breath test reported that early satiety was the only symptom associated with delayed GE.²⁴ Postprandial fullness or vomiting is regarded as one of the dysmotility symptoms. Sarnelli et al⁵ studied the relationship between delayed GE and the presence or severity of individual symptoms in dyspeptic patients, using an eight-item questionnaire to assess symptom severity and breath test technology to assess GE. Delayed GE was associated with postprandial fullness and vomiting, regardless of their severity. Despite the weakness in comparing the symptoms that patients complained of, by simply dividing the symptoms into postprandial fullness, early satiety, and epigastric pain, this study demonstrated the delayed GE time in postprandial fullness and early satiety, the symptoms regarded as dysmotility symptoms by clinicians. This study examined whether the GE was associated with vomiting or nausea that occurred during the ictal period in migraine patients. However, there was no significant association between nausea, vomiting and GE in migraine group, which indicates that GE is likely to have less effect on these symptoms.

This study has some limitations. Our data lacked information about factors regarded as affecting GE, such as height, weight and body mass index except age and sex. If we had many more

subjects with FD, we might have been able to obtain more reliable information on the association between dyspeptic symptoms and GE parameters. Second, in our study, the mean gastric $T_{1/2}$ of controls was prolonged, as compared with that in the previous data.¹⁷ This might be because there was relatively large proportion of young and female subjects enrolled. In fact, the volume and content of ingested food, mental status, age and physical exercise are known associated factors that alter GE.²⁵⁻³¹ Therefore, we tried to obtain our own data on GE times in our hospital, because we thought it was important to collect unique data using GE scintigraphy in an individual hospital. Third, we captured just the main or most discomforting symptoms because we chose FD patients among the patients who had undergone GE scintigraphy in a single hospital. Therefore, the lack of objective symptomatic analysis was also a limitation of this study. Lastly, this study has the limitation of a single-center study targeting a small number of patients. There was also a small number of FD patients in this study because FD patients were selected to match the gender and age of the migraine and control group from the subjects who had undergone GE scintigraphy although the migraine and normal control groups were collected prospectively to conduct gastric scintigraphy during the interictal period. Therefore, further studies targeting more patients would be needed.

In conclusion, using gastric scintigraphy, this study demonstrated that GE in FD was more delayed than in migraineurs. In particular, we designed the study to exclude anyone who had experienced gastrointestinal symptoms during the interictal period from the migraine groups, thereby eliminating the overlap between migraine and FD. Therefore, this study produced different results from previous studies.^{12,13,19-21} In other words, it could be suggested that unlike FD, the migraine without dyspeptic symptoms does not affect GE during interictal period; nausea and vomiting complained during ictal period could be affected by another mechanism rather than delayed GE.

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