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# 파킨슨 병 환자에서 MRI를 이용한 위 운동성 측정: 위 용량 및 위 운동성과 소화기계 증상 간의 연관성 분석

Quantitative MRI evaluation of gastric motility in patients with Parkinson's disease: Correlation of dyspeptic symptoms with volumetry and motility indices

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서울대학교 대학원

의학과 영상의학 전공

조 정 흠

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Abstract

# Quantitative MRI evaluation of gastric motility in patients with Parkinson's disease: Correlation of dyspeptic symptoms with volumetry and motility indices

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**Objectives**: To investigate the correlation between dyspeptic symptoms and gastric motility parameters measured by magnetic resonance imaging (MRI) using volumetry and motility indices in patients with Parkinson's disease (PD).

**Materials and Methods**: In this IRB-approved study, MRI datasets obtained from August 2014 to May 2016 in 38 PD patients were retrospectively analyzed. Patients underwent a 120-minute-long MRI study using a liquid test meal and 8 sets of scans.

Gastric content volume (GCV) and total volume (TGV), gastric half emptying time ($T_{1/2}$), motility index (GMI), accommodation (GA), and emptying (GE) values were acquired. These measurements were compared between patients according to the presence of gastric symptoms: early satiety (n = 25), epigastric pain (n = 13), and dyspepsia (n = 28).

**Results**: Patients with early satiety showed significantly decreased GE of GCV and TGV ($p < 0.001$ and $p = 0.017$). Dyspeptic patients had significantly decreased GE of GCV and GMI ($p = 0.001$ and $p = 0.029$). GE of GCV at 90 and 120 minutes were significantly lower in patients with early satiety ($p = 0.001$ and $p = 0.002$). GE of GCV and GMI at 90 minutes were significantly decreased in patients with dyspepsia ($p = 0.004$ and $p = 0.002$). $T_{1/2}$ of GCV was prolonged in patients with early satiety, epigastric pain, and dyspepsia ($p = 0.004$, $p = 0.041$, and $p = 0.023$). $T_{1/2}$ of TGV also delayed in patients with early satiety ($p = 0.023$). GMI at 90 minutes was significantly correlated with dyspepsia on multivariable analysis ($p = 0.028$).

**Conclusion**: Gastric motility can be quantitatively assessed by MRI, showing decreased GMI, delayed GE, and prolonged $T_{1/2}$ in PD patients with early satiety or dyspepsia.

**Key words:** Stomach, Parkinson's disease, Magnetic Resonance Imaging, Gastric Emptying, Dyspepsia

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# INTRODUCTION

Parkinson's disease (PD) is the second most prevalent degenerative disease in people above 65 years, and affects 1% of the population above 60 years (1). Gastrointestinal dysfunction is frequent in PD, involving approximately 30% of patients (2). Symptoms include dysphagia, nausea, bloating, delayed gastric emptying, and constipation, which are thought to be due to decreased gastrointestinal motility. Of these, gastroparesis is a significant problem in PD patients (3), and has a detrimental effect on regulation of the level of levodopa, which is absorbed only in the small bowel (4, 5). However, there are few studies on the quantitative assessment of impaired gastric motility in PD patients (6, 7).

Unlike structural diseases manifested as fixed stenosis or obstruction which can be evaluated by computed tomography, functional impairment of gastric motility is a challenging disease to assess with conventional imaging studies taken at a single time point. Gastric scintigraphy, which is the gold standard for evaluating gastric emptying, has drawbacks such as radiation exposure and limited temporal and spatial resolution (8). Other assessment techniques such as gastric barostat (9), ultrasound imaging (10), and single photon emission computed tomography (11) which have been used for measuring gastric accommodation, have shortcomings of invasiveness (12), subjectiveness (13), and radiation exposure (14), respectively. On the other hand, according to previous studies (8, 15), magnetic resonance imaging (MRI) which is non-invasive and has no radiation exposure can allow simultaneous morphologic and functional evaluation of the stomach.

Although there were some reports on MRI assessment of impaired gastric

function in PD patients (6) and in diabetic patients (16), there is no study comparing gastric functional MRI measurements with clinical aspects in PD patients. Therefore, this study aims to investigate the correlation between dyspeptic symptoms and gastric motility parameters measured by MRI using volumetry and motility indices in PD patients.

# MATERIALS AND METHODS

Our study was performed from March 2017 to December 2017. All procedures were approved by the animal care and use committees of our institute (approval number: BA1608-206/050-01). This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (B-1712-436-103) and requirement of informed consent was waived (The data were analyzed anonymously). This study was conducted according to the Declaration of Helsinki.

## *Study population*

Patient data were collected prospectively for a randomized controlled trial testing the noninferiority of a novel prokinetic drug (17), which included patients diagnosed as idiopathic PD by UK Parkinson's disease Society Brain Bank criteria (18) with age of 20–80 years, from August 2014 to May 2016. This study is aimed to retrospectively compare various measurements on baseline MRI obtained before taking the drug, according to the presence of dyspeptic symptoms. Of the 42 patients who were assessed for eligibility, two patients were excluded for refusing to undergo MRI (n = 2). During the study, two patients dropped out due to loss of follow-up (n = 1) and aggravation of disease requiring increased drug doses for PD (n = 1). Finally, 38 patients were included for this retrospective analysis (Fig 1). Basic clinical information including body weight index (BMI), duration of PD, levodopa equivalent daily dose (LEDD), and medication duration were extracted from the prospectively collected database. Enrolled participants also answered the unified Parkinson's disease rating scale (UPDRS) questionnaire (19) and filled a

gastrointestinal symptom diary (20).

For analysis, patients were divided into groups according to the presence of dyspeptic symptoms; early satiety, epigastric pain, and dyspepsia. Dyspepsia was defined as present if either early satiety or epigastric pain was present.

## *MRI protocol*

After at least 6 hours of fasting, participants underwent MRI of the stomach in supine position, before and after drinking a 400-mL fluid meal (Nucare, 400 kcal, carbohydrate: protein: fat = 57:15:27; Daesang Wellife, Seoul, Korea). All images were obtained between 08:00 and 13:00 hours.

Patients were scanned with 3.0-T Ingenia or 1.5-T Intera MRI units (Philips Healthcare, Best, the Netherlands) with body coil (16-channel for Ingenia and 8-channel for Intera). Axial 3D fatsuppressed T1-weighted gradient echo sequence (mDixon for Ingenia and THRIVE for Intera) covering the stomach was used to measure the gastric volume before and after meal at 5, 10, 15, 30, 60, 90, and 120 minutes (Fig 2). For evaluation of proximal gastric motility, oblique sagittal images parallel to the long axis of gastric body were obtained before and after meal at 5, 10, 15, 30, 60, 90, and 120 minutes by using 3D balanced-turbo field echo (b-TFE) sequence. Distal stomach images were obtained at 30, 60, 90, and 120 minutes after meal by using the same b-TFE sequence with oblique coronal plane parallel to the long axis of gastric antrum. Further details of MR imaging parameters are listed in Table 1. We organized the MRI protocol according to previous studies and modified it according to our study purpose and institutional setting (6, 21).

## *Image analysis*

Gastric content volume (GCV) and total gastric volume (TGV) were measured by semi-automatic method using volume analysis software (Multi-Modality Tumor Tracking, Intellispace Portal version 5.0.2; Philips Healthcare, Best, the Netherlands) by one radiologist (Y.J.L. with 11 years of experience in body imaging). Regions of interest (ROIs) were drawn roughly along the margin of gastric contents and intraluminal air, respectively, on axial fat-suppressed T1-weighted images and the margin was carefully modified. Then, the volume of ROIs was calculated automatically by the software (Fig 3). TGV was defined as sum of gastric contents and air volume.

Gastric half emptying time ($T_{1/2}$) of GCV and TGV were derived respectively from the power exponential model which was described by Elashoff et al (22).

Gastric motility indices (GMIs) at 15, 30, 60, and 90 minutes after meal were calculated from measurements in b-TFE images by one radiologist (J.C. with 3 years of experience in body imaging). The gastric wave was measured at the location where sinusoid wave was most prominently visible. Usually, it was measured at the proximal stomach in the 15-minute-delayed scan, and at the mid to distal stomach afterwards. Wavelengths, number of waves within serially obtained 30 images, and amplitudes of gastric peristaltic waves were measured on the b-TFE images (Fig 4). Wavelength was defined as the distance between the two end points of the inward deflection of the most prominent sinusoid wave. GMI was calculated for each participant using the following equation, which was modified from previously reported formula (6):

$$\text{GMI } [mm^2/\text{s}] = \frac{\text{Wavelength} \times \text{Number of waves}}{\text{Total scan time}} \times \text{Amplitude}$$

Gastric accommodation (GA) and gastric emptying (GE) at x minutes after ingestion of test meal (x = 5, 10, 15, 30, 60, 90, and 120 minutes) were defined as following formulas:

$$\text{GA} = \frac{\text{Gastric volume at 5 minutes - Gastric volume before ingestion}}{\text{Gastric volume before ingestion}}$$

$$\text{GE (\%)} = 100 - \frac{\text{Gastric volume at x minutes - Gastric volume before ingestion}}{\text{Gastric volume at 5 minutes - Gastric volume before ingestion}} \times 100$$

GA and GE of TGV and GCV were calculated respectively. The radiologists were blinded to the presence of dyspeptic symptoms while analyzing the images.

## *Statistical analysis*

Statistical analysis was performed by using SPSS version 19.0 software (IBM, Armonk, NY) and R version 3.3.2 software (R Foundation for Statistical Computing, Vienna, Austria). $P < 0.05$ was considered as statistically significant. Clinical features which might affect gastric parameters such as age, BMI, duration of PD, LEDD, and medication duration were analyzed using independent t-test between PD patients with and without dyspeptic symptoms. GE of GCV and TGV, and GMIs were compared between PD patients with and without dyspeptic symptoms, using repeated measures ANOVA, and post hoc analysis was done using independent t-test with Bonferroni correction at each timepoint. GA and $T_{1/2}$ were also comparedusing Mann-Whitney tests. Generalized estimating equation was applied for multivariable analysis to determine significant independent clinical or imaging features that might

be correlated with the presence of dyspeptic symptoms in PD patients. Clinical or imaging features which showed statistical significance in the aforementioned univariable analyses were used as independent variables for the generalized estimating equation.

# RESULTS

All participants ingested the fluid meal and underwent MRI without complication. Table 2 shows the characteristics of included PD patients. Twenty-eight patients experienced dyspeptic symptoms related to meal; early satiety in 15 patients, epigastric pain in 3 patients, and both in 10 patients. The remaining 10 patients did not complain of any dyspeptic symptoms. There was no statistically significant difference of age, BMI, duration of PD, LEDD, and medication duration between PD patients with and without dyspeptic symptoms in each group (S1 Table).

The range of measured GCV and TGV were 0.5–551.0 mL and 6.6–864.4 mL, respectively. The coefficients of variation, obtained from the ratio of gastric air volume to GCV, were between 0.6 and 1.3.

The mean $T_{1/2}$ of GCV and TGV of 38 patients were 113.82 minutes (range 60.85–166.79) and 98.98 minutes (range 53.66–144.30), respectively.

Mean GE of GCV and TGV, and GMIs at each time points were compared between patients with and without the dyspeptic symptoms (Fig 5, Table 3, S2 and S3 Tables). Patients with early satiety showed significantly decreased GE of GCV and TGV ($p < 0.001$ and

$p = 0.017$, respectively) compared with asymptomatic patients. For epigastric pain, there was a significant difference in GE of GCV between the two groups over time ($p = 0.029$). On the other hand, there was no statistically significant difference in GE of TGV and GMI between the patients with and without epigastric pain. Patients who had dyspepsia also showed significant decrease in the GE of GCV and GMI ($p = 0.001$ and $p = 0.029$, respectively). Independent t-test with Bonferroni correction

showed significant difference of GE of GCV at 90 and 120 minutes ($p$ = 0.001 and $p$ = 0.002) between the patients with and without early satiety. GE of GCV and GMI at 90 minutes ($p$ = 0.004 and $p$ = 0.002, respectively) were significantly decreased in patients with dyspepsia.

The comparison results of GA and $T_{1/2}$ of GCV and TGV are presented in Table 4. GA did not show statistical difference between patients with and without dyspeptic symptoms. On the other hand, $T_{1/2}$ of GCV was significantly prolonged in patients with early satiety, epigastric pain, or dyspepsia ($p$ = 0.004, $p$ = 0.041, and $p$ = 0.023, respectively). $T_{1/2}$ of TGV also prolonged in patients with early satiety ($p$ = 0.023).

Multivariable analysis showed one statistically significant MR imaging feature, GMI at 90 minutes ($p$ = 0.028), in patients with and without dyspepsia (S4 Table).

# DISCUSSION

In this study, we performed a quantitative MRI analysis using volumetry and motility indices and evaluated the correlation of dyspeptic symptoms and various MRI measurements in PD patients.

Gastric volume measurement by using MRI has been demonstrated to be reliable compared with other methods, such as barostat, gastric scintigraphy, or $^{13}$C-breath test (15, 23). The non-invasive nature of MRI can provide a more tolerable method in GE and GA assessment, and is more capable of evaluating physiological characteristics encompassing both secretion and air in the stomach (24). Moreover, gastric motility can be estimated visually and quantitatively by MRI at the same time (6, 25).

In our study, $T_{1/2}$, GE, GA, and GMI were compared between patients with and without dyspeptic symptoms including early satiety, epigastric pain, and dyspepsia. The $T_{1/2}$ of GCV and TGV in PD patients were prolonged compared with those of healthy volunteers in previous studies using MRI (21) and gastroscintigraphy (26). This corresponds with several previous studies showing impaired gastric emptying in PD patients (6, 27). Fauehauf et al. (28) demonstrated that there is a correlation between GCV estimated by MRI and fullness in healthy controls and patients with functional dyspepsia. These findings may suggest that retention of the gastric contents in the stomach could be one of the causes of dyspeptic symptoms such as fullness and epigastric discomfort. In accordance with previous studies, PD patients with early satiety showed delayed GE, prolonged $T_{1/2}$, and decreased GMI compared to patients without the symptom in our study. To the

best of our knowledge, this is the first study to correlate dyspeptic symptoms and gastric MRI measurements in PD patients.

On the other hand, there was no statistically significant difference of gastric measurements between PD patients with and without epigastric pain, except for the overall trend of decreased GE of GCV. This could be attributed to the pathophysiology of delayed gastric emptying in PD patients. Although it is not clearly understood, the neuronal and hormonal abnormalities in PD are due to alpha-synuclein deposition in central (dorsal motor nucleus of the vagus nerve) and enteric nervous system. In PD patients, the stomach is one of the primary sites of alphasynuclein deposition (29). Therefore, decreased motility of the stomach or gastroparesis, rather than gastric outlet obstruction or stenosis, may be accompanied by early satiety, rather than epigastric pain. This is in keeping with a previous study reporting higher prevalence of bloating and nausea than abdominal pain in PD patients (30).

There is scarce data on the optimal timing to notice a significant difference by gastric imaging to reflect gastric dysfunction. The difference of various MRI measurements between the groups was prominent after 90 minutes in this study. This is in line with a previous study which reported a gastric half emptying time of PD patients with delayed gastric emptying to be 89.5 minutes on liquid meal gastric scintigraphy (23). We also observed a trend of increasing GMI until 90 minutes after ingestion. Although there is no such study measuring GMI timely by MRI, it is consistent with a previous study showing maximal gastric emptying rate at 119 minutes after ingestion of liquid meal containing $^{13}$C-glycine (31). Based on our

results and previous studies, it may be necessary to obtain images until at least 90 minutes after ingestion of test meal to observe a significant difference in future studies assessing impaired gastric function of PD patients.

In terms of MRI volumetry, GCV seems to be better correlated with dyspeptic symptoms than TGV in PD patients. This finding may be owing to the technical difficulty in measuring the air volume due to susceptibility artifacts on MR images. In addition, the relative amount of air ingested in each patient showed great variability compared to the gastric content in our study, with coefficient of variance between 0.6 and 1.3, which also may dilute the potentially significant differences between certain groups.

As GMI at 90 minutes was the only significant imaging feature for dyspepsia on multivariable analysis, future studies on imaging assessment of gastric motility should include similar motility indices to overcome the simplicity of volumetry alone and offer more comprehensive information. Although we have adopted a rather plain measurement of gastric peristaltic waves, more sophisticated techniques such as motility mapping or gastrointestinal tagging may be of value and provide promising results for evaluating dyspepsia (32).

When assessing bowel motility by imaging, it is crucial to control the clinical factors which might influence the motility. According to previous studies (26, 33), UPDRS is one of the confounding factors in evaluation of gastric emptying of PD patients, unlike age, sex, and BMI. However, in this study, there was no statistically significant difference of UPDRS among all of the compared groups. Although there is a possibility that levodopa medication in our patients had various

effects on UPDRS and gastric motor function, the number of patients in our study might have been too small to have sufficient statistical power as it was originally designed to show the non-inferiority of a new prokinetic drug (17).

There are several limitations in this study. First, the sample size in this retrospective study was predetermined for a prospective clinical trial with a different study purpose. The numbers of patients in each symptom group might not be optimal to show a statistically significant difference by MRI volumetry or motility indices. A total of 36 patients were required for the prospective clinical trial from a priori power analysis with a non-inferiority limit of -10%, based on a previous study reporting the standard deviation of GE rate at 120 minutes to be 10% in healthy subjects (21). Nonetheless, as the significant differences in GE of GCV in certain comparison groups exceed 10%, our results can still provide valuable information. Moreover, we were able to show a general trend of decreased GE or GMI in symptomatic patients, especially with early satiety. In addition, our study included more patients than previous reports on gastric motility (6, 15, 16, 21, 25). A future prospective study with a larger number of patients may be warranted. Secondly, fluid meal was used for evaluating gastric volume. Although it is not a routine meal for patients, it is convenient for ingestion and enables better visualization with less susceptibility artifacts on MRI. Many studies showed that it is feasible to evaluate gastric function with MRI using a liquid meal (21, 23, 34–36) or a semi-solid meal such as pudding or scrambled egg with water (6, 25). Gastric emptying measured by gastric scintigraphy is generally known to be delayed for solid meals compared to liquid meals (37). Therefore, the usage of a solid test meal might have resulted in

fewer numbers of significant MRI-derived parameters obtained within 120 minutes after ingestion. Accordingly, our results should be interpreted with attention. Thirdly, we were not able to compare the data between healthy volunteers and PD patients, which could have given important information to understand the pathophysiology of PD.

In conclusion, gastric motility can be quantitatively assessed by MRI, showing decreased GMI, delayed GE, and prolonged $T_{1/2}$ in PD patients with early satiety or dyspepsia. Therefore, MRI may become a comprehensive tool providing objective parameters for the evaluation of impaired gastric function in dyspeptic patients

# References

1. Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. J Neural Transm (Vienna) 2017;124(8):901-905.

2. Rodriguez-Violante M, Cervantes-Arriaga A, Villar-Velarde A, Corona T. Prevalence of non-motor dysfunction among Parkinson's disease patients from a tertiary referral center in Mexico City. Clin Neurol Neurosurg 2010;112(10):883-885.

3. Soykan I, Sivri B, Sarosiek I, Kiernan B, McCallum RW. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. Dig Dis Sci 1998;43(11):2398-2404.

4. Muller T, Erdmann C, Bremen D, Schmidt WE, Muhlack S, Woitalla D, Goetze O. Impact of gastric emptying on levodopa pharmacokinetics in Parkinson disease patients. Clin Neuropharmacol 2006;29(2):61-67.

5. Doi H, Sakakibara R, Sato M, Masaka T, Kishi M, Tateno A, Tateno F, Tsuyusaki Y, Takahashi O. Plasma levodopa peak delay and impaired gastric emptying in Parkinson's disease. J Neurol Sci 2012;319(1-2):86-88.

6. Unger MM, Hattemer K, Moller JC, Schmittinger K, Mankel K, Eggert K, Strauch K, Tebbe JJ, Keil B, Oertel WH, Heverhagen JT, Knake S. Real-time visualization of altered gastric motility by magnetic resonance imaging in patients with Parkinson's disease. Mov Disord 2010;25(5):623-628.

7. Tanaka Y, Kato T, Nishida H, Yamada M, Koumura A, Sakurai T, Hayashi Y, Kimura A, Hozumi I, Araki H, Murase M, Nagaki M, Moriwaki H, Inuzuka T. Is there a delayed gastric emptying of patients with early-stage, untreated Parkinson's

disease? An analysis using the $^{13}$C-acetate breath test. J Neurol 2011;258(3):421-426.

8. Feinle C, Kunz P, Boesiger P, Fried M, Schwizer W. Scintigraphic validation of a magnetic resonance imaging method. Gut 1999;44(1):106-111.

9. Boeckxstaens GE, Hirsch DP, van den Elzen BD, Heisterkamp SH, Tytgat GN. Impaired drinking capacity in patients with functional dyspepsia: relationship with proximal stomach function. Gastroenterology 2001;121(5):1054-1063.

10. Gilja OH, Hausken T, Wilhelmsen I, Berstad A. Impaired accommodation of proximal stomach to a meal in functional dyspepsia. Dig Dis Sci 1996;41(4):689-696.

11. Bredenoord AJ, Chial HJ, Camilleri M, Mullan BP, Murray JA. Gastric accommodation and emptying in evaluation of patients with upper gastrointestinal symptoms. Clin Gastroenterol Hepatol 2003;1(4):264-272.

12. de Zwart IM, Haans JJ, Verbeek P, Eilers PH, de Roos A, Masclee AA. Gastric accommodation and motility are influenced by the barostat device: Assessment with magnetic resonance imaging. Am J Physiol Gastrointest Liver Physiol 2007;292(1):G208-214.

13. Undeland KA, Hausken T, Aanderud S, Berstad A. Lower postprandial gastric volume response in diabetic patients with vagal neuropathy. Neurogastroenterol Motil 1997;9(1):19-24.

14. Bouras EP, Delgado-Aros S, Camilleri M, Castillo EJ, Burton DD, Thomforde GM, Chial HJ. SPECT imaging of the stomach: comparison with barostat, and effects of sex, age, body mass index, and fundoplication. Gut 2002;51(6):781-786.

15. de Zwart IM, Mearadji B, Lamb HJ, Eilers PH, Masclee AA, de Roos A, Kunz P.

Gastric motility: comparison of assessment with real-time MR imaging or barostat measurement initial experience. Radiology 2002;224(2):592-597.

16. Borovicka J, Lehmann R, Kunz P, Fraser R, Kreiss C, Crelier G, Boesiger P, Spinas GA, Fried M, Schwizer W. Evaluation of gastric emptying and motility in diabetic gastroparesis with magnetic resonance imaging: effects of cisapride. Am J Gastroenterol 1999;94(10):2866-2873.

17. Shin CM, Lee YJ, Kim JM, Lee JY, Kim KJ, Choi YJ, Kim N, Lee DH. DA-9701 on gastric motility in patients with Parkinson's disease: A randomized controlled trial. Parkinsonism Relat Disord 2018.

18. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55(3):181-184.

19. Fahn S ER, UPDRS program members. Unified Parkinsons Disease Rating Scale. In: Fahn S, Marsden CD, Goldstein M, Calne DB, ed. Recent developments in Parkinson’s disease, vol 2. 1st ed. Florham Park, NJ. Macmillan Healthcare Information 1987; 153–163.

20. Park H, Lee JY, Shin CM, Kim JM, Kim TJ, Kim JW. Characterization of gastrointestinal disorders in patients with parkinsonian syndromes. Parkinsonism Relat Disord 2015;21(5):455-460.

21. Min YW, Min BH, Kim S, Choi D, Rhee PL. Effect of DA-9701 on Gastric Motor Function Assessed by Magnetic Resonance Imaging in Healthy Volunteers: A Randomized, Double-Blind, Placebo-Controlled Trial. PloS one 2015;10(9):e0138927.

22. Elashoff JD, Reedy TJ, Meyer JH. Analysis of gastric emptying data. Gastroenterology 1982;83(6):1306-1312.

23. Hoad CL, Parker H, Hudders N, Costigan C, Cox EF, Perkins AC, Blackshaw PE, Marciani L, Spiller RC, Fox MR, Gowland PA. Measurement of gastric meal and secretion volumes using magnetic resonance imaging. Phys Med Biol 2015;60(3):1367-1383.

24. Marrinan S, Emmanuel AV, Burn DJ. Delayed gastric emptying in Parkinson's disease. Mov Disord 2014;29(1):23-32.

25. Carbone SF, Tanganelli I, Capodivento S, Ricci V, Volterrani L. Magnetic resonance imaging in the evaluation of the gastric emptying and antral motion: feasibility and reproducibility of a fast not invasive technique. Eur J Radiol 2010;75(2):212-214.

26. Hellmig S, Von Schoning F, Gadow C, Katsoulis S, Hedderich J, Folsch UR, Stuber E. Gastric emptying time of fluids and solids in healthy subjects determined by $^{13}C$ breath tests: influence of age, sex and body mass index. J Gastroenterol Hepatol 2006;21(12):1832-1838.

27. Heetun ZS, Quigley EM. Gastroparesis and Parkinson's disease: a systematic review. Parkinsonism Relat Disord 2012;18(5):433-440.

28. Fruehauf H, Steingoetter A, Fox MR, Kwiatek MA, Boesiger P, Schwizer W, Fried M, Thumshirn M, Goetze O. Characterization of gastric volume responses and liquid emptying in functional dyspepsia and health by MRI or barostat and simultaneous C-acetate breath test. Neurogastroenterol Motil 2009;21(7):697-e637.

29. Braak H, de Vos RA, Bohl J, Del Tredici K. Gastric alpha-synuclein

immunoreactive inclusions in Meissner's and Auerbach's plexuses in cases staged for Parkinson's disease-related brain pathology. Neurosci Lett 2006;396(1):67-72.

30. Edwards LL, Pfeiffer RF, Quigley EM, Hofman R, Balluff M. Gastrointestinal symptoms in Parkinson's disease. Mov Disord 1991;6(2):151-156.

31. Achour L, Meance S, Briend A. Comparison of gastric emptying of a solid and a liquid nutritional rehabilitation food. Eur J Clin Nutr 2001;55(9):769-772.

32. de Jonge CS, Smout A, Nederveen AJ, Stoker J. Evaluation of gastrointestinal motility with MRI: Advances, challenges and opportunities. Neurogastroenterol Motil 2018;30(1)

33. Goetze O, Nikodem AB, Wiezcorek J, Banasch M, Przuntek H, Mueller T, Schmidt WE, Woitalla D. Predictors of gastric emptying in Parkinson's disease. Neurogastroenterol Motil 2006;18(5):369-375.

34. Fruehauf H, Menne D, Kwiatek MA, Forras-Kaufman Z, Kaufman E, Goetze O, Fried M, Schwizer W, Fox M. Inter-observer reproducibility and analysis of gastric volume measurements and gastric emptying assessed with magnetic resonance imaging. Neurogastroenterol Motil 2011;23(9):854-861.

35. Teramoto H, Shimizu T, Yogo H, Nishimiya Y, Hori S, Kosugi T, Nakayama S. Assessment of gastric emptying and duodenal motility upon ingestion of a liquid meal using rapid magnetic resonance imaging. Exp Physiol 2012;97(4):516-524.

36. Bickelhaupt S, Froehlich JM, Cattin R, Raible S, Bouquet H, Bill U, Patak MA. Software-supported evaluation of gastric motility in MRI: a feasibility study. J Med Imaging Radiat Oncol 2014;58(1):11-17.

37. Bredenoord AJ. Diagnostic Techniques. In: Bredenoord AJ, Smout A, Tack J, ed.

A Guide to Gastrointestinal Motility Disorders. 1st ed. Switzerland. Springer International Publishing. 2016; 21–28

**Table 1. MR Imaging Parameters**

| **Sequence** | **3D FS T1-weighted GRE** | | **3D b-TFE** | | | |
|---|---|---|---|---|---|---|
| **Scan plane** | **Axial** | | **Oblique sagittal** | | **Oblique coronal** | |
| **Tesla** | 3 T | 1.5 T | 3 T | 1.5 T | 3 T | 1.5 T |
| **TR (ms)** | 4.2 | 4.05 | 2.16 | 3.4 | 2.16 | 3.36 |
| **TE (ms)** | 1.45 | 1.96 | 1.08 | 1.7 | 1.08 | 1.68 |
| **FOV (mm)** | 320×320 | 315×350 | 400×400 | 272×340 | 400×400 | 360×360 |
| **Matrix** | 280×212 | 160×112 | 200×200 | 224×224 | 200×200 | 224×179 |
| **ST (mm)** | 5 | 5 | 10 | 10 | 10 | 10 |
| **SI (mm)** | 2.5 | 2.5 | 10 | 10 | 10 | 10 |
| **Sense factor** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Acquisition time** | 10 seconds within one breath hold | | 3 minutes with free breathing, 1 second per image (30 images of 5 second intervals at 5 consecutive planes) | | | |

Note-FS, fat-suppressed, GRE, gradient echo, b-TFE, balanced-turbo field echo, TR, repetition time, TE, echo time, FOV, field-of-view, ST, slice thickness, SI, slice interval

**Table 2. Patient demographics**

| Characteristic | Value |
|---|---|
| Age (years) | 69 (64–72) |
| Male | 70 (66–73) |
| Female | 68 (58–72) |
| Gender | |
| Male (%) | 20 (53) |
| Female (%) | 18 (47) |
| BMI (mean ± SD, kg/m2) | 23.1 ± 3.0 |
| UPDRS (mean ± SD) | 22.3 ± 9.1 |
| Disease duration (mean ± SD, months) | 62.5 ± 45.6 |
| LEDD (mean ± SD, mg/day) | 635.5 ± 404.6 |
| Duration with levodopa (mean ± SD, months) | 49.8 ± 44.9 |
| Patients with dyspeptic symptom (%) | 28 (74) |
| Early satiety (%) | 25 (66) |
| Epigastric pain (%) | 13 (34) |
| MRI scanner | |
| 1.5-T (%) | 7 (18) |
| 3.0-T (%) | 31 (82) |

Note—Age is presented as median value with interquartile range in parentheses. BMI, body mass index, UPDRS, unified Parkinson's disease rating scale, LEDD, levodopa equivalent daily dose, SD, standard deviation

**Table 3. Comparison of gastric motility index in patients with or without dyspepsia**

| | Dyspepsia (+) | Dyspepsia (-) | *p*-value |
|---|---|---|---|
| **15 minutes** | 5.0 ± 2.1 | 6.8 ± 3.3 | 0.112 |
| **30 minutes** | 5.1 ± 2.3 | 6.8 ± 3.3 | 0.095 |
| **60 minutes** | 8.1 ± 3.8 | 10.2 ± 6.3 | 0.216 |
| **90 minutes** | 13.1 ± 4.4 | 19.3 ± 6.6 | 0.002 |
| **RM-ANOVA*** | | | 0.029 |

Note–Except for P-value, data are presented as mean ± standard deviation.
*Results of repeated measures ANOVA

**Table 4. Comparison of gastric accommodation and half emptying time**

| | Gastric accommodation | | | Gastric half emptying time | | |
|---|---|---|---|---|---|---|
| | **Symptom (+)** | **Symptom (-)** | ***p*-value** | **Symptom (+)** | **Symptom (-)** | ***p*-value** |
| **Gastric content volume** | | | | | | |
| **Early satiety** | 101.67 ± 154.84 | 76.41 ± 85.54 | 0.88 | 145.98 ± 96.65 | 83.96 ± 32.18 | 0.004 |
| **Epigastric pain** | 57.00 ± 81.39 | 111.77 ± 153.23 | 0.25 | 165.98 ± 125.57 | 103.33 ± 44.14 | 0.041 |
| **Dyspepsia** | 94.60 ± 147.56 | 88.64 ± 94.59 | 0.91 | 139.22 ± 93.48 | 84.28 ± 35.52 | 0.023 |
| **Total gastric volume** | | | | | | |
| **Early satiety** | 18.86 ± 18.77 | 22.09 ± 18.43 | 0.45 | 118.61 ± 78.69 | 63.70 ± 33.15 | 0.023 |
| **Epigastric pain** | 18.33 ± 18.88 | 20.81 ± 18.59 | 0.43 | 119.05 ± 69.72 | 97.63 ± 50.80 | 0.26 |
| **Dyspepsia** | 19.81 ± 20.56 | 20.41 ± 11.57 | 0.26 | 139.22 ± 93.48 | 113.26 ± 62.31 | 0.14 |

Note–Except for *p*-value, data are presented as mean ± standard deviation.

**Figure 1. Flow diagram of enrolled patients.** The analyzed patients were divided into three groups according to the presence of gastric symptoms: early satiety (n = 25), epigastric pain (n = 13), and dyspepsia (n = 28)

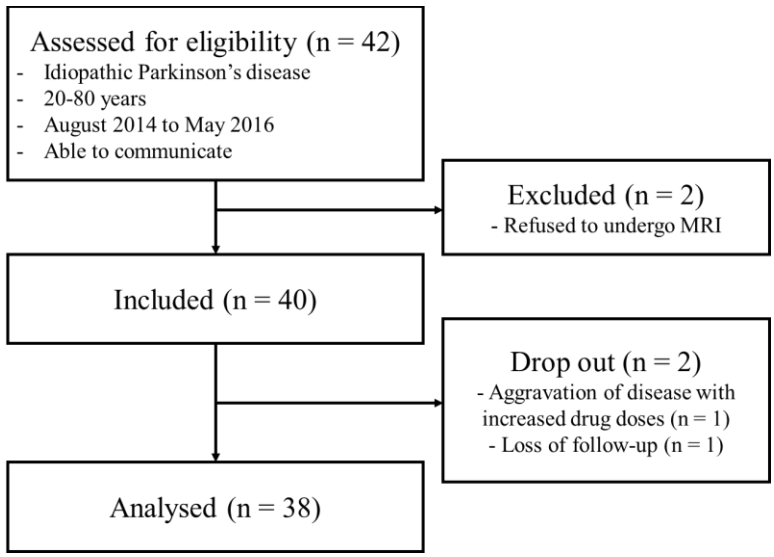


**Figure 2. Timetable for obtaining MR images.** MR images with axial 3D fat-suppressed T1-weighted gradient echo (GRE) sequence and oblique sagittal 3D balanced-turbo field echo (b-TFE) sequence were obtained before and after meal until 120 minutes. Oblique coronal 3D b-TFE sequence was also used from 30 minutes after meal. TGV, total gastric volume, GCV, gastric content volume, GMI, gastric motility index

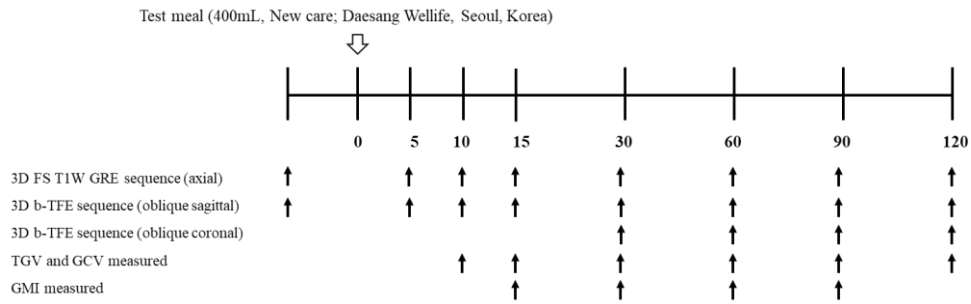


**Figure 3. Gastric volume measurement of a 68-year-old man with Parkinson's disease.** In axial T1-weighted image, regions of interest (ROI) of gastric contents and air were drawn by a radiologist with volume analysis software. The volume of ROI was calculated automatically. TGV, total gastric volume, GCV, gastric content volume

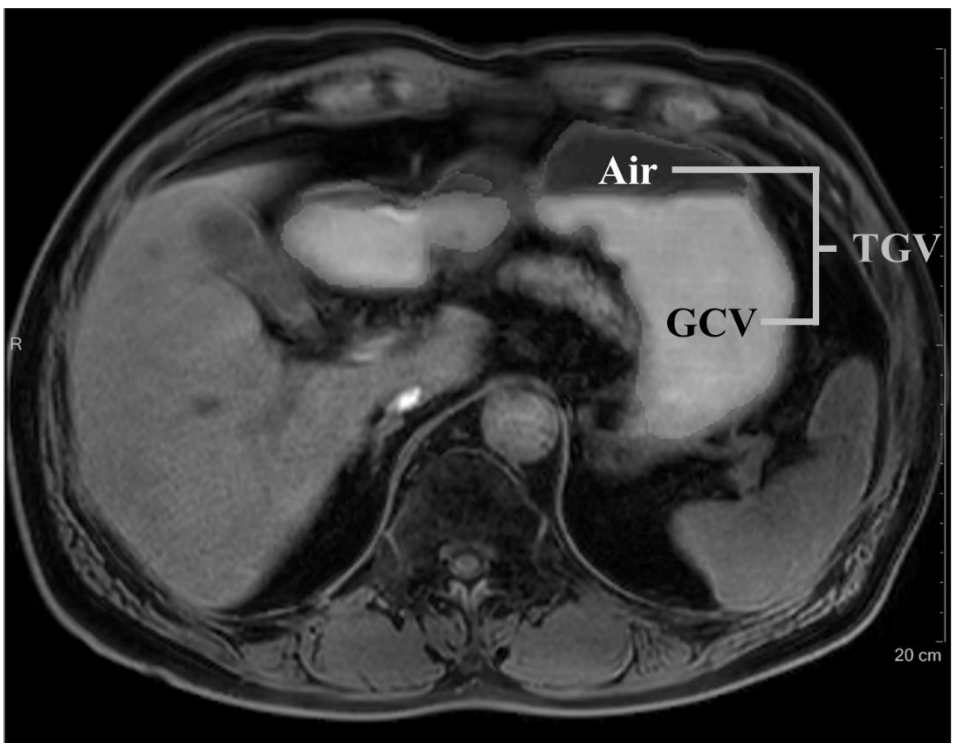


**Figure 4. Measurements for calculating gastric motility index of a 68-year-old man with Parkinson's disease.** Wavelength (X, straight arrow) and amplitude (d, curved arrow) of gastric peristaltic waves were measured in the 3D balanced-turbo field echo MR image. Number of waves (not shown in this image) was also obtained from the same sequence. Gastric motility index was calculated based on these measurements

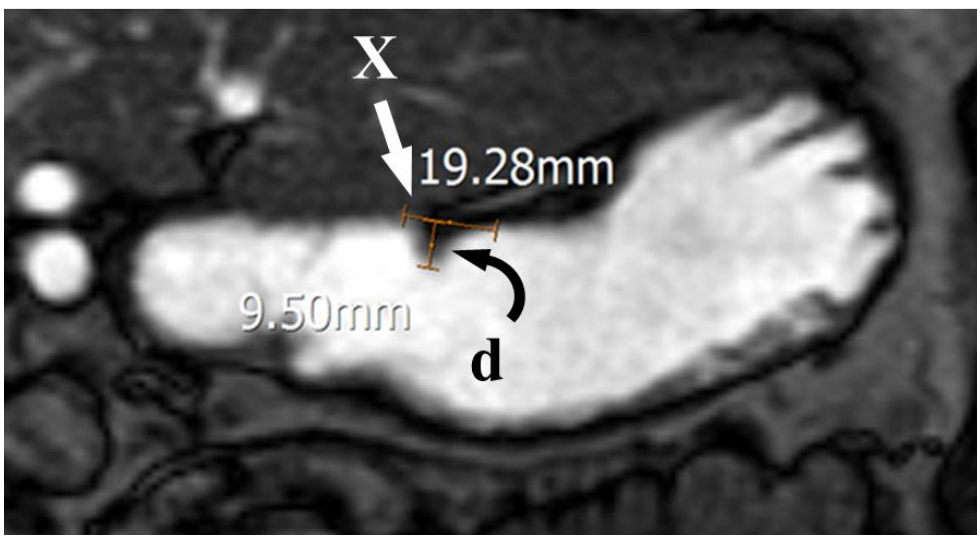
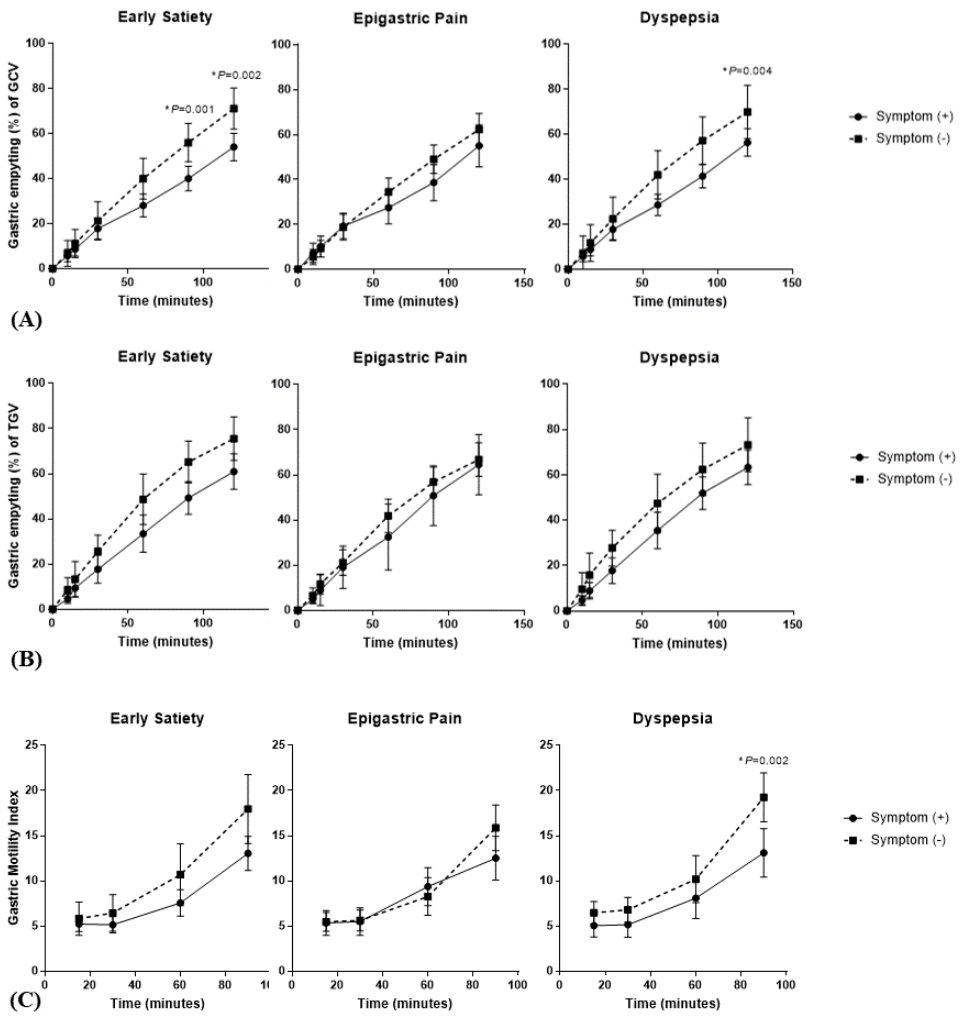


**Figure 5. Line graphs of gastric emptying and gastric motility index in patients with each symptom.** A. Gastric emptying of gastric content volume B. Gastric emptying of total gastric volume C. Gastric motility index, GCV, gastric content volume, TGV, total gastric volume, repeated measures ANOVA was used for comparison between patients with and without dyspeptic symptoms and post hoc analysis was done using independent t-test with Bonferroni correction.



**Supplemental Table 1. Comparison of clinical features between patients with and without symptoms**

| | Early satiety | | | Epigastric Pain | | | Dyspepsia | | |
|---|---|---|---|---|---|---|---|---|---|
| | (+) | (-) | *p*-value | (+) | (-) | *p*-value | (+) | (-) | *p*-value |
| **Age (years)** | 67 ± 7 | 69 ± 7 | 0.40 | 66 ± 6 | 68 ± 7 | 0.37 | 67 ± 7 | 69 ± 7 | 0.28 |
| **BMI (kg/m2)** | 23.4 ± 3.0 | 22.7 ± 2.9 | 0.54 | 23.2 ± 3.8 | 23.1 ± 2.5 | 0.95 | 23.2 ± 3.2 | 22.9 ± 2.5 | 0.80 |
| **UPDRS** | 21.8 ± 10.1 | 23.3 ± 7.0 | 0.63 | 23.4 ± 11.7 | 21.5 ± 7.5 | 0.47 | 21.6 ± 10.1 | 24.2 ± 5.1 | 0.32 |
| **Disease duration (months)** | 65 ± 51 | 48 ± 25 | 0.18 | 57 ± 36 | 60 ± 49 | 0.83 | 63 ± 49 | 49 ± 26 | 0.40 |
| **LEDD (mg/day)** | 666 ± 469 | 577 ± 243 | 0.53 | 721 ± 573 | 591 ± 287 | 0.45 | 646 ± 457 | 605 ± 212 | 0.78 |
| **Duration with levodopa (months)** | 54 ± 49 | 34 ± 28 | 0.12 | 45 ± 36 | 49 ± 47 | 0.80 | 52 ± 48 | 35 ± 27 | 0.31 |

Note—Data are mean ± standard deviation (SD). BMI, body mass index. UPDRS, unified Parkinson's disease rating scale. LEDD, levodopa equivalent daily dose.

**Supplemental Table 2. Comparison of clinical features between patients with and without symptoms**

| | Early Satiety | | | | | |
|---|---|---|---|---|---|---|
| | GE of GCV | | | GE of TGV | | |
| | **Symptom (+)** | **Symptom (-)** | ***p*-value** | **Symptom (+)** | **Symptom (-)** | ***p*-value** |
| **10 minutes** | 5.8 ± 6.6 | 6.7 ± 9.5 | 0.73 | 4.7 ± 5.1 | 8.6 ± 9.0 | 0.10 |
| **15 minutes** | 8.7 ± 7.4 | 11.2 ± 10.4 | 0.40 | 9.3 ± 9.6 | 13.3 ± 12.9 | 0.29 |
| **30 minutes** | 17.8 ± 11.5 | 21.2 ± 14.1 | 0.43 | 17.7 ± 14.9 | 25.6 ± 11.9 | 0.11 |
| **60 minutes** | 28.0 ± 12.2 | 40.0 ± 15.0 | 0.01 | 33.4 ± 19.9 | 48.6 ± 18.5 | 0.03 |
| **90 minutes** | 40.0 ± 13.2 | 56.0 ± 14.0 | 0.001 | 49.3 ± 17.6 | 65.2 ± 15.4 | 0.009 |
| **120 minutes** | 54.0 ± 14.8 | 71.1 ± 15.2 | 0.002 | 61.0 ± 19.2 | 75.6 ± 15.9 | 0.02 |
| **RM-ANOVA*** | | | < 0.001 | | | 0.02 |

Note-continued on the next page

| | Epigastric Pain | | | | Dyspepsia | | | |
|---|---|---|---|---|---|---|---|---|
| | GE of GCV | | | GE of TGV | GE of GCV | | | GE of TGV |
| | (+) | (-) | *p*-value | *p*-value | (+) | (-) | *p*-value | *p*-value |
| **10 minutes** | 7.3 ± 7.1 | 5.5 ± 7.9 | 0.50 | | 5.7 ± 6.3 | 7.2 ± 10.9 | 0.60 | |
| **15 minutes** | 10.2 ± 7.7 | 9.2 ± 9.0 | 0.74 | | 8.8 ± 7.3 | 11.7 ± 11.3 | 0.36 | |
| **30 minutes** | 19.3 ± 9.5 | 18.8 ± 13.9 | 0.91 | | 17.8 ± 12.0 | 22.4 ± 13.5 | 0.32 | |
| **60 minutes** | 27.5 ± 12.0 | 34.5 ± 15.0 | 0.15 | | 28.6 ± 12.4 | 41.9 ± 15.1 | 0.009 | |
| **90 minutes** | 38.7 ± 13.3 | 49.0 ± 15.4 | 0.05 | | 41.3 ± 13.4 | 57.1 ± 14.8 | 0.004 | |
| **120 minutes** | 55.1 ± 15.6 | 62.4 ± 17.3 | 0.21 | | 56.3 ± 15.8 | 69.9 ± 16.6 | 0.03 | |
| **RM-ANOVA*** | | | 0.03 | 0.34 | | | 0.001 | 0.58 |

Note–Except for *p*-value, data are mean ± standard deviation. GE, gastric emptying. GCV, gastric content volume. TGV, total gastric volume. *Results of repeated measures ANOVA.

**Supplemental Table 3. Results of generalized estimating equation**

| | Early Satiety *p*-value | Dyspepsia *p*-value |
|---|---|---|
| **GE of GCV at 90 min** | 0.89 | 0.34 |
| **$T_{1/2}$ of GCV** | 0.10 | 0.18 |
| **GMI at 90 min** | - | 0.03 |

Note–GE, gastric emptying, T1/2, half emptying time, GCV, gastric content volume, GMI, gastric motility index

# 논 문 초 록

**목적:** 파킨슨 병 환자에서 위 자기공명영상을 촬영 후, 정량적 지표들을 구하고, 이를 소화기계 증상과의 연관성을 평가하고자 한다.

**대상 및 방법:** 2014 년 8 월부터 2016 년 5 월까지 38 명의 파킨슨병 환자가, 400 mL 의 유동식을 먹고, 120 분 정도 소요되는 위 자기공명영상(MRI)을 촬영하였다. 이 영상의 각 시간에서 위 내용물 부피와 위 전체 부피를 측정하였고, 이를 이용하여, 시간에 따른 식후 위 적응 및 위 배출능, 그리고 위 내용물의 배출 반감기를 구하였다. 또한 영화 자기공명영상 기법(Cine MRI)을 확인하여, 위벽의 연동 운동에서 파장, 파고, 지나간 파의 수 등을 측정하여 위 운동성 지표(Gastric motility index)를 얻었다. 파킨슨 병 환자들은 unified Parkinson's disease rating scale (UPDRS) 및 소화기계 증상 일기 작성 등을 통해, 식사 중 이른 포만감 및 식후 명치부위 통증 등의 소화기계 증상의 유무를 보고하였고, 둘 중 하나라도 증상이 있는 사람은 소화불량이 있다고 정의하였다. 이를 통해, 소화기계 증상과 식후 위 적응, 위 배출능, 위 내용물의 반감기, 그리고 위 운동성 지표 간의 관계를 확인하였다.

**결과:** 파킨슨 병 환자 중 식사 중 이른 포만감 및 식후 명치부위 통증을 호소한 환자는 각각 25, 13 명이었고, 둘 중 하나라도 갖고 있는 사람은 28 명 이었다. 식사 중 이른 포만감을 보인 환자는 위 내용물 및 위 전체의 위 배출능이 감소되어 있었다($p < 0.001$ 와 $p = 0.017$). 소화불량이 있는 환자는 위 내용물의 위 배출능 및 위 운동성 지표가 감소되어 있었다($p = 0.001$ 과 $p = 0.002$). 식사 중 이른 포만감을 가진 환자에서, 특히 90 분과 120 분에서의 위 내용물의 위 배출능이 감소하여 있었고($p = 0.001$ 와 $p = 0.002$), 소화불량 환자에서는 90 분에서의 위 내용물의 위 배출능과 위 운동성 지표가 감소되어

있었다($p$ = 0.004 와 $p$ = 0.002). 위 내용물의 배출 반감기는 식사 중 이른 포만감 및 식후 명치부위 통증, 소화불량이 있는 환자에게서 모두 연장되어 있었다($p$ = 0.004, $p$ = 0.041, 그리고 $p$ = 0.023). 위 전체의 배출 반감기는 식사 중 이른 포만감을 보인 환자에게서 연장되어 있었다 ($p$ = 0.023). 다변량 분석에서는 90 분에서의 위 운동성지표가 소화불량과 연관이 있었다 ($p$ = 0.028).

**결론:** 식사 중 이른 포만감이나 소화불량이 있는 파킨슨 병 환자에게서 위 운동성 지표가 감소하였고, 위 배출이 지연되었으며, 위 배출의 반감기가 연장되었다. 상기 결과는 위의 운동성을 위 자기공명영상을 통해 정량적으로 분석이 가능함을 시사한다.

**주요어:** 위, 파킨슨 병, 자기공명영상, 위 배출, 소화불량
**학번:** 2019-37318