J Neurogastroenterol Motil, Vol. 28 No. 3 July, 2022
pISSN: 2093-0879 eISSN: 2093-0887
https://doi.org/10.5056/jnm22074
Journal of Neurogastroenterology and Motility

Editorial

Role of Nutrient Drinking Test in Functional Dyspepsia

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Article: Efficacy of slow nutrient drinking test for evaluating postprandial distress symptom in Japanese patients with functional dyspepsia
Watanabe T, Masaoka T, Kameyama H, Kanai T
(J Neurogastroenterol Motil 2022;28:424-430)

Functional dyspepsia (FD) is common prevalent. At least 1 in 10 people suffers from FD.[1,2] To date, the pathophysiology of FD is not well understood. However, several mechanisms contributing to FD have been suggested. It can be distinguished from environmental, biological, psychologic, and physiological factors. Among these mechanisms, there are physiologic factor such as acid, gastric accommodation (GA), hypersensitivity to gastric distension, and delayed gastric emptying.[3] Considering these aspects, FD is probably a heterogeneous disorders of gastric sensorimotor function. Given the abnormality of the sensorimotor function, it is possible to develop physiologic test in FD, as high-resolution manometry is a golden standard diagnostic test of achalasia. The most common pathophysiological mechanism in FD is impaired GA, which appears in 40% of patients, with hypersensitivities to gastric distention in about one-third of patients and delayed gastric emptying in about 25% of patients.[4] In the case of FD, tests that diagnose or predict to treatment responses are insufficient. Slow nutrient drinking testing (NDT) in FD has been proposed as a potential biomarker for the presence and severity of gastric sensorimotor dysfunction.[5] In particular, NDT is a useful method to check for abnormalities in GA.

A slow NDT was the first test to report by Tack et al[6] in the literature, in a 1998 article evaluated the role of impaired GA in FD. After this, many NDT studies show the most consistent distinction between health person and FD patient, relevance with impaired GA and reproducibility. Most of the studies are from Western and Europe, and there are very few studies in Asia.[6-13] In this issue of *Journal of Neurogastroenterology and Motility*, Watanabe et al[14] reported efficacy of slow nutrient drinking test among patients with FD in Japan. NDT was applied to total 42 participants (26 healthy controls and 16 FD patients). The primary outcome is the ending time of the NDT, which help to distinguish Japanese patients with FD from healthy controls. The test ending time was significantly shorter in patients with FD than in healthy controls (22.3 ± 10.6 vs 45.0 ± 7.5 minutes, respectively; $P < 0.001$, Fig. 1A and 1B). The optimal cut-off time differentiated patients with FD from healthy controls was 30 minutes. At the cutoff time, the area under the curve was 0.91 with 87.5% sensitivity and 92.3 specificity (Fig. 2). This result is those that have already been proven in previous studies. Interestingly, in this study, FD patients were classified into epigastric pain syndrome (EPS), postprandial distress syndrome (PDS), and both mixed groups, and each patient group was 3, 6, and 7, respectively. The difference in the severity of meal-related

Received: May 21, 2022 Revised: June 14, 2022 Accepted: June 21, 2022

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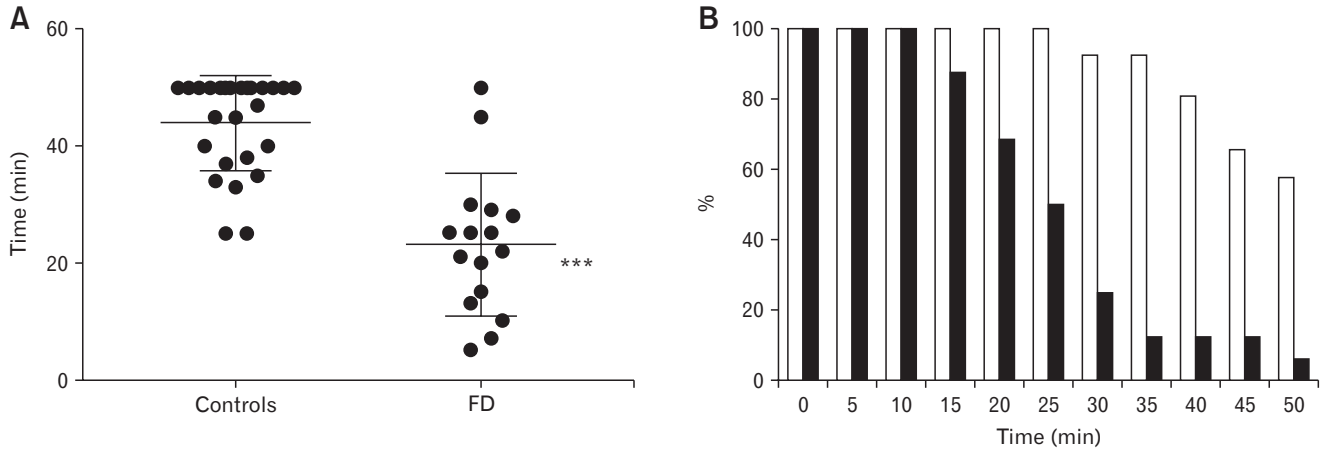

Figure 1. The test ending time. (A) Scatter diagrams of the test ending time. (B) Rate of participants who passed each time point in both groups. Open columns indicate the group of healthy participants. Closed columns indicate the group of patients with functional dyspepsia (FD). Adapted from Watanabe et al.[14] ***$P < 0.001$.

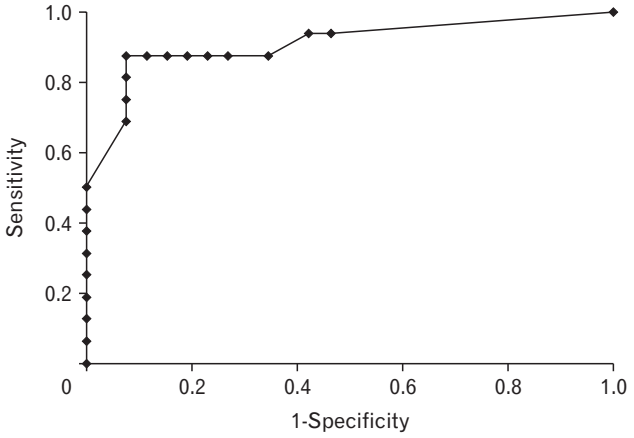

Figure 2. Receiver operating characteristic curve in the test ending time. Adapted from Watanabe et al.[14]

symptoms (eg, hunger, expected amount to eat, and satiation) and abdominal symptoms (eg, bloating, postprandial fullness, nausea, belching, and epigastric pain) appeared from the beginning of the examination (Fig. 3 and 4). The difference in the severity of meal-related symptoms and abdominal symptoms between the 2 groups was consistently greater in patients with FD than in the healthy participants. Although univariate analysis emphasizes a stronger association with PDS symptoms, especially early satiation, than EPS symptoms (OR, 104.00 vs 7.00; Table), it seems difficult to find statistical significance in numbers that are too small enough to make multivariate analysis impossible. It is difficult to say that this difference alone suggests the possibility that NDT can be more useful for evaluating PDS symptoms. It has already been known that impaired GA, delayed gastric emptying, and visceral hypersensitivity after meals are already involved in both EPS and PDS. It can also appear in the form of overlapping syndrome with EPS and PDS at the same time.[15] This study once again demonstrated the usefulness of NDT in distinguishing between healthy people and patients with FD, and the ending time of the NDT as a reference value for clinical applications in the future.

However, this study has several limitations. It was a single and tertiary center study. First, although using the calculated required sample size from previous study, sample size is too small. More FD patients are needed for multivariate analysis to identify the presence of PDS symptoms as a significant factor for shortening the test time. Second, many of the referred patients were refractory and more severe symptoms. Multicenter studies including general clinics or hospitals and patients with mild FD symptoms are required to determine the efficacy of NDT in evaluating FD symptoms.

Results of NDT studies were similar in Western and Asia.[6-13] NDT is easy-to-performing technique that measures the amount of nutrient solution that can be taken before feeling full or uncomfortable. A NDT is a simple non-invasive and reproducible method proven to quantify meal-induced satiety and gastric accommodation. It can be used to evaluate impaired accommodation and early satiety. Biomarker are indicator of physiological/pathological states that can be objectively estimated to detect differences between groups and therapeutic effects. NDT showed sufficient possibility as a potential biomarker for the presence and severity of gastric sensorimotor dysfunction.[5] However, this test is a time- and labor-consuming test, and in order to be actually used in clinical practice in the future, it needs to be simplified with standardized methods, and objective reference variables must be developed. NDT reflects

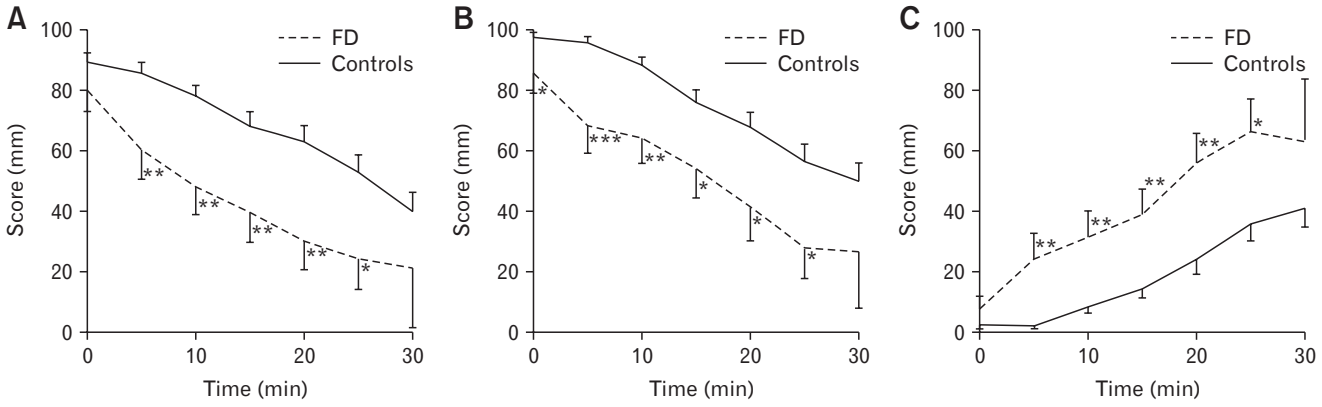

Figure 3. Severity of meal-related symptoms ([A] hunger, [B] expected amount to eat, and [C]satiation) during the test assessed using the visual analog scale. FD, patients with functional dyspepsia. Adapted from Watanabe et al.[14] *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

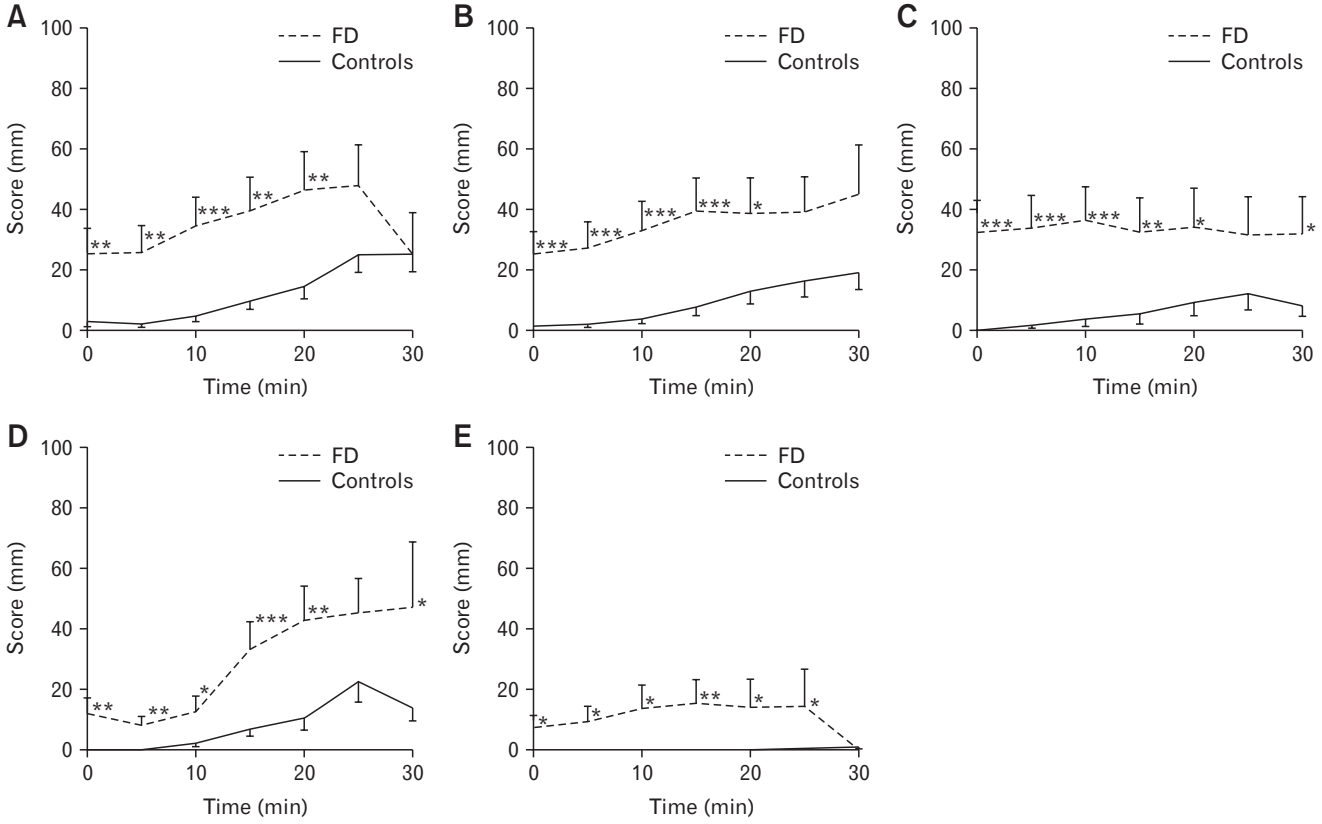

Figure 4. Severity of abdominal symptoms ([A] bloating, [B] postprandial fullness, [C] nausea, [D] belching, and [E] epigastric pain) during the test assessed using the visual analog scale. FD, patients with functional dyspepsia. Adapted from Watanabe et al.[14] *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

only part of a heterogeneous pathophysiology of FD. Therefore, NDT cannot be generalized test for all FD patients.

Financial support: None.

Conflicts of interest: None.

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Table. Univariate Analysis to Detect Contributing Factors to the Test End Time Below the Cutoff Time (Adapted From Watanabe et al[14])

Factors	Univariate analysis		
	OR	95% CI	*P*-value
Age	0.75	0.43-1.30	0.304
Sex	0.37	0.10-1.36	0.135
BMI	16.53	1.14-240.25	0.040
HADS-A	0.82	0.69-0.97	0.019
HADS-D	0.89	0.76-1.03	0.110
GERDQ	0.84	0.63-1.13	0.254
Presence of EPS symptoms	7.00	1.45-33.70	0.015
Presence of PDS symptoms	104.00	9.78-1106.18	< 0.001

BMI, body mass index; HADS-A, Hospital Anxiety and Depression Scale; HADS-D, Hospital Anxiety and Depression Scale; GERDQ, Gastroesophageal Reflux Disease Questionnaire; EPS, epigastric pain syndrome; PDS, postprandial distress syndrome.

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