

## Clinical Features of Both Functional Dyspepsia and Gastroparesis

To clarify the pathophysiology of functional dyspepsia (FD) and its relationship with the better understood syndrome of gastroparesis. Adult patients with chronic upper gastrointestinal symptoms were followed up prospectively for 48 weeks in multi-center registry studies. Patients were classified as having gastroparesis if gastric emptying was delayed; if not, they were labeled as having FD if they met Rome III criteria. Study analysis was conducted using analysis of covariance and regression models.

A total of 944 patients were enrolled during a 12-year period; 720 (76%) were in a gastroparesis group and 224 (24%) were in the FD group. Baseline clinical characteristics and severity of upper gastrointestinal symptoms were highly similar. The 48-week clinical outcome was also similar, but at this time, 42% of patients with an initial diagnosis of gastroparesis were reclassified as FD, based on gastric emptying results at this time point. Conversely, 37% of patients with FD were reclassified as having gastroparesis. Change in either direction was not associated with any difference in symptom severity changes. Full-thickness biopsies of the stomach showed loss of interstitial cells of Cajal and CD-206 macrophages in both groups, compared with obese controls.

It was concluded a year after initial classification, patients with FD and gastroparesis as seen in tertiary referral centers at least, are not distinguishable based on clinical and pathologic features, or based on assessment of gastric emptying. Gastric-emptying results are labile and do not reliably capture the pathophysiology of clinical symptoms in either condition. FD and gastroparesis are unified by characteristic pathologic features and should be considered as part of the same spectrum of truly “organic” gastric neuromuscular disorders.

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Pasricha, P., Grover, M., Yates, K., et al for the National Institute of Diabetes and Digestive and Kidney Diseases/National Institute of Health Gastroparesis Clinical Research Consortium. “Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features.” *Gastroenterology* 2021; Vol. 160, pp. 2006-2017.

## Refractory Reflux Symptoms: A Guide for Discontinuation of PPI Treatment

A proportion of patients with gastroesophageal reflux symptoms are refractory to PPI therapy. In order to develop a diagnostic approach to identify candidates appropriate for PPI cessation and to examine the clinical utility of prolonged wireless reflux monitoring to predict the ability to discontinue PPIs, a double-blinded, clinical trial performed over 3 years at 2 centers was carried out.

Adults were enrolled with troublesome esophageal symptoms of heartburn, regurgitation, and/or chest pain and inadequate PPI response. Participants underwent prolonged wireless reflux monitoring (off PPIs for greater than 7 days), and a 3-week PPI cessation intervention. Primary outcome was tolerance of PPI cessation (discontinued or resumed PPIs). Symptom burden was quantified using the reflux symptom questionnaire, electronic diary (RESQ-eD).

Of 128 enrolled, 100 participants met inclusion criteria (mean age 48.6 years; 41 men, 34 participants, 34% discontinued PPIs). The strongest predictor of PPI discontinuation was number of days with acid exposure time (AET) greater than 4%. Participants with 0 days of AET greater than 4% had a 10x increased odds of discontinuing PPI than participants with 4 days of AET greater than 4%. Reduction in symptom burden was greater among the discontinued vs. resumed PPI group.

It was concluded among patients with typical reflux symptoms, inadequate PPI response and absence of severe esophagitis, acid exposure on reflux monitoring predicted the ability to discontinue PPIs without symptom escalation. Up-front reflux monitoring of acid suppression can limit unnecessary PPI use and guide personalized management.

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Yadlapati, R., Mishia, M., Gayawali, C., et al. “Ambulatory Reflux Monitoring Guides Proton Pump Inhibitor Discontinuation in Patients with Gastroesophageal Reflux Symptoms: A Clinical Trial.” *Gastroenterology* 2021; Vol. 160, pp. 174-182, January 2021

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### Safety of FMT Treatment for Recurrent *C. Difficile* Infection

Fecal microbiota transplantation (FMT) is highly effective for treating recurrent *Clostridioides difficile* infection (CDI). A prospective survey-based study was conducted from September 2012 to June 2018 in patients undergoing FMT for recurrent CDI.

Data on demographics and comorbidities were abstracted from medical records. Patients were contacted at 1 week, 1 month, 6 months, 1 year and greater than 2 years post-FMT (long-term). Symptoms and new medical diagnoses were recorded at each time point. Data was weighted to account for survey nonresponse bias. Multivariate logistic regression models for adverse events were built using age, sex, time of survey, and comorbidities.

Overall, 609 patients underwent FMT. Median age was 56 years (18-94), 64.8% were women, and 22.8% had IBD. At short-term followup (N = 609), greater than 60% of patients had diarrhea and 19 (33%) had constipation. At 1

year, 9.5% reported additional CDI episodes. On multivariable analysis, patients with IBD, dialysis-dependent kidney disease and multiple FMTs had higher risk of diarrhea; risk of constipation was higher in women and lower in IBD. For long-term follow-up (N = 447), median time of follow-up was 3.7 years (2-6.8). Overall, 73 new diagnoses were reported; 13% gastrointestinal, 10% weight gain, 11.8% new infections deemed unrelated to FMT. Median time to infections was 29 months post-FMT.

It was concluded that FMT appears safe with low risk of transmission of infections. Several new diagnoses were reported that require exploration in future studies.

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Saha, S., Mara, K., Pardi, D., and Khanna, S. "Long-Term Safety of Fecal Microbiota Transplantation for Recurrent *Clostridioides Difficile* Infection." *Gastroenterology* 2021; Vol. 160, pp. 1961-1969.

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