

New classification Rome IV functional dyspepsia and subtypes

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Comment on: Aziz I, Palsson OS, Törnblom H, *et al.* Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: a cross-sectional population-based study. *Lancet Gastroenterol Hepatol* 2018;3:252-62.

Received: 02 September 2018; Accepted: 10 September 2018; Published: 19 September 2018.

doi: 10.21037/tgh.2018.09.12

View this article at: <http://dx.doi.org/10.21037/tgh.2018.09.12>

Functional dyspepsia (FD) is one of the gastrointestinal disorders and can be severely disturbed with quality of life (QOL). Visceral hypersensitivity (1), disturbed gastric accommodation (2) and disturbed gastric motility are mostly reported in FD patients (3-5). According to the Rome III classification, FD symptoms were chiefly consisted of four symptoms, such as bothersome postprandial fullness, early satiety, epigastralgia and epigastric burning (6). FD patients were divided two groups. One group was epigastric pain syndrome (EPS) and the other was postprandial distress syndrome (PDS). These two groups require different treatments. EPS patients were mainly treated with acid secretion inhibitors, whereas PDS patients were mainly treated with prokinetic drugs, such as mosapride and acotiamide (7).

Recently, Rome IV classification has been reported the definition of FD determined by bothersome clinical symptoms (8,9). In the Rome IV classification of FD patients, slight modifications were mentioned as compared to last Rome III classification. In new Rome IV classification, not only postprandial fullness, but also EPS symptom and early satiation should be determined as “bothersome symptoms”. Then, Rome IV classification involves not only PDS and EPS, but also the overlap of PDS and EPS. PDS-EPS overlapped syndrome in the hospital-based population is more frequent than in the general population (10).

Aziz et al. have tried to determine enrolled subjects fitted into Rome IV criteria using online questionnaire in the USA, Canada, and the UK. *Aziz et al.* have demonstrated

that almost ten percentage in the adult population fitted into symptoms-based criteria for Rome IV FD (11). They have reported that the proportion of Rome IV FD in the USA was significantly higher than in Canada (8%) and UK (8%) (11). They have also reported that 9% participants accompanying with symptom-based diagnosis for Rome IV FD patients, 6% having PDS, 2% EPS, and 2% having the overlapping variant (11). Then, in our data, although we evaluated clinical symptoms, quality of life, sleep disturbance and anxiety in FD subgroups, these parameters and the score of questionnaires were not significantly linked to the criteria of respective subgroups (12). Anyway, the definition of subtypes of FD patients is important for the determination of the treatment for FD patients. Recently, Chen *et al* have demonstrated that FD subgroups had various regional brain activities at rest and under stress and compared to PDS patients, EPS patients exhibited more significant differences in the distribution of brain activities from healthy volunteers (13).

In addition, *Aziz et al.* have reported that the proportion of subgroups was 61% PDS, 18% EPS and the incidence of irritable bowel syndrome (IBS) was also significantly higher among those with overlapping PDS and EPS than in those with EPS alone and was lowest in those with PDS alone (11). Ford *et al* have also reported that the incidence of IBS is 8 times higher in subjects with FD and suggests that IBS and FD share the process of the progression of their diseases (14). In our data, the severity of symptom, such as heartburn and hunger in the overlapped syndrome were significantly higher compared to that in FD patients (15).

Then, since FD patients, especially those with EPS, has been reported to overlap with other diseases such as chronic pancreatitis, the administration of PPI and H₂-blocker in the treatment of EPS remains controversial (16-18). Then, the reason why certain populations of EPS are resistant for the treatment using anti-acid therapy or prokinetics are considered as the involvement with several other overlapped diseases. We have also reported that almost 40% of FD patients with abnormalities of pancreatic enzyme was determined as early chronic pancreatitis (ECP) using endosonography (19). Our results suggest that the measurement of early phase of gastric emptying may be a useful tool to distinguish ECP patients from FD patients. Gastric emptying is partly regulated by ghrelin and glucagon-like peptide 1 (GLP-1) production. Further studies will be needed to clarify whether the inflammation in gastrointestinal tract affect ghrelin and GLP-1 production, respectively (20).

When we can distinguish FD patients with pancreatic enzyme abnormalities from ECP, the treatment for ECP using camostat mesilate, pancrelipase, and rabeprazole triple therapy was significantly effective compared to that for FD using acotiamide and rabeprazole combination therapy (20). In Japan, acotiamide alone or acotiamide and proton pump inhibitor combination therapy were effective for PDS subtype, whereas certain populations in EPS subtype were resistant for the treatment for FD patients. Measurement of pancreatic enzyme, brain MRI, endosonography may be useful for the determination of the strategy for EPS or PDS-EPS overlap syndrome.

Acknowledgements

Funding: The Ministry of Education, Culture, and Science and from the Ministry of Health, Japan (16K09294).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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doi: 10.21037/tgh.2018.09.12

Cite this article as: Futagami S, Yamawaki H, Agawa S, Higuchi K, Ikeda G, Noda H, Kirita K, Akimoto T, Wakabayashi M, Sakasegawa N, Kodaka Y, Ueki N, Kawagoe T, Iwakiri K. New classification Rome IV functional dyspepsia and subtypes. *Transl Gastroenterol Hepatol* 2018;3:70.