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Chairman of Chinese Digestive Psychosomatic Union
Chief of Chinese Association of Psychosomatic Digestive Diseases
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Clinical Characteristics and Therapeutic Advances in Functional Dyspepsia Combined with Gastroesophageal Reflux Disease (Part 2)

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Abstract: Functional dyspepsia (FD) symptoms and gastroesophageal reflux disease (GERD) symptoms often coexist, forming an “overlap syndrome.” These symptoms are often intertwined, and the pathophysiological mechanisms are interrelated. This overlap syndrome significantly impairs patients' quality of life and poses challenges to clinical diagnosis and treatment. This review analyzes the clinical characteristics and diagnostic difficulties of the overlap syndrome and, based on the latest international guidelines and evidence-based medical evidence, elaborates on patient-centered treatment principles. This article aims to provide diagnostic and therapeutic ideas and strategies for the scientific management of FD combined with GERD in clinical practice.

***Key words*:** Functional dyspepsia; gastroesophageal reflux disease; overlap syndrome; visceral hypersensitivity; brain-gut axis; neuromodulators

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Introduction

Functional dyspepsia (FD) and gastroesophageal reflux disease (GERD), which are among the most prevalent upper gastrointestinal (GI) disorders, respectively represents the most common type of functional gastrointestinal disorders (FGIDs) and acid-related motility disorders. These two conditions often coexist, forming an "overlap syndrome".[1] Epidemiological data indicate that the co-occurrence of these two conditions far exceeds random probability, suggesting a shared pathophysiological basis, such as the generalization of visceral hypersensitivity, gastric and duodenal dysmotility, and the dysregulated brain-gut axis. [1-3] This overlap is not merely a simple addition of symptoms but may form a unique "overlap syndrome" with distinct characteristics, leading to more complex symptoms in patients (such as the coexistence of epigastric pain, postprandial fullness, and reflux and heartburn), more severe impairment of quality of life, and poor response to traditional monotherapy strategies targeting either FD or GERD. At present, although the Rome IV diagnostic criteria provide a framework for the diagnosis of comorbidity of these two conditions, [4] there is still a lack of systematic consensus on their intrinsic connections and optimal management pathways in clinical practice. Therefore, based on our previous review addressing the classification of FD overlapping with GERD, [5] this review summarizes the symptomatic characteristics and pathophysiological mechanisms of FD-GERD overlap, and elaborates on evidence-based integrative therapeutic principles, with the aim of providing clear diagnostic and therapeutic strategies for clinical practice and improving patient outcomes.

4. Symptomatic characteristics and shared pathophysiological mechanisms of FD overlapping with GERD

Epidemiological evidence shows that the symptomatic overlap between FD and GERD is common, with a co-occurrence rate exceeding 30%, suggesting the existence of shared pathophysiological processes [6,7].

4.1 Clinical characteristics of overlap syndromes

The clinical characteristics of overlapping FD and GERD symptoms include: 1) Mixed and intertwined symptoms. Patients often report the coexistence of epigastric pain/fullness (characteristic symptoms of FD) and retrosternal heartburn/regurgitation (characteristic symptoms of GERD). These symptoms frequently interact with each other and are difficult to distinguish. For example, postprandial fullness may exacerbate regurgitation symptom, while frequent reflux can also trigger or worsen upper abdominal discomfort. 2) Overlapping symptom triggers. meals, psychological stress, and specific foods (such as high-fat or spicy diets) can simultaneously trigger or aggravate both FD and GERD symptoms. 3) Expanded symptom spectrum. Patients with overlapping conditions are usually more prone to atypical symptoms, such as belching, nausea, chronic cough, and globus pharyngeus (the sensation of a lump in the throat). They are also more likely to have other FGIDs, such as irritable bowel syndrome (IBS), which further complicates their clinical presentation [6,7].

4.2 Diagnosis of overlap syndromes

The diagnostic approaches for overlap syndrome include: 1) Symptom diagnostic scales. Commonly used symptom questionnaires (e.g., the GerdQ questionnaire) are inadequate to precisely differentiate whether symptoms originate from the gastroduodenal region or the esophagus, nor can they distinguish GERD from functional esophageal disorders. 2) Endoscopy. Gastroscopy is an essential step to rule out organic lesions (such as esophagitis and ulcers). However, negative endoscopic findings (i.e., non-erosive changes) do not exclude GERD (non-erosive reflux disease, NERD) or functional esophageal disorders. In such cases, the value of symptom assessment and functional testing becomes particularly prominent. 3) Functional testing. Functional evaluation is recommended for overlap patients with refractory symptoms, unclear diagnoses, or failure of empirical therapy. For instance, gastric emptying scintigraphy can help to identify FD patients with concurrent

delayed gastric emptying, thereby providing a rationale for the use of prokinetic agents. High-resolution manometry (HRM) can be applied for assessment of esophageal motility. 4) 24-hour multichannel intraluminal impedance-pH monitoring (MII-pH). It has been considered as the "gold standard" for differentiating GERD, reflux hypersensitivity, and functional heartburn. It can objectively record the frequency and duration of acid, weakly acidic, and non-acidic reflux events, and calculate the symptom association probability (SAP) between symptoms and reflux episodes [6].

4.3 Shared pathophysiological mechanisms of FD and GERD

The high comorbidity rate between FD and GERD suggests the existence of shared pathophysiological mechanisms, which may include: 1) Generalization of visceral hypersensitivity. Visceral hypersensitivity may concurrently involve the stomach, duodenum, and esophagus, leading to aberrant perception of various stimuli in patients. 2) Continuity of motor dysfunction. Delayed gastric emptying and elevated intragastric pressure may facilitate the occurrence of transient lower esophageal sphincter relaxations (TLESRs), thereby increasing the frequency of gastroesophageal reflux events. 3) Central sensitization and psychiatric comorbidities. Alterations in the functions of the central nervous system, such as anxiety and depression, can lower the sensory thresholds in both the stomach and esophagus and simultaneously leading to dysmotility. These central factors serve as critical drivers for the overlap of these disorders and the chronicity of their symptoms.

5. Treatment principles for concurrent FD and GERD

The management of patients with concurrent FD and GERD should follow a comprehensive strategy that is stepwise, individualized, and pathophysiology-oriented [8-10].

5.1 Basic management.

1) Helicobacter pylori testing and eradication. All FD patients should be tested for H. pylori (HP), and eradication therapy is recommended for the HP-positive patients. This is an etiological treatment supported by evidence-based medicine that may improve symptoms in a subset of FD patients.

2) Dietary modifications. It is recommended to adopt a small, frequent meal pattern and avoid eating too rapidly. Intake of high-fat, spicy, and overly sweet foods, as well as caffeine, carbonated beverages, and alcohol, should be reduced, as these may simultaneously exacerbate both FD and GERD symptoms. For patients with postprandial distress syndrome (PDS), a low-FODMAP diet may be beneficial.

3) Lifestyle adjustments. Smoking cessation and weight control are advised. To specifically relieve reflux symptoms, it is recommended to avoid lying flat within 2-3 hours after meals and to elevate the head of the bed during nighttime sleep.

4) Patient education and psychological support. Educating patients about the brain-gut interactions, helping them to establish realistic treatment expectations and alleviating their illness-related anxiety are essential. These measures are the cornerstone of all therapeutic interventions.

5.2 First-line empirical therapy: According to current guideline recommendations, initial treatment may be selected based on the predominant symptoms.

1) For patients with predominant symptoms of reflux/heartburn or epigastric pain (EPS), proton pump inhibitors (PPIs) are preferred, administered once daily 30 min before breakfast, with a duration of 4–8 weeks.

2) For patients with predominant symptoms of postprandial fullness or early satiety (PDS), prokinetic agents are preferred, such as domperidone, mosapride, or itopride.

3) For patients displaying overlapping symptoms without an obviously predominant symptom, initial combination therapy with PPIs and prokinetic agents can be employed.

5.3 Second-line and optimization therapy. For patients with inadequate response to first-line treatment after 4–8 weeks, diagnostic reassessment should be performed, with adjustment of the treatment regimen considered.

1) Neuromodulators/centrally acting agents. They constitute the cornerstone of second-line therapy. Low-dose tricyclic antidepressants (e.g., amitriptyline 10–25 mg) are the most evidence-based option for alleviating visceral hypersensitivity and improving refractory epigastric pain as well as functional chest pain/heartburn. Selective serotonin reuptake inhibitors (e.g., escitalopram) may also be considered. Agents with combined dopamine antagonist and prokinetic properties, such as levo-sulpiride, represent an additional therapeutic option.

2) Switching to or combining with alternative agents. Prokinetic drugs with different mechanisms of action may be trialed, or combination therapy with evidence-based herbal medicine, such as compound preparations containing peppermint oil, may be employed.

5.4 Mechanism-based precision interventions.

1) For patients with functional testing indicating reflux hypersensitivity, PPI dosage should be reduced or discontinued. In addition, application of neuromodulators is recommended.

2) For patients with extremely poor treatment response, re-evaluation for overlooked organic or motility disorders (e.g., gastroparesis, achalasia) is warranted.

5.5 Multidisciplinary integrated management for refractory cases. For refractory FD overlapping with GERD, psychobehavioral interventions may be employed. Cognitive behavioral therapy and gut-directed hypnotherapy have demonstrated efficacy in improving FD and functional esophageal symptoms, particularly in patients with significant psychological distress or suboptimal response to pharmacotherapy [11]. Additionally, emphasis should be placed on multidisciplinary team collaboration, wherein gastroenterologists work jointly with psychiatrists/psychologists, nutritionists, and pain management specialists to develop comprehensive treatment plans integrating biological, psychological, and social factors for complex, refractory patients.

Outlook and Conclusion

The overlap syndrome of FD and GERD reflects the complexity and continuum of symptoms in FGIDs. The Rome IV diagnostic framework provides tools for precise clinical identification. Modern management has evolved beyond simple acid suppression or prokinetic monotherapy toward an integrated treatment model based on predominant symptoms and underlying pathophysiological mechanisms, with heightened emphasis on the roles of neuromodulation and psychological intervention. Future novel therapies targeting duodenal low-grade inflammation, intestinal microecology, and specific neurotransmitter pathways hold promise for delivering fundamental relief to these patients. At present, clinicians should strive to perform meticulous symptom profiling and mechanistic assessment, implementing individualized stepwise treatment to maximize improvement in patients' quality of life.

References

1. Geeraerts A, Van Houtte B, Clevers E, Geysen H, Vanuytsel T, Tack J, Pauwels A. Gastroesophageal Reflux Disease-Functional Dyspepsia Overlap: Do Birds of a Feather Flock Together? Am J Gastroenterol. 2020;115(8):1167-1182.
2. Gwee KA, Lee YY, Suzuki H, Ghoshal UC, Holtmann G, Bai T, Barbara G, Chen MH, Chua ASB, Gibson PR, Hou X, Liu J, Nakajima A, Pratap N, Sachdeva S, Siah KTH, Soh AYS, Sugano K, Tack J, Tan VPY, Tang X, Walker M, Wu DC, Xiao YL, Zulkifli KK, Toh C. Asia-Pacific guidelines for managing functional dyspepsia overlapping with other gastrointestinal symptoms. J Gastroenterol Hepatol. 2023;38(2):197-209.
3. Ohara S, Kawano T, Kusano M, Kouzu T. Survey on the prevalence of GERD and FD based on the Montreal definition and the Rome III criteria among patients presenting with epigastric symptoms in Japan. J Gastroenterol. 2011;46(5):603-611.

4. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. Gastroenterology. 2016:S0016-5085(16)00223-7.
5. Chen SL. Clinical characteristics and therapeutic advances in functional dyspepsia combined with gastroesophageal reflux disease (Part 1). Psychosom Gastroenterol. 2026;12(2):6-10.
6. Geeraerts A, Van Houtte B, Clevers E, Geysen H, Vanuytsel T, Tack J, Pauwels A. Gastroesophageal reflux disease-functional dyspepsia overlap: do birds of a feather flock together? Am J Gastroenterol. 2020;115(8):1167-1182.
7. Quach DT, Ha QV, Nguyen CT, Le QD, Nguyen DT, Vu NT, Dang NL, Le NQ. Overlap of gastroesophageal reflux disease and functional dyspepsia and yield of esophagogastroduodenoscopy in patients clinically fulfilling the Rome IV criteria for functional dyspepsia. Front Med (Lausanne). 2022;9:910929.
8. Byun SY, Jung KW. Overlap Between Gastroesophageal Reflux Disease and Functional Dyspepsia: Do We Need a New Management Paradigm? J Neurogastroenterol Motil. 2025 Apr 30;31(2):129-130.
9. Pasricha PJ, Talley NJ. Functional Dyspepsia. N Engl J Med. 2026 Jan 8;394(2):166-176.
10. Gwee KA, Lee YY, Suzuki H, Ghoshal UC, Holtmann G, Bai T, Barbara G, Chen MH, Chua ASB, Gibson PR, Hou X, Liu J, Nakajima A, Pratap N, Sachdeva S, Siah KTH, Soh AYS, Sugano K, Tack J, Tan VPY, Tang X, Walker M, Wu DC, Xiao YL, Zulkifli KK, Toh C. Asia-Pacific guidelines for managing functional dyspepsia overlapping with other gastrointestinal symptoms. J Gastroenterol Hepatol. 2023 Feb;38(2):197-209.
11. Browne PD, den Hollander B, Speksnijder EM, van Wering HM, Tjon A Ten W, George EK, Groeneweg M, Bevers N, Wessels MMS, van den Berg MM, Goede J, Teklenburg-Roord STA, Frankenhuis C, Benninga MA, Vlieger AM. Gut-directed hypnotherapy versus standard medical treatment for nausea in children with functional nausea or functional dyspepsia: protocol of a multicentre randomised trial. BMJ Open. 2019 Apr 11;9(4):e024903.