

Research Progress on Pathogenesis and Traditional Chinese-Western Medicine Diagnosis and Treatment of Functional Dyspepsia

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Abstract: Functional dyspepsia (FD) is a highly prevalent functional gastrointestinal disorder in clinical practice, characterized by postprandial fullness, early satiation, epigastric pain, and epigastric burning. Its recurrent episodes substantially impair patients' quality of life. According to the Rome IV criteria, FD is subclassified into postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), and overlapping presentations of the two subtypes are frequently observed. From the perspective of modern medicine, the pathogenesis of FD is closely associated with gastrointestinal motility disorders, visceral hypersensitivity, brain-gut axis dysfunction, *Helicobacter pylori* infection, gut microbiota dysbiosis, and psychosocial factors. In traditional Chinese medicine (TCM), FD falls under the disease categories of "Pi Man (stiffness-fullness syndrome)" and "Wei Wan Tong (epigastric pain)". Its core pathogenesis lies in disordered middle-jiao Qi movement and impaired ascending-descending functions of the spleen and stomach induced by dietary irregularities, emotional disturbances, external pathogenic invasion, and constitutional deficiency. Western-medicine therapeutic strategies mainly include symptomatic interventions such as acid suppression, prokinetic agents, *Helicobacter pylori* eradication, and anxiolytic-antidepressant therapy. Guided by syndrome differentiation-based treatment, TCM adopts oral herbal formulas combined with external therapies including acupuncture, auricular-point pressing, and acupoint application. Each therapeutic system possesses its unique strengths. This review summarizes research advances regarding FD pathogenesis as well as TCM-western-medicine diagnosis and treatment, and identifies existing limitations within integrated TCM-western-medicine frameworks, so as to provide references for clinical management and scientific research.

Keywords: Functional dyspepsia; Pi Man (stiffness-fullness syndrome); Pathogenesis; Integrated traditional Chinese and Western medicine; Diagnostic and therapeutic progress

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1. Introduction

Functional dyspepsia (FD) refers to a functional gastrointestinal disorder without organic lesions, manifested by one or more symptoms including postprandial fullness, early satiation, epigastric pain, and epigastric burning.^[1] The disease is protracted and recurrent, hard to achieve complete cure, and markedly compromises patients' quality of life. Based on the Rome IV criteria, FD is divided into post-prandial distress syndrome (PDS) and epigastric pain syndrome (EPS); co-existence of both subtypes is common in clinical settings.

With an accelerated pace of life, elevated psychological stress, and altered dietary patterns in modern society, the prevalence of FD keeps rising year-on-year. The global prevalence of FD ranges from 11.5 % to 14.5% ^[2]. The prevalence among European adults is approximately 10%, among whom 60% present with PDS. In China, the prevalence of FD reaches 18–45%, distinctly higher than that in foreign regions, accounting for onethird of patients seeking gastroenterological outpatient care ^[3,4]. A domestic multi-center survey reported that postprandial fullness occurred in 57.12% of FD patients and early satiation in 40.21%, indicating higher clinical frequency of PDS ^[5]. The high prevalence in China is correlated with high *Helicobacter pylori* infection rates, predilection for spicy and greasy food, and disrupted work-rest rhythms. Economically developed regions demonstrate higher FD prevalence than less-developed counterparts, which is attributable to greater psychological stress burden.

Although FD carries no mortality risk, persistent abdominal discomfort is frequently complicated by emotional disturbances and sleep disorders, interfering with patients' work, study, and social activities. Therefore, research on FD and optimization of therapeutic regimens are of great practical significance for improving patients' quality of life.

2. Research progress on pathogenesis of FD

2.1. Pathogenesis from modernmedicine perspective

FD results from interactions of multiple contributing factors, and its pathogenesis has not been fully elucidated. Major mechanisms are summarized as follows:

(1) Gastrointestinal motility disorders\

A predominant trigger for PDS. Patients exhibit delayed gastric emptying, disordered food transit, and increased duodenal retroperistalsis, which give rise to postprandial fullness and early satiation ^[6].

(2) Visceral hypersensitivity

Predominantly observed in EPS patients. 30–50% of patients display heightened gastrointestinal nociceptive perception and impaired gastric accommodation, aggravating abdominal distension and epigastric pain.

(3) Braingut axis dysfunction

Aberrant bidirectional signaling between the brain and the gut. Anxiety and depression impair gastrointestinal function; in turn, gastrointestinal complaints exacerbate mood disturbances, forming a vicious cycle. Abnormal activation of cerebral nociceptive regulatory regions has been documented.

(4) *Helicobacter pylori* (Hp) infection

The causal relationship between Hp and FD remains controversial. Persistent symptoms after Hp eradication are observed in subsets of Hp-positive patients, suggesting that Hp participates in the pathogenesis of partial FD cases. Empiric eradication therapy is only recommended for such Hppositive patients in clinical practice.

(5) Gut microbiota dysbiosis

Reduction of beneficial commensal bacteria and overgrowth of pathogenic bacteria disrupt intestinal barrier integrity and interfere with brain-gut signaling. Probiotic preparations can be adopted as adjuvant therapy.

(6) Psychological-psychiatric factors

FD patients exhibit high comorbidity rates of anxiety, depression, and insomnia. Psychological stress suppresses gastrointestinal motility, elevates visceral sensitivity, and also compromises patients' treatment adherence.

2.2. TCM etiology and pathogenesis

No disease term equivalent to functional dyspepsia exists in classic TCM literature. According to clinical manifestations, FD is categorized under “Pi Man (stiffness-fullness syndrome)” and “Wei Wan Tong (epigastric pain)”. The concept of “Pi Man” was first recorded in *Huang-Di Nei-Jing (Huangdi's Internal Classic)*. *Lan-Shi Mi-Cang (Secret Records of the Orchid Chamber)*, compiled by Li Gao, contains a special chapter addressing “epigastric pain”. Zhang Jing-yue and Yu Tuan further differentiated epigastric pain from true cardiac pain, and proposed food retention, phlegmfluid retention, and emotional imbalance as key precipitants for epigastric pain. Shen Jin-ao emphasized that liver-wood invading spleen constitutes an important pathogenic link for epigastric pain.

Ancient texts documented that external cold/damp pathogenic factors can obstruct the middle-jiao and impair spleen-stomach transportation and transformation. Constitutional spleen/stomach deficiency leads to insufficient transportation capacity and dampness stagnation, which also triggers this disorder. Treatises by Zhu Dan-xi and Li Dong-yuan indicated that dietary overstrain, emotional disharmony, deficiency, and cold exposure can all induce epigastric stiffness and pain.

In summary, modern TCM theory holds that FD is caused by dietary indiscretion, emotional disturbance, external pathogenic invasion, and spleen-stomach deficiency, which induce Qi stagnation in the middle-jiao and dysfunctional ascending-descending activities of the spleen and stomach. Its pathogenesis is characterized by intermingled deficiency and excess, with mutual transformation between these two pathological states. Common clinical syndromes include liver-stomach disharmony, spleen-deficiency Qi stagnation, spleen-stomach deficiency, spleen-stomach damp-heat, and cold-heat complex. Liver-stomach disharmony and spleen-deficiency Qi stagnation are the most prevalent. Liver-wood overacting on spleen, impaired spleen transportation, and stomach failing to descend represent core pathological processes.

3. Progress in TCM Diagnosis and Treatment

3.1. Oral herbal medicine

Decoctions constitute the primary TCM therapeutic modality, with flexible modification according to syndrome patterns. Liu Xin-rong et al. achieved favorable clinical outcomes using modified Tiao-Wei Jian-Pi Decoction for FD patients^[7]. Master Xu Jing-fan, a nationally renowned TCM physician, attached great importance to the dampness pathogen in PDS management and prioritized activating the spleen and eliminating dampness. He adopted Er-Chen Decoction-related formulas to regulate Qi and resolve dampness. For patients with damp-heat accompanied by insufficient stomach yin, he prioritized heat-

clearing and fluid-generating therapy before activating the spleen and resolving dampness. He also applied herbal tea substitutes to improve patients' medication adherence ^[8].

Chinese patent medicines feature convenient administration and are widely used in clinical practice. Studies demonstrated that Zhizhu Kuanzhong Capsule yields superior efficacy for FD with liver-stomach disharmony syndrome compared with spleenstomach Qi-deficiency syndrome ^[9]. Combined application of Shen-Shu Jian-Yun Tiao-Qi Decoction and Zhizhu Kuanzhong Capsule for FD with spleen-deficiency Qi-stagnation syndrome improves gastric emptying capacity and lowers recurrence rates ^[10]. Reliable therapeutic effects can be obtained when patent medicines are prescribed under accurate syndrome differentiation.

3.2. External TCM therapies

External therapies possess advantages of convenient manipulation and minimal adverse effects, and are frequently combined with oral herbal medicine to enhance therapeutic efficacy. Herbal hotcompress package combined with fiveelement music therapy can regulate spleen-stomach function, soothe liver and calm spirit, and ameliorate negative emotions among FD patients ^[11]. Auricular-point pressing is suitable for FD with liver-stomach disharmony syndrome, featuring minimal discomfort and suitability for long-term intervention ^[12]. Acupoint catgut embedding at acupoints including Zhongwan (CV12), Zusanli (ST36), Pishu (BL20) and Weishu (BL21) exerts definite therapeutic effects on FD ^[13]. Vitamin B1 acupoint injection at Zusanli (ST36) and Hegu (LI4) is easy to operate and cost-effective, and is suitable for popularization in primary-care medical institutions ^[14].

Acupuncture combined with herbal medicine represents a distinctive TCM therapeutic modality. Professor Xiang Xian-de integrated zangfu and six-meridian syndrome differentiation, implementing combined acupuncture-herbal therapy supplemented with psychological counseling to achieve simultaneous regulation of body and mind ^[15]. Herbal formulas can also be combined with Western medicine agents. The combination of Shen-Ling Bai-Zhu San and mosapride modulates 5-hydroxytryptamine receptors, facilitates acetylcholine release, enhances gastrointestinal smooth-muscle contraction, and improves gastrointestinal motility, which illustrates the value of integrated TCM-Western-medicine therapy ^[16].

4. Progress in Western-medicine diagnosis and treatment

4.1. Pharmacological therapy

Western-medicine treatment mainly adopts empirical symptomatic therapy, with medication selection tailored to FD subtypes. Protonpump inhibitors (PPIs) for acid suppression are indicated for patients presenting with nonmealrelated symptoms such as epigastric pain and epigastric burning. Prokinetic agents including mosapride, domperidone, and acotiamide are prioritized for meal-related symptoms such as postprandial fullness and early satiation. *Helicobacter pylori*-positive patients can receive eradication therapy. Digestive enzymes and probiotics serve as adjuvant interventions. For patients with inadequate response to the above-mentioned regimens and concurrent mood disorders, anxiolytic-antidepressant agents can be added ^[17].

Systematic reviews have validated that PPIs effectively alleviate dyspeptic symptoms and improve quality of life ^[18]. Among prokinetic agents, metoclopramide and cinitapride exhibit prominent therapeutic effects, while cinitapride carries lower risks of adverse events ^[19]. Domperidone is associated with QT-interval prolongation and cardiac risks; dosage and treatment course should be strictly controlled among elderly

patients and individuals with cardiovascular comorbidities. Acotiamide is an FD-targeted prokinetic agent approved overseas, yet its clinical popularization in China remains limited.

Helicobacter pylori eradication is only recommended for Hp-positive FD patients. Persistent symptoms post-eradication in partial patients confirm that Hp is not the sole pathogenic factor. Systematic reviews on antidepressants indicated that tricyclic antidepressants are effective for FD, exerting both analgesic and visceral-sensation-modulating effects. Selective serotonin reuptake inhibitors (SSRIs) mainly regulate central emotional status and demonstrate no statistically significant benefits for gastrointestinal manifestations^[20].

4.2. Non-pharmacological interventions

For patients with poor pharmacological response, psychological-behavioral interventions such as cognitive-behavioral therapy, hypnotherapy and mindfulness-based stress reduction can be implemented. Existing evidence indicates that behavioral interventions improve both gastrointestinal symptoms and anxiety-depressive mood compared with routine nursing care and placebo controls^[21]. Nevertheless, psychological therapy resources are scarce in China. Long treatment courses and high costs restrict their wide application. Internet-based remote psychological intervention represents a promising future direction.

5. Challenges and prospects

FD has complex multifactorial pathogenesis, and radical curative approaches are still unavailable. Integrated TCM-western-medicine therapy holds great therapeutic potential, whereas multiple challenges persist. Future research directions are proposed as follows:

- (1) Conduct highquality multi-center clinical trials to enrich evidencebased medical foundations;
- (2) Promote objective quantification of TCM syndrome differentiation, clarify pathological features corresponding to distinct syndromes, and refine therapeutic-effect evaluation criteria;
- (3) Optimize integrated TCM-western-medicine regimens, and select monotherapy or combined therapy flexibly according to individual patient conditions;
- (4) Address both somatic and psychological manifestations, and explore synergistic mindbody intervention strategies combining TCM and Western medicine;
- (5) Carry out gut-microbiota-oriented research to interpret the pharmacological mechanisms of TCM interventions and identify novel therapeutic targets.

Disclosure statement

The authors declare no conflict of interest.

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