

World Journal of *Gastroenterology*

World J Gastroenterol 2020 February 7; 26(5): 456-561



**MINIREVIEWS**

- 456** Diet and functional dyspepsia: Clinical correlates and therapeutic perspectives
Pesce M, Cargiolli M, Cassarano S, Polese B, De Conno B, Aurino L, Mancino N, Sarnelli G
- 466** Endoscopic Kyoto classification of *Helicobacter pylori* infection and gastric cancer risk diagnosis
Toyoshima O, Nishizawa T, Koike K

ORIGINAL ARTICLE**Basic Study**

- 478** lncRNACNN3-206 activates intestinal epithelial cell apoptosis and invasion by sponging miR-212, an implication for Crohn's disease
Li N, Shi RH

Case Control Study

- 499** Upregulation of miR-34c after silencing E2F transcription factor 1 inhibits paclitaxel combined with cisplatin resistance in gastric cancer cells
Zheng H, Wang JJ, Yang XR, Yu YL

Retrospective Cohort Study

- 514** Severity of acute gastrointestinal injury grade is a good predictor of mortality in critically ill patients with acute pancreatitis
Ding L, Chen HY, Wang JY, Xiong HF, He WH, Xia L, Lu NH, Zhu Y

Retrospective Study

- 524** Development of a prognostic model for one-year surgery risk in Crohn's disease patients: A retrospective study
Yao JY, Jiang Y, Ke J, Lu Y, Hu J, Zhi M
- 535** Nomograms predicting long-term survival in patients with invasive intraductal papillary mucinous neoplasms of the pancreas: A population-based study
Wu JY, Wang YF, Ma H, Li SS, Miao HL

CASE REPORT

- 550** New tight junction protein 2 variant causing progressive familial intrahepatic cholestasis type 4 in adults: A case report
Wei CS, Becher N, Friis JB, Ott P, Vogel I, Grønbaek H

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Yan-Tao Tian, MD, Professor, Department of Pancreatic and Gastric Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (WJG, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2019 edition of Journal Citation Report® cites the 2018 impact factor for WJG as 3.411 (5-year impact factor: 3.579), ranking WJG as 35th among 84 journals in gastroenterology and hepatology (quartile in category Q2). CiteScore (2018): 3.43.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yun-Jie Ma*

Proofing Production Department Director: *Yun-Xiaoqian Wu*

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Subrata Ghosh, Andrzej S Tarnawski

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

EDITORIAL OFFICE

Ze-Mao Gong, Director

PUBLICATION DATE

February 7, 2020

COPYRIGHT

© 2020 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Diet and functional dyspepsia: Clinical correlates and therapeutic perspectives

Marcella Pesce, Martina Cargiolli, Sara Cassarano, Barbara Polese, Barbara De Conno, Laura Aurino, Nicola Mancino, Giovanni Sarnelli

ORCID number: Marcella Pesce (0000-0001-5996-4259); Martina Cargiolli (0000-0001-9378-7882); Sara Cassarano (0000-0002-0616-3711); Barbara Polese (0000-0001-5173-2453); Barara De Conno (0000-0001-6205-8513); Laura Aurino (0000-0002-9060-2595); Nicola Mancino (0000-0002-7940-1952); Giovanni Sarnelli (0000-0002-1467-1134).

Author contributions: Pesce M and Sarnelli G conceived the manuscript and contributed to drafting, critical revision and editing; Cargiolli M, Polese B and Cassarano S carried out literature review and analysis and contributed to writing the manuscript. De Conno B, Aurino L and Mancino N contributed to this paper with literature review and analysis and editing; all authors gave final approval of the paper.

Conflict-of-interest statement: No potential conflicts of interest.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Marcella Pesce, Martina Cargiolli, Sara Cassarano, Barbara Polese, Barbara De Conno, Laura Aurino, Nicola Mancino, Giovanni Sarnelli, Department of Clinical Medicine and Surgery, “Federico II” University of Naples, Naples 80131, Italy

Marcella Pesce, GI Physiology Unit, University College London Hospital, London NW1 2BU, United Kingdom

Corresponding author: Giovanni Sarnelli, MD, PhD, Associate Professor, Department of Clinical Medicine and Surgery, Federico II University of Naples, Via Pansini 5, Naples 80131, Italy. sarnelli@unina.it

Abstract

Hypervigilance and symptoms anticipation, visceral hypersensitivity and gastroduodenal sensorimotor abnormalities account for the varied clinical presentation of functional dyspepsia (FD) patients. Many patients recognize meals as the main triggering factor; thus, dietary manipulations often represent the first-line management strategy in this cohort of patients. Nonetheless, scarce quality evidence has been produced regarding the relationship between specific foods and/or macronutrients and the onset of FD symptoms, resulting in non-standardized nutritional approaches. Most dietary advises are indeed empirical and often lead to exclusion diets, reinforcing in patients the perception of “being intolerant” to food and self-perpetuating some of the very mechanisms underlying dyspepsia physiopathology (*i.e.*, hypervigilance and symptom anticipation). Clinicians are often uncertain regarding the contribution of specific foods to dyspepsia physiopathology and dedicated professionals (*i.e.*, dietitians) are only available in tertiary referral settings. This in turn, can result in nutritionally unbalanced diets and could even encourage restrictive eating behaviors in severe dyspepsia. In this review, we aim at evaluating the relationship between dietary habits, macronutrients and specific foods in determining FD symptoms. We will provide an overview of the evidence-based nutritional approach that should be pursued in these patients, providing clinicians with a valuable tool in standardizing nutritional advises and discouraging patients from engaging into indiscriminate food exclusions.

Key words: Functional dyspepsia; Dietary habits; Food intolerances; Fermentable oligosaccharides, disaccharides, monosaccharides and polyols; Gluten-sensitivity; Diet

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Manuscript source: Invited manuscript

Received: November 15, 2019

Peer-review started: November 15, 2019

First decision: December 12, 2019

Revised: December 24, 2019

Accepted: January 19, 2020

Article in press: January 19, 2020

Published online: February 7, 2020

P-Reviewer: Triantafyllou K, Liu S

S-Editor: Wang JL

L-Editor: A

E-Editor: Ma YJ



Core tip: The spread on the internet of indiscriminate exclusion diets and food intolerance tests often reinforces in patients with functional dyspepsia (FD) the idea of being allergic or intolerant to foods. Physicians are often uncertain regarding the contribution of specific foods in FD and the lack of guidelines and dedicated dietitians, ultimately, leads to conflicting and uneven dietary advises. Here, we provide a pathophysiological-based review of the putative causal relationship between specific foods and symptoms generation in FD and then provide an evidence-based standardized dietary approach, applicable in clinical practice. Moving forward, international guidelines are eagerly awaited to standardize FD dietary management.

Citation: Pesce M, Cargiolli M, Cassarano S, Polese B, De Conno B, Aurino L, Mancino N, Sarnelli G. Diet and functional dyspepsia: Clinical correlates and therapeutic perspectives. *World J Gastroenterol* 2020; 26(5): 456-465

URL: <https://www.wjnet.com/1007-9327/full/v26/i5/456.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v26.i5.456>

INTRODUCTION

Current guidelines^[1] define functional dyspepsia (FD) as a complex and multifactorial condition characterized by a broad spectrum of symptoms centered in the gastroduodenal region. It is a highly prevalent disorder, reaching prevalence as high as 40% of the general population in western countries^[2] and it is characterized by a highly varied clinical presentation, ranging from upper abdominal bloating to nausea and vomiting. The high degree of overlap with gastro-esophageal reflux^[3] and other functional gastrointestinal disorders (FGDIs) accounts for the complexity in categorizing dyspeptic patients into clinically and pathophysiological meaningful subgroups.

Though, Rome criteria^[4,5] have identified two main subgroups based on the principal clinical pattern: Epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS).

EPS is characterized by the recurrence of epigastric pain or burning, independently from meal. On the contrary, PDS is unequivocally related to early post-prandial onset of fullness or early satiation. However, food ingestion seems to elicit also meal-unrelated symptoms such as pain or burning in over 75% of patients with PDS; hence, a clear-cut distinction between these two symptomatic presentations is challenging in real-world clinical practice^[6]. Dyspepsia pathophysiology is heterogeneous and complex and both cognitive and behavioral factors, such as anticipation and arousal, and/or gastric sensorimotor dysfunction are well-established factors at play in FD symptoms induction and perception^[6,7]. Aside from the role of central nervous system and gastric dysfunction, increasing evidences also demonstrated that duodenal abnormalities (duodenal hypersensitivity and small intestinal dysmotility) and subtle mucosal inflammation (duodenal eosinophilia and mast cell infiltration) could also play a role in generating FD symptoms^[8-11].

Since the meals are recognized as triggers for at least a subset of symptoms, dietary and lifestyle modifications often represent the first line management in FD patients^[12], despite the scanty quality evidence produced so far.

In this review, we summarize the current evidences regarding the role of diet in FD, focusing on the proposed underlying pathophysiological mechanisms. We will then explore the current treatment strategies in FD and the possible future targeted dietary treatments.

CALORIC INTAKE AND FD SYMPTOMS

Defective accommodation of the proximal stomach and delayed gastric emptying are recognized as two of the main mechanisms implicated in FD pathogenesis; hence, several studies investigated the potential role of caloric intake and food intake on symptoms development^[13,14].

Tack *et al*^[15] confirmed a possible correlation between caloric intake and gastric accommodation demonstrating that FD patients exhibited significantly higher satiety scores compared to controls, with maximum satiety reached at significantly lower

caloric amount in patients. However, this eating behavior does not necessarily correlate with a consistent weight loss, as one would expect^[16-18].

Furthermore, Boeckxstaens *et al*^[19] also described an impaired drinking capacity for both water and nutrient liquid meal in FD patients compared to healthy volunteers, even though no association with specific symptoms pattern had emerged.

This evidence suggests that probably meal volume and gastric distension could be implicated in triggering symptoms, rather than caloric intake *per se*^[19]. Therefore, the consumption of small and frequent meals may be a reasonable advice in order to reduce FD symptoms. Beyond the effect of caloric intake and food amount itself, nutrient composition should not be underestimated.

NUTRIENT COMPOSITION AND FD SYMPTOMS

In the last decade, the interest on the correlation between physicochemical properties of macronutrients and dyspeptic symptoms is growing. Indeed, food consumption can influence gastrointestinal functions by means of either mechanical or chemical stimulation. A recent review, systematically analyzing over 6400 studies, concluded that wheat and high fat foods are two of the major players in FD^[20].

Proteins, carbohydrates and lipids could all be implicated in symptoms onset, but the latter seems to be the most effective in eliciting the symptoms. Although a high protein intake may induce an increase of satiety in healthy subjects, little is known about the impact of high-protein meals on dyspeptic symptoms^[21].

The role of carbohydrates on FD symptoms is still unclear, too. In the cross-sectional study “Study on the Epidemiology of Psychological, Alimentary Health and Nutrition”, a large cohort of subjects has been evaluated to assess the potential effects of carbohydrates, in terms of glycemic index and load. The high glycemic load seemed to be associated with an increased risk of uninvestigated chronic dyspepsia and heartburn, in male subjects with normal body weight^[22].

It is plausible that a high intake of carbohydrates could induce PDS-like symptoms due to its possible effect on gastric fundus accommodation. Furthermore, a high glycemic index meal physiologically determines an increase of glucagon-like peptide 1 and cholecystokinin (CCK) release, which can, in turn, delay gastric emptying and induce prolonged satiety.

An analysis of recent literature showed that the most common culprit foods, recognized by FD patients, appeared to be high in concentration of either gluten (grain/wheat products, takeout foods, processed foods) or fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) (fruit, wheat and grain products, soft drinks, processed foods)^[16,20].

FODMAPs are a group of poorly absorbed and osmotically active carbohydrates, naturally contained in a wide array of common foods. Due to their physiological effects, FODMAPs are widely accepted as potential triggers for gastrointestinal symptoms in functional gastrointestinal disorders, particularly in irritable bowel syndrome (IBS) and residual functional bowel symptoms in inflammatory bowel diseases^[23-25]. The combination of abnormal gas production, caused by an increased intestinal fermentation, and the luminal water retention secondary to their osmotic activity, seems to enhance abdominal distension and to induce abdominal pain and bloating in patients with altered visceral sensitivity^[24]. Besides these well-known effects, their impact on FD physiopathology could be linked to qualitative changes in microbiome composition and/or on duodenal homeostasis secondary to an enhanced duodenal inflammation^[24].

On the contrary, the role of lipids in FD has been better characterized. It has been demonstrated that a high fat-meal can induce greater nausea, pain and fullness both respect to a low-calorie meal and an equicaloric meal, high in carbohydrates for the same volume. The main mechanisms by which fatty foods could exacerbate FD symptoms are related to delayed gastric emptying and hypersensitivity to gastrointestinal hormones^[26].

It is known that an intraduodenal lipid infusion can increase the sensitivity of the proximal stomach to distention, probably due to a fat specific effect on CCK release^[26]. Indeed, the administration of a CCK-A receptor antagonist seems to overturn the inhibition of gastric motility and emptying caused by the ingestion of a high-fat meal^[26-28].

SPECIFIC FOODS

Although the contribution of specific foods identified as triggers from FD patients is

empirical and diversified, some causal relationships between specific culprit foods and symptoms have been demonstrated. The retrospective nature of most studies and the lack of a standardized method to verify the food-symptom association accounts for the difficulty in drawing up an ultimate list of culprit or beneficial foods. Some of the most frequently reported triggering foods are fatty and acidic foods, wheat products and several types of fruit such as watermelon and fruit juices^[16,24,29-31]. Despite the known evidences about fatty foods, almonds seem not to aggravate FD symptoms as expected^[29]. This effect might be related to the high content of tryptophan, a serotonin precursor. Serotonin (5-hydroxytryptamine) is a key neurotransmitter involved in the regulation of gastrointestinal motility and sensory function. Indeed, the stimulation of serotonergic 5-HT₁ and 5-HT₄ receptors induce gastric smooth muscle contractions, enhancing gastric emptying and seem to improve abdominal symptom in FD patients^[32,33]. The culprit effect of pepper and chili may be mediated by its main active ingredient, capsaicin. Indeed, this alkaloid can exacerbate FD symptoms inducing hyperalgesia, through the activation of the transient receptor potential vanilloid subtype 1 (TRPV1) receptors, expressed on sensory afferent neurons^[34-36]. Nonetheless, chronic capsaicin administration could lead to TRPV1 downregulation and reduce visceral hypersensitivity. Effectively, in a small-sized (30 FD subjects) randomized control trial over placebo, red pepper powder (*Capsicum annuum*) significantly improved overall symptom scores, including epigastric pain, fullness, and nausea^[37]. Capsaicin is the paradigmatic example of how complex is the interplay between food ingestion and FD symptoms, with nutrients that can be at both beneficial or culprit foods, depending on the compensatory downregulation of visceral nociceptors.

The prevalent dyspepsia subtype also seems to play a role in predicting the response to dietary interventions. Being prevalently meal-related, PDS subtype has been the most studied pattern for nutritional intervention in FD. In a recent survey on 1304 Chinese FD patients, the authors found that unhealthier dietary habits, such as dining irregularly, having night snacks, skipping breakfast, and dining out, were more frequently associated with FD. The authors also evaluated the impact of specific dietary habits and dyspepsia subtypes, concluding that, although there was a large degree of overlap; certain foods, such as alcohol and coffee, were associated with EPS-FD^[38]. Only few other studies have analyzed the impact of diet on the prevalent symptom pattern, revealing possible links between the consumption of specific foods and epigastric burning (coffee, pepper, chocolate and onions), fullness (red meat, wheat products, beans, fried foods, sweets, chocolate) and bloating (carbonated drinks, onions, bananas, milk)^[16,20].

A factor that has to be taken into account is the lack of effective methods to assess potential food intolerances and allergies in most studies. The effect on FD symptoms could actually be influenced by the presence of gluten or lactose intolerance^[31]. Further studies are needed to deepen this aspect.

Analogously to the culprit foods, very few data is available about putative “beneficial” foods and most of these studies have investigated herbal supplements, often used as complementary and alternative treatments^[39,40]. In particular, caraway seeds, apple, quince and rock candy seem to have beneficial effects on FD symptoms^[15,20,29]. Oil extracts of both peppermint (*Mentha piperita*) and caraway seeds (*Carum carvi*), as single supplements or in combination^[41] have been proven beneficial in treating FD symptoms, but little is known about their physiological activity. The antiemetic action of menthol and peppermint oil seems to be related to an allosteric effect on 5-HT₃ receptors; however, this may be clinically irrelevant^[42]. Peppermint oil has been traditionally used in FD and IBS due to its choleric action and spasmolytic effects in the esophagus, lower stomach and duodenal bulb and colonic spasm during barium enema^[43]. In several trials, peppermint and caraway oil were found to be more effective than placebo in improving dyspeptic symptoms, with an average decreased intensity of epigastric pain compared to placebo^[44].

Furthermore, the consumption of rice seems to be safe and well tolerated by FD patients^[45,46]. One could speculate that the lower content of gluten and FODMAPs compared to wheat and grain products could be involved in this favorable effect, but there are no evidences demonstrating this association to date.

Another emerging beneficial actor is ginger, thanks to its anti-inflammatory and antiemetic properties and its action on gastrointestinal motility^[46]. The main polyphenolic components of ginger, gingerols and shogaols, have an inhibitory effect on cholinergic M₃ and serotonergic 5-HT₃ receptors improving gastric motility, reducing nausea and vomiting and inducing an acceleration of gastric emptying^[47-51]. Despite the increasing knowledge of its physiological effects, in a small-sized open study, involving 11 FD patients, Ginger had no impact on gastric sensation, dyspeptic symptoms or gut peptides/hormones, while it displayed prokinetic effects^[50]. **Table 1** provides an overview of the role of specific foods and their contribution to FD

symptoms.

NUTRITIONAL APPROACH

In current clinical practice, dietary measures are often provided by physicians rather than nutritionists or dieticians and are frequently not supported by strong scientific evidences or are not systematically studied^[52].

No standardized nutritional guidelines for FD are available, to date.

This reflects the poor methodology and quality evidence and the considerable heterogeneity in dietary assessment methodology (food frequency questionnaires, 24-h recall methods) and outcomes measures (gastrointestinal symptoms scores, gastroduodenal motility, gastric emptying rates *etc.*), observed in published food-based trials^[20]. Most studies also fail to exclude the most common food intolerances (*i.e.* lactose intolerance) and/or are country or region-specific, exposing to an interpretation bias of published results.

A recent survey from China found a positive association between dyspepsia and irregular eating habits (skipping meals, dining out *etc.*), regardless of FD phenotype^[38]. According to the above, it is reasonable to advice the consumption of smaller and more frequent meals during the day. Moreover, a reduction of spicy, hot, acid-stimulating and high-fat foods seems to be effective in a subgroup of patients.

Due to its efficacy in reducing abdominal symptoms as pain, flatulence and bloating a dietician-led low-FODMAP diet can be now considered as a viable first-line therapy in IBS^[53]. Despite the known pathogenic and clinical overlap with IBS currently, there is lack of evidence demonstrating the effect of a FODMAPs reduction in FD^[54,55]. Only one recent Asiatic review examined the feasible role of low-FODMAPs diet in the management of FD^[56]. In 2017, Tan^[56] speculates on several expected mechanism of action by which a reduction of these carbohydrates could improve dyspeptic symptoms. Specifically, the reduction of both intestinal fermentation and osmotic load could correlate with a decreased stimulation of mechanoreceptors. On the other hand, a decreased production of short chain fatty acids could either reduce chemoreceptors stimulation or modulate immune response.

To date, the increasing evidences showing an implication of wheat-containing foods in inducing FD symptom, led several authors to investigate the effects of gluten-free regimens in FD patients^[30,31,57,58]. However, the gluten-free diet results in a marked reduction of dietary FODMAPs as well, offering potential interpretation biases^[59]. A specific investigation on the differential impact of gluten and FODMAPs restrictions on FD symptoms is necessary to clarify the mechanisms by which these nutrients could act on FD pathogenesis.

Taking to account the beneficial effect of ginger mentioned above, it could be reasonable to encourage its addition to diet. However, the effectiveness of ginger action seems to be dose-related and influenced by the instability and the ease of oxidation typical of polyphenolic compounds and their different bioavailability. Indeed, gingerols and shogaols concentrations strongly differ based on product type (fresh, dry, ground, crystallized...)^[60]. The role of dietary manipulations and specific foods in FD pathophysiology is summarized in [Figure 1](#).

CONCLUSION

At present, googling the entries “dyspepsia AND diet” leads to over 2570000 hits, witnessing the public interest on this topic. This combined with the lack of standardized dietary guidelines for FD, the uneven information provided by specialists and the vast diffusion of not validated nutritional advices results in an increasingly frequent tendency of patients to self-manage their symptoms. FD patients often tend to self-diagnose with “food intolerances” and arbitrarily restrict their diet, solely on the basis of their personal experience or anecdotal information from questionable sources. These improvised elimination diets are often nutritionally unbalanced and, if prolonged, could therefore cause nutritional deficiencies. Furthermore, long-term exclusion diets could enhance anxiety toward that food, increasing visceral hyperalgesia and contributing to symptoms anticipation.

This improper loop leads functional patients to perpetuate these eating-avoidant behaviors and to erroneously convince themselves of being “intolerant” to specific trigger foods^[61-63].

In spite of the growing public interest and pressing requests for standardized dietary advices from patients, very few randomized controlled trials were included in the present review and most available evidences represent extrapolations from

Table 1 Role of specific foods and their contribution to functional dyspepsia symptoms

Food	Active molecules	Study characteristics	Outcomes measurement	Proposed mechanisms of action	Effects	Ref.
Fatty foods	Lipids	Cross-sectional study (4 health subjects); Loxiglumide <i>vs</i> Loxiglumide plus fat Randomized crossover study (20 FD patients); Duodenal infusion of saline <i>vs</i> lipid solutions	Gastrointestinal contractile activity (manometry) Gastric volume measurement (gastric barostat)	Increased CCK release	(1) Hypersensitivity to gastrointestinal hormones; (2) Delayed gastric emptying; and (3) Symptoms exacerbation	[27] [28]
Almond	Tryptophan	Cross-sectional study (384 FD patients); Symptoms correlation with the intake of 114 different foods Double-blind RCT over placebo; Tandospirone <i>vs</i> placebo	Gastrointestinal symptoms measurement (VAS)	Indirect stimulation of serotonergic 5-HT1 and 5-HT4 receptors	(1) Improved gastric emptying; and (2) Symptoms improvement	[29] [33]
Pepper and Chili	Capsaicin	Cross-sectional study (121 FD patients); Symptom generation according to TRPV1 genotypes and the intake of spicy food Randomized crossover study (20 IBS-D patients); Standard meal <i>vs</i> spicy meal <i>vs</i> chili Double-blind trial over placebo (30 FD patients); Pepper <i>vs</i> placebo	TRPV1 polymorphisms (on blood samples) Gastrointestinal symptoms measurement (VAS) Gastrointestinal symptoms measurement (VAS)	Regulation of TRPV1 receptors	(1) Hyperalgesia (acute administration); and (2) Reduced visceral hypersensitivity (chronic administration)	[35] [36] [37]
Peppermint and Caraway oil		Cross-over study (6 health subjects); Peppermint caraway oil combination (enteric <i>vs</i> non enteric coated capsules) Randomized, double-blind trial over placebo (96 FD patients); Peppermints caraway oil <i>vs</i> placebo	Gastrointestinal motility (manometric study) Gastrointestinal symptoms measurement (VAS)	Allosteric effect on 5-HT3 receptors	(1) Antiemetic, Choleretic and spasmolytic action; and (2) Symptoms improvement	[41] [44]
Ginger	Gingerols and Shogaols	Double-blind trial over placebo (24 health subjects); Ginger <i>vs</i> placebo Randomized, double-blind trial over placebo (126 FD patients); inger <i>vs</i> placebo RCT over placebo (11 FD patients); inger <i>vs</i> placebo	Gastric emptying (US) Gastrointestinal symptoms score (VAS) Gastrointestinal symptoms (VAS) Gastric emptying (US), circulating hormones (GLP-1, motilin and ghrelin)	Inhibition of cholinergic M3 and serotonergic 5-HT3 receptors	(1) Enhanced gastric emptying; (2) Improved gastric motility; (3) Reduced nausea and vomiting; and (4) reduced inflammation	[47] [48] [50]

FODMAPs	FOS, GOS, Lactose, Fructose (excess), Polyols	Randomized crossover study (30 IBS patients and 8 health subjects); LFD <i>vs</i> Australian diet	Gastrointestinal symptoms score (VAS)	Increased intestinal fermentation Increased osmotic load	(1) Abnormal gas production; (2) Luminal water retention and abdominal distension; (3) Symptoms exacerbation; and (4) Enhanced duodenal inflammation
---------	---	---	---------------------------------------	---	--

[25]

5-HT1: 5-hydroxytryptamine subtype 1; 5-HT4: 5-hydroxytryptamine subtype 4; CCK: Cholecystokinin; FD: Functional dyspepsia; FODMAPs: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols; FOS: Fructo-oligosaccharides; GOS: Galacto-oligosaccharides; LFD: Low fodmaps diet; M3: Muscarinic receptor subtype 3; TRPV1: Transient receptor potential vanilloid subtype 1; GLP1: Glucagon-like peptide 1, US: Ultrasound, GI: Gastrointestinal; VAS: Visual analogue scale.

observational studies. Complicating the matter further stands the high degree of overlap between FD, gastro-esophageal reflux disease and IBS. For instance, the effects of a low-FODMAPs diet in FD could be overshadowed by the overlap with IBS symptoms, under- or over-estimating the effects of this dietary approach in FD patients^[56].

Taking into account the above considerations, it is vital to pursue a uniform and evidence-based nutritional approach in the management of FD patients and to design high-quality studies evaluating the impact of nutritional intervention. The growing number of mobile and smartphone-based apps, designed to collect dietary data and to objectively record nutritional interventions, offers the possibility to overcome the current limitations.

Therefore, well-structured and standardized guidelines are eagerly awaited in order to standardize the nutritional approach and satisfy FD patients unmet clinical needs.

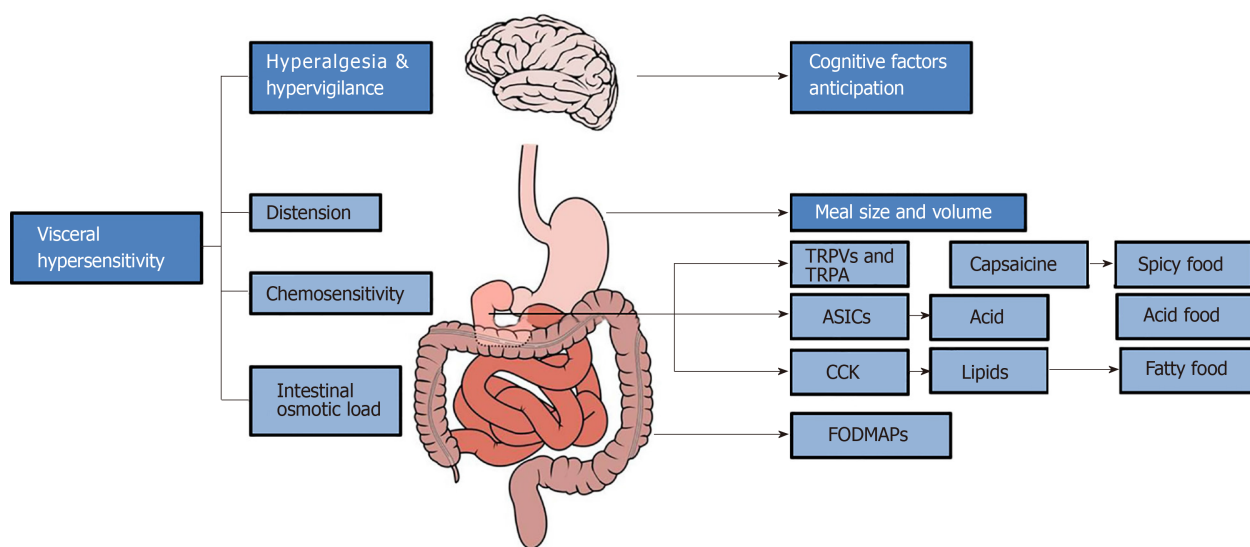


Figure 1 Role of dietary manipulations and specific foods in functional dyspepsia pathophysiology. ASICs: Acid-sensing ion channels; CCK: Cholecystokinin; FD: Functional dyspepsia; FODMAPs: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols; TRPA: Transient receptor potential ankyrin; TRPV: Transient receptor potential vanilloid.

REFERENCES

- 1 Tack J, Talley NJ. Functional dyspepsia--symptoms, definitions and validity of the Rome III criteria. *Nat Rev Gastroenterol Hepatol* 2013; **10**: 134-141 [PMID: 23399526 DOI: 10.1038/nrgastro.2013.14]
- 2 Mahadeva S, Ford AC. Clinical and epidemiological differences in functional dyspepsia between the East and the West. *Neurogastroenterol Motil* 2016; **28**: 167-174 [PMID: 26331919 DOI: 10.1111/nmo.12657]
- 3 D'Alessandro A, Zito FP, Pesce M, Andreozzi P, Efficie E, Cargiolli M, Maione F, De Palma GD, Cuomo R, Sarnelli G. Specific dyspeptic symptoms are associated with poor response to therapy in patients with gastroesophageal reflux disease. *United European Gastroenterol J* 2017; **5**: 54-59 [PMID: 28405322 DOI: 10.1177/2050640616650061]
- 4 Vanheel H, Carbone F, Valvekens L, Simren M, Tornblom H, Vanuytsel T, Van Oudenhove L, Tack J. Pathophysiological Abnormalities in Functional Dyspepsia Subgroups According to the Rome III Criteria. *Am J Gastroenterol* 2017; **112**: 132-140 [PMID: 27958284 DOI: 10.1038/ajg.2016.499]
- 5 Stanghellini V, Chan FK, Hasler WL, Malagelada JR, Suzuki H, Tack J, Talley NJ. Gastrointestinal Disorders. *Gastroenterology* 2016; **150**: 1380-1392 [PMID: 27147122 DOI: 10.1053/j.gastro.2016.02.011]
- 6 Tack J, Bisschops R, Sarnelli G. Pathophysiology and treatment of functional dyspepsia. *Gastroenterology* 2004; **127**: 1239-1255 [PMID: 15481001 DOI: 10.1053/j.gastro.2004.05.030]
- 7 Feinle-Bisset C, Meier B, Fried M, Beglinger C. Role of cognitive factors in symptom induction following high and low fat meals in patients with functional dyspepsia. *Gut* 2003; **52**: 1414-1418 [PMID: 12970132 DOI: 10.1136/gut.52.10.1414]
- 8 Komori K, Ihara E, Minoda Y, Ogino H, Sasaki T, Fujiwara M, Oda Y, Ogawa Y. The Altered Mucosal Barrier Function in the Duodenum Plays a Role in the Pathogenesis of Functional Dyspepsia. *Dig Dis Sci* 2019; **64**: 3228-3239 [PMID: 30673985 DOI: 10.1007/s10620-019-5470-8]
- 9 Friesen CA, Schurman JV, Colombo JM, Abdel-Rahman SM. Eosinophils and mast cells as therapeutic targets in pediatric functional dyspepsia. *World J Gastrointest Pharmacol Ther* 2013; **4**: 86-96 [PMID: 24199024 DOI: 10.4292/wjgpt.v4.i4.86]
- 10 Wang X, Li X, Ge W, Huang J, Li G, Cong Y, Li F, Liu Z, Liu Z, Li Y, Yuan H. Quantitative evaluation of duodenal eosinophils and mast cells in adult patients with functional dyspepsia. *Ann Diagn Pathol* 2015; **19**: 50-56 [PMID: 25735567 DOI: 10.1016/j.anndiagpath.2015.02.001]
- 11 Walker MM, Aggarwal KR, Shim LS, Bassan M, Kalantar JS, Weltman MD, Jones M, Powell N, Talley NJ. Duodenal eosinophilia and early satiety in functional dyspepsia: confirmation of a positive association in an Australian cohort. *J Gastroenterol Hepatol* 2014; **29**: 474-479 [PMID: 24304041 DOI: 10.1111/jgh.12419]
- 12 Karamanolis GP, Tack J. Current management of functional dyspepsia: impact of Rome III subdivision. *Ann Gastroenterol* 2012; **25**: 96-99 [PMID: 24714074]
- 13 Mazzawi T, Bartsch E, Benammi S, Ferro RMC, Nikitina E, Nimer N, Ortega LJ, Perrotte C, Python JV, Rosalina S, Sharp A, Stevano R, Hatlebakk JG, Hausken T. Gastric Emptying of Low- and High-Caloric Liquid Meals Measured Using Ultrasonography in Healthy Volunteers. *Ultrasound Int Open* 2019; **5**: E27-E33 [PMID: 30648161 DOI: 10.1055/a-0783-2170]
- 14 Pilchiewicz AN, Horowitz M, Holtmann GJ, Talley NJ, Feinle-Bisset C. Relationship between symptoms and dietary patterns in patients with functional dyspepsia. *Clin Gastroenterol Hepatol* 2009; **7**: 317-322 [PMID: 18929687 DOI: 10.1016/j.cgh.2008.09.007]
- 15 Tack J, Caenepeel P, Piessevaux H, Cuomo R, Janssens J. Assessment of meal induced gastric accommodation by a satiety drinking test in health and in severe functional dyspepsia. *Gut* 2003; **52**: 1271-1277 [PMID: 12912857 DOI: 10.1136/gut.52.9.1271]
- 16 Carvalho RV, Lorena SL, Almeida JR, Mesquita MA. Food intolerance, diet composition, and eating patterns in functional dyspepsia patients. *Dig Dis Sci* 2010; **55**: 60-65 [PMID: 19160046 DOI: 10.1007/s10620-008-0698-8]
- Filipović BF, Randjelovic T, Kovacevic N, Milinić N, Markovic O, Gajić M, Filipović BR. Laboratory

- 17 parameters and nutritional status in patients with functional dyspepsia. *Eur J Intern Med* 2011; **22**: 300-304 [PMID: 21570652 DOI: 10.1016/j.ejim.2011.01.012]
- 18 Tack J, Caenepeel P, Fischler B, Piessevaux H, Janssens J. Symptoms associated with hypersensitivity to gastric distention in functional dyspepsia. *Gastroenterology* 2001; **121**: 526-535 [PMID: 11522735 DOI: 10.1053/gast.2001.27180]
- 19 Boeckxstaens GE, Hirsch DP, van den Elzen BD, Heisterkamp SH, Tytgat GN. Impaired drinking capacity in patients with functional dyspepsia: relationship with proximal stomach function. *Gastroenterology* 2001; **121**: 1054-1063 [PMID: 11677196 DOI: 10.1053/gast.2001.28656]
- 20 Duncanson KR, Talley NJ, Walker MM, Burrows TL. Food and functional dyspepsia: a systematic review. *J Hum Nutr Diet* 2018; **31**: 390-407 [PMID: 28913843 DOI: 10.1111/jhn.12506]
- 21 Ryan AT, Feinle-Bisset C, Kallas A, Wishart JM, Clifton PM, Horowitz M, Luscombe-Marsh ND. Intraduodenal protein modulates antropyloroduodenal motility, hormone release, glycemia, appetite, and energy intake in lean men. *Am J Clin Nutr* 2012; **96**: 474-482 [PMID: 22854403 DOI: 10.3945/ajcn.112.038133]
- 22 Keshmeli AH, Haghighatdoost F, Azadbakht L, Daghighzadeh H, Feinle-Bisset C, Afshar H, Feizi A, Esmailzadeh A, Adibi P. Dietary glycaemic index and glycaemic load and upper gastrointestinal disorders: results from the SEPAHAN study. *J Hum Nutr Diet* 2017; **30**: 714-723 [PMID: 28634998 DOI: 10.1111/jhn.12480]
- 23 Colombel JF, Shin A, Gibson PR. AGA Clinical Practice Update on Functional Gastrointestinal Symptoms in Patients With Inflammatory Bowel Disease: Expert Review. *Clin Gastroenterol Hepatol* 2019; **17**: 380-390.e1 [PMID: 30099108 DOI: 10.1016/j.cgh.2018.08.001]
- 24 Eswaran S, Farida JP, Green J, Miller JD, Chey WD. Nutrition in the management of gastrointestinal diseases and disorders: the evidence for the low FODMAP diet. *Curr Opin Pharmacol* 2017; **37**: 151-157 [PMID: 29156449 DOI: 10.1016/j.coph.2017.10.008]
- 25 Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology* 2014; **146**: 67-75.e5 [PMID: 24076059 DOI: 10.1053/j.gastro.2013.09.046]
- 26 Vanheel H, Farré R. Changes in gastrointestinal tract function and structure in functional dyspepsia. *Nat Rev Gastroenterol Hepatol* 2013; **10**: 142-149 [PMID: 23318268 DOI: 10.1038/nrgastro.2012.255]
- 27 De Giorgio R, Stanghellini V, Ricci Maccarini M, Morselli-Labate AM, Barbara G, Franzoso L, Rovati LC, Corinaldesi R, Barbara L, Go VL. Effects of dietary fat on postprandial gastrointestinal motility are inhibited by a cholecystokinin type A receptor antagonist. *Ann N Y Acad Sci* 1994; **713**: 226-231 [PMID: 8185163 DOI: 10.1111/j.1749-6632.1994.tb44069.x]
- 28 Feinle C, Meier O, Otto B, D'Amato M, Fried M. Role of duodenal lipid and cholecystokinin A receptors in the pathophysiology of functional dyspepsia. *Gut* 2001; **48**: 347-355 [PMID: 11171824 DOI: 10.1136/gut.48.3.347]
- 29 Akhondi-Meybodi M, Aghaei MA, Hashemian Z. The role of diet in the management of non-ulcer dyspepsia. *Middle East J Dig Dis* 2015; **7**: 19-24 [PMID: 25628849]
- 30 Elli L, Tomba C, Branchi F, Roncoroni L, Lombardo V, Bardella MT, Ferretti F, Conte D, Valiante F, Fini L, Forti E, Cannizzaro R, Maiero S, Londoni C, Lauri A, Fornaciari G, Lenoci N, Spagnuolo R, Basilisco G, Somalvico F, Borgatta B, Leandro G, Segato S, Barisani D, Morreale G, Buscarini E. Evidence for the Presence of Non-Celiac Gluten Sensitivity in Patients with Functional Gastrointestinal Symptoms: Results from a Multicenter Randomized Double-Blind Placebo-Controlled Gluten Challenge. *Nutrients* 2016; **8**: 84 [PMID: 26867199 DOI: 10.3390/nu8020084]
- 31 Santolaria S, Alcedo J, Cuartero B, Diez I, Abascal M, García-Prats MD, Marigil M, Vera J, Ferrer M, Montoro M. Spectrum of gluten-sensitive enteropathy in patients with dysmotility-like dyspepsia. *Gastroenterol Hepatol* 2013; **36**: 11-20 [PMID: 23103052 DOI: 10.1016/j.gastrohep.2012.07.011]
- 32 Mawe GM, Hoffman JM. Serotonin signalling in the gut--functions, dysfunctions and therapeutic targets. *Nat Rev Gastroenterol Hepatol* 2013; **10**: 473-486 [PMID: 23797870 DOI: 10.1038/nrgastro.2013.105]
- 33 Miwa H, Nagahara A, Tominaga K, Yokoyama T, Sawada Y, Inoue K, Ashida K, Fukuchi T, Hojo M, Yamashita H, Tomita T, Hori K, Oshima T. Efficacy of the 5-HT_{1A} agonist tandospirone citrate in improving symptoms of patients with functional dyspepsia: a randomized controlled trial. *Am J Gastroenterol* 2009; **104**: 2779-2787 [PMID: 19638966 DOI: 10.1038/ajg.2009.427]
- 34 Vanheel H, Vicario M, Vanuytsel T, Van Oudenhove L, Martinez C, Keita ÁV, Pardon N, Santos J, Söderholm JD, Tack J, Farré R. Impaired duodenal mucosal integrity and low-grade inflammation in functional dyspepsia. *Gut* 2014; **63**: 262-271 [PMID: 23474421 DOI: 10.1136/gutjnl-2012-303857]
- 35 Lee SY, Masaoka T, Han HS, Matsuzaki J, Hong MJ, Fukuhara S, Choi HS, Suzuki H. A prospective study on symptom generation according to spicy food intake and TRPV1 genotypes in functional dyspepsia patients. *Neurogastroenterol Motil* 2016; **28**: 1401-1408 [PMID: 27094759 DOI: 10.1111/nmo.12841]
- 36 Gonlachanvit S, Mahayosnond A, Kullavanijaya P. Effects of chili on postprandial gastrointestinal symptoms in diarrhoea predominant irritable bowel syndrome: evidence for capsaicin-sensitive visceral nociception hypersensitivity. *Neurogastroenterol Motil* 2009; **21**: 23-32 [PMID: 18647268 DOI: 10.1111/j.1365-2982.2008.01167.x]
- 37 Bortolotti M, Coccia G, Grossi G, Miglioli M. The treatment of functional dyspepsia with red pepper. *Aliment Pharmacol Ther* 2002; **16**: 1075-1082 [PMID: 12030948 DOI: 10.1046/j.1365-2036.2002.01280.x]
- 38 Xu JH, Lai Y, Zhuang LP, Huang CZ, Li CQ, Chen QK, Yu T. Certain Dietary Habits Contribute to the Functional Dyspepsia in South China Rural Area. *Med Sci Monit* 2017; **23**: 3942-3951 [PMID: 28809820 DOI: 10.12659/msm.902705]
- 39 Chiarioni G, Pesce M, Fantin A, Sarnelli G. Complementary and alternative treatment in functional dyspepsia. *United European Gastroenterol J* 2018; **6**: 5-12 [PMID: 29435308 DOI: 10.1177/2050640617724061]
- 40 Lacy BE, Talley NJ, Locke GR, Bouras EP, DiBaise JK, El-Serag HB, Abraham BP, Howden CW, Moayyedi P, Prather C. Review article: current treatment options and management of functional dyspepsia. *Aliment Pharmacol Ther* 2012; **36**: 3-15 [PMID: 22591037 DOI: 10.1111/j.1365-2036.2012.05128.x]
- 41 Micklefield GH, Greving I, May B. Effects of peppermint oil and caraway oil on gastroduodenal motility. *Phytother Res* 2000; **14**: 20-23 [PMID: 10641042 DOI: 10.1002/(sici)1099-1573(200002)14:1<20::aid-ptr542>3.0.co;2-z]
- 42 Heimes K, Hauk F, Verspohl EJ. Mode of action of peppermint oil and (-)-menthol with respect to 5-HT₃ receptor subtypes: binding studies, cation uptake by receptor channels and contraction of isolated rat

- ileum. *Phytother Res* 2011; **25**: 702-708 [PMID: [21077259](#) DOI: [10.1002/ptr.3316](#)]
- 43 **Chumpitazi BP**, Kearns GL, Shulman RJ. Review article: the physiological effects and safety of peppermint oil and its efficacy in irritable bowel syndrome and other functional disorders. *Aliment Pharmacol Ther* 2018; **47**: 738-752 [PMID: [29372567](#) DOI: [10.1111/apt.14519](#)]
 - 44 **May B**, Köhler S, Schneider B. Efficacy and tolerability of a fixed combination of peppermint oil and caraway oil in patients suffering from functional dyspepsia. *Aliment Pharmacol Ther* 2000; **14**: 1671-1677 [PMID: [11121917](#) DOI: [10.1046/j.1365-2036.2000.00873.x](#)]
 - 45 **Gonlachanvit S**. Are rice and spicy diet good for functional gastrointestinal disorders? *J Neurogastroenterol Motil* 2010; **16**: 131-138 [PMID: [20535343](#) DOI: [10.5056/jnm.2010.16.2.131](#)]
 - 46 **Miwa H**, Ghoshal UC, Fock KM, Gonlachanvit S, Gwee KA, Ang TL, Chang FY, Hongo M, Hou X, Kachintorn U, Ke M, Lai KH, Lee KJ, Lu CL, Mahadeva S, Miura S, Park H, Rhee PL, Sugano K, Vilaichone RK, Wong BC, Bak YT. Asian consensus report on functional dyspepsia. *J Gastroenterol Hepatol* 2012; **27**: 626-641 [PMID: [22142407](#) DOI: [10.1111/j.1440-1746.2011.07037.x](#)]
 - 47 **Wu KL**, Rayner CK, Chuah SK, Changchien CS, Lu SN, Chiu YC, Chiu KW, Lee CM. Effects of ginger on gastric emptying and motility in healthy humans. *Eur J Gastroenterol Hepatol* 2008; **20**: 436-440 [PMID: [18403946](#) DOI: [10.1097/MEG.0b013e3282f4b224](#)]
 - 48 **Giacosa A**, Guido D, Grassi M, Riva A, Morazzoni P, Bombardelli E, Perna S, Faliva MA, Rondanelli M. The Effect of Ginger (*Zingiber officinalis*) and Artichoke (*Cynara cardunculus*) Extract Supplementation on Functional Dyspepsia: A Randomised, Double-Blind, and Placebo-Controlled Clinical Trial. *Evid Based Complement Alternat Med* 2015; **2015**: 915087 [PMID: [25954317](#) DOI: [10.1155/2015/915087](#)]
 - 49 **Abdel-Aziz H**, Windeck T, Ploch M, Verspohl EJ. Mode of action of gingerols and shogaols on 5-HT₃ receptors: binding studies, cation uptake by the receptor channel and contraction of isolated guinea-pig ileum. *Eur J Pharmacol* 2006; **530**: 136-143 [PMID: [16364290](#) DOI: [10.1016/j.ejphar.2005.10.049](#)]
 - 50 **Hu ML**, Rayner CK, Wu KL, Chuah SK, Tai WC, Chou YP, Chiu YC, Chiu KW, Hu TH. Effect of ginger on gastric motility and symptoms of functional dyspepsia. *World J Gastroenterol* 2011; **17**: 105-110 [PMID: [21218090](#) DOI: [10.3748/wjg.v17.i1.105](#)]
 - 51 **Nikkhah Bodagh M**, Maleki I, Hekmatdoost A. Ginger in gastrointestinal disorders: A systematic review of clinical trials. *Food Sci Nutr* 2019; **7**: 96-108 [PMID: [30680163](#) DOI: [10.1002/fsn3.807](#)]
 - 52 **Ansari S**, Ford AC. Initial management of dyspepsia in primary care: an evidence-based approach. *Br J Gen Pract* 2013; **63**: 498-499 [PMID: [23998837](#) DOI: [10.3399/bjgp13X671821](#)]
 - 53 **Gibson PR**. The evidence base for efficacy of the low FODMAP diet in irritable bowel syndrome: is it ready for prime time as a first-line therapy? *J Gastroenterol Hepatol* 2017; **32** Suppl 1: 32-35 [PMID: [28244668](#) DOI: [10.1111/jgh.13693](#)]
 - 54 **Outlaw WM**, Koch KL. Dyspepsia and its overlap with irritable bowel syndrome. *Curr Gastroenterol Rep* 2006; **8**: 266-272 [PMID: [16888867](#)]
 - 55 **Wang A**, Liao X, Xiong L, Peng S, Xiao Y, Liu S, Hu P, Chen M. The clinical overlap between functional dyspepsia and irritable bowel syndrome based on Rome III criteria. *BMC Gastroenterol* 2008; **8**: 43 [PMID: [18808723](#) DOI: [10.1186/1471-230X-8-43](#)]
 - 56 **Tan VP**. The low-FODMAP diet in the management of functional dyspepsia in East and Southeast Asia. *J Gastroenterol Hepatol* 2017; **32** Suppl 1: 46-52 [PMID: [28244670](#) DOI: [10.1111/jgh.13697](#)]
 - 57 **Kaess H**, Kellermann M, Castro A. Food intolerance in duodenal ulcer patients, non ulcer dyspeptic patients and healthy subjects. A prospective study. *Klin Wochenschr* 1988; **66**: 208-211 [PMID: [3361798](#) DOI: [10.1007/bf01728198](#)]
 - 58 **Du L**, Shen J, Kim JJ, He H, Chen B, Dai N. Impact of gluten consumption in patients with functional dyspepsia: A case-control study. *J Gastroenterol Hepatol* 2018; **33**: 128-133 [PMID: [28452428](#) DOI: [10.1111/jgh.13813](#)]
 - 59 **De Giorgio R**, Volta U, Gibson PR. Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction? *Gut* 2016; **65**: 169-178 [PMID: [26078292](#) DOI: [10.1136/gutjnl-2015-309757](#)]
 - 60 **Baliga MS**, Haniadka R, Pereira MM, D'Souza JJ, Pallaty PL, Bhat HP, Popuri S. Update on the chemopreventive effects of ginger and its phytochemicals. *Crit Rev Food Sci Nutr* 2011; **51**: 499-523 [PMID: [21929329](#) DOI: [10.1080/10408391003698669](#)]
 - 61 **Lee IS**, Preissl H, Giel K, Schag K, Enck P. Attentional and physiological processing of food images in functional dyspepsia patients: A pilot study. *Sci Rep* 2018; **8**: 1388 [PMID: [29362408](#) DOI: [10.1038/s41598-017-19112-0](#)]
 - 62 **Reed-Knight B**, Squires M, Chitkara DK, van Tilburg MA. Adolescents with irritable bowel syndrome report increased eating-associated symptoms, changes in dietary composition, and altered eating behaviors: a pilot comparison study to healthy adolescents. *Neurogastroenterol Motil* 2016; **28**: 1915-1920 [PMID: [27353222](#) DOI: [10.1111/nmo.12894](#)]
 - 63 **Mari A**, Hosadurg D, Martin L, Zarate-Lopez N, Passananti V, Emmanuel A. Adherence with a low-FODMAP diet in irritable bowel syndrome: are eating disorders the missing link? *Eur J Gastroenterol Hepatol* 2019; **31**: 178-182 [PMID: [30543574](#) DOI: [10.1097/MEG.0000000000001317](#)]



Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

