

Lian-Sheng Ma

Editor-in-Chief

World Journal of Gastroenterology

15 Sep 2023

Dear Dr Prof. Ma,

Re: Manuscript reference No. 86823

Please find attached a revised version of our manuscript "*Colorectal Motility Patterns and Psychiatric Traits in Functional Constipation and Constipation-Predominant Irritable Bowel Syndrome: A Study from Eastern China*", which we would like to resubmit for publication as a "Observational study" in "*World Journal of Gastroenterology*".

Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. I have revised the manuscript according to the Editorial Office's comments and suggestions. Uniform presentations are used for figures showing the same or similar contents decomposable. Decomposable Figures (in which all components are movable and editable) are provided and organized into a single PowerPoint file with copyright information in the bottom right-hand side. Standard three-line tables are also provided. The manuscript has been sent to a professional English language editing company to polish the language and the English Language Certificate issued by AJE has been obtained. Reference Citation Analysis has been used to supplement and improve the highlights of the latest cutting-edge research results.

In the following pages are our point-by-point responses to each of the comments of the reviewers. Revisions in the text are shown using yellow highlight for additions. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in *World Journal of Gastroenterology*.

Responses to the comments of Reviewer #1

1. *I am not qualified to comment on the gastrointestinal aspects of the differences between functional constipation (FC) and irritable bowel syndrome with constipation (IBS-C). However, it is somewhat surprising that the authors claim that there is limited data on these disorders from China. A recent systematic review*

and meta-analysis on prevalence and risk factors for functional constipation from China identified 39 population-based cross-sectional studies on the subject (Chen et al. Front Med (Lausanne). 2022 Feb 16; 9:815156. doi: 10.3389/fmed.2022.815156). Significantly enough, this meta-analysis found a higher prevalence of anxiety, depression, and poor sleep quality among persons with FC compared with those without FC. Similarly, a recent bibliometric analysis of studies of depression and anxiety in IBS showed that the largest number of publications were from the USA (833, 32.51%), followed by China (316, 12.33%), UK (302, 11.79%), Sweden (172, 6.71%), and Australia (162, 6.32%) [Chen et al. 2022 Front. Public Health 10:947097. doi: 10.3389/fpubh.2022.947097]

Responses: Thanks for the comments. There are indeed many studies of psychiatric features on FC or IBS-C from China. However, clinical studies which attempt to illuminate distinctive physiological mechanisms between FC and IBS-C are predominantly from Western countries, and data from Chinese populations remain scarce. In our study, we compared not only psychiatric features, but also colorectal motility, and the correlations between psychiatric and colorectal motility characteristics between FC and IBS-C patients. I have revised the manuscript to make these innovative points clearer and more logical.

- 2. The second limitation of such hospital-based studies, particularly from specialty clinics is that there is a significant referral bias affecting hospital attendees. For a very long time it has been known that people who attend hospitals with functional bowel complaints differ from those in the community not in the nature of bowel symptoms, but in their psychosocial profile. Hospital attendees have a very high rates of depressive, anxiety, or somatoform disorders. Symptoms of depression and anxiety are also far more common in them as are maladaptive personality traits. Consultations are often triggered by stressful life events and studies have also shown an association with childhood abuse (Farthing 1995, BMJ; Zamani et al. Aliment Pharmacol Ther. 2019 Jul;50(2):132-143; Staudacher et al. Lancet Gastroenterol Hepatol. 2021 May;6(5):401-410; Hu et al. BMC Gastroenterol. 2021 Jan 7;21(1):23). Therefore hospital-based studies may not be representative of the actual psychosocial profile of functional bowel disorders. There are two implications of these facts for the present study. Firstly, hospital-based studies have to be supplemented by community-based studies to reveal the true profiles of different functional bowel disorders. The authors should comment on this significant limitation of their study. Secondly, the range of psychological and psychological problems associated with these disorders is much wider than investigated in this study. This is another limitation that deserves an explanation.*

Response: We deeply appreciate the reviewer's suggestion. We agree with the reviewer's comments. Following the reviewer's suggestion, we have added these limitations in the Discussion section, and highlighted the added contents with yellow color in the revised manuscript.

Responses to the comments of Reviewer #2

1. *Nice study about the Psychiatric and colonic motility in IBS-C and FC patients. The comments are as follows: 1. There are already studies and known facts about the patients of Chronic constipation and its association with Psychiatric symptoms in many and also impairment of colonic motility. This study is not new.*

Response: We appreciate the reviewer's positive evaluation of our work. There are indeed many studies on psychiatric symptoms and colonic motility of chronic constipation. However, the comparison of colorectal motility, psychiatric features, and the association of colorectal motility patterns and psychiatric traits between FC and IBS-C groups, especially in Chinese population has not been fully studied. In our study, we compared not only colorectal motility and psychiatric features, but also the correlations between psychiatric and colorectal motility characteristics in FC and IBS-C patients. Our findings underscored both overlaps and distinctive patterns of colon transit, dyssynergic pattern, anorectal sensation, psychological distress, and also associations of psychiatric and colorectal motility characteristics between FC and IBS-C in Eastern Chinese populations. Moreover, we used the Hamilton scales which have better application reliability and validity to assess psychological distress. The Sitzmarks capsule we used to assess colonic transit time was the only radiopaque markers approved by FDA. These mentioned above are all our innovation and highlights.

2. *There is significant mismatch in the number of patients in IBS-C Vs FC. Conclusions drawn are not without errors.*

Responses: Thanks for the comments. Our study recruited all the patients diagnosed with FC and IBS-C from the Anhui provincial hospital's motility clinic between December 2019 and February 2023. The ratio of IBS-C patients and FC patients represents the true outcomes in our center. Our conclusions are entirely based on our investigation and results reported in previous literature.

3. *The exact clinical usefulness of the study is not new.*

Responses: Thanks for the comments. Actually, we have got some novel and meaningful results, parts of which have never been reported in China, or are discrepant from western studies. for example:

- 1) Our study showed a higher prevalence of RSARM and elevated anal resting pressure in FC patients compared to IBS-C patients, suggesting that DD might be more prevalent among Chinese FC patients. Furthermore, we observed that nearly half of the FC patients with RSARM exhibited Type IV dyssynergia, a prevalence nearly double that of IBS-C patients, implying distinct pathogeneses of DD in FC and IBS-C patients. Our data also showed that IBS-C patients with NTC were more likely to experience anxiety compared to those with STC. However, we found no significant correlations between psychological stress and colonic motility in FC patients.

These findings have never been reported in China. The associations of psychological stress and colonic motility in our study are discrepant from results of western studies, indicating that emotional factors may have varying effects on colonic motility between these two patient groups.

- 2) In our study, we speculated that FC patients with Type IV dyssynergia and IBS-C patients with Type III dyssynergia are more likely to have DD, and further BET or defecography might not be necessary for these patients. Our results suggested Type I or II dyssynergia cannot rule out the need for CTT in CC patients, while it might not be necessary for FC patients with Type IV dyssynergia and IBS-C patients with Type III dyssynergia to undergo CTT, but further BET or defecography might still be necessary.

The correlations of CTT and ARM are rarely studied. What we have found in this study could provide guidance for constipation patients to choose appropriate colorectal tests.

Responses to the comments of Reviewer #3

1. *Good but need some revision*

Responses: We appreciate the reviewer's positive evaluation of our work. We apologize for the language problems in the original manuscript. We have sent our revised manuscript to a professional English language editing company to polish the language.

We would like to thank you all again for taking the time to review our manuscript.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

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