OPEN

Clinical Characteristics of Different Primary Constipation Subtypes in a Chinese Population

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Goal: To investigate the clinical characteristics of different primary constipation subtypes, including symptom clusters, psychological problems, quality of life (QOL), and to explore the role of constipation symptoms and the mental state in the QOL of constipation subtypes.

Background: Patients with chronic constipation (CC) may be unsatisfied with their therapy and suffer recurrent symptoms. Different constipation subtypes require different treatments; therefore, it is important to identify the features of different constipation subtypes.

Study: CC patients (n = 206) visiting our gastroenterology clinic were studied. CC subtypes were diagnosed using the Rome-IV criteria. We used validated questionnaires to investigate the symptom severity, mental state, and QOL of patients. QOL was assessed with the Patient Assessment of Constipation Quality of Life (PAC-QOL) and SF-36 questionnaire. Results of symptom, mental and QOL scores are expressed as means with 95% confidence interval.

Results: Three groups of CC patients differed in their constipation scoring system and the Patient Assessment of Constipation Symptoms (PAC-SYM) total scores, and both were significantly higher in the functional defecation disorder (FDD) group compared with that in the normal transit constipation (NTC) group. FDD patients tended to have more severe "abdominal symptoms," "rectal symptoms" than NTC group. No significant difference in General Anxiety Disorder 7-item or Patient Health Questionnaire-9 results was found among the 3 groups. Significantly more patients with FDD suffered more "physical discomfort" and had poorer QOL in the "physical function" dimension of SF-36. FDD and NTC patients mainly showed associations between CC-related QOL and constipation severity, while slow transit constipation patients' QOL was significantly associated with anxiety and depression.

Conclusion: Patients with FDD suffer more severe constipation symptoms and have a lower QOL than patients in other CC subgroups. FDD and NTC patients' QOL is mainly linked to constipation symptoms, while that of slow transit constipation is mainly related to mental states such as anxiety and depression.

Key Words: chronic constipation, constipation subtypes, anxiety, depression, quality of life

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C onstipation is a common complaint worldwide. Chronic constipation (CC, course > 6 mo) can be divided into 2 main categories: primary and secondary. Primary constipation is a common functional gastrointestinal disorder characterized by reduced bowel movements and/or difficult defecation. The prevalence of constipation in the general population is ~20%, although it can vary from 2% to 27% in the United States,^{1,2} and 16% to 20% in China,³ depending on the definition used and the population studied. Female gender, increasing age, socioeconomic status, and educational level seemed to affect the prevalence of constipation.⁴

The most common constipation symptoms include abdominal pain or discomfort, hard stools, feeling of incomplete evacuation, excessive straining, sense of anorectal blockage, and the need for manual maneuvers.²

CC requires different management approaches depending on whether the colonic transit time is normal or prolonged, and whether the outlet function is abnormal.⁵ The American Gastroenterological Association divides primary constipation into 3 main types: functional defecation disorder (FDD), slow transit, and normal transit.⁶ Different subtypes have different clinical manifestations and need different therapeutic regimens; therefore, it is important to identify the characteristics of different constipation subtypes in order to guide treatment for refractory patients. High-resolution anorectal manometry (HR-ARM),⁷ balloon expulsion test (BET),⁸ and colon transit time (CTT)⁹ are useful tools to distinguish the different constipation subtypes.

Constipation has a significant impact on quality of life (QOL), affecting both physical and emotional wellbeing.^{10,11} Patients with constipation may experience poorer QOL.¹² Previous studies reported that CC causes greater school and work absenteeism, as well as loss of productivity.^{10,12,13} QOL in CC has been shown to be affected by gender, age, disease severity, and psychiatric symptoms; however, the relationship with CC subtype is unclear. A study from Mexico showed QOL differences in patients with different constipation subtypes, and the patients with irritable bowel syndrome with constipation (IBS-C) were the most affected compared with the other subtypes.¹⁴

In the present study, we investigated patients with primary constipation to identify the clinical symptoms, mental state, and QOL associated with the different subtypes. To better understand the QOL of patients suffering from different CC subtypes, we studied the factors that may be associated with disease-specific QOL.

MATERIALS AND METHODS

Participants

This is a retrospective clinical study. The data were collected between January 2014 and January 2018 at the

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TABLE 1. Constipation Symptoms					
Constipation Severity	FDD, n = 124 (M/F 46/78)	STC, n = 36 (M/F 8/28)	NTC, n = 46 (M/F 6/40)	F	Р
CSS	15.78 (15.13, 16.44)	15.25 (13.57, 16.93)	13.67 (12.40, 14,94)	4.52	0.012
PAC-SYM	1.50 (1.41, 1.59)	1.35 (1.16, 1.54)	1.27 (1.12, 1.42)	3.51	0.032
Abdominal	1.08 (0.95, 1.21)	0.90 (0.66, 1.13)	0.83 (0.66, 1.00)	2.62	0.076
Rectal	0.63 (0.50, 0.76)	0.57 (0.36, 0.79)	0.49 (0.28, 0.69)	0.73	0.482
Stool	2.36 (2.22, 2.51)	2.17 (1.88, 2.47)	2.08 (1.87, 2.29)	2.38	0.095

CSS: FDD versus NTC: P = 0.003; PAC-SYM: FDD versus NTC: P = 0.013; Abdominal: FDD versus NTC: P = 0.038; Stool: FDD versus NTC: P = 0.043. CSS indicates constipation scoring system; F, female; FDD, functional defecation disorder; M, male; NTC, normal transit constipation; PAC-SYM, the Patient Assessment of Constipation Symptoms; STC, slow transit constipation.

gastrointestinal motility clinic of the First Affiliated Hospital of Nanjing Medical University. Patients who were diagnosed with CC via the Rome IV questionnaires¹⁵ were further classified into 3 subtypes¹⁶: normal transit, slow transit, and FDD. The exclusion criteria were as follows: (1) pregnant patients, or those with structural diseases (like tumor, rectocele or intussusception) diagnosed by colonoscopy and/or barium enema; (2) a history of gastrointestinal surgery; (3) underlying chronic conditions (eg, endocrine, metabolic, neurological, diagnosed with anxiety or a depressive disorder); (4) taking drugs that could affect defecation, such as antidepressants, spasmolytics, or opioids, with the exception of hypnotics; and (5) patients with abuse history. As a result, 206 patients with CC were eligible in our study.

Ethical Considerations

This study was performed according to the ethical standards for human experimentation. The clinical research committee of the First Affiliated Hospital of Nanjing Medical University approved the study protocol. All patients involved in our study were voluntary and informed consent was obtained from all participants after explaining the aim of the study.

Methods

Every enrolled patient was subjected to HR-ARM, BET, and CTT examinations, and completed the following questionnaires.

Constipation Symptoms

The Constipation Scoring System (CSS) scale¹⁷ was used to measure the severity of the constipation symptoms, in which higher scores suggested more severe constipation. We used the Patient Assessment of Constipation Symptoms (PAC-SYM)¹⁸ to measure patients' subjective feelings about constipation, specifically those related to abdominal symptoms, rectal symptoms, and defecation symptoms, with higher scores indicating more severe symptoms.

Anxiety and Depression Symptoms

General Anxiety Disorder 7-item (GAD-7)¹⁹ and Patient Health Questionnaire-9 (PHQ-9)²⁰ were adopted to measure the severity of anxiety and depression symptoms, respectively. The reliability and validity of these tools have been verified.^{21,22} In both questionnaires, higher scores suggested more severe mental symptoms.

QOL

The self-reported Patient Assessment of Constipation Quality of Life (PAC-QOL) questionnaire specifically assesses the QOL of patients diagnosed with constipation.²³ It contains 28 items divided into 4 subscales (physical discomfort, psychosocial discomfort, worry/anxiety, and satisfaction with treatment). We calculated the subscale scores by taking the mean of the items in each subscale. The subscale scores varied from 0 (absent) to 4 (very severe). The total scores were calculated by taking the mean of the subscales. Higher total and subscale scores indicated poorer constipation-related QOL.

The SF-36 questionnaire measures general healthrelated QOL and includes 8 dimensions: physical functioning, role limitations due to physical health, pain, general health, vitality, social functioning, role limitations due to emotional problems, and emotional well-being.²⁴ In contrast to PAC-QOL, a higher score for each subscale indicated better health-related QOL.

Subgroups

According to the colonic transit and anorectal function, patients with CC were classified into 3 subtypes: FDD, slow transit constipation (STC), and normal transit constipation (NTC), although overlap is not uncommon. FDD are characterized by primarily impaired rectal evacuation, with normal or delayed colonic transit. Incomplete rectal evacuation is associated with poor coordination of the pelvic floor and the anal sphincter.²⁵ It may result from inadequate rectal propulsive forces and/or increased resistance to evacuation.² STC is mostly characterized by reduced phasic colonic motor activity, resulting in a prolonged intestinal transit time and lack of the urge to defecate. NTC is a common subtype and is characterized by constipation

TABLE 2. Anxiety and Depression						
Mental State	FDD, n = 124 (M/F 46/78)	STC, n = 36 (M/F 8/28)	NTC, n = 46 (M/F 6/40)	F	Р	
GAD-7	5.77 (5.01, 6.53)	3.92 (2.53, 5.30)	5.35 (4.22, 6.48)	2.79	0.064	
PHQ-9	5.52 (4.80, 6.23)	4.33 (3.10, 5.57)	5.15 (4.08, 6.23)	1.32	0.270	

GAD-7: FDD versus STC: P = 0.019.

F indicates female; FDD, functional defecation disorder; GAD-7, General Anxiety Disorder 7-item; M, male; NTC, normal transit constipation; PHQ-9, Patient Health Questionnaire-9; STC, slow transit constipation.

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TABLE 3. Constipation-related Quality of Life					
PAC-QOL Items	FDD, n = 124 (M/F 46/78)	STC, n = 36 (M/F 8/28)	NTC, n = 46 (M/F 6/40)	F	Р
PAC-QOL	1.71 (1.59, 1.82)	1.55 (1.34, 1.76)	1.69 (1.50, 1.89)	0.86	0.424
PD	1.54 (1.41, 1.68)	1.20 (0.94, 1.46)	1.13 (0.91, 1.35)	6.51	0.002
PSD	1.11 (0.98, 1.25)	0.92 (0.71, 1.13)	1.12 (0.85, 1.39)	0.93	0.395
W/A	1.68 (1.52, 1.83)	1.51 (1.22, 1.81)	1.87 (1.63, 2.11)	1.72	0.181
Satisfaction	2.85 (2.70, 3.00)	2.92 (2.63, 3.21)	2.73 (2.49, 2.98)	0.501	0.607

PD: FDD versus STC: P = 0.017; FDD versus NTC: P = 0.002.

F indicates female; FDD, functional defecation disorder; M, male; NTC, normal transit constipation; PAC-QOL, Patient Assessment of Constipation Quality of Life; PD, physical discomfort; PSD, psychosocial discomfort; STC, slow transit constipation; W/A, worry/anxiety.

occurring in the presence of normal colonic transit time and normal defecatory function. According to some previous studies, patients with NTC are regarded as belonging to the irritable bowel syndrome (IBS) group.²⁶ Anorectal manometry, BET, defecography, and colonic transit test can be helpful in classifying CC categories.⁷ Overlap patients have been excluded in order to clarify the results clearly. CC patients were not allowed to take laxatives 3 days before HR-ARM, BET, and CTT examinations to exclude the medicine interference in the results of tests.

HR-ARM

A novel solid-state HR-ARM device (Manoscan AR 360; Given Imaging, Yoquem, Israel) with 12 sensors was used. Patients were studied in the left lateral decubitus position with hips flexed to 90 degrees, after defecation. The catheter was placed with the rectal balloon 3 cm proximal to the superior aspect of the external anal sphincter. Parameters were collected in the following order: anal pressure at rest (20 to 30 s), during squeeze (3 attempts for a maximum duration of 20 to 30 s), and bearing down as in defecation (typically 20 to 30 s, 3 times).²⁶ Rectal sensation was simultaneously evaluated by incrementally distending the rectal balloon by 10 mL from 0 to 300 mL; threshold volumes for first sensation, urgency, and maximum discomfort were recorded.

BET

We measured the time taken for patients to expel a balloon filled with 50 mL of warm water from the rectum while seated a commode in privacy. If 3 minutes went by with no expulsion, the balloon was removed²⁷ and the BET result was regarded as positive. BET is used as a screening tool for FDD.

CTT

CTT was evaluated using radiopaque marker techniques. Patients ingested 20 radiopaque markers (tube-shaped, with a diameter of 2 mm and a length of 6 mm) on day 1, and erect abdominal plain radiographs were obtained 48 and 72 hours later. The x-rays were analyzed to count the number and distribution of the markers. Delayed colon transit was recognized when there were >4 markers throughout the colon at 72 hours.^{9,28}

Statistical Analysis

All data input, data processing, and statistical analysis were performed using SPSS version 20.0 (IBM Corp., Armonk, NY). The different constipation subtype scores were compared using parametric statistics for CSS, GAD-7, PHQ-9, and each of the areas of the PAC-SYM, PAC-QOL, and SF-36 questionnaires. Differences among the 3 groups were analyzed using 1-way analysis of variance (ANOVA). Continuous data were expressed as means with 95% confidence intervals (CIs). The relationship between QOL and constipation symptom severity, anxiety as well as depression symptoms in different subtypes were analyzed using the Pearson correlation. Statistical significance was set at a *P*-value <0.05.

RESULTS

Among the 425 patients with CC who visited the outpatient gastroenterology motility center, 306 were eligible to participate in the study. However, only 231 patients (ranging from 13 to 81 y old) with the mean age of 46.95 (\pm 16.26 SD) years completed all the examinations (HR-ARM, BET, and CTT) and questionnaires. Among them, there were 25 patients of overlap subtype and were excluded afterwards. In the end, 206 CC patients were enrolled for our study.

SF-36 Items	FDD, $n = 124$ (M/F 46/78)	STC, $n = 36$ (M/F 8/28)	NTC, $n = 46$ (M/F 6/40)	F	P		
Physical functioning	88.55 (85.99, 91.12)	95.14 (90.79, 99.48)	93.70 (90.32, 97.07)	4.66	0.011		
Role limitations due to physical health	64.67 (57.04, 72.30)	67.36 (53.09, 81.63)	73.91 (62.85, 84.98)	0.84	0.435		
Pain	83.74 (80.08, 87.40)	86.33 (80.42, 92.24)	86.78 (82.43, 91.13)	0.57	0.57		
General health	45.37 (41.44, 49.31)	52.92 (44.13, 61.70)	52.20 (45.18, 59.21)	2.36	0.097		
Vitality	64.34 (60.50, 68.18)	71.11 (64.04, 78.19)	65.11 (58.61, 71.60)	1.42	0.245		
Social functioning	71.63 (67.25, 76.02)	81.60 (74.56, 88.64)	76.63 (70.34, 82.92)	2.83	0.061		
Role limitations due to emotional problems	61.71 (54.01, 69.40)	62.96 (48.00, 77.92)	62.32 (49.18, 75.45)	0.01	0.987		
Emotional well-being	63.50 (59.91, 67.10)	68.89 (62.42, 75.36)	60.91 (53.96, 67.87)	1.55	0.215		

Physical functioning: FDD versus STC: P = 0.01; FDD versus NTC: P = 0.028; Social functioning: FDD versus STC: P = 0.024. F indicates female; FDD, functional defecation disorder; M, male; NTC, normal transit constipation; STC, slow transit constipation.

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FIGURE 1. The role of chronic constipation and mental health in quality of life of FDD patients. CSS indicates constipation scoring system; FDD, functonal defecation disorder; GAD, General Anxiety Disorder 7-item; PAC-QOL, Patient Assessment of Constipation Quality of Life; PHQ-9, Patient Health Questionnaire-9. [full core]

CC Subtype Comparison

The complete 206 patient data sample consisted of 124 patients with FDD (M/F: 46/78), 36 with STC (M/F: 8/28), and 46 with NTC (M/F: 6/40). We compared age, BMI, gender, constipation duration, symptom severity, psychological state, and QOL scores among them. Patients' ages, BMIs and duration of constipation in 3 groups showed no significant difference while there was a gender difference among 3 subtypes (P=0.005) and a significant difference between FDD and NTC (P=0.002).

Severity of Constipation Symptoms

The comparison among the three groups showed a significant difference (P = 0.012) by the CSS score. Upon comparing individual groups, the FDD group (15.78; 95% CI: 15.13-16.44) had a higher score, compared with that in the NTC group (13.67; 95% CI: 12.40-14.94) (P = 0.003). Three groups also differed significantly in their PAC-SYM total scores (P = 0.032) and the FDD group (1.50; 95% CI: 1.41-1.59) showed a significantly higher score than that in the NTC group (1.27; 95% CI: 1.12-1.42) (P = 0.013). Besides, the FDD group had more severe abdominal and rectal symptoms than the NTC group, with significant differences (P = 0.038 and 0.043) (Table 1).

Anxiety and Depression

The mean GAD-7 and PHQ-9 scores for the entire data sample were 5.35 (n = 206; SD = 4.17) and 5.23 (n = 206; SD = 3.87), respectively. Further ANOVA analysis demonstrated no significant difference among the CC subtypes in terms of mean GAD-7 (P=0.064) and PHQ-9 values (P=0.27). However, the FDD group (5.77; 95% CI: 5.01-6.53) showed a significantly higher GAD-7 score than that in the STC group (3.92; 95% CI: 2.53-5.30) (P=0.019) (Table 2).

PAC-QOL

In Table 3, ANOVA analysis showed a significant difference (P=0.002) for the "physical discomfort" score among the 3 groups. There was also a difference in this subscale when comparing the FDD (1.54; 95% CI: 1.41-1.68) and STC groups (1.20; 95% CI: 0.94-1.46) (P=0.017) as well as the FDD and NTC groups (1.13; 95% CI: 0.91-1.35) (P=0.002). In relation to PAC-QOL total score and scores for other subscales, no significant differences were observed (P-values all > 0.05).

SF-36

As shown in Table 4, there was a statistically significant difference in "physical function" scores among the 3 groups (P=0.011). The FDD group showed a significantly lower score (88.55; 95% CI: 85.99-91.12) than that of the STC group (95.14; 95% CI: 90.79-99.48) (P=0.01) and the NTC group (93.70; 95% CI: 90.32-97.07) (P=0.028), signifying that the patients with FDD experienced a poorer physical condition than those with STC and NTC.

There was no significant difference among the 3 groups for "social function" of SF-36; however, there was a difference in this subscale between the FDD group and STC group (P = 0.024, 71.63; 95% CI: 67.25-76.02 vs. 81.60; 95% CI: 74.56-88.64), indicating that patients with FDD suffered more social dysfunction than those with STC.

One-way ANOVA demonstrated no statistically significant difference in SF-36 scores for other dimensions (physical limitation, emotional well-being, pain, general health, energy, and mental health) among FDD, STC, and NTC (*P*-values all > 0.05).

The Role of CC and Mental Health in QOL

As shown in Figures 1–3, the total scores for PAC-QOL were positively associated with the CSS scores in patients with FDD and NTC (P both <0.05). Their correlation indexes were over 0.30, which indicated that constipation severity significantly impaired constipation-related



FIGURE 2. The role of chronic constipation and mental health in quality of life of STC patients. CSS indicates constipation scoring system; GAD, General Anxiety Disorder 7-item; PHQ-9, Patient Health Questionnaire-9; STC, slow transit constipation.

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FIGURE 3. The role of chronic constipation and mental health in quality of life of NTC patients. CSS indicates constipation scoring system; GAD, General Anxiety Disorder 7-item; NTC, normal transit constipation; PHQ-9, Patient Health Questionnaire-9.

QOL, especially in the FDD and NTC subgroups. The GAD-7 and PHQ-9 scores were both obviously correlated with the PAC-QOL total scores in all 3 subgroups, especially in the STC group (correlation indexes of 0.695 and 0.59). In addition, CSS was related to the "physical function" scores of SF-36 only in FDD patients (correlation indexes 0.30, P = 0.001). Furthermore, the STC subgroup showed "physical function" scores in SF-36 were significantly correlated with the GAD-7 and PHQ-9 scores (correlation indexes -0.345 and -0.364).

DISCUSSION

Early diagnostic testing for constipation is not routinely recommended in the absence of alarm signs. A treat-and-test approach is practical and cost effective when testing and can be pursued in patients who are refractory to conservative treatment.¹¹ The specific recognition of CC subtypes can guide clinicians to treat refractory patients with high efficiency.

In this investigation of CC patients' manifestations at a tertiary care clinic, we found that FDD patients had more severe constipation symptoms and a significantly worse disease-specific, as well as general, QOL compared with those in the STC and NTC subtypes. Constipation symptoms mainly contributed to the QOL in patients with FDD and NTC, while patients with STC showed a close association between mental state and QOL. To the best of our knowledge, the data and analysis is unique in demonstrating subtype-specific clinical differences in a Chinese CC population.

CC is known to interfere with a patient's physical wellbeing and health-related QOL including mental health, daily activities, and work productivity. Regarding the impact of CC on the daily lives of patients, 69% considered that it impairs their academic or occupational performance.13 A systematic review in 2010 indicated all SF-36 domains were impaired in constipation patients as compared with those in healthy controls.²⁹ However, limited data is available regarding the effect of CC subtype on patients' daily life. Early identification of different CC subtypes could help physicists to choose the correct therapies for patients. Early diagnosis of FDD is very useful in clinical practice, because the response to biofeedback (BFB) therapy is better than that to standard therapy.^{30,31} Patients with NTC should never be treated with extreme measures, but only be relieved by modified lifestyle and oral drugs. Furthermore, patients with STC commonly experience clinical worsening in response to routine laxatives; however, sacral nerve root neuromodulation and subtotal colectomy with ileorectal anastomosis for highly selected STC cases will be more beneficial.³² Our aim was to investigate the clinical characteristics of different subtypes to provide clues to treat patients with CC more efficiently.

On the basis of the results of our study, FDD patients showed significantly more severe symptoms than other constipation subtypes, both in the subjective (PAC-SYM) and objective (CSS) rating scales. Patients with the FDD subtype usually manifest with prolonged straining and incomplete evacuation. FDD is mainly associated with anal canal relaxation deficiency, paradoxical contraction, or dyssynergic defecation.³³ FDD responds poorly to routine treatments, including lifestyle modification, laxatives, and surgery. The first-line treatment for FDD is BFB.³⁴ BFB delivered by experienced therapists is effective to relieve constipation symptoms and improve patients' QOL.²⁶

Previous studies have shown an obvious link between constipation and mental disorders. Mood disorders, such as anxiety and depression, are more prevalent in individuals with CC than in the general population.35 Nehra et al³⁶ reported that 65% of CC patients had psychological problems. In a nonselected population of constipated patients, severe anxiety was an independent factor to predict constipation symptoms and the only predictive factor for choosing coping strategies.³⁷ Increased anxiety is associated with increased rectal compliance.³⁸ Depression may play an important role in the slow transit of the intestines. In our study, patients with FDD showed more anxiety than those with STC significantly, though no statistical difference in depression severity was seen among 3 subtypes. Patients with FDD made more complaints of physical discomfort; therefore, we speculated that anxiety might worsen the pelvic dysfunction in the FDD subtype and constipation might aggravate anxiety disorder in CC patients in turn.

Patients with chronic disorders not only suffer from physical discomfort, but are also affected socially and mentally.³⁹ Patients with functional gastrointestinal disorders, especially CC, have been shown to experience poorer QOL.¹² A previous study reported that CC disrupted productivity on 1.2 to 3.2 days per month, the duration of this disruption depending on the prominence of abdominal symptoms.40 From our findings, patients with FDD had more severe constipation symptoms and poorer diseaserelated QOL than the other 2 subtypes, especially for the "physical discomfort" item, which was in agreement with previous studies. According to the SF-36 tool, patients with FDD were the most affected group, when compared with those with STC and NTC, even though the difference was only in the "physical function" dimension. However, in another study that investigated the QOL of different CC subtypes based on ROME III criteria, patients with IBS-C (most are NTC) were the most affected group compared with the other groups, according to SF-36, even though the differences were in only a few aspects.14

In relation to the factors contributing to QOL of CC patients, we investigated the relationship between constipation

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severity, anxiety, depression, and disease-specific QOL, as well as general QOL. There was no doubt that constipation has an important impact on QOL, regardless of culture or nationality.¹⁴ It has been reported that PAC-QOL scores were worse in constipated patients with more severe symptoms than that in those with mild to moderate constipation.⁴¹ Our results also suggested that constipation severity plays a vital role in constipation-related QOL of FDD and NTC groups compared with that in the STC group. With regards to general QOL, constipation only had a slight impact on the "physical function" dimension in FDD patients, while no significant relationship was seen between constipation symptoms and general QOL in patients with STC or NTC. We speculate that these findings result from different mechanisms of constipation and severity of physical symptoms of different CC subtypes.

With respect to the influence of mental state on QOL of different CC patients, anxiety, and depression were closely associated with disease-specific QOL and the "physical function" dimension of general QOL in individuals with STC. Anxiety and depression were demonstrated to play a role in the constipation-related QOL of patients with FDD and NTC; however, no significant relationship was found between mental state and the "physical function" dimension of SF-36 in these 2 subtypes. No similar previous studies have reported these correlations.

A major strength of this study is the detailed classification of CC patients based on the ROME IV criteria and the use of well-validated, robust questionnaires. This was the first study conducted among a Chinese population to evaluate the QOL of patients with CC, both generally and by specific subgroups. In addition, determining the different characteristics of the CC subtypes might help clinicians to choose more specific and efficient therapies for patients with CC. However, some important limitations should be mentioned. First, a potential limitation was that our findings may not be easily generalized to patients with CC in the primary care setting, because the sample was derived from a single third-class hospital. Our patients suffered from severe rather than varying degrees of constipation. Second, our sample sizes of STC and NTC are relatively small and the sex ratios are different in 3 subgroups, which may lead to statistic bias. In further studies, we will enlarge our samples and conduct the subgroup analysis based on gender in order to eliminate the effect of gender-related differences in CC subtypes, and then we will draw a more robust conclusion. Third, there are more factors known to affect the QOL in CC other than disease severity and mental state. We might have underestimated the impact of other factors. We hope that future research will be conducted to address these defects.

According to this study, patients with different CC subtypes had different clinical features; therefore, systematized evaluations of patients with CC are particularly important for their better long-term management, especially for refractory patients. However, patients with defecatory difficulty continue to represent a significant management challenge for physicians. BFB therapy, although effective for patients with FDD, is time-consuming and available only in certain centers. The literature on the management of refractory patients lacks high quality comparative studies.

CONCLUSIONS

The results of the present study suggested that constipated patients with FDD suffer more severe physical symptoms and have lower QOL than patients in other CC subgroups. The QOL of patients with FDD and NTC is mainly linked to constipation symptoms, while the QOL of patients with STC is mostly related to mental state, such as anxiety and depression. Thus, clinicians need to pay special attention to patients with CC whose symptoms interfere in their daily activities and social reactions, which are more prominent in the FDD subtype than in the other subtypes. To improve the QOL of patients with CC, it seems reasonable that more attention should be paid to relieving constipation for patients with FDD and NTC, while to improving mental health of patients with STC. To date, CC remains a poorly understood and under-investigated issue, despite being very common. It is high time that clinicians and modern medicine united to control this disorder.

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