Clinical Value of Positive BET and Pelvic Floor Dyssynergia in Chinese Patients with Functional Defecation Disorder

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Research Article

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Abstract

Background

Functional defecation disorder (FDD) is a common subtype of functional constipation (FC). Balloon expulsion test (BET) and high resolution anorectal manometry (HR-ARM) are significant tools but their results are not always consistent.

Aims

To investigate the characteristics of patients with positive BET and pelvic floor dyssynergia (PFD) and explore the value of both positive results in FDD diagnosis.

Methods

We retrospectively diagnose FC subtypes and enrolled FDD patients based on Rome-IV criteria. They underwent HR-ARM, BET and CTT tests. Then they were classified to 2 groups and further stratified by FDD subtypes. Validated questionnaires were applied to investigate patients' constipation, anxiety/depression and quality of life.

Results

335 FDD patients were finally enrolled. They were classified into 2 groups according to whether BET and PFD were both positive (consistent or not). 84.48% showed consistent results. These patients had significantly higher anal residual pressure, lower anal relaxation rate, MDI and a more negative RAPG (Ps < 0.05). The specific distribution of FDD phenotypes in two groups showed significant difference ($P = 0.021$). Males suffered a more negative RAPG ($P < 0.001$) and age was correlated with anal relaxation rate ($P < 0.001$). 177 individuals among them were investigated with validated questionnaires. Scores for Defecation Symptoms, Physical Discomfort and GAD-7 score were significantly high in Consistent Group (Ps < 0.05). GAD-7 score was associated with Defecation Symptoms ($P < 0.001$) while anal residual pressure, GAD-7 and Defecation Symptoms score were linked to Physical Discomfort (Ps < 0.05). The diagnostic specificity and PPV for FDD rose significantly with positive BET and PFD.

Conclusion

FDD patients with positive BET and PFD suffer severe defecation symptoms, anxiety and impaired QOL. Positive BET and PFD could be an ideal tool for screening FDD.

Introduction

Functional constipation (FC) is a common disease impairing patients' well-being worldwide but some individuals are dissatisfied with their therapy, which is probably related to not targeting the underlying pathophysiology. Functional defecation disorder (FDD) is an important but under-recognized subtype of FC, referring to the paradoxical contraction and/or inadequate relaxation of the pelvic floor muscles during attempted defecation[1], which affects nearly one half of constipated patients[2]. FDD impairs patients' mental health and quality of life (QOL) much more than other subtypes[3]. There are three FDD phenotypes based on High resolution anorectal manometry (HR-ARM): high anal sphincter pressure during defecation, inadequate propulsive force, and hybrid of both disturbance[4] so it's essential to identify pathophysiology of FDD. HR-ARM and balloon expulsion test (BET) are pivotal in investigation of anorectal disorders[5] and more relevant with treatment outcomes[6].

BET is a convenient, inexpensive and accessible tool used for identifying patients with FDD. It provides an assessment of patients' ability to evacuate artificial stool during simulated defecation within the laboratory environment. However, its sensitivity and specificity are not consistent in various studies. Positive BET alone does not sufficiently predict response to biofeedback treatment. HR-ARM indirectly evaluates anorectal function by measuring recto-anal pressures and motor coordination and assessing rectal sensation, reflexes, and rectal compliance for FDD diagnosis. However, this test costs much more and less accessible in primary clinics.

There is no single gold standard for FDD diagnosis[7]. In a majority of FDD cases, positive BET is consistent with pelvic floor dyssynergia (PFD), defined as the failure to relax or paradoxical contraction of puborectalis muscle and anal sphincters during straining on manometry, imaging and/or EMG[8, 9]. However, there is exception. Our study aimed to find difference between patients with and without positive BET and PFD and explore the associated factors. Furthermore, we tried to assess the value of positive BET and PFD in detecting FDD individuals.

Methods

It's a retrospective clinical study, conducted on patients in the gastrointestinal motility clinic of the First Affiliated Hospital of Nanjing Medical University from January 2015 to October 2019. We used Rome IV criteria retrospectively to enroll the target patients. Patients with drug-induced, organic lesion-associated constipation, a history of prior anorectal surgery, inflammatory bowel disease or an abuse history were excluded. This study was approved by the Ethical Committee of the First Affiliated Hospital with Nanjing Medical University (No. 2020-SR-061).

Every enrolled patient was subjected to HR-ARM, BET, and colonic transit time (CTT) tests.

HR-ARM. A high resolution solid-state anorectal manometry device (Manoscan AR 360; Given Imaging, Yoquem, Israel) with 12 sensors was used in this study. Patients underwent it in the left lateral decubitus position with hips flexed to 90° after using enemas. The proficient doctor placed the catheter with a rectal balloon 3 cm proximal to the superior aspect of the external anal sphincter. The absolute parameters

were collected in the following order: Anal resting pressure (20 to 30 s), anal sphincter length, duration of sustained squeeze, anal pressure during squeeze (three attempts for a maximum duration of 20 to 30 s), rectal and anal residual pressure during attempted defecation (typically 20 to 30 s, three times)[10]. 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.

In this study, not only absolute pressure values but also quantification of pressure changes in the rectum and anus during attempted defecation were recorded and interpreted (anal relaxation rate, MDI and RAPG). Manometric defecation index (MDI) is the ratio of rectal pressure to anal pressure during simulated defecation (rectal /anal pressure). RAPG was defined by the difference between the rectal pressure and anal pressure during attempted defecation (rectal pressure minus anal pressure)[11].

BET. We measured the time taken for patients to expel a balloon filled with 50 mL of warm water from the rectum in the left lateral decubitus position in privacy. If 3 minutes went by with no expulsion, the balloon was removed[12] and the BET was regarded as positive.

CTT. CTT was evaluated using radiopaque marker techniques[13]. Patients ingested 20 radiopaque markers (tube-shaped, with a diameter of 2 mm and a length of 6 mm) on day 1 morning. Erect abdominal plain radiographs were obtained 48 and 72 hours later. The X-rays were analyzed to count the remanent number and distribution of the markers. Delayed colon transit was recognized when more than 4 markers were observed throughout the colon at 72 hours. When remanent radiopaque markers are scattered in the whole digestive tract, STC could be diagnosed. While more than half of remanent markers were in sigmoid colon and rectum, patients are considered as FDD[14]. This has been shown to be reproducible in 70% of the patients being evaluated for constipation[15].

Diagnostic criteria for FDD

The ROME IV diagnostic criteria for FDD are as follows[16]. During repeated attempts to defecate must satisfy at least 2 of the following: (a) evidence of impaired evacuation based on balloon expulsion test; (b) inappropriate contraction of the pelvic floor muscles or inadequate propulsive forces by manometry or EMG; and (c) impaired rectal evacuation by imaging. In this study, we diagnosed patients with FDD when they had two or more abnormal results of f HR-ARM, BET and CTT tests. ROME IV separates FDD into two subtypes: (1) paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation (dyssynergic defecation, DD); (2) inadequate propulsive forces during attempted defecation (inadequate defecatory propulsion, IDP).

Group

Patients were classified into 2 groups according to whether BET and PFD were both positive or not. Then data were further stratified by FDD subtypes based on HR-ARM results (IDP: rectal defecation pressure < 40mmHg and DD: anal relaxation rate < 20% or RAPG < 0 with normal rectal defecation pressure).

177 out of 335 patients completed the following questionnaires.

Living habits. We investigated patients' daily water intake, physical exercises and sleep quality.

Constipation Symptoms. FDD patients were asked about their spontaneous bowel movements (SBMs) (times per week), stool consistency using Bristol Stool Formation Scale(BSFS)and defecation time during last 6 months. Then we used Constipation Symptoms (PAC-SYM)[17] to measure patients' subjective feelings about constipation, with higher scores indicating more severe symptoms.

Anxiety and depression symptoms. General Anxiety Disorder 7-item (GAD-7)[18] and Patient Health Questionnaire-9 (PHQ-9)[19] were adopted to measure anxiety and depression symptoms, respectively. In both questionnaires, higher scores suggested more severe mental symptoms.

QOL. The Patient Assessment of Constipation Quality of Life (PAC-QOL) questionnaire specifically assesses constipated patients' QOL[20]. It contains 28 items divided into four subscales (physical discomfort, psychosocial discomfort, worry/anxiety, and satisfaction with treatment). The subscale scores varied from 0 (absent) to 4 (very severe). Higher total and subscale scores indicated poorer constipation-related QOL.

Statistical analysis

Statistical analyses were conducted with SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous data were presented as mean ± SD; otherwise, the data were presented as median (interquartile range). Categorical data were analyzed using chi-square tests, and continuous variables were analyzed using independent-sample *t*-tests or rank-sum tests. Spearman's correlation was used to measure the relationships between variables. Statistical significance was set at a *P*-value less than 0.05.

Results

Demography

62.73% FC patients (534) were diagnosed as FDD (335) and finally enrolled. They were classified into 2 groups according to positive BET and PFD (consistent or not). In total, 84.48% FDD (283) patients showed both positive BET and PFD. Two groups did not differ in BMI, constipation duration, daily water intake, exercise frequency and sleep quality (Table 1). There were older (52.81 ± 15.73 and 42.17 ± 14.74,$P < 0.001$) and more males in Consistent Group ($P < 0.001$).

Table 1
Demographic data

	Consistent Group(n = 283)	Inconsistent Group(n = 52)	t/Z	P
BMI	22.42 ± 2.86	21.78 ± 2.68	1.357	0.177
Constipation Duration	5.00(8.00)	7.00(6.25)	-1.603	0.109
Water Intake	2.00(2.00)	2.00(0.50)	-0.70	0.484
Sleep quality	2.00(2.00)	2.00(1.00)	-0.234	0.815
Exercise frequency	1.00(2.00)	2.00(2.00)	-1.067	0.286

FDD patients were further separated into IDP (197) and DD (138) subgroup. 80.71% (159 out of 197) patients were with positive BET and PFD results in IDP Group and 89.86% (124 out of 138) in DD Group, respectively (P = 0.023).

HR-ARM variables analyses

As shown in Table 2, Consistent Group showed significantly higher anal residual pressure, lower anal relaxation rate, a more negative median RAPG and lower MDI than Inconsistent Group (Ps < 0.001). DD was predominant in Consistent Group compared with that in Inconsistent Group (43.82% vs 26.92%, P = 0.023). Hybrid phenotype of FDD was the most in Consistent Group, followed by high anal sphincter pressure phenotype while inadequate propulsive force phenotype was the mainstream in Inconsistent Group. The specific distribution of FDD phenotype had significant difference (P = 0.021).

Table 2
HR-ARM variables of Consistent Group and Inconsistent Group In Total FDD patients

Total FDD patients	**BET consistent with PFD (n = 283)**	**BET inconsistent with PFD (n = 52)**	***t/Z***	***P***
Anal resting pressure (mm Hg)	85.50(31.5)	87.95(39.47)	0.578	0.563
Anal sphincter length (cm)	3.80(1.30)	3.35(1.08)	3.048	0.002
Duration of sustained squeeze (s)	19.20(10.10)	17.75(8.70)	0.872	0.383
Maximum squeeze pressure(mm Hg)	223.00(101.10)	213.95(69.63)	0.427	0.669
Rectal defecation pressure (mm Hg)	37.80(24.80)	31.10(17.00)	1.558	0.119
Anal residual pressure (mm Hg)	99.30(38.40)	63.55(26.38)	7.355	< 0.001
First sensation volume (mL)	40.00(30.00)	40.00(31.25)	0.50	0.617
Urge to defecate (mL)	100.00(70.00)	100.00(50.00)	0.943	0.346
Maximum tolerable volume (mL)	150.00(110.00)	150.00(73.75)	0.433	0.665
Anal relaxation rate (%)	-10.15(43.64)	28.55(29.93)	8.393	< 0.001
RAPG (mm Hg)	-61.61 ± 34.06	-30.69 ± 24.71	6.248	< 0.001
MDI	0.38(0.28)	0.49(0.33)	3.635	< 0.001
Abbreviations: RAPG rectal and anal pressure gradient; MDI: manometric defecation index				

Furthermore, similar results were observed in both FDD subtypes (*P*s < 0.001, Table 3–4). In terms of rectal sensation, in DD Group, volume for urge to defecate was larger in Consistent Group than that in Inconsistent Group (*P* = 0.044).

Table 3
HR-ARM Variables of Consistent Group and Inconsistent Group in IDP

IDP	BET consistent with PFD (n = 159)	BET inconsistent with PFD (n = 38)	*t/Z*	*P*
Anal resting pressure (mm Hg)	89.10(35.60)	81.25(44.25)	0.288	0.773
Anal sphincter length (cm)	3.80(1.30)	3.45(1.08)	1.921	0.055
Duration of sustained squeeze (s)	20.00(10.40)	18.60(8.98)	0.709	0.478
Maximum squeeze pressure(mm Hg)	225.50(93.10)	211.00(78.32)	0.553	0.581
Rectal defecation pressure (mm Hg)	31.20(19.80)	31.30(16.15)	0.879	0.380
Anal residual pressure (mm Hg)	98.35 ± 30.98	69.95 ± 24.04	4.95	< 0.001
First sensation volume (mL)	40.00(30.00)	40.00(35.00)	0.004	0.997
Urge to defecate (mL)	100.00(70.00)	100.00(66.25)	0.042	0.966
Maximum tolerable volume (mL)	150.00(100.00)	165.00(120.00)	0.451	0.652
Anal relaxation rate (%)	-6.33(34.70)	-21..02(27.90)	5.836	< 0.001
RAPG (mm Hg)	-68.83 ± 32.55	-38.47 ± 22.62	5.083	< 0.001
MDI	0.31(0.20)	0.40(0.27)	4.414	0.003

Abbreviations: RAPG rectal and anal pressure gradient; MDI: manometric defecation index;

Table 4
HR-ARM Variables of Consistent Group and Inconsistent Group In DD

DD	BET consistent with PFD (n = 124)	BET inconsistent with PFD (n = 14)	*t/Z*	*P*
Anal resting pressure (mm Hg)	83.90(30.83)	84.70(31.22)	0.032	0.975
Anal sphincter length (cm)	3.80(1.10)	3.25(1.12)	1.581	0.114
Duration of sustained squeeze (s)	18.85(8.83)	18.10(8.73)	0.638	0.523
Maximum squeeze pressure(mm Hg)	229.55(110.67)	211.65(78.58)	0.063	0.949
Rectal defecation pressure (mm Hg)	52.45(25.38)	55.00(32.90)	0.448	0.654
Anal residual pressure (mm Hg)	109.08 ± 38.38	79.51 ± 34.57	3.45	0.001
First sensation volume (mL)	40.00(27.50)	40.00(23.00)	1.053	0.292
Urge to defecate (mL)	100.00(67.50)	80.00(60.00)	2.017	0.044
Maximum tolerable volume (mL)	150.00(100.00)	130.00(78.75)	1.297	0.195
Anal relaxation rate (%)	-17.97(49.29)	17.51(48.25)	3.498	< 0.001
RAPG (mm Hg)	-49.14 ± 30.97	-17.34 ± 30.21	3.651	< 0.001
MDI	0.54(0.30)	0.80(0.58)	3.001	0.003

Abbreviations: RAPG rectal and anal pressure gradient; MDI: manometric defecation index

In total FDD patients, males showed significantly higher anal residual pressure (101.2[36.85] vs 88.45[45.50], $P < 0.001$), lower anal relaxation rate (-26.34% [52.11%] vs 3.48% [34.53%], $P < 0.001$) and lower RAPG (-62.37 ± 35.09 vs -52.97 ± 33.85, $P = 0.014$) than females. Male patients made up higher percentage in Consistent Group (45.94% vs 13.46%, $P < 0.001$). Due to the small number of males in Inconsistent Group (only 7 patients), data analysis separated by gender could not be performed. It's indicated that male gender was associated with anal residual pressure ($P < 0.001$), anal relaxation rate ($P < 0.001$) and RAPG ($P = 0.037$) in total FDD patients. Patients in Consistent Group were older (52y vs 41.5y, $P = 0.001$). Besides, age was negatively correlated with anal relaxation rate (r=-0.236, $P < 0.001$). However, no correlation was seen between age and anal residual pressure, RAPG or MDI.

The similar results were observed in IDP patients, in other words, there were more males (X^2 = 15.15, P< 0.001) and patients were older (Z = 2.83, P = 0.005) in Consistent Group. However, DD patients did not differ in gender and age between Consistent and Inconsistent Group.

Clinical manifestation evaluation

177 FDD patients were investigated by validated questionnaires. Among them, 128 patients were with both positive BET and PFD. Compared with Inconsistent Group, score for Defecation Symptoms was significantly high (P = 0.021) while other items in PAC-SYM showed no difference (Table 5). SBMs, BSFS and defecation duration did not differ between two groups. Mental evaluation suggested GAD-7 score was higher in Consistent Group (P = 0.036), however, PHQ-9 scores were not significantly different between two groups.

Table 5
Constipation symptoms of patients with FDD

Constipation Symptoms	**Consistent Group(n = 128)**	**Inconsistent Group(n = 49)**	***t/Z***	***P***
SBMs	2.00(4.00)	1.50(3.00)	0.847	0.397
Bristol Stool Type	2.00(3.00)	2.00(3.00)	0.027	0.978
Defecation Duration	3.00(1.00)	2.00(1.00)	1.067	0.286
PAC-SYM				
Abdominal Symptoms	1.00(1.00)	1.00(1.00)	0.564	0.573
Rectal Symptoms	0.33(1.00)	0.33(0.84)	0.737	0.461
Defecation Symptoms	2.40(1.20)	2.00(1.20)	2.312	0.021
Total Score	1.42(0.75)	1.42(0.75)	1.754	0.079
Abbreviations: SBMs: spontaneous bowel movements; PAC-SYM: patient assessment of constipation symptom				

As shown in Table 6, score for Physical Discomfort was significantly higher in Consistent Group (P = 0.01) whereas there was no difference in Psychosocial Discomfort, Worry/Anxiety, Satisfaction items and PAC-QOL total score. However, when analyzing constipation and related QOL in IDP and DD patients separately, no significant difference was observed between Consistent and Inconsistent Groups.

Table 6
Constipation related QOL of patients with FDD

PAC-QOL	Consistent Group(*n* = 128)	Inconsistent Group(*n* = 49)	*t/Z*	*P*
Physical Discomfort	1.50(1.00)	1.00(1.13)	-2.578	0.01
Psychosocial Discomfort	1.00(1.12)	1.00(1.00)	-0.325	0.745
Worry/Anxiety	1.73 ± 0.94	1.53 ± 0.89	1.296	0.198
Satisfaction	3.00(1.20)	2.80(1.40)	-1.498	0.134
Total score	1.70 ± 0.67	1.57 ± 0.67	1.174	0.244
Abbreviations: PAC-QOL: patient assessment of constipation quality of life				

Furthermore, score for Defecation Symptoms was correlated with GAD-7 score (r = 0.323, $P < 0.001$). Physical Discomfort was correlated with anal residual pressure (r = 0.167, $P = 0.027$), GAD-7 (r = 0.344, $P < 0.001$) as well as Defecation Symptoms score (r = 0.388, $P < 0.001$).

Diagnostic value of positive BET and PFD

534 FC patients were included in our analyses. The diagnostic sensitivity and specificity of BET for FDD was 95.82% and 66.83% while the diagnostic sensitivity and specificity of PFD was 87.46% and 71.86%, respectively. BET had a positive predictive value (PPV) of 82.95% and a negative predictive value (NPV) of 90.47% while PFD had a PPV of 83.95% and a NPV of 77.30%. The diagnostic specificity and PPV rose to 100% when BET and PFD were both positive.

We further studied the diagnostic value of positive BET and PFD in FDD subtypes. The diagnostic sensitivity was 80.51% and specificity was 63.42% in IDP patients. The diagnostic sensitivity and specificity in DD patients was 89.86% and 60.35%, respectively.

Discussion

The prevalence of FDD worldwide ranges from 13–81% of FC patients depending on different population and definitions[2]. Our study retrospectively investigated a consecutive Chinese FC population and 62.73% were FDD. The high prevalence might be related to the severe symptoms and unsatisfied treatment experience of patients in our hospital. In view of the difficulty in telling FDD from other FC subtypes with symptoms alone, anorectal physiological testing and imaging are warranted[21].

Function testings need to be carried out in specialist centers, including ARM, BET, CTT test, defecography, EMG, etc[22]. However, given the limited availability of these investigations in primary clinics, the work-up for FDD often remains inadequate[23]. Current guidelines from the American Gastrointestinal Association

(AGA) recommend ARM with or without BET as a basic test[24], followed by EMG, barium or magnetic resonance(MR) defecography if necessary[25, 26]. ARM and BET are pivotal in identifying patients with FDD[27, 28]. However, limited agreement between these tests has been achieved and there is no single gold standard for FDD diagnosis[7].

We diagnosed FDD using BET, HR-ARM and CTT. The majority of our patients with FDD showed fine agreement in BET and HR-ARM results. Compared with other physiology testings such as barium or MR defecography, currently ARM and BET are more available, less costly and correlated with treatment outcomes[6]. BET is utilized as a direct tool to indicate defecation dysfunction while HR-ARM as an indirect tool. BET can be used to assess rectoanal coordination and the abnormal result is indicative of an impaired defecatory maneuver and may predict the response to biofeedback therapy[29]. HR-ARM provides a comprehensive assessment of rectoanal pressures and motor coordination combined with an assessment of rectal sensation and rectoanal reflexes[30]. The pressure measurements can identify rectoanal dyssynergia as a cause of FDD[31]. PFD identified by HR-ARM have been widely used to diagnose and classify FDD due to its convenience and availability in clinical practice[11].

84.48% patients with FDD in our study were found showing positive BET and PFD, revealing good consistency between BET and PFD. Compared to other patients with FDD, these patients showed high anal residual pressure, low anal relaxation rate, RAPG and MDI. During normal defecation, there is a rise in rectal pressure, which is synchronized with a relaxation of the external anal sphincter and a decrease in anal pressure. The inability to perform this coordinated movement represents the main pathophysiology mechanism in FDD. This may be related to inadequate pushing force, paradoxical anal sphincter contraction, impaired anal sphincter relaxation, or a combination of above[32, 33]. Anal residual pressure indicates whether there is a failure in anal relaxation during attempted defecation. Besides, the quantitative parameters of pressure changes in the rectum and anus during attempted defecation, such as anal relaxation rate, MDI and RAG, are useful to diagnose FDD[11] and MDI serves as a simple and useful quantitative measure of rectoanal coordination during defecation[34]. According to our findings, FDD patients with positive BET and PFD mainly had problems with impaired anal sphincter relaxation and paradoxical anal sphincter contraction, which may be associated with abnormal external anal sphincter (EAS) and/or puborectalis muscle contraction[35].

A previous study suggested impaired defecation in patients with FDD was mainly attributed to increased resistance to evacuation, rather than weak propulsive force and DD would be more predominant than IDP in FDD[11]. Our study showed the percentage of consistent results was larger in DD patients. Furthermore, high anal sphincter pressure phenotype of FDD was more frequently observed when BET and PFD were both positive. These findings revealed patients with DD usually have both positive BET and PFD. Meanwhile, their impairment of EAS and/or puborectalis muscle contraction is likely more severe.

Zakari et al found that men had higher median resting anal pressures and mean squeeze pressures compared to women[36]. Different from its results, no difference of resting anal pressure and squeeze

pressure between genders was observed in our study. Instead, the percentage of males is larger in Consistent Group and males tended to suffer much more paradoxical anal sphincter contraction and impaired anal sphincter relaxation. A previous study found that males with FC were significantly more likely to suffer defecation dysfunction than female patients[37]. In addition, our results showed increasing age played a negative role in anal relaxation dysfunction during defecation and patients with positive BET and PFD were older than other patients with FDD. The findings above indicated male and age might predict severe defecation dysfunction.

Four of the six symptoms in Rome IV criteria for constipation are highly indicative of FDD: straining, sensation of incomplete evacuation, sensation of anorectal obstruction/blockage, and manual maneuvers to facilitate defecation[38]. While the BSFS is commonly used in clinical practice, a previous study did not find a report of hard or lumpy stools associated with FDD[39]. In this study, defecation symptoms assessed by PAC-SYM were more severe in Consistent Group. However, SBMs, BSFS and defecation duration did not differ between two groups. It suggested FDD patients with positive BET and PFD might have more severe clinical manifestation, especially the defecation dysfunction symptoms. Furthermore, constipation is associated with high psychological stress and impaired QOL[40] and FDD carries a significant impact on them[3, 41]. Our findings suggested FDD patients with positive BET and PFD suffered more anxiety and impaired QOL, particularly physical health related QOL. Furthermore, we found that anxiety played a role in defecation symptoms and the impaired QOL might be related to anxiety and defecation symptoms. Depression did not make sense whether BET was consistent with PFD in this study. More relevant evidence concerning the relationship between symptoms, mental health and QOL in FDD patients is warranted.

BET has a diagnostic accuracy sufficient to identify patients without FDD. Patients with negative BET may not need other onerous tests to exclude FDD[12]. In our study, positive BET alone had a good diagnostic sensitivity and NPV for FDD as well as its two subtypes so it could be used as an excluding tool. Besides, BET was reported to have high specificity as a diagnostic tool for FDD[42]. According to the 3 minutes criteria of BET based on ARM and EMG during biofeedback training, PPVs were 93% and 100%, respectively[43]. However, the specificity and PPV of BET in our study were relatively low compared to some previous studies. The difference might be attributed to patients without FDD failing BET with left lateral decubitus position. When positive BET was combined with PFD, the specificity and PPV rose evidently to 100%, indicating that positive BET and PFD can be used as a good screening tool for FDD.

A digital rectal examination (DRE) is helpful to assess the anal sphincter and puborectalis muscle tone during squeezing and attempted defecation[44], which could indicate PFD. DRE has been reported with a sensitivity of 75% and specificity of 87% for identifying DD[45]. Based on our findings, PFD identified by DRE and BET might be sufficient for screening FDD when ARM or defecography is not available in primary clinics.

This study investigated the characteristics of FDD patients with positive BET and PFD. We also explored possible pathophysical mechanism and associated risk factors of patients' severe symptoms and impaired QOL. Furthermore, we evaluated the diagnostic value of positive BET and PFD and then suggested BET combined with DRE being applied in primary clinics to help identify FDD.

However, there are also some limitations as follows. First, this study was performed with data retrospectively analyzed in a single tertiary care center, which might result in data scarcity and lack of universality. Second, Other diagnostic tests that might be helpful to diagnose FDD, such as defecography or EMG, were only performed in a minority of our patients. Furthermore, position is a key component as demonstrated in a study recruiting 25 healthy people that found an increase in dyssynergia in the left lateral position (36%) compared with the seated position (20%)[46]. Left lateral position was adopted in BET in our study, which might cause false positive result and low specificity of BET. However, concordance between BET performed in the left lateral position or seated position was observe in a previous study[47].

Complex procedures are needed to diagnose FDD and it is hard for primary care or secondary gastroenterology practices outside referral centers[42] to tell FDD from other constipation subtypes. We found that positive BET and PFD could be an ideal screening tool to identify FDD, in which PFD could be diagnosed by ARM or DRE instead. FDD patients with positive BET and PFD suffer severe defecation symptoms, anxiety and impaired QOL. Paradoxical anal sphincter contraction or impaired anal sphincter relaxation might be the key factor.

In conclusion, patients with FDD request more concern and need to be treated properly based on clinical manifestations and specific pathophysiology. Positive BET and PFD shed light on diagnosing FDD more conveniently.

Declarations

Autor contributions: designed the study: Ya Jiang, Lin Lin; collected and analyzed the data: Ya Jiang and Yan Wang ; wrote the paper: Ya Jiang; revised the paper: Yurong Tang.

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This study was approved by the Ethical Committee of the First Affiliated Hospital with Nanjing Medical University(No. 2020-SR-061) and it agrees with the 1975 Helsinki declaration. All patients involved have signed the informed consent.

The authors have no conflicts of interest to disclose.

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