

## Effects of Comorbid Depressive Symptoms and Diabetes Mellitus on Functional Dyspepsia in Older Patients

### ABSTRACT

**Objective:** Diabetes mellitus (DM) is a global epidemic; comorbid depressive symptoms are highly prevalent worldwide and commonly manifests as physical symptoms, including functional dyspepsia (FD), a gastrointestinal psychosomatic disorder. This study aimed to explore the effects of comorbid depressive symptoms and DM on FD in older patients.

**Methods:** In total, 420 older patients with DM completed measures of depression, anxiety, and FD. Relevant demographic characteristics and medical information were self-reported and obtained from the hospital information system.

**Results:** Among older patients with DM, 30.48% had depressive symptoms. Patients with depressive symptoms were more likely to have FD than those without (42.19% vs. 20.21%,  $P = .000$ ). Dyspepsia symptoms were more frequent in patients with depression ( $P = .022$ ). The greater the amount of dyspepsia symptoms, the higher the depression symptoms score ( $P = .000$ ). Furthermore, dyspepsia symptoms were positively correlated with depressive symptoms ( $r$  values were 0.292, 0.311, 0.297, 0.369; all had  $P < .05$ ). Both FD subtypes, postprandial distress, and epigastric pain syndromes affected depressive symptoms ( $P < .05$ ). Smoking was significantly associated with FD ( $P < .05$ ). Diabetes mellitus complications, such as diabetic neuropathy, different therapeutic methods, and anxiety symptoms, influenced FD overlap ( $\chi^2$  values were 6.298, 16.314, and 30.744;  $P < .05$ ). Anxiety (odds ratio = 1.832, 95% Confidence Intervals (CI) 1.185-2.834) was a risk factor for FD in comorbid depressive symptoms and diabetes ( $P < .05$ ).

**Conclusion:** Comorbid depressive symptoms and DM overlapped with physical symptoms, such as FD, in older patients with DM. Lifestyle, diabetic factors, and anxiety were the associated risk factors.

**Keywords:** Diabetes mellitus, functional dyspepsia, depressive symptoms, older patients

### Introduction

Diabetes mellitus (DM) is a common, chronic metabolic disorder caused by elevated plasma glucose levels. The incidence of DM has increased significantly over the past decade and is a growing epidemic worldwide.<sup>1</sup> The prevalence of diabetes has doubled since 1980, and in 2014, an estimated 422 million adults had DM.<sup>2</sup> In China, 140 million people have DM, a number that is expected to reach 174 million in 2045.<sup>3</sup> Recent research predicted that older adults with DM will continue to experience diminished quality of life because of the disease itself, DM complications, and related treatments.<sup>4</sup>

As defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, DM is a mood disorder with several combined symptoms that can alter the functionalities of patients with diabetes.<sup>5</sup> Studies have confirmed that patients with diabetes have a higher prevalence of depression than those with normal glucose metabolism.<sup>6,7</sup> Globally, the prevalence of depression was found to be 2-3 times higher in patients with DM than in the general population.<sup>8</sup> Depression, which is a common medical crisis worldwide, can occur with or



Zhen-peng Huang<sup>1</sup> 

Yan-bin Chen<sup>1</sup> 

Bin-bin Wen<sup>2,1</sup> 

Hui-xian Guan<sup>1</sup> 

Bin Wu<sup>1</sup> 

<sup>1</sup>Faculty of Nursing, Guangxi University of Chinese Medicine, Nanning, Guangxi, China  
<sup>2</sup>Xiangya School of Nursing, Central South University, Changsha, Hunan, China

**Corresponding author:**  
Zhen-peng Huang or Bin-bin Wen  
✉ huang\_zhenpeng@126.com or wenbinbin0906@163.com

**Received:** February 28, 2024  
**Revision Requested:** March 18, 2024  
**Last Revision Received:** March 31, 2024  
**Accepted:** April 23, 2024  
**Publication Date:** August 10, 2024

**Cite this article as:** Huang Z, Chen Y, Wen B, Guan H, Wu B. Effects of comorbid depressive symptoms and diabetes mellitus on functional dyspepsia in older patients. *Alpha Psychiatry*. 2024;25(4):465-471.



without psychotic features.<sup>8</sup> However, most patients with depression first complain of the manifestation of physical symptoms. Indeed, 60% of patients present with physical symptoms, and 20% of those who received a diagnosis of psychotic depression present with somatic complaints.<sup>9</sup> Another study found that approximately 80% of patients with depression presented with physical rather than psychological complaints.<sup>9</sup>

Functional dyspepsia (FD) is defined by certain characteristic symptoms, including postprandial fullness, epigastric pain, epigastric burning, and early satiation, which occur for at least 6 months.<sup>10</sup> Recent large-scale studies have reported a worldwide prevalence of FD at 10%-30%.<sup>11</sup> Functional dyspepsia is widely known as a gastrointestinal psychosomatic disorder; its known risk factors include psychological disturbances, social factors, and lifestyle habits, such as smoking.<sup>11</sup> A recent meta-analysis found a positive association between depression and FD.<sup>12</sup> Furthermore, our previous study found that approximately half of the participants with depressive symptoms also had FD.<sup>13</sup> However, the prevalence, correlation, and risk factors regarding FD in DM with comorbid depressive symptoms, especially in older patients, have remained unknown thus far. Identifying the relationships and risk factors of FD in DM with depressive symptoms, especially in older patients with DM, could reduce the patients' healthcare-related burdens and improve their quality of life.

This study aimed to explore prevalence, correlation, and risk factors regarding FD among older patients with DM and comorbid depressive symptoms.

## Methods

### Patients

Older patients admitted to Ruikang Hospital affiliated with Guangxi University of Chinese Medicine and the First Affiliated Hospital of Guangxi University of Chinese Medicine who were diagnosed with DM between January and December 2022 were recruited.

The study's inclusion criteria were as follows. In order to be accepted, prospective study participants had to (1) be diagnosed with DM based on World Health Organization diagnostic criteria; (2) be aged 60 years or older; (3) ensure they had no reading or communication barriers; (4) have no history of antianxiety or anti-depression drug administration; and (5) ensure that their participation in the study was voluntary.

Prospective study participants with the following exclusion criteria were rejected: (1) patients who had no access to the World Health Organization DM diagnostic criteria; (2) patients with cognitive dysfunction who could not complete this study; (3) patients who had

received antianxiety or anti-depression treatments in the recent 6 months; and (4) patients who could not cooperate or participate voluntarily in the study.

The appropriate medical research formula for estimating sample size holds that the average prevalence of comorbidity of depression and diabetes is approximately 30%. Therefore, the sample size of this study needed to reach at least 323 participants.<sup>8,14</sup> In total, 420 participants were enrolled in this study.

This study was approved by the Institutional Ethics Committee of Ruikang Hospital affiliated with Guangxi University of Chinese Medicine (No. KY2022-042). All patients participated in this study voluntarily and provided written informed consent. This study was performed in accordance with the relevant guidelines and regulations of the Declaration of Helsinki.

### Measures and Questionnaires

The validated Chinese version of the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7) was administered to all older patients with DM to identify those with generalized anxiety disorder. Scores were calculated for each item in the GAD-7; total scores of above 5 points were identified as indicating the presence of an anxiety disorder. A total of 5-9 points indicated mild anxiety disorder, 10-14 points indicated moderate anxiety disorder, and scores higher than 15 points indicated severe anxiety disorder. The Cronbach's alpha for the GAD-7 was 0.92.<sup>15</sup>

The Chinese version of the Patient Health Questionnaire 9 (PHQ-9) was used to screen older patients with DM for depressive symptoms. Each item score of the PHQ-9 was calculated—total scores above 5 points were classified as indicating depressive symptoms; 5-9 points indicated mild depressive symptoms; 10-14 points indicated moderate depressive symptoms; 15-19 points indicated moderate to severe depressive symptoms; and scores higher than 20 points indicated severe depressive symptoms. The Cronbach's alpha for the PHQ-9 was 0.88.<sup>16</sup>

The Rome IV diagnostic questionnaire for functional gastrointestinal disorders in adults was used to identify participant's FD-related gastrointestinal symptoms. The questionnaire assesses postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), which include symptoms such as postprandial fullness, early satiation, epigastric pain, and/or burning sensation occurring in the last 3 months, and the course of the disease for at least 6 months.<sup>17</sup> The Cronbach's alpha for this questionnaire was 0.84. Additionally, laboratory and imaging tests, such as endoscopy, abdominal ultrasound, and routine blood tests, were used to rule out organic, systemic, or metabolic diseases that were likely to explain the FD gastrointestinal symptoms observed in this study.

Relevant demographic characteristics were self-reported by all patients; 6 items were included in the questionnaire as follows: educational level (junior middle school or below, senior high school, or college or above), marital status (married, divorced, or widowed), mode of living (living alone, with family and friends, or in a nursing home), smoking (yes or no), alcohol consumption (yes or no), and medical insurance (yes or no).

### MAIN POINTS

- In this study, 30.48% of older patients with diabetes mellitus (DM) had depressive symptoms.
- Older patients with DM who also had depression were more likely to have functional dyspepsia (FD) symptoms.
- Comorbid depressive symptoms and DM overlap with physical symptoms such as FD in older patients. Lifestyle, diabetic factors, and anxiety are risk factors.

Relevant medical information was self-reported by all older patients with DM and obtained from the hospital information system. Four items were included in the questionnaire as follows: initial consultation (yes or no), family history (yes or no), course of disease (<1 year, 1-5 years, 6-10 years, 11-20 years, or >20 years), regular blood glucose monitoring (yes or no), complications (yes or no), names of complications (diabetic macroangiopathy, diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, diabetic foot, diabetic ketoacidosis, or other complications), comorbidity excluding depression (yes or no), and treatments (lifestyle interventions, oral hypoglycemic agents, insulin injections, or comprehensive therapies).

### Statistical Analysis

Statistical analyses were performed using IBM SPSS for Windows, version 25.0 (IBM SPSS Corp.; Armonk, NY, USA). In this paper, continuous variables are presented as mean (standard deviations). Categorical variables are expressed as proportions and percentages. The associations between relevant factors and study outcomes are presented as odds ratios (OR) and 95% confidence intervals (95% CI).

This study analyzed comparisons of continuous variables after ensuring the normality and homogeneity of the variance. If the normality and homogeneity of the variance were satisfied, the variables were compared using Student's *t*-test; if they were not satisfied, the variables were compared using the Mann-Whitney *U*-test. Categorical variables were compared using the chi-square test, Fisher's exact test, or the Ridit test.

Correlation analysis was performed between the dyspepsia symptoms and the comorbid depressive symptoms and DM. The independent factors associated with DM in patients with depressive symptoms and FD were analyzed using multivariate logistic regression. Statistical significance was indicated as a 2-sided  $P < .05$ .

## Results

### Prevalence of Comorbid Depressive Symptoms and Diabetes Mellitus

Among older patients with DM who participated in this study, 198 (47.14%) were male, and 222 (52.86%) were female. The participants' ages ranged from 60-92 years (68.362 (6.478)).

In total, 30.48% of the patients had comorbid depressive symptoms and DM; 95 (70.32%) had mild depressive symptoms, 30 (23.44%) had moderate depressive symptoms, 2 (1.56%) had moderate-to-severe depressive symptoms, and 1 (0.78%) had severe depressive symptoms. Most patients with DM and comorbid depressive symptoms experienced only mild depressive symptoms.

### Prevalence of Comorbid Depressive Symptoms and Diabetes Mellitus Overlapping with Functional Dyspepsia

In total, 26.90% of the patients also had FD, and 42.19% with depressive symptoms also had FD; conversely, only 20.21% of those who did not have depressive symptoms suffered from FD ( $\chi^2 = 35.393$ ,  $P = .00$ ). Patients with comorbid depressive symptoms were more likely to have physical gastrointestinal symptoms, such as FD.

### Effects of Comorbid Depressive Symptoms and Diabetes Mellitus on Dyspepsia Symptoms

Dyspepsia symptoms, including postprandial fullness, early satiation, epigastric pain, and epigastric burning, were more obvious in older

**Table 1.** Impact of Functional Dyspepsia-Related Comorbid Depressive Symptoms and Diabetes Mellitus on Dyspepsia Symptoms [n (%)]

Dyspepsia Symptoms	DM with Depressive Symptoms	DM Without Depressive Symptoms	
Postprandial fullness	43 (79.63%)	45 (76.27%)	$\chi^2 = 0.059$ , $P = .808$
Early satiation	26 (48.15%)	20 (33.90%)	$\chi^2 = 2.115$ , $P = .146$
Epigastric pain and/or burning	34 (62.96%)	26 (44.07%)	$\chi^2 = 3.597$ , $P = .058$
Numbers of dyspepsia symptoms	1.909 ± 0.908	1.525 ± 0.858	$t = -2.314$ , $P = .022$

DM: Diabetes Mellitus.

patients with comorbid depressive symptoms and DM, although this difference was not statistically significant (all had  $P > .05$ ). The number of dyspepsia symptoms was significantly higher in patients with depressive symptoms than in those without depressive symptoms ( $t = -2.314$ ,  $P = .022$ ) (Table 1).

Additionally, the number of dyspepsia symptoms impacted depression; the higher the number of dyspepsia symptoms, the higher the PHQ-9 score ( $F = 22.260$ ,  $P = .000$ ). Moreover, among patients with comorbid depressive symptoms and DM, those who had only 1 dyspepsia symptom experienced milder depressive symptom severity than those with 2 or 3 dyspepsia symptoms; furthermore, the number of dyspepsia symptoms had a positive correlation with the comorbid depressive symptoms and DM (all had  $P < .05$ ) (Table 2).

Further analysis showed that dyspepsia symptoms, such as postprandial fullness, early satiation, epigastric pain, and epigastric burning, had a positive correlation with comorbid depressive symptoms and DM (the *r* values were 0.292, 0.311, 0.297, and 0.369 for the aforementioned symptoms, respectively; all had  $P < .05$ ) (Table 3).

### Effects of Comorbidity of Depressive Symptoms and Diabetes Mellitus on the Subtype of Functional Dyspepsia

Functional dyspepsia subtypes, including PDS and EPS, had an impact on patients with depressive symptoms (all had  $P < .05$ ). Additionally, the depressive symptom severity in patients with only PDS or EPS was mild compared to that of those with overlapping PDS and EPS (all had  $P < .05$ ). However, there was no significant difference between PDS and EPS with regard to their impact on depressive symptom severity ( $P > .05$ ) (Table 4).

**Table 2.** The Number of Dyspepsia Symptoms and Diabetes Mellitus with Depressive Symptoms

Dyspepsia Symptoms	Incidence [n (%)]	Scores of PHQ-9 <sup>†</sup>
0	307 (73.10)	3.323 (2.699)
1 <sup>‡</sup>	64 (15.24)	4.234 (3.221)
2 <sup>‡</sup>	17 (4.05)	6.471 (3.727)
3 <sup>‡*</sup>	32 (7.61)	7.438 (4.990)

Scores of PHQ-9 are expressed as mean (SD [standard deviation]).

<sup>†</sup> $F = 22.260$ ,  $P = .000$ .

<sup>‡</sup> $P = .008$ .

<sup>\*</sup> $P = .000$ .

<sup>\*</sup> $P = .292$ .

**Table 3.** Correlation Between Dyspepsia Symptoms and Diabetes Mellitus with Depressive Symptoms

Dyspepsia Symptoms	DM with Depressive Symptoms
Postprandial fullness	$r = 0.292, P = .000$
Early satiation	$r = 0.311, P = .000$
Epigastric pain and/or burning	$r = 0.297, P = .000$
Numbers of dyspepsia symptoms	$r = 0.369, P = .000$

DM, diabetes mellitus.

### Impact of Social Factors on Functional Dyspepsia in Patients with Comorbid Diabetes Mellitus and Depressive Symptoms

Various social factors can affect FD in patients with comorbid DM and depressive symptoms. This study's results showed that patients with comorbid DM and depressive symptoms who smoke are more likely to have FD symptoms ( $P < .05$ ). In patients with depressive symptoms, gender, age, educational level, marital status, mode of living, regular alcohol consumption, and possession of medical insurance were not significantly related to the likelihood of having FD ( $P > .05$ ) (Table 5).

### Impacts of Diabetic Factors on Functional Dyspepsia in Patients with Comorbid Diabetes Mellitus and Depressive Symptoms

Various diabetic factors can affect whether patients with comorbid depressive symptoms also have FD. This study confirmed that DM complications such as diabetic neuropathy; different therapeutic methods (insulin injections); comprehensive therapies (lifestyle interventions, oral hypoglycemic agents, and insulin injections); and anxiety disorders significantly influenced FD occurrence in patients with depressive symptoms (all  $P < .05$ ).

However, whether patients had an initial consultation, a relevant family history of the disease, course of disease, regular blood glucose monitoring, presence of complications, and comorbidity excluding depressive symptoms had no significant impact on FD in patients with comorbid depressive symptoms and DM ( $P > .05$ ) (Table 6).

### Performing Multivariable Logistic Regression Analyses on Certain Selected Factors Associated with Functional Dyspepsia in Comorbid Depressive Symptoms and Diabetes Mellitus

A multivariable logistic regression model was constructed to identify the association between social and disease factors and FD in patients with DM and depressive symptoms. Anxiety disorder (OR=1.832, 95% CI 1.185-2.834) was an independent risk factor associated with FD in patients with comorbid depressive symptoms and DM ( $P < .05$ ) (Table 7).

**Table 4.** Impact of Comorbidity of Depressive Symptoms and Diabetes Mellitus on Functional Dyspepsia Subtype

Subtype of FD	Incidence [n(%)]	Scores of PHQ-9 <sup>†</sup>
PDS <sup>#,+</sup>	51 (45.13)	4.549 (3.534)
EPS <sup>#,*</sup>	30 (26.55)	4.967 (3.296)
Overlap PDS and EPS <sup>+,*</sup>	32 (28.32)	7.438 (4.990)

EPS: Epigastric Pain Syndrome; FD: Functional Dyspepsia; PDS: Postprandial Distress Syndrome.

<sup>†</sup>F=5.615,  $P = .005$ .<sup>#</sup> $P = .646$ .<sup>+</sup> $P = .002$ .<sup>\*</sup> $P = .015$ .**Table 5.** Impact of Social Factors on Functional Dyspepsia in Patients with Comorbid Diabetes Mellitus and Depressive Symptoms

Variables	Category	Depressive Symptoms with FD	Depressive Symptoms without FD	
Gender	Male	28 (51.85%)	22 (37.29%)	$\chi^2 = 2.424, P = .120$
	Female	26 (48.15%)	37 (62.71%)	
Age		67.093 ± 6.208	68.509 ± 6.642	$z = -0.335, P = .737$
Educational level	Junior middle school or below	29 (53.70%)	27 (45.76%)	$\chi^2 = 0.895, P = .639$
	Senior high school	17 (31.48%)	20 (33.90%)	
	College or above	8 (14.82%)	12 (20.34%)	
Marital status	Married	48 (88.89%)	50 (84.75%)	$\chi^2 = 1.107, P = .575$
	Divorced	0 (0%)	1 (1.69%)	
	Widowed	6 (11.11%)	8 (13.56%)	
Mode of living	Living alone	3 (5.56%)	4 (6.78%)	$\chi^2 = 1.042, P = .594$
	With family and friends	51 (94.44%)	54 (91.53%)	
	Nursing home	0 (0%)	1 (1.69%)	
Smoking		8 (14.81%)	2 (3.39%)	$\chi^2 = 4.427, P = .035$
Alcohol consumption		6 (11.11%)	3 (5.08%)	$\chi^2 = 0.648, P = .421$
Medical insurance		51 (94.44%)	56 (94.92%)	$\chi^2 = 0.110, P = .740$

## Discussion

This study found that about one-third of the older patients with DM suffered from depressive symptoms. The general prevalence of depressive disorders in China is 6.91%.<sup>18</sup> Therefore, the prevalence of depression is approximately 4.4 times higher in older patients with DM than in the general population. Other studies confirm that older patients with DM face a greater risk of developing comorbid depressive symptoms.<sup>19,20</sup>

However, the mechanisms underlying the comorbidity of the depressive symptoms and DM remain unclear. Some studies suggest that depression is an independent risk factor for subsequent development of DM, which, in turn, may increase the risk of developing or worsening depression.<sup>21</sup> Some health risk behaviors associated with depression (e.g., smoking) and psychobiological factors (e.g., increased cortisol levels and increased inflammatory factors) can increase the risk of developing insulin resistance.<sup>22</sup> Moreover, DM complications can cause functional impairment, decreased memory, and cognitive impairment via dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis.<sup>23</sup> The current study confirmed that psychobiological factors can impact the comorbidity of depressive symptoms and DM and, furthermore, lead to or overlap with dyspepsia symptoms.

**Table 6.** Impact of Diabetic Factors on Functional Dyspepsia in Patients with Comorbid Diabetes Mellitus and Depressive Symptoms [n (%)]

Variables	Category	Depressive Symptoms with FD	Depressive Symptoms Without FD	
Initial consultation		9 (16.67)	9 (15.25)	$\chi^2 = 0.042, P = .838$
Family history	Yes	10 (18.52)	15 (25.42)	
	No	44 (81.48)	44 (74.58)	$\chi^2 = 0.872, P = .350$
Course of disease	Less than 1 year	10 (18.52)	7 (11.86)	
	1-5 years	11 (20.37)	10 (16.95)	
	6-10 years	11 (20.37)	13 (22.03)	
	11-20 years	10 (18.52)	17 (28.81)	
	More than 20 years	12 (22.22)	12 (20.34)	
Blood glucose monitoring regularly		16 (29.63)	27 (45.76)	$\chi^2 = 3.368, P = .067$
Diabetic complication		40 (74.07)	40 (67.80)	$\chi^2 = 0.331, P = .565$
	Diabetic macroangiopathy	21 (38.89)	19 (32.20)	$\chi^2 = 0.159, P = .690$
	Diabetic nephropathy	10 (18.52)	5 (8.47)	$\chi^2 = 1.575, P = .210$
	Diabetic retinopathy	24 (44.44)	20 (33.90)	$\chi^2 = 1.139, P = .286$
	Diabetic neuropathy	44 (81.48)	28 (47.46)	$\chi^2 = 6.298, P = .012$
	Diabetic foot	2 (3.70)	1 (1.69)	$\chi^2 = 0.038, P = .951$
	Diabetic ketoacidosis	2 (3.70)	3 (5.08)	$\chi^2 = 0.006, P = .936$
	Other complications	0 (0)	2 (3.39)	$\chi^2 = 0.441, P = .507$
Comorbidity except for depression		46 (85.19)	48 (81.36)	$\chi^2 = 0.296, P = .586$
Treatment				$\chi^2 = 16.314, P = .001$
	Lifestyle intervention	2 (3.70)	6 (10.17)	$\chi^2 = 0.944, P = .331$
	Oral hypoglycemic agent	17 (31.48)	19 (32.20)	$\chi^2 = 0.007, P = .934$
	Insulin injection	17 (31.48)	3 (5.08)	$\chi^2 = 11.736, P = .001$
	Comprehensive therapy	32 (59.26)	17 (28.81)	$\chi^2 = 10.641, P = .001$
Anxiety disorder	Mild	19 (35.19)	12 (20.34)	
	Moderate	10 (18.52)	0 (0)	
	Severe	5 (9.26)	0 (0)	
	Total	34 (62.96)	12 (20.34)	$\chi^2 = 30.744, P = .000$

The worldwide prevalence of uninvestigated dyspepsia is 21%.<sup>24</sup> In Korea and China, the prevalence of FD in older people is 11% and 2.4%, respectively.<sup>25</sup> The present study observed a higher prevalence of FD in older patients with DM. Functional dyspepsia is a gastrointestinal psychosomatic disorder, and it has been reported that psychological and physiological factors play an equal role in the development of DM. Patients with DM face an increased risk of developing psychosomatic and somatopsychic symptoms, including FD and gastroesophageal reflux.<sup>26</sup> This study found that the comorbidity of depressive symptoms and DM was common in older patients with FD.

Furthermore, several underlying mechanisms influenced the comorbidity of depressive symptoms and DM overlap in those with underlying FD. First, gastrointestinal motor dysfunction exacerbates dyspepsia symptoms.<sup>10</sup> Diabetic delayed gastric emptying can directly worsen dyspepsia symptoms, including nausea, vomiting, and postprandial fullness occurrence.<sup>27</sup> Mechanical stimulation and inflammatory mediators also stimulate the mechanical and chemical hypersensitivity of the stomach in patients with comorbid depressive symptoms and DM; these have been associated with epigastric pain.<sup>28</sup> In contrast, gut-brain axis dysfunction also influences FD.<sup>29</sup> The central and peripheral nervous systems overlap with the key pathways

**Table 7.** The Multivariable Logistic Regression Analyses Conducted on Selected Factors Associated with Functional Dyspepsia in Comorbid Depressive Symptoms and Diabetes Mellitus

Selected Factors	B	SE	Wald	df	Sig.	Exp (B)	95% CI for Exp (B)
Smoking	-0.228	0.523	0.190	1	0.663	0.796	(0.286, 2.218)
Diabetic retinopathy	-0.272	0.359	0.573	1	0.449	0.762	(0.377, 1.541)
Treatment	-0.062	0.920	0.004	1	0.947	0.940	(0.155, 5.701)
Anxiety disorder	0.606	0.222	17.413	1	0.006	1.832	(1.185, 2.834)
Numbers of dyspepsia symptoms	22.233	2768.280	0.000	1	0.993	1.231	(0.000)

of the gut–brain axis, including functions such as neurotransmitter release and regulation of dysfunction, when DM is associated with depression.<sup>30</sup> Additionally, dysfunction in the HPA axis with its neuroendocrine mediators can also lead to mood disorders, for example, depression and FD.<sup>23,29</sup>

Recent studies suggest that environmental and social risk factors can also have significant effects on FD. Research confirms that unhealthy diets and lifestyles can induce and exacerbate FD symptoms.<sup>31,32</sup> The current study found that unhealthy diets and lifestyles, such as regular alcohol consumption, can lead to or affect depressive symptoms and FD. Furthermore, DM complications, such as diabetic neuropathy and different therapeutic methods, contributed toward depressive symptoms. Moreover, with the progression of DM, diabetic complications gradually increase and patients require comprehensive therapies, such as lifestyle interventions, oral hypoglycemic agents, and insulin injections; these could aggravate depression and FD, thereby reducing the patients' quality of life.<sup>33</sup>

Anxiety disorder was also found to be an independent risk factor associated with FD in patients with comorbid depressive symptoms and DM. Recent studies suggest that dyspepsia symptoms are much more severe and easy to detect in FD patients who experience psychological distress related to both anxiety and depression than in those with only depression or those without mood disorders.<sup>34</sup>

This study had several limitations. First, this cross-sectional study was designed to explore the effect of comorbid depressive symptoms and DM on FD presence in older patients; further prospective clinical studies are necessary. Furthermore, self-report questionnaires such as the GAD-7 and PHQ-9 used in this study may suffer from social desirability biases that could distort results.

In conclusion, this study confirmed that physical symptoms, such as dyspepsia, commonly occur in older patients with DM and depressive symptoms. Unhealthy lifestyles and diabetic factors play a key role in the occurrence of FD in older patients with comorbid depressive symptoms and DM. Additionally, anxiety disorder was confirmed as a risk factor for FD co-occurrence.

**Availability of Data and Materials:** The data and materials that support the findings of this study are available from the corresponding author upon reasonable request.

**Ethics Committee Approval:** This study was approved by the Institutional Ethics Committee of Rui kang Hospital affiliated with Guangxi University of Chinese Medicine (number: KY2022-042).

**Informed Consent:** Written informed consent was obtained from all the patients who participated in the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – Z.P.H.; Design – Z.P.H.; Supervision – B.B.W., B.W.; Resources – Y.B.C., B.B.W., B.W.; Materials – Z.P.H., Y.B.C., B.B.W.; Data Collection and/or Processing – Z.P.H., Y.B.C., B.B.W., H.X. G.; Analysis and/or Interpretation – Z.P.H.; Literature Search – Z.P.H.; Writing – Z.P.H.; Critical Review – Z.P.H., Y.B.C., B.B.W., H.X.G., B.W.

**Acknowledgments:** We would like to thank all the study participants for their assistance in this study.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

**Funding:** The authors declare that this study received no financial support.

## References

- Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The growing epidemic of diabetes mellitus. *Curr Vasc Pharmacol*. 2020;18(2):104-109. [\[CrossRef\]](#)
- World Health Organization. *Global Report on Diabetes 2016*. Available at: <https://www.who.int/publications/i/item/9789241565257>. Accessed 21 April 2016
- Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. [\[CrossRef\]](#)
- Sayyed Kassem L, Aron DC. The assessment and management of quality of life of older adults with diabetes mellitus. *Expert Rev Endocrinol Metab*. 2020;15(2):71-81. [\[CrossRef\]](#)
- American Psychiatric Association, Task F. *Diagnostic and Statistical Manual of Mental Disorders DSM-5*. 5th ed. Washington, DC: American Psychiatric Association; 2013.
- Pearce M, Garcia L, Abbas A, et al. Association between physical activity and risk of depression: a systematic review and meta-analysis. *JAMA Psychiatry*. 2022;79(6):550-559. [\[CrossRef\]](#)
- Chen S, Zhang Q, Dai G, et al. Association of depression with pre-diabetes, undiagnosed diabetes, and previously diagnosed diabetes: a meta-analysis. *Endocrine*. 2016;53(1):35-46. [\[CrossRef\]](#)
- Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. *J Affect Disord*. 2012;142(suppl):S8-S21. [\[CrossRef\]](#)
- Lipowski ZJ. Somatization and depression. *Psychosomatics*. 1990;31(1):13-21. [\[CrossRef\]](#)
- Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. *Lancet*. 2020;396(10263):1689-1702. [\[CrossRef\]](#)
- Oshima T. Functional dyspepsia: current understanding and future perspective. *Digestion*. 2024;105(1):26-33. [\[CrossRef\]](#)
- Lin S, Gao T, Sun C, Jia M, Liu C, Ma A. The association between functional dyspepsia and depression: a meta-analysis of observational studies. *Eur J Gastroenterol Hepatol*. 2019;31(8):911-918. [\[CrossRef\]](#)
- Huang ZP, Huang F, Wang MJ, et al. Lifestyle and social factors exacerbated on the prevalence of mood disorders and functional dyspepsia among neonatal nurses in China. *Front Psychiatry*. 2022;13:905401. [\[CrossRef\]](#)
- Wang X, Ji X. Sample size estimation in clinical research: from randomized controlled trials to observational studies. *Chest*. 2020;158(15):S12-S20. [\[CrossRef\]](#)
- Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. [\[CrossRef\]](#)
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613. [\[CrossRef\]](#)
- Whitehead WE. *Rome IV Diagnostic Questionnaire for Adults Functional Gastrointestinal Disorders*. Raleigh, NC: The Rome Foundation; 2016:149-187.
- Lu J, Xu X, Huang Y, et al. Prevalence of depressive disorders and treatment in China: a cross-sectional epidemiological study. *Lancet Psychiatry*. 2021;8(11):981-990. [\[CrossRef\]](#)
- Pashaki MS, Mezel JA, Mokhtari Z, et al. The prevalence of comorbid depression in patients with diabetes: a meta-analysis of observational studies. *Diabetes Metab Syndr*. 2019;13(6):3113-3119. [\[CrossRef\]](#)
- Park M, Reynolds CF 3rd. Depression among older adults with diabetes mellitus. *Clin Geriatr Med*. 2015;31(1):117-137. [\[CrossRef\]](#)

21. Golden SH, Lazo M, Carnethon M, et al. Examining a bidirectional association between depressive symptoms and diabetes. *JAMA*. 2008;299(23):2751-2759. [\[CrossRef\]](#)
22. Fernandes BS, Salagre E, Enduru N, Grande I, Vieta E, Zhao Z. Insulin resistance in depression: a large meta-analysis of metabolic parameters and variation. *Neurosci Biobehav Rev*. 2022;139:104758. [\[CrossRef\]](#)
23. Hauger RL, Saelzler UG, Pagadala MS, Panizzon MS. The role of testosterone, the androgen receptor, and hypothalamic-pituitary-gonadal axis in depression in ageing Men. *Rev Endocr Metab Disord*. 2022;23(6):1259-1273. [\[CrossRef\]](#)
24. Walker MM, Talley NJ. Functional dyspepsia in the elderly. *Curr Gastroenterol Rep*. 2019;21(10):54. [\[CrossRef\]](#)
25. Kim SE, Kim N, Lee JY, et al. Prevalence and risk factors of functional dyspepsia in health check-up population: a nationwide multicenter prospective study. *J Neurogastroenterol Motil*. 2018;24(4):603-613. [\[CrossRef\]](#)
26. Bonetto S, Gruden G, Beccuti G, Ferro A, Saracco GM, Pellicano R. Management of dyspepsia and gastroparesis in patients with diabetes. A clinical point of view in the year 2021. *J Clin Med*. 2021;10(6):1313. [\[CrossRef\]](#)
27. Sarnelli G, Caenepeel P, Geypens B, Janssens J, Tack J. Symptoms associated with impaired gastric emptying of solids and liquids in functional dyspepsia. *Am J Gastroenterol*. 2003;98(4):783-788. [\[CrossRef\]](#)
28. Farré R, Vanheel H, Vanuytsel T, et al. In functional dyspepsia, hypersensitivity to postprandial distention correlates with meal-related symptom severity. *Gastroenterology*. 2013;145(3):566-573. [\[CrossRef\]](#)
29. Labanski A, Langhorst J, Engler H, Elsenbruch S. Stress and the brain-gut axis in functional and chronic-inflammatory gastrointestinal diseases: a transdisciplinary challenge. *Psychoneuroendocrinology*. 2020;111:104501. [\[CrossRef\]](#)
30. Vanner S, Greenwood-Van Meerveld B, Mawe G, et al. Fundamentals of neurogastroenterology: basic science. *Gastroenterology*. 2016. [\[CrossRef\]](#)
31. Huang ZP, Wang K, Duan YH, Yang G. Correlation between lifestyle and social factors in functional dyspepsia among college freshmen. *J Int Med Res*. 2020;48(8):300060520939702. [\[CrossRef\]](#)
32. Amerikanou C, Kleftaki SA, Valsamidou E, et al. Food, dietary patterns, or is eating behavior to blame? Analyzing the nutritional aspects of functional dyspepsia. *Nutrients*. 2023;15(6):1544. [\[CrossRef\]](#)
33. An D. A study on the clinical characteristics of functional dyspepsia patients with or without depression. *Asian J Surg*. 2022;45(1):605-606. [\[CrossRef\]](#)
34. Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of functional dyspepsia with depression and anxiety: a systematic review. *J Gastrointest Liver Dis*. 2021;30(2):259-266. [\[CrossRef\]](#)