Association between gastrointestinal symptoms and depression among older adults in Taiwan: A cross-sectional study

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Abstract

Background: Older adults with depression more frequently experience somatic and gastrointestinal (GI) problems compared with people without depression and younger adults with depression. However, whether GI symptoms are predictive of elevated rates of depression among older adults is unclear.

Methods: We enrolled 106 older adults (>60 years old); 69 had late-life depression (LLD), and 37 were controls. All participants gave ratings on the Gastrointestinal Symptom Rating Scale (GSRS) and Hamilton Depression Rating Scale. Food consumption was assessed using a food frequency questionnaire, and a Mediterranean diet score was used as a covariate.

Results: Compared with the controls, patients with LLD reported higher levels of depressive and GI symptoms and reported more reflux, abdominal pain, and dyspepsia symptoms, and these symptoms were correlated with Hamilton Depression Rating Scale scores (GSRS total: $\beta = 0.47$; reflux: $\beta = 1.47$; abdominal pain: $\beta = 1.98$; dyspepsia: $\beta = 1.02$; all $p < 0.01$). After demographic variables and Mediterranean diet score were controlled for, a logistic regression analysis indicated that total GSRS score was an independent determinant of LLD (odds ratio: 1.20, 95% CI: 1.04-1.38). Moreover, a stratified analysis by depression severity indicated that higher total GSRS score may contribute to greater depression severity (odds ratio: 1.25, 95% CI: 1.04-1.52).

Conclusion: We provide evidence that GI symptoms are associated with depressive symptoms among patients with LLD. Older people with more specific GI symptoms, such as reflux, abdominal pain, and dyspepsia, are potentially at greater risk of having LLD.

Keywords: Gastrointestinal symptoms; Late-life depression; Mediterranean diet

1. INTRODUCTION

Late-life depression (LLD) is a major psychiatric disorder in older adults, with prevalence rates ranging from 7% to 49%.[1] Older adults with depression may have more somatic and gastrointestinal (GI) symptoms than either older adults without depression[2] or younger adults with major depressive disorder (MDD).[3] Several studies have identified some generalized physical complaints as predictors of psychiatric comorbidity.[4] However, whether GI symptoms are predictive of elevated rates of depression among older adults remains unclear. Furthermore, few studies on older adults with depression have investigated GI symptoms using GI-specific symptom questionnaire scales, such as the Gastrointestinal Symptom Rating Scale (GSRS). In other fields of research, the bidirectional route of communication between the gut and central nervous system, referred to as the gut-brain axis, has been of interest in recent years.[5] Psychological factors, such as depression, anxiety, and the occurrence of traumatic life events, have been reported to be closely related to the causal mechanisms underlying functional GI disorders.[6] Dysbiosis and inflammation of the gut have also been identified as causes of several mental illnesses, including anxiety and depression.[7] Studies investigating the relationship between depression and GI symptoms have not controlled for crucial variables, such as diet, that may influence both depression and functional GI disorders.[8] Furthermore, relatively little research on this topic has focused on older adults.

Thus, this study investigated the correlation between specific GI symptoms and depressive symptoms in older adults after diet is controlled for. Specifically, we examined the influence of a Mediterranean diet pattern (MDP) on the risk of depression in

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older adults. We hypothesized that older adults with certain GI symptoms have a higher risk of having more depressive symptoms.

2. METHODS

2.1. Participants

Our study was conducted at the psychiatric outpatient department of Taipei Veterans General Hospital. We recruited patients between the ages of 60 and 89 years who had a Diagnostic and Statistical Manual of Mental Disorders, 5th Edition diagnosis of MDD made by a board-certificated psychiatrist[9] into the LLD group. Participants in the control group were recruited using posters placed in the community surrounding the hospital. The exclusion criteria were having (1) a diagnosis of a major neurocognitive disorder; (2) any one major psychiatric comorbidity (such as schizophrenia or bipolar disorder); (3) any one physical comorbidity (such as organic GI diseases—including liver cirrhosis, fatty liver disease, peptic ulcer, inflammatory bowel disease, or any malignancy—or a history of receiving chemotherapy or radiation for any cancer); (4) any known active bacterial, fungal, or viral infection; (5) received new prebiotic or probiotics within 90 days prior to enrollment; and (6) a record of GI tract surgery, appendectomy, or cholecystectomy surgery in the preceding 1 year. The participants in the control group underwent the Mini-International Neuropsychiatric Interview with a psychiatrist to exclude patients with any psychiatric illness. We conducted a detailed review of the participants' medical history and performed anthropometric measurements to exclude those with physical comorbidities. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics review committee. All participants provided written informed consent prior to participating in the study.

2.2. Assessment of depressive and GI symptoms

All participants completed the 17-item Hamilton Depression Rating Scale (HAMD)[10] and 15-item GSRS.[11] The 17-item HAMD is a commonly used and widely validated measure of depressive symptoms, where ratings are given by clinicians. The GSRS comprises sections on the five symptom clusters of reflux syndrome, diarrhea, constipation, abdominal pain, and dyspepsia, where ratings are given by clinicians. The GSRS uses a 7-point scale with 1 representing "no bothersome symptoms" and 7 representing "very bothersome symptoms." The GSRS has been reported to be valid and reliable when used to measure GI symptoms, such as gastroesophageal reflux disease and dyspepsia.[12]

2.3. Assessment of food consumption

Food consumption was assessed with the assistance of a trained dietitian using a semiquantitative food frequency questionnaire with documented validity.[13] Participants were asked how often they consumed various types of food and beverages that fall under one of nine categories during the previous 1 month. We evaluate the adherence of participants to the MDP according to a 9-point dietary score, which was previously reported by Trichopoulou et al.[14] The Mediterranean diet score (MedDietScore) was calculated by assigning a score of 0 or 1 to each of the nine food groups; scores of 0 and 1 indicated that the participant's consumption patterns in the given food category did not and did accord with the MDP, respectively. Specifically, for each food category, 1 point was awarded for food intake with a (1) high ratio of monounsaturated fatty acids to saturated fatty acids; (2) high intake of legumes, at one or more servings per week; (3) high intake of whole grains, at one or more servings per day; (4) high intake of nuts, at one or more servings per week; (5) high intake of fruits, at three or more servings per day; (6) high intake of vegetables, at four or more servings per day; (7) high intake of fish, at four or more servings per week; (8) low intake of red and processed meat, at less than two and three servings per day for women and men, respectively; and (9) moderate intake of alcohol, at 0.5 to 1 drink daily for women and 1 to 2 drinks daily for men. The total score ranged from 0 (minimal adoption) to 9 (maximum adoption).

2.4. Other covariates assessments

For the baseline assessment, we gathered sociodemographic data (eg, sex, age, and education) and anthropometric data (eg, weight and height). The weight and height of the participants were measured by an assisting nurse, and body mass index (BMI) was calculated, defined as weight (in kilograms) divided by squared height (in meters).

2.5. Statistical analyses

Categorical variables were compared using chi-square tests, and continuous variables were compared using Student's t tests. All tests were based on two-tailed alternatives. Analysis of variance with post hoc analysis was used to compare HAMD scores and GSRS scores between the four groups of patients with LLD who were taking different types of antidepressant drugs. Linear regression was used to assess the correlation between total HAMD score and GSRS score, with adjustment for age, sex, years of education, BMI, and MedDietScore. Sex-stratified subgroup analyses were also conducted to investigate the role of sex in the association between HAMD score and GSRS score among patients with LLD. The HAMD-17 has two items that are related to appetite and GI (items 11 and 12), which may overlap with the psychometric construct of the GSRS. Thus, to prevent any consequently spurious inferences as to the predictive power of GI symptoms, we summed all subscores of HAMD except item 11 and item 12 in the linear regression model. Before the analysis, we tested for multicollinearity using the variance inflation factor. We also performed logistic regression with adjustment for demographic data (age, sex, years of education, BMI, and diabetes mellitus) to calculate the odds ratios (ORs) of developing LLD. A subgroup analysis using logistic regression models for subscales of GSRS was performed to assess the risks of developing LLD. Furthermore, logistic regression analyses for subgroups stratified by depression severity were also conducted to explore the effects of disease severity on the risk of LLD. With reference to a large study that established severity cutoff scores on the HAMD,[15] we classified patients into mild depression (8-16), moderate depression (17-23), and severe depression (≥24) groups according to the ranges of HAMD. For all variables, significance was defined as a two-tailed p value of <0.05. All data processing and statistical analyses were performed using Statistical Package for Social Science software version 17 and Statistical Analysis Software (version 9.1; SAS Institute, Cary, NC, USA).

3. RESULTS

We enrolled 69 patients with LLD and 37 controls. The patients with LLD had a lower average educational level compared with the controls and reported higher levels of depressive symptoms and GI symptoms (Table 1). Specific GI symptoms that were more prevalent in patients with LLD were reflux syndrome, abdominal pain, and dyspepsia (all $p < 0.01$) (Table 1). MedDietScore did not significantly differ between patients with LLD and the controls. Among the 69 patients with LLD, 14 (20.3%) did not take antidepressants and 55 (79.7%) took antidepressants. Among these 55 patients taking antidepressants, 18 (26.1%) took selective serotonin reuptake inhibitors, 14 (20.3%) took serotonin-norepinephrine reuptake inhibitors,

Table 1

Clinical and demographic characteristics of the patients with late-life depression and the controls

Mean (SD) or n (%)	LLD (n = 69)	Control (n = 37)	*p*
Age	72.4 (8.3)	67.5 (5.5)	<0.01
Sex (female), n (%)	53 (76.8)	22 (59.5)	0.05
Edu (y)	9.0 (5.1)	12.3 (4.5)	<0.01
BMI (kg/m^2)	23.8 (3.0)	24.0 (3.4)	0.80
DM (yes), n (%)	14 (20.3)	5 (13.5)	0.28
MedDietScore	1.8 (1.0)	1.8 (1.3)	0.97
HAMD total score	14.4 (6.4)	1.8 (1.8)	<0.01
GSRS total score	6.3 (4.1)	3.5 (3.3)	<0.01
GSRS: Reflux syndrome	1.2 (1.4)	0.5 (0.9)	<0.01
GSRS: Diarrhea syndrome	1.1 (1.1)	1.0 (1.1)	0.61
GSRS: Constipation syndrome	1.4 (1.5)	0.8 (1.0)	0.02
GSRS: Abdominal pain	0.7 (1.0)	0.3 (0.5)	<0.01
GSRS: Dyspepsia	2.1 (2.0)	1.0 (1.4)	<0.01

BMI = body mass index; DM = diabetes mellitus; GSRS = Gastrointestinal Symptom Rating Scale; HAMD = Hamilton Depression Rating Scale; LLD = late-life depression; MedDietScore = Mediterranean diet score.

and 23 (33.3%) took agomelatine. To investigate the influence of the various medications on GI symptoms, analysis of variance tests were performed, and no significant difference in any of the symptom clusters of GSRS was noted among patients taking medications in the different groups (Table 2). Linear regression results indicated a modest correlation between GSRS total score and HAMD total score (β: 0.47, $p < 0.01$) (Table 3). The subscales were also included in the analyses, and we found that reflux syndrome (β: 1.47, 95% CI: 0.46-2.48), abdominal pain (β: 1.98, 95% CI: 0.41-3.55), and dyspepsia (β: 1.02, 95% CI: 0.36-1.68) were significantly correlated with HAMD total score without somatic subscores (Table 3). Sex-stratified subgroup analyses further indicated that the correlation between HAMD score and GSRS score was only present among female patients with LLD (Table 4).

Logistic regression analyses with demographic variables and MedDietScore controlled for revealed that total GSRS score was an independent determinant of LLD (OR: 1.20, 95% CI: 1.04-1.38) (Table 5). Subgroup analyses for subscales of GSRS indicated that older adults with more reflux (OR: 1.97, 95% CI: 1.14-3.41), abdominal pain (OR: 2.41, 95% CI: 1.05-5.52), or dyspepsia (OR: 1.57, 95% CI: 1.13-2.18) had a greater risk of LLD (Table 5). Among the patients with LLD, 31, 21, and 5 were defined as having mild, moderate, and severe depression, respectively. Logistic regression analyses for subgroups stratified by depression severity indicated that GSRS score was the only variable that potentially contributed to a higher depression severity (OR: 1.25, 95% CI: 1.04-1.52) (Table 6). This correlation was only noted when the mild and moderate depression groups were compared.

Table 3

Linear regression model for the association between the depressive symptoms and gastrointestinal symptoms in patients with late-life depression (n = 69)[a]

GSRS score	HAMD total scores without somatic subscores β (95% CI)	*p*
GSRS total score	0.47 (0.14-0.81)	<0.01
Subscale		
GSRS: Reflux syndrome	1.47 (0.46-2.48)	<0.01
GSRS: Diarrhea syndrome	-0.34 (-1.64 to 0.98)	0.61
GSRS: Constipation syndrome	-0.23 (-1.17 to 0.71)	0.62
GSRS: Abdominal pain	1.98 (0.41-3.55)	<0.01
GSRS: Dyspepsia	1.02 (0.36-1.68)	<0.01

[a]Adjusted for demographic data and Mediterranean diet score.
GSRS = Gastrointestinal Symptom Rating Scale; HAMD = Hamilton Depression Rating Scale.

4. DISCUSSION

The key finding of our study was that patients with LLD had higher levels of GI symptoms, including reflux syndrome, abdominal pain, and dyspepsia, than did the controls. Certain GI symptoms, such as reflux syndrome, abdominal pain, and dyspepsia, were significantly correlated with depressive symptoms among patients with LLD. Older adults with more GI symptoms, especially reflux syndrome, abdominal pain, and dyspepsia, may have a higher risk of LLD.

Our observations that patients with LLD had more reflux symptoms accord with those in the literature. In a cross-sectional study using Taiwan's National Health Insurance Research Database, patients over 65 years old with MDD were noted to have a higher prevalence of gastroesophageal reflux disease relative to the general population.[16] This finding may be attributable to the lower threshold for bodily sensation due to psychiatric factors and to the altered perception of esophageal stimuli in patients with depression.[17] An association between depression and dyspepsia was reported in the adult population,[18] and our findings suggest a higher level of dyspepsia in patients with LLD than in people without depression. Dyspeptic symptoms may be attributable to visceral hypersensitivity, which was reported to be associated with emotion dysregulation.[19] A previous study linked altered alpha-adrenoceptor function and depression to a G-protein beta-3 subunit gene polymorphism.[20] The genetic architecture of GI syndromes and the effects of interactions between gene polymorphisms and the environment warrant further investigation to determine the roles of interoceptive awareness and central nervous system dysregulation in GI syndromes. In addition, a study reported increased activation of brain regions such as the anterior cingulate cortex, thalamus, and prefrontal cortex in response to visceral stimuli in adult patients with irritable bowel syndrome, a GI disorder characterized by abdominal pain in the absence of an organic disorder.[21] The aforementioned brain regions that process

Table 2

Comparison of gastrointestinal symptoms among patients with late-life depression taking different types of antidepressant drugs (n = 69)

GSRS score	SSRI (n = 18)	SNRI (n = 14)	Agomelatine (n = 23)	Nonmedication (n = 14)	*p*
GSRS total score	6.3 (3.4)	6.1 (4.3)	6.1 (4.5)	6.9 (4.5)	0.96
GSRS: Reflux syndrome	1.2 (1.0)	0.9 (1.2)	1.5 (1.8)	1.3 (1.2)	0.65
GSRS: Diarrhea syndrome	1.2 (1.1)	0.9 (1.0)	1.0 (1.1)	1.4 (1.1)	0.66
GSRS: Constipation syndrome	1.2 (1.2)	2.0 (1.6)	1.5 (1.9)	0.9 (0.9)	0.27
GSRS: Abdominal pain	0.8 (0.9)	0.4 (0.6)	0.8 (1.3)	0.8 (0.7)	0.66
GSRS: Dyspepsia	2.1 (2.1)	1.9 (1.9)	2.0 (1.7)	2.7 (2.4)	0.68

GSRS = Gastrointestinal Symptom Rating Scale; SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Table 4

Linear regression model for the association between the depressive symptoms and gastrointestinal symptoms in male patients (n = 16) and female patients (n = 53)[a]

	HAMD total scores without somatic subscores			
	Male		Female	
GSRS score	β (95% CI)	*p*	β (95% CI)	*p*
GSRS total score	-0.12 (-1.46 to 1.22)	0.84	0.57 (0.25-0.9)	<0.01
Subscale				
GSRS: Reflux syndrome	-0.9 (-5.45 to 3.65)	0.66	1.74 (0.77-2.72)	<0.01
GSRS: Diarrhea syndrome	-1.46 (-5.38 to 2.46)	0.42	-0.11 (-1.47 to 1.26)	0.88
GSRS: Constipation syndrome	-0.99 (-4.83 to 2.86)	0.57	-0.18 (-1.11 to 0.74)	0.69
GSRS: Abdominal pain	0.19 (-12.57 to 12.96)	0.97	2.13 (0.73-3.53)	<0.01
GSRS: Dyspepsia	0.39 (-2.55 to 3.34)	0.77	1.06 (0.44-1.68)	<0.01

[a]Adjusted for demographic data and Mediterranean diet score.
GSRS = Gastrointestinal Symptom Rating Scale; HAMD = Hamilton Depression Rating Scale.

GI sensory information largely overlap with regions involved in emotional regulation, which may form a structural foundation for the coexistence of abdominal pain and depression.[22,23]

The correlation between depression and GI symptoms cannot be explained using a single model because various interactions are involved.[24] The brain-gut axis may involve bidirectional communication in the development of GI symptoms. A high depression level in patients with functional GI disorder was reported in a previous study, and depression was considered to be an important predictor of functional dyspepsia and irritable bowel syndrome.[25] Our findings indicate that functional GI symptoms may be independent predictors of depression in older adults. We further stratified GI symptoms by GSRS subscale measure and found that reflux syndrome, abdominal pain, and dyspepsia are possible determinants of depression in old age. Our subgroup analyses further indicated that the association between depressive symptoms and GI symptoms was present only among female patients. However, this result may be biased because of the small number of male participants with LLD. Moreover, subgroup analysis stratified by depression severity indicated that a higher total GSRS score contributes to greater depression severity only in the comparison of groups with mild and moderate depression. No differences were observed between other groups, possibly because of our small sample of patients with severe depression.

Diet has been generally accepted for its role in the pathophysiology of GI disorders.[26] Adherence to an MDP, characterized by abundant intake of plant-based foods and olive oil and a moderate intake of fish, has been linked to a lower likelihood of depressive symptoms in older adults.[27] The protective role of the MDP against depression encompasses positive synergic actions, anti-inflammatory functions, and protection from oxidative stress.[28,29] In Taiwan, the excessive intake of meat by men and women aged 19-64 years results in an excessive intake of protein, cholesterol, and saturated fat. Older adults (>65 years) were noted to have a low intake of dietary fiber.[30] Difficulty chewing and swallowing may influence the amount of fiber consumed among older adults.[30] This may explain why we found no significant difference in MedDietScore between the patients with LLD and the controls. Moreover, the GSRS total score and subscores remained related to depression even after MedDietScore was controlled for, suggesting that diet may not fully explain the presence of depressive symptoms in older patients. Despite the increasing emphasis on the brain-gut axis, the role of diet in this pathway remains uninvestigated.

Because depression in older adults remains underdiagnosed and inadequately treated, patients with LLD often have a poor long-term prognosis, a more chronic disease course, and a higher relapse rate. The findings of our study can aid clinical practice in highlighting the importance of considering an older adult patient's history of somatic symptoms, particularly GI symptoms. Clinicians should be aware that LLD may present without typical subjective mood symptoms but with a more pronounced frequency of somatic symptoms. Knowledge of a patient's co-occurring or even preceding GI symptoms can help physicians pay more attention to older patients with depression to provide them with suitable and timely treatment. Future studies should investigate the relationship between mental illness and the GI tract in older adults.

Table 5

Logistic regression analyses for adjusted odds ratio of late-life depression (n = 106)

Variables	Adjusted odds ratio (95% CI)	*p*
Age	1.11 (1.02-1.19)	0.01
Sex	2.57 (0.83-7.93)	0.10
Edu	0.93 (0.83-1.03)	0.17
BMI	0.94 (0.80-1.10)	0.43
DM	0.86 (0.19-3.88)	0.86
MedDietScore	0.69 (0.57-1.45)	0.69
GSRS total score	1.20 (1.04-1.38)	0.01
GSRS: Reflux syndrome	1.97 (1.14-3.41)	0.02
GSRS: Diarrhea syndrome	0.99 (0.65-1.49)	0.94
GSRS: Constipation syndrome	1.21 (0.84-1.74)	0.32
GSRS: Abdominal pain	2.41 (1.05-5.52)	0.04
GSRS: Dyspepsia	1.57 (1.13-2.18)	< 0.01

BMI = body mass index; DM = diabetes mellitus; GSRS = Gastrointestinal Symptom Rating Scale; MedDietScore = Mediterranean diet score.

Table 6

Adjusted odds ratios for the risk of moderate depression (n = 21) versus mild depression (n = 31)

	Moderate vs mild depression	
Variables	Adjusted OR (95% CI)	*p*
Age	1.07 (0.96-1.19)	0.21
Sex	0.98 (0.14-6.99)	0.98
Edu	0.97 (0.86-1.11)	0.68
BMI	1.13 (0.85-1.50)	0.40
DM	1.50 (0.22-10.36)	0.68
MedDietScore	0.83 (0.43-1.60)	0.58
GSRS total score	1.25 (1.04-1.52)	0.02

BMI = body mass index; GSRS = Gastrointestinal Symptom Rating Scale; MedDietScore = Mediterranean diet score; OR = odds ratio.

Our study had the following limitations. First, our sample size was small, particularly for the subsamples of the control group and male patients with LLD. Future studies should recruit more participants to produce findings with higher statistical power. Second, participants with depression were taking medication. Psychotropic medications, particularly antidepressant medications, have known GI side effects. We did not account for this influence, which potentially affected our results. Third, we had an insufficient number of participants with more severe depression. Thus, we could not investigate the association between GI symptoms and depression among subgroups of patients with different symptom severities. Fourth, we did not account for lifestyle factors, such as smoking and sedentary behavior; these factors have a known influence on reflux symptoms. Finally, GI symptoms were recorded retrospectively. This constitutes a limitation because the occurrence of mood disturbances may increase recall effects because retrospective ratings of symptoms are biased by the participant's feelings as they complete the questionnaire, leading to positive or negative recall.

Our findings provide evidence supporting the association between GI symptoms and depressive symptoms among patients with LLD. Older people with more specific GI symptoms, such as reflux, abdominal pain, and dyspepsia, may have a higher risk of LLD. Future studies that account for neurobiological and genetic factors should be conducted to further elucidate the relationship between GI symptoms and depression. Clinicians should remain vigilant to signs of mental disorders when evaluating older patients with GI symptoms.

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