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Original Article

Masculinity, Rather Than Biological Sex, Is Associated With Psychological Comorbidities in Patients With Irritable Bowel Syndrome

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Background/Aims
Irritable bowel syndrome (IBS) generally shows sex differences, and psychiatric comorbidities play an important role in its pathogenesis. We aim to measure the levels of gender roles and investigate their relationship with psychiatric factors in patients with IBS versus healthy controls.

Methods
Patients diagnosed with IBS by Rome III and whose colonoscopy findings were normal were enrolled at multiple sites in Korea. The participants completed the Korean Sex Role Inventory–Short Form (KSRI-SF) to assess masculinity and femininity, the stress questionnaire, the Hospital Anxiety Depression Scale (HADS), and the 36-item Short Form Health Survey questionnaire to assess the quality of life (QOL).

Results
In total, 102 patients with IBS (male:female = 35:67; mean age 42.6 ± 16.7 years) and 55 controls (male:female = 20:35; mean age 42.4 ± 11.1 years) were recruited. IBS patients had higher stress (9.69 ± 8.23 vs 4.56 ± 8.31, $P < 0.001$) and HADS scores (16.12 ± 7.17 vs 10.22 ± 5.74, $P < 0.001$) than the control group, but showed no significant difference in KSRI-SF scores. No significant differences in HADS and KSRI-SF scores were found between males and females. However, IBS patients whose symptoms worsened due to stress and patients with anxiety or depression had significantly lower masculinity. QOL was poorer in IBS patients than in controls. In stepwise multivariate analyses, the anxiety score, depression score, and the degree of daily life disturbance, not masculinity, were associated with the QOL of IBS patients.

Conclusions
IBS patients had higher stress, more psychiatric comorbidities, and lower QOL than controls. Low masculinity, rather than sex, was associated with stress and psychological comorbidities, which deteriorated the QOL in IBS patients.
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Key Words
Anxiety; Depression; Irritable bowel syndrome; Masculinity; Stress, psychological

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Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal (GI) disorder of unclear etiology that is characterized by recurrent abdominal pain associated with a change in bowel frequency or stool form.[1] According to the Rome Foundation Global Study in 33 countries, the worldwide prevalence of IBS is 3.8% and 10.1% by the Rome IV and III criteria, respectively.[2] The prevalence of IBS in South Korea based on the Rome III criteria was 15.6%, which is slightly higher than the global prevalence.[3] The prevalence of IBS in females is twice as high as in males, and the global survey reaffirmed this finding, with a female-to-male odds ratio of 1.8.[2,4] The reason for the sex difference in the prevalence of IBS is not completely understood. In general, the prevalence of depression and anxiety in females is approximately twice as high as in males;[5,6] therefore, sex differences in the prevalence might be associated with psychiatric comorbidities in patients with IBS. A recent study found that overlap functional GI disorder including IBS was more associated with depression and anxiety and had more severe symptoms, and these phenomena were more prominent in women.[7] Another study also revealed sex differences in IBS tight junction protein pathophysiology.[8]

In our previous study, we showed that depression and anxiety were strongly associated with patients with IBS compared with healthy controls, regardless of the IBS subtype.[9] However, it was impossible to analyze psychological comorbidities according to sex in that systematic review and meta-analysis because most studies did not attempt to obtain sex-specific data. Moreover, most studies investigating psychological factors in patients with IBS have focused on anxiety and depression. Therefore, it is recommended to perform routine sex or gender analysis and investigate other variables such as the quality of relationships, social support, health perceptions, traumatic and stressful events, childhood experiences, and socioeconomic disparities.[4]

The role of sex and gender in disease has recently attracted attention as a novel variable in biomedical science.[10,11] "Sex" refers to a biological concept that classifies an individual into male and female based on the reproductive organs and functions derived from the chromosomal type and sex hormones. In contrast, "gender" refers to socio-cultural attitudes and behavioral traits appropriate to men and women, termed masculinity or femininity.[4,10] In this manuscript, sex differences and gender roles were studied simultaneously, but the terms "male" and "female" were used for uniformity. In a study of cardiovascular patients, female sex was not correlated with the recurrence of post-acute coronary syndrome or major adverse cardiac events. Instead, feminine roles and personality traits, which showed significant correlations with high anxiety, were associated with cardiovascular outcomes compared to masculine characteristics.[12] As gender roles are associated with depression and anxiety, suggesting that they may be possible indicators of mental health,[13,14] it could be hypothesized that gender-related characteristics may interplay with psychiatric comorbidities in the pathogenesis of IBS. Surprisingly, only 2 studies on gender-related characteristics in IBS have been reported, despite the definite sex difference. One study surveyed only patients with IBS and showed that femininity was correlated positively with symptom preoccupation, rejection of physician reassurance, and hypochondriasis characterized by high anxiety.[15] Another study with only male participants showed that patients with IBS exhibited less masculinity than healthy controls.[16] No study has explored the correlation between gender roles and psychiatric comorbidities by comparing patients with IBS and healthy controls in both sexes. In this study, we measured psychological comorbidities and gender scores in Korean patients with IBS and assessed the relationship between psychological comorbidities and gender scores, as well as their impact on quality of life (QOL).

Materials and Methods

Study Population

Participants aged 20 to 70 were consecutively recruited from 6 gastroenterology clinics of secondary and tertiary university hospitals from 2017 to 2018. The flow of the study process is summarized in Figure 1. All patients who met the Rome III criteria for IBS[17] underwent routine laboratory tests, abdominal imaging,

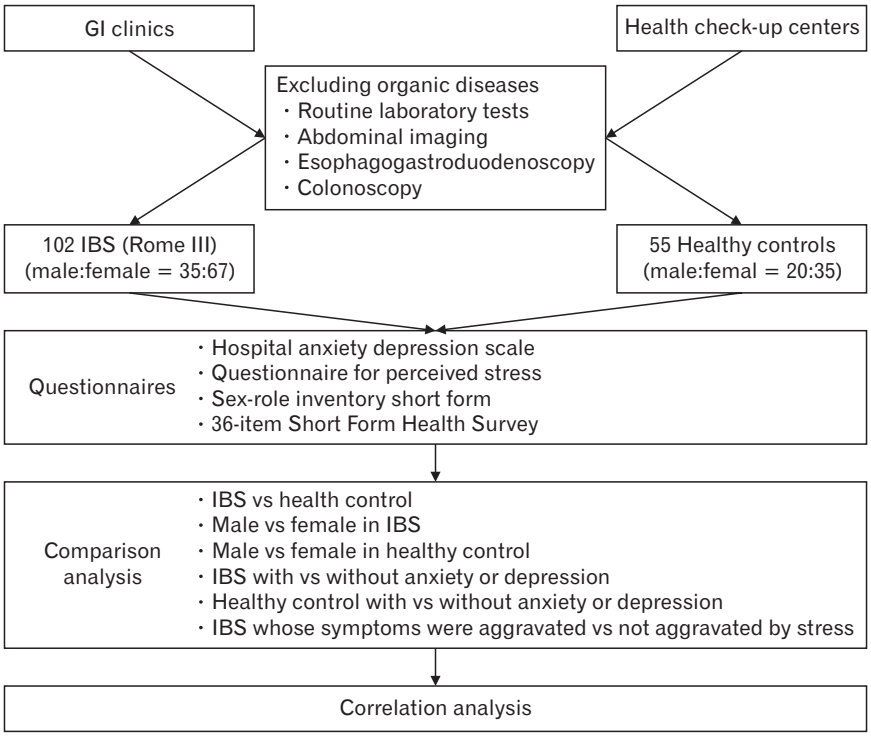

Figure 1. The flow chart of the study process. GI, gastrointestinal; IBS, irritable bowel syndrome.

esophagogastroduodenoscopy, and colonoscopy to exclude organic diseases. Subjects without any GI symptoms were enrolled in health check-up centers as controls. The exclusion criteria were as follows: a history of inflammatory bowel disease; major abdominal surgery (except appendectomy); pregnant or lactating women; severe systemic diseases including malignancy; hepatic and biliary disease; psychiatric disorders requiring medication. The study protocol was approved by the Institutional Review Board of all participating hospitals: Keimyung University Dongsan Hospital (No. 2016-10-006), Wonkwang University School of Medicine, Sanbon Hospital (No. IRB 2016-31), Kyung Hee University Hospital (KHUH 2017-07-081), Seoul National University Hospital Gangnam Center (No. H-1803-052-928), Gyeongsang National University Changwon Hospital (No. 2017-08-009), and The Catholic University of Korea (No. PC16QIMI0061). Written informed consent was obtained from all participants.

Questionnaires

Rome III criteria

The validated Korean Rome III questionnaire was used to diagnose IBS.[18] The Rome III criteria for IBS[19] were defined as recurrent abdominal pain or discomfort for at least 3 days per month in the past 3 months with 2 or more of the following: improvement with defecation, onset associated with a change in frequency of stool, and onset associated with a change in the form of stool. Patients scored their usual defecations using the Bristol Stool Form Scale (BSFS), a diagnostic tool that classifies the stool form into 7 categories. Stools described as BSFS type 1 or 2 were considered hard or lumpy stools, and stools described as BSFS type 6 or 7 were considered loose (mushy) or watery stools.[17] To evaluate the degree of the impact of IBS symptoms on patient's daily lives, patients were asked to answer on a 10-point Likert scale ranging from 0 for "none" to "very serious" in response to the question "Do your IBS symptoms interfere with your daily life or work?"

Psychological comorbidities

Anxiety and depressive symptoms were assessed using the validated Korean version of the Hospital Anxiety Depression Scale (HADS).[20,21] The HADS consists of 14 questions: 7 questions related to anxiety and 7 questions related to depression. Each question is answered on a 4-point Likert scale, ranging from 0, indicating "strongly disagree," to 3, representing "strongly agree." The total scores for each anxiety and depressive symptom range from 0 to 21

and are judged as follows: 0-7 points are normal, 8-10 points are borderline abnormality, and 11-21 points are abnormal.[20]

Assessment of perceived stress

Perceived stress was assessed using a questionnaire for 12 types of stress.[22] Participants answered the question, "Does stress worsen your symptoms?" and if they answered "yes," they were asked to choose the severity for each stress on a 7-point Likert scale, ranging from 0, indicating "none," to 6, representing "extremely severe." The types of stress were as follows: conflict with a spouse; child problems; conflict with a sibling; economic loss or business failure; conflict with family-in-law; unemployment, retirement, and promotions; poverty or hardship; conflict with friends; conflict with parents; family member's chronic illness; my chronic disease; and other stress.

Gender role-related scores

The validated Korean version of the Sex Role Inventory–Short Form (KSRI-SF) was used to evaluate gender roles.[23] The KSRI-SF, which measures masculinity-femininity and gender roles, was developed and validated in Korea based on the theory of Bem's androgyny and later used in several studies.[23,24] Compared to the Bem Sex Role Inventory, which consists of 60 questions, KSRI-SF has the advantage of easily measuring the properties of gender roles with high reliability in a short time.[23] The KSRI-SF consists of 10 questions: 5 questions related to masculinity and 5 questions related to femininity. The KSRI-SF was adapted from the Korean Sex Role Inventory, which was developed based on the Bem Sex Role Inventory.[25] Each item is rated on a 7-point Likert scale, ranging from 1, indicating "not at all," to 7, representing "always."

36-item Short Form Health Survey

The validated Korean version of 36-item Short Form Health Survey (SF-36) version 2 was used to evaluate the health-related QOL of the participants.[26,27] It consists of 36 items and 1 multi-item scale for each of its 8 conceptual QOL domains. The domains related to physical health include physical functioning (10 items), role limitations due to physical health problems (4 items), bodily pain (2 items), and perceptions of general health (5 items). The domains that relate to mental health include vitality (4 items), social functioning (2 items), role limitations due to emotional problems (3 items), and mental health (5 items). A score ranging from 0 to 100, with 0 indicating the worst and 100 representing the best condition, is calculated for each QOL domain, and higher scores indicate better QOL. The scores from all 8 domains are combined to create more comprehensive indicators of physical and mental health: the physical component summary and the mental component summary (MCS).

Statistical Methods

The continuous variables are presented as mean ± SD or median with interquartile range (IQR). Categorical variables were evaluated with the chi-square test or the Fisher exact test. Continuous variables were evaluated using the *t* test or the Wilcoxon rank sum test. Differences between IBS patients and controls were assessed using the chi-square and *t* tests. Both univariate and multivariate analyses were performed to identify risk factors for IBS, with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). The level of statistical significance was $P < 0.05$ for all analyses.

Results

Baseline Characteristics

In total, 102 patients with IBS (male:female = 35:67) and 55 controls (male:female = 20:35) were recruited (Table 1). The sub-

Table 1. Demographic Characteristics of Participants

Characteristics	IBS (n = 102)	Control (n = 55)	Total (n = 157)	*P*-value
Age (yr)	42.6 ± 16.7	42.4 ± 11.1	42.5 ± 14.9	0.760
Sex				
Male	35 (34.3)	20 (36.4)	55 (35.03)	0.797
Female	67 (65.7)	35 (63.6)	102 (64.97)	
BMI (kg/m^2)	22.4 ± 3.6	22.7 ± 4.2	22.5 ± 3.8	0.817
Education level				
Elementary school	8 (7.8)	3 (5.45)	11 (7.0)	0.003
Middle school	17 (16.7)	3 (5.5)	20 (12.7)	
High school	23 (22.6)	3 (5.5)	26 (16.6)	
University	47 (46.1)	34 (61.8)	81 (51.6)	
Postgraduate school	7 (6.9)	10 (18.2)	17 (10.8)	
Marital status				
Single	41 (40.2)	18 (32.7)	59 (37.6)	0.741
Married	51 (50.0)	34 (61.8)	85 (54.1)	
Divorce	3 (2.9)	1 (1.8)	4 (2.6)	
Bereavement	6 (5.9)	2 (3.6)	8 (5.1)	
Et cetera	1 (1.0)	0 (0.00)	1 (0.6)	

IBS, irritable bowel syndrome; BMI, body mass index.
Categorical data were analyzed using the chi-square test (chi-square statistic) or the Fisher exact test (table probability), and continuous data were analyzed using the Wilcoxon rank sum test (z-statistic).
Data are presented as mean ± SD or n (%).

Table 2. Hospital Anxiety and Depression Scale in Patients With Irritable Bowel Syndrome and Controls

Category	IBS (n = 102)	Control (n = 55)	*P*-value
HADS-A score	8.0 (6.0-11.0)	5.0 (0.0-13.0)	< 0.001
Judgment of anxiety			
Normal	47 (46.1)	47 (85.5)	< 0.001
Borderline abnormality	29 (28.4)	4 (7.3)	
Abnormal	26 (25.5)	4 (7.3)	
HADS-D score	8.0 (5.0-10.0)	5.0 (3.0-9.0)	< 0.001
Judgment of depression			
Normal	49 (48.0)	39 (70.9)	0.006
Borderline abnormality	29 (28.4)	12 (21.8)	
Abnormal	24 (25.3)	4 (7.3)	
HADS total score	16.12 ± 7.17	10.22 ± 5.74	< 0.001

IBS, irritable bowel syndrome; HADS-A, Hospital Anxiety Depression Scale-Anxiety; HADS–D, Hospital Anxiety Depression Scale–Depression.
Categorical data were analyzed using the chi-square test (chi-square statistic) and continuous data were analyzed using the Wilcoxon rank sum test or independent *t* test.
Data are presented as median (interquartile range), n (%), or mean ± SD.

types of IBS based on the BSFS during the most recent 3 months were as follows: constipation-predominant IBS (7, 6.9%), diarrhea-predominant IBS (34, 33.3%), and mixed IBS (61, 59.8%). Seventy-one (69.9%), 11 (10.8%), and 20 (19.6%) patients with IBS complained of abdominal pain, abdominal discomfort, and both abdominal pain and discomfort, respectively, during the last 3 months.

Psychiatric Comorbidities in Patients With Irritable Bowel Syndrome and Healthy Controls

Patients with IBS exhibited significantly higher HADS scores than the control group. When participants were classified as normal, borderline abnormal, and abnormal based on the HADS score, there were significantly more borderline abnormal and abnormal anxiety and depression cases in IBS patients than in the controls (Table 2). In a subgroup analysis by sex, there was no statistical difference in the stress and HADS scores between males and females in both IBS patients and the control group. Patients with IBS exhibited significantly higher stress scores than controls (median 7.5, IQR 4.0-15.0 vs median 0.0, IQR 0.0-6.0; $P < 0.001$). Eighty out

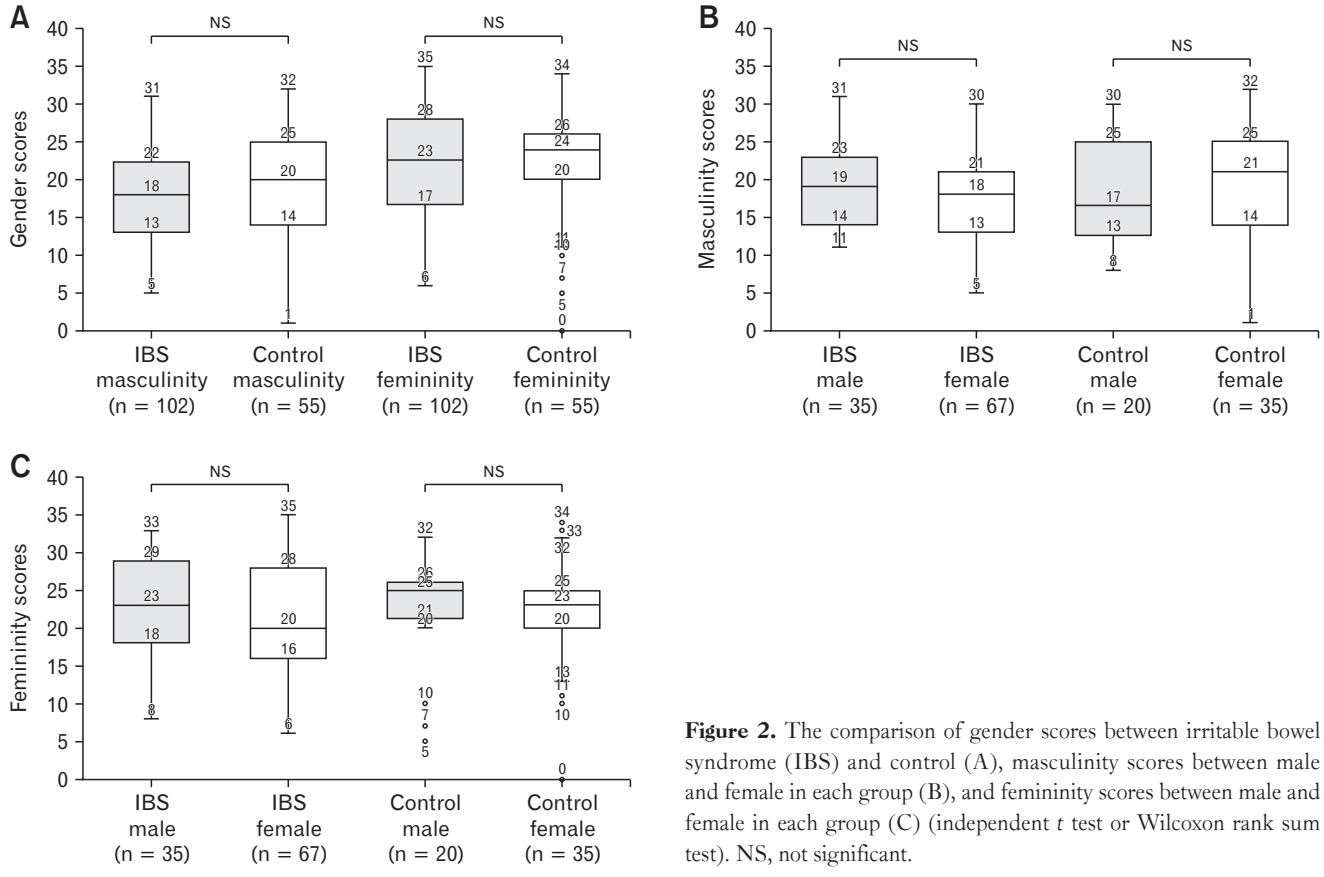

Figure 2. The comparison of gender scores between irritable bowel syndrome (IBS) and control (A), masculinity scores between male and female in each group (B), and femininity scores between male and female in each group (C) (independent *t* test or Wilcoxon rank sum test). NS, not significant.

of 102 (78.4%) patients with IBS answered that psychological stress aggravated their bowel symptoms. There were no differences in the total stress scores between males and females in both IBS patients and the control group.

Gender Role Scores and Their Relationship to Psychological Variables in Patients With Irritable Bowel Syndrome and Controls

There were no statistically significant differences in the masculinity and femininity scores between IBS patients and the control group. Interestingly, the masculinity and femininity scores were not different between males and females in both groups (Fig. 2). In a subgroup analysis, the masculinity scores were significantly lower in IBS patients with anxiety (16.7 ± 5.7 vs 19.7 ± 6.1, $P = 0.011$) or depression (16. 5 ± 6.1 vs 19.9 ± 5.5, $P = 0.004$) in comparison with IBS patients without anxiety or depression (Fig. 3A and 3B). In contrast, there was no significant difference in gender scores between controls with anxiety and controls without anxiety. The femininity scores (median 20. 0, IQR 14.5-25.0 vs median 25.0, IQR 21.0-27.0; $P = 0.024$) were lower in the controls with depression than the controls without depression (Fig. 3C and 3D).

Correlation Among Psychiatric Comorbidities, Stress, and Gender Roles and Their Impacts on Daily Life and Quality of Life

Patients with high anxiety or depression scores (range 11-21) reported significantly more disturbance scores in their daily life and work due to GI symptoms than patients with low scores (range 0-10) (high anxiety vs low anxiety: median 6.0, IQR 5.0-8.0 vs median 5.0, IQR 2.0-7.0, $P = 0.017$; high depression vs low depres-

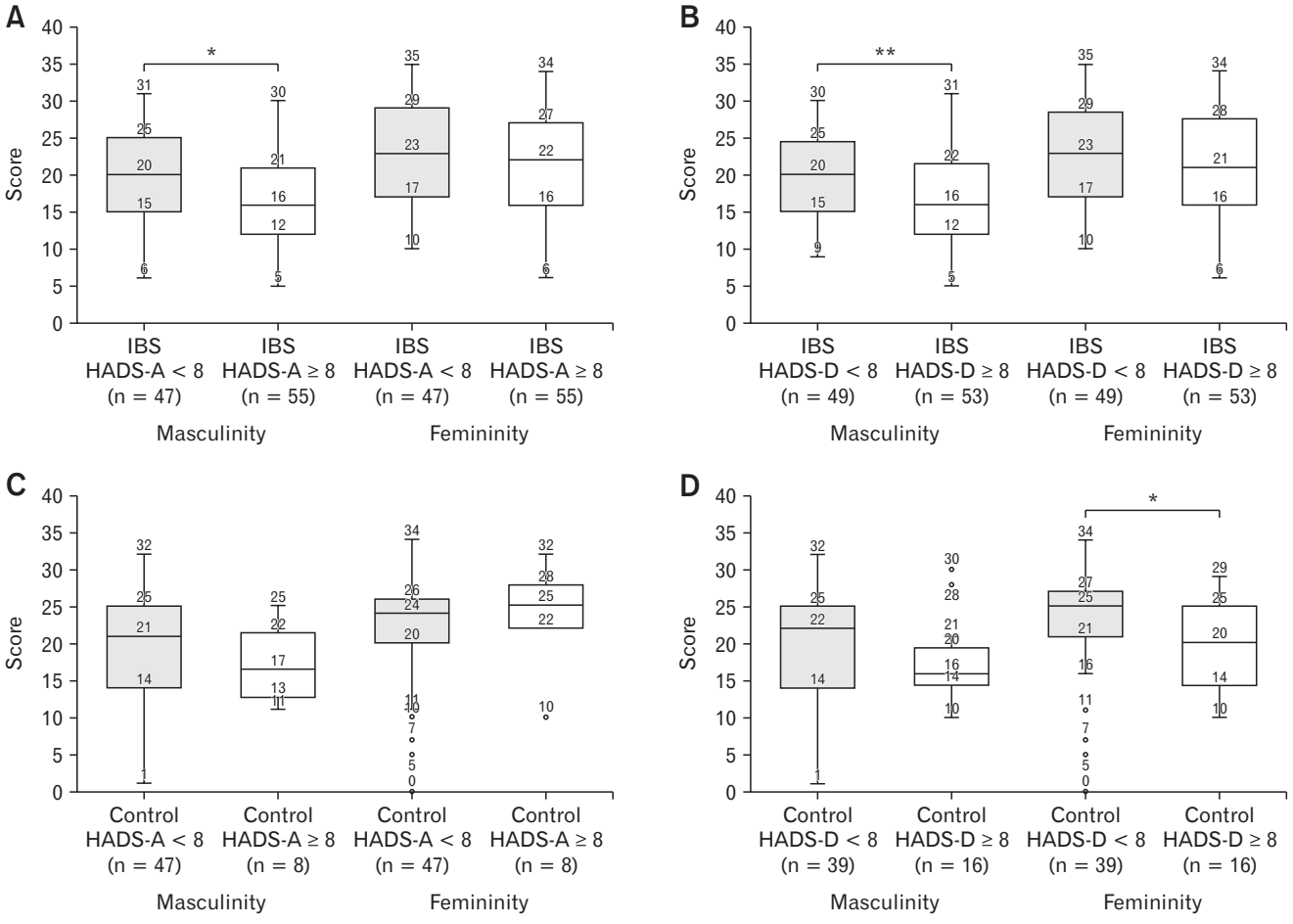

Figure 3. The subgroup analysis for gender scores based on the presence of anxiety in patients with irritable bowel syndrome (IBS) (A), based on the presence of depression in patients with IBS (B), based on the presence of anxiety in control (C), and based on the presence of depression in control (D). *$P < 0.05$, **$P < 0.01$, independent t test or Wilcoxon rank sum test. HADS-A, Hospital Anxiety Depression Scale–Anxiety; HADS-D, Hospital Anxiety Depression Scale–Depression.

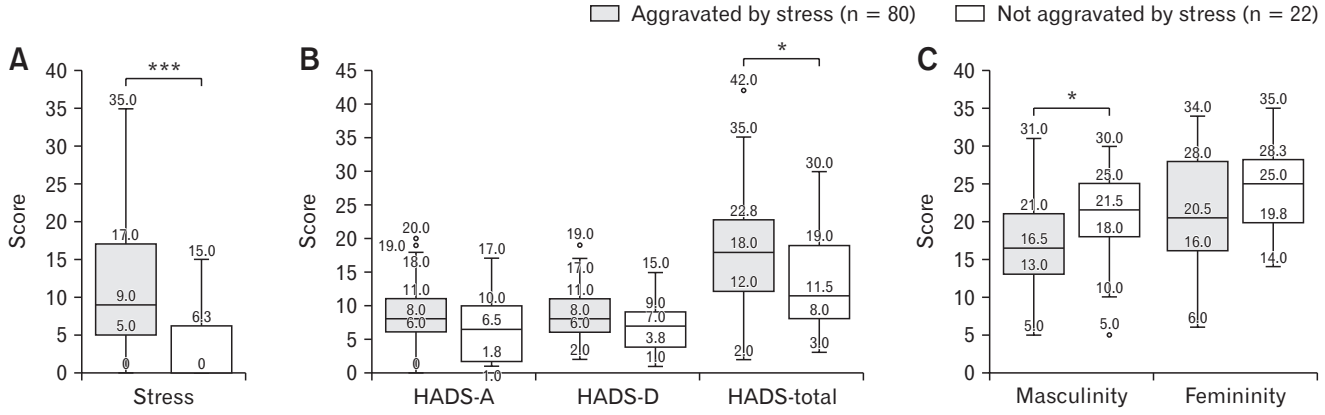

Figure 4. Differences between patients with irritable bowel syndrome (IBS) whose symptoms were aggravated and not aggravated by stress. Comparison of stress scores (A), anxiety and/or depression (B), and gender score (C) among IBS patients with and without stress-aggravated symptoms. *$P < 0.05$, ***$P < 0.001$, independent *t* test or Wilcoxon rank sum test. HADS-A, Hospital Anxiety Depression Scale–Anxiety; HADS-D, Hospital Anxiety Depression Scale–Depression.

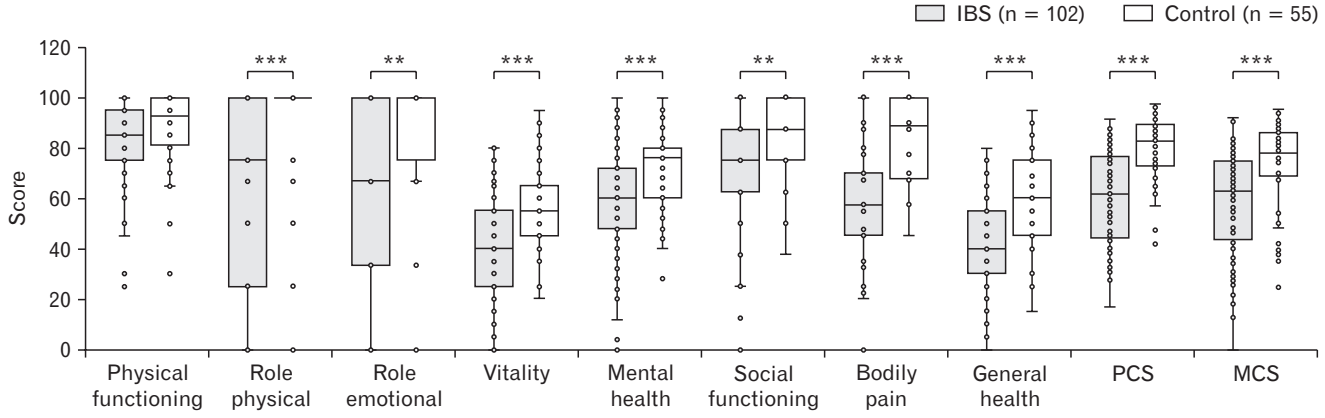

Figure 5. The comparison of quality of life (36-item Short Form Health Survey scales) between patients with irritable bowel syndrome (IBS) and controls. **$P < 0.01$, ***$P < 0.001$, independent *t* test or Wilcoxon rank sum test. PCS, physical component summary; MCS, mental component summary.

Table 3. Bivariate Associations Between Daily Life Disturbance, Quality of Life, and Psychological Variables

Variables	Daily life disturbance	Stress	HADS-A	HADS-D	Masculinity	Femininity	PCS	MCS	QOL-total
Daily life disturbance	1								
Stress	0.239[a]	1							
HADS-A	0.364[b]	0.363[b]	1						
HADS-D	0.264[b]	0.363[b]	0.565[b]	1					
Masculinity	−0.089	−0.038	−0.323[b]	−0.385[b]	1				
Femininity	−0.075	−0.088	−0.159	−0.236[a]	0.330[b]	1			
PCS	−0.461[b]	−0.310[b]	−0.464[b]	−0.480[b]	0.182	0.077	1		
MCS	−0.356[b]	−0.307[b]	−0.617[b]	−0.628[b]	0.249[a]	0.119	0.659[b]	1	
QOL-total	−0.441[b]	−0.338[b]	−0.600[b]	−0.614[b]	0.239[a]	0.110	0.896[b]	0.925[b]	1

[a]$P < 0.05$, [b]$P < 0.01$.
HADS-A, Hospital Anxiety Depression Scale–Anxiety; HADS-D, Hospital Anxiety Depression Scale–Depression; PCS, physical component summary; MCS, mental component summary; QOL, quality of life.

sion: median 7.0, IQR 5.0-8.0 vs median 5.0, IQR 2.0-7.0, $P = 0.024$; $P = 0.032$). The patients with IBS whose symptoms were aggravated by stress had significantly higher stress scores, higher total HADS scores, and lower masculinity scores than those who did not (Fig. 4). The QOL was poorer in patients with IBS than in controls, both physically and mentally (Fig. 5). In IBS patients with anxiety, the SF-36 score was lower in almost all areas, except bodily pain, than in IBS patients without anxiety. In the IBS patients with depression, the SF-36 score was lower in vitality, mental health, and general health than in the IBS patients without depression. The

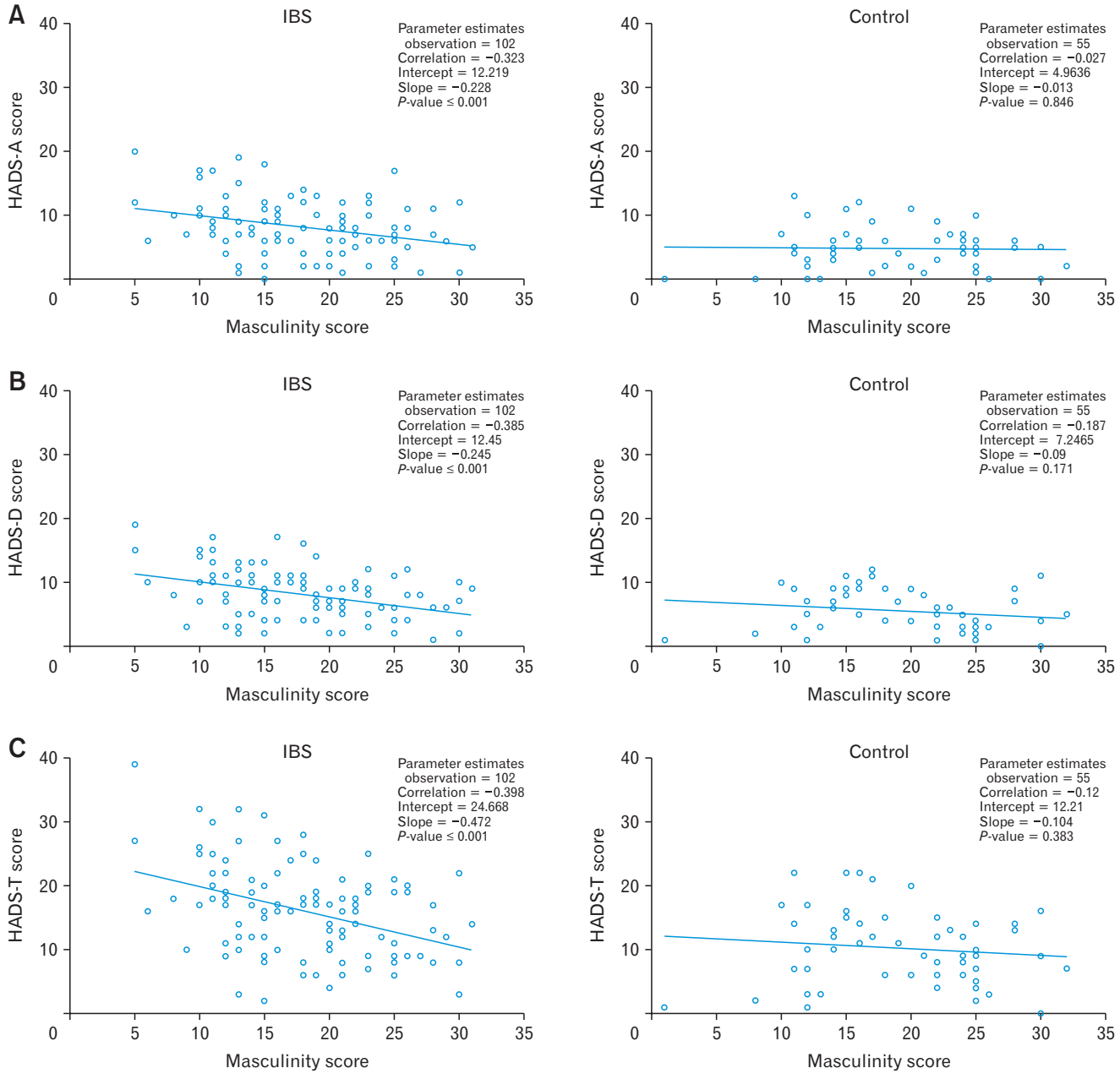

Figure 6. Correlation between psychiatric comorbidity and gender roles. (A) Scatter plot of anxiety scores by masculinity scores in patients with irritable bowel syndrome (IBS) and controls. (B) Scatter plot of depression scores by masculinity scores in patients with IBS and controls. (C) Scatter plot of total Hospital Anxiety Depression Scale (HADS) scores by masculinity scores in patients with IBS and control. HADS-A, Hospital Anxiety Depression Scale–Anxiety; HADS-D, Hospital Anxiety Depression Scale–Depression; HADS-T, Hospital Anxiety Depression Scale–Total.

Table 4. Stepwise Regression Analysis of Variables Associated With Quality of Life in Patients With Irritable Bowel Syndrome

	Unstandardized coefficients		Standardized coefficients	*t*	*P*-value	Adjusted R^2	F	*P*-value
	B	SE	β					
HADS-D	−3.425	0.785	−0.376	−4.360	< 0.001	0.498	33.677	< 0.001
HADS-A	−2.486	0.730	−0.304	−3.404	0.001			
Daily life disturbance	−2.955	0.982	−0.231	−3.008	0.003			

HADS-A, Hospital Anxiety Depression Scale–Anxiety; HADS-D, Hospital Anxiety Depression Scale–Depression.

masculinity score was inversely related to anxiety and depression and positively related to the MCS and total QOL scores in the IBS group. However, femininity was only related to depression and was not related to QOL.

In contrast, these relationships between gender scores and psychological variables were not observed in the control group. No correlation was found between masculinity and HADS scores in the control group (Table 3 and Fig. 6). Among various parameters, the anxiety score, depression score, and degree of daily life disturbance, but not masculinity or femininity scores, were significantly associated with the QOL of patients with IBS in stepwise multivariate analyses ($R^2 = 0.498, P < 0.001$) (Table 4).

Discussion

In this study, we measured gender role scores in patients with IBS and discovered that lower masculinity, rather than sex, was associated with anxiety and depression in patients with IBS; however, unlike anxiety and depression, masculinity did not directly affect QOL.

Psychosocial factors play an important role in the pathogenesis of IBS, and IBS is commonly associated with depression and anxiety.[28] The current study reaffirmed the results of our previous meta-analysis, according to which patients with IBS were significantly more depressed and anxious than healthy controls.[9] In addition to psychological factors, stress affects the onset and exacerbation of IBS symptoms. Stress can cause GI motor disorders and immune dysfunction, which provides a fundamental mechanism for changes in visceral hypersensitivity. Epidemiological studies have shown that early adverse life events are commonly noted in IBS patients, and chronic life stressors affect symptom intensity and treatment response.[29] Chronic GI symptoms again exacerbate the stress response of IBS patients.[30] Psychological factors can moderate the stress effect on IBS symptoms.[31] In the current study, we measured scores of various life stressors in terms of human relations, family problems, and socioeconomic factors, and found higher stress scores in IBS patients than in healthy people. Our data showed that patients whose symptoms were exacerbated by stress had a similar degree of daily life disturbances as patients without stress-induced exacerbation; however, the stress and total HADS scores were significantly higher. This finding means that anxiety and depression are closely related to stress and interact with each other in patients with IBS. Therefore, stress and psychological distress, such as anxiety and depression, should be systematically identified in IBS patients. Treatment strategies could be determined depending on the presence or absence of accompanying stress and psychological distress.[32]

The prevalence of IBS is typically higher in females, and this difference is greater in patients in tertiary hospitals with severe symptoms. Symptoms also differ between males and females. Increased bowel movements and diarrhea are more common in males, while nausea is more frequent in females.[33] In the current study, the number of females in consecutively enrolled patients with IBS was twice as high as that of males, although the prevalence could not be determined. Sex hormones could affect various mechanisms of IBS pathogenesis, including visceral perception and gut permeability.[34] However, there was no sex difference in the change of visceral sensitivity, at least in healthy young volunteers.[35] Considering that the prevalence of depression and anxiety is higher in females than in males, accompanying psychiatric distress could be the main contributor to sex differences in patients with IBS.[36] However, the sex difference in psychiatric distress of patients with IBS has not been completely elucidated because it usually has not been investigated in previous studies. Thus, we could not determine the effect of sex on depression and anxiety among IBS patients in our previous meta-analysis. A subsequent meta-analysis reported that when more females were included, more severe depression was associated with patients with IBS than in the control group. However, it is difficult to generalize because there was no direct comparison between males and females, and 20 out of 24 studies in the meta-analysis were con-

ducted in a single country (China).[37] In the current study, we conducted a sex analysis on psychiatric distress and surprisingly found no significant differences in depression, anxiety, and stress between males and females in the patients with IBS. Therefore, differences between males and females should be explained comprehensively based on various factors, such as gender effects (eg, including psychological influence and body image), which are particularly frequently observed in patients with IBS, along with sex differences in hormone and stress response.[38]

In this respect, we noted the impact of gender roles in IBS. Some recent studies have reported that gender role characteristics affect diseases, rather than biological sex. The concept of gender roles (masculinity and femininity) is defined as the generalization of appropriate male and female characteristics, and the application of this concept might enhance our understanding of the pathogenesis of IBS.[39] The gender role questionnaire was based on the Bem Sex Role Inventory, which was developed in the 1970s. Therefore, it may not fit well with the behavioral characteristics of males and females in modern society. In that sense, masculinity and femininity have recently been recognized in other terms as instrumentality and expressiveness.[40] The androgyny model suggests that males and females with high masculine and feminine characteristics show the greatest psychological adjustment because they might adapt to a wider range of situations.[41]

Only 2 studies to date have investigated the relationship between gender roles and IBS.[15,16] However, these studies were only conducted among patients with IBS or male patients, and no previous study has evaluated both male and female patients with IBS and healthy controls. We have raised the question of whether gender-related characteristics play a role in psychiatric distress in both sexes of patients with IBS. Several studies have shown that masculinity, not femininity, is related to anxiety and depression.[41,42] Interestingly, we found that gender scores were not significantly different between males and females in patients with IBS and healthy control, similar to HADS scores. However, a subgroup analysis according to psychological distress revealed differences in gender role scores according to stress, depression, and anxiety. The patients with IBS whose symptoms were aggravated by stress or patients with anxiety or depression had lower masculinity. In contrast, healthy controls showed no association between anxiety and gender scores. Rather, healthy controls with depressive mood showed significantly lower femininity. Considering the results of a study in acute coronary syndrome patients, according to which femininity is related to anxiety,[12] the relationship between gender roles and psychological comorbidities should be interpreted in the context of disease-specific aspects.

Our study confirmed that IBS patients had a lower QOL than normal controls, which was more pronounced in IBS patients with anxiety and depression, as reported in previous studies.[43] A correlation analysis showed that the masculinity score was positively related to the MCS and total QOL score; however, femininity was not related to QOL. These relationships between gender scores and psychological variables were not observed in the control group. Interestingly, in stepwise multivariate analyses, only the anxiety score and depression score, not masculinity, were directly associated with the QOL of patients with IBS.

It is not clear why low masculinity was associated with IBS. One study suggested that the level of sex hormones may affect masculinity and femininity; therefore, the role of low masculinity in IBS may be due to differences in underlying sex hormones.[44] Another explanation is that, as observed in this study, low masculinity increases anxious traits and subsequently affects IBS symptoms and QOL. Conversely, low masculinity in patients with IBS may result from psychological distress and social life disturbance caused by chronic GI symptoms. Future studies need to clarify whether the low masculinity in patients with IBS is a cause or effect.

Based on the findings that gender role imbalance is associated with psychological distress, it is necessary to determine whether severe gender role imbalance is present in patients with higher depression and anxiety. One study suggested that increasing instrumentality in patients with social anxiety disorder might be beneficial for treatment.[45] However, gender role imbalance could be considered a personality trait rather than an abnormal psychological condition. Future research is needed to clarify whether treatments targeting psychological comorbidities, such as neuromodulators, cognitive behavioral therapy, and psychotherapy, will be effective in improving gender role imbalance, resulting in improved QOL. The limitations of our study were that we did not conduct an analysis according to the IBS subtype due to the small number of patients with each subtype. Research on subtypes is needed with a larger number of patients in the future. Furthermore, the gender role scores used in this study were developed in the 1970s and may not be suitable for modern society. The results may also vary depending on the culture of each country. Therefore, further research is needed using new gender variables that are suitable for each culture.[46]

In conclusion, there was no significant difference in psychological comorbidity scores and gender role scores between males and females in patients with IBS. However, low masculinity is associated with anxiety and depression, which deteriorate the QOL. In the therapeutic approach to patients with IBS, multidisciplinary treatment is needed, considering not only symptoms but also psy-

chological factors and underlying gender-related characteristics.

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