INTRODUCTION

Inflammatory bowel disease (IBD), of which ulcerative colitis (UC) and Crohn’s disease (CD) are two subset disorders, is an idiopathic disease with chronic or relapsing inflammation of the gastrointestinal tract. While the pathogenesis of IBD is unclear, it is currently understood that the complex interaction between genetic, environmental, and immunological factors contributes to the disease course and progression. In Korea, the incidence of UC and CD increased from 0.22 to 3.62 and near to 0.2 to 1.68 per 100,000, respectively, from 1986 to 2005.

Patients with IBD have physical symptoms, such as diarrhea, rectal bleeding, and abdominal pain, and often develop various complications, including intestinal stricture, perforation, fistula, and abscess. Additionally, the disease’s incurability and unpredictable clinical course have a negative impact on patients’ quality of life and increase their psychological burden. Previous studies have reported that a significant proportion of patients with IBD have high rates of psychiatric comorbidity, especially depression and anxiety. An inadequate treatment may lead to a vicious cycle of poor treatment compliance, hormonal changes, frequent relapse, and deterioration of disease. Therefore, it is important to discover depression and anxiety in patients with IBD and provide them with appropriate psychiatric treatment.

Various factors associated with depression or anxiety in patients with IBD have been suggested in previous studies, but few are consistently reported. Previously mentioned risk factors for depression in patients with UC are disease activity, hospitalization, sex, other concomitant diseases, and surgery.
cal history. Risk factors for depression in patients with CD include disease activity, socioeconomic status, immunosuppressive drug use, surgical history, and age. In addition, the risk factors for anxiety are the time of diagnosis for UC and abdominal pain and socioeconomic status for CD. However, it was difficult to find a significant factor that consistently affects psychiatric symptoms in various studies. In addition, when comparing depression and anxiety levels in patients with UC and CD, some studies reported that there were no significant differences, while some reported higher levels of psychiatric symptoms in patients with CD.

Due to the chronic nature of IBD, which is difficult to treat and frequently recurs, the comorbidity of depression and anxiety also tends to become chronic during the long-term disease course. People who have chronic depression and anxiety often have cognitive distortions that lead to negative and pessimistic thoughts about their environment and themselves. It has been reported that not only the clinical symptoms of IBD itself but also the problems in life arising from the disease have a great influence on the course of treatment and compliance, but the rate of receiving treatment is low.

Therefore, the objective of this study was to identify and compare the depression and anxiety levels of patients with UC and CD in Korea using well-established psychometric instruments. The factors affecting depression and anxiety of each disease were also analyzed. Furthermore, the cognitive distortion level during the long-term course of IBD and its correlation with depression and anxiety were examined.

METHODS

Study patients

This study was conducted at Kyung Hee University Hospital, Seoul, Republic of Korea, and included patients with a confirmed diagnosis of UC or CD who were evaluated and treated in the Department of Gastroenterology from March 2018 to June 2018. Diagnoses of UC and CD were made based on the established clinical, endoscopic, radiological, and histopathological criteria. All patients were asked to complete questionnaires proven reliable and valid in obtaining the relevant information required in this study. The exclusion criteria were refusal to participate in the study, inability to fully comprehend or complete the questionnaires, and history of psychiatry clinic visit. Written informed consent was obtained from all patients. The study protocol was approved by the Institutional Review Board of Kyung Hee University Hospital (KHUH 2018-01-083).

Demographic and clinical presentation

Patient demographic and clinical data were collected from electronic medical records and administered questionnaires. Sociodemographic variables, such as age, sex, educational level, employment status, income level, marital status, family history of IBD, body mass index (BMI), and smoking or alcohol use were recorded. The collected clinical data included disease type (UC vs. CD), disease duration after diagnosis, number of IBD-related hospitalizations and surgeries, medical treatment (5-aminosalicylic acid (5-ASA), immunosuppressant, corticosteroid, anti-tumor necrosis factor-alpha (anti-TNF-α), and others), history of treatment discontinuation, and presence of comorbidities. Disease activity was assessed using the partial Mayo Clinic score for UC and Harvey Bradshaw index for CD.

Psychometric tools

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a well-validated depression screening tool, which is a self-reporting questionnaire consisting of nine items that are used to assess the depression level over the past 2 weeks. Each item is scored on a 4-point Likert scale (0–3), so the total score can range between 0 and 27. Scores of 0–4, 5–9, 10–14, 15–19, and 20–27 indicate minimal, mild, moderate, moderately severe, and severe depression, respectively. According to earlier studies, an individual with PHQ-9 score ≥10 is interpreted as having major depression with a sensitivity of approximately 90% and specificity of 77–88%.

Hospital and Anxiety Depression Scale (HADS)

The HADS, originally devised by Zigmond and Snith in 1983, is a self-reporting questionnaire to measure the levels of anxiety (A) and depression (D). Each scale comprises seven items, and each item on the questionnaire is scored on a 4-point Likert scale (0–3). Thus, one can score between 0 and 21 for either anxiety or depression. A higher score depicts a greater level of anxiety and depression. Cutoff scores are available where scores <8 are considered non-cases, 8–10 as mild, 11–14 as moderate, and 15–21 as severe cases of psychological morbidity. A score ≥11 indicates clinically significant depression. Since the HADS focuses on non-physical symptoms, it is useful in assessing anxiety and depression in patients with significant physical or chronic illness.

Anxious Thoughts and Tendencies (AT&T) Scale

The AT&T scale, originally developed by Ganellen et al. and later revised by Uhlenhuth et al., is an instrument designed to identify anxiety-prone cognitive style. Such cognitive style is marked by cognitive distortions, including catastrophizing, intrusive negative thoughts, and selective abstraction focusing on negative aspects of a situation. It contains 15 items.
on a 4-point Likert scale (0–3), with a higher score representing a greater predisposition to anxiety in general. According to the study by Uhlenhuth et al., AT&T scores observed in individuals with all anxiety disorders were higher than those in individuals in the reference group, with the highest scores observed in individuals who have panic disorder with agoraphobia. The second highest scores were noted in those with generalized social phobia, while the lowest scores were observed in individuals with specific social phobias.

Statistical analysis
In the comparative analysis of patients with UC and CD, categorical variables were analyzed using chi-square test or Fisher's exact test, while continuous variables were analyzed using Wilcoxon rank sum test. In the subgroups (UC and CD), we analyzed the variables that were correlated with different levels of depression and anxiety defined by PHQ-9, HADS-D, and HADS-A.

PHQ-9 scores were subcategorized into 0–4, 5–9, and ≥10, and HADS-A and D scores were subcategorized into 0–7, 8–10, and ≥11. In the comparison of the three ordinal groups, categorical variables were analyzed using chi-square test (or Fisher's exact test), and continuous variables were analyzed using the Jonckheere-Terpstra test. Furthermore, after screening variables with p-value <0.1 through simple multinomial logistic regression, multiple multinomial logistic regression was performed with selected variables. In addition, multiple generalized linear model (GLM) was established to examine the association between AT&T and depression or anxiety scales (PHQ-9, HADS-D, and HADS-A).

The p-value of all analyses was based on the significance level of 0.05, and statistical analyses were performed using the SAS 9.4 program (SAS Institute Inc., Cary, NC, USA).

RESULTS
Demographic and clinical characteristics
Of the 369 patients with IBD enrolled in the study, 187 had UC (50.7%), while 182 had CD (49.3%). Table 1 demonstrates baseline sociodemographic characteristics of the study population. The mean age of patients with CD was lower than that of patients with UC (33.83±11.37 vs. 45.46±14.09 years, p<0.001). In both UC and CD groups, there were more men than women (60.96% in UC, 75.82% in CD). There was a larger number of patients with CD with education level of university graduation or higher compared to that of patients with UC (62.09% vs. 52.94%, p<0.001). When the patients’ marital statuses were collected, there were more patients with UC

Table 1. Demographic characteristics of the study population

| Variable                  | UC (N=187)     | CD (N=182)     | p-value  |
|---------------------------|----------------|----------------|----------|
| Age (year)                | 45.46±14.09    | 33.83±11.37    | <0.001*  |
| Sex                       |                |                | 0.002*   |
| Male                      | 114 (60.96)    | 138 (75.82)    |          |
| Female                    | 73 (39.04)     | 44 (24.18)     |          |
| BMI (kg/m²)               | 23.04±2.87     | 22.28±3.63     | 0.003*   |
| Alcohol use               | 82 (43.85)     | 89 (48.90)     | 0.331    |
| Smoking                   |                |                |          |
| Current smoker            | 19 (10.16)     | 30 (16.48)     | 0.074    |
| Education level           |                |                |          |
| University graduation or high | 99 (52.94) | 113 (62.09)    | <0.001*  |
| Marital status            |                |                | <0.001*  |
| Married                   | 116 (62.03)    | 76 (41.76)     |          |
| Never married             | 59 (31.55)     | 102 (56.04)    |          |
| Divorced/ Separated/ Widowed | 12 (6.42)    | 4 (2.2)        |          |
| Employment status, working| 141 (75.40)    | 149 (81.87)    | 0.155    |
| Income                    |                |                | 0.057    |
| Low                       | 49 (26.35)     | 66 (36.67)     |          |
| Moderate                  | 71 (38.17)     | 67 (37.22)     |          |
| High                      | 66 (35.48)     | 47 (26.11)     |          |
| Family history of IBD     | 17 (9.09)      | 12 (6.59)      | 0.373    |

Data are presented as mean±SD or number (%). *p<0.05. UC: ulcerative colitis, CD: Crohn's disease, BMI: body mass index, IBD: inflammatory bowel disease
who were married or separated than were patients with CD. In patients with UC, the number of never married individuals was higher than that in patients with CD. There were no significant differences in alcohol or tobacco use, family history of IBD, employment status, and income between patients with UC and CD.

The clinical characteristics of the study population are shown in Table 2. Patients with UC had a higher rate of disease remission, while there was a larger number of patients with CD with mild or moderate to severe disease activity. Patients with UC more frequently used 5-ASA, whereas patients with CD more frequently used immunosuppressant and anti-TNF-α. IBD-related hospitalizations or surgeries and history of steroid or biologics use were all significantly more common in patients with CD compared to those in patients with UC. Moreover, there was a higher rate of treatment discontinuation in patients with CD than in patients with UC. No significant differences in disease duration and presence of comorbidity existed between the two groups.

### Psychosocial comorbidities

Table 3 shows the average scores of psychometric scales used in the study population. The average scores of PHQ-9 and HADS in both patients with UC and CD were below the cutoff scores for mild depression or anxiety although the average PHQ-9 score in patients with CD (4.87±4.66) was extremely close to the cutoff score of 5. There were no significant differences in the average scores between the UC and CD.

### Table 2. Clinical and therapeutic characteristics of the study population

| Characteristic                                           | UC (N=187)          | CD (N=182)          | p-value |
|----------------------------------------------------------|---------------------|---------------------|---------|
| Disease duration (year)                                  | 8.98±7.70           | 9.28±5.39           | 0.138   |
| Disease activity                                         |                     |                     | <0.001* |
| Remission                                               | 104 (55.61)         | 43 (23.63)          |         |
| Mild                                                     | 54 (28.88)          | 82 (45.05)          |         |
| Moderate to severe                                       | 29 (15.51)          | 57 (31.32)          |         |
| Presence of comorbidity                                  | 7 (3.72)            | 9 (4.92)            | 0.571   |
| DM                                                       | 2 (1.07)            | 3 (1.65)            | 0.682   |
| Malignancy                                               | 3 (1.60)            | 3 (1.65)            | 1.000   |
| Liver disease                                            | 2 (1.07)            | 1 (0.55)            | 1.000   |
| Cerebrovascular accident                                 | 0                   | 1 (0.55)            | 0.493   |
| Myocardial infarction                                    | 0                   | 2 (1.10)            | 0.243   |
| Others (CHF, COPD, AIDS, dementia, peripheral vascular disease) | 0                   | 0                   |         |
| Current treatment                                        |                     |                     |         |
| 5-aminosalicylic acid                                    | 174 (93.05)         | 144 (79.12)         | <0.001* |
| Immunosuppressant (azathioprine, 6-MP, MTX)              | 84 (44.92)          | 113 (62.09)         | <0.001* |
| Steroid                                                  | 9 (4.81)            | 6 (3.30)            | 0.461   |
| Anti-TNF alpha (infliximab, adalimumab, golimumab)       | 35 (18.72)          | 124 (68.13)         | <0.001* |
| Others (filgotinib, tofacitinib, ustekinumab, vedolizumab) | 30 (16.04)          | 11 (6.04)           | 0.002*  |
| Number of IBD-related hospitalizations                   | 0.78±1.34           | 1.51±1.83           | <0.001* |
| Number of IBD-related surgeries                          | 0.06±0.42           | 0.60±0.89           | <0.001* |
| History of steroid use                                   | 114 (60.96)         | 129 (70.88)         | 0.037*  |
| History of biologics use                                 | 63 (33.69)          | 115 (63.19)         | <0.001* |
| History of treatment discontinuation                      | 2 (1.07)            | 11 (6.04)           | 0.010*  |

Data are presented as mean±SD or number (%). *p<0.05. UC: ulcerative colitis, CD: Crohn’s disease, IBD: inflammatory bowel disease
CD groups. The depression and anxiety levels in patients with IBD assessed using the PHQ-9 and HADS are presented in Table 4. More patients with CD had mild or moderate to severe depression than did patients with UC based on the PHQ-9 scores, but the difference was not statistically significant. In addition, the level of depression measured using the HADS-D was not significantly different in the two groups. The number of patients with mild or moderate to severe levels of anxiety measured using the HADS-A was slightly larger in the UC group than in the CD group, yet the difference was not statistically significant.

**Multivariable analysis of factors associated with depression in patients with IBD**

Using the established cutoff scores of 5 and 10 for PHQ-9 and 8 and 11 for HADS-D, the study patients were categorized into subgroups of mild depression and suspected clinically significant depression based on each scale. The subgroup with mild depression included patients with PHQ-9 scores of 5–9 and HADS-D scores of 8–10. The other subgroups with suspicious clinically significant depression were comprised of patients with PHQ-9 score ≥10 and HADS-D score ≥11.

In patients with UC, divorced, separated, or widowed status and treatment with anti-TNF-α were significantly associated with mild depression based on the PHQ-9 scale. Age was also associated with this subgroup with an odds ratio of 0.93, suggesting that younger age was associated with mild depression. In the suspicious clinically significant depression group with PHQ-9 score ≥10, BMI was a significant predictor of depression with an odds ratio of 0.81. When categorized by HADS-D, never married status in patients with UC was significantly associated with suspicious clinically significant depression (Table 5).

In patients with CD, alcohol use and never married status had significant association with mild depression assessed using the PHQ-9 scale. Employment at the time of survey had an odds ratio of 0.15 in the group with suspicious clinically significant depression assessed using the PHQ-9 scale, indicating that having a job had protective effect against depression. Moderate to severe disease activity had strong association with both mild and suspicious clinically significant depression assessed using the PHQ-9 scale. We found no significant predictor of depression in patients with CD when the HADS-D was used (Table 6).

**Multivariable analysis of factors associated with anxiety in patients with IBD**

The same cutoff scores of 8 and 11 were used in the HADS-A to categorize patients into subgroups with mild anxiety and suspicious clinically significant anxiety. In patients with UC, female sex had a significant association with mild anxiety, while never married status was associated with suspicious clinically significant anxiety (Table 7). In patients with CD, steroid use had a strong association with mild depression with an odds ratio of 17.03 (Table 8). However, this result may be of limited value since there were only six patients with CD who used steroid.

**Association between anxiety-prone cognitive style and depression or anxiety level**

The average AT&T scale scores were not significantly different between patients with UC and CD. When the patients were categorized according to the depression or anxiety levels based on the PHQ-9 and HADS, there was no significant difference in the average AT&T scores between patients with UC and CD. However, as the depression or anxiety level increased, the average AT&T scores also significantly increased in both patients with UC and CD (p<0.001) (Table 9). We obtained the same results after adjusting for other significant variables (UC, disease activity; CD, alcohol use, marital status, employment status, income) in the GLM (p<0.001).

**DISCUSSION**

This study aimed to investigate the depression and anxiety levels, risk factors, and accompanying cognitive distortion in patients with IBD. The average depression and anxiety levels in patients with IBD were not clinically significant. How-
ever, 35% of patients with UC and 45% of patients with CD complained of feeling depressive based on the PHQ-9 scale, whereas 25% of patients with UC and those with CD had depressive mood based on the HADS-D. In addition, 20% of patients with UC and 14% of patients with CD had depressive mood based on the HADS-D. In addition, never married or separated status was a significant risk factor of depression in patients with UC and CD. In addition, never married status was a significant risk factor of anxiety in patients with UC. In patients with CD, the anxiety level was higher in patients who were never married compared to married patients, although the difference was not statistically significant. A weak support system is a known risk factor for depression or anxiety, and it is believed that marriage is an important factor constituting the support system of patients. Particularly, the support system becomes more important when considering characteristics of diseases that need to be treated and managed on a long-term basis. Moreover, current employment status is one of the important indicators reflecting the patient’s daily life mainte-

Table 5. Multivariable analysis of factors associated with depression in patients with UC

|                      | PHQ-9: 5–9 |                      | PHQ-9 ≥10 |                      |
|----------------------|------------|----------------------|------------|----------------------|
|                      | OR         | 95% CI               | p-value    | OR                  | 95% CI               | p-value    |
| Education level      |            |                      |            |                      |
| University graduation or high | 0.48 | 0.19–1.22           | 0.123      | 3.40                | 0.67–17.33           | 0.142      |
| Married              | 1.00       |                      |            |                      |
| Never married        | 1.26       | 0.47–3.41            | 0.647      | 2.62                | 0.73–9.46            | 0.142      |
| Divorced/separated/widowed | 7.72 | 1.90–31.41           | 0.004*     | inf                 | inf                 | 0.979      |
| Anti-TNF-α           | 4.34       | 1.64–11.49           | 0.003*     | 0.88                | 0.16–4.81            | 0.884      |
| History of steroid use | 2.32 | 0.97–5.55            | 0.060      | 0.85                | 0.26–2.76            | 0.791      |
| Age                  | 0.93       | 0.89–0.97            | 0.002*     | 0.98                | 0.94–1.04            | 0.545      |
| BMI                  | 1.02       | 0.89–1.17            | 0.796      | 0.81                | 0.66–1.00            | 0.047*     |
|                      |            |                      |            |                      |
|                      | OR         | 95% CI               | p-value    | OR                  | 95% CI               | p-value    |
| Alcohol use          | 0.81       | 0.31–2.16            | 0.675      | 0.35                | 0.08–1.45            | 0.148      |
| Married              | 1.00       |                      |            |                      |
| Never married        | 0.60       | 0.22–1.65            | 0.321      | 3.83                | 1.18–12.42           | 0.026*     |
| Divorced/separated/widowed | inf | inf                 | 0.970      | 1.73                | 0.24–12.61           | 0.588      |
| Employment status, working | 0.84 | 0.30–2.38           | 0.740      | 0.45                | 0.14–1.43            | 0.175      |
| Disease activity     |            |                      |            |                      |
| Remission            | 1.00       |                      |            |                      |
| Mild                 | 0.56       | 0.20–1.59            | 0.276      | 0.22                | 0.05–1.10            | 0.065      |
| Moderate to severe   | 0.91       | 0.27–3.09            | 0.883      | 0.67                | 0.15–2.95            | 0.600      |
| Other (filgotinib, tofacitinib, ustekinumab, vedolizumab) | 1.97 | 0.60–6.44           | 0.263      | 2.56                | 0.68–9.64            | 0.164      |
| BMI                  | 0.92       | 0.78–1.08            | 0.282      | 0.91                | 0.73–1.13            | 0.378      |

Multivariable analysis was performed after selecting variables with p<0.1 from univariate logistic regression analysis. *p<0.05, the references for comparative analysis were 0–4 for PHQ-9 and 0–7 for HADS-D. UC: ulcerative colitis, PHQ-9: Patient Health Questionnaire-9, HADS: Hospital and Anxiety Depression Scale, anti-TNF-α: anti-tumor necrosis factor-alpha, BMI: body mass index, OR: odds ratio, CI: confidence interval, inf: infinite.
nance, and it is consistent with the results of previous studies, which revealed that socioeconomic deprivation was an important factor in depression.\textsuperscript{15,38,39} In this study, employed patients with CD had lower risk of developing depression compared to unemployed patients. Although not statistically significant, a similar trend was observed in patients with UC.

In the case of the therapeutic agent, the use of anti-TNF-\(\alpha\) agent increased the risk of having depressive mood in patients with UC based on the PHQ-9 scale. Anti-TNF-\(\alpha\) agents include infliximab, adalimumab, and golimumab, of which infliximab is the most commonly used. Generally, topical or oral 5-ASA or oral steroid is initially administered in the treatment sequence; then, immunosuppressants and biologics, such as anti-TNF-\(\alpha\) agents, are administered if symptoms persist.\textsuperscript{40} It can be assumed that the frustration experienced by the patient during this process may be the cause of depression.

### Table 6. Multivariable analysis of factors associated with depression in patients with CD

|                | PHQ-9: 5–9 | PHQ-9 \(\geq\) 10 |
|----------------|------------|-------------------|
|                | OR         | 95% CI p-value    | OR     | 95% CI p-value    |
| Alcohol use    | 2.16       | 1.02–4.58 0.045*  | 1.71   | 0.63–4.65 0.296   |
| Married        | 1.00       |                   |        |                   |
| Never married  | 2.86       | 1.04–7.84 0.041*  | 1.80   | 0.47–6.88 0.391   |
| Divorced/separated/widowed | inf | inf 0.979 | inf | inf 0.987 |
| Employment status, working | 0.63 | 0.18–2.22 0.468 | 0.15 | 0.04–0.67 0.012* |
| Income         |            |                   |        |                   |
| Low            | 1.00       |                   |        |                   |
| Moderate       | 0.76       | 0.27–2.11 0.596   | 1.01   | 0.25–4.10 0.992   |
| High           | 0.64       | 0.20–2.12 0.466   | 0.97   | 0.16–5.87 0.972   |
| Disease activity |         |                   |        |                   |
| Remission      | 1.00       |                   |        |                   |
| Mild           | 1.65       | 0.64–4.24 0.300   | 3.82   | 0.86–16.95 0.078   |
| Moderate to severe | 3.28 | 1.16–9.23 0.025* | 10.82 | 2.30–51.01 0.003* |
| Steroid        | 4.78       | 0.38–60.19 0.226  | 3.11   | 0.17–58.59 0.448   |
| Age            | 1.04       | 0.99–1.09 0.098   | 0.95   | 0.88–1.02 0.169   |

|                | PHQ-9: 0–7 | HADS-D \(\geq\) 11 |
|----------------|------------|-------------------|
|                | OR         | 95% CI p-value    | OR     | 95% CI p-value    |
| Female         | 0.39       | 0.10–1.54 0.180   | 0.70   | 0.16–3.02 0.631   |
| Married        | 1.00       |                   |        |                   |
| Never married  | 1.40       | 0.36–5.36 0.627   | 1.32   | 0.31–5.71 0.711   |
| Divorced/separated/widowed | inf | inf 0.985 | inf | inf 0.987 |
| Employment status, working | 0.72 | 0.15–3.48 0.681 | 0.22 | 0.04–1.13 0.070 |
| Income         |            |                   |        |                   |
| Low            | 1.00       |                   |        |                   |
| Moderate       | 0.93       | 0.24–3.63 0.913   | 0.49   | 0.07–3.66 0.488   |
| High           | 1.05       | 0.22–4.94 0.951   | 3.69   | 0.61–22.29 0.155   |
| Disease activity |         |                   |        |                   |
| Remission      | 1.00       |                   |        |                   |
| Mild           | 1.43       | 0.39–5.22 0.586   | 2.01   | 0.45–8.93 0.358   |
| Moderate to severe | 3.29 | 0.90–12.01 0.071 | 2.50 | 0.54–11.65 0.244 |
| Steroid        | 5.99       | 0.41–87.05 0.190  | 12.42  | 0.93–165.31 0.056 |
| Anti-TNF-\(\alpha\) | 0.42 | 0.17–1.08 0.071 | 0.55 | 0.18–1.69 0.298 |
| Age            | 1.01       | 0.96–1.07 0.686   | 0.98   | 0.92–1.05 0.623   |

Multivariable analysis was performed after selecting variables with p<0.1 from univariate logistic regression analysis. *p<0.05, the references for comparative analysis were 0-4 for PHQ-9 and 0-7 for HADS-D. CD: Crohn's disease, PHQ-9: Patient Health Questionnaire-9, HADS: Hospital and Anxiety Depression Scale, anti-TNF-\(\alpha\): anti-tumor necrosis factor-alpha, OR: odds ratio, CI: confidence interval, inf: infinite
Moreover, patients are required to visit the clinic every week for both induction and maintenance of anti-TNF-\(\alpha\) agent, which is administered intravenously. Again, this may cause daily and work life discomfort and disturbances and deteriorate the patient’s quality of life.

Increased disease activity in patients with IBD is a known risk factor of psychological distress. According to Precelli et al.,41 various intestinal and extra-intestinal symptoms related to moderate to severe disease activity in IBD may lead to discomfort and frustration, thereby increasing the risk of depression. Although it appears to be a risk factor for depression in UC as well, it was not statistically significant, and it can be expected that patients with CD have increased risk of depression because there have been reports that CD has a more chronic course compared to UC and can be accompanied by abdominal pain even in remission.42

### Table 7. Multivariable analysis of factors associated with anxiety in patients with UC

|                          | HADS-A: 8–10 OR | 95% CI   | p-value | HADS-A ≥11 OR | 95% CI   | p-value |
|--------------------------|-----------------|----------|---------|-----------------|----------|---------|
| Female                   | 4.15            | 1.32–13.04 | 0.015*  | 1.10           | 0.30–4.02 | 0.882   |
| Alcohol use              | 0.79            | 0.26–2.36 | 0.666   | 0.43           | 0.10–1.86 | 0.256   |
| Married                  | 1.00            |          |         | 1.00           |          |         |
| Never married            | 2.12            | 0.74–6.10 | 0.162   | 5.03           | 1.16–21.76 | 0.031*  |
| Divorced/separated/widowed | inf        | inf       | 0.968   | 4.19           | 0.57–30.79 | 0.160   |
| Employment status, working | 1.59       | 0.42–6.01 | 0.497   | 0.21           | 0.04–1.03 | 0.054   |
| Income                   |                |          |         |                |          |         |
| Low                      | 1.00            |          |         | 1.00           |          |         |
| Moderate                 | 0.56            | 0.16–1.97 | 0.364   | 1.44           | 0.25–8.23 | 0.680   |
| High                     | 0.78            | 0.18–5.43 | 0.742   | 3.91           | 0.64–23.80 | 0.139   |
| History of biologics use | 0.51            | 0.14–1.78 | 0.289   | 1.06           | 0.30–3.76 | 0.931   |
| History of steroid use   | 0.52            | 0.19–1.45 | 0.210   | 1.67           | 0.40–7.06 | 0.486   |
| BMI                      | 0.87            | 0.71–1.06 | 0.175   | 0.94           | 0.72–1.22 | 0.623   |

Multivariable analysis was performed after selecting variables with p<0.1 from univariate logistic regression analysis. *p<0.05, the references for comparative analysis were 0-7 for HADS-A. UC: ulcerative colitis, HADS: Hospital and Anxiety Depression Scale, BMI: body mass index, OR: odds ratio, CI: confidence interval, inf: infinite

### Table 8. Multivariable analysis of factors associated with anxiety in patients with CD

|                          | HADS-A: 8–10 OR | 95% CI   | p-value | HADS-A ≥11 OR | 95% CI   | p-value |
|--------------------------|-----------------|----------|---------|-----------------|----------|---------|
| History of treatment discontinuation | inf   | inf   | 0.971   | 1.03           | 0.06–17.30 | 0.981   |
| 5-aminosalicylic acid    | 1.22            | 0.25–5.84 | 0.807   | 0.35           | 0.06–1.91 | 0.224   |
| Steroid                 | 17.03           | 2.24–129.20 | 0.006*  | 9.82           | 0.55–174.14 | 0.119   |
| Anti-TNF-\(\alpha\)     | 0.42            | 0.15–1.23 | 0.113   | 0.61           | 0.12–3.15 | 0.559   |

Multivariable analysis was performed after selecting variables with p<0.1 from univariate logistic regression analysis. *p<0.05, the references for comparative analysis were 0-7 for HADS-A. CD: Crohn’s disease, HADS: Hospital and Anxiety Depression Scale, anti-TNF-\(\alpha\): anti-tumor necrosis factor-alpha, OR: odds ratio, CI: confidence interval, inf: infinite

### Table 9. Average scores of AT&T scale according to the level of depression and anxiety in patients with IBD

|                  | PHQ-9: 0–4 | PHQ-9: 5–9 | PHQ-9: 10–21 | p-value \(\dagger\) |
|------------------|------------|------------|--------------|----------------------|
| UC               | 19.87±5.47 | 25.41±7.64 | 34.53±8.50   | <0.001*              |
| CD               | 19.01±4.57 | 24.00±5.18 | 30.21±7.92   | <0.001*              |
| HADS-D: 0–7      | HADS-D: 8–10 | HADS- D: 11–21 | p-value \(\dagger\) |
| UC               | 20.11±5.54 | 28.50±7.87 | 33.68±8.34   | <0.001*              |
| CD               | 20.40±5.39 | 26.38±6.80 | 28.90±8.30   | <0.001*              |
| HADS-A: 0–7      | HADS-A: 8–10 | HADS-A: 11–21 | p-value \(\dagger\) |
| UC               | 19.91±4.79 | 31.48±6.83 | 37.50±7.84   | <0.001*              |
| CD               | 20.44±4.58 | 30.12±6.03 | 39.63±6.97   | <0.001*              |

\(\dagger\)p<0.05, \* adjusting for other significant variables (UC: disease activity, CD: alcohol use, marital status, employment status, income) in generalized linear model. IBD: inflammatory bowel disease, UC: ulcerative colitis, CD: Crohn’s disease, AT&T scale: Anxious Thoughts and Tendencies scale, PHQ-9: Patient Health Questionnaire-9, HADS: Hospital and Anxiety Depression Scale

Moreover, patients are required to visit the clinic every week for both induction and maintenance of anti-TNF-\(\alpha\) agent, which is administered intravenously. Again, this may cause daily and work life discomfort and disturbances and deteriorate the patient’s quality of life.

Increased disease activity in patients with IBD is a known risk factor of psychological distress. According to Precelli et al.,41 various intestinal and extra-intestinal symptoms related to moderate to severe disease activity in IBD may lead to discomfort and frustration, thereby increasing the risk of depression. Although it appears to be a risk factor for depression in UC as well, it was not statistically significant, and it can be expected that patients with CD have increased risk of depression because there have been reports that CD has a more chronic course compared to UC and can be accompanied by abdominal pain even in remission.42

In patients with UC, the risk of developing depression
somewhat decreased as the age increased by 1 year. Young people are more socially active than middle-aged individuals and thus may be at a greater risk of depression resulting from decreased quality of life associated with IBD. In addition, the risk of depression somewhat decreased as BMI increased by 1 unit. Already, a positive correlation between obesity and depression has been demonstrated in many studies. However, the average BMI of patients with CD participating in this study was normal at 22.28, and malnutrition in patients with IBD is one of the targets of treatment. Considering that the disease causes abdominal pain or discomfort or that dietary control is sensitive due to the nature of the disease, proper oral intake may be linked to an effect of preventing depressive symptoms. Given this, increased BMI can be understood as a result that reflects the patient’s proper dietary intake.

The risk factors of anxiety, other than previously mentioned marital status, include female sex and steroid use. Considering that the prevalence of anxiety disorders is higher in women than in men, it can be assumed that women with IBD are more susceptible to anxiety. In this study, female sex was a significant predictor of anxiety in patients with UC. Although not statistically significant, more female patients with CD had anxiety than male patients with CD did. Women with IBD may frequently develop anxiety in marriage, pregnancy, childbirth, lactation, and parenting due to the chronic course of illness and treatment. Steroid use was another predictor of anxiety in patients with CD. This may be due to the side effects of steroids, such as weight gain, moon face, acne caused by hormonal changes, and osteoporosis. However, there were only nine patients with steroid treatment in the UC subgroup, so further research on a larger study population is needed.

Catastrophic thinking refers to distorting the irrational negative perception of the consequences of a particular event. In this process, the patient has emotional burden, adversely affecting the result of rational coping and treatment and compliance, which can be used to measure the tendency of anxiety vulnerable accidents through the AT&T scale. In this study, the mean AT&T scores significantly increased as the severity of depression and anxiety assessed using PHQ-9, HADS-D, and HADS-A increased. According to Khawaja and Dyer, the mean AT&T scores were 26.01 in the control group and 39.15 in patients with anxiety disorder. In another study by Lee et al., the mean AT&T scores were 23.47 in the control group and 29.83 in patients with panic disorder with or without agoraphobia. This result reflects changes in cognitive distortions, such as catastrophes, that occur when psychiatric symptoms, such as depression and anxiety, are present for a long time. In this study, a significant cognitive distortion level was observed when depression and anxiety levels were moderate or higher. In particular, when the anxiety level assessed using the HADS-A was moderate to severe, the AT&T scores were 37.50 in patients with UC and 39.63 in patients with CD. Cognitive distortion also causes the tendency to recognize and judge situations as extreme or negative. Considering this, it is important to check the depression and anxiety level periodically in patients with IBD and consult the department of psychiatry, especially if it is prolonged. As mentioned earlier, it should be considered whether there is cognitive distortion and, if any, cognitive therapy is necessary. Given that cognitive distortion was a significant outcome variable in this study, further studies on the correlation between cognitive distortion and depression or anxiety may provide more advanced results. To date, few studies have yet examined the relationship between disease specific factors and cognitive style in IBD patients. Thus, further study on a wider spectrum of cognitive characteristics of IBD patients by using various tools, in addition to catastrophic thinking identified by AT&T may be needed.

Although this study is limited to only patients who visited a single tertiary hospital, it is a considerable scale regarding the limited number of patients with IBD in Korea. Recently, interest and research on depression and anxiety accompanying IBD have been active, but there are still few in Korea. In particular, studies on the depression or anxiety level of patients with IBD are rare. Unlike other studies that used cutoff points to determine only the presence or absence of depression or anxiety, this study identified the size of the corresponding group according to severity. We also attempted to identify factors that should be taken more seriously when approaching and treating patients with IBD by classifying the variables that affect them according to severity. Additionally, the necessity to correct cognitive distortions along with the treatment of depression and anxiety was identified. Based on this study, cognitive evaluation should be included in clinical setting, which may be expected to provide fundamental research data for future studies. However, since it is a cross-sectional study, the depression and anxiety levels according to the changes in the risk factors could not be determined. Moreover, it is possible that some risk factors may have been omitted since the mean depression and anxiety scores were not significantly high in these study participants. Perhaps the exclusion of patients with history of psychiatry clinic visit may have contributed to the low depression and anxiety scores observed in this study. To compensate for this, a screening for patients with significantly high depression and anxiety levels may be useful in identifying associated risk factors. When the risk factors were analyzed by range of scores, most of the significant risk factors were inconsistent in the subgroups by range of scores which made the results difficult to fully explain. Since this study only used self-reported scales, the objec-
Activity of these self-reported measures may be limited. Further studies with psychiatric evaluation performed by a psychiatrist are expected to improve the objectivity of the measures.

In conclusion, psychological distress in patients with IBD requires considerable attention. Screening of patients needing treatment and research on programs to manage their psychological burden are necessary. Additional future research on the risk factors of depression or anxiety in patients with UC and CD may be helpful to both physicians and patients in the management and treatment of the disease.

Acknowledgments

This work was supported by a grant from Kyung Hee University in 2017 (KHU-20170855).

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

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Depression, Anxiety in IBD Patients

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