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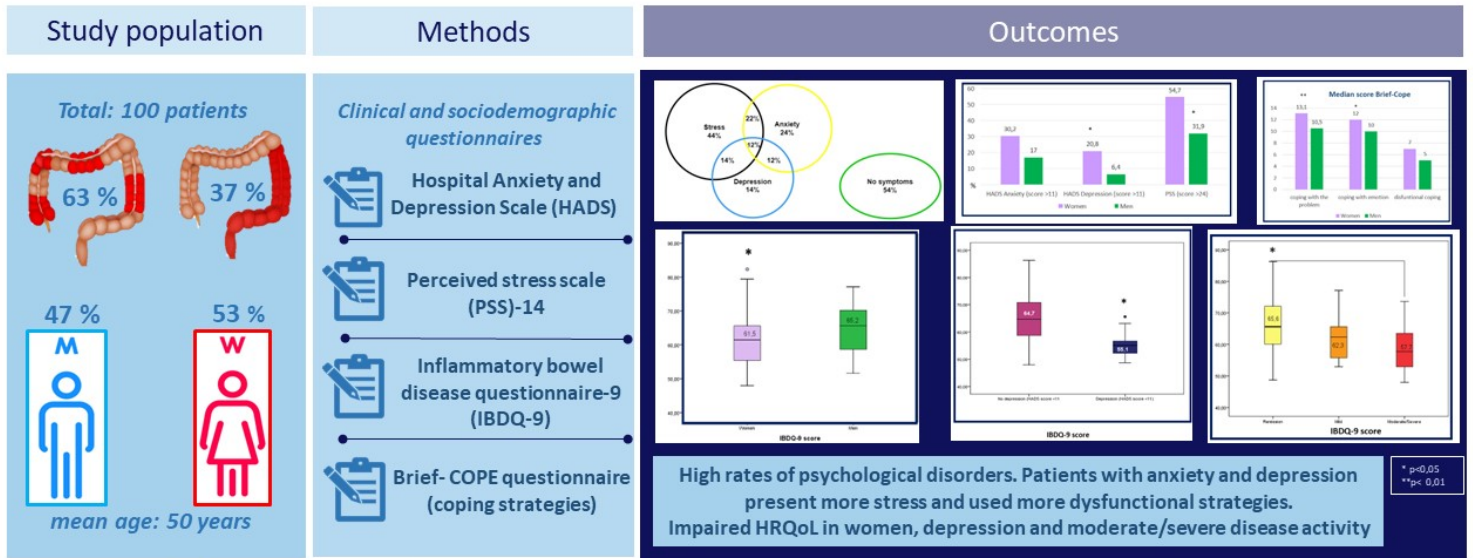
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Psychological disorders and coping strategies in patients with Inflammatory Bowel Disease. Their impact in health-related quality of life



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Psychological disorders and coping strategies in patients with inflammatory bowel disease. Their impact on health-related quality of life

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ABSTRACT

Background and objectives: inflammatory bowel disease (IBD) has a major impact on psychological well-being. This condition is associated with a high level of anxiety and mood disorders, but stress prevalence and how an individual copes with IBD have not been sufficiently explored. The objective of this study was to assess the impact of the disease on psychological disorders and to identify coping strategies used by patients with IBD, as well as to analyze the relationship between these variables and sociodemographic and clinical variables.

Methods: a cross-sectional prospective study was performed including 126 consecutive patients. Those with psychiatric conditions prior to the onset of the IBD were excluded. Independent variables were measured using a sociodemographic and

clinical questionnaire. The patients completed the Hospital Anxiety and Depression Scale (HADS), the Perceived Stress Scale (PSS) and the BRIEF COPE questionnaire. Quality of life was measured using the nine-item IBD Quality of Life (IBDQ-9).

Results: the final cohort comprised 100 patients (37 with ulcerative colitis and 63 with Crohn's disease). The prevalence rates of the variables of stress, anxiety and depression were high (44 %, 24 % and 14 %, respectively). Stress and depression were higher in females ($p < 0.05$), without differences regarding other sociodemographic and clinical variables. Moreover, higher levels of anxiety and depression were found to be associated with stress and dysfunctional coping strategies ($p < 0.01$).

Conclusions: patients with IBD, particularly women, have high rates of psychological disorders. Those with anxiety and depression presented more stress and used more dysfunctional strategies. These conditions must be considered for a multidisciplinary management.

Keywords: Inflammatory bowel disease. Crohn's disease. Ulcerative colitis. Anxiety. Depression. Psychological stress. Coping. Quality of life.

INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic relapsing and chronic inflammatory condition whose nature of the disease, the unpredictability of flare-ups, and the challenges of managing symptoms affect the psychological well-being of patients and can impair their health related quality of life (HRQoL) (1,2). The psychological burden associated to IBD has been previously documented, with anxiety and depression prevalences of at least twice compared to the general population (3-5).

Stress is an individual concept that depends on the patient's abilities to adapt to a challenge. It has been reported that psychological stress could be a trigger of IBD deterioration and be involved in the immune modulation, gut microbiome changes and intestinal permeability in IBD, but the link between psychological stress and IBD remains poorly understood (6,7). Coping strategies play a vital role in managing the psychological impact and navigate the challenges posed by chronic diseases (8,9).

Coping strategies can be classified into two broad categories: functional strategies that include problem-focused coping and emotion-focused coping, and dysfunctional strategies. Problem-focused coping involves actively addressing the stressor, whereas emotion-focused coping involves managing the emotional distress associated with the problem. Dysfunctional strategies refer to maladaptive or unhealthy ways that may provide temporary relief or distraction, including substance abuse and avoidance or withdrawal from social interactions, but they ultimately exacerbate the negative consequences and hinder effective problem-solving (10).

While previous studies have explored the relationship between coping strategies and psychological well-being in various chronic conditions, limited research has focused on patients with IBD. On the other hand, despite there being a significant number of studies that have focused on HRQoL in IBD, only a small number of them have considered all these psychological variables together (11).

The purpose of this study was to analyze the impact of the onset of an inflammatory bowel disease on psychological symptoms and the prevalence of anxiety, depression and stress in patients with IBD and to evaluate the associations between these psychological factors and clinical and sociodemographic variables. Understanding the magnitude of the problems of the psychological sphere is essential to be able to design a comprehensive treatment for patients with IBD, which combines medical and psychological interventions.

METHODS

Design and study population

A cross-sectional prospective study was designed. The study population consisted of 150 consecutive patients with IBD who attended the IBD Unit at the Hospital Universitario Fundación Alcorcón between December 2022 and February 2023. This is a third-level hospital and the integral care unit of Inflammatory Bowel Disease attends to a total of 800 patients with this pathology.

The inclusion criteria were diagnosis of CD or UC based on conventional criteria and age 18 years or more. The exclusion criteria were the diagnosis of IBD less than a year before, psychological or psychiatric conditions prior to the onset of the intestinal

disease, and limitations to complete the questionnaires.

The study was approved by the local ethics committee (2022/2216) and the patients signed an informed consent prior to participation.

Variables and questionnaires

The information concerning demographic variables was collected via a short questionnaire. These variables included age, gender, smoking habit and marital and employment status. Clinical data (type, localization, extension and duration of the IBD disease), previous surgeries, type of treatment, anemia and the presence of musculoskeletal, cutaneous or ocular extraintestinal manifestations (EIMs), or other chronic comorbidities, were collected from clinical records.

The disease activity was assessed by the partial Mayo score and Harvey-Bradshaw Index, defining remission in ulcerative colitis patients as a Mayo score < 2 and in Crohn's disease as a Harvey-Bradshaw score < 4 .

Patients completed five self-administered questionnaires to evaluate anxiety, depression, perceived stress, health-related quality of life and coping strategies. Anxious and depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) (12). This instrument consists of 14 items with subscales for anxiety and depression. The total score in each subscale ranges from 0 to 21, with a score greater than 11 suggesting a clinically significant impairment.

For the evaluation of stress, the perceived stress scale (PSS)-14 was used. This scale is a self-administered instrument that consists of 14 items, each one rated on a five-point Likert-type scale, ranging from 0 = "never" to 4 = "very often". A higher score corresponds to a higher level of perceived stress, and a score equal to or greater than 24 indicates a high level of stress in the last month (13).

The Inflammatory Bowel Disease Questionnaire-9 (IBDQ-9) was used to document health related quality of life (14). It is an abbreviated version of the 36-IBD questionnaire (15).

Coping strategies were evaluated using the Brief-COPE questionnaire (16) and consists of 14 subscales with two items each. Response options range from 0 (not at all) to 3 (a lot of the time). The subscales are grouped into three strategies: problem-focused

(active coping, instrumental support use and planning), emotion-focused (emotional support use, positive reframing, humor, acceptance and religion), and dysfunctional or maladaptive strategies (self-distraction, denial, substance use, behavioral disengagement, venting and self-blame). Problem and emotion-focused are considered as adaptive coping strategies (11,17).

For all the instruments, versions adapted to the Spanish population were used. Sample size was calculated using OpenEpi and expected prevalences of anxiety and depression (A&D) were obtained from Iglesias-Rey et al. (20 % and 10 %, respectively) (11,18). The minimum sample size (95 % confidence interval [CI]) required was 97, with a precision of 6 % for anxiety and 8 % for depression.

Statistical analyses

Sociodemographic, clinical and psychological characteristics of patients are displayed as frequencies (proportions) for categorical variables and as means or medians and interquartile ranges (IQR) for quantitative variables. Categorical variables were compared using the Chi-squared test. Quantitative variables between groups were compared using the Student's t-test for parametric data and the Mann-Whitney U test in other cases. ANOVA was used for analysis of more than two groups. Spearman's correlation was used to assess the association between the quantitative results of the different scales. The accepted level of statistical significance was lower than 0.05

RESULTS

Of the 150 patients who were invited, 126 agreed to participate. Twenty-six patients did not meet inclusion criteria because of psychiatric conditions before the onset of inflammatory bowel disease, or IBD diagnosed less than a year before. Therefore, the final study cohort comprised 100 patients: 63 with CD and 37 with UC (women: 53 %).

The demographic and clinical characteristics are shown in table 1.

More patients with CD were on immunosuppressant and biological treatments, and had previous surgeries for IBD and more EIMs, than with UC ($p < 0.01$). It should be noted that patients with CD required sick leave in the last year more frequently than those with UC ($p = 0.044$). Regarding clinical activity, more UC patients than CD

patients were considered in remission, although the differences were not significant.

Psychological measures

Considering the HADS and PSS scales, the proportion of patients with clinically significant anxiety, depression and stress were 24 %, 14 % and 44 %, respectively, without differences in the percentage between UC and CD, although patients with CD showed higher anxiety scores than UC (9 [IQR 6-11] vs 7 [IQR 4-9.5]; $p = 0.042$). No significant differences were found regarding depression and stress between CD and UC (Fig. 1).

The mean of health-related quality of life (IBDQ-9) score was 63.8 (IQR 56.7-69.6), which was similar in both diseases. The coping strategies most often used by patients with IBD were focused on the problem (mean 13, IQR [9-16]) and focused on emotion (11 IQR) (7,14,7), with no differences between CD and UC.

Differences of psychological conditions, HRQOL and coping strategies depending on social and clinical variables

Females had significantly higher levels of stress (54.7 % vs 31.9 %, p value = 0.022) and depression (20.8 % vs 6.4 %, p value = 0.012) than males (Fig. 2). Depression was also more frequent among patients under treatment with steroids (28.6 %) or immunosuppressive/biological treatment (16.9 %) vs no treatment (9.8 %), $p = 0.001$ and $p = 0.002$, respectively. Patients with moderate or severe activity also suffer more depression than those with mild activity or remission ($p = 0.028$) (Fig. 3), had lower HRQoL scores ($p = 0.04$), and used more dysfunctional strategies ($p = 0.01$). Females scored lower in IBDQ-9 ($p = 0.047$) than males.

Regarding coping strategies, females use good functional ones, based on focusing on the problem (p value = 0.008) or based on the emotion (p value = 0.012), more frequently than males. Disease duration, behavior, treatment or clinical activity were not significant predictors of good or bad coping.

Correlations between psychological variables and coping strategies

All patients with significant anxiety, depression or stress used significantly more dysfunctional coping strategies than those without symptoms (all p -values < 0.001) and scored lower in HRQoL (all p -values < 0.001). Patients with higher levels of perceived stress and anxiety needed more sick leave compared with those without symptoms (Table 3). There was a positive correlation between anxiety and depression with stress (Fig. 3).

DISCUSSION

It is known that the diagnosis of a chronic disease poses a significant burden on mental health (19). We have identified the significant impact of inflammatory bowel disease on the onset of stress, anxiety and depression in this Spanish cohort of 100 patients. A&D comorbidities have a considerable prevalence (24 % and 14 %, respectively). Rey-Iglesias et al. (11) also evaluated these clinical disorders in Spain, but unlike our study, depression was twice as prevalent as anxiety in their cohort (20.1 % and 10.5 %, respectively). A recent meta-analysis by Barberio et al. (4) also found a higher prevalence of anxiety than depression, which was also higher than ours (32 % and 25 %, respectively). We must point out that our study excluded patients with previous psychological disorders or a recent IBD diagnosis, as many patients' experience heightened levels of anxiety and depression just right the onset of the disease. Our intention was to find out how IBD diagnosis can determinate the subsequent appearance of symptoms in the psychological sphere.

Our results show that depression was significantly associated with the activity of the disease and the use of steroids or immunosuppressive and biological treatment, probably as an indirect measure of the degree of IBD severity. Other studies have found higher prevalences for A&D during periods of exacerbation compared with remission, reaching 80 % and 60 %, respectively (1,20,21). On the other hand, Navabi et al. also described that patients with anxiety or depression were more likely to use anti-tumor necrosis factor (anti-TNF) and steroids, and that psychological symptoms were indeed associated with surgical history, disease complications, smoking and female gender (5). No association was found with tobacco and surgical history, which could be related to the sample size.

Stress means the individual physiological and behavioral reaction to pressure. Distress affects cognitive function and reduces our ability to rest and resolve problems (22). Chronic disease patients are known to frequently suffer from stress, which has been related to more severe disease, uncontrolled pain, younger age at diagnosis and lower socioeconomic status (23,24). Stress however, has not been extensively studied in Spanish IBD populations. A recent study during the COVID pandemic showed rates of 18 % (25), while international studies reflect percentages between 32-44 % (26). In our study, the proportion of patients with significant stress was as high as 44 %, comparable to those studies with greater rates, and reflects the importance of this disorder in IBD setting. On the other hand, this is correlated with the existence of anxiety and depression, as we proved in our study. Depending on the severity of the symptoms, patients may benefit from pharmacological together with psychological treatment, alongside referral to Psychiatry (3).

Our results show that women suffered more frequently from stress, and moreover, they have more depression and worst HRQoL than men. Different authors agree that patients with IBD have a higher probability to develop affective disorders compared with the general population, female gender represents a risk factor (2,5,27). However, the reason for the differences is not clear and probably involves biological and psychological factors, thus, healthcare professionals should pay special attention to them.

The impact of stress, anxiety and depression on patient well-being is evident, and related to inferior HRQoL scores in our sample. Patients with moderate-severe activity also scored lower on the IBDQ-9, compared to those who were in remission. Similar results are shown by Casellas et al. in patients during a flare (1). Some other studies have also pointed out the role of age, type of disease (CD worst HRQoL than UC), the need for hospitalizations or extraintestinal manifestations (2,5,28,29). We could not demonstrate this in our study, possibly because of the sample size. Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) are complementary tools to measure patients' well-being and should be added in clinical settings to assess patients' assessment of their health status (30). Even though disease severity is a determinant of quality of life, under-diagnosed and under-treated mental

disorders may impact outcomes, health-care use and associated costs. Our results do point out that high levels of stress and anxiety were also associated with an increase in the need for sick leave in the last year, as an indirect measure of quality of life.

Finally, the coping strategies used by IBD patients to deal with the disease have been studied. This process depends on various individual and external factors (31). From our study, we can conclude that IBD patients mostly use strategies focused on the problem, followed by those focused on emotion, and that women use more adaptive strategies than men. The vast use of emotion-focused coping in women may be explained by their adherence to the traditional female roles of mother and family caretaker, despite their disease. Nevertheless, patients with activity, anxiety or depression, without differences between the type of disease, use more dysfunctional strategies, which correlated with reduced quality of life. As avoidance behaviors can manifest in non-compliance or lack of follow-up care, which can trigger flares in IBD, this aspect should be explored routinely (11,32). Some studies have evaluated the efficacy of psychological intervention programs aimed at patients with IBD and high levels of stress (33,34), but this purpose was beyond the scope of our study.

The strength of this study rests on the analysis of several psychological comorbidities, with validated psychometric questionnaires, and their relationship with coping strategies and quality of life. Limitations include the single-center study design, the absence of a healthy control group, and the insufficient IBD sample size for some analyses. Due to the cross-sectional design, only relationships between variables could be established, but contributions of causality were not defined.

In conclusion, this study indicates that stress, anxiety and depressive symptoms are very common in IBD patients and are significant predictors of worse quality of life and for the use of dysfunctional coping strategies. Our results support the need for a psychological assessment of IBD. The evaluation of mental disorders and non-adaptive response, as well as the derivation to mental health specialists, should be evaluated in clinical care of the patient, particularly in women. This justifies including psychological interventions in their management, as recommended in recent guidelines on the management of IBD (35).

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Table 1. Main sociodemographic and clinical characteristics of the subjects and results questionnaires

Variable		CU (n = 37)	EC (n = 63)	Total (n = 100)	p valor
Age (years): median (IQR)		51.0 (42.0-70.0)	48.0 (41.0-61.0)	50 (42.0-62.7)	0.42
Female (%)		21 (56.8 %)	32 (50.8 %)	53 (53 %)	
Marital status (single): n (%)	Single/divorced	6 (16.7 %)	15 (23.8 %)	21 (21 %)	0.45
Children (yes): n (%)		27 (77.1 %)	44 (71 %)	71 (71 %)	0.510
Employed status: n (%)	Self-employed	3 (8.3 %)	6 (9.5 %)	9 (9 %)	0.71
	Employee	17 (47.2 %)	36 (57.1 %)	53 (53 %)	
	Unemployed	3 (8.3 %)	5 (7.9 %)	8 (8 %)	
	Retired	13 (36.1 %)	16 (25.4 %)	29 (29 %)	
Sick leave last year (yes): n (%)		2 (5.9 %)	13 (22.4 %)	15 (15 %)	0.04*
Location UC: n (%)	E1 (proctitis)	15 (40.5 %)	-	-	-
	E2 (left-sided)	6 (16.2 %)	-	-	
	E3 (pancolitis)	15 (40.5 %)	-	-	
Location CD: n (%)	Ileal	-	37 (58.73 %)	-	-
	Colonic	-	9 (14.3 %)	-	
	Ileocolic	-	18 (28.6 %)	-	
Behavior CD: n (%)	Inflammatory	-	44 (69.8 %)	-	-
	Stenosing	-	10 (15.9 %)	-	
	Fistulizing	-	19 (15.9 %)	-	
	Perianal	-	13 (20.6 %)	-	
Smoking habit	No smoking	21 (56.8 %)	30 (47.6 %)	51 (51 %)	0.21
	Ex-smoker	13 (35.1 %)	19 (30.2 %)	32 (32 %)	
	Current smoker	3 (8.1 %)	14 (22.2 %)	17 (17 %)	
Extraintestinal manifestations: n (%)		8 (21.7 %)	20 (31.7 %)	21 (21 %)	0.01**
Years of diagnosis (years): median (IQR)		14.4 (6.2-19.9)	11.7 (5.7-18.5)	12.49 (5.8-19.4)	0.51
Surgery for IBD: n (%)		2 (5.4 %)	20 (31.7 %)	22 (22 %)	0.002**
Treatment during	No treatment/5-	26 (70.3 %)	15 (23.8 %)	41 (41 %)	0.000**



Treatment during	ASA				0.000**
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Treatment during					0.000**
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last year: <i>n</i> (%)	No treatment/5-ASA				
	Anti-TNF/other biologic	9 (24.3 %)	37 (58.7 %)	46 (46 %)	
	Immunosuppressive	2 (5.4 %)	11 (17.5 %)	13 (13 %)	
	Steroids	1 (2.7 %)	6 (9.5 %)	7 (7 %)	0.26

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Treatment during last year: <i>n</i> (%)					
Disease activity*: <i>n</i> (%)	Remission/mild	34 (91.9 %)	50 (79.4 %)	84 (84 %)	0.11
	Moderate/severe	3 (8.1 %)	13 (20.6 %)	16 (16 %)	
Smoking habit: <i>n</i> (%)	No smoking	21 (56.8 %)	30 (47.6 %)	51 (51 %)	0.21
	Ex-smoker	13 (35.1 %)	19 (30.2 %)	32 (32 %)	
	Current smoker	3 (8.1 %)	14 (22.2 %)	17 (17 %)	
Anemia: <i>n</i> (%)		2 (5.2 %)	5 (7.9 %)	7 (7 %)	1.00
CRP: mean (IQR)		1 (0.3-4.5)	3 (0.3-4.7)	1.5 (0.3-4.5)	0.26
Fecal calprotectin: mean (IQR)		54 (8-109)	106 (27-260)	69 (20-212)	0.29

IQR: interquartile range; CD: Crohn's disease; UC: ulcerative colitis; IBD: inflammatory bowel disease; CRP: C-reactive protein; 5-ASA: 5-aminosalicylic acid; anti-TNF: anti-tumor necrosis factor. *Disease activity based on Mayo partial and Harvey-Bradshaw score, respectively.

Table 2. Influence of anxiety, depression and stress on coping strategies, sick leave and HRQoL

Variable		HADS: anxiety <i>n</i> (%)		HADS: depression <i>n</i> (%)		PSS (stress) <i>n</i> (%)	
		Score < 11	Score > 11	Score < 11	Score > 11	Score < 24	Score > 24
HRQoL (95 % CI)		65.7 (63.9-67.5)	57.6 (54.8-60.3) †	65.16 (63.3-68.9)	55.4 (52.8-57.9) †	66.7 (65.2-68.2)	60.1 (58.6-61.5) †
Sick leave last year (yes): <i>n</i> (%)		8 (11.3 %)	7 (33.3 %)*	11 (14.1 %)	4 (28.6 %)	4 (7.4 %)	11 (28.9 %) [†]
Coping strategies: mean (95 % CI)	Coping with the problem	11.8 (10.6-12.9)	12.2 (10.3-14.2)	12.0 (10.9-13.0)	11.3 (8.6-14.2)	11.95 (10.9-12.9)	11.8 (10.8-12.7)
	Coping with emotion	10.8 (9.8-11.9)	10.8 (9.0-12.7)	11.1 (10.1-12.0)	9.4 (6.4-12.5)	11.0 (10.1-11.9)	10.5 (9.6-11.4)
	Dysfunctional	6.20 (5.2-7.2)	11.5 (8.9-14.1) [†]	6.51 (5.6-7.4)	13.4 (9.4-17.3) [†]	5.4 (4.6-6.2)	11.1 (10-12.2) [†]

HADS: Hospital Anxiety and Depression Scale; PSS: Perceived Stress Scale; HRQoL: health related quality of life; CI: confidence interval. *Significance < 0.05; †significance < 0.01.

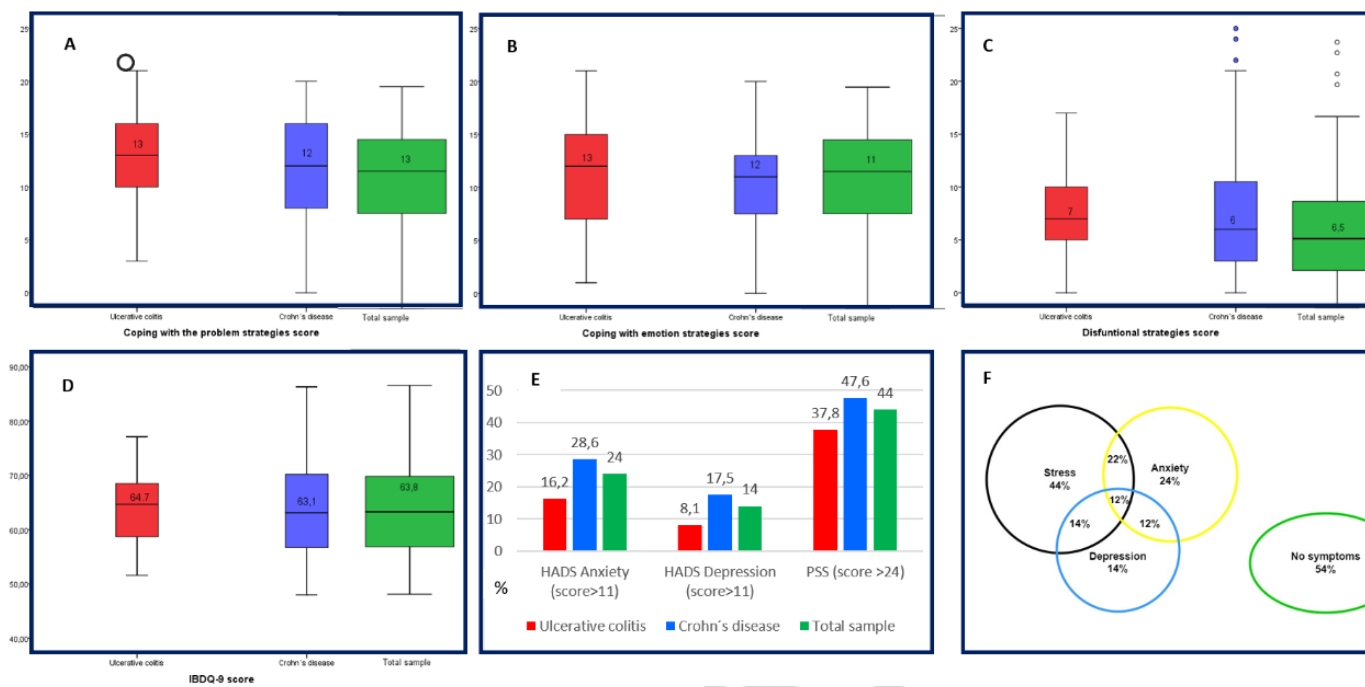


Fig. 1. Median score of coping strategies (A-C) and Inflammatory Bowel Disease Questionnaire-9 (IBDQ-9) (D) depending on the type of IBD. E. Prevalence of stress, anxiety and depression symptoms depending on type of IBD. F. Coexistence of symptoms of depression, anxiety and stress according to the results in the total sample. HADS: Hospital Anxiety and Depression Scale; PSS: Perceived Stress Scale. *Significance < 0.05; **significance < 0.01.

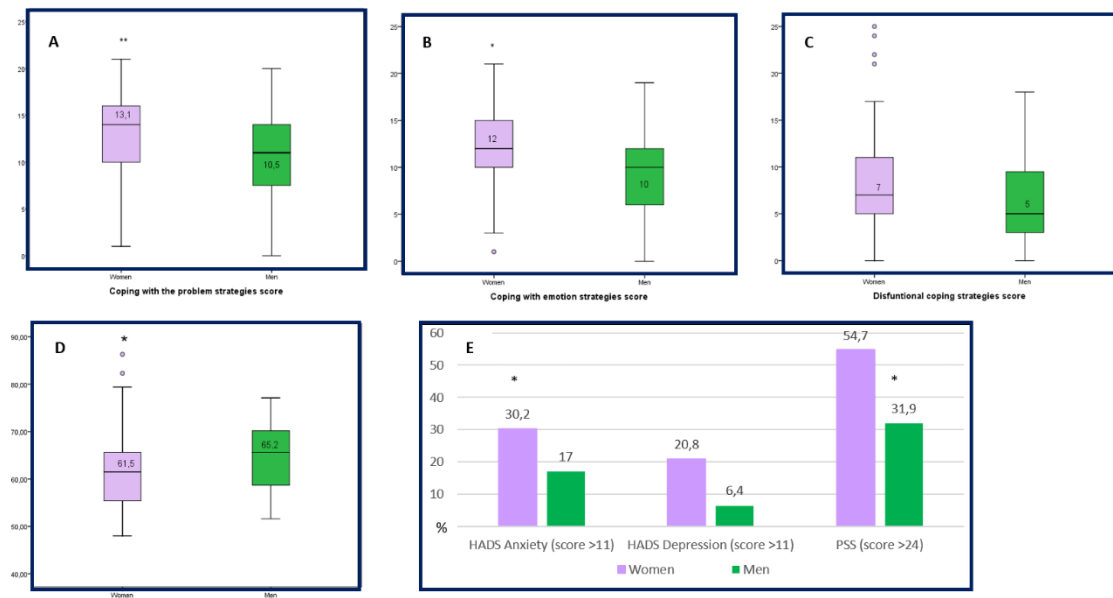


Fig. 2. Median score of coping strategies (A-C) and Inflammatory Bowel Disease Questionnaire-9 (IBDQ-9) (D) depending on sex. E. Prevalence of stress, anxiety and depression symptoms depending on sex. HADS: Hospital Anxiety and Depression Scale; PSS: Perceived Stress Scale. *Significance < 0.05; ***significance < 0.01.

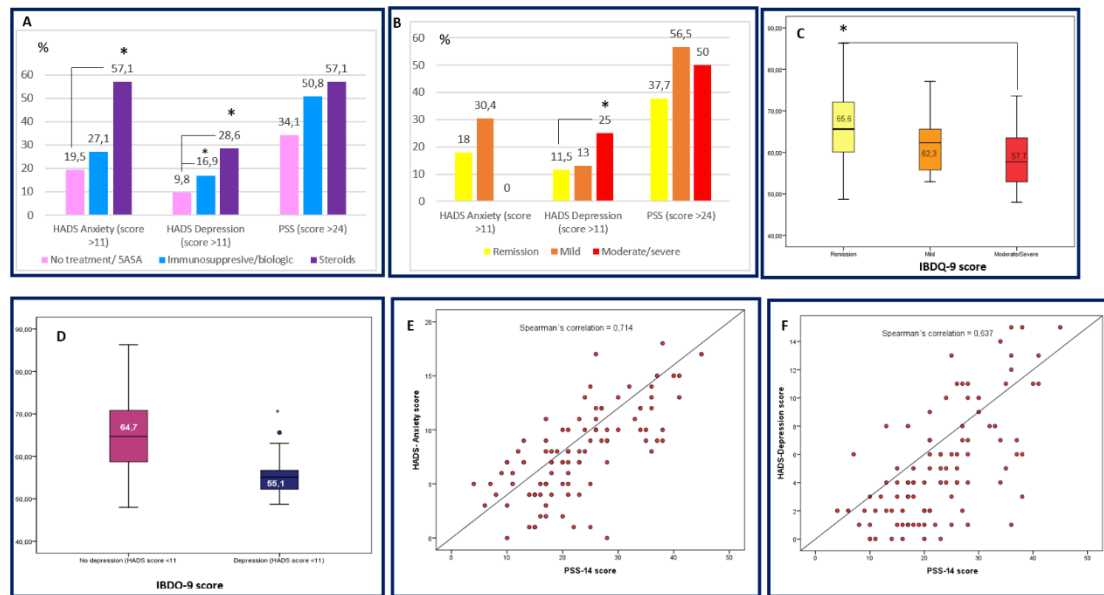


Fig. 3. Prevalence of stress, anxiety and depression symptoms depending on type of treatment (A) or clinical activity (B). Median score of Inflammatory Bowel Disease Questionnaire-9 (IBDQ-9) depending on clinical activity (C) and existence of depression (D). Correlation between stress (PSS-14) and HADS-Anxiety (E) and HADS-Depression (F) score. HADS: Hospital Anxiety and Depression Scale; PSS: Perceived Stress Scale; 5-ASA: 5-aminosalicylic acid.