Journal of Coloproctology

www.jcol.org.br

Original Article

Comparative analysis of anxiety and depression prevalence between individuals with and without inflammatory bowel disease

Carlos Henrique Marques dos Santos ^{a,*}, Amanda Cristine Alcântara Galindo^b, Bárbara Alencar da Silva^b, Camila Rodrigues Dantas^b, Isadora Albuquerque de Araújo Guilherme^b, José Elias Basmage Nunes Gomes^b, Kayque Michel Dallacqua^b, Mariana Pereira de Souza^b, Patricia Szlachta Senna^b

^a Universidade Anhanguera (UNIDERP), Campo Grande, MS, Brazil

^b Universidade Anhanguera (UNIDERP), Curso de Medicina, Campo Grande, MS, Brazil

ARTICLE INFO

Article history:

Received 1 June 2020

Accepted 11 July 2020

Available online 14 September 2020

Keywords:

Inflammatory bowel disease

Crohn's disease

Ulcerative colitis

Depression

Anxiety

ABSTRACT

Rationale: Inflammatory bowel diseases – Crohn's Disease (CD) and Ulcerative Colitis (UC) – are chronic disorders associated, for several reasons, with psychological symptoms and stigmatization of patients.

Aim: To compare individuals with and without inflammatory bowel diseases in relation to the prevalence of anxiety and depression.

Method: The psychological aspect was analyzed using two globally validated questionnaires – the Patient Health Questionnaire (PHQ-9) and the General Anxiety Disorder questionnaire (GAD-7) – in addition to a sociodemographic questionnaire. Data collection was carried out in three groups, each one consisting of 100 individuals; the first comprising outpatients with a diagnosis of inflammatory bowel diseases, the second comprising outpatients without a diagnosis of inflammatory bowel diseases and the third by non-outpatients without a diagnosis of inflammatory bowel diseases.

Results: The groups were similar regarding gender, ethnicity, marital status and tobacco use. As for social class, the IBD group showed a predominance of class E (46%), the outpatient group a predominance of class D (44%) and the non-outpatient group, class C (44%) ($p < 0.001$). The non-outpatient group also had a higher number of young individuals (mean = 36.69 years) ($p < 0.001$). There was a higher number of individuals with depression and anxiety in the IBD and outpatient control groups when compared to the non-outpatients' group ($p < 0.001$), but with no difference between the two first groups. There was a higher number of individuals with severe degree anxiety in the IBD group (36%) compared to the non-outpatients' group (8%) ($p < 0.001$).

* Corresponding author.

E-mail: carlos.marques@anhanguera.com (C.H. Santos).

<https://doi.org/10.1016/j.jcol.2020.07.006>

2237-9363/© 2020 Sociedade Brasileira de Coloproctologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Conclusion: Greater severity and a prevalence of anxiety and depression were observed in the group with inflammatory bowel diseases.

© 2020 Sociedade Brasileira de Coloproctologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Análise comparativa da prevalência de ansiedade e depressão entre indivíduos portadores e não portadores de doença inflamatória intestinal

R E S U M O

Palavras-chave:

Doença inflamatória intestinal
Doença de Crohn
Retocolite ulcerativa
Depressão
Ansiedade

Racional: Doenças inflamatórias intestinais – Doença de Crohn (DC) e Retocolite Ulcerativa (RCU) – são desordens crônicas associadas, por diversos fatores, a sintomas psicológicos e estigmatização dos portadores.

Objetivo: Comparar indivíduos portadores e não portadores de doenças inflamatórias intestinais em relação à prevalência de ansiedade e depressão.

Método: O aspecto psicológico foi analisado através de dois questionários mundialmente validados – o Questionário sobre Saúde do Paciente (PHQ-9) e o questionário de Transtorno Geral de Ansiedade (GAD-7) – além de um questionário sociodemográfico. A coleta foi realizada em três grupos, cada um composto por 100 indivíduos, sendo o primeiro composto por pacientes ambulatoriais com diagnóstico de doenças inflamatórias intestinais, o segundo por pacientes ambulatoriais sem diagnóstico de doenças inflamatórias intestinais e o terceiro por indivíduos não ambulatoriais sem diagnóstico de doenças inflamatórias intestinais.

Resultados: Os grupos foram semelhantes quanto a gênero, etnia, estado civil e uso de tabaco. Quanto à classe social, o grupo doenças inflamatórias intestinais apresentou predominância de classe E (46%), o grupo Controle Ambulatorial predominância de classe D (44%) e o grupo Controle Parque de classe C (44%) ($p < 0,001$). O grupo controle parque teve também maior número de indivíduos jovens (média = 36,69 anos) ($p < 0,001$). Observou-se maior número de indivíduos com depressão e ansiedade nos grupos doenças inflamatórias intestinais e Controle ambulatorial em comparação ao grupo Controle parque ($p < 0,001$), mas sem diferença entre os primeiros. Houve maior número de indivíduos com ansiedade grau severo no grupo DII (36%) em comparação ao grupo Controle parque (8%) ($p < 0,001$).

Conclusão: No grupo portador de doenças inflamatórias intestinais foi observada maior severidade e prevalência de ansiedade e depressão.

© 2020 Sociedade Brasileira de Coloproctologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The two clinical forms of Inflammatory Bowel Disease (IBD) are Crohn's Disease (CD) and Ulcerative Colitis (UC), which are idiopathic and incurable chronic intestinal disorders with unpredictable evolution, requiring long-term treatment.¹ Although these diseases differ from each other in terms of location, epithelial tissue involvement and pathophysiology, they have another factor in common, in addition to constituting IBDs: the impaired mental health in these patients.

People with IBD live with unpleasant symptoms such as diarrhea, abdominal pain, and possible complications such as strictures and fistulas, which can result in hospitalizations and surgical procedures.² These manifestations, combined with the uncertain evolution, foster exacerbated concerns, so that these fears may imply emotional impairment and may culminate in the most common psychiatric disorders in IBD: anxiety and depression.³

The importance of these disorders is also described by the epidemiology, which shows significant numbers. The prevalence of depressive symptoms in IBD ranges from 9.3% to 68%, whereas for anxiety, it ranges from 22.5% to 80%.⁴ Moreover, in comparison with the general population, individuals with IBD are two to four-fold more likely to develop depressive disorders throughout their lives and three to five-fold more likely to develop anxiety disorders.⁵

Therefore, the study of these patients is necessary for a psychological intervention, starting with the diagnosis. Considering that such studies are scarce in Brazil, and the incidence of CD and UC has progressively increased,⁶ it is necessary to carry out studies that indicates the number of patients with these psychiatric disorders associated with IBD and whether these numbers follow global trends recorded in the literature regarding the evolution of these conditions associated with IBD. Therefore, the aim of this study is to compare individuals with and without IBD in relation to the prevalence of anxiety and depression.

Objective

To compare individuals with and without IBD in relation to the prevalence of anxiety and depression.

Method

This study was approved by the Research Ethics Committee of Universidade Anhanguera - Uniderp, under the Certificate for Ethical Appreciation Presentation n. 92636418.8.0000.5161 and carried out according to the required ethical standards.

This was a descriptive cross-sectional study, which involved the application of questionnaires to three different groups, in which the inclusion criteria were: age older than 18 and literate. The first, called the IBD group, consisted of 100 adult patients followed at the Coloproctology Outpatient Clinics at Hospital Universitário Maria Aparecida Pedrossian (HU) of Universidade Federal de Mato Grosso do Sul and Hospital Regional de Mato Grosso do Sul (HR) in the municipality of Campo Grande, state of Mato Grosso do Sul, Brazil, diagnosed with CD or UC. The second group, called the Ambulatory Control group, consisted of 100 patients followed at the HU and HR Coloproctology Outpatient Clinics, who did not have IBD. The third group consisted of non-IBD patients who frequented the Ayrton Senna park, called the Park Control group, consisting of 100 adult patients who declared themselves healthy and did not have IBD.

The data collection instruments comprised the General Anxiety Disorder (GAD-7) questionnaire, the Patient Health Questionnaire (PHQ-9), a sociodemographic questionnaire and another questionnaire, exclusively applied to the IBD Group.

Specifically, GAD-7 is an instrument for the assessment, diagnosis and monitoring of generalized anxiety disorder (usually called anxiety), consisting of seven items, arranged on a four-point scale: 0 (not once that symptom occurred in a period of two weeks) and 3 (that symptom occurred almost every day in a period of two weeks), therefore its score ranges from 0 to 21. A positive indicator is considered with a score ≥ 10 , thus, the lower the number of the sum (closer to 0) the lower the positive indicator for the disorder and the closer to the maximum sum (21), the greater the intensity of the pathology. It was created by Spitzer, Kroenke, Williams and Löwe,⁷ validated by Kroenke, Spitzer, Williams, Monahan and Löwe⁸ according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). The translation into Portuguese was carried out by Pfizer - (Copyright© 2005 Pfizer Inc., New York, NY) with registered use in Brazil.⁹ The aforementioned literature by those who created and validated it, identified a sensitivity of 89% and a specificity of 82%.

The PHQ-9 is used to assess, diagnose and monitor the presence or absence of major depressive disorder (commonly called depression).¹⁰ It has validation records,¹¹ and it was translated into Portuguese by Pfizer, and there are also studies carried out in Brazil¹² that used this instrument. Its creation was in accordance with the DSM-IV criteria and allows the diagnosis and screening of depression levels. It consists of

nine items arranged on a scale identical to that of GAD-7, with the same function of its sum and its score ranges from 0 to 27. Questionnaires that assess the presence of depression in individuals with IBD, were validated by a specific study, which demonstrated that PHQ-9 has greater sensitivity (95%) when compared to other equally validated questionnaires.^{13,14} Both PHQ-9 and GAD-7 are copyrighted questionnaires, which belong to Pfizer. However, this company grants free permission to copy and reproduce them.

The sociodemographic questionnaire, which was prepared by the authors of the present study, covers topics related to age, gender, marital status, level of schooling, housing conditions, economic status, smoking status, health insurance and concomitant diseases.

The last questionnaire, which was applied exclusively to the IBD group, comprised four questions related to the time of diagnosis, surgery and /or hospitalizations due to IBD and psychological assistance.

Patients in the IBD group were approached after an educational lecture on the quality of life and coping with IBD topic, previously planned by the authors. The data collection sites included the HU and HR Coloproctology Outpatient Clinics.

Regarding the group of patients without IBD, they were also approached at the Coloproctology Outpatient Clinics of the HU and HR, among patients who were waiting for their respective medical appointments.

As for the group of non-IBD patients that frequented the Ayrton Senna Park, the approach was carried out by talking to people who were inside the park.

The same data collection procedures were carried out for the three groups: after reading and signing the Free and Informed Consent Form (FICF), the participants received the GAD-7, PHQ-9 and sociodemographic study questionnaires. Subsequently, they were instructed on the project objective and on questionnaire self-administration. The questionnaires were privately and individually filled-in, without the need for identification and placed inside an opaque folder immediately after being delivered to the researchers.

At the end, all study participants were instructed by receiving information about places where psychological health services are provided and ways to have access to these services through the Unified Health System, through an information leaflet.

As for data treatment, the comparison between age and different groups was performed using One-Way ANOVA, followed by the Tukey post-test. The assessment of the association of categorical variables, both sociodemographic ones and those related to IBD with different groups of patients or with different diagnoses of IBD or with signs of anxiety and depression, was performed using the chi-square test, with Bonferroni correction when necessary. The other study results are presented as descriptive statistics or in tables. The statistical analysis was performed using the SPSS statistical software, version 23.0, considering a significance level of 5%.

Results

There was no significant difference between the groups regarding the participants' gender ($p=0.114$) and ethnicity

Table 1 – Prevalence of individuals with positive indicators for depression in the PHQ-9 questionnaire.

Level of depression	Group			p-value
	IBD	Ambulatory control	Park control	
Negative (≤ 10)	58.0 (58)b	69.0 (69)b	87.0 (87)a	0.001
Moderate (10 – 14)	19.0 (19)a	14.0 (14)a	8.0 (08)a	
Moderately severe (15 – 19)	9.0 (09)a	7.0 (07)a	4.0 (04)a	
Severe (≥ 20)	14.0 (14)a	10.0 (10)a	1.0 (01)b	
The results are shown as relative frequency (absolute frequency). p-value in the Chi-Square Test. Different letters on the line indicate a significant difference between the groups (Chi-square test with Bonferroni correction, $p < 0.05$).				

Table 2 – Prevalence of patients with positive indicators for anxiety in the GAD-7 questionnaire.

Degree of severity GAD-7	Grupo			p-value
	IBD	Ambulatory control	Park control	
Negative (< 10)	45.0 (45)b	62.0 (62)b	80.0 (80)a	< 0.001
Moderate (10 – 14)	19.0 (19)a	17.0 (17)a	12.0 (12)a	
Severe (≥ 15)	36.0 (36)a	21.0 (21)a	8.0 (08)b	
The results are shown as relative frequency (absolute frequency). p-value in the Chi-Square Test. Different lowercase letters on the line indicate a significant difference between the groups (Chi-square test, with Bonferroni correction, p<0.05).				

($p = 0.054$). As for marital and smoking status, the indicators were similar, with no statistical significance. As for the social class, a difference was found between the three groups: the IBD group showed a predominance of class E (46%), the Ambulatory Control group a predominance of class D (44%) and the Park Control group, class C (44%), considered the statistical significance (p -value < 0.001). The Park Control group belonged to a younger age group when compared to the IBD group ($p < 0.001$), with a mean age of 36.69 years.

As shown in Table 1, the IBD group obtained a 42.0% positive indicator for depression, a considerably higher number ($p = 0.001$) when compared to the Park Control group (13.0%), but with no statistically significant difference when compared to the Outpatient Control group (31.0%).

Similar values were also found for anxiety (Table 2), with a prevalence of 55.0%, compared to the Park Control group (20.0%). Moreover, a higher frequency of severe anxiety was observed in patients with IBD (36.0%) when compared to the individuals who frequented the park (8%).

Discussion

The present study highlighted a group with a majority of women (54%), with a mean age of 44.77 years, non-whites and non-smokers. These data show a sociodemographic profile of IBD patients similar to that found in the Brazilian literature^{14–16}; however, it differs mainly in terms of income, ethnicity and mean age when compared to the international literature.^{17–19}

As for the Outpatient Control group and the Park Control group, similarities can be observed regarding gender, ethnicity, marital status and smoking status; however, they differ in terms of age, social class and occupation. Regarding age, the Park Control group comprised an age group with fewer elderly individuals, a result that was consistent with the study by Pet-

roski et al.,²⁰ which stated that young individuals more often frequent public parks, when compared to older ones.²⁰

It was observed that the IBD group had a higher frequency of depression. A similar pattern was found in the literature, when it demonstrated that 9.3%–68% of IBD patients have depressive disorders, while the world population has 11.1%.^{3,21,22}

Regarding the GAD-7 questionnaire, the prevalence of anxiety was three-fold higher in the IBD group, and previous studies found similar values^{4,22}; this can be up to 15-fold higher than the anxiety index in the world's population (3.6%).²³

Therefore, the highest percentage of anxiety and depression in the IBD group, in contrast to the other groups in the present study and the general population, confirms the hypothesis that IBD patients have higher rates of anxiety and depression, as the literature already supports.^{24,25}

The reason for the high rates of psychiatric comorbidities is due to two main reasons: the symptomatological characteristic of the disease, susceptible to psychosocial suffering^{26–28}; and the intrinsic and bidirectional communication between the brain and the intestine.^{29,30} Therefore, it is important to note that IBD predisposes to and worsens psychiatric comorbidities, especially mood and anxiety disorders, which also influence the course of the disease, leading to its exacerbation.^{2,14,31–34}

However, as mentioned before, when correlating the prevalence of depression in the group with IBD with the Ambulatory Control group (Table 2), no statistical difference was observed. To understand this result, it is necessary to emphasize that individuals in the Ambulatory Control group have chronic and acute coloproctological comorbidities, which were not differentiated and characterized during the research. For comparative purposes, the study by Lewis³⁵ shows a similar result, which concluded that patients with IBD have a higher prevalence of depression when compared to the healthy control group; however, when compared to the group

of patients other chronic diseases, no significant differences are observed.

Other studies have described that individuals with chronic diseases, such as asthma, arthritis and diabetes, have higher rates of depression and anxiety compared to healthy control groups.^{36,37} Hence, these data showed that other diseases, as well as CD and UC, are also associated with an increased incidence of these psychiatric disorders.

Considering this problem, the importance of a multidisciplinary approach when treating patients with chronic diseases becomes clear. Therefore, it is necessary to expand the human, structural and financial resources for the identification and treatment of psychiatric disorders, especially in patients with IBD, since anxiety and depression are of great importance for the natural history of the disease.^{38,39}

Another potentially influential factor regarding such result, is that in general, people who frequent public parks practice outdoor activities.⁴⁰ Because physical activity is an effective means of preventing and treating anxiety and depressive disorders, it is possible that this factor may have influenced the lower frequency found among these individuals.^{41,42} However, to understand whether the practice of physical exercises influences the prevalence of anxiety and depression in IBD patients and in the other assessed groups, further studies are required to provide data on this association.

According to the obtained results, the positive indicator for depression in the IBD group was not correlated with age ($p=0.323$) and social class ($p=0.644$). The same was observed for anxiety in relation to the abovementioned variables.

The lack of interaction between epidemiological characteristics and anxiety and depression disorders suggests that there are other factors that directly interfere with them, which need to be assessed in future studies. For instance, we mention other agents that have been previously mentioned in the literature: use of corticosteroids, disease remission, frequency and severity of symptoms, treatment adherence.^{21,29,43}

Therefore, this study showed that the population with IBD, due to the biopsychosocial impacts of the pathology, has higher rates of anxiety and depression, just as it has been observed in the world's population with IBD.

Consequently, the importance of further studies focusing on the psychological care of patients with IBD and other chronic pathologies becomes evident, aiming to expand the prevention, diagnosis and treatment of these disorders.

We emphasize that this article has limitations, such as data obtained from a single center and, mainly, the evaluation of a specific moment, which, especially in individuals with IBD, can be of great relevance, since the active disease phases can have greater emotional impact than phases when the disease is in remission. Thus, further studies are required on the topic, aiming to provide subsidies for health professionals, aiming to improve care for patients with IBD. Therefore, comprehensive and multidisciplinary care is essential for health and quality of life improvement.

Conclusion

It can be concluded that individuals with IBD had a higher prevalence of anxiety and depression, and these conditions

were more severe in intensity than in the other groups. Moreover, they are closely related to more disadvantaged social classes.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Xavier RJ, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. *Nature*. 2007;448:427–34.
- Zaterka S, Eiseig J. *Tratado de Gastroenterologia: da Graduação à Pós-graduação*. 2. ed. São Paulo: Editora Ateneu; 2016.
- Szigethy E, Weaver E, Click B, Kogan J, Shrank W, Mcauliff K, et al. Psychiatric Characterization of Patients Enrolled in IBD Subspecialty Home. *Am J Gastroenterol*. February 2018;113:S2.
- Cardozo W, Sobrado C. *Doença inflamatória intestinal*. 2. ed. São Paulo: Manoele; 2015. p. 614–26.
- Graff LA, Walker JR, Bernstein CN. Depression and anxiety in inflammatory bowel disease: a review of comorbidity and management. *Inflamm Bowel Dis*. 2009;15:1105–18.
- Souza M, Belasco A, Aguilar JN. Perfil epidemiológico dos pacientes portadores de doença inflamatória intestinal do estado de Mato Grosso. *Rev Bras Coloproctol*. 2008;28:324–8.
- Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166:1092–7.
- Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. 2007;146:317–25.
- Bergerot CD, Laros BJA, de Araujo BTCCF. Avaliação de ansiedade e depressão em pacientes oncológicos: comparação psicométrica. *Psico-USF*. 2014;19:187–97.
- Kroenke K, Spitzer R. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatr Ann*. 2002;32:509–15.
- Martin A, Rief W, Klaiberg A, Braehler E. Validity of the brief patient health questionnaire mood scale (PHQ-9) in the general population. *Gen Hosp Psychiatry*. 2006;28:71–7.
- Osório FL, Mendes AV, Crippa JA, Loureiro SR. Study of the discriminative validity of the PHQ-9 and PHQ-2 in a sample of Brazilian women in the context of primary health care. *Perspect Psychiatr Care*. 2009;45:216–27.
- Bernstein CN, Zhang L, Lix LM, Graff LA, Walker JR, Fisk JD, et al. CIHR Team in Defining the Burden and Managing the Effects of Immune-mediated Inflammatory Disease. The validity and reliability of screening measures for depression and anxiety disorders in inflammatory bowel disease. *Inflamm Bowel Dis*. 2018;24:1867–75.
- Starcevic V, Portman ME. The status quo as a good outcome: how the DSM-5 diagnostic criteria for generalized anxiety disorder remained unchanged from the DSM-IV criteria. *Aust N Z J Psychiatry*. 2013;47:995–7.
- Arantes JAV, Santos CHM, Delfino BM, Silva BA, Souza RMM, Souza TMM, et al. Epidemiological profile and clinical characteristics of patients with intestinal inflammatory disease. *J Coloproctol (Rio J)*. 2017;37:273–8.
- Shirazi KM, Somi MH, Bafandeh Y, Saremi F, Mylanchy N, Rezaeifar P, et al. Epidemiological and clinical characteristics of inflammatory bowel disease in patients from northwestern Iran. *Middle East J Dig Dis*. 2013;5:86–92.
- Rubin Dt, Feld Ld, Goeppinger Sr, Margolese J, Rosh J, Rubin M, et al. The Crohn's and colitis foundation of america survey of

- inflammatory bowel disease patient health care access. *Inflamm Bowel Dis.* 2016;23:224-32.
18. Kochar B, Barnes EL, Long MD, Cushing KC, Galanko J, Martin CF, et al. Depression is associated with more aggressive inflammatory bowel disease. *Am J Gastroenterol.* 2018;113:80-5.
 19. Petroski EL, Silva DAS, Reis RS, Pelegrini A. Estágios de mudança de comportamento e percepção positiva do ambiente para atividade física em usuários de parque urbano. *Motricidade.* 2009;5:17-31.
 20. Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients with Inflammatory Bowel Disease: a systematic review. *J Psychosom Res.* 2016;87:70-80.
 21. Molina MRAL, Wiener CD, Branco JC, Jansen K, Souza LDM, Tomasi E, et al. Prevalência de depressão em usuários de unidades de atenção primária. *Rev Psiq Clín.* 2012;39:194-7.
 22. Organização Mundial de Saúde-OMS. Depression and other common mental disorders: global health estimates. Geneva: WHO; 2017. Disponível em: <http://apps.who.int/iris/bitstream/10665/254610/1/WHO-MSD-MER-2017.2-eng.pdf>. Acesso em: 26/07/2019.
 23. Häuser W, Janke KH, Klump B, Hinz A. Anxiety and depression in patients with inflammatory bowel disease: comparisons with chronic liver disease patients and the general population. *Inflamm Bowel Dis.* 2011;17:621-32.
 24. Addolorato G, Capristo E, Stefanini GF, Gasbarrini G. Inflammatory bowel disease: a study of the association between anxiety and depression, physical morbidity, and nutritional status. *Scand J Gastroenterol.* 1997;32:1013-21.
 25. Falcão LTM, Martinelli VF. Associação de doença inflamatória intestinal com ansiedade e depressão: avaliação dos fatores de risco. *GED Gastroenterol Endosc Dig.* 2016;35:52-8.
 26. Cohen RD. The quality of life in patients with Crohn's disease. *Aliment Pharmacol Ther.* 2002;16:1603-9.
 27. Bernklev T, Jahnsen J, Lygren I, Henriksen M, Vatn M, Moum B. Health-related quality of life in patients with inflammatory bowel disease measured with the Short Form-36: psychometric assessments and a comparison with general population norms. *Inflamm Bowel Dis.* 2005;11:909-18.
 28. Janke KH, Klump B, Gregor M. Determinants of life satisfaction in inflammatory bowel disease. *Inflamm Bowel Dis.* 2005;11:272-86.
 29. Bonaz B, Bernstein C. Brain-gut interactions in inflammatory bowel disease. *Gastroenterology.* WB Saunders. 2013;144:36-49.
 30. Martin-Subero M, Anderson G, Kanchanatawan B, Berk M, Maes M, et al. Comorbidity between depression and inflammatory bowel disease explained by immune-inflammatory, oxidative, and nitrosative stress; tryptophan catabolism; and gut-brain pathways. *CNS Spectr.* 2016;21:184-98.
 31. Kiebles J, Doerfler B, Keefer L. Preliminary evidence supporting a framework of psychological adjustment to inflammatory bowel disease. *Inflammatory Bowel Dis.* 2010;16:1685-95.
 32. Byrne G, Rosenfeld G, Leung Y, Qian H, Raudzus J, Nunez C, et al. Prevalence of anxiety and depression in patients with inflammatory bowel disease. *Can J Gastroenterol Hepatol.* 2017;2017:6496727.
 33. Mikocka-Walus A, Pittet V, Rossel JB, von Känel R, IBD S. Cohort Study Group. Symptoms of depression and anxiety are independently associated with clinical recurrence of inflammatory bowel disease. *Clin Gastroenterol Hepatol.* 2016;14:829-35, e1.
 34. Spiller RC, Thompson WG. Transtornos intestinais. *Ar Gastroenterol.* 2012;49:39-50.
 35. Lewis K, Marrie RA, Bernstein CN, Graff LA, Patten SB, Sareen J, et al. CIHR Team in defining the burden and managing the effects of immune-mediated inflammatory disease. The prevalence and risk factors of undiagnosed depression and anxiety disorders among patients with inflammatory bowel disease. *Inflamm Bowel Dis.* 2019;25:1674-80.
 36. Nakagawa R, Yamaguchi S, Kimura S, Sadamasu A, Yamamoto Y, Sato Y, et al. Association of anxiety and depression with pain and quality of life in patients with chronic foot and ankle diseases. *Foot Ankle Int.* 2017;38:1192-8.
 37. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B, et al. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet.* 2007;370:851-8.
 38. Liu CS, Adibfar A, Herrmann N, Gallagher D, Lanctôt KL. Evidence for inflammation-associated depression. *Curr Top Behav Neurosci.* 2017;31:3-30.
 39. Leonard BE. Inflammation and depression: a causal or coincidental link to the pathophysiology. *Acta Neuropsychiatr.* 2018;30:1-16.
 40. Pierone JM, Vizzotto MM, Heleno MGV, Farhat CAV, Serafim AP. Qualidade de vida de usuários de parques públicos. *Boletim Psicol.* 2016;66:99-112.
 41. Dunn AL, Trivedi MH, O'Neal HA. Physical activity dose-response effects on outcomes of depression and anxiety. In *Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]*. Centre for Reviews and Dissemination (UK). 2001.
 42. Rebar AL, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C. A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. *Health Psychol Rev.* 2015;9:366-78.
 43. Burisch J, Munkholm P. The epidemiology of inflammatory bowel disease. *Scandinavian J Gastroenterol.* 2015;50: 942-51.