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"CAROL DAVILA" BUCURESTI

DOCTORAL SCHOOL

MEDICINE

TOOLS TO ASSESS THE QUALITY OF CARE OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A DEDICATED TERTIARY CENTER

PHD THESIS ABSTRACT

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CONTENTS

Working hypothesis and general objectives

In this doctoral thesis we started from the premise of assessing the experience of IBD patients and their quality of life, aiming to identify factors associated with the perception of an improvement in quality of life.

Second, we wanted to validate a series of simplified tools to assess patients' quality of life and in this way to make the case for routine use in inflammatory bowel disease centers.

The main purpose of the benchmarking exercise was to provide a detailed assessment of the quality of patient care from the patients' perspective.

Recurring themes of insufficient information, as well as the need for improved communication and easy access to help were highlighted at most stages of the patient journey.

Within the Gastroenterology I Clinic of the University Emergency Hospital of Bucharest, we have developed a tertiary center dedicated to the specialized treatment of inflammatory bowel diseases, with the aim of providing patient-centered care adapted to the principles of modern medicine. In line with the latest international recommendations - in particular the ECCO guidelines and the STRIDE II consensus - we have adopted a proactive approach, based on treat-to-target treatment and continuous monitoring of disease progression, with a focus on clinical, endoscopic and, increasingly, quality of life goals.

To assess the effectiveness of this integrated approach and to quantify the quality of care provided, we designed a comprehensive prospective analysis of patient well-being using validated patient-reported outcomes (PRO) instruments. Thus, in this work we used three complementary instruments: the IBD-Disk questionnaire, the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) and the Beck Depression Inventory (BDI). They allow a multidimensional assessment of quality of life, covering areas such as self-perceived disability, psychological distress and the impact of gastrointestinal symptoms on daily functioning.

We initially reviewed the rationale for the existence of tertiary care centers for inflammatory bowel disease. Then we analyzed in three different studies the various tools for measuring patients' quality of life and their role in increasing quality of care in completely different situations-from the impact of therapy change and the nocebo effect, to disability and depression as well as the implementation of simple tools to measure them.

The primary objectives of the thesis focus on three key directions.

First, we investigated the impact of switching from originator biologic therapy to biosimilars, both from the perspective of clinical efficacy and patient-perceived quality of life

and acceptability. Second, we analyzed the presence of depressive symptoms in patients with IBD, simultaneously using two instruments - the IBD-Disk and the Beck Depression Inventory - to identify overlaps, differences, and potential complementary clinical utilities. Thirdly, the paper comprises a longitudinal evaluation, conducted over a five-year period (2019-2023), in which patients' quality of life was systematically monitored using the IBD-Disk and SIBDQ questionnaires, translated and culturally adapted into Romanian.

Through this initiative, we aimed not only to analyze individual patient outcomes, but also to identify predictive models to support personalized and value-based medicine. The results obtained provide important insights into how the integration of PROs into current clinical practice can optimize the management of inflammatory bowel diseases and contribute to the achievement of therapeutic goals defined in international consensus.

The statistics were performed at the department of markerting and medical informatics of UMF Carol Davila, the studies benefiting from a complex and robust analysis that generated solid results that were published in journals with impact factor 4.3 and 0.9. Several publications in indexed journals and communications at national congresses allowed the realization of this thesis.

Research methodology for the 3 studies carried out

1. Impact of changing therapy in inflammatory bowel disease

This observational, multicenter, prospective, observational study was conducted in two specialized centers in Bucharest, aiming to assess the impact of non-medical replacement of originator Adalimumab with biosimilars in patients with inflammatory bowel disease (IBD). Fifty-three patients (27 men and 26 women) diagnosed with Crohn's disease or ulcerative colitis according to standard endoscopic, radiologic and histologic criteria were included. Follow-up was performed using a tight control approach [4].

Disease extent was classified according to the Montreal system [4], and severity was assessed by the Mayo score (ulcerative colitis) [4] and the Harvey-Bradshaw Index (HBI) (Crohn's disease) [2]. All patients were in clinical remission after induction treatment with originator Adalimumab (Humira).

In the context of the policy of the National Health Insurance House on monthly prescription, patients were gradually switched to one of the biosimilars available in Romania: Hukyndra, Imraldi or Hyrimoz [3]. The choice of biosimilar was not standardized, the decision being made by the treating physician together with the patient. The dose (40 mg subcutaneously every two weeks) and mode of administration (pen injector) remained unchanged after the transition.

Clinical evaluations were performed monthly for 12 months after the change. The characteristics of the products used (volume, composition, presence of citrate, latex and shelf life at room temperature) are presented highlighting similarities and differences between the available formulations of Adalimumab on the Romanian market.

2. IBD Disk- BDI correlation analysis

The observational, cross-sectional, non-interventional study was conducted in the Department of Internal Medicine I and Gastroenterology of the University Emergency Hospital of Bucharest and included 82 consecutive patients diagnosed with inflammatory bowel disease (IBD), with a mean age of 43.11 ± 13.07 years. The majority of patients were male (63.4%) and had Crohn's disease (61.0%). The sample size provides adequate statistical power for an estimated effect size of high magnitude (0.80) [5].

Inclusion criteria were confirmed diagnosis according to ECCO guidelines, age >18 years and informed consent. Patients with psychiatric conditions or antidepressant

treatment were excluded. Disease remission was defined by Harvey-Bradshaw score <5 for Crohn's disease and partial Mayo score ≤2 for ulcerative colitis. Participants completed two questionnaires: the Beck Depression Inventory (BDI), to assess depressive symptoms [316-319], and the IBD-Disk, to measure IBD-related disability [5].

The BDI comprises 21 items with scores ranging from 0 to 3, with a total score ranging from 0 to 63, indicating the severity of depressive symptoms. The IBD-Disk is a simplified, self-administered version of the IBD-DI, which assesses ten dimensions of disability on a visual scale from 0 to 10, resulting in a total score between 0 and 100. The values are plotted as a polygon, providing a visual picture of the impact of the disease on the patient [320]. The questionnaire was used in a translated and validated version in Romanian, with demonstrated applicability in international studies [5].

Statistical analysis was performed in SPSS v26.0, using Spearman correlation for the relationships between questionnaires and scores, logistic regression to assess the predictive ability of scores in relation to clinical remission and Mann-Whitney test for comparing means. The significance level was $p<0.05$.

3. IBD Disk- SIBDQ correlation analysis

The observational, cross-sectional, single-center study was conducted between 2019 and 2023 in the Department of Internal Medicine I and Gastroenterology of the University Emergency Hospital of Bucharest. A total of 83 consecutive patients with inflammatory bowel disease (IBD), with a mean age of 41.54 ± 14.14 years, were included, of whom 60.2% had Crohn's disease and 39.8% ulcerative colitis. Statistical calculation confirmed that the sample size was adequate to detect a large effect size (0.80) with a significance level $\alpha = 0.05$ [5].

Inclusion criteria assumed confirmed diagnosis according to ECCO guidelines, age >18 years and informed consent. Disease remission was defined by Harvey-Bradshaw score <5 for Crohn's disease and partial Mayo score ≤2 for ulcerative colitis. Demographic data, clinical parameters and fecal calprotectin were recorded. Patients completed two validated questionnaires: the **SIBDQ** - an IBDQ-derived instrument used to assess quality of life, with scores between 10 and 70, where scores below 50 indicate significant impairment [5]; and the **IBD-Disk** - a simplified, self-administered version of the IBD-DI, with total score between 0 and 100, quantifying disability in IBD [1,5].

Statistical analysis was performed with SPSS v26. The following were applied: Spearman correlation for the association between questionnaire scores, **Cronbach's Alpha**

coefficient to assess internal consistency ($\alpha \geq 0.7$ indicating acceptable reliability) [6], exploratory factor analysis (EFA) to identify latent structure [6], and repeated measures **ANOVA** for time course [6]. The predictive performance of the scores in relation to clinical remission was assessed by the **ROC** curve, interpreted according to AUC (with values >0.7 indicating diagnostic utility) [6]. **The Chi-square** test for association of categorical variables [6] and **the Mann-Whitney** test for comparison of means in non-Gaussian distributions were also used. The significance threshold was set at $p < 0.05$.

Summary of chapters

Chapter 1. Inflammatory bowel diseases

1.1 Definition and epidemiology

Inflammatory Bowel Diseases (IBD), mainly Crohn's Disease and Ulcerative Colitis, are chronic immune-mediated diseases, with a common onset in young adults and a course marked by relapses and remissions [7]. Undetermined colitis occurs in 5-15% of patients, and microscopic colitis is only diagnosed histologically [7]. The prevalence of IBD exceeds 0.3% in Europe, North America and Oceania, while the incidence is rapidly increasing in newly industrialized countries such as China or Brazil [7]. Crohn's disease is more common in North America and ulcerative colitis in Europe [7]. In Asia, ulcerative colitis predominates, but the difference with Crohn's is fading [7]. Incidence varies by sex and age, with a peak between 15-29 years [7]. A north-south gradient has also been noted in the northern hemisphere, suggesting a possible link with vitamin D deficiency [7].

1.2. Pathogenesis

The pathogenesis of IBD involves genetic factors, intestinal dysbiosis, abnormal immune response and environmental factors [9]. Genes such as *NOD2*, *IL23R* and *ATG16L1* are implicated especially in Crohn's disease [9], and certain mutations may influence the course and response to treatment [10]. Immune dysregulation leads to chronic inflammation mediated by proinflammatory cytokines [10]. Dysbiosis and microbial imbalance favor immune activation [10]. Factors such as smoking, diet, antibiotics or stress may trigger or aggravate the disease [9,10]. Appendectomy increases the risk of Crohn's disease but protects against ulcerative colitis [10,11], and lack of microbial exposure in childhood supports the hygiene theory [11]. Physical activity, high-fiber diet and breastfeeding are protective [11].

1.3. Classification

Crohn's disease can affect the entire digestive tract, with a predilection for the ileum and colon. The Montreal classification (age, localization, phenotype) is commonly used and has prognostic value [11]. CDAI and HBI scores assess disease activity but do not include biological or endoscopic data [12]. PDAI assesses the severity of perianal disease [13].

Ulcerative colitis affects the colon, starting from the rectum. The Montreal classification defines the extent of inflammation (E1-E3), with therapeutic and prognostic implications [14]. The Truelove and Witts score assesses clinical severity [14], and the Mayo score integrates symptoms and endoscopic appearance and is useful in monitoring and research [15].

1.4. Positive diagnosis of inflammatory bowel diseases

The diagnosis of IBD is based on clinical symptoms (diarrhea, abdominal pain, rectal pain), ileo-colonoscopy with biopsies (gold standard), and biological and imaging investigations [16].

Crohn's disease has varied symptoms and can lead to complications such as strictures or fistulas [17]. CRP and fecal calprotectin are useful markers [18], and endoscopy and imaging (MRI, CT, CEV) are essential for diagnosis and monitoring [18,19].

Ulcerative colitis starts rectally, with rectal rectorrhea and tenderness [19]. Inflammatory markers and calprotectin help to assess activity [20]. Colonoscopy shows ongoing inflammation and histology confirms the diagnosis [20]. Imaging is used only in special cases [20].

1.5. Extraintestinal manifestations

Extraintestinal manifestations occur in up to 40% of patients with IBD and may affect the joints, skin, eyes, liver, lungs, cardiovascular, nervous and renal systems [20]. The most common are arthritis, erythema nodosum, uveitis and primary sclerosing cholangitis [21]. Thromboembolic, cardiovascular, neurological, pulmonary and renal complications may also occur, sometimes preceding digestive symptoms [22]. These manifestations require early recognition and multidisciplinary approach.

1.6. Differential diagnosis of IBD

The differential diagnosis of inflammatory bowel disease (IBD) is complex and involves the exclusion of infectious, neoplastic and inflammatory nonIBD conditions. Digestive infections (e.g. *C. difficile, Salmonella, Campylobacter*) can mimic IBD, requiring

specific microbiologic tests [23]. In endemic areas, intestinal tuberculosis is an important differential diagnosis of Crohn's disease, being suggested by cascading granulomas and positive PCR [23].

Neoplastic diseases (colorectal carcinoma, lymphoma) may present with similar symptoms, but are differentiated by imaging and histology [23]. Ischemic colitis occurs suddenly, especially in the elderly, and is characterized by mucosal necrosis [23]. Microscopically microscopic colitis requires biopsies for diagnosis, with endoscopically normal mucosa [24]. Other causes include radiation-induced colitis, drugs or celiac disease.

Correct diagnosis requires the integration of clinical, endoscopic, histologic, imaging and microbiologic data to avoid inappropriate immunosuppressive treatments and to guide correct management

1.7. Treatment in inflammatory bowel diseases

The therapeutic management of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), has evolved from a symptomatic to a treat-to-target approach, aiming at sustained remission and mucosal healing [25]. Treatment is tailored according to severity, localization and prognostic factors, including aminosalicylates, corticosteroids, immunomodulators, and biologic or small molecule therapies [25].

Corticosteroids induce remission in moderate-severe forms, but are not recommended for maintenance due to adverse effects [25]. Budesonide MMX is effective in mild-to-moderate UC with reduced systemic effects [27].

In Crohn's disease, 5-ASAs are considered ineffective [25]. Tiopurines and methotrexate are used in maintenance of remission but not in induction [26]. Anti-TNF agents (infliximab, adalimumab, certolizumab) are effective in moderate-severe forms, especially in combination with immunomodulators [25,26]. Ustekinumab (anti-IL-12/23) and risankizumab (anti-IL-23) are indicated after failure of anti-TNF therapies [26]. Vedolizumab is a safe alternative in patients at high infectious risk [26,28]. JAK inhibitors (e.g. upadacitinib) are novel oral options but require careful monitoring [25]. Surgery remains indicated in complicated cases and postoperative relapse is common [27].

In ulcerative colitis, 5-ASAs remain the mainstay of treatment in mild-moderate forms, including for maintenance [25]. Tiopurines are useful in relapse prevention, whereas methotrexate is not recommended [25]. Anti-TNF (infliximab, adalimumab, golimumab) are effective in moderate-severe forms [28]. Ustekinumab is indicated in patients refractory to other therapies [28]. Vedolizumab is preferred in patients with comorbidities or infectious risk

[28]. JAK inhibitors (tofacitinib, upadacitinib) are oral options for patients with prior biologic failure [25].

Surgery is reserved for refractory or complicated cases (e.g. dysplasia, toxic megacolon), with total proctocolectomy as a curative solution [25,28].

Biosimilars offer cost-effective options that are equivalent in efficacy and safety to the original biologics, with support from ECCO and AGA guidelines [28].

1.8. Complications in inflammatory bowel diseases

Crohn's disease can lead to fistulae (40%) [18], abscesses (15-20%) [29], strictures [29], perianal damage, metabolic deficiencies (e.g. vitamin B12) and treatment-related complications such as infection or toxicity [29].

Ulcerative colitis can be complicated by toxic megacolon and colonic perforation [29], bleeding [29], strictures and increased risk of colorectal cancer in extensive and long-lasting forms [30].

Chapter 2. Quality of life of patients with inflammatory bowel disease

2.1. Psychosocial aspects and quality of life in IBD patients

Inflammatory bowel disease (IBD) profoundly affects the psychological, social and professional dimensions of patients' lives, beyond the physical manifestations. The prevalence of anxiety and depression is high, affecting up to 30-40% of patients, especially during periods of increased disease activity [31]. These comorbidities negatively influence quality of life (HRQoL), adherence to treatment and disease progression by exacerbating inflammation and triggering relapses [31]. The psychosocial impact is reflected in stigma, social isolation, decreased self-esteem and educational or occupational difficulties [32]. Psychological interventions such as cognitive-behavioural therapy and screening for emotional disturbances are recommended by ECCO and AGA guidelines [32]. Although biological remission is achieved, up to 50% of patients continue to have a suboptimal quality of life [33], with notable socio-economic effects [31].

2.2 Depression, anxiety and the role of stress in IBD

Depression, anxiety and stress are common psychological comorbidities with a major impact on the course of inflammatory bowel disease (IBD), affecting quality of life, adherence to treatment and relapse rates [33]. Depression is present in up to 60% of patients in the active phases of the disease and is associated with systemic inflammation through neuroimmune

mechanisms [34]. Anxiety, reported in about 40% of patients, negatively influences symptom perception and healthcare utilization [35]. Psychological stress contributes to activation of the gut-brain axis and disruption of the intestinal barrier, being correlated with disease activity and relapses [36]. In addition, defecation imperfectivity, common in ulcerative colitis, profoundly affects patients' social and professional life, being correlated with disease severity and risk of surgery, despite its exclusion from classical scores [36]. Psychological screening and multidisciplinary approach are essential in the integrated care of IBD patients [35].

2.3. Coping in IBD

Coping is an essential element in the adaptation of patients with inflammatory bowel disease (IBD) to the challenges of chronic disease. Active, problem-solving-oriented coping strategies are associated with higher quality of life and better psychological adjustment, whereas avoidant styles (e.g. denial, disengagement) correlate with increased anxiety, depression and disability [37]. Interventions such as cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT) have been shown to be effective in promoting adaptive coping and reducing psychological distress [37]. Current guidelines recommend integrating psychological support and education to improve coping strategies and overall outcomes for patients with IBD [35].

2.4. PRO tools in inflammatory bowel disease - clinical use

Patient-reported outcomes (PROs) provide a subjective but essential perspective on the impact of inflammatory bowel disease (IBD) on quality of life, complementing objective assessments such as endoscopy or biomarkers [37]. PROs address multiple dimensions - physical symptoms, emotional state, social functioning - and are increasingly integrated into personalized medicine [37]. Instruments such as the IBDQ, SIBDQ, IBD-Control and PROMIS are validated and used for patient monitoring, optimization of therapeutic decisions and early detection of relapse [38]. Limitations of these questionnaires include the influence of psychosocial factors, overlap of symptoms with other conditions and logistical difficulties in clinical integration [37]. However, digitization and international initiatives for standardization (e.g. ICHOM, ECCO) support the use of PROs as an integral part of a patient-centered approach, with benefits in adherence, communication and therapeutic efficiency [38].

Chapter 3. Tertiary centers for inflammatory bowel diseases

The care of patients with inflammatory bowel disease (IBD) varies significantly between centers, with higher quality in dedicated centers with multidisciplinary expertise [39]. Although international and national guidelines (e.g., AGA, ECCO, CCFA, Romanian IBB

Society) have proposed clear sets of measures to standardize and improve care [40], implementation remains uneven, influenced by institutional and systemic factors. Recent studies show that patients' perceptions of quality of care are correlated with their ability to manage symptoms, but topics such as mental health or fatigue are insufficiently explored in clinical practice. The need for validated tools to audit the impact of illness on quality of life is emphasized.

Chapter 4. Impact of changing therapy in IBD

This study of non-medical switching to an Adalimumab biosimilar, conducted among 53 patients with inflammatory bowel disease, confirmed the efficacy of Adalimumab biosimilars in the management of patients with IBD, with excellent results at six and twelve months of follow-up. Furthermore, the study demonstrates that switching from the originator product to a biosimilar is safe, therapeutically effective and cost-effective.

No differences were observed between the three biosimilars used in this study.

This observational study is the first analysis conducted in Romania showing that Adalimumab biosimilars are as effective as the originator Adalimumab in clinical practice applied to IBD patients. Our results support the idea that the widespread use of biosimilars does not affect therapeutic efficacy and patient safety.

Future studies of longer duration are needed to confirm the safety, efficacy and reduction of adverse effects after treatment change including nocebo involvement. IBD disk is a useful and easy to use tool including in monitoring adverse effects and impact on patient's quality of life.

Chapter 5. IBD Disk - BDI correlation analysis

In this study we observed an increased burden of illness on daily life correlated with disease activity. Symptoms of depression and anxiety were common among IBD patients.

Our results suggest that IBD-Disk correlates well with the Beck Depression Inventory. Both scores correlated with illness activity.

We encourage the use of the IBD-Disk questionnaire during routine visits and regular patient follow-up as a useful and easy-to-use tool both for screening for depressive symptoms and for assessing quality of life in IBD patients.

Chapter 6. IBD Disk - SIBDQ correlation analysis

The main aim of this thesis was to validate and compare two international questionnaires translated into Romanian - SIBDQ and IBD Disk - for the assessment of quality of life in patients with inflammatory bowel disease (IBD) in Romania. The study, conducted prospectively between 2019-2023, showed that both instruments have good internal consistency and validity. The SIBDQ-Ro correlated better with clinical and endoscopic remission, reflecting the impact of the disease on daily life, while the IBD Disk-Ro was more sensitive to biological changes, correlating with increased calprotectin levels. The combined use of the two questionnaires provides a more complete picture of the disease course, supporting efficient and personalized monitoring of IBD patients.

Conclusions

In this PhD thesis, a fundamental objective was the development and consolidation of a tertiary center of excellence in the diagnosis, treatment and monitoring of patients with inflammatory bowel diseases (IBD) in the Gastroenterology Department of the University Emergency Hospital of Bucharest. This approach started from the imperative need to provide patients with IBB with specialized medical care, structured according to the latest international standards and clinical practice guidelines. To this end, we aimed not only to implement a modern therapeutic model based on proactive principles, such as the treat-to-target strategy and the use of biomarkers and validated clinical scores, but also to integrate patient-centered approaches through the systematic assessment of quality of life and patient-reported outcomes (PROs).

Through the efforts of the multidisciplinary team involved, we have managed to achieve this ambitious goal, fulfilling the essential criteria for the recognition of a centre of excellence: the existence of a well-organized patient flow, the implementation of international therapeutic algorithms, the use of innovative biological therapies, standardized monitoring of clinical, endoscopic and psychosocial evolution, as well as active involvement in research and continuing medical education. The Centre's work has been organized to ensure a clear, efficient and safe patient pathway from diagnosis to maintenance of remission and functional recovery, with a focus on quality of life and reduction of disability.

The importance of centres of excellence in the management of inflammatory bowel diseases is increasingly recognized internationally, as they provide an optimal setting for the application of the most advanced therapies, promoting evidence-based medicine and relevant patient outcomes. The presence of a dedicated team of gastroenterologists, surgeons, psychologists, nutritionists and specialized nurses allows for an integrated approach to the disease, tailored to the clinical complexity and systemic impact of the disease. At the same time, centres of excellence contribute significantly to increasing the quality of care, reducing medical errors, standardizing treatment and increasing patient satisfaction.

In conclusion, the formation of a tertiary center of excellence for IBD is an essential achievement of this work, with a direct impact on improving the prognosis, therapeutic efficiency and quality of life of our patients. This model can serve as an example for the expansion of networks of specialized IBB centers in Romania, with a view to aligning with leading European and international practices.

A second major objective of this thesis was to evaluate the impact of switching from originator biologic therapy to biosimilar on the clinical and psychosocial status of patients with inflammatory bowel diseases, especially in the context of the controversies related to the potential nocebo effect. Given the increasing accessibility of biosimilars and international recommendations for cost optimization in health care systems, this transition has become an increasingly common practice in specialized centers, including our clinic. However, concerns about patient acceptability and the risk of the nocebo effect compromising therapeutic efficacy justify the need for clear clinical evidence.

In our study, we prospectively investigated this transition using both objective biological indicators and validated quality of life assessment tools such as the IBD Disk and IBD Control questionnaires. The results demonstrated that switching from originator therapy to biosimilar did not negatively impact clinical remission, biomarkers of inflammation or perceived quality of life. Thus, the therapeutic efficacy was maintained and the collected data indicate a stability of the patients' overall health status after the switch.

Although some cases showed a slight increase in anxiety before treatment change, these were not statistically significant and did not correlate with clinically relevant variations. These observations suggest that although the psychological component may influence the patient's perception of treatment, the nocebo effect did not manifest significantly in our cohort. Importantly, correct information, effective communication between doctor and patient, and trust in a well-organized therapeutic system probably contributed to preventing the occurrence of adverse psychosomatic effects.

Therefore, we conclude that, with rigorous monitoring and a patient-centered approach, switching from the original biologic therapies to biosimilars is safe, well tolerated and does not compromise either clinical efficacy or quality of life. These results support the integration of biosimilars into routine practice as equivalent therapeutic options with significant economic benefit and without major risk to the patient, contrary to the fears frequently expressed in the medical literature and in everyday practice.

A third key objective of this thesis was to assess the degree of depression and anxiety among patients diagnosed with inflammatory bowel disease (IBD) using two distinct but complementary instruments: the Beck Depression Inventory (BDI), a validated psychological questionnaire for measuring the severity of depression, and the IBD Disk, a modern, multidimensional, digital, multidimensional instrument developed to assess the global impact of the disease on the patient's overall quality of life and functionality.

Based on the existing data in the literature, which show an increased prevalence of affective symptoms in patients with IBD, we aimed not only to quantify the severity of depression and anxiety, but also to compare the performance of the two questionnaires in reflecting the patient's psychological status and its relationship with disease activity. Our study revealed a statistically significant correlation between the scores obtained on the BDI and those obtained on the IBD Disk, confirming that the psychological dimension captured by Beck is to a relevant extent also reflected by the global score of IBD-related disability as perceived by the patient.

Moreover, a clear association was observed between the increased values of the two scores and the intensity of clinical disease activity, suggesting that depressive and anxiety symptoms are influenced not only by the chronic context of the disease, but also by the severity of active manifestations. This correlation supports the need to integrate psychological assessment into the standard monitoring of patients with IBD.

Therefore, the implementation of IBD Disk as a screening tool for affective symptoms in clinical practice is justified. Having the added advantage of digital use and ease of administration, this questionnaire may become a valuable tool for periodic assessment of psychosocial status, thus contributing to holistic care and personalization of therapeutic strategies. Our study validates the use of the IBD Disk not only as a tool to measure functional disability, but also as a sensitive indicator for depressive and anxiety-like disorders among IBD patients.

The final goal of this thesis was to evaluate the performance of two internationally validated questionnaires - SIBDQ (Short Inflammatory Bowel Disease Questionnaire) and IBD Disk - in their Romanian translated version, in order to use them in clinical practice in Romania. The study was conducted prospectively over a five-year period (2019-2023), in a tertiary center of excellence in the management of inflammatory bowel diseases, and included a representative cohort of patients with Crohn's disease and ulcerative colitis.

Comparative analysis of the two HRQoL instruments showed similar performance in terms of overall assessment of patients' status, with both questionnaires demonstrating high internal consistency and good validity. However, subtle differences in sensitivity between the two scales were noted in statistical correlations with various clinical and biological parameters.

Thus, the SIBDQ-Ro scores were found to have a stronger correlation with clinical and endoscopic remission, confirming the usefulness of this tool in assessing the patient's general well-being and symptomatologic control. The SIBDQ, with its multidimensional structure including domains such as emotional and social functioning, accurately reflects the impact of

disease activity on daily life, supporting its value as an outcome marker in patient-centered practice.

On the other hand, IBD Disk-Ro correlated better with abnormal levels of fecal calprotectin, an objective marker of intestinal inflammation. This observation suggests that the IBD Disk, although designed as a tool to assess functional disability, has the ability to also capture subclinical inflammatory changes, thus providing valuable information on the inflammatory status of the patient even before the onset of overt clinical manifestations.

The results obtained therefore support the use of both questionnaires in parallel in a complementary manner. Their integration into monitoring algorithms for IBD patients could contribute not only to a more accurate assessment of quality of life, but also to the early detection of disease relapses, allowing early therapeutic interventions. In conclusion, the study validates both SIBDQ-Ro and IBD Disk-Ro as useful and feasible tools in Romanian gastroenterological practice, and emphasizes the importance of a multidimensional approach in the follow-up of patients with inflammatory bowel diseases.

Based on the results obtained in this thesis, several relevant directions for future research in the field of inflammatory bowel disease (IBD) are outlined. First, longitudinal evaluation of the SIBDQ-Ro and IBD Disk-Ro scores in predicting relapse is needed to validate their usefulness in routine practice. Second, implementing these instruments in digital format provides an opportunity to study the role of remote monitoring in increasing adherence and optimizing treatment.

Another important direction is to extend the process of cultural validation to other internationally used PRO instruments in order to harmonize clinical practices. Also, the correlation between clinical phenotypes and quality of life scores could provide valuable data for individualizing therapies.

In addition, given the demonstrated relationship between PRO scores and psychological status, the initiation of multidisciplinary interventions integrating psychological support into the management of IBD patients is warranted. Last but not least, a more detailed exploration of the impact of the transition from original biologic therapies to biosimilars is needed, taking into account possible differences related to the patient's psychological profile or level of awareness. These directions may help to strengthen a patient-centred approach and increase the quality of care in specialized centres.

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