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REVIEWS

Patient-Reported Outcomes: a Compass Through Inflammatory Bowel Disease Journey

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Abstract

Inflammatory bowel disease (IBD) are chronic inflammatory conditions which have a major impact on the patients' quality of life. Patient reported outcomes (PROs) help empower the patients giving them a voice in their treatment decision and improving communication between patients and doctors. PROs represent a foundation for a tailored approach of IBD monitoring and treatment and are very important in both research and routine clinical management. Improved PROs tools will facilitate their use in daily practice, in turn improving the delivery of value-based healthcare and, in the long term, good clinical care of the patients. This review is focused on the main principles regarding PROs role and their importance in IBD care.

Keywords: patient reported outcomes, inflammatory bowel disease, quality of care, individualized treatment

Rezumat

Bolile inflamatorii intestinale sunt condiții inflamatorii cronice cu evoluție fluctuanta cu afectare sistemica si simptome proteiforme. Efectele bolii sunt considerabile, având o influență semnificativă asupra calității vieții pacientului. Rezultatele raportate de pacienți (PRO) contribuie la o imagine reala si nemediata asupra percepției acestora privind efectele pe care le are boala asupra vieții lor, oferindu-le o voce și un sentiment de mai mare control asupra deciziei privind tratamentul. PROs îmbunătățesc substanțial comunicarea dintre pacient și medic, ajutând astfel medicii să ia decizii mai precise în ceea ce privește tratamentul si reprezintă o bază pentru o abordare personalizata a fiecărui pacient. Instrumentele de măsurare PRO oferă structură și standardizare atât in scop de cercetare dar si in activitatea clinica de rutina din domeniul bolilor inflamatorii intestinale. Utilizarea acestora în practica zilnică va îmbunătăți la calitatea asistenței medicale și, pe termen lung, o mai buna îngrijire a pacienților.

Cuvinte cheie: rezultatele raportate de pacient, boala inflamatorie intestinală, calitatea îngrijirii, tratament individualizat

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INTRODUCTION

Inflammatory bowel disease (IBD) commonly known as Crohn disease (CD) and Ulcerative colitis (UC) are chronic inflammatory condition with flare-ups and remissions, affecting quality of life (QoL) of the patients and necessitating lifelong medical care.[1] Both diseases have a general commonality in their pathogenesis and are derived from a dysregulated or aberrant mucosal immune response to antigenic components of the normal commensal microbiota that reside within the intestine. Usually, IBD is diagnosed in early adulthood with a peak incidence between ages of 15-25 years but lately adult or late onset patterns of disease are described with increased frequency.[5,6,17]

The symptoms associated with IBD are proteiform and can vary by disease location and severity and can reduce general health related quality of life (HRQoL), which is an important indicator for patient care in the disease management.[16,17] IBD's can impact many aspects of the patients' quality of life, such as bowel control, fatigue, social isolation and fear of developing complications, cancer or need of complicated surgical procedures with irreversible impact on their daily life.[1,14] They are also associated with significant psychosocial burden and may have a detrimental impact on one's ability to work, leading to decreased productivity, absenteeism, all of which increase financial strain.

Therefore, the target of IBD treatment is not only to limit the impact of comorbidities, prevent further complications by inducing and maintaining deep clinical remission but also improving health-related quality of life (HRQoL).[2,11]

Patient-reported outcomes (PROs) are any reports given directly by the patient regarding his health, that was not modified by the doctor or anybody.

In the last years, several questionnaires have been developed and validated and PROs started to represent an important end point and a significant therapeutic objective.

These well-designed questionnaires can be useful in monitoring the disease activity together with other parameters such as biomarkers, endoscopy and cross-sectional imaging. By incorporating them into the assessment process, healthcare providers try to evaluate the patient real condition, leading to treatment plans that are better aligned with the patient needs and expectations. This type of information can empower the patients giving them a voice and a sense of control in their treatment decision and improving communication between patients and doctors.[3,18]

Classical physicians developed indices of disease activity or severity including the Harvey-Bradshaw Index or the Mayo Score may disproportionately present the specific patient experiences; fatigue is highly prevalent in patients with IBD and has a negative impact on PROs and contributes to poor HRQoL elements but is not assessed in these scores.[12,16,19]

In clinical trials, valid PROs are quintessential because they provide information on the evolution of the patient's quality of life. In real life clinical setting they might represent a tool to tailor treatment. By capturing more precisely the disease activity, they can serve for an individual therapy approach making it crucial to implement PROs more widely in clinical routine.[3,9]

Recently PRO's gained a lot of recognition in individualized managing IBD, with studies highlighting their effectiveness and also their current limitations.[11,13,18]

PATIENT-REPORTED OUTCOMES': SIGNIFICANCE IN THE TREATMENT OF IBD

Defining Patient-Reported Outcomes

PROs are instruments that generate numerical data from information given directly by the patient, without any modifications. They can be subtracted to address various life and disease symptoms like fatigue, pain, depressive symptoms, and movement disabilities, which are the most significant domains that need to be addressed during IBD patient care.

Disease-specific PRO measures are constructed for a specific patient population, a specific disease, functions or symptoms. Several disease-specific PROs have been developed for different chronic inflammatory disease conditions, including IBD.[7,16,18]

The European Medicines Agency (EMA) has provided another definition of PRO as "any outcome evaluated directly by the patient themselves and based on the patient's perception of a disease and its treatment," and described it as an umbrella term which covers both single and multi-dimension measures of symptoms, HRQ-oL, health status, adherence to treatment, and satisfaction with treatment.[1]

As the illness's impact extends beyond physical symptoms to mental health and daily activities, PROs

provide valuable insights into patients' daily feelings and behaviours, providing insights not accessible through medical evaluations alone.[2,13]

Some frequently used PROS instruments in IBD include the Inflammatory Bowel Disease Questionnaire (IBDQ), SIBDQ (Short Inflammatory Bowel Disease Questionnaire) and the IBD-Control.

The CONFIDE study, which was a large-scale survey conducted in USA and several European countries found that up to half of cases of UC patients experienced bowel urgency at least once a day and that many of them not bringing forward this issue, the most common reason being embarrassment.[18]

The use of a PRO instrument can significantly aid the conversation between patient and the physician, ensuring that all aspects of the patient views and concerns are assessed, and allowing dynamic comparison with previous reports in this way serving as a tool to adjust therapy.[11,12]

The Significance of PROs in IBD Management

Research indicates that doctors often underestimate the severity of some IBD symptoms, leading to underestimation of disease severity and impact on patients' life.[3,5,11] Assessing various facets of IBD that are not easily captured through objective clinical measures, PROs are increasingly recognized as valuable tools capable to offer the physician a deeper inside on patients' evolution.

A study using the Patient Reported Outcomes Measurement Information System (PROMIS) revealed that patients with IBD experience worsening symptoms such as anxiety, depression, sleep disturbance, fatigue, pain interference, and satisfaction with their social role. Measuring these using PRO's allows better adjustments of therapy.

The CONFIDE study reported that the patients often avoid discussing bowel urgency due to embarrassment and shame, while health care practitioners often did not proactively discuss such symptoms, because they expected the patient to bring it up or due to insufficient time during appointments. Bowel urgency negatively impacts QoL in UC patients, while absence correlates with improved clinical outcomes, including better endoscopic findings and lower levels of biomarkers such as fecal calprotectin and high-sensitivity C-reactive protein (hsCRP), emphasizing the importance of severity in disease activity.[1,18]

Another study described comparable results using a two item PRO of stool frequency and rectal bleeding. Such two-item PRO scales are frequently used in IBD although there is a need to allow for regional and cultural differences; further development and assessment of PROs in IBD would be valuable to provide more guidance for physicians and to allow subsequent inclusion in treatment guidelines.[1,21]

Patient-reported metrics, such as the Inflammatory Bowel Disease Self-Efficacy Scale (IBD-SES), IBDQ, and fatigue-specific PROs, assess the disease's impact on patient life, evaluating symptoms from bowel to systemic. The IBD-SES, a 13-item scale, measures patient confidence in disease management and treatment compliance, with improved validity, reliability, and psychometric properties, increasing usage likelihood.[17,19,21]

Nevertheless, even upgrade PROs will not completely fill the inequalities of symptoms and endoscopic disease activity and thus need to be regarded as important cornerstones but not the exclusive therapy guidance parameters.[3,7]

Role in Clinical Trials and Benefits in Routine Clinical Practice

PROs are important tools to observe and record the patient health status in clinical trial environment and to compare the outcomes between treatment groups, without information on individual patient results.

PROs are increasingly used in clinical trials to measure patient experiences, such as QoL and symptom management, which are not fully captured by traditional endpoints, such as stool frequency and abdominal pain.[1,4]

PROs can aid in patient-centered drug development, providing data to demonstrate the effectiveness of new therapies, such as in IBD trials, assessing bowel urgency, fatigue, and pain.

Trials can use PROs to evaluate treatment effectiveness and patient quality of life, adjusting therapies to manage inflammation and daily symptoms. Asking patients to report their symptoms will lead to a better connection to the clinical trial process, which will improve retention rates this being very important particularly in IBD, where disease activity can fluctuate over time.[1,11,16,17]

In some studies, the use of PROs, showed that a higher-than-expected proportion of patients reported longer corticosteroid use highlighting the need for further education to reduce corticosteroid use.[1,14]

The IBD-Control Questionnaire aids physicians in assessing disease control, identifying patients needing

treatment changes, and identifying symptoms impacting daily life. PROs reveal fatigue or psychological stress, enabling clinicians to provide comprehensive care and personalized medicine, based on patient's specific needs and preferences. Anxiety and depression, which are bidirectionally related, can worsen the severity of IBD, negatively impacting quality of life, with higher prevalence in patients with IBD compared to healthy controls as an evaluation conducted by Mikocka-Walus revealed (19.1% vs. 9.6% for anxiety and 21.2% vs. 13.4% for depression).[2,5,11,19] By tracking these symptoms therapies can be adjusted before clinical deterioration occurs. This proactive approach can prevent complications, enabling interventions and improve long-term outcomes.[1,11]

Also in routine practice, PROs can provide valuable data that may reduce the need for frequent invasive procedures or unnecessary medical visits allowing an individualized approach.[1,12]

The integration of PROs into both clinical trials and routine clinical practice offers significant advantages. In trials, they ensure that patient voices are heard and incorporated into drug development, while in practice, they provide critical insights into disease management and patient QoL.[11,12]

CURRENT OBSTACLES OF PROS IN IBD

PROs must be valid, reliable, and consistent and easy to use for both research and clinical use. However, some are limited by cost, lack of provider education, and questionable validity or reliability. Sometimes their use is limited by their complexity or length. One example is the lengthy IBDQ-32. Efforts to develop shorter versions, like the 13-item IBD-SES, aim to alleviate this burden without sacrificing the tools psychometric properties, but further validation is required to ensure these shorter tools are equally effective as these shorter versions may miss crucial patient experience details.[1,10,13,14]

Another limit is that some patients will find it difficult to self-assess accurately their symptoms if they are dealing with a lot of flare-ups or their going under complex treatment.[1,11,12] PROs rely on how patients interpret their symptoms, so, factors such as personal beliefs, emotional status or pain tolerance may influence this report introducing a certain level of variability and can complicate the results. For example, two patients with similar disease severity will report different levels of pain or fatigue because of their personal perception not due to differences in disease activity. Also, the same patient might report different levels of their symptoms over time due to fluctuations in their energy or mood levels even because of other unrelated stress factors.[1,12,18]

Multiple instruments, such as the Harvey Bradshaw Index (HBI), the Simple Clinical Colitis Activity Index (SCCAI), and the IBD-Control Questionnaire are used to measure different facets of disease activity and patient well-being but some elements of a patient's experience may be improperly evaluated through these indices.[1,3,7]

PROs are often less sensitive to subtle changes in disease activity compared to clinical or endoscopic measures. In clinical trials this can be problematic when trying to capture early or mild improvements in response to therapy. Traditional endpoints such as endoscopic remission or biomarkers like calprotectin may show improvement before patients report feeling better through PROs. This can lead to a mismatch between clinical findings and PROs complicating treatment adjustments.

Another challenge is the overlap of IBD symptoms with conditions like irritable bowel syndrome (IBS) or psychological disorders, making it difficult to differentiate between true disease activity and symptoms related to other conditions. Patients may report high symptom scores on PROs even when their IBD is in endoscopic remission, leading to confusion about the true state of their condition.[20]

Many PROs are now collected through digital platforms or mobile apps, which presents a barrier for certain types of patients, particularly older adults or those with limited access to technology. Despite advancements in using these tools, there remains a need for objective correlations with clinical outcomes like endoscopy findings and biomarkers.[1,3,4,17]

There is no comprehensive routine integration of PRO's into electronic health records (EHR) systems for the moment limiting their utility in real clinical decision making.[4]

Addressing all these limitations will help ensure that PROs can better serve their purpose of providing a comprehensive understanding of disease impact from the patient's perspective in the management of IBD.[11]

FUTURE POTENTIAL OF PROS IN IBD MANAGEMENT

Remote or mobile tools can be used to collect highly subjective PROs outside the clinical setting. Telemedicine

systems have proven useful in disease activity monitoring. Further attempts should be tested, such as allowing patients to complete general well-being at home on request of the attending physician, 24 hours before a medical appointment.[2,3,15,22]

Advances in technology, like web portals and smartphone applications, are revolutionizing clinical practice by enabling rapid data accumulation. The Center for Inflammatory Bowel Disease at University of California Los Angeles (UCLA) developed an IBD scoring system to monitor disease activity. Digital PRO assessment improves patient access to clinics and health literacy, enhancing their QoL.[1,11,22]

Integrating PROs into future IBD management prioritizes patients' most important symptoms, shifting the system to a patient-centered approach. This helps healthcare providers develop personalized treatment strategies, improving patients' QoL by alleviating symptoms like bowel urgency and fatigue, not just to manage inflammation.[3,7,9]

CONCLUSIONS

PRO`s are becoming the basis of tailor-made solutions in the clinical management of IBD patients. Implementation and development of PRO`s is not limited to capturing more precise disease activity, they are also crucial in providing evidence of therapy benefits and in facilitating communication with patients offering an image of their evolution. The development of newer, simpler and validated PRO instruments will allow their routine application in daily practice and will improve the delivery of value-based healthcare and, ultimately, better clinical care of patients.[11,12,18]

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