



Treating the Whole Disease: A Call for Holistic Care for Patients with Inflammatory Bowel Disease

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The disease course of inflammatory bowel diseases (IBD) is unpredictable, with alternating periods of flares and remission [1]. Disease flares occur yearly in half of IBD patients, despite the enlarging therapeutic armamentarium that includes highly targeted biologics and small molecules [1]. Currently, two thirds of patients do not achieve clinical remission [2], and even in clinical remission, patients can experience IBS-like and extraintestinal symptoms, fatigue, depression and anxiety, which negatively impact quality of life (QoL). In order to improve QoL and better predict disease flares, incorporating assessment of psychosocial factors during the diagnostic and therapeutic stages of the illness is essential. Being modifiable, these factors can be targeted by psychological interventions, with consequent improvements in QoL and social functioning.

One important modifiable factor is illness perception [3], which refers to the cognitive and emotional representations patients form about aspects of their illness. According to the common-sense model, illness perceptions influence the way patients cope with their illness, with consequent effects on outcome, medical or otherwise. The impact of illness perceptions on QoL has been demonstrated in many chronic illnesses including Crohn's disease [4, 5]. More importantly, illness perceptions have a greater impact on QoL than do related clinical factors.

In a recent issue of *Digestive Diseases and Sciences*, Okegunna et al. [6] developed an advanced model aimed at predicting flares. Besides clinical characteristics, this model included modifiable lifestyle and psychosocial factors including fatigue, stress, anxiety, depression and life events. A cohort of 429 Dutch patients from both academic

and general hospitals was prospectively followed for almost 2 years. Data with regard to disease activity and psychosocial factors were measured with validated questionnaires on the MyIBDcoach™ remote monitoring platform. Both self-reported questionnaires and objective disease markers (calprotectin and endoscopic findings) were used to define a disease flare. Five G-LASSO models were developed, combining numerous covariates (baseline characteristics, lifestyle, psychosocial). During follow-up, 46% of patients developed a flare. Not surprisingly, stress, depression, anxiety, and pain scores were significantly higher in those who flared than those in remission. The model that included baseline variables and MyIBDcoach™ patient-reported outcomes performed significantly better (accuracy: 71%, ROC-AUC: 77%, sensitivity: 59%, specificity: 91%, PPV: 91%, NPV: 59%) than the model with only baseline variables (accuracy: 63%, ROC-AUC: 65%, sensitivity: 51%, specificity: 81%, PPV: 81%, NPV: 52%).

Using data from a remote monitoring platform and advanced modeling techniques, the authors successfully confirmed a strong relationship between psychosocial factors and disease flares. Obviously, the data need to be validated and important variables such as illness perceptions and coping are lacking. Nevertheless, the results of the present study support the concept of the brain-gut axis. There is convincing evidence that the brain and gut are intrinsically linked by neurological, endocrine and immunological pathways, which can become dysregulated in IBD [7]. Firstly, the brain-gut axis has a bidirectional effect on the prognosis of IBD. People with IBD are at increased risk of depression and anxiety. Furthermore, patients with IBD who also have depression and anxiety have more adverse outcomes, including disease flares, escalation of therapy, hospitalization, emergency department visits and surgery [7]. Secondly, a third of individuals with IBD who are endoscopically in remission suffer from persistent IBS-like symptoms. These patients are more than twice as likely to have depression and anxiety compared to those without IBS-like symptoms [8].

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A mechanistic explanation for the dysregulated brain-gut axis has recently been described by Schneider et al. [9] Using a mouse model of restraint stress and three cohorts of people with IBD, the authors reported the substantial contribution of the enteric nervous system toward enhancing the effect of psychological stress on intestinal inflammation. Elevated levels of glucocorticoids in stressed mice stimulated the generation of an inflammatory subset of enteric glia cells that produced colony-stimulating factor 1 that promoted the production of tumor necrosis factor by monocytes, leading to intestinal inflammation. Furthermore, glucocorticoids caused transcriptional immaturity in enteric neurons, acetylcholine deficiency, and dysmotility via transforming growth factor β 2.

Despite the important influence of lifestyle and psychosocial factors on disease course and QoL, current treatments primarily target inflammation. Access to more immunosuppressive drugs, treat-to-target strategies and top-down therapy has, unfortunately, not substantially improved outcomes. In an attempt to break through the therapeutic ceiling, clinicians now focus on combining novel therapies (termed advanced combination therapy), which thus far has been associated with disappointing results, high rates of adverse effects, and high healthcare costs.

Therefore, we support the implementation of a holistic care model, integrating clinical, psychosocial and lifestyle factors in order to improve clinical outcomes and QoL. A holistic care model provides a framework for a patient-centered and personalized treatment [10]. Care can be effectively delivered by a multidisciplinary team, including gastroenterologists, nurses, psychologists and dieticians, with patient-experts as advisers. Likewise, patients are more actively engaged in their own care and thereby improving their self-management skills and adherence. As shown by Keefer et al. [11] resilience-based integrated care given by a multidisciplinary team reduced emergency department visits, unplanned hospitalizations, and use of opioids and corticosteroids, compared with standard IBD care.

In summary, these promising results show the potential of holistic care to improve clinical outcomes, patient satisfaction and cost-effectiveness.

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Data Availability No datasets were generated or analyzed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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