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INVITED COMMENTARY

Taking IBD Treatment in STRIDE: How Objective Disease Assessment Is Essential for the Successful Implementation of Treat-to-Target Strategies

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The treatment goals for patients with inflammatory bowel disease (IBD) have evolved over time: in the pre-biologics era, the primary focus of patients and medical professionals alike was on achieving rapid symptom regression, avoiding chronic steroid-based therapies, and minimizing the need for surgery. With the introduction of innovative biologic-based therapies, this perspective has significantly broadened—"treat-to-target" strategies have gained prominence in an effort to enhance the short- and long-term outcomes in patients with IBD. To implement this approach, patients are regularly monitored through a "tight control" regimen, utilizing objective inflammatory biomarkers and imaging, which accurately reflect disease activity independently of the patient's subjective perceptions. In 2015, the initial Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) consensus recommended that physicians prioritize achieving endoscopic remission and resolving subclinical inflammation as primary treatment goals in IBD [1]. The updated STRIDE recommendations, known as STRIDE-II (published in 2021), also takes into consideration the restoration and maintenance of the patients' quality of life as a formal treatment goal [2].

In this issue of *Digestive Diseases and Sciences*, Pablo Vega and colleagues conducted a comprehensive real-world study across 14 Spanish IBD centers to assess the frequency of achieving optimized treatment goals according to the STRIDE-II criteria in 396 patients [3]. The study revealed that 53.1% (104/196) of patients with Crohn's disease (CD) and 41.5% (83/200) of patients with ulcerative colitis (UC) did not attain optimal disease control according to STRIDE-II recommendations. These individuals experienced diminished quality of life, increased healthcare resource utilization and direct costs, and loss of work productivity when compared with those who achieved optimal disease control. This is particularly remarkable considering that 72.7% of patients with CD and 40.9% of patients with UC received treatment with targeted immunomodulators (TIM). Apart from the new IL23 antibodies, targeted immunomodulators encompass the full spectrum of biologics and small molecules, such as anti-tumor necrosis factor-α antibodies, interleukin (IL)12/IL23 antibodies, integrin antagonists, selective sphingosine-1-phosphate-receptor-1 modulators, and Janus kinase inhibitors. The authors demonstrate that in this patient population, over half of the patients treated with TIM exhibited suboptimal disease control or failed to respond to treatment, with a concomitant high incidence of steroid overuse in patients with CD and UC.

This study highlights the frequent inadequacy of disease control not only in daily practice but also in patients receiving treatment in specialized centers, where the STRIDE-II criteria are routinely used as a benchmark. Nevertheless, the definition of suboptimal disease control is not solely based on objective 'red flags,' such as the lack of normalization of inflammatory markers like CRP or fecal calprotectin or the absence of improvement as assessed by endoscopic or radiologic imaging. In the Spanish population, fecal calprotectin analyses were conducted in less than half of the patients, and imaging was utilized in < 15% of cases. In over half of the cases where patients exhibited suboptimal disease control, long-term impaired quality of life was the primary reason for this assessment. Using the short IBD questionnaire (SIBDQ) [4], authors documented a diminished quality of life in 55.8% of patients with CD and an even higher percentage, 72.3%, in patients with UC during the initial evaluation. Even though ensuring a satisfactory quality of life is undoubtedly of high importance for individuals with IBD, it is affected by multiple factors, many independent of anti-inflammatory therapy, and its assessment of entirely

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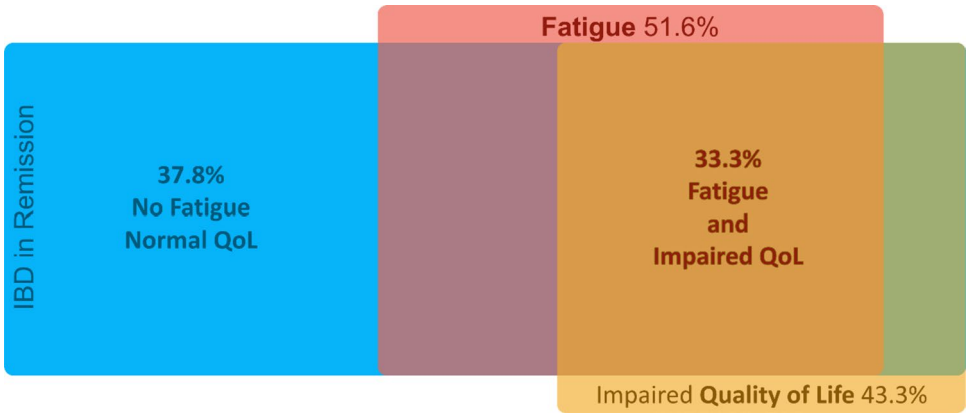

Fig. 1 Prevalence of fatigue and quality of life in patients with IBD in clinical remission. Among those in remission, one-third experience both normal quality of life and are free from fatigue, while two-thirds of patients encounter either fatigue, impaired quality of life, or both simultaneously. $N = 91$, QoL = quality of life. Clinical remission was defined as a partial Mayo Score < 2 for UC and Harvey–Bradshaw Index < 5 for CD. Fatigue was defined as > 21 points on the Fatigue Assessment Scale (FAS) and impaired quality of life was defined as IBDQ-32 Score < 180. Unpublished data, extracted from (5)

subjective. Even in clinical remission, 43% of patients with IBD report impairment of their quality of life, 51% suffer from fatigue, and one-third of the patients endure both simultaneously (Fig. 1). Fatigue is a burdensome and highly prevalent issue, not only in patients with active IBD but also in those with inactive disease [5]. In addition to the targeted treatment of inflammation, considerations for evolving treatment concepts should also encompass fatigue, including the possibility of underlying subclinical depression.

The suboptimal implementation of treat-to-target monitoring in IBD has been documented in other real-world studies as well. A study based on a commercial US database revealed a low colonoscopy rate following the initiation of therapy. In this study, only 40% of patients with CD underwent a colonoscopy 3–15 months after starting treatment with a biologic or immunomodulator, a rate that remained relatively stable over time [6]. Another prospective study, the Prospective Adult Research Cohort with IBD (SPARC IBD), investigated how many patients received a colonoscopy within 3–15 months after commencing advanced therapy. It reported higher proportions, reaching up to 63.2% in individual centers, but as low as 26.6% in others [7].

Why do these gaps in monitoring exist and what can be done to narrow them? The German National guideline for the treatment of Crohn's disease states clearly that after the initiation or alteration of therapy, biochemical markers, such as CRP and/or fecal calprotectin, as well as intestinal sonography should be used in addition to clinical assessment to evaluate the treatment response within the first 3 months. This recommendation was given particular importance by the rating of a Choosing Wisely recommendation [8]. If, as suggested in the STRIDE-II concept, elevated serum or stool biomarkers, verified, if necessary, through endoscopy, are adequate for documenting the extent and severity of the disease and for making substantial treatment changes, then these markers should be monitored after the initiation of a new therapy. Nonetheless, the question remains: why is this approach not consistently put into daily practice? The Vega et al. dataset lacked data regarding physician-level, patient-level, and other factors that may help answer these questions. Patients often do not consider normalization of inflammatory markers and endoscopic findings as their primary treatment goals and often avoid the corresponding assessments, particularly endoscopies [9]. In this context, bedside bowel ultrasound, as a point-of-care examination, can transform the landscape, serving as a serial assessment of treatment response, offering a noninvasive and highly feasible, patient-friendly procedure. Nevertheless, although it remains essential to demonstrate that the consistent implementation of the STRIDE-II concept indeed improves patient outcomes and the achievement of sustainable therapeutic goals, this evidence is currently still pending. Through further research aimed at understanding the reasons behind the practice gaps in monitoring treatment response and subsequent testing of interventions to bridge these gaps, enhanced patient outcomes in IBD and in other areas are possible.

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