Digestive and Liver Disease xxx (xxxx) xxx

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Review Article

Quality of life in patients with moderate to severe ulcerative colitis and the impact of treatment: A narrative review

Alessandro Armuzzi[a,b,*], Giuseppina Liguori[c]

[a] Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo Agostino Gemelli, 8, Rome 00168, Italy
[b] Dipartimento Universitario di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy
[c] Medical Department, Inflammation and Immunology, Pfizer Italy

ARTICLE INFO

Article history:
Received 6 November 2020
Accepted 2 March 2021
Available online xxx

Key words:
Ulcerative colitis
Quality of life
JAK inhibitors
Biological agents

ABSTRACT

As a chronic inflammatory disease, ulcerative colitis has significant negative impact on the quality of life (QoL) of patients. Since the disease affects many aspects of QoL, comprising multiple domains, treatments that induce and maintain remission can provide benefits beyond hard clinical endpoints. Effective treatment of ulcerative colitis can restore QoL and return it to normal or near normal levels. Biological therapies have shown consistent improvement in the QoL of patients with ulcerative colitis during the induction phase, with benefits that are generally maintained in the long-term. Current medical treatment options broadly comprise aminosalicylates, corticosteroids, thiopurines, and calcineurin inhibitors, as well as biologic therapies. Conventional therapies do not always adequately control disease in a sizeable portion of patients, while anti-TNF antibodies are associated with several issues such as contraindications, intolerance, primary non-response, and loss of response in some patients. JAK inhibitors have been associated with clinical improvements in disease manifestations and long-term improvement in QoL outcomes. However, additional studies are needed to better understand the comparative effects of different treatments on QoL and patient preferences for therapy. Herein, the available evidence is reviewed regarding the impact of various treatments on QoL in patients with moderate to severe ulcerative colitis.

© 2021 The Authors. Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l.
This is an open access article under the CC BY-NC-ND license
(http://creativecommons.org/licenses/by-nc-nd/4.0/)

1. Introduction

Ulcerative colitis is a chronic inflammatory disease that affects the colon, with a peak of disease onset at an age between 30 and 40 years [1]. The disease is characterized by a relapsing remitting course and is responsible for considerable disability and high direct and indirect costs [2]. While there does not appear to be any gender-related differences, both the incidence and prevalence are increasing worldwide [3,4].

Ulcerative colitis most commonly presents with bloody stool and diarrhea, as well as with urgency, incontinence, and fatigue [1]. Roughly 1 in 6 patients may present with severe disease in which fever and weight loss can also occur [5]. Diagnosis of ulcerative colitis is based on symptoms, endoscopic findings, histology, and exclusion of possible differential diagnoses and enteric infections [5].

The treatment strategy depends on several factors including disease severity, colonic extension, patient age and comorbidities, duration, and frequency of relapses [1]. In any case, the overarching goal is to induce and maintain clinical and endoscopic remission in the long-term, in order to minimize disability and prevent colectomy or development of colorectal cancer. Indeed, treatment goals have gradually evolved from treatment of symptoms to more stringent outcomes such as maintenance of steroid-free clinical remission, prevention of hospital admission and surgery, and mucosal healing (i.e. endoscopic and histologic remission). Towards this end, therapeutic targets that can affect the natural history of the disease and improve the patient's quality of life (QoL) have been established [6] and are continuously refined according to the most recent evidence [7]. These include more detailed mucosal healing criteria and use of biomarkers such as fecal calprotectin.

In addition to clinical and endoscopic targets, improving the QoL is now recognized as a major and ultimate goal of treatment [6,7].

The current therapeutic armamentarium has been expanding recently. Notwithstanding, many patients do not enter remission

* Corresponding author.
E-mail address: alessandro.armuzzi@unicatt.it (A. Armuzzi).

https://doi.org/10.1016/j.dld.2021.03.002
1590-8658/© 2021 The Authors. Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Please cite this article as: A. Armuzzi and G. Liguori, Quality of life in patients with moderate to severe ulcerative colitis and the impact of treatment: A narrative review, Digestive and Liver Disease, https://doi.org/10.1016/j.dld.2021.03.002

with biologics and about one-third of patients with severe disease still require surgery [8]. It is also relevant that each type of treatment has specific characteristics that influence the choice of therapy by both patients and physicians. Indeed, patients and physicians may not always have the same preferences for treatment of ulcerative colitis, which highlights the need for good and effective communication during the shared decision-making process [9].

The present review will explore the impairments in QoL in patients with moderate to severe ulcerative colitis and how various treatments can improve overall well-being.

2. Main tools for the assessment of QoL in ulcerative colitis

A large number of measures have been used to quantify health-related QoL in ulcerative colitis [10]. These include, but are not limited to, the Inflammatory Bowel Disease Questionnaire (IBDQ), Shortened Inflammatory Bowel Disease Questionnaire (SIBDQ), 9-item IBDQ (IBDQ-9), Rating Form of IBD Patient Concerns (RFIPC), Edinburgh IBD Quality of Life Questionnaire (EIBDQ), IBD disability score, IBD disability index, and Social Impact of Chronic Conditions–Inflammatory Bowel Disease (SICC-IBD) questionnaire [10]. Each of these covers different domains that may include symptoms, social functioning, emotional dysfunction, sexual functioning, disease control, general health, etc. [11]. It has been noted that the majority of HRQoL measures are likely to have problems with methodological quality [10]. Moreover, the large variety of measures used renders comparison difficult. As noted by others, the most widely used tool appears to be the IBDQ [10,11]. However, other tools have also been used to evaluate the quality of life such as the EuroQol-5D-5 L and the IBD-Fatigue scale [12,13]. Among the unmet needs in patients with ulcerative colitis, it has been highlighted that there is a greater consensus is warranted in terms of assessment of QoL [14]. Lastly, it is clear that the choice of one measurement tool over another depends on the information that is being sought after and the particular purpose for which it is being utilized.

3. Impact of ulcerative colitis on quality of life

The gastrointestinal symptoms and fecal incontinence associated with ulcerative colitis have a dramatic impact on patients' QoL, spanning psychological, physical, sexual, and social domains [15-17]. As a result of the poor control of body functions, in contrast to what is dictated by social rules, patients with ulcerative colitis may perceive a certain degree of social stigmatization, which leads to further negative consequences and the desire to separate from group interactions [15,18]. A multicenter European study reported that, compared to the general population, patients with moderate to severe ulcerative colitis have increased morbidity, poorer health-related QoL, and severe impairment of social and professional activities, accompanied by higher percentages of both sick leave and unemployment [12]. A large study in 1326 patients with moderate to severe ulcerative colitis in the US and Europe reported that active disease was significantly associated with impairments in health-related QoL, as well as employment and leisure activities [19]. Among patients with ulcerative colitis, depression and anxiety appear to be the most frequent psychiatric disorders [20], and more than 40% of patients refer the presence of fatigue [21]. Stress and sleeping disorders have also been noted [22]. Interestingly, both psychological and biological mechanisms appear to be responsible for psychiatric comorbidities. Indeed, a range of complex interactions including alterations in the brain gut-axis and immunological aberrations have been hypothesized to be involved [20]. Since patients with active disease refer significantly more disease-related symptoms, this can lead to an altered perception of their illness. This was shown in a prospective cohort study from Italy in patients with IBD, where ≥80% of active patients referred greater fatigue and difficulty in sleeping, loss of strength, and pain [23]. In any case, patients' perception of their functional disability, and not necessarily their clinical disease activity, appears to be related to greater symptoms of anxiety and depression [20]. This is an important aspect to consider, and highlights that psychological comorbidities can affect the course of the disease [20]. It has been further postulated that the decreased QoL observed in moderate to severe ulcerative colitis may well relate to disruption of routine activities, given the impact of the disease on multiple domains, as mentioned above [24]. Poorer social and interpersonal functioning, self-perception, and self-esteem are likely to be associated with IBD-related complications. These include factors such as chronic changes in bowel function, surgical scars, and ostomy, which can adversely impact QoL.

In younger individuals, QoL aspects are also particularly relevant. This was shown in study on 262 patients with inflammatory bowel disease aged 10–20 years, 115 of whom had ulcerative colitis [25]. In the entire group of patients, the negative perceptions of illness and associated depression strongly correlated with lower health-related QoL compared to either demographic or disease-related factors. In addition, in the group of patients with ulcerative colitis, greater anxiety was also significantly associated with lower health-related QoL. This stresses the need to look beyond disease severity and place greater focus on the patient's perception of functional disability [26].

A number of studies have demonstrated that ulcerative colitis has a major impact on sexual QoL in both men and women [27]. In both genders, depression has been linked to greater impairment of sexual QoL [28]. In men, active disease, aggravated by the inability to control smoking, drinking, and eating habits has been linked to both sexual dysfunction and infertility [29]. Moreover, it has been reported that patients with inflammatory bowel disease (IBD) have fewer children compared to the general population, which may be related to alterations in fertility due psychological issues [30]. Unexpectedly, active disease has been associated with greater problems in sexual functioning [31]. The negative impact of IBD on sexual health was further highlighted by a Spanish Working Group which recommended that in managing patients with IBD, its burden should be actively explored [32].

Body image dissatisfaction is common in patients with IBD, and has been associated with disease activity and treatment with steroids [33]. In addition to anxiety and depression, body image dissatisfaction is also associated with lower QoL, self-esteem and sexual satisfaction, leading to substantial psychological impairment [33]. As such, it has been recommended that evaluation of body image dissatisfaction be part of comprehensive assessment since illness perceptions are strongly associated with QoL [34]. Indeed, since patients with active ulcerative colitis experience clinically meaningful burden of disease across most QoL domains, a comprehensive framework has been advocated for disease management that extends to cognitive, emotional, and behavioral factors, in addition to medical and psychological care [35].

4. The importance of treatment in restoring quality of life

A prospective observational study in 115 patients with IBD found that clinical remission normalized the health-related QoL in 82% of patients with ulcerative colitis, which importantly, was not related to the type of treatment [36]. In fact, while patients with active ulcerative colitis have significant burden of disease across most QoL domains, those with inactive disease have negligible disease burden that is comparable to the general population [37]. Accordingly, a systematic literature review concluded that treatments which induce and maintain remission reestablish both physical and mental health status [37]. Indeed, a recent cross-sectional study

of 201 patients with ulcerative colitis found that impaired disability was mainly related to disease activity (odds ratio 6.54, 95% CI 3.21–13.22) as well as the presence of extraintestinal manifestations OR 2.48, 95%, CI 1.11–5.54), and limited alcohol consumption (OR 0.39, 95% CI 0.20–0.76) [38]. Work overload has also been perceived as the cause of the disease more frequently in active patients compared to patients in remission [23].

The ECCO-EpiCom study on 1560 patients with IBD reported that both medical and surgical treatment improved health-related QoL during the first year of disease based on increases in SIBDQ scores (in Western Europe from 48.8 to 55.7) [39]. However, while biological therapy improved QoL in patients with Crohn's disease, patients with ulcerative colitis who needed surgery or biological therapy had lower perceptions of health-related QoL. This indicates that there are shortcomings to current therapies. Indeed, a significant fraction of patients do not achieve substantial improvement in QoL, which emphasizes the need for complete restoration of health and the need for global care [6,36]. Moreover, many patients still experience symptoms at least once weekly, even when in remission [40]. Accordingly, treatments that effectively induce and maintain remission are needed since the benefits of treatment of ulcerative colitis extend well beyond hard clinical endpoints [6,41]. To achieve this comprehensive objective, a multidisciplinary approach and collaboration between primary and secondary care has been advocated [42].

As with any disease, patient preferences for treatment should also be considered as part of any overall management plan. A Danish survey found that the most important attribute of medical treatments was effectiveness within 8 weeks [43]. In that analysis, in addition to the desire for fast onset of action, respondents also preferred that they wanted to avoid taking steroids and favored oral formulations. Moreover, about half of patients managed with conventional treatments refer that they are dissatisfied with their treatment, and that effectiveness and rapidity of onset were the most highly appreciated attributes [44].

5. Biological therapies and quality of life

Several reviews and meta-analyses concluded that biologics have the potential to improve health-related QoL in patients with ulcerative colitis [45-47]. Indeed, there is now good evidence demonstrating that treatment with biological agents will lead to meaningful benefits on QoL. A systematic review and meta-analysis concluded that induction treatment with infliximab, adalimumab, golimumab, or vedolizumab increases the QoL vs placebo, although there is less evidence for the effectiveness of these agents as maintenance therapy [46]. The main trials on biologics and QoL discussed below are summarized in Table 1.

A recent study analyzed clinical outcomes and health-related QoL in 463 patients with moderate to severe ulcerative colitis in daily practice treated with adalimumab [48]. At 26 weeks, in addition to benefits on clinical outcomes, significant improvement was seen in the European Quality of Life-5 Dimensions-5 Level, various measures of work productivity, and ability to perform daily activities.

Two trials have assessed the effects of infliximab on QoL. In 2007, Feagan et al. analyzed pooled data from the ACT 1 and 2 studies on 728 patients with moderate to severe ulcerative colitis [49]. After 8 weeks of treatment with infliximab, significant improvements compared to placebo were seen in the physical (PCS) and mental component summaries (MCS) of the Medical Outcomes Study 36-Item Short Form Health Survey, and continued benefit was seen through week 54 [for infliximab 5 and 10 mg: PCS 6.8 and 5.9, respectively, MCS 5.9 and 6.4, respectively, placebo PCS 3.7, MCS 3.0; $P < 0.01$ for all comparisons). In 2019, Gheorghe published the results of a small real-life study on biosimilar infliximab in 85 patients with IBD [50]. After 30 weeks of therapy, of the 47 patients with ulcerative colitis, 55.3% showed a clinical response and 48.9% were in remission. In the pooled population, significant improvement in the Short Inflammatory Bowel Disease Questionnaire was reported.

Two other trials have assessed the effects of treatment with an anti-TNFα agent (infliximab or adalimumab) on QoL. In the small observational trial by Casellas et al. on 54 patients with IBD (11 with ulcerative colitis), after one year, restoration of health to normal as measured by the IBDQ-36 questionnaire was seen in most patients, which was significantly more frequent in ulcerative colitis (all patients) vs. Crohn's disease (67%) [51]. Meijs et al. compared the effectiveness of therapy with infliximab or adalimumab ($n = 29$) to surgery (restorative proctocolectomy with ileal pouch-anal anastomosis; $n = 29$) [52]. There were no significant differences in multiple measures of health-related QoL or disability, with the exception of stool frequency and anti-diarrhea medication use which was significantly higher in patients treated with surgery. Thus, treatment with infliximab or adalimumab appears to be at least as effective as surgery in improving patient's QoL.

A Phase 4 open label, single arm study has examined the effectiveness of golimumab in 205 patients with moderate to severe ulcerative colitis [53]. At the end of the induction phase, 140 patients achieved clinical response and continued into the maintenance phase. Significant improvements were observed from baseline to week 6 for the Inflammatory Bowel Disease Questionnaire (IBDQ) total score and in each of the IBDQ subdomains (bowel symptoms, emotional function, systemic symptoms and social function). Significant improvement was also seen in the EuroQol Group 5 Dimensions Health Questionnaire score. Of note, these improvement in health-related QoL were maintained up to week 54.

Feagan et al. analyzed maintenance phase data from a randomized study to examine the benefits of vedolizumab on health-related QoL [54]. Data were available for 126 patients randomized to placebo, for 122 patients randomized to vedolizumab every 8 weeks and for 125 patients receiving vedolizumab every 4 weeks. Compared with placebo-treated patients, at week 52, vedolizumab-treated patients had greater improvements (152–201%) in IBDQ, and EQ-5D visual analogue scale and utility scores. Of interest, the improvements in QoL were greater in patients who had lower disease activity at baseline and no prior failure of anti-TNFα agent.

Sands et al. assessed the effects of ustekinumab as 8-week induction therapy and 44-week maintenance therapy in 961 patients with moderate-to-severe ulcerative colitis, measuring changes in IBDQ to evaluate quality of life [55]. Through week 8, the authors reported that median changes from baseline in IBDQ score significantly greater in both ustekinumab induction dose groups (130 mg or a weight-range–based dose that approximated 6 mg/kg body weight) vs. placebo.

Thus, considering the limited evidence, treatment with biological agents appears to be associated with meaningful and benefits on QoL in patients with ulcerative colitis receiving maintenance therapy [45,46].

6. JAK inhibitors and quality of life in ulcerative colitis

Janus kinase (JAK) inhibitors have been a significant addition to the treatment options available for moderate to severe ulcerative colitis. JAK inhibitors reduce the activity of one or more of the JAK enzymes (JAK1, JAK2, JAK3, TYK2), thereby interfering with the JAK-STAT signaling pathway thus the activity of many inflammatory cytokines [56]. Several JAK inhibitors are under investigation in moderate to severe ulcerative colitis, including filgotinib, upadacitinib, and peficitinib [56]. To date, however, tofacitinib is the only JAK inhibitor that has been approved by Food and Drug Administration (FDA) and the European Medicines Agency (EMA)

Table 1
Main trials investigating effects of biologics on health-related quality of life in patients with ulcerative colitis.

Author, year	Interventions	No. patients	Time of assessment of QoL outcomes	QoL outcomes
Travis, 2017 [40]	Adalimumab 40 mg EOW	463	26 weeks	Significant improvements from baseline in SIBDQ, EQ-5D-5 L, and VAS. Parallel improvements in work productivity [11% absolute decrease in absenteeism; 25% absolute decrease in impairment while working; and 27% absolute decrease in impairment of ability to perform daily activities].
Feagan, 2007 [41]	Infliximab 10 mg/kg Infliximab 5 mg/kg Placebo	242 242 244	8–54 weeks	Improvement in total IBDQ score significantly greater in the both infliximab groups vs. placebo at 8 weeks. Improvement significantly greater in both infliximab groups for PCS and MCS vs. placebo at 8 weeks. Continued benefit was seen at weeks 30 and 54 with infliximab maintenance therapy.
Gheorghe, 2019 [42]	Infliximab biosimilar (mean dose 5.0 ± 0.6 mg/kg)	47	30 weeks	SIBDQ was significantly improved from baseline to end of treatment
Casellas, 2012 [43]	Adalimumab 40 mg Infliximab 5 mg/kg	4 7	1 year	Normalization of HR-QoL achieved in all 11 UC patients
Meijs, 2014 [44]	Surgery Infliximab or adalimumab	30 30	1 year	No significant differences in multiple measures of HR-QoL or disability, except for stool frequency and anti-diarrhea medication use which was significantly higher in patients treated with surgery
Probert, 2018 [45]	Golimumab 50 or 100 mg Q4W	205	54 weeks	Significant improvements from baseline to week 6 were observed for IBDQ total score and each IBDQ domain score (bowel symptoms, emotional function, systemic symptoms and social function), as well as the EQ-5D index score and associated visual analogue scale score. Improvement of HR-QoL was sustained through week 54.
Feagan, 2017 [46]	Vedolizumab 300 mg Q8W Vedolizumab 300 mg Q8W Placebo	122 125 126		Vedolizumab-treated patients had greater improvements in IBDQ, EQ-5D VAS, and EQ-5D utility scores vs. placebo.
Sands, 2019 [47]	Ustekinumab 130 mg Ustekinumab ≅ 6 mg/kg Placebo	320 322 319	52 weeks	Through week 8, median changes from baseline in IBDQ were significantly greater in both ustekinumab groups vs. placebo.

PCS/MCS, Physical and Mental Component Summaries; IBDQ, Inflammatory Bowel Disease Questionnaire; SIBDQ, short IBDQ.

Table 2
Main trials investigating effects of JAK inhibitors on health-related quality of life in patients with ulcerative colitis.

Author, year	Interventions	No. patients	Time of assessment of QoL outcomes	QoL outcomes
Sands, 2018 [49]	Peficitinib (25 mg QD, 75 mg QD, 150 mg QD, 75 mg BID) Placebo	176 43	8 weeks	Proportion of patients with *a* >20-point increase in IBDQ score from baseline was numerically greater for peficitinib ≥75 mg QD vs. placebo
Panes, 2015 [50]	Tofacitinib (0.5 mg, 3 mg, 10 mg, or 15 mg BID) Placebo	146 48	8 weeks	Improvement from baseline was significantly greater ($P = 0.001$) for tofacitinib 15 mg BID versus placebo. For tofacitinib 15 mg BID, most patients reported satisfaction or extreme satisfaction, definite preference for tofacitinib, and definite willingness to use tofacitinib again
Panes, 2018 [51] OCTAVE Induction 1	Tofacitinib 10 mg BID Placebo	476 122	8 weeks	In OCTAVE Induction 1 and 2, mean changes from baseline IBDQ were significantly greater with tofacitinib 10 mg BID versus placebo; mean changes from baseline SF-36v2 PCS/MCS were also greater with 10 mg BID versus placebo.
Panes, 2018 [51] OCTAVE Induction 2	Tofacitinib 10 mg BID Placebo	429 112	8 weeks	
Panes, 2018 [51] OCTAVE Sustain	Tofacitinib 10 mg BID Tofacitinib 5 mg BID Placebo	197 198 198	52 weeks	Changes in IBDQ were maintained with both doses of tofacitinib. Changes in SF-36v2 PCS/MCS were maintained with 5 mg and 10 mg BID.

PCS/MCS, Physical and Mental Component Summaries; IBDQ, Inflammatory Bowel Disease Questionnaire.

for treatment of moderate to severe ulcerative colitis. A small number of trials have investigated the effects of JAK inhibitors on QoL in patients with ulcerative colitis (Table 2).

Sands et al. evaluated changes in the IBDQ following treatment with peficitinib in a Phase 2B trial in 219 patients [57]. It was found that the proportion of patients with *a* >20-point increase in the IBDQ score from baseline at Week 8 was numerically greater for patients receiving peficitinib ≥75 mg qd compared to placebo (18 vs. 22–25), which was the dose at which numerically greater increases in clinical response were observed.

Considering patient-reported outcomes with tofacitinib, Panes et al. carried out an analysis on 195 patients randomized to tofacitinib or placebo [58]. After 8 weeks, compared to placebo, patients receiving tofacitinib reported significant and dose-dependent improvement in both the IBDQ and the Inflammatory Bowel Disease Patient-Reported Treatment Impact (IBD PRTI) survey (baseline range 123.2–134.5; Week 8 range 149.6–175.4). Moreover, most patients reported satisfaction or extreme satisfaction, together with a definite preference for tofacitinib and a definite willingness to use it again.

The changes in QoL in patients with moderate to severe colitis receiving tofacitinib during the induction and maintenance phases has also been reported using data from the randomized, placebo-controlled OCTAVE trials [59]. Significant improvement in the IBDQ [OCTAVE 1 and OCTAVE 2, respectively; tofacitinib 28.9 and 31.5; placebo [15.4 and 17.2; $p < 0.0001$]; and SF-36v2® Health Survey [OCTAVE 1 and OCTAVE 2, respectively; tofacitinib: PCS 6.8 and 6.8; MCS 6.8 and 7.6; placebo: PCS 2.5 and 4.6; MCS 3.5 and 4.4; $p<0.01$]. was seen after 8 weeks of induction therapy that was maintained throughout 52 weeks of maintenance therapy (tofacitinib 5 mg [−1.3] and 10 mg BID [0.6], placebo [−20.2; $p < 0.0001$]. Onset of action is an important consideration for patients.

Lastly, a Confidence in Network Meta-Analysis assessed the impact of medical therapies (infliximab, adalimumab, golimumab, vedolizumab or tofacitinib) on health-related QoL in 14 randomized trials in patients with moderate to severe colitis [46]. The study concluded that there was good evidence to suggest that induction treatment with infliximab, adalimumab, golimumab, vedolizumab, or tofacitinib improves QoL vs. placebo. Data on maintenance therapy and QoL are scarce and available only for adalimumab, vedolizumab, and tofacitinib, showing sustained benefits. This study has several limitations due to the heterogeneity of trials and further studies on QoL are needed.

Conclusions

There are several unmet needs in the treatment of ulcerative colitis. Conventional therapies often result in treatment failure or unacceptable side effects, and despite treatment roughly one-half of patients still have ongoing disease activity [44,60]. Even if a large number of therapeutic options are now available, concerns about long-term efficacy and safety, which have the potential to impact the patient's QoL, still remain [14]. Moreover, even in many patients who are asymptomatic, health-related QoL may still not be restored to normal, which suggests that disease burden is still present [51]. Lastly, total proctocolectomy is still needed in around 15% of patients since they are refractory to medical therapy or develop complications [61]. Thus, new therapeutic opportunities are greatly needed in moderate-to-severe ulcerative colitis.

The availability of biologics has provided the possibility to optimize the overall management of moderate to severe ulcerative colitis, with lower rates of surgery and better clinical and patient-reported outcomes in the long term [62]. Notwithstanding, many patients continue to experience a sizeable number of symptoms with disease-related physical and psychological burden [63]. QoL issues are crucial to the management of patients as is evident from a review of the literature. There is increasing recognition that patient preferences for treatment when establishing the optimal therapy, and can also affect adherence to a prescribed treatment [64,65]. Patients with moderate to severe ulcerative colitis now have an increasing number of therapeutic choices, and patient preference is increasingly recognized to play a major role in patient care [64]. Assessment of quality of life is an important aspect, since its improvement is a foremost aim of therapy.

While it is clear that moderate to severe ulcerative colitis has significant impact on QoL those who suffer from it, covering all health-related domains, QoL in these patients and the benefits that treatment can have on it have not been widely studied [14,47]. While out of scope of the present review, it is noted that there is also the need for consensus regarding assessment of QoL, fatigue, psychological symptoms, social problems, and disability [14].

From review of the literature, it is clear that effective treatment of moderate-to-severe ulcerative colitis can restore QoL and return it to normal or near normal levels [45,47]. This has been further indicated by the recent STRIDE-II survey, which confirmed that meeting therapeutic goals with a treat-to-target strategy can restore QoL [7]. Biological therapies have shown improvement in the QoL of patients with ulcerative colitis during the induction phase, with benefits that are maintained during maintenance treatment [45,47]. Studies have indicated that small molecules are also associated with clinical improvements in disease manifestations as well as long-term improvement in QoL measures [57-59, 66]. With these aspects in mind, it should be stressed that relevant attributes spanning three domains (efficacy, complications and risk, and health-related QoL) have been identified that can aid prescribers in making shared decisions regarding therapy [41]. Newer therapies, including biological agents and JAK inhibitors, have made a definite contribution to overall management and are associated not only with clinical benefits, but benefits on the patient's QoL as well.

Declaration of Competing Interest

The authors declare they have no conflicts of interest related to this work. Giuseppina Liguori is a Pfizer employee.

Acknowledgements

None.

Disclosures

Alessandro Armuzzi received an honorarium from Pfizer in connection with the development of this manuscript. Medical writing and editorial support was provided by Patrick Moore on behalf of Health Publishing & Services Srl. and was funded by Pfizer.

Compliance with ethical standards

This is a review article for which ethical approval was not required.

References

[1] Ungaro R, Mehandru S, Allen PB, et al. Ulcerative colitis. Lancet 2017;389:1756–70.
[2] Cohen RD, Yu AP, Wu EQ, et al. Systematic review: the costs of ulcerative colitis in Western countries. Aliment Pharmacol Ther 2010;31:693–707.
[3] da Silva BC, Lyra AC, Rocha R, et al. Epidemiology, demographic characteristics and prognostic predictors of ulcerative colitis. World J Gastroenterol 2014;20:9458–67.
[4] Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012;142:46–54. e42.
[5] Dignass A, Eliakim R, Magro F, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. J Crohns Colitis 2012;6:965–90.
[6] Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): determining Therapeutic Goals for Treat-to-Target. Am J Gastroenterol 2015;110:1324–38.
[7] Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the international organization for the study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterology 2020 Dec 21 S0016-5085(20)35572-4. doi:10.1053/j.gastro.2020.12.031.
[8] Rubin DT, Dubinsky MC, Martino S, et al. Communication between physicians and patients with ulcerative colitis: reflections and insights from a qualitative study of in-office patient-physician visits. Inflamm Bowel Dis 2017;23:494–501.
[9] Kariburyo MF, Xie L, Teeple A, et al. Predicting pre-emptive discussions of biologic treatment: results from an openness and preference survey of inflammatory bowel disease patients and their prescribers. Adv Ther 2017;34:1398–410.
[10] Alrubaiy L, Rikaby I, Dodds P, et al. Systematic review of health-related quality of life measures for inflammatory bowel disease. J Crohns Colitis 2015;9:284–92.
[11] Chen XL, Zhong LH, Wen Y, et al. Inflammatory bowel disease-specific health-related quality of life instruments: a systematic review of measurement properties. Health Qual Life Outcomes 2017;15:177.
[12] Van Assche G, Peyrin-Biroulet L, Sturm A, et al. Burden of disease and patient-reported outcomes in patients with moderate to severe ulcerative colitis in the last 12 months - Multicenter European cohort study. Dig Liver Dis 2016;48:592–600.

[13] Varbobitis I, Kokkotis G, Gizis M, et al. The IBD-F patient self-assessment scale accurately depicts the level of fatigue and predicts a negative effect on the quality of life of patients with IBD in clinical remission. Inflamm Bowel Dis 2020.
[14] Daperno M, Armuzzi A, Danese S, et al. Unmet medical needs in the management of ulcerative colitis: results of an Italian delphi consensus. Gastroenterol Res Pract 2019;2019:3108025.
[15] Lenti MV, Cococcia S, Ghorayeb J, et al. Stigmatisation and resilience in inflammatory bowel disease. Intern Emerg Med 2020;15:211–23.
[16] Subasinghe D, Navarathna NM, Samarasekera DN. Faecal incontinence and health related quality of life in inflammatory bowel disease patients: findings from a tertiary care center in South Asia. World J Gastrointest Pharmacol Ther 2016;7:447–52.
[17] Ueno F, Nakayama Y, Hagiwara E, et al. Impact of inflammatory bowel disease on Japanese patients' quality of life: results of a patient questionnaire survey. J Gastroenterol 2017;52:555–67.
[18] Dibley L, Norton C, Whitehead E. The experience of stigma in inflammatory bowel disease: an interpretive (hermeneutic) phenomenological study. J Adv Nurs 2018;74:838–51.
[19] Armuzzi A, Tarallo M, Lucas J, et al. The association between disease activity and patient-reported outcomes in patients with moderate-to-severe ulcerative colitis in the United States and Europe. BMC Gastroenterol 2020;20:18.
[20] Nowakowski J, Chrobak AA, Dudek D. Psychiatric illnesses in inflammatory bowel diseases - psychiatric comorbidity and biological underpinnings. Psychiatr Pol 2016;50:1157–66.
[21] Chavarria C, Casanova MJ, Chaparro M, et al. Prevalence and factors associated with fatigue in patients with inflammatory bowel disease: a multicentre study. J Crohns Colitis 2019;13:996–1002.
[22] Liu R, Tang A, Wang X, et al. Assessment of quality of life in Chinese patients with inflammatory bowel disease and their caregivers. Inflamm Bowel Dis 2018;24:2039–47.
[23] Vegni E, Gilardi D, Bonovas S, et al. Illness perception in inflammatory bowel disease patients is different between patients with active disease or in remission: a prospective cohort study. J Crohns Colitis 2019;13:417–23.
[24] Knowles SR, Graff LA, Wilding H, et al. Quality of life in inflammatory bowel disease: a systematic review and meta-analyses-part I. Inflamm Bowel Dis 2018;24:742–51.
[25] Stapersma L, van den Brink G, van der Ende J, et al. Illness perceptions and depression are associated with health-related quality of life in youth with inflammatory bowel disease. Int J Behav Med 2019;26:415–26.
[26] Walter JG, Kahn SA, Noe JD, et al. Feeling fine: anxiety and depressive symptoms in youth with established IBD. Inflamm Bowel Dis 2016;22:402–8.
[27] Mantzouranis G, Fafliora E, Glanztounis G, et al. Inflammatory bowel disease and sexual function in male and female patients: an update on evidence in the past ten years. J Crohns Colitis 2015;9:1160–8.
[28] Roseira J, Magro F, Fernandes S, et al. Sexual quality of life in inflammatory bowel disease: a multicenter, national-level study. Inflamm Bowel Dis 2020;26:746–55.
[29] Park YE, Kim TO. Sexual dysfunction and fertility problems in men with inflammatory bowel disease. World J Mens Health 2020;38:285–97.
[30] Leenhardt R, Riviere P, Papazian P, et al. Sexual health and fertility for individuals with inflammatory bowel disease. World J Gastroenterol 2019;25:5423–33.
[31] Ates Bulut E, Toruner M. The influence of disease type and activity to sexual life and health quality in inflammatory bowel disease. Turk J Gastroenterol 2019;30:33–9.
[32] Barreiro-de Acosta M, Marin-Jimenez I, Panadero A, et al. Recommendations of the Spanish working group on crohn's disease and ulcerative colitis (GETECCU) and the association of Crohn's disease and ulcerative colitis patients (ACCU) in the management of psychological problems in inflammatory bowel disease patients. Gastroenterol Hepatol 2018;41:118–27.
[33] McDermott E, Mullen G, Moloney J, et al. Body image dissatisfaction: clinical features, and psychosocial disability in inflammatory bowel disease. Inflamm Bowel Dis 2015;21:353–60.
[34] Rochelle TL, Fidler H. The importance of illness perceptions, quality of life and psychological status in patients with ulcerative colitis and Crohn's disease. J Health Psychol 2013;18:972–83.
[35] Kiebles JL, Doerfler B, Keefer L. Preliminary evidence supporting a framework of psychological adjustment to inflammatory bowel disease. Inflamm Bowel Dis 2010;16:1685–95.
[36] Casellas F, Barreiro de Acosta M, Iglesias M, et al. Mucosal healing restores normal health and quality of life in patients with inflammatory bowel disease. Eur J Gastroenterol Hepatol 2012;24:762–9.
[37] Yarlas A, Rubin DT, Panes J, et al. Burden of ulcerative colitis on functioning and well-being: a systematic literature review of the SF-36(R) health survey. J Crohns Colitis 2018;12:600–9.
[38] Marinelli C, Zingone F, Inferrera M, et al. Factors associated with disability in patients with ulcerative colitis: a cross-sectional study. J Dig Dis 2020;21:81–7.
[39] Burisch J, Weimers P, Pedersen N, et al. Health-related quality of life improves during one year of medical and surgical treatment in a European population-based inception cohort of patients with inflammatory bowel disease–an ECCO-EpiCom study. J Crohns Colitis 2014;8:1030–42.
[40] Lonnfors S, Vermeire S, Greco M, et al. IBD and health-related quality of life – discovering the true impact. J Crohns Colitis 2014;8:1281–6.
[41] Louis E, Ramos-Goni JM, Cuervo J, et al. A Qualitative research for defining meaningful attributes for the treatment of inflammatory bowel disease from the patient perspective. Patient 2020.
[42] Lamb CA, Kennedy NA, Raine T, et al. British society of gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68:s1–s106.
[43] Hagelund LM, Elkjaer Stallknecht S, Jensen HH. Quality of life and patient preferences among Danish patients with ulcerative colitis - results from a survey study. Curr Med Res Opin 2020:1–9.
[44] Peyrin-Biroulet L, Van Assche G, Sturm A, et al. Treatment satisfaction, preferences and perception gaps between patients and physicians in the ulcerative colitis CARES study: a real world-based study. Dig Liver Dis 2016;48:601–7.
[45] LeBlanc K, Mosli MH, Parker CE, et al. The impact of biological interventions for ulcerative colitis on health-related quality of life. Cochrane Database Syst Rev 2015:CD008655.
[46] Paschos P, Katsoula A, Salanti G, et al. Systematic review with network meta-analysis: the impact of medical interventions for moderate-to-severe ulcerative colitis on health-related quality of life. Aliment Pharmacol Ther 2018;48:1174–85.
[47] Whitehead L. The impact of biological interventions for ulcerative colitis on health-related quality of life. Am J Nurs 2016;116:21.
[48] Travis S, Feagan BG, Peyrin-Biroulet L, et al. Effect of adalimumab on clinical outcomes and health-related quality of life among patients with ulcerative colitis in a clinical practice setting: results from InspirADA. J Crohns Colitis 2017;11:1317–25.
[49] Feagan BG, Reinisch W, Rutgeerts P, et al. The effects of infliximab therapy on health-related quality of life in ulcerative colitis patients. Am J Gastroenterol 2007;102:794–802.
[50] Gheorghe C, Svoboda P, Mateescu B. Effectiveness and safety of biosimilar infliximab (CT-P13) in a real-life setting in patients with Crohn's disease or ulcerative colitis. J Drug Assess 2019;8:129–34.
[51] Casellas F, Robles V, Borruel N, et al. Restoration of quality of life of patients with inflammatory bowel disease after one year with antiTNFalpha treatment. J Crohns Colitis 2012;6:881–6.
[52] Meijs S, Gardenbroek TJ, Sprangers MA, et al. Health-related quality of life and disability in patients with ulcerative colitis and proctocolectomy with ileoanal pouch versus treatment with anti-TNF agents. J Crohns Colitis 2014;8:686–92.
[53] Probert CS, Sebastian S, Gaya DR, et al. Golimumab induction and maintenance for moderate to severe ulcerative colitis: results from GO-COLITIS (Golimumab: a Phase 4, UK, open label, single arm study on its utilization and impact in ulcerative Colitis). BMJ Open Gastroenterol 2018;5:e000212.
[54] Feagan BG, Patel H, Colombel JF, et al. Effects of vedolizumab on health-related quality of life in patients with ulcerative colitis: results from the randomised GEMINI 1 trial. Aliment Pharmacol Ther 2017;45:264–75.
[55] Sands BE, Sandborn WJ, Panaccione R, et al. Ustekinumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med 2019;381:1201–14.
[56] Troncone E, Marafini I, Del Vecchio Blanco G, et al. Novel therapeutic options for people with ulcerative colitis: an update on recent developments with janus kinase (JAK) inhibitors. Clin Exp Gastroenterol 2020;13:131–9.
[57] Sands BE, Sandborn WJ, Feagan BG, et al. Peficitinib, an oral janus kinase inhibitor, in moderate-to-severe ulcerative colitis: results from a randomised, phase 2 study. J Crohns Colitis 2018;12:1158–69.
[58] Panes J, Su C, Bushmakin AG, et al. Randomized trial of tofacitinib in active ulcerative colitis: analysis of efficacy based on patient-reported outcomes. BMC Gastroenterol 2015;15:14.
[59] Panes J, Vermeire S, Lindsay JO, et al. Tofacitinib in patients with ulcerative colitis: health-related quality of life in phase 3 randomised controlled induction and maintenance studies. J Crohns Colitis 2018;12:145–56.
[60] Varyani F, Argyriou K, Phillips F, et al. Profile of tofacitinib in the treatment of ulcerative colitis: an evidence-based review of recent data. Drug Des Devel Ther. 2019;13:4091–105.
[61] D'Amico F, Parigi TL, Fiorino G, et al. Tofacitinib in the treatment of ulcerative colitis: efficacy and safety from clinical trials to real-world experience. Therap Adv Gastroenterol 2019;12:1756284819848631.
[62] Weisshof R, El Jurdi K, Zmeter N, et al. Emerging therapies for inflammatory bowel disease. Adv Ther 2018;35:1746–62.
[63] Farrell D, McCarthy G, Savage E. Self-reported symptom burden in individuals with inflammatory bowel disease. J Crohns Colitis 2016;10:315–22.
[64] Bewtra M, Johnson FR. Assessing patient preferences for treatment options and process of care in inflammatory bowel disease: a critical review of quantitative data. Patient 2013;6:241–55.
[65] Hodgkins P, Swinburn P, Solomon D, et al. Patient preferences for first-line oral treatment for mild-to-moderate ulcerative colitis: a discrete-choice experiment. Patient 2012;5:33–44.
[66] Lohan C, Diamantopoulos A, LeReun C, et al. Tofacitinib for the treatment of moderately to severely active ulcerative colitis: a systematic review, network meta-analysis and economic evaluation. BMJ Open Gastroenterol 2019;6:e000302.