Quality of life in patients with IBD during the COVID-19 pandemic in the Netherlands

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ABSTRACT

Objective COVID-19 has put a strain on regular healthcare worldwide. For inflammatory bowel disease (IBD), gastrointestinal surgeries were postponed and changes in treatment and diagnostic procedures were made. As abrupt changes in treatment regimens may result in an increased morbidity and consequence well-being of patients with IBD, the aim of this study was to determine the effect of the COVID-19 pandemic on health-related quality of life (HRQoL) in patients with IBD.

Design All patients with IBD who completed both Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-Item Short Form Health Survey (SF-36) questionnaire between 31 August and 13 September 2020 were included in our cohort study. The primary end point was to determine the HRQoL in patients with IBD, measured by the IBDQ and SF-36 questionnaire. The secondary end point was determining which factors influence the HRQoL in patients with IBD.

Results 582 patients with IBD filled in the IBDQ and SF-36 questionnaire. The HRQoL in our study population was low according to the questionnaires on both physical and mental subscales. In addition, multivariate analysis showed that increased age, female sex and patients who underwent surgery had a significantly lower HRQoL, most frequently on the physical domains in both questionnaires. Conclusion Patients with IBD had an overall low HRQoL during the COVID-19 pandemic. Furthermore, older patients, women and patients who underwent surgical procedures had the lowest physical HRQoL.

INTRODUCTION

The first wave of the COVID-19 pandemic has led to an increase in patients with COVID-19 requiring hospital healthcare. This influx called for measures to limit the impact of the virus on the healthcare system by prioritising care. As a consequence, only (semi)acute procedures, typically those involving oncological, acute gastrointestinal, vascular and trauma surgery, were able to be continued.1-3 This meant that many types of elective surgical procedures, including gastrointestinal surgery due to inflammatory bowel disease (IBD), were postponed. In addition,
changes in medical treatment and diagnostic procedures for patients with IBD were made.\textsuperscript{4-10} Therefore, non-urgent care, including treatment of patients with IBD, has a lower healthcare priority. Furthermore, basic measures were taken in the Netherlands to reduce the spread of COVID-19, including the advice to stay at home if possible and to limit the number of social contacts.\textsuperscript{11}

IBD is a chronic and multifactorial disease comprising ulcerative colitis (UC) and Crohn’s disease (CD) and has an increasing prevalence around the world.\textsuperscript{12} Treatment of IBD symptoms as a result of inflammatory activity consists of immunosuppressive medication, combined with a possible surgical procedure.\textsuperscript{13} Most patients requiring surgery are facing inadequate control of IBD-specific symptoms, experiencing intolerable side effects or presenting with complications of the disease such as intestinal bowel obstruction, fistula, perforations or stenosis.\textsuperscript{13-15} Symptom monitoring remains one of the key components of the disease course in patients with IBD.\textsuperscript{15,16} Therefore, to objectify the disease course in patients with IBD, their health-related quality of life (HRQoL) is measured. Treatment of patients with IBD requires a complex and multidisciplinary approach, and abrupt changes in treatment regimens and options may result in an increased morbidity and consequent well-being of patients with IBD. Therefore, the aim of this study is to determine the HRQoL during the COVID-19 pandemic in patients with IBD in the Netherlands.

\section*{Materials and Methods}

\subsection*{Study design and patient selection}

This study consisted of a self-administered single-point survey, in which details on demographics, IBD medication and the physical and emotional impact of the COVID-19 lockdown period were collected. The survey was distributed electronically to all panel members registered in the national database of the Dutch Crohn’s and Colitis Association. This panel consisted of patients with IBD who would like to be involved in IBD healthcare and research. The panel was composed of patients from as many different regions and age groups as possible to obtain a representative view of the IBD population in the Netherlands and currently consists of 1932 patients.\textsuperscript{17} Participants were included if they were older than 18 years and filled in both the Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-Item Short Form Health Survey (SF-36) questionnaire between 31 August and 15 September 2020. Patients were excluded when the final diagnosis was not yet determined or when they were diagnosed with proctitis, as proctitis can have other causes besides CD and UC.

\subsection*{HRQoL assessment}

\textbf{36-Item Short Form Health Survey}

SF-36 is a non-disease-specific questionnaire to assess all the domains for a general health condition, containing 36 items. This questionnaire is further categorised into eight groups: physical functioning, role limitations due to physical health problems, bodily pain, general health perception, vitality, social functioning, role limitations due to emotional problems and mental health. In addition, the physical component scale (PCS) is the sum of physical functioning, role limitations due to physical problems, bodily pain and general health domains, and the mental component scale (MCS) is the sum of vitality, social functioning, role limitations due to emotional problems and mental health domains. Social functioning scores range from 0 to 100, with a higher score indicating a better health condition.\textsuperscript{18,19}

\subsection*{Inflammatory Bowel Disease Questionnaire}

The IBDQ is a disease-specific QoL questionnaire. It consists of 32 items, which are divided into four domains: bowel-related symptoms, systematic symptoms, emotional function and social function. Responses are graded on a seven-point scale in which 1 indicates the worst function and 7 the best function. The total IBDQ score gives a possible range of 32–224, with a higher score indicating a better QoL.\textsuperscript{20,21}

\subsection*{End points and definitions}

The primary end point was to ascertain the patient-reported outcome measured using the IBDQ and SF-36 questionnaire. The secondary end point was determining the effect of age, gender, type of IBD and operation performed on different domains of the HRQoL.

Patients were stratified according to the type of IBD, including CD and UC. Patients who underwent a previous surgical procedure, during or before the COVID-19 pandemic, were stratified by the number of surgical procedures performed. Patients who underwent a previous surgical procedure were stratified into five categories as well: previous 0–5 years, previous 6–10 years, previous 11–15 years, previous 16–20 years and longer than 20 years. Types of medical treatment included, but were not limited to, biologicals (eg, infliximab, adalimumab, golimumab, vedolizumab, ustekinumab and tofacitinib), corticosteroids (eg, prednis(ol)one, budesonide, beta-methasone and beclometasone), immunosuppressants (eg, azathioprine, ciclosporin, mercaptopurine, methotrexate and thioguanine), mesalamines (eg, sulfasalazine and mesalazine), supportive medication (eg, loperamide and cholestyramine) and research medication.

\subsection*{Statistical analysis}

Descriptive statistics were used to describe the patient and treatment characteristics. Continuous data are reported as mean and standard deviation (SD).

Multivariate linear regression was used to determine which factors determine QoL in the different domains of both HRQoL questionnaires. P values below 0.05 were considered significant.

All calculations were performed using RStudio V.1.2.5001 (with R V.x64 3.6.3).
RESULTS
Baseline characteristics
Between 31 August and 13 September 2020, 582 (30.6%) patients with IBD completed both questionnaires. Of these patients, 179 (32.8%) were men. The mean age of the study population was 52.8 years (SD=14.9, range=13–85 years), and the mean age of IBD diagnosis was 35 years. The diagnosis of CD was the most frequent type of IBD in 327 (56.2%) patients and UC in 255 (43.8%) patients. In 193 (35.0%) patients, a surgical intervention for IBD was performed. Most of these patients (80.8%) were diagnosed with CD compared with 19.2% with UC. The mean time between the year of IBD diagnosis and first surgery was 7 years. The majority of the surgical patients (33.7%) were operated once. Of the 193 surgical patients, 37 (19.2%) required more than five surgical procedures. In total, 480 (82.5%) patients received medical therapy at the time of questionnaire (table 1).

QoL using SF-36 and IBDQ
Figure 1 presents the general health of the patients with IBD using the mean scores of the SF-36 questionnaire. The mean scores on the PCS and MCS were 36.3 and 50.8, respectively. The highest mean score was observed for the mental health domain (mean score=73.2) and the lowest score for the physical functioning domain (mean score=45.3). Furthermore, figure 2A,B displays the disease-specific health status of the participants using the mean scores of the IBDQ. The total IBDQ score in our study population is 171.3 (SD=31.04). The mean scores on the physical components of the IBDQ were 54.4 and 22.8 for bowel symptoms and systemic symptoms, respectively. Emotional function and social function contributed to the mental domains of the IBDQ with mean scores of 65.5 and 28.6, respectively.

Factors associated with HRQoL
Multivariate analysis of the SF-36 questionnaire showed that higher age was a significant predictor of a lower score on physical functioning (p<0.001) and PCS (p=0.006) and of higher score on vitality (p=0.041) and MCS (p=0.005). Furthermore, female gender was a significant contributor to a lower median score of the SF-36 for physical functioning (p=0.013), role limitations due to physical health problems (p=0.028), bodily pain (p=0.007), social functioning (p=0.017) domains and the PCS (p=0.003). Finally, a history of surgical IBD procedure was a significant predictor of a lower median score on the role limitations due to physical health problems domain (p=0.026) and PCS (p=0.08). Type of IBD was not a significant contributor to the HRQoL domains of the SF-36 (table 2).

Multivariate analysis of the IBDQ showed that a history of IBD surgery performed was a significant predictor of a lower score in bowel symptoms, systemic symptoms, social function and the total IBDQ scores, with p values of 0.033, 0.049, <0.001 and 0.014, respectively. Furthermore, higher age (p=0.003) was a significant predictor of scoring higher on the emotional function domain. In addition, in scoring on systemic symptoms, female gender (p=0.001) was a significant predictor to result in a lower mean score. Type of IBD was not a significant contributor to the HRQoL domains of the IBDQ (table 3).

DISCUSSION
This study analysed 582 patients with IBD who completed the SF-36 and IBD-specific questionnaires during the COVID-19 pandemic. The overall HRQoL in our IBD participants during the pandemic is low. Furthermore, older patients, women and patients who have undergone surgery have a significant lower physical HRQoL.

During the pandemic, healthcare measures in different disciplines were taken to facilitate the intensive care
capacity for patients with COVID-19, while at the same time non-COVID-19 care was minimalised to reduce the pressure on healthcare. A recent study describes a decrease in IBD care performed as a result of the pandemic. Due to changes in the healthcare priority, the HRQoL of the patients with IBD may have decreased. This study describes the HRQoL of patients with IBD during the COVID-19 pandemic.

This study showed an overall low HRQoL based on the SF-36 questionnaire, in our study population. The SF-36 questionnaire showed that our study population had lower scores compared with a recent study during the COVID-19 pandemic with non-chronically ill patients, indicating an inferior general health in our patients with IBD during the lockdown. Furthermore, HRQoL measured by the SF-36 questionnaire showed that patients with IBD experienced a lower physical HRQoL during the pandemic compared with Dutch patients with IBD outside the pandemic as shown in earlier pre-pandemic studies (mean PCS=45.7–63). This may be explained by the healthcare changes needed during the pandemic, including reduced performance of diagnostic endoscopy, reduced access to outpatient clinic visits and postponement of surgical procedures. Due to this postponement of regular care and altered medical treatment, patients with IBD may have a higher risk of physical adverse outcomes. Therefore, the low HRQoL score, focused on the general health, in our patients with IBD may be explained by these possible consequences of the healthcare postponement as a result of the pandemic.

This study displays that our Dutch patients with IBD score low on the IBDQ, the disease-specific questionnaire for IBD, indicating an overall low HRQoL. These scores were lower compared with pre-pandemic studies in the Dutch IBD population (mean total IBDQ score=173–181, mean bowel symptoms=53–57, mean systemic symptoms=24–26, mean emotional function=65–68 and mean social function=29–30). The changed measures during the pandemic, described previously, come with uncertainty and stress, which could explain the low score of the emotional function and social function domains of the IBDQ in our study population. Optimal IBD course consists of clinical symptoms combined with monitoring of biomarkers such as faecal calprotectin and C reactive protein. However, during the pandemic, outpatient clinic visits were cancelled, resulting in reduced ability to collect blood for possible follow-up of biomarkers. Our data regarding the bowel function and systemic symptoms subscales of the IBDQ and PCS of the SF-36 illustrated worsening of intestinal problems during the pandemic compared with previously mentioned Dutch pre-pandemic studies. As IBD
care is partially based on the patients' clinical symptom experience, postponement of IBD care may result in more disease activity and thereby in further clinical deterioration.13 16 35–37 This may lead to additional care, which

Table 2 Multivariate analysis of predictors determining different outcomes of the domains from the SF-36 questionnaire

| Parameter | Estimate | SE  | z value | P value |
|-----------|----------|-----|---------|---------|
| PF        |          |     |         |         |
| Age       | −0.143   | 0.023 | −6.154  | <0.001  |
| Sex       | −1.844   | 0.736 | −2.507  | 0.013   |
| CD        | 0.252    | 0.743 | 0.339   | 0.735   |
| Surgery   | −1.354   | 0.769 | −1.761  | 0.079   |
| RP        |          |     |         |         |
| Age       | −0.064   | 0.128 | −0.500  | 0.617   |
| Sex       | −8.924   | 4.036 | −2.211  | 0.028   |
| CD        | 0.531    | 0.602 | 0.131   | 0.896   |
| Surgery   | −9.4     | 4.208 | −2.234  | 0.026   |
| BP        |          |     |         |         |
| Age       | −0.104   | 0.067 | −1.555  | 0.120   |
| Sex       | −5.788   | 2.125 | −2.723  | 0.007   |
| CD        | 1.974    | 2.145 | 0.92    | 0.358   |
| Surgery   | −4.25    | 2.221 | −1.913  | 0.056   |
| GH        |          |     |         |         |
| Age       | −0.005   | 0.059 | −0.079  | 0.937   |
| Sex       | −0.377   | 1.889 | −0.200  | 0.842   |
| CD        | 0.932    | 1.909 | 0.488   | 0.625   |
| Surgery   | −3.261   | 1.977 | −1.650  | 0.100   |
| VT        |          |     |         |         |
| Age       | 0.141    | 0.069 | 2.048   | 0.041   |
| Sex       | −3.843   | 2.187 | −1.757  | 0.080   |
| CD        | 3.45     | 2.208 | 1.562   | 0.119   |
| Surgery   | −1.78    | 2.286 | −0.779  | 0.437   |
| SF        |          |     |         |         |
| Age       | −0.066   | 0.072 | −0.924  | 0.356   |
| Sex       | −5.496   | 2.284 | −2.406  | 0.017   |
| CD        | 0.221    | 2.308 | 0.096   | 0.924   |
| Surgery   | −4.3     | 2.39  | −1.799  | 0.073   |
| RE        |          |     |         |         |
| Age       | 0.165    | 0.118 | 1.398   | 0.163   |
| Sex       | 0.717    | 3.734 | 0.192   | 0.848   |
| CD        | −4.944   | 3.764 | −1.314  | 0.19    |
| Surgery   | −2.888   | 3.899 | −0.741  | 0.459   |
| MH        |          |     |         |         |
| Age       | 0.101    | 0.055 | 1.831   | 0.068   |
| Sex       | 0.273    | 1.744 | 0.156   | 0.876   |
| CD        | −0.727   | 1.761 | −0.413  | 0.680   |
| Surgery   | −1.315   | 1.823 | −0.722  | 0.471   |
| PCS       |          |     |         |         |
| Age       | −0.067   | 0.024 | −2.773  | 0.006   |
| Sex       | −2.233   | 0.758 | −2.947  | 0.003   |
| CD        | 0.713    | 0.771 | 0.925   | 0.356   |
| Surgery   | −2.116   | 0.790 | −2.677  | 0.008   |

Table 2 Continued

| Parameter | Estimate | SE  | z value | P value |
|-----------|----------|-----|---------|---------|
| MCS       |          |     |         |         |
| Age       | 0.096    | 0.0344 | 2.804   | 0.005   |
| Sex       | 0.030    | 1.078  | 0.028   | 0.978   |
| CD        | −0.671   | 1.097  | −0.612  | 0.541   |
| Surgery   | −0.725   | 1.124  | −0.645  | 0.519   |

Table 3 Multivariate analysis of predictors determining different outcomes of the domains from the IBDQ

| Parameter | Estimate | SE  | z value | P value |
|-----------|----------|-----|---------|---------|
| BS        |          |     |         |         |
| Age       | 0.035    | 0.03 | 1.166   | 0.244   |
| Sex       | −1.779   | 0.954 | −1.865  | 0.063   |
| CD        | 1.211    | 0.976 | 1.241   | 0.215   |
| Surgery   | −2.14    | 1.002 | −2.137  | 0.033   |
| SS        |          |     |         |         |
| Age       | 0.031    | 0.018 | 1.786   | 0.075   |
| Sex       | −1.814   | 0.561 | −3.235  | 0.001   |
| CD        | 0.186    | 0.572 | 0.326   | 0.745   |
| Surgery   | −1.159   | 0.587 | −1.975  | 0.049   |
| EF        |          |     |         |         |
| Age       | 0.105    | 0.035 | 2.993   | 0.003   |
| Sex       | 0.079    | 1.108 | 0.071   | 0.943   |
| CD        | −0.371   | 1.13  | −0.328  | 0.743   |
| Surgery   | −2.181   | 1.153 | −1.892  | 0.059   |
| SF        |          |     |         |         |
| Age       | 0.001    | 0.019 | 0.070   | 0.944   |
| Sex       | −0.812   | 0.594 | −1.366  | 0.173   |
| CD        | 0.337    | 0.605 | 0.557   | 0.578   |
| Surgery   | −2.475   | 0.622 | −3.981  | <0.001  |
| IBDQ total|          |     |         |         |
| Age       | 0.178    | 0.091 | 1.949   | 0.052   |
| Sex       | −3.854   | 2.865 | −1.345  | 0.179   |
| CD        | 1.631    | 2.928 | 0.557   | 0.578   |
| Surgery   | −7.408   | 2.993 | −2.475  | 0.014   |

BS, bowel Symptoms; CD, Crohn’s disease; EF, emotional function; IBDQ, Inflammatory Bowel Disease Questionnaire; SF, social function; SS, systemic symptoms.
results in a larger strain on overall healthcare during the pandemic. Therefore, maintenance of IBD care is essential.

Our multivariate analysis showed that there were no significant differences in HRQoL between patients with UC and patients with CD. This is in line with the previous literature. Furthermore, this study showed that a history of surgery was a significant predictor for a lower HRQoL for several different physical and emotional domains of both HRQoL questionnaires. These findings are presented in previous studies as well. However, due to our study design, our findings should be interpreted cautiously as other studies describe that surgical intervention can play an important role in improving HRQoL in patients with IBD on the long term. Furthermore, this study shows that increased age and female patients with IBD scored lower on the physical aspects of the HRQoL questionnaires, which is described previously. This study illustrates that increased age is a significant predictor for a higher HRQoL score on the emotional function domain of the IBDQ and vitality domain and MCS of the SF-36. The vitality domain of the SF-36 makes an important contribution to the overall emotional health of patients and focuses, for example, on level of energy, dispiritedness and fatigue experience. The higher results on emotional health and vitality domains may indicate that disease-adapting and disease-coping ability is better in older patients with IBD compared with younger patients. This association between the contribution made by increased age on the mental HRQoL is reported earlier.

This study has some limitations. First, our study has not included clinical follow-up data of our participants. However, because IBD treatment is partly based on symptoms of the patients, and therefore the HRQoL, this study gives a good indication of the current health status of our study population during the rapidly spread pandemic. Second, the data from the questionnaires were collected online, with potential under-representation of older patients. The average age of our study population is almost 53 years. This is in line with previous IBD studies. Third, as the survey was conducted just after the first wave, all respondents experienced the full first wave of the COVID-19 pandemic. However, the influence of other factors on the HRQoL in patients with IBD, such as social isolation, cannot be directly determined. Finally, due to the unexpected onset of the COVID-19 pandemic and because it was the first time that we invited all patients of the Dutch Crohn’s and Colitis Association to participate in filling out the IBDQ and SF-36, we were not able to provide a pre-COVID-19 control group. However, we used four Dutch IBD studies to serve as pre-COVID-19 control groups from similar background populations, to compare our data as closely as possible.

More research is warranted to follow up our study population to obtain advanced information to determine their HRQoL outside the pandemic. Furthermore, additional research is required to determine the effect and predictors of postponed IBD care on clinical deterioration, thereby enabling to determine for which patients with IBD a delay of treatment is feasible and for which patients delay of IBD care could lead to increased morbidity and thereby an increased demand for healthcare resources.

In conclusion, this study shows that the HRQoL in patients with IBD during the COVID-19 pandemic is low. Furthermore, this study showed that older female patients have the lowest physical HRQoL. In the event of a next wave of the COVID-19 pandemic, caution in postponing IBD care is essential to prevent a decrease in the HRQoL of patients with IBD.

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