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To cite this article: Lauran Vogelaar, Rita van den Berg-Emons, Hans Bussmann, Robert Rozenberg, Reinier Timman & Christien J. van der Woude (2015) Physical fitness and physical activity in fatigued and non-fatigued inflammatory bowel disease patients, Scandinavian Journal of Gastroenterology, 50:11, 1357-1367, DOI: 10.3109/00365521.2015.1046135

To link to this article: http://dx.doi.org/10.3109/00365521.2015.1046135

Published online: 20 May 2015.

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ORIGINAL ARTICLE

Physical fitness and physical activity in fatigued and non-fatigued inflammatory bowel disease patients

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Abstract

Objective. To assess physical fitness and physical activity in inflammatory bowel disease (IBD) patients and whether fatigue is associated with impaired physical fitness and impaired physical activity. Materials and methods. Ten patients with quiescent IBD and fatigue (fatigue group [FG]) based on the Checklist Individual Strength-Fatigue score of ≥35 were matched for age (±5 years) and sex with a non-fatigue group (NFG) with IBD. Physical fitness was measured with a cyclo-ergometric-based maximal exercise test, a submaximal 6-min walk test, and a dynamometer test to quantify the isokinetic muscle strength of the knee extensors and flexors. Level of physical activity was measured with an accelerometer-based activity monitor. Results. The patients in both groups did not differ in regard to medication use, clinical characteristics, and body composition. However, medium-to-large effect sizes for impaired physical fitness (both cardiorespiratory fitness and muscle strength) and physical activity were seen between the patients in the FG and the NFG. Especially, intensity of physical activity was significantly lower in the FG patients compared with the NFG patients (effect size: 1.02; p = 0.037). Similar results were seen when outcomes of the FG and NFG were compared with reference values of the normal population. Conclusion. Fatigued IBD patients show an impaired physical fitness and physical activity compared with non-fatigued IBD patients. This gives directions for a physical component in fatigue in IBD patients. Therefore, these new insights into fatigue indicate that these patients might benefit from an exercise program to improve physical fitness and physical activity.

Key Words: fatigue, inflammatory bowel disease, physical activity, physical fitness

Introduction

Despite more effective treatments for patients with inflammatory bowel disease (IBD), many patients still suffer from disabling fatigue, which is associated with decreased quality of life (QoL) [1–5]. Several factors such as disease activity, perceived stress, depressive coping, female gender, and psychological well-being contribute to fatigue in IBD patients. Moreover, we showed in a previous study that solution-focused therapy, a psychological intervention, is effective in reducing fatigue and subsequently in increasing QoL [5–13]. However, although effective in the majority, there are still patients who suffer from invalidating fatigue.

Previous studies among cancer patients and liver transplant recipients showed evidence for a relationship between fatigue, impaired physical fitness and impaired physical activity [14–16]. Cardiorespiratory fitness (VO2peak) in liver transplant recipients was related with severity of fatigue and QoL, but no indications of impaired muscle strength was observed [17]. Furthermore, the level of daily physical activity measured with an accelerometer was related with fatigue in liver transplant recipients [18]. In cancer patients the etiology of fatigue is poorly understood,
and literature on fatigue and objective physical components is scarce. However, literature suggests associations between impaired muscle strength, impaired physical activity and fatigue [15,19]. Moreover, most research on fatigue in cancer patients focused on exercise interventions and showed reduction of fatigue by these interventions [16,20–25].

Therefore, we hypothesize that fatigue in IBD patients might be partly related to impaired physical fitness and impaired physical activity. However, data on the association between physical activity and physical fitness and fatigue in IBD patients is lacking. For the development of an exercise intervention to reduce fatigue, more objective knowledge of these associations is necessary.

The aim of this study was to assess the level of physical fitness (cardiorespiratory fitness and muscle strength) and daily physical activity in IBD patients and whether fatigue is associated with impaired physical fitness and impaired physical activity.

**Methods**

**Study design**

We performed a matched cross-sectional study in fatigued and non-fatigued IBD patients. This study was conducted in accordance with the protocol International Conference on Harmonization Guidelines for Good Clinical Practice, the Declaration of Helsinki, and local national regulations governing clinical study conduct. The protocol was approved by the medical ethics committee of the Erasmus Medical Center (Erasmus MC, registration number: MEC-2010-249; NL33396.078.10). The study was not designed for an interim analysis and no Data Safety Monitoring Board was assigned. All patients gave written informed consent. Patients were enrolled at the Erasmus MC in The Netherlands from November 2010 to October 2011. Patients were randomly selected from the IBD outpatient population.

**Sample size.** For the sample size calculation, we applied data from the study of van den Berg-Emmons et al. [18]. They reported correlation between −0.81 and −0.84 between severity of fatigue and daily physical activity within a group of liver transplant recipients. Applying a two-sided α-level of 0.05, power 0.80, nine cases are needed for a correlation of 0.80. In a study of van Ginneken et al. correlations between −0.50 and −0.61 were reported between cardiorespiratory fitness and severity of fatigue within a group of liver transplant recipients [17]. Again applying a two-sided α-level of 0.05, power 0.80, 28 cases are needed for a correlation of 0.50, and 18 cases for a correlation of 0.60. Combining these results we felt confident in applying a sample size of 20.

Therefore we decided to include 10 patients in the fatigue group (FG) and 10 patients in the non-fatigue group (NFG). Patients were matched for sex and age (maximal difference: ±5 years).

**Patients and fatigue measurement**

Men and women aged ≥18 years, diagnosed with IBD which was radiologically or endoscopically/histologically confirmed, were included. Patients had to be in remission of the disease, defined as Harvey Bradshaw Index score of <5 or Clinical Activity Index score of <10 and C-reactive protein value of <10 mg/L (reference value: 0–9 mg/L). Fatigue was defined as a Checklist Individual Strength-fatigue (CIS-fatigue) score of ≥35 and non-fatigue as a CIS-fatigue score of <35 [26].

Pregnant women or breastfeeding women, surgery within 12 weeks prior to the screening visit, short bowel syndrome, a history of lymphoproliferative disease or cancer, other than skin basocellular carcinoma, gastrointestinal disease other than IBD, and contraindication for maximal exercise testing according to the Physical Activity Readiness Questionnaire (PAR-Q) were not included [27].

**Measurements**

**Physical fitness.**

**Cardiorespiratory fitness – cyclo-ergometric exercise test:** Cardiorespiratory fitness was measured with a progressive maximal cyclo-ergometric exercise test (ER800, Jaeger Toennies, Breda, The Netherlands) (Figure 1).

The test was preceded by a 4-min warm-up period (20 Watt [W]). The test started at 20 W, followed by an increase in resistance of 15 or 20 W/min, depending on the ability of the patients. Individual test protocols were chosen aimed for a test duration of 8–12 min according to the American College of Sports Medicine criteria [28]. Subjects were instructed to use a pedal rate of 60 rpm and were encouraged to achieve maximal effort.

The test was terminated when the subject was subjectively exhausted, or when the patient was unable to maintain the instructed pedal rate. Breathing gas exchange and heart rate (HR) were monitored continuously using a breath-by-breath gas analysis system (Oxycon Pro, Jaeger Toennies, Breda, The Netherlands).
The respiratory exchange ratio (RER) was calculated during the test. An RER of ≥1.1 indicates maximal exercise [29–31]. The predicted maximum HR was calculated with the formula of Tanaka: 208 – (0.7 × age) [32].

Subjective strain was measured immediately after the final stage by the Borg Category Ratio Scale (Borg-CR10 scale) [33,34]. Patients were asked to indicate how strenuous they had experienced the test by giving a number from 0 (no effort at all) to 10 (maximal effort). Cardiorespiratory fitness was defined as the highest mean oxygen uptake during 30 s of exercise (\(VO_2\text{peak} \text{ L min}^{-1}\)). Ventilatory threshold (VT) was defined as an increase in VE/without a concomitant increase in VE/ [35,36].

**Cardiorespiratory fitness: 6-min walk test.** Furthermore, cardiorespiratory fitness was also measured with the submaximal 6-min walk test (6MWT) [37]. Patients were instructed to walk, not run, as far as they could along a 30-m marked track during a 6-min period. Standardized encouragement was provided with the following phrases: “you are doing well” and “keep up the good work”. Patients were allowed to stop and rest during the test but were instructed to resume walking as soon as they felt able to do so. The 6-min walk distance (6MWD) was recorded.

**Muscle strength.** Isokinetic muscle strength of the knee extensors and flexors was assessed in both legs using a Biodex® dynamometer (Shirley, New York, USA), recording strength as torque in Newton meters. The patients were seated against a backrest, firmly strapped at the hip and thigh. The rotational axis was aligned with the lateral femoral epicondyle. After three familiarization repetitions, isokinetic strength was measured at 60°/s (60°/s) with 5 maximal contractions and at 180°/s (180°/s) with 15 maximal contractions. Maximal effort was encouraged. Peak torque (PT) was defined as the maximum torque generated by the patients throughout a series of repetitions at each velocity. The mean PTs were separately calculated from all torques of both legs at each velocity.

**Physical activity.** For assessment of the level of daily physical activity an activity monitor (AM) (Temec Instruments BV, Kerkrade, The Netherlands) was used. The AM is based on long-term ambulatory monitoring of signals from body-fixed accelerometers and consists of four accelerometers, a portable data recorder, and a computer with analysis software [38]. After the measurement, data were downloaded onto a computer for analysis by the Kinematic Analysis part of the Vitagraph Software [39]. A detailed description of the activity detection procedure has been described previously [38,40]. Data were calculated for 1 day (24-h period) and the following variables were assessed: duration of dynamic activities (walking, including climbing/descending stairs and running, cycling, general non-cyclic movement) as percentage of a 24-h period; number of transitions (contains all transitions except the lying transitions such as the transition from lying prone to lying supine); and number of walking periods (>10 s). In addition, body motility was assessed, addressing mean motility over a 24-h period (representing intensity of daily physical activity) and motility during walking (representing walking speed) [38,41,42].

The AM system was set up at each participant’s home to minimize influence on the normal physical activity pattern. To avoid measurement bias, we instructed the participants to continue their ordinary daily life activities. The principles of the AM were explained to the participants after all measurements had been made.

**Descriptive parameters**

**Body composition.** Height (cm) and body mass (kg) were measured without shoes. Body mass index (BMI, kg m\(^{-2}\)) was calculated from height and body mass. Body fat was estimated using skinfold measurements with a Harpenden Skin-Fold Caliper (Burgess Hill, UK). The mean of the two measurements was used as representative for each site. Percentage body fat was predicted from skinfold thickness according to the method of Durnin and Womersley [43,44]. Fat-free mass was calculated as total body mass minus body fat.

**Questionnaires.** The Harvey Bradshaw Index (HBI) [45] or Clinical Activity Index (CAI) [46], a
questionnaire focusing on current medication use and side-effects, were filled in.

A HBI score of <5 or a CAI score of <10 in addition to a C-reactive protein value of <10 mg/L are considered to reflect remission of the disease.

Demographics, disease phenotype (Montreal Classification) were collected from medical records [47].

Measurement protocol

Before inclusion, the CIS, HBI, or CAI, a questionnaire focusing on current medication use and side effects to medication were filled in. After inclusion, the level of daily physical activity with an AM was measured. Maximal 1 week thereafter, the fitness measurements were performed. During the day of the fitness measurements, patients refrained from high intensity exercise (running, walking/climbing briskly up a hill, fast cycling, aerobics, fast swimming, competitive sports and games, heavy shoveling or digging ditches, carrying/moving heavy loads >20 kg).

The order of the tests was standardized: patients started with the 6MWT, body composition measurements, and the isokinetic muscle strength test, followed by a questionnaire (PAR-Q) [27] and finally the progressive maximal cyclo-ergometric exercise test. Exercise tests were performed under supervision of a physician.

Table I. Baseline characteristics.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Fatigue</th>
<th>Non-fatigue</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; mean (sd)</td>
<td>36.4 (12.3)</td>
<td>38.2 (11.0)</td>
<td></td>
</tr>
<tr>
<td>Female (frequency)</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Crohn’s disease (frequency)</td>
<td>7</td>
<td>8</td>
<td>1.00</td>
</tr>
<tr>
<td>Ulcerative colitis (frequency)</td>
<td>3</td>
<td>2</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Body composition</strong></td>
<td>Mean (sd)</td>
<td>Mean (sd)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175 (11)</td>
<td>176 (11)</td>
<td>0.80</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>72 (12)</td>
<td>80 (13)</td>
<td>0.16</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23 (2)</td>
<td>26 (5)</td>
<td>0.15</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>27 (9)</td>
<td>30 (10)</td>
<td>0.44</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>52 (10)</td>
<td>56 (10)</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td>Frequency</td>
<td>Frequency</td>
<td></td>
</tr>
<tr>
<td>5-ASA</td>
<td>2</td>
<td>2</td>
<td>1.00</td>
</tr>
<tr>
<td>Immunosuppressives</td>
<td>7</td>
<td>3</td>
<td>0.074</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>1</td>
<td>0</td>
<td>0.305</td>
</tr>
<tr>
<td>Biologics (anti-TNF)</td>
<td>0</td>
<td>2</td>
<td>0.136</td>
</tr>
<tr>
<td>Side effects of medication</td>
<td>4</td>
<td>1</td>
<td>0.139</td>
</tr>
<tr>
<td><strong>CIS-fatigue</strong></td>
<td>Mean (sd)</td>
<td>Mean (sd)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>44.8 (8.6)</td>
<td>18.2 (6.9)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Notes: Chi-square test for dichotomous variables, independent samples t-test for continuous variables.
Abbreviations: 5-ASA = 5-aminosalicylic acid; CIS = Checklist Individual Strength; sd = standard deviation.
participants recruited at the Erasmus MC, measured
with the same AM system and protocol [38,52].
Data were analyzed with SPSS Software for
Windows, version 20 (SPSS Inc, Chicago, IL, USA).
Results were considered significant when two-sided
p-Values were <0.05.

Results

Baseline characteristics

Baseline characteristics according to type of disease,
body composition, medication use, and side effects to
medication were not significantly different between

the FG and NFG (Table I). Mean age was
37.3 (11.4 standard deviation [sd]). Table I also
shows the baseline fatigue scores. No differences
were observed in clinical characteristics of the disease
between the FG and NFG (Table II). Moreover, there
were no differences in co-morbidity between the FG
and NFG.

Outcomes

Table III shows the results of the maximal cyclo-
ergometric exercise tests. The outcomes were indic-
ative for maximal performed tests in both groups.

The mean modified Borg-CR10 score of the FG
was 5.3 (2.2 sd) and 5.5 (1.9 sd) for the NFG
(p = 0.831), which indicates that patients experienced
the maximal cyclo-ergometric exercise test on average
as heavy (= Borg-CR10 score of ≥5).

The effect sizes of the different variables were
medium to large comparing the FG with the NFG,
except from number of transitions. Especially, the FG
showed a significantly lower intensity of daily physical
activity (motility) compared with the NFG (mean:
FG: 0.022, NFG: 0.028) (effect size: 1.02;
P = 0.037) (Table IV).

Between the FG and NFG, both related to their
normed reference values, medium-to-large effect sizes
for physical fitness and physical activity were seen.
Details of these results are presented in Table V.

Discussion

This study showed an impaired physical fitness
(cardiorespiratory fitness and muscle strength) and
physical activity in fatigued IBD patients compared
with non-fatigued IBD patients. The same was seen
when outcomes of both fatigued and non-fatigued

Table II. Clinical characteristics.

<table>
<thead>
<tr>
<th>Montreal classification – CD</th>
<th>Fatigue</th>
<th>Non-fatigue</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (%)</td>
<td>n = 7</td>
<td>n = 8</td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>14.3</td>
<td>12.5</td>
<td>0.379</td>
</tr>
<tr>
<td>A2</td>
<td>42.8</td>
<td>75.0</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>42.9</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>Location (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1</td>
<td>71.4</td>
<td>75.0</td>
<td>0.988</td>
</tr>
<tr>
<td>L2</td>
<td>14.3</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>L3</td>
<td>14.3</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>L4</td>
<td>100</td>
<td>100</td>
<td>1.00</td>
</tr>
<tr>
<td>+L4</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Behavior (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>57.1</td>
<td>62.5</td>
<td>0.535</td>
</tr>
<tr>
<td>B2</td>
<td>42.9</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>B3</td>
<td>0</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>42.9</td>
<td>25.0</td>
<td>0.464</td>
</tr>
<tr>
<td>Disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean HBI (sd)</td>
<td>3.4 (1.0)</td>
<td>2.4 (1.4)</td>
<td>0.114</td>
</tr>
<tr>
<td>Montreal classification – UC</td>
<td>n = 3</td>
<td>n = 2</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>33.3</td>
<td>50.0</td>
<td>0.233</td>
</tr>
<tr>
<td>A2</td>
<td>66.7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>0</td>
<td>50.0</td>
<td></td>
</tr>
<tr>
<td>Location (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E1</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>E2</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>E3</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Severity (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S0</td>
<td>100</td>
<td>100</td>
<td>1.00</td>
</tr>
<tr>
<td>S1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>S2</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>S3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean CAI (sd)</td>
<td>2.7 (0.6)</td>
<td>2.0 (0.0)</td>
<td>0.184</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bowel resection (%)</td>
<td>50</td>
<td>60</td>
<td>0.653</td>
</tr>
<tr>
<td>Stoma (%)</td>
<td>10</td>
<td>0</td>
<td>0.305</td>
</tr>
</tbody>
</table>

Note: Chi-square test for dichotomous variables, independent
samples t-test for continuous variables.
Abbreviations: CD = Crohn’s disease; UC = ulcerative colitis;
HBI = Harvey Bradshaw Index; CAI = Clinical Activity Index;
sd = standard deviation.

Table III. Results of cyclo-ergometric exercise test.

<table>
<thead>
<tr>
<th></th>
<th>Fatigue</th>
<th>Non-fatigue</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. RER</td>
<td>1.14 (0.1)</td>
<td>1.14 (0.1)</td>
<td>0.986</td>
</tr>
<tr>
<td>Max. HR % of predicted*</td>
<td>89 (10.1)</td>
<td>96 (7.1)</td>
<td>0.084</td>
</tr>
</tbody>
</table>

Note: Independent samples t-test for continuous variables.
*Maximal HR as percentage of predicted maximum heart rate
(calculated with the formula of Tanaka: 208 – (0.7×age)) [32].
Abbreviations: sd = standard deviation; Max. = maximal;
HR = heart rate; RER = respiratory exchange ratio.
IBD patients were compared to reference values of non-IBD healthy persons.

To our knowledge, this is the first study which shows a medium effect size for lower cardiorespiratory fitness (VO
\textsubscript{2peak}, VT, and 6MWD) in fatigued IBD patients compared with non-fatigued IBD patients. This finding is consistent with literature on cancer patients and liver transplant recipients, which demonstrated a relationship between impaired cardiorespiratory fitness and severity of fatigue [17,22]. The origin of the impaired cardiorespiratory fitness is possibly a less active behavior, as part of sickness behavior [53–56]. Since we know that disease activity is an important determinant of fatigue complaints, this sickness behavior may be induced by circulating cytokines (IL-1, IL-6, and TNF-\(\alpha\)) during active disease [3,5,7,57–60]. Therefore, it can be hypothesized that sickness behavior and the direct negative effect of the cytokines IL-6 and TNF-\(\alpha\) on muscle performance induce lowering of physical activity. Lowering of physical activity could result in impaired physical fitness, thereby leading to further deteriorating of fatigue complaints (Figure 2) [17,54,57,61–68]. Because physical exercise lowers proinflammatory cytokines, physical exercise could interfere in this cascade [65,66,69].
Impaired cardiorespiratory fitness is known to be related to lower muscle strength [70,71].

Our study found a medium effect size for lower muscle strength (PT extension 60°/s, PT flexion 60°/s, PT flexion 180°/s) and a large effect size for lower PT extension 180°/s in fatigued IBD patients compared with non-fatigued IBD patients. Previous studies in IBD also showed impaired muscle strength in these patients, but fatigue was not investigated in these studies [72–74]. Only one study showed an association between impaired muscle strength and fatigue severity in IBD patients [61]. Because we measured the muscle strength both at 60°/s and 180°/s, combined with flexion and extension of both lower limbs, we were able to show a broader spectrum of muscle performance.

The etiology of the impaired muscle strength seems multifactorial. The use of corticosteroids is one of the factors associated with impaired muscle strength [75–77]. However, in our study only one patient in the fatigue group used corticosteroids at the time of participation. Although we are unaware of the former corticosteroid use in these patients, it is unlikely that impaired muscle strength in fatigue patients was induced by corticosteroid use.

Nutritional status, in a previous study defined as lower BMI, was found as a factor of impaired muscle strength [78]. We could not confirm this, because no differences were found in BMI and fat-free mass between fatigued and non-fatigued patients. It might be that cytokines negatively influence muscle strength in IBD patients [61,67,68]. Beside the negative effect of cytokines on muscle strength, reduced physical activity is associated with lower muscle strength [79,80]. We showed medium effect sizes for reduced physical activity in fatigued IBD patients compared with non-fatigued IBD patients. This is in line with a previous reported relationship between lower physical activity and severity of fatigue in liver transplant recipients [18].

This finding is in contrast with a previous study which showed no difference in physical activity between fatigued IBD patients and a healthy control group [61]. However, this latter study did not report on the intensity of physical activity, which was significantly lower in our fatigued IBD patients.

Our results of impaired physical fitness and physical activity in fatigued IBD patients are important for optimization of fatigue management and must be regarded in addition to fatigue-associated factors, such as disease activity, perceived stress, and depressive coping. Previously it was shown that optimal management of disease activity, stress, and coping is effective to reduce fatigue [13,81–84]. Despite that
these aforementioned interventions are effective in the majority of IBD patients, there are still patients suffering from severe fatigue. As previous studies showed positive effects of exercise interventions on QoL in IBD patients and also on fatigue in other patients with chronic disorders [16,20,21,85–95], we suppose that a multidisciplinary approach to reduce the fatigue burden is needed.

This study has some limitations: first, patients were not screened for disease activity using calprotectin at inclusion [96]. For measuring disease activity, we used the HBI and CAI. Although these questionnaires are validated and widely used in trials, they are more prone to subjective results of disease activity.

Second, no data on cytokines were obtained. Although it is difficult to draw a conclusion in regard to cytokines in a small sample size, it is worth investigating the possible influence of cytokines on muscle performance and physical activity.

Conclusion

Fatigued IBD patients showed impaired physical fitness and physical activity compared with non-fatigued IBD patients. These results offer new possibilities to optimize fatigue management for IBD patients. Further research is warranted using exercise interventions, to confirm whether exercise reduces fatigue complaints in IBD patients.

Acknowledgments

The authors thank Emiel Sneekes and Herwin Horemans for contributing to the study by data processing and for their assistance in data analyses, Badr Nouhaili and Sylvii-An de Schipper for practical assistance and data collection. Contributors: All authors have read and approved the final manuscript. LV participated in the conception and design, acquisition of data, analysis and interpretation of data, and drafting of the manuscript. RB participated in the conception and design of the study, and critical revision of the manuscript for important intellectual content. RT participated in the conception and design of the study, performed the statistical analysis and critical revision of the manuscript for important intellectual content. HB participated in critical revision of the manuscript for important intellectual content. RR participated in critical revision of the manuscript for important intellectual content. CW had full access to all data of the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, study concept and design, acquisition of data, and critical revision of the manuscript for important intellectual content.

Funding: No funding was obtained.

Declaration of interest: All authors state that there are no potential conflicts of interest during the work under consideration for publication.

References

[12] Casellas F, Lopez-Vivancos J, Badia X, Vilaseca J, Malagelada JR. Influence of inflammatory bowel disease...


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