The Case for Increased Physical Activity in Chronic Inflammatory Bowel Disease: A Brief Review

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Abstract

Regular physical activity reduces the risk of colon cancer, but there is little information on the merits of such activity in the prevention and management of chronic inflammatory bowel disease (CIBD). The present systematic review thus documents current levels of habitual physical activity and aerobic and muscular function in CIBD, and examines the safety, practicality and efficacy of exercise programmes in countering the disease process, correcting functional deficits and enhancing quality of life. A systematic search of the Ovid/Medline database from January 1996 to May 2015 linked the terms physical activity/motor activity/physical fitness/physical training/physical education/training/exercise/exercise therapy with Crohn's disease/colitis/ulcerative colitis/inflammatory bowel disease, supplementing this information by a scanning of reference lists and personal files. 12 of 16 published studies show a low level of habitual physical activity in CIBD, with sub-normal values for aerobic power, lean tissue mass and muscular strength. 3 of 4 studies suggest physical activity may reduce the risk of developing IBD, and 11 interventions all note that exercise programmes are well tolerated with some decreases of disease activity, and functional gains leading to an increased health-related quality of life. Moreover, programme compliance rates compare favourably with those seen in the treatment of other chronic conditions. More information on mechanisms is needed, but regular moderate aerobic and/or resistance exercise improves the health status of patients with CIBD both by modulating immune function and by improving physical function. A regular exercise programme should thus become an important component in the management of CIBD.

Introduction

Chronic inflammatory bowel disease (CIBD) includes both ulcerative colitis and Crohn's disease, affecting about 0.25 % of the North American population. It carries a substantial direct economic cost (for example, $1.2 B/year in Canada [56]), but it remains a poorly understood syndrome, possibly linked to an inappropriate immune responses [18]. In the form of ulcerative colitis (UC), it is localized to the intestines, but as Crohn's disease (CD) it may also affect the mouth, oesophagus, stomach and anus [2]; there are other differences in the 2 expressions of CBID, including differing loci of genetic susceptibility [40]. One Danish study reported that with appropriate medical management, the overall mortality for UC was normal [71], whereas in 2013 the global mortality from CIBD remained a substantial 0.8/100 000 [13]. Moreover, CIBD is a significant risk factor for colonic cancer [63]; it reduces the age at which such cancers develop [45], and it increases the risk 2–3 fold [38].

Given uncertainties regarding aetiology, much treatment of CIBD is empirical, and the discussion of therapeutic options often fails to consider the potential benefits of an increase in what are typically low levels of habitual physical activity. The primary aims of the present brief review are to document current patterns of habitual physical activity in CIBD, to assess their impact upon functional capacity, and to examine the safety and practicality of exercise programmes in countering the disease process, correcting loss of function, and enhancing the patient's overall quality of life.

Methods

The Ovid/Medline database was scanned systematically and without restriction from January 1996 to May 2015. The terms physical activity/motor activity, physical fitness, and physical training/physical education and training/exercise and exercise therapy (192 761 citations) were paired with Crohn's disease/colitis/ulcerative colitis/inflammatory bowel disease (41 751 citations) to yield 90 references. A scanning of the abstracts indicated 36 items relevant to the present review for which the full text was obtained; these were supplemented with papers drawn from reference lists and the author's personal files.
Because of the complex nature of CIBD, its interaction with physical activity likely depends upon its phenotype, location and activity, the use of corticosteroids, and biosocial factors such as age, education, socio-economic status and associated anxiety and depression. Given the limited amount of information that is available, all relevant papers have been considered although the quality of contributions has been weighed in terms not only of experimental design, but also clarity regarding such details. Articles have been analyzed with respect to current levels of habitual physical activity in CIBD, current levels of functional capacity, the role of physical activity in the prevention of CIBD, acute and chronic responses to exercise in CIBD, and practical experience of compliance with exercise programming in CIBD.

Results

Current levels of habitual physical activity in IBD

16 groups of investigators [5, 6, 11, 16, 27, 36, 42, 43, 50, 53, 59, 60, 67, 70, 72, 74] have evaluated habitual physical activity in patients from various age groups and with variously defined CIBD, using subjective and objective measures of physical activity that have included occupational categorization, completion of interviews or questionnaires, accelerometry and use of other objective sensors (▸ **Table 1**). 12 of the 16 studies found levels of physical activity that were significantly lower in patients with CIBD than in controls, the difference generally being more marked for those classed as CD than for those with UC ([27, 43, 53] but not [16]). In 1 study where physical activity was not significantly less than that of controls, the patients selected were children, more with UC than with CD [6]. In a second study, patients with medical or psychiatric abnormalities were excluded, and despite similar accelerometer readings, the patients had greater subjective and objective muscle fatigue than controls [67]. A third negative report [11] included more cases with UC than with CD, and diagnostic criteria were not standardized. In the fourth negative study [60], 23% of those with CD reported greater fatigue, and 21% noted reduced leisure activities, although a brief interview by the principal investigators had found similar proportions of patients and controls reporting high, moderate or low levels of physical activity
Thus, a level of habitual physical activity that is lower than that of controls and below current minimum recommendations for general health is a relatively consistent finding in CIBD. It could be argued that in some patients, specific features of the disease such as an exercise-induced diarrhoea or a substantial ileostomy made it difficult to undertake physical activity [7], but other surveys were conducted when patients were in remission (23), and in at least one questionnaire study [36] (and likely in the occupational comparisons) the low levels of physical activity preceded the development of clinical illness.

Current levels of functional capacity in IBD

As might be anticipated from the low levels of habitual physical activity, patients with CD commonly show an impaired functional capacity relative to age- and sex-matched controls or population norms, with an associated accumulation of body fat and a deterioration of bone health.

Aerobic functional capacity

Only 4 groups of investigators [7, 17, 18, 50, 74] have discussed the influence of CIBD upon aerobic functional capacity (▸ **Table 2**). The characteristics of the patients are quite varied; some in 2 of the 4 groups [7, 50] had received surgical treatment and one group [17, 18] was in remission. Conclusions concerning aerobic function are based upon peak cycle ergometer and treadmill performance, gait speed measurements, and patient perceptions of reduced aerobic function at an interview. All 4 studies reported some loss of aerobic function. Brevinge et al. [7] found that the degree of impairment (when normalized for loss of body mass) was small in patients who had not undergone surgery, but increased progressively in relation to the extent of any intestinal resection. Moreover, losses were generally greater than might have been predicted from the decrease of lean tissue mass [7], possibly reflecting problems in the absorption of food, electrolyte imbalances and altered metabolism. Zaitman et al. [74] further noted that losses of aerobic function were inversely related to habitual physical activity and grip strength

Lean tissue mass

Lean tissue mass has been measured relatively frequently in CIBD [3, 6–8, 10, 20, 22, 24, 29, 61, 64–66, 69, 72–74], usually by computed tomography or by bio-impedance techniques (▸ **Table 3**). Often, it has been evaluated as a marker of nutrition rather than as a marker of functional status. Evidence for a decrease in lean tissue mass is fairly conclusive. In 13/18 studies, values were lower than in controls, although (since the loss of lean tissue is generally more marked in CD than in UC [29]), the reported extent of loss was influenced by the relative proportions of cases with UC and CD in the patient samples. Often, a low lean tissue mass was associated with a low level of habitual physical activity, suggesting inactivity as one contributing factor [66, 70, 74]. A second issue has been whether the disease process was active or in remission [24]; although the adverse effect of CD upon lean tissue mass can persist into remission for as long as several years [61, 64, 70], 4 of the 5 studies reporting a normal lean tissue mass were of patients in remission [10, 22, 24, 72], and one concerned only women with UC [74]; in 2 of the 5 negative trials, leg-muscle strength was nevertheless lower than in controls [24, 72]. Wiskin et al. [73] noted that lean tissue mass was inversely related to disease activity; in this series, the loss of lean tissue was sometimes masked by an accumulation of body fat, although in other studies abnormalities of fat metabolism led also to a reduction in body fat content [10]. Bechtold et al. [3] noted a correlation between a low serum albumin and muscle wasting, and Brevinge et al. [7] pointed specifically to a malabsorption of nutrients following extensive intestinal resection; even in the absence of surgical intervention, nutrient intake can be adversely affected by dietary modifications, chronic inflammation and diarrhoea [22]. A further possible factor leading to muscle wasting, not always clearly documented, is prolonged steroid treatment [65]. Bechtold et al. [3] found no difference of muscle cross-sectional area with steroid treatment in adolescents, Dubner et al. [20] reported an improvement of muscle

Table 1 Current physical activity in patients with chronic inflammatory bowel disease (CBID).

Author	Subjects	Activity determination	Findings	Comments
Bøggild et al. [5]	Danes aged 20–59 yrs; analysis of 6 296 first hospital admissions for CIBD	Physical activity at work, based on extended International Standard Classification of Occupations	Sedentary work increased risk of hospitalization from CIBD	All cases in Danish population register first admitted to hospital with CIBD
Boot et al. [6]	Children, 22 CD, 33 UC, unspecified controls	Interview	Mean physical activity not significantly less than in controls	Diagnoses made using Dutch consensus guidelines
Chan et al. [11]	177 cases of incident UC, 75 cases of incident CD among 300,724 participants in cancer survey	Questionnaire (5-level classification)	Reported physical activity of affected individuals developing UC or CD did not differ relative to 4 matched controls per case	Methods of case identification varied from one centre to another
Cuciono & Sonnenberg [16]	2 399 deaths from CD, 2 419 deaths from UC as reported to US National Center for Health Statistics, 1991–1996	US Vital Statistics on occupational activity, expressed as proportional mortality ratios	Low risk in farmers, miners and labourers, high risk in sales persons & secretaries	Effects appear similar for UC and CD
Hlavaty et al. [27]	190 cases of CD, 148 cases of UC, 355 controls (case-control study); diagnosis based on clinical, endoscopic, radiologic and histologic criteria	44-item questionnaire included question on sporting activities	Association of CIBD with <2 sporting activities/wk as a child (odds ratios 2.7 for CD, 2.0 for UC)	CD also associated with smoking
Klein et al. [36]	55 recent-onset cases of UC, 33 cases of CD referred by regional gastroenterologists, matched controls (76 orthopaedic clinic, 68 general population)	Questionnaire included item on time spent in various levels of physical activity	Physical activity of patients low, spent less time than controls in strenuous activity	Low activity level present before onset of clinical disease
Lustyk et al. [42]	54 women (29 diagnosed, 25 suspected CIBD based on Rome criteria), 35 controls free of GI symptoms	1-month diary covering housework, mild, moderate and strenuous activity and 1-month symptom diary	CIBD group less active than controls, difference persisted when controlled for educational level	Among patients, symptoms (especially fatigue) inversely related to habitual physical activity
Mack et al. [43]	637 cases of self-reported UC, 474 CD, 113,685 control participants in Canadian Health Measures Survey	Questionnaire on health and time spent on 21 activities in previous 3 months	In CD, odds ratios to be classed as inactive (1.34) and active (0.69); similar but smaller effects & ns trends for UC	Most people with CD or UC did not meet public health guidelines for physical activity
Ojerskog et al. [50]	29 cases of UC, 1 case of CD, 1 case of familial polyposis before & after conversion to continent ileostomy	Interview by psychiatrist before & after conversion; leisure activity 1 of 11 topics	Hindrance of sport and bathing reported in 19/31 with traditional ileostomy, 4/30 with continent ileostomy	60 % reported facilitation of leisure activities
Persson et al. [53]	152 cases CD, 145 cases UC (all new cases hospitalized in Stockholm county, Leonard-Jones score), random population sample of 305 controls	Postal questionnaire; single question on physical activity, 5yrs ago & current	Relative risks with weekly & daily exercise: CD 0.6, 0.5, ns benefit in UC (RR 0.9)	"regular participation in any recreational, leisure or sports activity (e. g. long walks)"
Sonnenberg [59]	12,014 patients granted rehabilitation for CIBD (ICD classifications 555 & 556)	Occupation determined from 2-digit occupational code	Occupations involving physical exercise and work in open air have lower risk of CD and UC	Risk of CIBD also increased by irregular hours and shift work
Sørensen et al. [60]	106 cases of CD (adults, >1 yr duration), 75 age- & sex-matched previously healthy acute hospital admissions with illness of <28 days duration	Interview by principal investigator, 3-level classification of physical activity	Similar proportions of 2 groups classed as high, moderate or low physical activity	CD group had slightly higher SES than controls. Note: 23 % of those with CD reported greater fatigue, and 21 % noted reduced leisure activities
van Langenberg et al. [67]	27 cases of CD at CIBD clinic, 27 controls	Tri-axial accelerometer worn at waist for 7 days	Habitual physical activity similar in CD and controls	CD group had greater fatigue; those with medical or psychiatric co-morbidities excluded
Werkstetter et al. [70]	26 IBD in remission, 13 IBD mildly active (27 CD, 12 UC), 39 age- & sex-matched adolescent controls	Sensewear arm band physical activity monitor	Trend to shorter duration of physical activity (0.44 h/d less activity > 3 METs) & lower step count (−1 339/day) in CD	Lean body mass also reduced in patients
Wiroth et al. [72]	41 adult cases of CD in remission (CD activity index <150) 26 healthy controls	Activity questionnaire (occupation, sport & leisure) & 7-day accelerometer record	Neither method showed difference of physical activity between 2 groups, but decreased sport index in CD	Strength of CD group lower than that of controls
Zaltman et al. [74]	23 women with UC, 23 age & BMI matched controls	Baecke physical activity questionnaire (score 3–15)	Physical activity 30 % lower in patients with UC	Loss of lower limb strength & mobility associated with low level of physical activity

CD = Crohn’s disease; CIBD = chronic inflammatory bowel disease; ns = non-significant; SES = socio-economic status; UC = ulcerative colitis

Z-scores over 12 months of treatment that included the use of glucocorticoids, and Wiroth et al. [72] observed an increase of lower limb endurance with recent use of steroids. However, Bryant et al. [8] noted an odds ratio of 2.03 for sarcopaenia in older patients who had received more than 12 months of steroid treatment, and Jahnsen et al. [29] saw a decrease of lean tissue mass that was concentrated in patients who had received steroids.

Table 2 Current aerobic function in patients with CIBD.

Author	Subjects	Measurement techniques	Findings	Comment
Brevinge et al. [7]	29 CD patients following procto-colectomy & 23 matched reference individuals	Supine cycle ergometry to voluntary exhaustion, questionnaire appraisal of perceived aerobic fitness	Maximal cycle ergometer loading reduced 9% if no resection, rising to loss of 40% if extensive bowel resection	Loss of aerobic power greater than loss of lean tissue; patients unaware of loss of aerobic power unless extensive resection
D'Inca et al. [17,18]	6 cases of CD, 6 controls	Treadmill	Lower maximal oxygen intake in CD	
Ojerskog et al. [50]	29 UC, 1 CD, 1 familial polyposis before & after construction of continent ileostomy	Interview by psychiatrist	6/31 had reduction of working capacity with conventional ileostomy	13/27 had greater working capacity after continent ileostomy – fewer toilet visits, able to dress more freely
Zaltman et al. [74]	23 women with UC, 23 matched controls	4-m gait speed	UC 17% slower gait than controls	Habitual physical activity & greater grip strength protect against slowing of gait

CD = Crohn's disease; CIBD = chronic inflammatory bowel disease; ns = non-significant; UC = ulcerative colitis

Muscular strength, muscular endurance and bone development

7 groups of investigators [8,24,25,65,67,70,72,74] have looked at various aspects of muscular function in CIBD (▶ **Table 4**). As might be anticipated from the low levels of habitual physical activity and loss of lean tissue mass, all 7 studies found some decreases of strength, although the adversely affected muscle groups varied from one study to another. A low lean tissue mass was seen even during remission of CD [24,25]. The strength impairment correlated with self-reported fatigue [67], and in some [65,70] but not all reports [72] was also correlated with the low lean tissue mass.

The reduced muscular cross-section in CIBD was typically associated with a low thickness of cortical bone and a reduced trabecular bone density [20,69]. As many as 60% of patients with Crohn's disease are sarcopaenic, 30–40% of patients with Crohn's disease also develop osteopaenia, and 15% show osteoporosis, thus doubling the risk of fractures [1,6,39]. In those with osteoporosis, the prevalence of vertebral fracture was 22%, even in patients under the age of 30 years [35]. In the 143 cases of IBD studied by Bechtold et al. [3], bone disease was thought secondary to muscle wasting. However, the problem is probably multifactorial, reflecting among other issues the inflammatory process itself, a poor absorption of nutrients, the frequent use of corticosteroids, and a lack of physical activity. One formal study of 120 patients, based on a self-reported 7-level classification of habitual physical activity, found no significant relationship between this measure of activity and bone density [55]; however, an important weakness in this report was that observers did not classify the reported physical activity in terms of the impact stimulus that it delivered to the bones

Bone parameters generally seem to be enhanced along with increased muscle growth if the patient with CIBD engages in greater habitual physical activity. However, it remains unclear how far the increased physical activity is directly strengthening muscle and bone and how far both tissues are responding positively to associated improvements in nutrition, reduced levels of pro-inflammatory cytokines, and decreases in corticosteroid treatment.

Physical activity in the prevention of IBD

A recent review [4] suggested that regular physical activity might play a role in preventing the development of CIBD, possibly by increasing the production of the muscle-derived anti-inflammatory myokine interleukin (IL)-6 [51] and heat-shock proteins [52], and inhibiting the release of pro-inflammatory mediators from visceral fat. 4 of 5 published studies [11,33,36,53,59] support this hypothesis in showing an association between regular physical activity and a reduced risk of developing CIBD

Klein et al. [36] questioned habitual physical activity in recent onset cases (53 UC and 33 CD), finding a low level of activity prior to the development of clinical disease. In 3 421 972 person years of follow-up in the Nurses Health Studies [33], 284 cases of CD and 363 cases of UC were identified. For CD, the risk of developing the condition was 0.64 among the most active quintile of nurses relative to the least active, with this difference persisting after statistical adjustments for smoking habits and body mass index; however, the level of physical activity was not significantly related to the risk of developing UC. Sonnenberg [59] examined a sample of 12 014 German patients, finding a low prevalence of CIBD among those whose occupation involved vigorous physical activity in the open air (although conceivably the onset of CIBD could have caused some subjects to change their occupation). Persson and colleagues [53] carried out a case-control comparison between 145 cases of UC and 305 controls. The risk of UC was inversely related to reported physical activity, with respective risk ratios of 0.6 and 0.5 for reports of weekly and daily exercise, although again in this report the onset of UC could have modified activity patterns.

Finally, a collaborative European study that included 177 incident cases of UC and 67 cases of CD did not find any association of either condition with a 5-level questionnaire assessment of habitual physical activity, even after adjusting for BMI, total energy intake and smoking habits [11].

Acute response to exercise in CIBD

Perhaps because of low levels of physical fitness, adolescents with CD metabolize a lesser proportion of fat than healthy individuals when they are exercising at a given fraction of maximal oxygen intake [49]. However, there have been few reports of other adverse responses to an acute bout of moderate aerobic exercise in those with CIBD

D'Incà et al. [17] tested the effects of an hour of treadmill exercise at 60% of maximal oxygen intake in 6 CD patients currently in remission. This level of physical activity caused no increase in stool frequency or the passing of faecal blood; there was no change in intestinal permeability, no evidence of lipid peroxidation, and any increase in oro-caecal transit time was identical with that seen in age-matched control subjects performing similar exercise.

Table 3 Measures of lean tissue mass in patients with CIBD.

Author	Subjects	Measures	Findings	Comments
Bechtold et al. [3]	143 adolescent cases of CIBD (45 UC, 98 CD; ESPGHAN criteria), compared to anthropometry Z-scores	Anthropometry & quantitative computed tomography & DXA	Mean muscle cross-sectional area significantly reduced in CIBD (z = −1.1)	Overall stunting of growth. Reduced bone cross-section linked to reduced muscle mass; history of steroids ns effect on muscle cross-section
Boot et al. [6]	Children, 22 CD, 33 UC, unspecified controls	Dual energy x-ray absorption & bio-impedance	Lean tissue mass lower than controls, CD > UC	35/55 cases had received steroid treatment, with negative effect on bone density
Brevinge et al. [7]	29 CD patients 1 yr or more after procto-colectomy & 23 matched reference individuals	Isotopic determinations of body water, body potassium & body nitrogen	Reduced lean tissue mass accounted for 74 % of variation in maximal cycle ergometer loading	Total body N2 shows 0.76 correlation with total nitrogen
Bryant et al. [8]	137 20–50 yr-old patients with CIBD (95 CD), 57 % with active disease	Dual energy x-ray absorptiometry	21 % of patients had lean body mass > 1 SD below population norms	59 % of those with low lean mass also had low grip strength; odds ratio of sarcopaenia 2.03 if > 12 months steroids
Capristo et al. [10]	18 cases of CD, 16 cases of UC, all in remission, 20 healthy volunteers	Bio-impedance	Fat-free mass tended to be lower in CD (ns)	Fat mass lower in CD than in UC and controls; no patients receiving steroids
Dubner et al. [20]	78 cases of incident CD in children	Quantitative computed tomography	Low initial muscle cross-sectional areas (Z-score = − 0.96) improved over 12 months treatment	Low muscle values associated with impaired bone mineral density
Filippi [22]	26 M, 28 F cases of CD in remission for > 3 months, aged 18–70 yr; 25 healthy controls	Anthropometry & bio-impedance	Fat-free mass did not differ significantly from controls	30 % of patients malnourished, all receiving 5-ASA maintenance treatment
Geerling et al. [24]	18 F, 14 M with CD (long-standing disease but in remission (Van Hees Index 146), 32 healthy controls	Dual energy x-ray absorptiometry	No difference of lean tissue mass	Hamstring strength less than in controls, quadriceps strength preserved
Jahnsen et al. [29]	60 cases CD, 60 cases UC, 60 healthy controls; small bowel resection in 27 cases with CD	Dual energy x-ray absorptiometry	Lean body mass lower in CD than in UC or controls	Bone mineral content also reduced in CD; loss of LBM only in 43 cases treated with steroids
Sylvester et al. [61]	42 children with CD (exclusions prior corticosteroid treatment or presence of other inflammatory conditions)	Dual energy x-ray absorptiometry	Low fat-free mass persisted over 2-yr follow-up when 27/42 received steroid treatment	Improvements of bone mineral composition associated with gains in fat-free mass.
Tjellesen et al. [64]	13 M, 18 F adults with long-standing CD compared to population norms; all in remission and none had received corticosteroids for 2 years	Dual energy x-ray absorptiometry	Z-score for muscle mass −1.74 Muscle mass not significantly correlated with energy intake or small intestinal resection	Fat mass increased as % of body mass
Valentini et al. [65]	94 adult cases CD, 50 cases UC, all in remission (12/94, 8/50 on corticosteroids), 61 healthy controls	Anthropometry, bio-impedance	Low body cell mass in M & F; decrease of LBM in males only. In women, prolonged corticosteroids associated with low LBM.	Associated decrease of grip strength
van Langenberg et al. [66]	27 adult cases of CD (2/27 on corticosteroids, 9/27 bowel resection), 22 controls	Quantitative computed tomography	Quadriceps cross-section reduced 14 % in CD	Muscle loss associated with lower physical activity & reduced capacity to activate protein synthesis
Werkstetter et al. [69]	82 children with CD, 20 with UC	Quantitative computed tomography	Initial Z-score for muscle cross-sectional area − 1.0	Treatment with 5-ASA, glucocorticoids and TNF-α antibodies increased muscle cross-sectional area
Werkstetter et al. [70]	27children with CD, 12 with UC, in remission for > 4 weeks	Bio-impedance	Reduced Z-score for muscle mass even during remission	Associated low habitual physical activity scores
Wiroth et al. [72]	41 adult cases of CD in remission for > 3 months, 25 controls	Bio-impedance	No difference in fat-free mass with CD	Lower limb endurance improved by recent use of steroids
Wiskin et al. [73]	55 adolescent children with IBD (37 CD, 18 UC; 22 had active disease)	Anthropometric estimate of fat-free mass	Fat-free mass inversely related to disease activity in CD; numbers insufficient to analyze in UC	Children had significant growth deficits; unclear whether active disease or growth deficit contributed to deficit of FFM
Zaltman et al. [74]	23 women with UC (15/23 active disease), 23 matched controls. Corticoid treatment in 9/23	Anthropometry & bio-impedance	No significant difference of lean tissue mass in UC	Associated low levels of habitual physical activity

ASA = acetylsalicylic acid; CD = Crohn's disease; CIBD = chronic inflammatory bowel disease; FFM = fat-free mass; LBM = lean body mass; IBD = inflammatory bowel disease; ns = non-significant; TNF-α = tumour necrosis factor alpha; UC = ulcerative colitis

Ploeger et al. [54] examined the effects of 30 min of cycling at 50 % of peak aerobic power, and of four 15-s bouts of maximal cycle ergometer exercise upon inflammatory cells and cytokine levels in an uncontrolled study of 15 youth with CD. Both types of exercise increased the numbers of immune cells and growth hormone (GH) concentrations and decreased levels of insulin-like growth factor (IGF)-1 much as in control subjects. Exercise also increased levels of IL-6 and Il-17 in the patients. The IL-6 was considered as muscle-derived and anti-inflammatory. The IL-17, not normally detectable in healthy individuals, and pos-

Table 4 Measures of muscle function in CIBD.

Author	Subjects	Measurement techniques	Findings	Comments
Bryant et al. [8]	137 20–50 year-old patients with CIBD (95 CD), 57 % with active disease	Handgrip dynamometer	59 % of patients with low lean body mass had grip strength > 1 SD below population norms	Odds ratio of sarcopaenia 2.03 if > 12 months steroids
Geerling et al. [24–25]	18 F, 14 M with CD (long-standing disease but in remission)	Upper leg circumference, isokinetic dynamometer	Quadriceps strength normal, reduced hamstring strength	Hamstring strength correlated with fat-free mass only in controls
Valentini et al. [65]	94 adult cases CD, 50 cases UC, all in remission (12/94, 8/50 on corticosteroids), 61 healthy controls	Handgrip dynamometer	Handgrip decreased 9 % in CD, 14 % in UC (no sex difference)	Associated with loss of lean tissue mass, but decrease of LBM in males only
van Langenberg et al. [67].	27 adult cases of CD (2/27 on corticosteroids, 9/27 bowel resection), 22 controls	Isokinetic dynamometer	CD show greater fatigue over 30 successive isokinetic contractions of quadriceps	Findings correlated with self-reported fatigue; associated with low Mg, low Vit. D3, low IGF-1 and high IL-6
Werkstetter et al. [70]	27children with CD, 12 with UC, in remission for > 4 weeks, 39 age- & sex-matched controls	Handgrip dynamometer	Z-score for grip strength − 1.02	Related to lower habitual physical activity and reduced LBM; LBM reduced even during remission
Wiroth et al. [72]	41 adult cases of CD in remission for > 3 months, 25 controls	Lower limb extensor strength, leg endurance & sit-up tests	Scores 24–26 % lower in CD	Strength not related to measures of habitual physical activity, LBM also had normalized
Zaltman et al. [74]	23 women with UC (15/23 active disease), 23 matched controls. Corticoid treatment in 9/23	Quadriceps & grip strength, timed sit-up	Quadriceps strength −6 %, sit-up speed −32 %, handgrip force normal	Strength loss associated with reduced habitual physical activity

CD = Crohn's disease; CIBD = inflammatory bowel disease; IGF = insulin-like growth factor; IL-6 = interleukin 6; LBM = lean body mass; ns = non-significant; UC = ulcerative colitis

sibly critical to the inflammation of Crohn's disease [46], was increased after both forms of exercise.

Chronic responses to an increase of physical activity in CIBD

Pérez [52] suggested many potential areas where an increase of habitual physical activity might help the person with Crohn's disease, including gains of nutrition, a reduction of disease activity, an enhanced mood state, and an improvement of body composition with a countering of fatigue, poor physical performance and bone mineral loss.

Nutrition

Undernutrition is a frequent problem in CD. Adolescent patients often show a resulting growth retardation, with an increased resting energy expenditure and a low body mass index (BMI) relative to controls of the same age [75]. Potential causes of impaired growth include chronic corticosteroid administration, an inhibition of appetite by inflammatory cytokines, an impaired absorption of nutrients in the diseased gut, a protein-losing enteropathy, and a diversion of food energy from normal growth to disease activity. Plainly, exercise programmes could have a favourable effect upon many of these issues

Disease activity

11 human studies [9, 15, 19, 21, 23, 30, 31, 34, 41, 47, 48] have looked at the influence of moderate exercise programmes upon disease activity in CIBD (**Table 5**). All 11 investigations have reported benefit in terms of reduced disease activity, although in some cases the experimental designs were not very satisfactory. Only 5 of the 11 studies were controlled [19, 21, 30, 34, 48], the exercise intervention was often poorly defined [21, 23], and sometimes included other lifestyle elements, and the largest of the 5 randomized studies referred to patients with irritable bowel syndrome rather than CD or UC [30]. Most studies were based upon moderate aerobic activity, but one specifically used resistance training [9]. Focusing upon the 4 controlled trials of CIBD, it is clear that the condition was not worsened by exercise, but positive changes were fewer: a lessening of constipation, but not pain or diarrhoea [19], a reduction of disease activity on the IBDQ scale, but no decrease of TNF-α [21], no change of Crohn's disease indices despite an improved reported quality of life [34], and improved scores on the IBDQ and Harvey Bradshaw index [48].

Animal experiments have allowed a comparison between moderate and much more vigorous exercise programmes. Thus, a study in a mouse model of colitis compared voluntary wheel exercise with forced treadmill running (8–12 m/min, 40 min/day, 5 days/wk for 6 weeks) [14]. As in the human studies, moderate voluntary running alleviated diarrhoea, and almost completely abolished the expression of inflammatory genes in the colonic mucosa. However, forced running worsened diarrhoea, led to expression of inflammatory genes (IL-6, IL-1-β and IL-17) in the colonic tissue and increased mortality. The treadmill-running group also showed increased colonic gene expression for the chemokine CCL6, suggesting that vigorous exercise may have increased bacterial penetration of the gut wall, and thus the tendency to inflammation.

Quality of life

Patients with IBD do not always show an initial impairment of quality of life relative to controls [70], but this is commonly the case [72]. 6 studies of varying quality [15, 21, 34, 41, 47, 48] have all reported an increase in the quality of life in patients with IBD following an increase of habitual physical activity, commonly linked to functional gains.

Endocrine and Immune function

One persistent hypothesis has been that exercise benefits patients with IBD because it modulates immune function, suppressing pro-inflammatory factors and augmenting the action of anti-inflammatory mechanisms. Plainly, while moderate activity could have such an effect, very vigorous activity seems likely to increase the tendency to inflammation, particularly if eccentric exercise is involved [58]. Regular moderate physical activity certainly reduces the level of pro-inflammatory prostaglandin E2 in the intestinal mucosa [44], and Chen and Noble [12] further hypothesized that exercise would be beneficial because of

Table 5 Beneficial effects of regular physical activity in CIBD.

Author	Subjects	Methodology	Findings	Comment
Activity of disease process				
Candow et al. [9]	12 adult cases of CD, no controls	12 wks resistance training, 3/wk, 3 sets of 8–10 reps at 60–70 % 1RM, 12 exercises	Disease activity as assessed by Harley & Bradshaw scale unchanged	Increased leg press (26 %) & chest press (21 %)
Crumbock et al. [15].	17 adult cases of CD, no controls	Physical activity questionnaire, IBDQ scale of disease activity	No relationship of disease activity to PA, stress or QOL	Uncontrolled correlational study
Daley et al. [19]	56 cases of CIBD randomized to experimental & usual care groups	Two 40-min exercise consultations that focused on walking over 12-week programme increased activity on Godin scale (36.7 vs. 15.0)	Exercise reduced constipation, but no pain or diarrhoea over 12 weeks	18.3 % recruitment of patients from hospital records; effects for > 12 weeks not tested
Eisenbruch et al. [21]	30 cases of UC in remission or low activity randomized to exercise & control	IBDQ scale, moderate exercise, 1/wk for 10 wks and lifestyle intervention	Disease activity reduced on IBDQ scale, but no change in TNF-α levels	Intervention included Mediterranean diet and stress management
Fraser & Niv [23]	6 cases of CIBD, no controls	3 weeks at Dead Sea spa, IBDQ, Harvey-Bradshaw scale of disease activity	Harvey-Bradshaw index decreased from 9.0 to 3.5 over 1 week	Hyperbaric environment, Dead Sea immersion, controlled life of spa as well as advice on greater physical activity
Johannesen et al. [30]	102 cases of IBS (ROME criteria) randomized (51 experimental, 51 control)	Physiotherapist, set target of 20–60 min of moderate to vigorous exercise 3–5 days/week, contacted patients 1–2 times/month for 12 weeks	Exercised group showed fewer symptoms on overall IBS disease severity scale (–51 vs. –5)	37/51 completed exercise programme; increase in peak oxygen intake of 0.11/min
Jones et al. [31]	Prospective 6-month study, 1 308 cases of CD & 540 cases of UC initially in remission	CD activity index vs. reported physical activity on Godin index	Activity score > median associated with a lower risk ratio for reactivation of CD and UC (respective unadjusted RRs 0.72 and 0.78).	Benefit significant for CD, ns for UC
Klare et al. [34]	30 cases of mild to moderate CD randomized to exercise or control	Indices of CD activity (Crohn's Disease Activity Index & Rachmilewitz index), 10 wks moderate supervised outdoor running 3 times/wk	No significant change of Crohn's indices relative to controls, although improved health-related quality of life	Exercisers completed 24/30 sessions
Loudon et al. [41]	12 cases of CD, no controls	HBI; 12-wk walking programme, 20–35 min sessions, 3/wk, covering average of 3.5 km per session	Lessening of disease activity (Harvey-Bradshaw index) 5.9 vs. 3.6 ($p < 0.02$)	Increase of aerobic capacity as predicted by Canadian aerobic fitness stepping test
Nathan et al. [47]	10 cases of CD, 1 case UC who had self-selected exercise, no controls	Walking, 3 of 11 working up a sweat	Subjective benefit, no worsening of CIBD	3 reported severe fatigue day following excessive exercise
Ng et al. [48]	32 cases of CIBD, mild disease or in remission, randomized to walking & controls	Moderate walking (30 min, 3 times/wk, for 3 months, average distance 3.1 km/session)	Exercisers improved scores on IBDQ; and index of stress. Harvey-Bradshaw index showed significant gain in exercisers, worsening in controls	No detrimental effects of exercise noted; gains seen after 1 month of exercise
Quality of life				
Crumbock et al. [15].	17 cases of CD, no controls	Physical activity questionnaire	More active individuals showed reduced stress & enhanced quality of life	Uncontrolled correlational study
Eisenbruch et al. [21]	30 cases of UC in remission or low activity randomized to exercise & control	Moderate exercise, 1/wk for 10 wks and lifestyle intervention	Gains on mental health & psychological health axes of SF-36 questionnaire	Intervention included Mediterranean diet and stress management
Klare et al. [34]	30 cases of mild to moderate CD randomized to exercise or control	10 wks moderate supervised outdoor running 3 times/wk	Significant gain on health-related quality of life scale	No changes of body composition; Exercisers completed 24/30 sessions
Loudon et al. [41]	12 cases of CD, no controls	12-wk walking programme, 20–35 min sessions, 3/wk, covering average of 3.5 km per session	Increase of physical health, well-being and quality of life on CIBD stress index and CIBD quality of life score	7 of 12 patients reported gains on stress index
Nathan et al. [47]	10 cases of CD, 1 case UC who had self-selected exercise, no controls	Walking, 3 of 11 subjects working up a sweat	Various subjective benefits reported from exercise – "feeling good, fatigued but energized, helped with lethargy & tiredness"	All 11 patients believed exercise was beneficial
Ng et al. [48]	32 cases of CIBD, mild disease or in remission, randomized to walking & controls	Moderate walking (30 min, 3 times/wk, for 3 months, average distance 3.1 km/session)	Enhanced quality of life as measured by CIBD stress index and CIBD questionnaire	No detrimental effects of exercise noted; gains seen after 1 month of exercise
Endocrine and immune responses				
D'Inca et al. [17–18]	6 cases of CD, 6 controls	Treadmill exercise at 60 % of maximal oxygen intake	No differences in the post-exercise polymorphonuclear respiratory burst, lipoperoxidation or oxidant stress	

Table 5 Beneficial effects of regular physical activity in CIBD.

Author	Subjects	Methodology	Findings	Comment
Eisenbruch et al. [21]	30 cases of UC in remission or low activity randomized to exercise & control	Moderate exercise, 1/wk for 10 wks and lifestyle intervention	No significant changes in lymphocyte sub-set numbers or production of TNF-α relative to controls.	Intervention included Mediterranean diet and stress management
Koek et al. [37]	31 cases of CD, 24 cases of UC, moderate activity levels, no controls	Measurement of expired NO	NO increased in active CIBD, both CD & UC, correlated with disease activity scores	Suggests CIBD is systemic disease
van Langenberg et al. [67]	27 adult cases of CD (2/27 on corticosteroids, 9/27 bowel resection), 22 controls	Measurements made prior to exercise tests	Increased levels of TBARS and decreased levels of IGF-1	Patients show low IGF-1 and high IL-6

CD = Crohn's disease; HBI = Harvey-Bradshaw Index; CIBD = Inflammatory Bowel disease; IBDQ = Inflammatory bowel disease questionnaire; IBS = irritable bowel syndrome; IGF-1 = insulin-like growth factor 1; IL-6 = interleukin 6; 1RM = 1 repetition maximum; PA = physical activity; RR = risk ratio; TNF-α; tumour necrosis factor alpha; UC = ulcerative colitis

Table 6 Patient compliance with exercise programmes in CIBD.

Author	Subjects	Programme	Compliance	Comments
Candow et al. [9]	12 cases of CD, no controls	12 wks resistance training, 3/wk, 3 sets of 8–10 reps at 60–70 % 1RM, 12 exercises	Programme "well tolerated"	Increased leg press (26 %) & chest press (21 %)
Chan et al. [11]	918 cases of IBD (54 % CD, 46 % UC)	On-line survey of exercise habits	80 % of patients had to stop exercising at some point because of severity of symptoms	Exercise generally made them feel better
Daley et al. [19]	56 cases of IBD randomized to experimental & usual care groups	2 exercise consultations that focused on walking over 12 weeks	Significant increase of activity reported on leisure index scale	
D'Incà et al. [17]	6 patients in remission	Cycle ergometer exercise at 60 % of maximal oxygen intake	Exercise did not elicit symptoms	
Eisenbruch et al. [21]	30 cases of UC randomized to exercise & control	Moderate exercise, 1/wk for 10 wks	1/15 dropped out due to miscarriage	
Fraser & Niv [23]	6 cases of IBD, no controls	3 weeks at Dead Sea spa	Full compliance	
Johannesen et al. [30]	102 cases of IBS (51 experimental, 51 control)	Physiotherapist, set target of 20–60 min of moderate to vigorous exercise 3–5 days/week	37/51 completed exercise programme	Motivation encouraged by training diary and cycle ergometer testing
Klare et al. [34]	30 cases of CD randomized to exercise or control	10 wks moderate outdoor running 3 times/wk	3 drop-outs from intervention (2 poor motivation, 1 injury)	Attendance averaged 24/30 sessions, 14/15 willing to repeat programme
Loudon et al. [41]	12 cases of CD, no controls	HBI; 12-wk walking programme, 20–35 min, 3/wk, covering average of 3.5 km per session	12/16 completed programme	
Nathan et al. [47]	10 cases of CD, 1 case UC, no controls	Walking, 3 of 11 subjects working up a sweat	Patients determined their own level of exercise, no drop-outs	3 subjects reported severe fatigue day following excessive exercise
Ng et al. [48]	32 cases of IBD, mild or in remission, no controls	Moderate walking (30 min, 3 times/wk, for 3/12)	All completed trial	
Ploeger et al. [54]	15 paediatric cases of CD in remission	30 min cycling at 50 % peak power or 6 bouts of 4 × 15 s cycling at 100 % peak power	16 of 20 subjects completed exercise protocols	
Robinson et al. [55]	117 cases of CD randomized to low impact exercise or control group	12 low-impact floor exercises, 2/wk for 12 months	85 % completed programme, only 25 % followed prescribed regimen	

CD = Crohn's disease; CIBD = inflammatory bowel disease; ns = non-significant; UC = ulcerative colitis

an increased production of heat shock proteins. Another potential effect is that exercise may induce an autophagy of the cells responsible for inflammation [26].

In practice, 1 uncontrolled and 3 controlled human studies [17, 18, 21, 37, 67] have shown little exercise-induced change of endocrine or immune function other than possible increases of TBARS and expired NO under resting conditions. However, several investigators have studied exercise responses in animals, some with colitis induced by irritant chemicals, and here benefit has generally been noted. Hoffman-Goetz et al. [28] carried out a controlled study in mice; 3 bouts of sustained and vigorous treadmill running increased levels of the anti-inflammatory cytokine IL-10 and decreased levels of TNF-α in intestinal lymphocytes relative to values for control animals. Szalai et al. [62] also found evidence of benefit from recreational levels of exercise (wheel-running) in rats with TNBS-induced colitis in terms of decreased pro-inflammatory genes, the induction of anti-inflammatory mediators, and modulation of the activity of HO and NOS enzymes. A controlled study of rats with an acetic acid-induced colitis confirmed that 6 weeks of moderate exercise on a running wheel (0.4 km/h, for 30 min, 3 days/wk) reduced markers of oxidative stress, and histological damage to the colon, in association with a reduction of stress as assessed by hole-board tests [32]. Saxena et al. [57] evaluated adiponectin-deficient mice where colitis had been induced by treatment with dextran sodium sulphate; again, some benefit was seen from vigorous exercise training (treadmill running for 55 min/day on a 5% slope at 18 km/h), particularly a decrease of pro-inflammatory cytokines

Practical experience of rehabilitation programming in CIBD

Although benefits can be demonstrated from an increase of physical activity under laboratory conditions, as in many chronic disorders, poor programme adherence could attenuate these benefits in clinical rehabilitation. The interest of CIBD patients must be maximized by such measures as a consideration of goals and objectives, development of group camaraderie, and a regular feedback of information about improvements in physical condition [52]. Initial acceptance of the illness also seems important to programme compliance [68].

13 studies (▸ **Table 6**) provide data on the acceptance of exercise programmes [9, 11, 17, 19, 21, 23, 30, 34, 41, 47, 48, 54, 55]. The patient response compares quite favourably with that reported in other clinical conditions. Most investigators have introduced a moderate-intensity aerobic regimen, and typically three-quarters of patients have completed group programmes of 3 months duration. Resistance exercise at 60% of 1 repetition maximum force was also well-tolerated in one study [9]. The single report where a high proportion of patients reported difficulty in completing the required regimen involved low impact exercises designed to enhance bone strength [55].

Discussion and Conclusions

The majority of reports to date have shown that patients with CIBD have a low level of habitual physical activity relative to age- and sex-matched control groups. In some instances, this may have been a consequence of the disease process, reflecting such factors as a diarrhoea exacerbated by exercise, difficulties in managing an ileostomy, or a poor overall state of nutrition, but in other studies the disease was of recent origin or in remission, and sometimes the lack of adequate physical activity ante-dated clinical manifestations of CIBD. A low level of physical activity may thus have contributed to the development of disease, possibly through a reduced modulation of pro-inflammatory cytokines.

The low level of habitual physical activity found in most CIBD patients has an adverse effect on overall health and increases the risk of developing many other chronic diseases. It also has various immediate negative consequences, including a low level of aerobic and muscular function, a reduction of lean tissue mass and an increased fragility of bone structure. There are thus strong arguments pointing to the need for rehabilitation programmes to enhance the physical capacities of individual patients. Moderate exercise, both aerobic and resistance, improves functional capacity and the quality of life, and it can be undertaken safely in CIBD without increasing activity of the disease process or causing adverse changes in endocrine and immune function. Programmes of moderate exercise should thus become an integral component in the treatment of IBD.

In terms of future research, there is a need to confirm whether a low level of habitual physical activity contributes to the development of CIBD, and if this is the case to explore the underlying mechanisms. The apparent difference in response of animals and humans to vigorous exercise also merits examination; does this indicate that animal models are not an effective way to evaluate responses in CIBD, or could benefits similar to those seen in animals be induced if humans took an appropriate exercise programme? Finally, there is scope for much applied research to examine the effectiveness of tactics to facilitate exercise for those with exercise-induced diarrhoea; possibilities include the use of stabilizing medications such as loperamide, the relief of the anxiety that sometimes precipitates defaecation by wearing protective underwear and choosing exercise locations close to toilet facilities.

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