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Malnutrition and impaired muscle strength in patients with Crohn's disease and ulcerative colitis in remission

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Abstract

Objective: This prospective, controlled, and multicentric study evaluated nutritional status, body composition, muscle strength, and quality of life in patients with inflammatory bowel disease in clinical remission. In addition, possible effects of gender, malnutrition, inflammation, and previous prednisolone therapy were investigated.

Methods: Nutritional status (subjective global assessment [SGA], body mass index, albumin, trace elements), body composition (bioelectrical impedance analysis, anthropometry), handgrip strength, and quality of life were assessed in 94 patients with Crohn's disease (CD; 61 female and 33 male, Crohn's Disease Activity Index 71 ± 47), 50 patients with ulcerative colitis (UC; 33 female and 17 male, Ulcerative Colitis Activity Index 3.1 ± 1.5), and 61 healthy control subjects (41 female and 20 male) from centers in Berlin, Vienna, and Bari. For further analysis of body composition, 47 well-nourished patients with inflammatory bowel disease were pair-matched by body mass index, sex, and age to healthy controls. Data are presented as median (25th–75th percentile).

Results: Most patients with inflammatory bowel disease (74%) were well nourished according to the SGA, body mass index, and serum albumin. However, body composition analysis demonstrated a decrease in body cell mass (BCM) in patients with CD (23.1 kg, 20.8–28.7, $P = 0.021$) and UC (22.6 kg, 21.0–28.0, $P = 0.041$) compared with controls (25.0 kg, 22.0–32.5). Handgrip strength correlated with BCM ($r = 0.703$, $P = 0.001$) and was decreased in patients with CD (32.8 kg, 26.0–41.1, $P = 0.005$) and UC (31.0 kg, 27.3–37.8, $P = 0.001$) compared with controls (36.0 kg, 31.0–52.0). The alterations were seen even in patients classified as well nourished. BCM was lower in patients with moderately increased serum C-reactive protein levels compared with patients with normal levels.

Conclusion: In CD and UC, selected micronutrient deficits and loss of BCM and muscle strength are frequent in remission and cannot be detected by standard malnutrition screening.

Keywords: Inflammatory bowel disease; Malnutrition; Body composition; Nutritional status; Quality of life; Muscle function; Gender specific

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Introduction

Nutritional status and body composition of patients with inflammatory bowel disease (IBD) in clinical remission are not adequately investigated, making it difficult for health professionals to find algorithms for adequate nutritional care.

For instance, it is generally believed that Crohn's disease (CD) causes more disturbances in nutritional status and body composition than ulcerative colitis (UC). But so far only three studies have evaluated patients with CD and UC at the same time [1–3] and these alterations occur mainly in those with UC [2]. The majority of studies were done only in patients with CD and most of them demonstrated decreased parameters of metabolically active tissue, such as lean body mass [3–5], midarm muscle circumference [6], or appendicular muscle mass [7]. But some investigators have concluded that lean body mass is normal [1,8] or even increased [2]. In addition, three studies have indicated that nutritional status is affected more in men than in women [2,3,9], whereas two other studies found no gender-related differences [5,6]. Results for muscle function and endurance also have varied from reduced [6,9,10] to normal [2] as compared with healthy controls.

These inconsistencies may have many reasons including a different degree of malnutrition in the study population or differences in the extent and duration of disease. However, four of the nine studies cited [2,3,6,9] included up to 33% of patients with active disease, which might also have influenced the results.

Malnutrition is a known challenge for patients with IBD. To identify malnutrition in clinical practice, routine nutritional screening and assessment using simple tools such as the subjective global assessment (SGA) [11] or nutritional risk screening [12] have been recommended for all patients. However, up to the present, it is not clear whether the use of such tools is also meaningful for patients with IBD in remission.

To answer the still open question of whether patients with CD and those with UC in remission do have changes in nutritional status, body composition, and muscle function, we performed a prospective, controlled, and multicenter study comparing patients with IBD with quiescent disease with healthy controls. In addition, we pair-matched a subgroup of well-nourished patients with no actual prednisolone intake by body mass index (BMI), sex, and age to healthy controls. This was done to differentiate between the acute effects of malnutrition or actual prednisolone therapy and the persistent effects of a chronic inflammatory disease. Furthermore, associations to inflammation and previous prednisolone therapy were investigated.

Materials and methods

Subjects

The study protocol was approved by the ethics committee of the Charité Universitätsmedizin Berlin and all subjects gave their informed consent before the start of the study.

Patients

In total, 144 patients with IBD in clinical remission (CD: $n = 94$, 37.7 ± 11.3 y of age; UC: $n = 50$, 42.8 ± 14.6 y of age) between 18 and 70 y of age were recruited in three centers (Berlin, Germany, $n = 113$; Vienna, Austria, $n = 23$; Bari, Italy, $n = 8$) from September 2004 to February 2006.

Remission was defined as a Crohn's Disease Activity Index (CDAI) <150 [13,14] or an Ulcerative Colitis Activity Index (CAI) <5 [15]. The CDAI and CAI are accepted gold standards for the assessment of disease activity in patients with CD and UC, respectively.

Disease duration ranged from 7.8 y (3.2–13.8) in CD to 9.0 y (5.5–14.5) in UC. Additional clinical data of the patients are presented in Table 1. The diagnosis and extent of disease were confirmed by standard criteria. Exclusion criteria were severe concomitant diseases, pregnancy, ostomy, deliberate adherence to an extreme diet (e.g., macrobiotics, vegan), celiac disease, proctitis, or proctosigmoiditis in UC and extensive small bowel resections in CD. Actual maintenance medication was recorded in all patients. Twenty-six patients took multivitamins and 15 patients were supplemented with intramuscular vitamin B12. A 5-y

Table 1
Patient characteristics

	CD ($n = 94$)	UC ($n = 50$)
Disease location and surgery (%)		
CD: terminal ileum	85	
CD: jejunum /Ileum	26	
CD: colon	88	
CD: upper gastrointestinal tract	38	
UC: pancolitis		54
UC: distal colitis		46
No. with bowel resection	38	3
Current disease-related medication (%)*		
5-Aminosalicylic acid	51	82
Immunosuppressants†	36	24
Prednisolone	12	8
Topical budesonide	16	10
No medication	19	10
Smoking (%)		
Never smoked	48	48
Stopped smoking	32	11
Active smoker	20	41
Prednisolone therapy in previous 5 y (%)	64	65
5-y prednisolone dose (g),‡ median (interquartile range)	2.4 (1.5–3.7)	2.9 (1.4–4.3)

CD, Crohn's disease; UC, ulcerative colitis

* Multiple answers possible.

† Total non-steroid immunosuppressants (azathioprine, methotrexate, and infliximab).

‡ Cumulative dose of prednisolone in the previous 5 y of all patients who had received prednisolone in previous 5 y.

history of glucocorticosteroid intake was available from 95 patients in the Berlin center.

Pair-matched analysis involved a subgroup of 47 well-nourished patients with IBD being in remission for at least 3 mo (41 female and 6 male, 30 with CD, 17 with UC). Well nourished was defined as an SGA grade A [11], a BMI within the normal range, and a serum albumin level >40 mg/L.

Controls

Sixty-one healthy controls were recruited by intranet announcement at the Charité Universitätsmedizin. Of these, 47 could be pair-matched to a corresponding patients with IBD according to BMI (±0.3 kg/m^2), age (±5 y), and sex. Health was defined as no acute or chronic disease, no intake of acute or chronic medication, and all standard routine blood parameters within the normal range at the time of assessment. Exclusion criteria consisted of not achieving at least one health criterion.

Methods

Nutritional status.

Nutritional status and malnutrition-associated risk were assessed by trained investigators using BMI, SGA [11], and serum albumin. Height and weight of the patients and controls were measured on the day of assessment, and their BMI was calculated as weight (kilograms) divided by squared height (meters). SGA refers to the overall evaluation of a patient by an experienced clinician. Review of the medical history includes assessment of weight and weight change, dietary intake, gastrointestinal symptoms, disease state, and a patient's functional status. SGA also includes a physical examination for negative changes in body composition such as loss of subcutaneous fat or muscle wasting and signs of edema or ascites (nutrition related). After evaluation, the patient is classified as well nourished (grade A), mild to moderately malnourished (grade B), or severely malnourished (grade C). A BMI <18.5 kg/m^2, SGA-B or SGA-C, or a serum albumin level <40 g/L indicated malnutrition, respectively.

Biochemical parameters.

A venous blood sample (50 mL) was obtained in patients and controls after an overnight fast and analyzed in the routine laboratory for C-reactive protein (CRP), blood count, albumin, total protein, cholesterol, erythrocytes, ferritin, hemoglobin, magnesium, selenium, zinc, vitamin B12, and folate levels. Interleukin-6 (IL-6) was determined with an enzyme immunoassay technique (Lincoplex, St. Charles, Missouri, USA).

Body composition.

Body composition was assessed using anthropometry and bioelectrical impedance analysis (BIA).

Anthropometric measurements were made in patients and controls at the non-dominant arm using a skinfold caliper (Holtain, Crymych, United Kingdom) and a flexible tape measure to calculate arm muscle area and arm fat area [16]. Midarm circumference was measured using a tape at the midpoint between the acromion and olecranon processes.

Bioelectrical impedance analysis was performed in patients and controls as described elsewhere [17] using a BIA 2000-M analyzer (Data Input, Darmstadt, Germany) applying an alternating electrical current of 800 μA at 50 kHz to measure resistance, reactance, and phase angle α. Body cell mass (BCM) was calculated as BCM_{BIA} = fat-free mass × 0.29 ×ln(α) [18] using the formulae for fat-free mass as total body water/0.732 and total body water = 0.69 × height^2/resistance +0.8 [19]. Measurements were taken in subjects after a 12-h overnight fast, voiding of the urine bladder, and lying in a supine position for 15 min.

Food intake.

Food intake was analyzed in patients and controls by using a food-frequency questionnaire adapted to German eating habits. It contains 67 food items and the subjects were asked to indicate the frequency of intake for each item (0 point, never; 1 point, rarely to once a month; 2 points, once a week to every second week; 3 points, several times a week to daily). The food items were summarized into eight food groups for analysis (meat, fish, milk products, non-sweet carbohydrates, fruits and vegetables, sweets, fast food, alcohol, oils and fats).

Muscle strength.

Handgrip strength was evaluated in patients and controls using the Jamar vigorimeter (Preston, Jackson, MI, USA). The subjects performed the test while sitting comfortably with the shoulder adducted and neutrally rotated, the elbow supported on a table and flexed to 90 degrees, and the forearm and wrist in neutral position. The subjects were instructed to perform a maximal contraction of the dominant hand. The test was repeated three times in an interval of 45 s and the highest value was recorded.

Quality of life.

Differences in qualities of life between patients and controls were assessed by comparing 11 non–disease-specific questions of the German version of the Inflammatory Bowel Disease Questionnaire [16].

Fecal calprotectin.

Seventy patients and 19 controls provided a fecal sample within 1 wk after the assessment. Fecal calprotectin, a non-invasive marker for intestinal inflammation, was analyzed using about 100 mg of stool with a monoclonal enzyme-linked immunosorbent assay technique (Calprotectin, mRP8-14, Immundiagnostik AG, Bensheim, Germany). Reference values given by the manufacturer are <15 mg/L including a borderline area of 10–15 mg/L.

Table 2
Gender-related analysis of nutritional status in all patients*

	CD	*P* CD vs UC	UC	*P* UC vs CON	CON	*P* CD vs CON
Women	61		33		41	
Well nourished (SGA, BMI, albumin)	48 (78.7%)	0.069†	20 (60.6%)		41 (100.0%)	
SGA grade A: well nourished	56 (92.0%)	0.066†	25 (76%)		41 (100.0%)	
Weight loss >5% in previous 3 mo	1 (1.6%)		5 (15.2%)		0 (0.0%)	
Albumin (<40 g/L)	4 (6.4%)		4 (12.3%)		0 (0.0%)	
Magnesium (<0.75 mmol/L)	19 (30.4%)		8 (24.2%)		4 (10.3%)	
Selenium (<0.89μmol/L)	33 (52.8%)		14 (42.4%)		14 (32.2%)	
Zinc (<10.1 μmol/L)	3 (4.8%)		0 (0.0%)		0 (0.0%)	
Folic acid (<2.8 μg/L)	0 (0.0%)		0 (0.0%)		0 (0.0%)	
Vitamin B12 (<199 ng/L)	4 (6.4%)		1 (3.0%)		0 (0.0%)	
Hemoglobin (<120 g/L)	9 (14.8%)		4 (12.1%)		0 (0.0%)	
Ferritin (<10 μg/L)	6 (9.8%)		1 (3.0%)		2 (2.9%)	
Men	33		17		20	
Well-nourished (SGA, BMI, albumin)	23 (69.7%)		12 (70.6%)		20 (100.0%)	
SGA: well nourished	30 (91.0%)		16 (94.0%)		20 (100.0%)	
Weight loss >5% in previous 3 mo	3 (9.1%)		1 (5.9%)		0 (0.0%)	
Albumin (<40 g/L)	6 (18.2%)		1 (5.9%)		0 (0.0%)	0.032‡
Magnesium (<0.75 mmol/L)	8 (24.2%)		3 (17.7%)	0.033‡	0 (0.0%)	
Selenium (<0.89μmol/L)	25 (77.3%)	0.01‡	6 (35.4%)		5 (25.0%)	0.001‡
Zinc (<10.1 μmol/L)	1 (3.0%)		1 (5.9%)		0 (0.0%)	
Folic acid (<2.8 μg/L)	1 (3.0%)		1 (5.9%)		0 (0.0%)	
Vitamin B12 (<199 ng/L)	5 (15.2%)		3 (17.7%)		0 (0.0%)	
Hemoglobin (<120 g/L)	2 (6.1%)		3 (17.7%)	0.036‡	0 (0.0%)	
Ferritin (<10 μg/L)	7 (21.2%)		3 (17.7%)		0 (0.0%)	0.096‡

BMI, body mass index; CD, Crohn's disease; CON, control; SGA, subjective global assessment; UC, ulcerative colitis
* Results are expressed as numbers of patients (percentages).
† Significances calculated with the chi-square test.
‡ Significances calculated with the Mann-Whitney U test.

Statistical analysis

We used SPSS 12.0 for Windows (SPSS, Inc., Chicago IL, USA) for all statistical analyses. Results were considered statistically different at $P < 0.05$ and data are expressed as mean ± SD or median (25th–75th percentile). The Kolmogorov-Smirnoff test was used to evaluate the normal distribution of datasets. Differences in body composition and nutritional status among patients from Berlin, Vienna, and Bari and among patients with CD, patients with UC, and healthy controls were analyzed with univariate analysis of variance. Pair-matched samples were analyzed with Wilcoxon's test. When non–pair-matched analyses were performed, the Mann-Whitney U test or chi-square test was used to analyze differences between groups. Correlations were calculated using Spearman's rank-order correlation coefficient.

According to detailed statistical analyses (analysis of variance) there was no difference in nutritional status and body composition among the three centers. All calculations were therefore performed in the combined group.

Results

Nutritional assessment

In total, 23.7% ($n = 22$) of patients with CD and 33.3% ($n = 16$) of patients with UC showed signs of malnutrition according to SGA, BMI, and plasma albumin values (Table 2). Female patients with UC seemed to be more severely affected but the difference was not statistically relevant.

When average group values for biochemical nutrition markers were compared, male but not female patients with IBD showed some impairment for selected parameters. When depicted as a percentage of individuals with values below the reference range, however, it was revealed that a considerable number of individuals, even healthy controls, had compromised values in some parameters (Table 2). All well-nourished patients had normal albumin, total protein, zinc, and folate levels, but selenium, magnesium, B12, and ferritin levels remained affected in a significant number of patients.

Body composition

We used anthropometry and BIA to assess BCM and fat mass and found good correlations between arm muscle area and lean body mass ($R = 0.606$, $P < 0.001$) or between arm fat area and fat mass ($R = .633$, $P < 0.001$), and only BIA results are presented in the rest of this report.

Analysis of body composition demonstrated a significantly decreased BCM in all patient groups, but lean body mass was affected only in male patients (Table 3). In female patients, an increased ratio between extracellular mass and BCM indicated increased extracellular water content and/or decreased BCM.

Table 3
Gender-related analysis of body composition in all patients*

	CD	*P* CD vs UC	UC	*P* UC vs CON	CON	*P* CD vs CON
Women (*n*)	61		33		41	
Age	39 (29–47)		42 (34–55)		40 (29–48)	
Body height (cm)	166 (160–171)		164 (162–170)		168 (161–173)	
Body weight (kg)	63.0 (55.0–69.0)		66.2 (56.2–76.5)		61.9 (55.0–66.6)	
BMI (kg/m^2)	22.1 (20.3–25.1)		24.3 (21.3–27.4)		21.8 (20.6–24.1)	
LBM (kg)	43.9 (39.9–46.6)		43.8 (41.0–47.0)		44.1 (42.5–48.1)	
BCM (kg)	21.5 (19.9–23.6)		21.9 (19.6–22.9)	0.029	22.9 (21.1–25.0)	0.024
FM (kg)	18.1 (14.7–24.4)		21.8 (15.4–28.3)		16.6 (14.1–19.9)	
TBW	32.2 (29.3–34.1)		32.1 (30.0–34.4)		32.3 (31.1–35.2)	
ECM/BCM index	1.02 (0.94–1.12)		1.02 (0.97–1.09)	0.008	0.96 (0.86–1.03)	0.007
Men (*n*)	33		17		20	
Age	36 (29–45)	0.026	54 (31–68)	0.036	35 (27–43)	
Body height (cm)	177 (173–184)		175 (171–180)		184 (180–188)	
Body weight (kg)	72.0 (63.9–84.4)		73.2 (68.6–85.3)		79.3 (73.4–89.1)	
BMI (kg/m^2)	22.3 (20.4–25.8)		24.5 (21.7–28.5)		23.7 (21.5–26.4)	
LBM (kg)	58.5 (53.5–61.5)		59.2 (54.8–62.8)	0.008	67.5 (60.1–70.5)	<0.001
BCM (kg)	30.2 (27.4–33.6)		31.5 (27.3–33.9)	0.002	36.0 (32.4–39.2)	<0.001
FM (kg)	12.7 (11.3–19.7)		15.3 (9.9–23.3)		15.2 (11.3–19.2)	
TBW	42.8 (39.1–45.1)		43.2 (40.1–46.0)	0.008	49.4 (43.9–51.6)	<0.001
ECM/BCM index	0.88 (0.82–0.95)		0.91 (0.81–1.04)	0.041	0.83 (0.76–0.92)	

BCM, body cell mass; BMI, body mass index; CD, Crohn's disease; CON, control; ECM, extracellular mass; FM, fat mass; LBM, lean body mass; TBW, total body water; UC, ulcerative colitis

* Results are expressed as median (25th–75th percentile); significances were calculated with the Mann-Whitney U test.

The features of malnutrition were different in patients with CD and those with UC. In malnourished patients with CD, BMI ($P = 0.036$) and fat mass ($P = 0.073$) were decreased, whereas BCM remained unaffected as compared with well-nourished patients with CD. However, malnourished patients with UC showed lower BCM ($P = 0.044$) and higher CRP ($P = 0.025$) values, whereas BMI and fat mass were similar as compared with well-nourished patients with UC.

The BMI pair-matching of well-nourished patients with no current prednisolone intake showed that derangements in body composition persisted even in the absence of obvious malnutrition (Table 4). Parameters of metabolically active mass, i.e., lean body mass and BCM, were decreased and fat mass increased. Although only trends for increased fat mass were seen in patients with CD, in the combined IBD group the difference became statistically relevant ($P = 0.012$). These results reflect a similar shift in body composition with decreased metabolically active mass and increased fat mass in patients with CD and those with UC.

Changes in body composition were not associated with location and duration of disease, current disease activity (CDAI, CAI), intestinal resections, and quality of life.

Table 4
Pair-matched analysis of patients with no nutritional risk and no actual intake of prednisolone*

	CD			UC			CD vs UC
	Patients	*P*	Controls	Patients	*P*	Controls	
General							
Number	30		30	17		17	
Age (y)	35 (26–43)		33 (26–42)	39 (27–49)		39 (28–52)	
Female (%)	86.7		86.7	88.2		88.2	
Body height (cm)	168 (162–174)		170 (166–175)	165 (163–171)		166 (160–175)	
Body weight (kg)	63.5 (54.8–67.3)		62.2 (56.9–71.2)	65.1 (57.8–67.9)		63.4 (58.3–69.4)	
BMI (kg/m^2)	22.0 (20.2–23.7)		21.8 (20.2–23.7)	23.1 (21.1–24.6)		23.3 (21.2–24.8)	
LBM (kg)	43.9 (39.5–46.6)	0.005	45.8 (42.3–48.4)	43.1 (40.8–46.8)	0.039	44.9 (42.6–52.3)	
BCM (kg)	21.4 (19.6–23.4)	0.001	23.0 (21.2–25.8)	22.3 (19.6–22.8)	0.011	23.6 (21.8–26.6)	
FM (kg)	17.5 (14.7–21.5)		15.1 (13.5–20.1)	19.0 (15.2–22.0)	0.032	14.8 (13.8–18.4)	
TBW	32.2 (28.8–34.1)	0.005	33.5 (31.0–35.5)	31.6 (29.9–34.3)	0.039	32.9 (31.2–38.3)	
ECM/BCM ratio	1.00 (0.93–1.07)	0.057	0.94 (0.87–1.04)	1.02 (0.97–1.08)	0.049	0.98 (0.84–1.02)	

BCM, body cell mass; BMI, body mass index; CD, Crohn's disease; ECM, extracellular mass; FM, fat mass; LBM, lean body mass; TBW, total body water; UC, ulcerative colitis

* Results are expressed as median (25th–75th percentile); significances calculated with Wilcoxon's test for pair-matched samples.

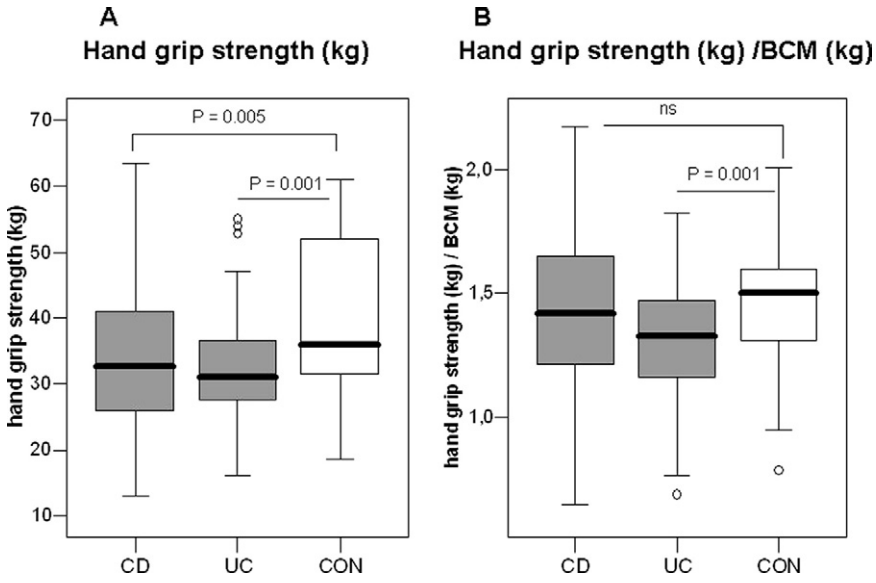

Fig. 1. Handgrip strength (A) and handgrip strength related to BCM (B) in 94 patients with CD and 50 patients with UC compared with 61 healthy controls. BCM, body cell mass; CD, Crohn's disease; CON, control; UC, ulcerative colitis.

Food intake

Food-frequency analysis resulted in a significantly lower intake of fruits and vegetables ($P < 0.001$), milk products ($P < 0.001$), fish ($P = 0.008$), and alcoholic drinks ($P < 0.001$) in patients with CU and those with CD as compared with controls. In contrast, intakes of meat, sweets, snacks, fast food, and oils/fat were comparable among all groups.

Muscle strength

Handgrip strength was significantly decreased in patients with CD and those with UC as compared with controls (Fig. 1A), with no gender-related differences seen. When relating handgrip strength to BCM (Fig. 1B), values were still lower in patients with UC but not in those with CD, which indicates compromised muscle function in those with UC. Handgrip strength remained decreased in well-nourished patients, but the ratio of handgrip strength to BCM was normal in both patient groups.

Quality of life

Quality of life was significantly decreased in patients with CD (58 points, 49.0–70.0, $P < 0.05$) and those with UC (57 points, 46.0–70.0, $P < 0.05$) as compared with controls (66 points, 61.0–75.0), and detailed analyses showed that the decrease was due to a compromised status in eight questions related to the extent of fatigue, frustration, impatience, restlessness, depression, relaxation, sleeplessness, and satisfaction with life. Interestingly, patients with IBD did not have more problems maintaining or achieving their desired weight than controls, and when weight problems were recorded, most often patients alluded to undesired weight gains.

Quality of life was associated with disease activity in patients with CD (CDAI, $r = -0.286$, $P = 0.018$) and those with UC (CAI, $r = -0.551$, $P < 0.001$), but not with any other parameter of nutritional status or body composition.

Association between body composition and inflammatory activity

Levels of CRP and IL-6 were normal in 76%, 86%, and 83% of patients, respectively (Fig. 2). In contrast, fecal calprotectin, a parameter of local intestinal inflammation, was elevated in 60.6% of patients, with comparable values for patients with CD and those with UC (CD 19.4 mg/L, 5.8–37.3; UC 17.3 mg/L, 0.8–40.1; controls 0 mg/L, 0–0, $P < 0.001$).

Patients with supranormal CRP values (≥8 mg/L) showed a significantly decreased BCM than did patients with normal CRP values (Fig. 3). IL-6 and calprotectin were not associated with changes in body composition in our patients.

Association between body composition and previous prednisolone therapy

To elucidate the possible long-term effects of prednisolone therapy on body composition, we compared BCMs of 96 patients (68 female and 28 male) who had received <1 g of prednisolone during the previous 5 y with those who received ≥1 g. BMI was similar in both groups (22.8 kg/m^2, 20.7–25.9, versus 22.7 kg/m^2, 20.2–25.8, $P = 0.786$). This analysis revealed a significant decrease in BCM in women with >1 g of prednisolone in the previous

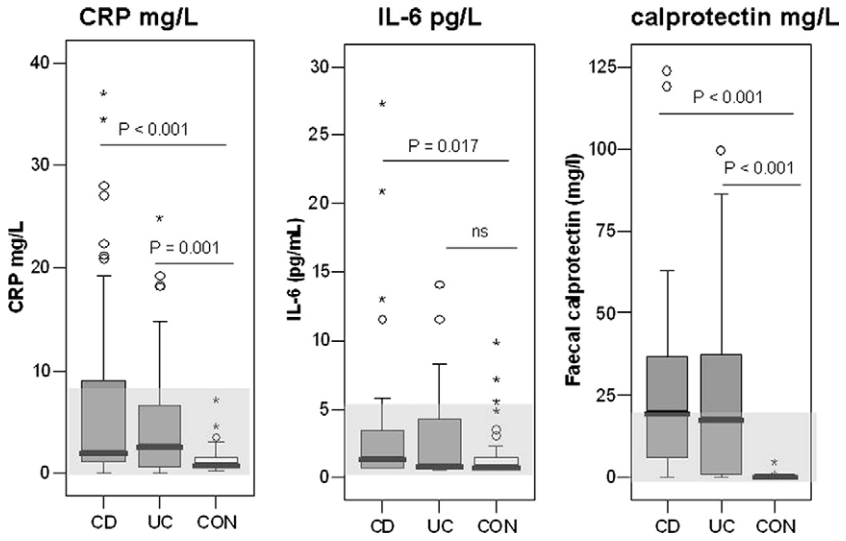

Fig. 2. Inflammatory status of patients with CD in remission ($n = 94$), patients with UC in remission ($n = 50$), and controls ($n = 50$). One CRP value is not shown in the CD group (58 mg/L), and two IL-6 values are not shown (CD 1 × 62.39, UC 1 × 48.47). Gray areas indicate normal range. CD, Crohn's disease; CON, control; CRP, C-reactive protein; IL-6, interleukin-6; UC, ulcerative colitis.

5 y (32.9% body weight, 29.5–35.0) as compared with those with <1 g of prednisolone (34.6% body weight, 32.6–37.0, $P = 0.015$). Interestingly, this effect could not be seen in men (42.7% body weight, 37.5–46.8, versus 43.5% body weight, 39.6–46.4, $P = 0.451$). In addition, only in women was BCM negatively correlated with cumulative prednisolone dose (Spearman's $\varphi = -0.318$, $P = 0.011$, in women versus $\varphi = 0.011$, $P = 0.957$, in men).

Discussion

In this prospective, controlled, and multicenter study we evaluated nutritional status, body composition, muscle strength, food intake, and quality of life in 144 patients with IBD in clinical remission and found decreased BCM, impaired handgrip strength, and selected micronutrient deficits in patients with CD and those with UC that persisted even in patients who were seemingly well nourished according to standard malnutrition assessments. The results were similar in all three centers from Austria, Germany, and Italy. In general, as pointed out by Jahnsen et al. [3] and Geerling et al. [2,9], male patients seemed to be more affected. However, our results clearly show that nutritional deficits occur in patients with CD and those with UC to a similar degree.

Three previous studies analyzed body composition and nutritional status in patients with CD and those with UC simultaneously and found conflicting results. Jahnsen et al.

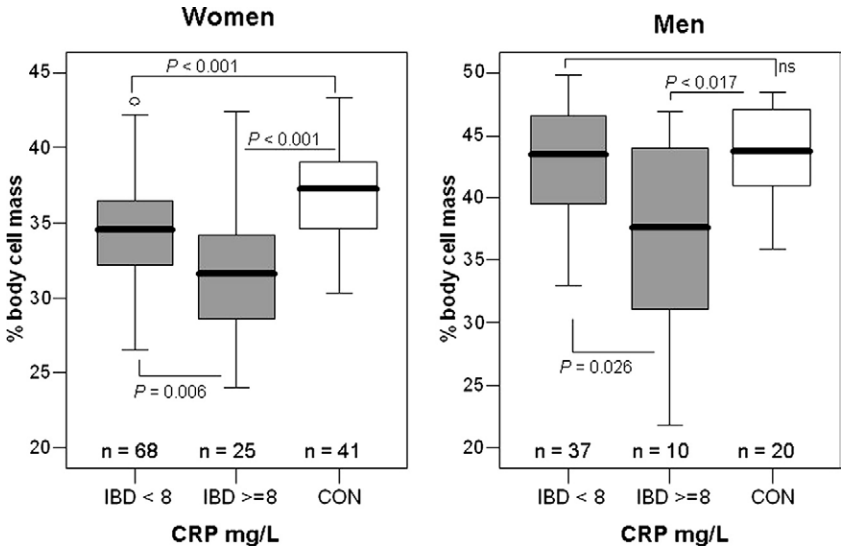

Fig. 3. Body cell mass is lower in patients with serum CRP values above the normal range, although the increases were unremarkable. Only one female patient with ulcerative colitis had a CRP value >40 mg/L. CON, control; CRP, C-reactive protein; IBD, inflammatory bowel disease.

[3] used dual-energy X-ray absorptiometry in 120 patients with IBD and concluded that body composition and nutritional status are compromised in patients with CD but not in those with UC. Capristo et al. [1] examined body composition in a probably too small sample of 18 patients with CD and 16 patients with UC using BIA and found decreased body weight and fat mass in patients with CD but not in those with UC. In contrast, Geerling et al. [2] found a deterioration of body composition mainly in male patients with UC, whereas body composition in those with CD was largely normal. Jahnsen et al. [3] included 40% of patients with UC and proctitis or proctosigmoiditis, i.e., mild forms of the disease with involvement of the rectum and sigmoid colon only. Thus they might have missed some patients with compromised nutritional status. We deliberately excluded such patients in our study, because we did not expect any effects on nutritional status or body composition in this group. We found similar alterations in body composition and nutritional status in patients with CD and those with UC. However, when we compared malnourished patients with IBD with well-nourished patients with IBD, the features of malnutrition were different in the two disease entities. In patients with CD malnutrition was mainly associated with loss of BMI and fat mass, probably due to increased malabsorption problems, whereas malnourished patients with UC predominantly showed a decreased BCM without any effects on BMI but accompanied by a further deterioration of muscle function.

To identify patients at nutritional risk, routine malnutrition screening using rapid and simple tools is generally recommended in all patients by the European Society of Clinical Nutrition and Metabolism [12,20] and many other national and international nutrition societies. To date it is unclear whether such tools are meaningful for patients with IBD in remission. So far only one group used a nutritional screening tool in quiescent IBD [4], reporting a low prevalence of malnutrition in patients with CD (6.3%). We used the combination of the SGA, BMI, and serum albumin to identify malnourished patients and found signs of predominantly mild to moderate malnutrition in 24% and 36% of patients with CD and UC, respectively. Although malnourished patients seemed more prone to macronutrient deficits than well-nourished patients, malnutrition screening was not adequately able to detect micronutrients deficits, low BCM, or compromised muscle strength.

Largely normal average IBD group values for biochemical nutritional markers obscured the fact that a significant number of patients had values below the reference range and that even healthy control subjects, despite careful recruitment, had suboptimal levels for some parameters. Particularly noticeable is the large number of healthy controls with compromised selenium values, reflecting the known problem of selenium deficiency in the general populations of Germany and Austria [21]. Because selenium is a potent antioxidant, supplementation in patients with IBD should at least be discussed. Two other recent publications [8,22] also have reported deficiencies of several other micronutrients independent of type and activity of disease in patients with IBD in remission.

We also evaluated possible mechanisms responsible for the decrease of BCM seen in our patients. Increased inflammatory parameters, such as CRP or IL-6, are known to aggravate sarcopenia in elderly individuals [23,24], but comparable longitudinal investigations in patients with chronic inflammatory diseases are lacking. We observed a decreased BCM in patients with CRP values above the normal range as compared with patients with normal CRP values, although the increases were mild and would normally be considered unremarkable in clinical practice (only one patient had a CRP value >40 mg/L). Our model does not allow distinguishing whether the decrease was the result of short-term or long-term exposure of supranormal CRP values. Surprisingly, fecal calprotectin, a measurement of intestinal inflammation, did not show any association to body composition in our patients.

Interestingly, previous prednisolone treatment was associated with a decrease in BCM in female patients, which persisted even after prednisolone withdrawal. Changes in body composition during systemic glucocorticosteroid treatment have been described previously [25–27]. However, apart from osteoporosis, such a persistent side effect of previous prednisolone therapy on body composition has not yet been reported. Use of glucocorticosteroids also reflects increased disease severity, and further research is necessary to determine whether the observed effect is the direct effect of prednisolone alone or the effect of a greater cumulative inflammatory burden.

Unfortunately, no information was available on physical activity in our patients or healthy subjects. However, it is reasonable to assume that patients with IBD are less physically active than healthy subjects because of several factors connected with their disease. Lesser physical activity could therefore have contributed to our findings. Physical exercise may improve muscle strength and body composition.

Conclusions

Our study showed that, in contrast to previous investigations, patients with CD and those with UC in remission show similar degrees of malnutrition and changes in body composition. Caretakers should be aware that micronutrient deficiencies, low BCM, and compromised muscle strength cannot be detected by standard malnutrition screening and assessment. We agree with Vagianos et al. [22] that multivitamin supplementation is warranted in quiescent IBD. In addition, eating habits in our patients were suboptimal and could be improved without harming the natural restrictions caused by the disease, and patients should be encouraged to increase their physical activity. Quality of life was associated with disease activity but not with malnutrition or body composition in patients with CD and those with UC in

remission. Future nutritional concepts for patients with IBD in remission should therefore include strategies for disease modification, e.g., through involvement of immune-modifying substances, rather than focusing on prevention and treatment of malnutrition alone.

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