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ORIGINAL ARTICLE

# Muscle Performance in Patients with Crohn's Disease in Clinical Remission

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**Background:** Because patients with Crohn's disease (CD) often show increased energy expenditure, nutritional deficiencies, and general fatigue, all which may persist after a flare, we hypothesized that CD could alter muscle mass and function. This study aimed to assess muscle strength and endurance in CD patients in clinical remission and the influencing factors.

**Methods:** Forty-one outpatients (17 men and 24 women; age, 37 ± 10 yr), in remission (CD Activity Index < 150) for >3 months, and 25 age-matched healthy controls (10 men and 15 women; age, 37 ± 13 yr) were evaluated. Evaluation included a sit-up test, hand-grip strength test, hand-grip endurance test, lower limb strength test, and lower limb endurance test (LE), as well as a measure of physical activity.

**Results:** No significant difference was found between CD and control groups regarding weight, height, body mass index, fat mass, and fat-free mass. Strength performance was lower in CD subjects compared with controls, particularly for lower limb indexes: lower limb strength test (−24.6%, $P < 0.001$), LE (−25.8%, $P < 0.001$), and sit-up test (−25.1%, $P < 0.001$). Previous disease severity, disease duration, the cumulative dose of glucocorticosteroids, current inflammation, and global habitual physical activity did not affect muscle performance. A recent use of steroids improved LE.

**Conclusions:** CD patients in clinical remission have decreased muscle function that may affect their quality of life. This pattern is reflected by reduced strength and endurance indexes, particularly for lower limbs. The reasons for these changes need further study. Strength training should be assessed in these patients.

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**Key Words:** Crohn's disease, habitual physical activity, muscle strength

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Crohn's disease (CD) is a chronic inflammatory bowel disease that affects well being and quality of life of patients,[1] with such symptoms as fatigue, diarrhea, abdominal, or musculo-articular pain and decreased self-reported physical activity. Among the factors that may explain these phenomena, muscle mass impairment is of particular interest. CD-induced malnutrition is a consequence of reduced dietary intake,[2] malabsorption,[3] and metabolic disturbances.[4,5] Malnutrition may have important consequences on body composition, and several studies have found decreased body weight, body mass index (BMI), body fat, or bone mineral density in CD patients comparatively to controls.[4,6–9] However, fat-free mass (FFM) has been found to be either identical[6,7] or decreased[8] in CD patients. Treatments of CD often include glucocorticosteroids (GCs) that may also have direct or indirect deleterious effects on body composition and particularly FFM. Indeed, several studies have showed that hypercortisolemia increases skeletal muscle catabolism,[10] which may affect the functional capacities of these patients.

In healthy adults, muscle mass has been shown to be positively regulated by nutritional factors such as protein intake[11,12] or zinc status.[13] Consequently, malnutrition observed in CD patients may induce deleterious effects on skeletal muscle mass and function. Impaired nutritional status is also associated with muscle fatigue.[14] In healthy subjects, muscle mass is a strong predictor of muscle strength,[15] and strength training has been shown to be an efficient mean to increase skeletal muscle mass.[16]

Very few studies have focused on exercise capacities in CD patients. Brevinge et al[17] found a reduced cycle ergometer exercise capacity in patients after small bowel resection, whereas D'Inca et al[9] reported a lower maximal oxygen consumption in CD patients compared with controls. To our

knowledge, only one study focused on skeletal muscle function in long-standing CD patients, showing insufficient protein intake and decreased hamstring strength.[6] These few studies have been performed in patients with active disease. However, thanks to new therapeutic classes and strategies (especially tumor necrosis factor-α blockade), remission is easier to achieve, and little is known about muscle function in these patients. This topic is of importance, because muscle weakness may partly explain the decreased quality of life reported by CD patients, therefore participating in disability.[1] Thus, the aim of this study was to investigate muscle performance in CD patients in clinical remission and to explore the relationship between muscle function, body composition, past disease severity, and associated treatments.

## MATERIALS AND METHODS

### Subjects

Between May 2001 and April 2003, a group of 41 CD outpatients, of both sexes, in clinical remission [CD Activity Index (CDAI) $< 150$] for at least 3 months, were consecutively recruited from the active list of inflammatory bowel disease cases in the Archet University Hospital in Nice, France. The diagnosis of CD was confirmed by histologic, endoscopic, radiologic, or clinical criteria. No patient had been receiving GCs for at least 2 months. Twenty-five sex- and age-matched healthy subjects were also recruited as the control group. The following exclusion criteria applied to patients and controls: age $<18$ or $>70$, known cardiovascular or muscular deficiencies, current pregnancy, neurologic diseases, sport training program for the last 6 months, and CDAI $> 150$.

### Study Design

Before inclusion in the study, all subjects were given a medical examination that included a health history and a resting electrocardiogram. Cumulative doses of GC—as well as the time of GC tapering—use of immunosuppressive drugs, and surgical episodes were recorded during this medical examination. After inclusion, subjects were instructed to report to the laboratory after an overnight fast, having abstained from strenuous physical activity for at least 48 hours. On the evaluation day, subjects were chronologically given anthropometric measurements, a body composition assessment, a light meal, muscle strength testings, and a habitual physical activity assessment (questionnaire). Each measure was made by a single investigator (R.A.J. for anthropometric measurements and body composition assessment and J.B.W. for muscle testing).

### Physical Characteristics

Patients were weighed at the same time of day, wearing only underwear and after emptying their bladder. A digital electronic scale (SECA, Birmingham, UK) was used for the measurement of body weight. Height was measured using a wall-mounted stadiometer. BMI was computed as the ratio between body weight and height squared. Body composition was assessed by bioelectrical impedance analysis using an alternating electric current of 50 μA at 2 frequencies (1 MHz and 5 KHz), as previously described and validated by Boulier et al.[18] A portable impedance analyzer (IMP BO1; L'impulsion, Caen, France) was used to calculate impedance and body composition (FFM and fat mass). Measurements were taken after a 12-hour overnight fast. The subjects had been supine for 30 minutes, arms relaxed at the sides without touching the body. Two stainless steel needles were inserted subcutaneously: one on the anterointernal side of a foot and the other in the first intermetacarpal space of the dorsal surface of the contralateral hand.

### Muscular Testing

Between anthropometric measurements and muscular testing, subjects were given a light meal to avoid hypoglycemia during the test protocol. Then, they completed a 5-minute warm-up on a friction-braked cycle ergometer (Monark, Stockholm, Sweden) at an intensity of 60% of the theoretical maximal heart rate. To test functional capacities of the lower limbs, time to complete a 12-repetition sit-up test (SUT) was measured to the nearest 0.01 second, using a digital chronometer (DigiSport, Germany). Seat height was adjusted to AU1 obtain a 90-degree knee angle while the subject was in the seated position.[19] Lower limbs' maximal isometric performance was measured bilaterally on a modified horizontal leg press (Vertex 2; Marcy, Alhambra, Calif.), fitted with 3 strain gauges (TME, Orgeval, France) under the foot platform.[20–22] To evaluate maximal isometric strength of leg extensors (LS), subjects were seated on the press with a 90-degree knee angle and a 150-degree hip angle. Subjects performed 3 trials lasting 3 to 4 seconds, and each trial was separated by a 2-minute passive recovery period. Afterward, a 1-repetition 15-second maximal isometric endurance test was completed for lower limbs (LE) with the same biomechanical settings.

Maximal isometric performances of the upper limbs were measured unilaterally using a hand-grip system made of a strain gauge (TME). The measures were taken on the nondominant forearm to avoid a training bias. Seated subjects were asked to hold the hand dynamometer, while keeping their arm toward the ground, and exert their maximal strength. As for the legs, 3 trials were performed for the maximal isometric handgrip strength test (HGS) and 1 trial for the maximal isometric hand-grip endurance test (HGE). Both evaluation devices were connected to the same microcomputer (P120E; Olivetti, Milan, Italy) through an analogic digital card (DAS 1000; Keithley Metrabytes, Taunton, Mass.), allowing us to record raw data at a frequency of 100 Hz, which was converted into Newtons using Excel (Microsoft, Seattle, Wash.). For both LS and HGS, the best peak force of the 3 trials was kept. For LE and HGE, mean force was calculated over the 15-second

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duration of each test. For each measurement, the same instructions and strong encouragement were given. Because we expected muscle strength to be dependent on FFM, results were normalized for FFM. Moreover, subjects were tested at the same ambient temperature (19°C–21°C) with a similar hygrometric level. The intraindividual variation for strength tests was <2% in each group of subjects.

### Habitual Physical Activity

Habitual physical activity was assessed with the help of a validated questionnaire[23] and accelerometry.[24] The self-administered questionnaire used in this study allowed us to calculate 3 activity indexes related to occupational physical activities (8 questions on the type of occupation, the fact of walking around at work, tiredness after work…), sport during leisure time (4 questions relative to the type of physical activity, to the fact of sweating during leisure time…), and physical activity during leisure time excluding sport (4 questions relative to watching television during leisure time, the time spent on locomotive activities…). All CD and control subjects were asked to complete this questionnaire on the evaluation day, after the muscular testings. A high score indicated that subjects were more physically active. Accelerometry measurements were performed in a subgroup of 21 CD patients and 24 controls during 7 consecutive days of free-living activities using triaxial accelerometers (RT3; StayHealthy, Monrovia, Calif.). All controls were assessed along with CD subjects matched for sex, age, and socio-economic status. Participants were instructed to wear the monitor all day long for the 1-week study period, excluding periods of bathing or other water activities. In respect to the manufacturer's advice, the accelerometer was "belt-worn." Each minute, accelerations were recorded and summarized in a magnitude vector. The habitual physical activity accelerometry index used in this study equaled the sum of 10,080 values and was expressed in counts.[24]

### Disease Severity and Treatments

To compare results according to disease severity, CD patients were separated into a "severe disease" group and a "moderate disease" group. The severe disease group included patients currently taking immunosuppressive drugs (n = 21) or who had been treated by infliximab (n = 2) or with a previous history of ≥2 surgical resections (n = 6). The moderate disease group included all other CD patients.

Results were also compared between patients who had been diagnosed >10 and <10 years ago. Effects of GC were assessed in CD patients by comparing CD patients with a low cumulative dose of GC (<10 g) and patients with a high cumulative dose of GC (≥10 g). They were also analyzed by looking at recent steroid use. A comparison was done between subjects who never took GC, subjects who stopped GC treatment during the last 6 months (with a free interval of >2 months), and those who stopped GC ≥6 months ago. Effects of current inflammation were assessed in CD patients by comparing CD patients with C-reactive protein levels <5 (15 patients) and ≥5 mg/L (23 patients; blood samples taken on the day of the study). Correlations were also assessed between muscle performance and C-reactive protein levels and GC dosage.

### Statistical Analysis

Data are presented as means ± SD. Comparison between CD and controls was done with Mann-Whitney *U* tests. Effects of disease severity, treatments, and sex were analyzed with Mann-Whitney *U* tests. Correlations between continuous variables were assessed using Spearman's correlation coefficients. The level of significance was set at $P < 0.05$. All statistical analysis were performed with Statistica 5.5 software (Statsoft, Tulsa, Okla.).

### Ethical Considerations

All subjects gave written informed consent to volunteer for this study, which met the requirements of the Local Standing Committee on Human Research.

## RESULTS

### Characteristics of Subjects

Main characteristics are presented in Table 1. No significant differences were observed for age, weight, height, body fat, or FFM between patients and controls. Among patients, 8 had never received GC, and 33 had received GC that had been discontinued >2 months before the study (6 patients had discontinued GC between 2 and 6 months before inclusion). In these patients, the cumulative dose of GC was <10 g in 22 and ≥10 g in 19, with a mean dose of 14.3 ± 17.0 g.

### Muscle Performances

Results of muscle performances, expressed as a function of FFM, in CD patients and controls are presented in Table 2. The SUT results showed that CD subjects were significantly slower to accomplish the 12 repetitions (−25.1%; $P < 0.001$), whatever sex was considered. CD patients had reduced values for lower limb isometric performances compared with controls (−24.8%; $P < 0.001$). There were no differences between CD and control groups concerning HGS and HGE.

When muscle performance results were analyzed by sex, no significant differences appeared between men and women in the control group. In contrast, CD women scored lower than men, even when results were corrected for FFM. This pattern was significant for LS, LE, HGS ($P < 0.05$), and HGE ($P < 0.01$).

### Habitual Physical Activity

Results are presented in Table 3. Total index (questionnaire) and 7-day counts (accelerometry) did not differ between CD and control subjects or between men and women. The only

 

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**TABLE 1.** Characteristics of Subjects

| | CD | | | Controls | | |
|---|---|---|---|---|---|---|
| | **Men (n = 17)** | **Women (n = 24)** | **Total (n = 41)** | **Men (n = 10)** | **Women (n= 15)** | **Total (n = 25)** |
| Age (yr) | 38 (11.8) | 37.4 (9.5) | 37.6 (10.4) | 43.6 (13.1) | 32.6 (11.2) | 37.0 (13.0) |
| Height (m) | 1.77 (0.06) | 1.62 (0.06) | 1.69 (0.09) | 1.76 (0.04) | 1.64 (0.06) | 1.69 (0.08) |
| Weight (kg) | 69.0 (9.2) | 58.2 (10.3) | 62.7 (11.1) | 74.9 (7.1) | 57.8 (5.6) | 64.6 (10.5) |
| BMI ($kg/m^2$) | 22.1 (3.5) | 22.1 (3.7) | 22.1 (3.6) | 24.0 (2.4) | 21.4 (1.6) | 22.5 (2.3) |
| FFM (kg) | 56.2 (6.4) | 42.9 (6.5) | 48.4 (9.2) | 58.0 (4.5) | 41.0 (4.4) | 47.8 (9.6) |
| Fat mass (kg) | 13.0 (5.1) | 15.3 (4.8) | 14.3 (5.1) | 16.4 (5.4) | 16.0 (4.2) | 16.2 (4.6) |
| Body fat (%) | 18.3 (6.0) | 25.8 (4.5) | 22.7 (6.3) | 21.7 (5.6) | 27.5 (5.5) | 25.2 (6.1) |
| C-reactive protein (g/L) | 11.6 (21.4) | 7.3 (7.7) | 9.1 (15.0) | | | |
| Disease duration (yr) | 12.8 (8.6) | 8.5 (4.7) | 10.3 (7.0) | | | |
| Disease location (n) (ileon and ileocolic/colic) | 14/3 | 18/6 | 32/9 | | | |
| Smoking habits (n) (CS/FS/NS) | 4/5/8 | 6/6/12 | 10/11/20 | 1/2/7 | 3/3/9 | 4/5/16 |
| Current immunosupressors use (n) | 9 | 12 | 21 | | | |
| Number of surgical episodes (n) | 1.8 (3.4) | 0.5 (0.6) | 1.1 (2.4) | | | |

Values are means (SD).
BM, body mass; BMI, body mass index; CS, current smokers; FS, former smokers; NS, nonsmokers.

significant differences were observed with the questionnaire for the estimation of work (with CD patients scoring higher) and sport indexes (with CD patients scoring lower).

## Disease Severity and Treatments

Neither disease severity (Fig. 1) nor duration (data not shown) influenced muscle performance. Similar findings were observed for the GC cumulative dose, regardless of the C-reactive protein levels and the history of GC usage (Table 4), except for higher LE values in patients who had received steroids 2 to 6 months before versus those who had never been on steroids, a finding that was confirmed by a positive correlation between GC dosage and LE ($r_2 = 0.50$; $P < 0.001$; Table 5).

## DISCUSSION

Very few studies have investigated the influence of CD on physical performance. To our knowledge, this study is the first to report, despite a normal FFM, decreased muscle performances in CD patients in clinical remission, independent of FFM, disease severity, disease duration, or treatment.

All these patients were considered to be in remission according to CDAI values. However, this index has been recently criticized as being based too much on clinical findings and medical history, both of which carry a certain level of subjectivity; indeed, high C-reactive protein levels found in some of our patients do not warrant complete remission because they reflect a persistent acute phase response.[25]

**TABLE 2.** Muscle Performances in CD Patients and Controls

| | CD | | | Controls | | |
|---|---|---|---|---|---|---|
| | **Men (n = 17)** | **Women (n = 24)** | **Total (n = 41)** | **Men (n = 10)** | **Women (n = 15)** | **Total (n = 25)** |
| HGS ($N/kg_{FFM}$) | 6.8 (1.1)§ | 5.8 (1.1) | 6.2 (1.2) | 6.7 (1.0) | 6.5 (1.5) | 6.6 (1.3) |
| HGE ($N/kg_{FFM}$) | 4.9 (0.6)¶ | 4.0 (1.0) | 4.4 (1.0) | 5.2 (1.0) | 4.8 (0.9) | 4.9 (1.0) |
| LS ($N/kg_{FFM}$) | 31.4 (7.4)§ | 27.0 (4.9)‡ | 28.8 (6.4)‡ | 37.8 (7.7) | 34.5 (6.0) | 35.8 (6.7) |
| LE ($N/kg_{FFM}$) | 23.2 (6.4)§ | 19.6 (3.7)‡ | 21.1 (5.2)‡ | 28.3 (6.3) | 25.4 (5.4) | 26.5 (5.8) |
| SUT (s) | 29.1 (6.6)† | 29.4 (4.6)‡ | 29.2 (5.5)‡ | 22.1 (3.7) | 21.7 (2.0) | 21.9 (2.8) |

Values are means (SD).
*Significantly different from controls, $P < 0.05$.
AU3 †Significantly different from controls, $P < 0.01$.
‡Significantly different from controls, $P < 0.001$.
§Significantly different from women, $P < 0.05$.
¶Significantly different from women, $P < 0.01$.

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**TABLE 3.** Habitual Physical Activity Indexes in CD Patients and Controls

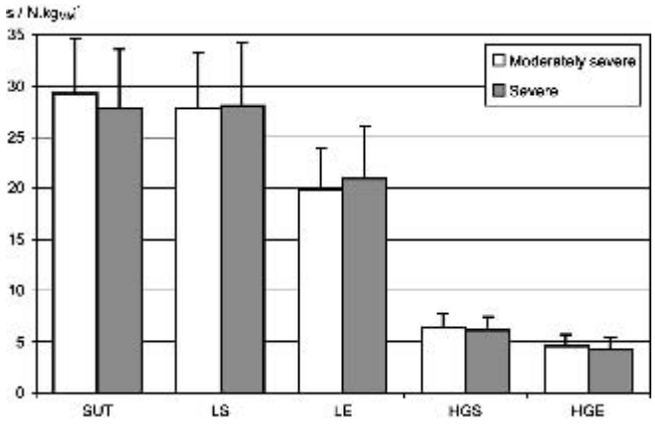
| Questionnaire | CD n = 41 | Controls n = 25 |
|---|---|---|
| Work | 2.94 (0.80)* | 2.51 (0.44) |
| Sport | 2.41 (1.10)* | 2.66 (0.74) |
| Leisure | 2.71 (0.52) | 2.76 (0.45) |
| Total | 8.06 (1.55) | 8.07 (0.99) |
| Accelerometry | n = 21 | n = 24 |
| Total counts | 1 513 787 (505 777) | 1 562 900 (409 915) |

Values are means (SD).
*Significantly different from controls, $P < 0.05$.

However, the CDAI is still widely accepted as a marker of disease activity, and our patients were therefore considered in clinical remission.

Body composition was similar in patients and controls, which is consistent with the remission status of the former. Indeed, metabolic features of active CD (higher resting energy expenditure and increased fat oxidation) explain the reduced fat mass[5,26] and FFM[8] usually observed in these patients. Weight and BMI results indicate that the majority of CD patients in remission may not be at risk for malnutrition. Nevertheless, appendicular muscle mass is only a compartment of FFM as measured by bioimpedance analysis, and we may have missed changes.

Muscle performance results show that CD patients were approximately 25% slower than controls to accomplish SUT, which is specific to several tasks of daily living. Although SUT dynamic contraction mode was different from the LS and LE isometric mode, the similar magnitude of differences observed is not surprising, because measurements were realized in the same standardized position: knee angle set at 90 degrees and maximal effort. Nevertheless SUT involves other abilities such as balance and mobility.




AU4 **FIGURE 1.** Comparison of muscle performances between patients with moderately severe (n = 18) and severe (n = 23) CD.

Concerning LS and LE, our results partially contradict those of Geerling et al,[6] who showed a lower isokinetic hamstring strength and similar quadriceps strength in patients compared with healthy controls. However, these differences may be caused by the inflammatory status, because 47% of CD patients in the study of Geerling et al had a CDAI >150, whereas no subject had a CDAI >150 in this study. Moreover, 41% of the patients evaluated in the study of Geerling et al received prednisone treatment while being evaluated. Finally, these authors used a different testing protocol (isokinetic) and a different way to express strength (N.m), which was uncorrected for FFM. Our results are similar to those of Brevinge et al,[17] who found a decreased power in CD patients undertaking a maximal pedaling task involving extensor muscles of the lower limb.

Results also show that women with CD are more affected by disease than men. Developing peak strength requires the activation of a maximum number of motor units, particularly the large fast IIb fibers. This capacity relies on motivation and practice to produce maximum voluntary neural drive to the muscles. Consequently, inactive CD women may not respond as well as CD men to these demands. Surface electromyography may help to understand such phenomenon. The lower performances observed in female patients should, however, be interpreted with caution, particularly for upper limbs, because the expression mode of strength ($N/kg_{FFM}$) is probably not adapted for intersex comparison of performances of small muscle masses like forearms. Normalization by forearm FFM would seem more reliable. Conversely, comparison of lower limbs parameters may be more reliable because muscle mass of the lower limbs accounts for an estimated 70% to 80% of total body muscle mass in healthy young subjects. The method used in this study to assess FFM did not permit evaluation of appendicular muscle mass or differentiation of muscle mass from bone mass. Thus, the assessment of global and appendicular body composition, through dual-energy absorptiometry, should be recommended in CD patients.

According to several authors, hand-grip strength tests are good predictors of physical fitness[27] and reliable indicators of evolution in several diseases such as liver cirrhosis or rheumatoid arthritis.[28] Thus, evaluation of upper limb muscular performance seemed to be of particular interest in CD patients. In our study, HGS and HGE were not statistically different between groups, suggesting that upper limb maximal strength is preserved with CD. These results suggest that upper limb capacities are less influenced by CD than those of lower limbs. This pattern is similar to the one observed during the aging process, where elderly people show a preserved arm

**TABLE 4.** Comparison of Muscle Performance in CD Patients Looking at History of GC Use

| | HGS ($N/kg_{FFM}$) | HGE ($N/kg_{FFM}$) | LS ($N/kg_{FFM}$) | LE ($N/kg_{FFM}$) | SUT (s) |
|---|---|---|---|---|---|
| GC stopped 2 to 6 months before (n = 6) | 6.1 (1.8) | 4.2 (1.4) | 31.4 (5.5) | 21.9 (4.1) | 30.3 (3.8) |
| GC stopped >6 months before (n = 27) | 6.2 (1.2) | 4.3 (1.0) | 28.7 (6.9) | 21.6 (5.6) | 28.7 (5.3) |
| GC never given (n = 8) | 6.4 (0.9) | 4.9 (0.6) | 26.5 (4.4) | 17.8 (3.2)* | 30.3 (7.5) |

Values are means (SD).
*Significantly different from patients "GC stopped 2 to 6 months before," $P < 0.05$.

function while leg function is often decreased.[29,30] In aging, this phenomenon is partly explained by the progressive disuse of leg muscles, which leads to a decrease of leg strength and power. In contrast, arm muscles are more often used in daily living activities, thus maintaining functional capacities of these limbs. A similar phenomenon remains a possible hypothesis in CD patients, which may be strengthened by the frequently reported asthenia and impossibility to undertake physical exercise in this population.

To confirm this hypothesis, we compared habitual physical activity between CD and control subjects. Interestingly, these results suggest that CD patients may not have a reduced daily life activity when in remission, whatever the measurement method used (questionnaire or accelerometry). Nevertheless, the decreased sport index in CD patients may negatively influence muscle performances, because high intensity exercises are less performed. On a metabolic point of view, this "detraining" may include a reduction of the muscle proton-buffering capacity, an inability to produce enough energy with anaerobic glycogenolysis and a reduction of the glycogen stores. Moreover, disuse may also negatively affect neural recruitment of powerful fast twitch muscle fibers. On the other hand, the increased work index may indicate that work activity perception is higher in CD patients, which may confirm an increased fatigability in this population.[31]

Nutritional deficiencies are another possible explanation for the impaired muscle function.[14,32] The main reason for decreased food intake often found in CD patients is anorexia, which probably results from high levels of proinflammatory cytokines.[8] CD patients can also show excessive intestinal losses from the gut of electrolytes and vitamins.[32] However, no patient had short bowel syndrome.

The lack of obvious influence of disease severity on body composition and muscle performances between CD subgroups gives results that are inconsistent with previous research in patients with active CD.[17] This confirms the hypothesis of a good reversibility of muscle damage after remission is achieved in these relatively young patients. On the other hand, long-term GC use does not induce deleterious effects on muscle endurance in our CD patients. This is suggested by the positive correlation that has been found between cumulative GC and LE and confirmed by the significant difference found between patients who never took GC and patients who stopped GC recently. These findings, which are contradictory to previous works,[33,34] may indicate that the negative effects of cumulative GC may be counteracted by a reduction of inflammation, which is known to induce deleterious effects on muscle. GC-induced muscle atrophy has been reported to be partially reversible,[35] particularly in adults. In our relatively young active CD population, regular physical exercise (during work or leisure activities) may act as a countermeasure to the negative effects of GC on body composition.[10] Irregular rhythm of GC intake may be an explanation, allowing our patients to normalize their body composition and muscle metabolism between episodes of GC treatments. Moreover, GC have been shown to induce deleterious effects on muscle mass and function mainly during a current administration, and none of our CD patients were on GC treatment during the study period, with a free interval of >2 months.

**TABLE 5.** Correlations Between GC Dosage and C-reactive Protein Levels and Muscle Performance in CD Patients

| | SUT (s) | HGS ($N/kg_{FFM}$) | HGE ($N/kg_{FFM}$) | LS ($N/kg_{FFM}$) | LE ($N/kg_{FFM}$) |
|---|---|---|---|---|---|
| GC | 0.24 | 0.07 | 0.11 | 0.08 | 0.50* |
| C-reactive protein | −0.10 | 0.07 | 0.23 | 0.16 | 0.11 |

Values are $r^2$.
*Significant correlation, $P < 0.001$.

Last, there was no influence of biologic inflammation on muscle performance, even if, despite a remission ascertained by CDAI scores, C-reactive protein levels slightly higher than the normal laboratory values (5 mg/L) may reflect a persistent subclinical inflammation. Inflammation has been shown to influence negatively muscle function in several inflammatory diseases,[36] because interleukin-6 concentration has been shown to induce lower muscle strength and power, concomitantly with reduced secretions of insulin-like growth factor-1,[37] which has important effects on muscle mass and function.[38,39] Therefore, drugs affecting cytokine production may influence muscle mass and function in a positive way. However, this needs to be put into perspective with the effects of the disease per se on muscle. Infliximab may have an acute effect, not necessarily positive, but the 2 patients with a history of infliximab prescription did not differ from the others. As for the 19 patients receiving azathioprine (which is known to down-regulate interleukin-6 in the serum), they too did not differ from patients who had not received this treatment. Unfortunately, we did not measure cytokine levels in plasma or in muscle, but this factor may play a key role in muscular deficiencies of CD patients and should therefore be explored. The evaluation of muscle metabolism with muscle biopsies or spectrometry may be of special interest to understand this phenomenon.

In conclusion, CD patients in clinical remission show a reduced skeletal muscle strength and endurance comparatively to control subjects, independently of FFM. Consequently, remission is not completely achieved in this population. Specific treatments such as GC, immunosuppressive drugs, or small bowel resections cannot be held responsible for the differences in muscular performances observed between CD and controls. Nevertheless, understanding the etiology of the reduced strength in CD patients warrants making the distinction between the deleterious effects of inflammation and those of treatments. Moreover, the global level of habitual physical activity does not seem to be involved in the reduction of muscular strength, although reduced sport activities may provide an explanation.

The potential therapeutic effects of resistance or endurance training should be tested in CD patients to reduce the deleterious effects of CD on their muscle function and enhance their quality of life. The therapeutic effect and the feasibility of endurance training has been recently shown in CD patients in remission.[9] We believe that resistance training may reduce the deleterious effects of CD on muscle function and enhance the quality of life of these patients, as in rheumatoid arthritis.[36]

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