



Original research

Fatigue in inflammatory bowel diseases: Relationship with age and disease activity



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ARTICLE INFO

Article history:

Received 15 May 2014

Accepted 15 June 2014

Available online 23 August 2014

Keywords:

Inflammatory bowel diseases

Crohn's disease

Ulcerative colitis

Fatigue

Quality of life

CD

UC

FIS

ABSTRACT

A higher rate of patients suffering from inflammatory bowel diseases (IBD) are reported to experience the symptom of fatigue compared with general population. Fatigue can impair quality of life of IBD patients by limiting their daily functioning.

However, this problem is poorly understood and addressed. Our aim was to investigate the impact of fatigue in IBD patients compared with controls, and to seek for relation between age and disease activity.

IBD patients aged between 16 and 75 years observed at our Unit from June 2011 through June 2012 were evaluated for fatigue. Patients were asked to fill the fatigue impact scale (FIS) questionnaire. A cohort of age- and sex-matched patients observed for other-than-IBD diseases were prospectively enrolled to act as controls. Patients diagnosed with malignancies were excluded from evaluation.

Each group included 16 patients, of whom half aged over 65 years.

Fatigue was more severe in IBD patients than in controls ($p = 0.02$), irrespective of age and disease activity. IBD patients with moderate to severe disease activity showed worse fatigue compared with controls at any age ($p < 0.0001$). Young IBD patients with low disease activity showed a trend toward worse FIS score when compared with old IBD counterparts ($p = 0.06$).

IBD significantly impacted on fatigue in our series. Considering IBD patients in remission, younger patients may experience worse fatigue. Further studies are needed to explore the effects of fatigue on quality of life and the potential of appropriate intervention strategies.

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1. Introduction

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic conditions

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characterized by periods of remission and relapse, affecting people at any age [1–3]. The aetiopathogenesis of IBD relies on complex immune mechanisms, and is mediated by a genetic/epigenetic predisposition and environmental factors [4–7]. Symptoms of IBD include diarrhoea, abdominal pain, fatigue, appetite and weight loss [8]. Moreover, IBD patients may often require both treatment with immunodepressants [1,2,9–12], which may be associated with significant side-effects [13–15], and invasive/repeated surgical procedures for primary disease [1,2,16–19] as well as for potential complications of the treatments [3,20–25]. Furthermore, IBD patients and their relatives are at increased risk of immune-driven cancerogenesis [26–28]. These observations justify the consistent impact of IBD on health related quality of life [20,29].

Even if fatigue is known to be a common concern in chronic diseases of the digestive system [30], there is lack of knowledge as

List of abbreviations

CD	Crohn's disease
CDAI	Crohn's disease activity index
IBD	inflammatory bowel diseases
SD	standard deviation
UC	ulcerative colitis
UCDAI	Ulcerative Colitis Disease Activity Index

well as of effective therapeutic interventions to treat fatigue in IBD. The condition is still unjustifiably overlooked in IBD patients, as clinicians tend to concentrate on controlling problems related to inflammation [31]. Our aim was to assess patient-reported fatigue in IBD patients and in controls, seeking for potential influences of age and disease activity.

2. Material and methods

All consecutive patients diagnosed with CD or UC aged between 16 and 75 years observed at our Unit from June 2011 through June 2012 were evaluated for inclusion.

Diagnosis of IBD was made following the accepted criteria [32,33]. Patients willing to participate were included. IBD patients with prior or current malignancies were excluded from the study. Patients observed for perianal CD were excluded.

A control group of patients diagnosed with other-than-IBD conditions was prospectively enrolled. Patients underwent surgery for benign diseases, hence excluding cancer patients [34–38], and were age- and sex-matched with IBD patients.

IBD patients and controls who were previously operated on for any disease were not included.

Each group comprised half patients aged over 65 years to allow sub-analyses.

2.1. Disease assessment

All patients underwent complete clinical examination. All IBD patients underwent endoscopy with biopsies to confirm the diagnosis [32,33]. Imaging modalities were selectively advocated [17,32,33,35,37–40]. Disease activity assessment in CD and UC patients was performed by means of Crohn's disease activity index (CDAI) [41] and Ulcerative Colitis Disease Activity Index (UCDAI) [42], respectively.

2.2. Fatigue assessment

Fatigue was assessed by means of the fatigue impact scale (FIS) questionnaire [43]. This is a self-reported instrument consisting of 40 questions, constructed to assess the impact of perceived fatigue on the following dimensions: physical functioning (10 items), cognitive functioning (10 items), and psychosocial functioning (20 items). Each question asks subjects to rate distress on a 5-point scale, ranging from 0 ("no problem") to 4 ("extreme problem"). The maximum total FIS score is 160, corresponding to highest fatigue perception.

2.3. Statistical analysis

Results of each group were compared, and sub-analyses were performed according to age (< and >65 years). FIS scores of young IBD patients were also compared with old IBD patients. Data are

expressed as mean \pm standard deviations (SD). The Mann–Whitney test was performed for calculations of differences between groups. Values of $p < 0.05$ were considered statistically significant.

3. Results

Sixteen patients per group (10 female) were enrolled, of whom 8 (50%) were >65-year-old per group. Patients with IBD had more severe overall fatigue compared with non-IBD controls (88 ± 70 vs 40 ± 25 , $p = 0.002$). Physical (IBD vs controls: all age, 25 ± 15 vs 12 ± 8 , $p = 0.02$) and psychosocial (36 ± 22 vs 21 ± 13 , $p = 0.04$) FIS scores were higher in IBD compared with controls while no differences were observed in cognitive FIS score (9 ± 7 vs 10 ± 8 , $p = 0.12$). Results were confirmed with subgroup analyses according to age (< and >65 year-of-age).

When only considering IBD patients with moderate to severe disease activity ($n = 5$, 31.3%), differences in overall FIS scores were even more apparent (IBD vs controls: all age, 100 ± 62 vs 40 ± 25 , $p < 0.0001$).

When only evaluating IBD patients with mild to low active disease ($n = 11$, 68.7%), young IBD patients showed a trend toward higher FIS score compared with older IBD patients (73 ± 60 vs 65 ± 80 , $p = 0.06$), and significantly higher fatigue than non-IBD young counterparts (73 ± 60 vs 31 ± 42 , $p = 0.001$).

4. Discussion

With our exploratory, pilot study we were able to demonstrate that IBD-associated fatigue affects the life of IBD patients, similarly to other chronic diseases [30,43].

IBD activity significantly impacted on perceived fatigue. Interestingly, old IBD patients in remission seemed to cope better with fatigue when compared with younger IBD patients. Patients aged <65 years tended to experience more severe fatigue than non-IBD controls.

Many factors may affect patient-perceived fatigue, and chronic illnesses [30,43,44] and conditions are one of the most important. However, also cancer patients may experience fatigue [45]. For this reason, we decided to put out from analyses patients diagnosed with malignancies [34–38,46–50] as this could have biased our results.

Our findings offer interesting and practical perspectives. Many factors may be responsible for higher fatigue perception in IBD, including depression and anxiety [51]. This advocates the need of further studies also evaluating these facets of IBD patients, which are frequently overlooked.

Disease duration and activity have previously been associated with higher fatigue levels [51]. Unsurprisingly, IBD patients with more active disease were much more fatigued than both IBD patients with mild disease and non-IBD patients.

We found that age may play a role in fatigue perception, as differences were observed in overall FIS score between young and old IBD patients in remission. Even if without reaching statistical significance, these may suggest that patients with longer disease, successfully controlled, may develop more effective coping strategies than younger patients. As a matter of fact, young IBD individuals in remission had significantly higher fatigue than same-age controls. It can be hence predicted that timely, fatigue-specific treatments may be needed in such patients, potentially reducing the levels of perceived fatigue, on condition that the baseline disease is controlled.

Further researches are compulsory to seek for potential associations between other factors which may play a role in perceived levels of fatigue. These may ultimately result in the development of accepted guidelines to strengthen and validate frameworks such as

the “health-related normality” [52], including psychological, behavioural, social, and medical strategies. Such approach could lead to achieve the optimal management of IBD-related fatigue at any age.

Ethical approval

Ethical approval was requested and obtained from the “Second University of Naples” ethical committee.

Funding

All authors have no source of funding.

Author contribution

Gianluca Pellino: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Guido Sciaudone: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Violetta Caserta: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Giuseppe Candilio: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

G Serena De Fatico: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Silvana Gagliardi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Isabella Landino: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Marta Patturelli: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Gabriele Riegler: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Ester Livia Di Caprio: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Silvestro Canonico: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Paolo Gritti: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Francesco Selvaggi: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Conflicts of interest

The authors have no conflict of interest or any financial support.

References

- [1] G. Pellino, G. Sciaudone, G. Candilio, et al., Complications and functional outcomes of restorative proctocolectomy for ulcerative colitis in the elderly, *BMC Surg.* 13 (Suppl. 2) (2013) S9, <http://dx.doi.org/10.1186/1471-2482-13-S2-S9>.
- [2] G. Pellino, G. Sciaudone, E. Miele, et al., Functional outcomes and quality of life after restorative proctocolectomy in paediatric patients: a case-control study, *Gastroenterol. Res. Pract.* 2014 (2014), <http://dx.doi.org/10.1155/2014/340341>, 340341.
- [3] G. Pellino, G. Sciaudone, G. Candilio, S. Canonico, F. Selvaggi, Rectosigmoid stump washout as an alternative to permanent mucous fistula in patients undergoing subtotal colectomy for ulcerative colitis in emergency settings, *BMC Surg.* 12 (Suppl. 1) (2012) S31, <http://dx.doi.org/10.1186/1471-2482-12-S1-S31>.
- [4] G. Latella, G. Rogler, G. Bamias, et al., Results of the 4th scientific workshop of the ECCO (I): pathophysiology of intestinal fibrosis in IBD, pii: S1873-9946(14)00120-2, *J. Crohns Colitis* (2014 Apr 11), <http://dx.doi.org/10.1016/j.crohns.2014.03.008> (Epub ahead of print).
- [5] R.B. Canani, P. Cirillo, G. Mallardo, et al., Effects of HIV-1 Tat protein on ion secretion and on cell proliferation in human intestinal epithelial cells, *Gastroenterology* 124 (2003) 368–376.
- [6] M. Romano, A. Cuomo, C. Tuccillo, et al., Vascular endothelial growth factor and cyclooxygenase-2 are overexpressed in ileal pouch-anal anastomosis, *Dis. Colon Rectum* 50 (2007) 650–659.
- [7] G. Pellino, G. Sciaudone, S. Canonico, F. Selvaggi, Nerve sheath in longstanding fibrostenosing Crohn's disease: is there a connection? *Inflamm. Bowel Dis.* 19 (2013) E16–E19.
- [8] C.C. Cronin, F. Shanahan, Exploring the iceberg – the spectrum of celiac disease, *Am. J. Gastroenterol.* 98 (2003) 518–520.
- [9] G. Sciaudone, G. Pellino, I. Guadagni, F. Selvaggi, Infliximab avoiding colectomy and maintaining remission in pediatric immunosuppressive-naïve ulcerative colitis achieving remarkable mucosal healing, *Panminerva Med.* 52 (2010) 91–92.
- [10] G. Sciaudone, G. Pellino, G. Riegler, F. Selvaggi, Infliximab in drug-naïve patients with failed ileorectal anastomosis for Crohn's disease: a new chance for sparing the rectum? *Eur. Surg. Res.* 46 (2011) 163–168, <http://dx.doi.org/10.1159/000324398>.
- [11] G. Sciaudone, C. Di Stazio, P. Limongelli, et al., Treatment of complex perianal fistulas in Crohn disease: infliximab, surgery or combined approach, *Can. J. Surg.* 53 (2010) 299–304.
- [12] D. Musto, L. Martorelli, A. Cirillo, F. Selvaggi, P. Esposito, M.I. Russo, G. Riegler, Distal esophageal involvement in Crohn disease: short treatment with adalimumab, *Endoscopy* 42 (Suppl. 2) (2010) E299.
- [13] G. Pellino, G. Sciaudone, G. Candilio, F. Campitiello, F. Selvaggi, S. Canonico, Effects of a new pocket device for negative pressure wound therapy on surgical wounds of patients affected with Crohn's disease: a pilot trial, *Surg. Innov.* 21 (2014) 204–212, <http://dx.doi.org/10.1177/1553350613496906>.
- [14] G. Sciaudone, G. Pellino, I. Guadagni, F. Selvaggi, Education and imaging: gastrointestinal: herpes simplex virus-associated erythema multiforme (HAEM) during infliximab treatment for ulcerative colitis, *J. Gastroenterol. Hepatol.* 26 (2011) 610.
- [15] G. Sciaudone, G. Pellino, I. Guadagni, et al., Disseminated *Cryptococcus neoformans* infection and Crohn's disease in an immunocompetent patient, *J. Crohns Colitis* 5 (2011) 60–63.
- [16] G. Pellino, G. Sciaudone, S. Canonico, F. Selvaggi, Role of ileostomy in restorative proctocolectomy, *World J. Gastroenterol.* 18 (2012) 1703–1707.
- [17] F. Selvaggi, G. Pellino, S. Canonico, G. Sciaudone, Is omitting pouchography before ileostomy takedown safe after negative clinical examination in asymptomatic patients with pelvic ileal pouch? An observational study, *Tech. Coloproctol.* 16 (2012) 415–420, <http://dx.doi.org/10.1007/s10151-012-0838-1>.
- [18] F. Selvaggi, A. Giuliani, C. Gallo, et al., Randomized, controlled trial to compare the J-pouch and W-pouch configurations for ulcerative colitis in the maturation period, *Dis. Colon Rectum* 43 (2000) 615–620.
- [19] F. Selvaggi, G. Sciaudone, A. Giuliani, P. Limongelli, C. Di Stazio, A new type of strictureplasty for the treatment of multiple long stenosis in Crohn's disease, *Inflamm. Bowel Dis.* 13 (2007) 641–642.
- [20] F. Selvaggi, G. Sciaudone, P. Limongelli, et al., The effect of pelvic septic complications on function and quality of life after ileal pouch-anal anastomosis: a single center experience, *Am. Surg.* 76 (2010) 428–435.
- [21] F. Selvaggi, G. Sciaudone, I. Guadagni, G. Pellino, Ileal pouch-anal anastomosis after stapled haemorrhoidopexy for unrecognized ulcerative colitis, *Colorectal Dis.* 12 (2010) e172.
- [22] G. Sciaudone, C. Di Stazio, I. Guadagni, F. Selvaggi, Rectal diverticulum: a new complication of STARR procedure for obstructed defecation, *Tech. Coloproctol.* 12 (2008) 61–63.
- [23] F. Selvaggi, G. Pellino, G. Sciaudone, Surgical treatment of recurrent prolapse after stapled haemorrhoidopexy, *Tech. Coloproctol.* (2014 Jun 24), <http://dx.doi.org/10.1007/s10151-014-1180-6> (Epub ahead of print).
- [24] F. Selvaggi, G. Sciaudone, A. Giuliani, New ambulatory treatment with radiofrequency for internal symptomatic hemorrhoids: morbidity evaluation, *Gastroenterol. Clin. Biol.* 29 (2005) 939–940.

- [25] G. Sciaudone, G. Pellino, I. Guadagni, A. Pezzullo, F. Selvaggi, Wireless capsule endoscopy years after Michelassi stricturoplasty for Crohn's disease, *Acta Chir. Belg.* 110 (2010) 213–215.
- [26] L. Egan, R. D'Inca, T. Jess, et al., Non-colorectal intestinal tract carcinomas in inflammatory bowel disease: results of the 3rd ECCO Pathogenesis Scientific Workshop (II), *J. Crohns Colitis* 8 (2014) 19–30, <http://dx.doi.org/10.1016/j.crohns.2013.04.009>.
- [27] F. Selvaggi, G. Pellino, S. Canonico, G. Sciaudone, Systematic review of cuff and pouch cancer in patients with ileal pelvic pouch for ulcerative colitis, *Inflamm. Bowel Dis.* 20 (2014) 1296–1308.
- [28] G. Pellino, G. Sciaudone, M. Patturelli, et al., Relatives of Crohn's disease patients and breast cancer: an overlooked condition, pii: S1743-9191(14)00121-6, *Int J Surg* 12 (Suppl. 1) (2014) S156–8, <http://dx.doi.org/10.1016/j.ijsu.2014.05.022>.
- [29] F. Selvaggi, A. Giuliani, G. Sciaudone, G. Riegler, C. Di Stazio, Quality of life in patients with ileal pouch for ulcerative colitis, *Chir. Ital.* 56 (2004) 239–246.
- [30] I.M. Minderhoud, B. Oldenburg, P.S. van Dam, G.P. van Berge Henegouwen, High prevalence of fatigue in quiescent inflammatory bowel disease is not related to adrenocortical insufficiency, *Am. J. Gastroenterol.* 98 (2003) 1088–1093.
- [31] J. Casati, B.B. Toner, E.C. de Rooy, D.A. Drossman, R.G. Maunder, Concerns of patients with inflammatory bowel disease: a review of emerging themes, *Dig. Dis. Sci.* 45 (2000) 26–31.
- [32] G. Van Assche, A. Dignass, J. Panes, et al., The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis, *J. Crohns Colitis* 4 (2010) 7–27.
- [33] A. Dignass, R. Eliakim, F. Magro, et al., Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis, *J. Crohns Colitis* 6 (2012) 965–990.
- [34] G. Pellino, G. Sciaudone, G. Candilio, et al., Early postoperative administration of probiotics versus placebo in elderly patients undergoing elective colorectal surgery: a double-blind randomized controlled trial, *BMC Surg.* 13 (Suppl. 2) (2013) S57, <http://dx.doi.org/10.1186/1471-2482-13-S2-S57>.
- [35] G. Pellino, G. Sciaudone, G. Candilio, et al., Stepwise approach and surgery for gallbladder adenomyomatosis: a mini-review, *Hepatobiliary Pancreat. Dis. Int.* 12 (2013) 136–142.
- [36] S. Canonico, R. Benevento, G. Perna, et al., Sutureless fixation with fibrin glue of lightweight mesh in open inguinal hernia repair: effect on postoperative pain: a double-blind, randomized trial versus standard heavyweight mesh, *Surgery* 153 (2013) 126–130, <http://dx.doi.org/10.1016/j.surg.2012.06.024>.
- [37] G. Gagliardi, S. Pucciarelli, C.R. Asteria, et al., A nationwide audit of the use of radiotherapy for rectal cancer in Italy, *Tech. Coloproctol.* 14 (2010) 229–235.
- [38] F. Selvaggi, A. Cuocolo, G. Sciaudone, et al., FGD-PET in the follow-up of recurrent colorectal cancer, *Colorectal Dis.* 5 (2003) 496–500.
- [39] F. Selvaggi, A. Cuocolo, A. Giuliani, et al., The role of scintigraphic defecography in the assessment of bowel function after restorative proctocolectomy for ulcerative colitis, *Int. J. Colorectal Dis.* 21 (2006) 448–452.
- [40] S.A. Müller-Lissner, D.C. Bartolo, J. Christiansen, et al., Interobserver agreement in defecography – an international study, *Z. Gastroenterol.* 36 (1998) 273–279.
- [41] R. Sostegni, M. Daperno, N. Scaglione, A. Lavagna, R. Rocca, A. Pera, Review article: Crohn's disease: monitoring disease activity, *Aliment. Pharmacol. Ther.* 17 (Suppl. 2) (2003) 11–17.
- [42] P.D. Higgins, M. Schwartz, J. Mapili, E.M. Zimmermann, Is endoscopy necessary for the measurement of disease activity in ulcerative colitis? *Am. J. Gastroenterol.* 100 (2005) 355–361.
- [43] J.D. Fisk, A. Pontefract, P.G. Ritvo, C.J. Archibald, T.J. Murray, The impact of fatigue on patients with multiple sclerosis, *Can. J. Neurol. Sci.* 21 (1994) 9–14.
- [44] M. Secondulfo, G. Riegler, L. De Magistris, M. Belletta, R. Fiandra, L. Caserta, F. Selvaggi, R. Carratù, Intestinal permeability assessment before and after ileal pouch-anal anastomosis, *Minerva Gastroenterol. Dietol.* 50 (2004) 155–163.
- [45] E. Ream, A. Richardson, Fatigue: a concept analysis, *Int. J. Nurs. Stud.* 33 (1996) 519–529.
- [46] P. Gritti, S. Lombardi, B. Nobile, et al., Alexithymia and cancer-related fatigue: a controlled cross-sectional study, *Tumori* 96 (2010) 131–137.
- [47] G. Sciaudone, G. Pellino, F. Selvaggi, Diagnostic pitfalls: cancerization in IBD versus mantle cell lymphoma presenting with multiple lymphomatous polyps, *Inflamm. Bowel Dis.* 17 (2011) E28–30.
- [48] F. Selvaggi, I. Guadagni, G. Pellino, M. De Rosa, G. Imbrogno, G. Sciaudone, Perianal Paget's disease happening with mucinous adenocarcinoma of the anal canal: managing rarities, *J. Cutan. Pathol.* 37 (2010) 1182–1183.
- [49] F. Selvaggi, G. Pellino, T. Pellegrino, G. Sciaudone, G. Candilio, G.S. De Fatico, I. Landino, S. Canonico, A. Cuocolo, Role of scintigraphy in differential diagnosis of adrenal lesions, *Minerva Chir.* 69 (2 Suppl. 1) (2014) 105–109.
- [50] G. Accardo, D. Esposito, F. Barbato, A. De Bellis, S. Iorio, V. Amoresano Paglionico, C. Colella, A. Dello Iacovo, F. Selvaggi, G. Docimo, G. Conzo, D. Pasquali, Pheochromocytoma: from the bench to the surgery, *Minerva Chir.* 69 (2 Suppl. 1) (2014) 97–103.
- [51] T. Piche, P. Ducrotté, J.M. Sabate, et al., Impact of functional bowel symptoms on quality of life and fatigue in quiescent Crohn disease and irritable bowel syndrome, *Neurogastroenterol. Motil.* 22 (2010), 626–e174.
- [52] N.J. Hall, G.P. Rubin, A. Dougall, A.P. Hungin, J. Neely, The fight for 'health-related normality': a qualitative study of the experiences of individuals living with established inflammatory bowel disease (ibd), *J. Health Psychol.* 10 (2005) 443–455.