Psychobiological Subtypes of Ulcerative Colitis: pANCA Status Moderates the Relationship between Disease Activity and Psychological Distress

Robert G. Maunder, MD¹, Gordon R. Greenberg, MD², Jonathan J. Hunter, MD¹, William J. Lancee, PhD¹, A. Hillary Steinhart, MD², and Mark S. Silverberg, MD, PhD²

¹ Department of Psychiatry, Mount Sinai Hospital and University of Toronto

² Division of Gastroenterology. Mount Sinai Hospital and University of Toronto

Abstract

Introduction—Studies of psychological factors in ulcerative colitis (UC) have produced inconsistent findings. This study sought to determine whether perinuclear antineutrophil cytoplasmic antibody (pANCA) demarcates subtypes which differ with respect to psychobiological interactions.

Methods—In 148 outpatients with UC, the strength of the relationship between current UC disease activity and psychological distress was assessed. pANCA was determined by ELISA and immunofluorescence, disease activity was determined by symptoms, physical examination and endoscopy using the St. Mark's index, and depressive symptoms and health anxiety were measured with self report scales. Pearson correlations between disease activity and depressive symptoms and between disease activity and health anxiety were calculated.

Results—In 74 pANCA negative subjects, the relationship between disease activity and measures of psychological distress was significant for disease activity-depression (partial correlation= 0.48, $p < 0.001$) and for disease activity-health anxiety (partial correlation= 0.64, $p < 0.001$), whereas in 74 pANCA positive subjects, no relationships were found (disease activity-depression: partial correlation= 0.18, $p = 0.14$; disease activity-health anxiety: partial correlation= 0.20, $p = 0.09$). The differences in the strength of correlation between pANCA positive and pANCA negative subjects were statistically significant for both disease activity-depression ($z = 2.0$, $p = 0.02$) and for activity-health anxiety ($z = 3.3$, $p < 0.001$).

Conclusions—pANCA status demarcates psychobiologically distinct subtypes of UC, such that the absence of pANCA is associated with greater psychobiological interaction. These findings have implications for clinical care and understanding the pathophysiology of intestinal inflammation.

Introduction

The course of ulcerative colitis (UC) may be influenced by psychological factors, such as stress (1;2). The evidence, however, is inconsistent, such that some well-designed studies support a psychobiological contribution to disease relapse while others fail to show such an effect (3;4). A plausible explanation for these disparate findings is that disease course is vulnerable to stress in some patients, but not in all (3;5). Thus, the hypothesis that UC is etiologically heterogeneous may explain why studies which fail to identify and stratify by pathophysiological subtypes that moderate the relationship between experience and disease course reach differing conclusions.

While a diagnosis of depressive illness is probably not more common in UC than in healthy persons (6;7), depressive symptoms have been reported to be greater at times of increased disease activity (8). Depressive symptoms may precede a relapse of disease activity in IBD (9), although the evidence for this temporal association is not consistent (1). Using the strategy of stratifying by psychological subtypes, we have reported that the strength of relationship between UC disease activity and concurrent depressive symptoms is moderated by attachment insecurity, a trait-like psychological vulnerability factor related to anxiety and dependency in interpersonal relationships (10), and varies from no relationship when attachment anxiety is low to a strong relationship in patients with high attachment anxiety (11).

If there is an important link between gut inflammation and psychological factors in a subset of UC patients, a biological marker of such patients would be useful for patient care and for research. First, markers of psychobiological subtypes could be used to identify which UC patients are appropriate for psychological interventions to prolong remission. The success of controlled trials to test therapeutic interventions may depend on appropriately selecting patients at high risk of stress-related relapse (5). Lastly, identification of psychobiologically distinct subtypes of UC would contribute to the understanding the pathogenesis of UC.

Currently, there are no established biological markers of psychobiological risk in UC. Perinuclear antineutrophil cytoplasmic antibody (pANCA) is an immune marker that is present in up to 70% of patients with UC, but is found in only 0–5% of healthy controls (12). pANCA is a marker of immunoregulatory disturbance in UC (13) and in various vasculidites, such as Wegener's granulomatosis, although it remains unclear what combination of genetic and environmental factors determine pANCA status (14). Previously, we found that attachment insecurity was more common in UC when pANCA absent as compared to pANCA positive UC (15). These findings lead us to hypothesize that pANCA may be a biological marker of psychobiologically distinct subtypes in UC. Therefore, the purpose of this study was to determine if pANCA moderates the strength of the association between UC disease activity and two forms of psychological distress, depressive symptoms and health anxiety.

Methods

Patients and procedures

Three hundred sixty-one patients with UC confirmed by endoscopy and biopsy, of at least 18 years of age, were identified by chart review and contacted by telephone by a research assistant. Patients who had had a colectomy or cardiovascular disease (an exclusion criteria for an aspect of the study not reported here) were excluded. Forty-one percent (148 subjects) consented to participate. Participants made 3 visits for assessment: (i) an assessment by a gastroenterologist which included history, physical examination, endoscopy and blood collection; (ii) completion of self-report measure of UC symptoms and psychological surveys, and (iii) a half-day in a stress laboratory for measurement of psychological and physiological variables that are reported elsewhere (16). All study visits occurred within a two week period with the order of visits determined by convenience (i.e. there was no fixed order to the three visits). Both investigators and subjects were blind to the results of pANCA testing at the time that other measurements were made. Subjects were paid \$90 Canadian (approximately \$80 US). This study was approved by the Research Ethics Boards of Mount Sinai Hospital and the University Health Network.

Evaluations

pANCA status was determined by previously described methods (17) at Prometheus Laboratories (San Diego, CA). Briefly, first the presence of ANCA was determined by fixed neutrophil ELISA. Indirect immunofluorescence staining was then performed on ANCA ELISA-positive samples to determine whether a predominantly perinuclear or cytoplasmic staining pattern was present. The specificity of the perinuclear staining pattern was finally confirmed by its disappearance after deoxyribonuclease treatment of the neutrophils. Results of the assay were considered positive when both the ANCA titer was above a cutoff of 12.1 EU/ml and indirect immunofluorescence revealed a perinuclear binding of ANCA that disappeared after deoxyribonuclease treatment (17).

Disease activity was measured with the St. Mark's index (18), which grades general health, abdominal pain, bowel frequency, stool consistency, blood in stool, anorexia, nausea and vomiting, abdominal tenderness, extraintestinal manifestations, fever, and sigmoidoscopic appearance, generating a summary index of severity with scores ranging from 0 to 22.

Depressive symptoms were measured with the Center for Epidemiologic Studies–Depression Scale (CES-D), a 20-item self-report screening instrument (19). In large community samples, a cut-off of 16 has identified 84% to 94% of subjects classified as depressed by the Schedule of Affective Disorder and Schizophrenia (SADS) structured interview, and a score of less than 16 has correctly identified 60% to 64% of subjects not classified as depressed on the SADS (20).

Health anxiety was measured as the sum of 3 scales of the Illness Behavior Questionnaire: “Psychological vs. Somatic” (e.g. “Do you ever think of illness as a punishment for something that you have done wrong in the past?”), disease conviction (e.g. “If the doctor told you that he or she could find nothing wrong with you, would you believe the doctor?”) and hypochondriasis (e.g. “Are you upset about the way other people take your illness?”). In

this scale 20 questions are answered yes or no, yielding a score of 0–20. Psychometrically, these scales have shown adequate test-retest reliability, a significant correlation between self-ratings and spouse ratings, and predicted differences between pain patients and general medical patients (21).

Statistical Analysis

Demographic variables, disease indices, and psychological variables were compared between pANCA positive and pANCA negative UC by T-test, Chi-square or Mann-Whitney U test.

The strength of the linear relationship between UC disease activity and psychological distress was expressed as a Pearson correlation co-efficient. The partial correlation between disease activity and depression was calculated for each pANCA group, correcting for age and gender (which were found to differ between pANCA positive and in pANCA negative UC). The *z* statistic was used to test the significance of the difference between two correlations: the correlation between disease activity and depression in pANCA positive and this correlation in pANCA negative UC. This analysis was repeated for the relationship between disease activity and health anxiety.

Because the St. Mark's index score includes self-reported symptoms, which can be influenced by patients' reporting style (22), analyses were repeated using only the items which are observed by the physician (abdominal tenderness, extraintestinal manifestations, fever, and sigmoidoscopic appearance).

Significance was set at $p < 0.05$ (two-tailed). Analysis was performed with SPSS 13.0 (SPSS Inc., Chicago, IL).

Results

Patients

Seventy-four subjects were pANCA positive and 74 were pANCA negative. The characteristics of the sample are shown in Table 1. More pANCA positive subjects than pANCA negative subjects were female (58% vs. 32%, $p < 0.01$) and pANCA negative subjects were somewhat older (45.6 ± 12.7 years vs. 41.6 ± 11.7 years, $p < .05$). Disease characteristics, current disease activity, depression and health anxiety did not differ by pANCA status (Table 1).

Psychobiological Interactions

In the entire cohort, significant relationships were found between depressive symptoms and disease activity (partial correlation= 0.32, 95% confidence interval 0.17–0.46, $p < 0.001$) and between health anxiety and disease activity (partial correlation= 0.41, 95% confidence interval 0.27–0.54, $p < 0.001$).

Stratification of the cohort by pANCA status yielded a significantly stronger relationship between disease activity and each measure of psychological distress in pANCA negative UC (Figure 1). The strength of relationship between disease activity and health anxiety differed

between pANCA negative UC and pANCA positive UC even when only physician observed signs of active disease were used (Table 2). The strength of relationship between physician observed signs of active disease and depression did not differ statistically between pANCA negative UC and pANCA positive UC, although the trend was in the same direction (Table 2).

Conclusions

This study shows a moderate to strong association between disease activity and psychological distress in patients who are pANCA negative which was not present in pANCA positive patients. The difference between pANCA groups was consistent for both depressive symptoms and health anxiety. The similarity of results with respect to both depression and health anxiety suggests that UC disease activity is related generally to psychological distress.

Correlations between disease activity and distress decrease somewhat when only physician-rated symptoms of UC are used, which is likely due to the lower variance in disease activity ratings that results from using only physician-observable signs. When testing the difference in these lower correlations between pANCA positive and pANCA negative UC, the difference remains significant for health anxiety but is not statistically significant for depression. Replication in a larger sample is required to test our interpretation that this is due to the decreased sensitivity inherent in limiting the measurement of disease activity to physician-rated signs.

The findings of this study are consistent with the hypothesis that pANCA negative UC is a distinct subtype characterized by psychobiological interaction. The identification of subtypes of UC with different psychobiological characteristics may explain inconsistencies in previous studies examining the relationship between disease course and psychological variables. Thus, psychobiological relationships which are only present in a subgroup of UC patients, would be diluted in studies that fail to distinguish UC subtypes, and lead to Type II error and inconsistency between studies.

Controlled trials of psychological interventions for maintenance of UC remission are needed, but are only likely to yield positive results if they are appropriately directed towards patients at high risk of psychologically-dependent relapse (5). Markers of risk, however, have been lacking. Our study suggests that pANCA status may be a useful marker psychobiological vulnerability in UC patients.

Our results further suggest that pANCA may allow for the identification of patients who are at higher risk of depression when their disease is active, and facilitate increased clinical vigilance for disease-associated depression and earlier psychological intervention. Identification of depressive risk is important in the clinical care of ulcerative colitis patients because co-morbid depression has a substantial impact on medical outcomes including increased symptom severity, unexplained physical symptoms, increased use of health care resources, and poor treatment adherence (23). Depression also increases the impact of active disease on health-related quality of life and function (24).

Why pANCA status is relevant to psychobiological interaction, and why the individuals at higher risk are those who *lack* this biological marker, remains unclear. pANCA has been linked to a UC phenotype suggestive of more severe disease course, including treatment-refractory UC (25), and occurrence of pouchitis after proctocolectomy and ileo-anal anastomosis (26–32) although the evidence for each of these associations is inconsistent (33–35). It is plausible that psychobiological factors would have greater impact on a less severe form of UC. Thus, one parsimonious explanation is that pANCA is a marker of a more severe subtype of UC in which psychological factors are irrelevant to disease course. The absence of pANCA would then identify the (possibly heterogeneous) remaining subtype(s) in which there is significant interaction between inflammation and psychological factors. It remains to be seen if a positive biological marker of the group with strong psychobiological interaction can be identified. For example, inflammatory processes and depression were found to share a genetic predisposition in a recent twin study (36). Because the current study measures a concurrent association between disease activity and distress, it is not possible to determine whether disease activity or distress occurred first in our patient population.

The conclusions of this study are limited by its design and the characteristics of the sample. In particular, the subtypes identified are distinct with respect to a concurrent association between disease activity and psychological distress, and we cannot determine causality or temporal sequence in that relationship. However, the nature of the relationship between disease and distress was not the primary focus of this analysis, since we evaluated the relationship only as an index of psychobiological interaction. The conclusions are also limited by the characteristics of the sample studied. The prevalence of pANCA in our sample of 50%, was somewhat lower than has typically been found in UC (37–39). Since pANCA positive patients may be more likely to require colectomy, the lower prevalence of pANCA may be explained by our exclusion of patients who had undergone colectomy. The participation rate of 41% is likely to be due to the time burden of participating in study procedures that are reported elsewhere (16). Nonetheless, it is possible that self-selection may have introduced a psychological bias.

In summary, for patients with UC a biological subclinical marker, pANCA demarcates a subgroup of UC patients in whom there is strong evidence for an interaction between psychological factors and disease activity. Identification of possible genetic differences between these subgroups, determination of the temporal sequence of disease activity and distress in pANCA negative UC, and the mechanisms underlying the moderating effect of pANCA remain areas for further study.

STUDY HIGHLIGHTS

What is Current Knowledge

- Psychological factors are inconsistently related to ulcerative colitis
- Depression adversely affects treatment of ulcerative colitis
- Depression adversely affects outcome of ulcerative colitis

What is New Here

- The absence of pANCA identifies patients with strong psychobiological interaction
- Identifying subtypes of ulcerative colitis explains previous inconsistencies.
- Identifying high risk patients promotes monitoring for depression

Acknowledgments

This study was supported by a research operating grant for the Canadian Institutes of Health Research (Grant number MOP-43985).

The authors thank Dr. Alvin Newman, Dr. Maria Cino, Dr. Rob Nolan and Dr. David Tannenbaum for their participation in this study.

Reference List

1. Levenstein S, Prantera C, Varvo V, Scribano M, Andreoli A, Luzi C, et al. Stress and exacerbation in ulcerative colitis: A prospective study of patients enrolled in remission. *Am J Gastroenterol.* 2000; 95:1213–1220. [PubMed: 10811330]
2. Bitton A, Sewitch MJ, Peppercorn MA, deB Edwardes MD, Shah S, Ransil B, et al. Psychosocial determinants of relapse in ulcerative colitis: A longitudinal study. *Am J Gastroenterol.* 2003; 98(10): 2203–2208. [PubMed: 14572569]
3. Maunder RG. Evidence that stress contributes to inflammatory bowel disease: evaluation, synthesis, and future directions. *Inflamm Bowel Dis.* 2005; 11(6):600–608. [PubMed: 15905709]
4. North CS, Clouse RE, Spitznagel EL, Alpers DH. The relation of ulcerative colitis to psychiatric factors: a review of findings and methods. *Am J Psychiatry.* 1990; 147:974–81. [PubMed: 2197886]
5. Levenstein S. Stress and ulcerative colitis: convincing the doubting Thomases. *Am J Gastroenterol.* 2003; 98(10):2112–2115. [PubMed: 14572553]
6. Walker EA, Roy-Byrne PP, Katon WJ, Li L, Amos D, Jiranek G. Psychiatric illness and irritable bowel syndrome: a comparison with inflammatory bowel disease. *Am J Psychiatry.* 1990; 147(12): 1656–61. [PubMed: 2103735]
7. Helzer JE, Stillings WA, Chammas S, Norland CC, Alpers DH. A controlled study of the association between ulcerative colitis and psychiatric diagnosis. *Dig Dis Sci.* 1982; 27:513–8. [PubMed: 7083987]
8. Porcelli P, Zaka S, Centonze S, Sisto G. Psychological distress and levels of disease activity in inflammatory bowel disease. *Ital J Gastroenterol.* 1994; 26:111–5. [PubMed: 8061336]
9. Mittermaier C, Dejacó C, Waldhoer T, Oefflerbauer-Ernst A, Miehsler W, Beier M, et al. Impact of depressive mood on relapse in patients with inflammatory bowel disease: a prospective 18-month follow-up study. *Psychosom Med.* 2004; 66(1):79–84. [PubMed: 14747641]
10. Maunder RG, Hunter JJ. Attachment and psychosomatic medicine: developmental contributions to stress and disease. *Psychosomatic Med.* 2001; 63(4):556–567.
11. Maunder RG, Lancee WJ, Hunter JJ, Greenberg GR, Steinhart AH. Attachment insecurity moderates the relationship between disease activity and depressive symptoms in ulcerative colitis. *Inflamm Bowel Dis.* 2005; 11(10):919–926. [PubMed: 16189422]
12. Rutgeerts P, Vermeire S. Clinical value of the detection of antibodies in the serum for diagnosis and treatment of inflammatory bowel disease. *Gastroenterology.* 1998; 115:1006–9. [PubMed: 9786723]
13. Shanahan, F. IBD-associated ANCA—current status. In: McLeod, RS, Martin, F, Sutherland, LR, Wallace, JL., Williams, CN., editors. *Trends in Inflammatory Bowel Disease Therapy 1996*. Dordrecht: Kluwer Academic Publishers; 1997.

14. Bartunkova J, Tesar V, Sediva A. Diagnostic and pathogenetic role of antineutrophil cytoplasmic antibodies. *Clinical Immunology*. 2003; 106:73–82. [PubMed: 12672398]
15. Maunder RG, Lancee WJ, Greenberg GR, Hunter JJ, Fernandes BJ. Insecure attachment in a subgroup with ulcerative colitis defined by ANCA status. *Dig Dis Sci*. 2000; 45(11):2127–2132. [PubMed: 11215726]
16. Maunder RG, Greenberg GR, Nolan RP, Lancee WJ, Steinhart AH, Hunter JJ. Autonomic response to standardized stress predicts subsequent disease activity in ulcerative colitis. *Eur J Gastroenterol Hepatol*. 2006; 18(4):413–420. [PubMed: 16538114]
17. Ruemmele FM, Targan SR, Levy G, Dubinsky M, Braun J, Seidman EG. Diagnostic accuracy of serological assays in pediatric inflammatory bowel disease. *Gastroenterology*. 1998; 115:822–9. [PubMed: 9753483]
18. Powell-Tuck J, Brown RL, Lennard-Jones JE. A comparison of oral prednisone given as single or multiple daily doses for active proctocolitis. *Scand J Gastroenterol*. 1978; 13:833–7. [PubMed: 364626]
19. Radloff LS. The CES-D scale: a self report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1:385–401.
20. Schutte, NS., Malouff, JM. *Sourcebook of Adult Assessment Strategies*. New York: Plenum; 1995.
21. Pilowsky, I. *Manual for the Illness Behaviour Questionnaire (IBQ): Recent Normative Data on General Hospital Psychiatric Inpatients and Pain Clinic Patients*. Adelaide: University of Adelaide; 1992.
22. Maunder RG, Greenberg GR. Comparison of a disease activity index and patients' self-reported symptom severity in ulcerative colitis. *Inflamm Bowel Dis*. 2004; 10(5):632–636. [PubMed: 15472526]
23. Katon W. The impact of major depression on chronic medical illness. *Gen Hosp Psychiatry*. 1996; 18(4):215–219. [PubMed: 8832253]
24. Wells KB, Stewart A, Hays RD, Burnam MA, Rogers W, Daniels M, et al. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. *Jama*. 1989; 262(7): 914–919. [PubMed: 2754791]
25. Sandborn WJ, Landers CJ, Tremaine WJ, Targan SR. Association of antineutrophil cytoplasmic antibodies with resistance to treatment of left-sided ulcerative colitis: results of a pilot study. *Mayo Clin Proc*. 1996; 71(5):431–6. [PubMed: 8628021]
26. Reumaux D, Colombel JF, Duclos B, Chaussade S, Belaiche J, Jacquot S, et al. Antineutrophil cytoplasmic auto-antibodies in sera from patients with ulcerative colitis after proctocolectomy with ileo-anal anastomosis. *Adv Exp Med Biol*. 1993; 336:523–5. [PubMed: 8296669]
27. Patel RT, Stokes R, Birch D, Ibbotson J, Keighley MR. Influence of total colectomy on serum antineutrophil cytoplasmic antibodies in inflammatory bowel disease. *Br J Surg*. 1994; 81(5):724–6. [PubMed: 8044563]
28. Yang P, Oresland T, Jarnerot G, Hulten L, Danielsson D. Perinuclear antineutrophil cytoplasmic antibody in pouchitis after proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis. *Scand J Gastroenterol*. 1996; 31(6):594–8. [PubMed: 8789899]
29. Esteve M, Mallolas J, Klaassen J, Abad-Lacruz A, Gonzalez-Huix F, Cabre E, et al. Antineutrophil cytoplasmic antibodies in sera from colectomised ulcerative colitis patients and its relation to the presence of pouchitis. *Gut*. 1996; 38(6):894–8. [PubMed: 8984029]
30. Sandborn WJ, Landers CJ, Tremaine WJ, Targan SR. Antineutrophil cytoplasmic antibody correlates with chronic pouchitis after ileal pouch-anal anastomosis. *Am J Gastroenterol*. 1995; 90:740–757. [PubMed: 7733080]
31. Vecchi M, Gionchetti P, Bianchi MB, Belluzzi A, Meucci G, Campieri M, et al. p-ANCA and development of pouchitis in ulcerative colitis patients after proctocolectomy and ileoanal pouch anastomosis. *Lancet*. 1994; 344:866–867.
32. Aisenberg J, Wagreich J, Shim J, Almer S, Peen E, Heimann T, et al. Perinuclear anti-neutrophil cytoplasmic antibody and refractory pouchitis. A case-control study. *Dig Dis Sci*. 2006; 40:1866–1872.

33. Reumaux D, Colombel JF, Masy E, Duclos B, Heresbach D, Belaiche J, et al. Anti-neutrophil cytoplasmic auto-antibodies (ANCA) in ulcerative colitis (UC): no relationship with disease activity. *Inflamm Bowel Dis.* 2000; 6(4):270–274. [PubMed: 11149558]
34. Yasuda N, Thomas P, Ellis H, Herbst F, Nicholls J, Ciclitira P. Perinuclear anti-neutrophil cytoplasmic antibodies in ulcerative colitis after restorative proctocolectomy do not correlate with the presence of pouchitis. *Scand J Gastroenterol.* 1998; 33(5):509–513. [PubMed: 9648991]
35. Kaditis AG, Perrault J, Sandborn WJ, Landers CJ, Zinsmeister AR, Targan SR. Antineutrophil cytoplasmic antibody subtypes in children and adolescents after ileal pouch-anal anastomosis for ulcerative colitis. *J Pediatr Gastroenterol Nutr.* 1998; 26(4):386–392. [PubMed: 9552133]
36. Vaccarino V, Bremner JD, Miller AH, Abramson JL, Jones L, Cheema FA. Depressive symptoms and inflammation: Is there a shared genetic vulnerability? *Psychosom Med.* 2006; 60(1):A29.
37. Abad E, Tural C, Mirapeix E, Cuxart A. Relationship between ANCA and clinical activity in inflammatory bowel disease: variation in prevalence of ANCA and evidence of heterogeneity. *J Autoimmun.* 1997; 10(2):175–80. [PubMed: 9185879]
38. Deusch K, Oberstadt K, Schaedel W, Weber M, Classen M. p-ANCA as a diagnostic marker in ulcerative colitis. *Adv Exp Med Biol.* 1993; 336:527–31. [PubMed: 8296670]
39. Rump JA, Worner I, Roth M, Scholmerich J, Hansch M, Peter HH. p-ANCA of undefined specificity in ulcerative colitis: correlation to disease activity and therapy. *Adv Exp Med Biol.* 1993; 336:507–13. [PubMed: 8296665]

Figure 1. Strength of relationship between ulcerative colitis disease activity (St. Mark's Index) and concurrent psychological distress in pANCA positive and pANCA negative UC.

Table 1

Characteristics of study participants.

	Full Sample n = 148	p-ANCA Absent n = 74	p-ANCA Present n = 74	Significance*
Age (years, mean $\pm$ SD)	43.6 $\pm$ 12.4	45.6 $\pm$ 12.7	41.6 $\pm$ 11.7	0.05
Gender (% female)	45%	32%	58%	0.002
Age of UC onset (years, mean $\pm$ SD)	30.4 $\pm$ 10.8	29.7 $\pm$ 10.0	31.2 $\pm$ 11.5	0.41
Duration of UC (years, mean $\pm$ SD)	15.0 $\pm$ 10.3	16.5 $\pm$ 10.5	13.5 $\pm$ 9.8	0.06
Most proximal extent (lifetime)				
Proctitis	28%	31%	26%	
Left-sided	27%	28%	26%	
Extensive	45%	41%	49%	0.35
Disease activity (St. Mark's Index): Mean $\pm$ SD	2.2 $\pm$ 2.7	2.0 $\pm$ 2.5	2.3 $\pm$ 2.8	0.46
Range	0 to 16	0 to 10	0 to 16	
St. Mark's score $\leq$ 2 (%)	53%	57%	49%	0.32
Ever treated with systemic steroid (lifetime, %)	57%	61%	54%	0.30
Current medication				
Systemic steroid (%)	9%	9%	8%	0.73
Antidepressant (%)	7%	5%	9%	0.51
Benzodiazepine (%)	2%	1%	3%	0.56
Smoking				
Ever smoke > 100 cigarettes (%)	41%	38%	45%	0.37
Smoke now (%)	11%	11%	12%	0.96
Depressive symptoms: Mean $\pm$ SD	11.0 $\pm$ 9.1	10.5 $\pm$ 9.0	11.4 $\pm$ 9.2	0.52
CESD score 16 (%)	26%	23%	28%	0.45
Health Anxiety: Mean $\pm$ SD	5.6 $\pm$ 4.1	5.4 $\pm$ 4.4	5.9 $\pm$ 3.9	0.48

* Significance of difference between pANCA positive and pANCA negative groups.

Table 2

Strength of relationship between disease activity and measures of psychological distress in pANCA positive and pANCA negative ulcerative colitis.

	pANCA absent n = 74	pANCA present n = 74	Significance of difference ¹	
			z	p
St. Mark's Index & Depression				
Correlation ²	0.48	0.18	2.0	0.02
95% Confidence Interval	0.28–0.63	0.05–0.39		
Significance ³	<0.001	0.14		
St. Mark's Index & Health Anxiety				
Correlation	0.64	0.20	3.3	<0.001
95% Confidence Interval	0.48–0.76	0.03–0.41		
Significance	<0.001	0.09		
MD-rated UC & Depression				
Correlation	0.35	0.14		
95% Confidence Interval	0.13–0.54	0.09–0.36	1.3	0.10
Significance	<0.001	0.26		
MD-rated UC & Health Anxiety				
Correlation	0.52	0.03	3.3	<0.001
95% Confidence Interval	0.33–0.67	–0.20–0.26		
Significance	0.003	0.83		

¹Tests the significance of the difference between correlations in pANCA positive and pANCA negative UC.

²Partial correlation, correcting for gender and age

³Tests that the correlation in this group is not 0.