

Anxiety, depression and psychotropic medication use in patients with persistent upper and lower gastrointestinal symptoms

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ABSTRACT

Background: Limited information is available about anxiety, depression and psychotropic medication use in patients referred for gastrointestinal endoscopy.

Aim: To determine anxiety and depression and its association with endoscopic findings in a representative sample of patients with persistent gastrointestinal symptoms prior to endoscopy.

Methods: Patients referred to the hospital for endoscopy between February 2002 and February 2004 were asked to score anxiety and depression on the Hospital Anxiety and Depression Scale 2 weeks prior to endoscopy. Information about endoscopic diagnoses was obtained from medical files.

Results: A total of 1298 subjects was studied (600 upper gastrointestinal endoscopies and 698 lower gastrointestinal endoscopies). Patients referred for upper gastroin-

testinal endoscopy used most psychotropic agents (24%; odds ratio = 3.1; 95% confidence interval = 2.3–4.2), especially patients with an organic abnormality when compared with patients without an organic abnormality (42% versus 8%; odds ratio = 8.6; 95% confidence interval = 5.4–14.0). Patients with colonic polyps were more anxious (odds ratio = 1.7; 95% confidence interval = 1.0–2.9) and depressed (odds ratio = 1.8; 95% confidence interval = 1.1–3.1) than other patients referred for lower gastrointestinal endoscopy.

Conclusions: There is no difference in anxiety nor depression between patients with and without organic abnormalities at endoscopy. Patients with colonic polyps are more anxious and depressed than other patients referred for lower gastrointestinal endoscopy. Psychotropic medication use is highest among patients with an organic abnormality in the proximal gastrointestinal tract.

INTRODUCTION

In the majority of patients with gastrointestinal (GI) symptoms (40–80%), no pathological cause for their symptoms can be found.^{1, 2} In search for an explanation for these symptoms, extensive research has been performed including psychological factors. Talley *et al.*, among others, concluded that patients with functional

dyspepsia (FD) or irritable bowel syndrome (IBS) who present for medical care tend to be more anxious and depressed than healthy controls.^{3–9} This also seems to be the case in subjects with functional GI symptoms who do not seek medical care.^{10–13}

Little information is available about anxiety and depression in patients in whom an organic cause for their symptoms has been found. Patients with duodenal ulcer had significantly lower levels of anxiety, general psychopathology, depression, a higher general level of functioning and less somatic complaints from different organ systems than patients with FD.^{14, 15} Pace *et al.*¹⁶

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recently found no difference in general psychological distress between patients diagnosed with IBS or inflammatory bowel disease. Yet, their study contained a limited number of patients and with the psychological questionnaire that was used, only the average severity of general psychological symptoms can be calculated but not specific scores for anxiety or depression.

The aim of this study was to determine the prevalence of anxiety and depression and its association with endoscopic findings in a representative sample of patients with upper or lower GI symptoms. In addition frequency of psychotropic medication use will be assessed.

MATERIALS AND METHODS

Subjects

Between February 2002 and February 2004, consecutive patients referred for upper or lower endoscopy to the Canisius-Wilhelmina Hospital in Nijmegen, The Netherlands, were asked to fill out a questionnaire 2 weeks prior to endoscopy. This is a general primary care district hospital. The questionnaire included enquiries on demographic information, alcohol and medication use, the presence and severity of upper and lower GI symptoms, anxiety and depression. Information about the endoscopy and histological findings were collected from medical files after completion of the questionnaire. All data were processed with Teleform automatic scanning software version 6.0 (Cardiff Software; Sunnyvale, CA, USA). All aspects of the protocol were approved by the Medical Ethical Committees of University Medical Center St Radboud and the Canisius-Wilhelmina Hospital both in Nijmegen, The Netherlands. For this study, data was used of patients who had no GI endoscopy in the last 6 months before enrolment.

Anxiety and depression

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). This is a self-completed questionnaire that has been validated and can be used in a variety of clinical settings.¹⁷⁻¹⁹ It consists of 14 items and is divided into an anxiety and a depression sub-scale, each comprising seven questions rated on a scale ranging 0-3, depending on the severity of the problem described in the question. This way utilities can be calculated that indicate the individuals

degree of anxiety or depression. A sub-scale score below 7 is considered normal, i.e. no signs of anxiety or depression.²⁰ A score of 7 to 21 was considered indicative for (mild) depression, although clinical signs might have been absent. Questions that were not filled out properly were not taken into further analysis and therefore incomplete subscales were excluded from analysis.

Endoscopy

Patients underwent a routine diagnostic upper or lower GI endoscopy. Outcomes were entered into a database. If necessary, histological data were obtained from biopsies taken during endoscopy. These biopsies were analysed by an experienced pathologist and results were entered into the same database. Results were extracted from that database and patients were divided into groups according to their most prominent endoscopic outcome. Patients were defined as having an organic disorder if their diagnosis was carcinoma, gastric or duodenal ulcer, reflux oesophagitis, hiatic hernia, colitis, polyps or diverticula's. When no endoscopic or histological explanation for symptoms could be found, they were defined as functional. Patients who underwent an endoscopy in the past 6 months before enrolment were excluded from further analysis.

Medication

Most patients included in the study used medication. Information on the use of psychotropic agents was obtained from the questionnaires and taken into further analysis (TCA's, SSRI's, other non-tricyclic agents and benzodiazepines).

Statistical analyses

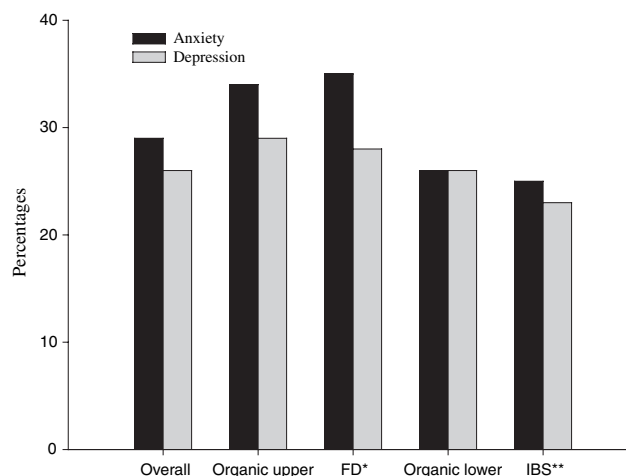
Statistical analysis was undertaken with SAS statistical software, version 8.0 (SAS Institute Inc, Minneapolis, MN, USA). Data at baseline were analysed by means of frequency tables and descriptive statistics. Patients with incomplete data were excluded from further analysis. Logistic regression analyses were performed to determine the odds ratios for anxiety and depression among disorders of the same part of the GI tract. Outcomes were adjusted for gender, age and psychotropic medication use. The latter was dichotomized into use and non-use. The same analyses were performed to deter-

mine odds ratios for medication use. Results were adjusted for age and gender. Overall, an alpha <0.05 was considered statistically significant.

RESULTS

Overall, 1969 out of the 3615 (54%) questionnaires that were sent were returned. Of these, 671 were excluded from further analysis as a result of improperly filled out questionnaires, or a recent GI endoscopy. Six hundred and fourteen (47%) subjects were male and mean age was 55 years (s.d. ± 15): 600 patients underwent an upper GI endoscopy and 698 a lower GI endoscopy (Table 1). Previous diagnostic intervention (i.e. endoscopy, X-ray or *Helicobacter pylori*-test) was reported by 731 patients, of which 493 (38%) patients had a previous endoscopy. Patients referred for lower GI endoscopy reported more previous endoscopic procedures (42%) than patients referred for upper GI endoscopy (33%) ($P < 0.01$) (Table 1).

In the total study population, mild to severe anxiety was reported by 29% and mild to severe depression by 26% (Figure 1). Use of psychotropic agents was higher among patients referred for upper GI endoscopy than among patients referred for lower GI endoscopy (24% vs. 9%; OR = 3.1; 95% CI = 2.3–4.2). Patients with an organic disorder of the proximal part of the GI tract used more antidepressants or benzodiazepines (42% vs. 8%; OR = 8.6; 95% CI = 5.4–14.0) in comparison to patients without an organic abnormality. Patients with



* Functional dyspepsia; ** Irritable bowel syndrome.

Figure 1. Percentages of anxiety and depression in patients with gastrointestinal diseases.

organic abnormalities in the proximal GI tract other than peptic ulcer, carcinoma or oesophageal reflux disease all used some sort of psychotropic medication. We found no difference in the use of psychotropic medication between patients without organic abnormalities referred for upper and lower GI endoscopy.

Patients with functional upper GI disease reported anxiety most often (35%) (Figure 1). Patients referred for upper GI endoscopy were more anxious than patients referred for lower GI endoscopy (OR = 1.6; 95% CI = 1.2–1.9). Thirty-nine per cent of the patients with peptic ulcer disease reported anxiety and 33% was depressed (Table 2). Overall, there was no difference in anxiety nor depression between patients with functional GI diseases and patients with an organic abnormality at upper GI endoscopy (OR = 1.2; 95% CI = 0.8–1.7 and OR = 0.9; 95% CI = 0.6–1.3 respectively) and at lower GI endoscopy (OR = 1.0; 95% CI = 0.6–1.5 and OR = 0.9; 95% CI = 0.6–1.4, respectively). However, patients diagnosed with colonic polyps were more anxious and depressed than other patients referred for lower GI endoscopy (OR = 1.7; 95% CI = 1.0–2.9 and OR = 1.8; 95% CI = 1.1–3.1, respectively) (Table 2).

DISCUSSION

The results from several studies showed that patients with functional GI disease are more anxious and depressed than healthy controls.^{4–10, 13, 16} However, data comparing patients with functional GI diseases with patients with an organic cause of their symptoms

Table 1. Demographics and endoscopic findings

Characteristics	No. of patients (%)
Age (years)	
18–50	444 (34)
>50	854 (66)
Gender	
Male	614 (47)
Female	684 (53)
Upper GI endoscopy	600 (46)
Organic upper GI disease	280 (47)
Functional upper GI disease	320 (53)
Lower GI endoscopy	698 (54)
Organic lower GI disease	133 (19)
Functional lower GI disease	565 (81)
Previous endoscopy	493 (38)
Other previous diagnostic interventions*	238 (18)

GI, gastrointestinal.

* X-ray or *Helicobacter pylori* test.

	No. of patients	Anxiety		Depression	
		%	OR (95% CI)*	%	OR (95% CI)*
Upper GI endoscopy	600	34	1.6 (1.2–1.9)	28	1.2 (0.9–1.5)
Carcinoma	7	14	0.4 (0.0–2.8)	50	2.2 (0.4–12.3)
Peptic ulcer	33	39	1.5 (0.7–3.2)	33	1.5 (0.7–3.1)
Reflux oesophagitis	132	33	1.0 (0.7–1.6)	28	1.1 (0.7–1.7)
Hiatic hernia	41	34	1.0 (0.5–2.0)	29	1.1 (0.5–2.1)
Other†	67	36	0.3 (0.1–0.6)	28	0.2 (0.1–0.5)
Functional‡	320	35	1.2 (0.8–1.7)	28	1.1 (0.8–1.6)
Lower GI endoscopy	698	25	0.7 (0.5–0.9)	24	0.8 (0.7–1.1)
Carcinoma	8	25	1.0 (0.2–4.6)	0	n.a.
Colitis	23	17	0.5 (0.1–1.4)	17	0.7 (0.2–2.0)
Polyps	78	32	1.7 (1.0–2.9)	33	1.8 (1.1–3.1)
Diverticles	16	13	0.4 (0.1–1.5)	31	1.1 (0.3–3.3)
Other†	8	13	0.1 (0.0–1.0)	0	n.a.
Functional‡	565	25	1.0 (0.6–1.5)	23	0.9 (0.6–1.4)

* ORs are among disorders of the same part of the gastrointestinal (GI) tract (i.e. proximal or distal) and adjusted for gender, age and use of psychotropic medication.

† Other organic abnormalities found at endoscopy, e.g. oesophageal varices, fungus, stomach resection.

‡ No abnormalities found at endoscopy.

Statistically significant differences are marked in bold.

are limited. This study was therefore performed to determine the prevalence of anxiety and depression and its association with endoscopic findings in a representative sample of patients with GI symptoms. Our results showed that patients referred for upper GI endoscopy are significantly more anxious than those referred for lower GI endoscopy. Although less anxious and depressed than patients referred for upper GI endoscopy, anxiety or depression is still reported by a quarter of all patients referred for lower GI endoscopy.

Psychotropic medication use among patients referred for GI endoscopy is high. There was no data available about reasons of prescription. Patients referred for upper GI endoscopy, especially those with an organic cause of their symptoms, consume more psychotropic medication than patients referred for lower GI endoscopy. This may have at least two explanations: as a lot of patients with GI symptoms are also anxious and depressed, it is very well possible that they use psychotropic medication to suppress their psychological complaints. Secondly, in The Netherlands, psychotropic agents are among the five most prescribed medicine.²¹ It is well known that antidepressants have GI side-effects. Thus it is possible that these patients have GI abnormalities as a side-effect of their psychotropic medication.

O'Malley *et al.*²² found that the presence of any psychiatric disorder makes it unlikely that upper GI

endoscopy will reveal significant GI abnormalities. Although their results lack evidence for an association with anxiety disorders, they conclude that mood and somatoform disorders are associated with endoscopy outcomes. This discrepancy with our study results might be explained by some differences in study design: first, we have included patients that might have been referred for a follow-up endoscopy, while the study by O'Malley included only patients with unexplained GI symptoms. In addition, they used a different diagnostic psychiatric test that assessed psychiatric disorders in general, including somatoform disorders, alcohol abuse and eating disorders whereas we used a validated specific anxiety and depression scale.^{17–19} Besides this, the study population of O'Malley *et al.* consisted of only 116 subjects, of whom only 29 (25%) had major endoscopic abnormalities.

There is no difference in anxiety and depression among patients referred for lower GI endoscopy between those with functional and organic causes of their symptoms. However, a remarkable conclusion is that patients diagnosed with colonic polyps are more anxious and depressed than other patients referred for lower GI endoscopy. There are some explanations imaginable for this finding: first, because of the genetic pattern, it is very well possible that these patients have relatives with colonic polyps or cancer and are anxious or depressed

Table 2. Anxiety and depression and findings at endoscopy

because they recognize the symptoms, or their physician told them that they are at increased risk of developing polyps themselves. Secondly, it is possible that some of them were already familiar with their diagnosis and were referred for a follow-up endoscopy. At last, as many groups were compared, it is possible that this finding is purely due to chance. Clinicians dealing with patients with colonic polyps should be aware of a possible psychological problem and take appropriate action when needed.

The division of patients according to endoscopy outcomes may have caused some limitations to the interpretation of results. For example, many patients with functional upper GI disease have an asymptomatic hernia. In addition, it is well known that at random endoscopy, polyps and diverticula's will be found in a significant part of the population.²³⁻²⁴ However, assuming that all subjects were referred for GI endoscopy for a legitimate reason (i.e. persistent GI symptoms), this division seems justifiable. The fact that many of these organic abnormalities are present in asymptomatic subjects, does not change anything to the possibility that they explain symptoms in patients presenting to the gastroenterology practice.

Although we included patients referred for their first endoscopy, one-third indicated to have had a previous endoscopy. It should be noted that high levels of anxiety or depression cannot be explained by fear for the procedure, as the HADS questionnaire measures generalized anxiety and depression only. Furthermore, we assumed that the effect of a previous endoscopy on anxiety or depression would be cancelled out after 6 months. Therefore, patients who had an endoscopy in the past 6 months before enrolment were excluded from further analysis. Besides, patients who underwent a previous endoscopy were not more anxious or depressed in comparison with patients with and without an organic abnormality who were referred for their first endoscopy.

The response rate to the first questionnaire is quite low. Possibly, this is because of the fact that all patients referred for GI endoscopy received a questionnaire. A certain part may have judged themselves not eligible for participation in this trial because they had a recent endoscopy, or insufficient control of the Dutch language. The low response rate may have given a distorted view of anxiety and depression rates in the studied population. It is very well possible that patients with an psychiatric disorder are more likely or unlikely than others to return the questionnaire.

In conclusion, patients referred for upper GI endoscopy are more anxious and use more psychotropic medication compared with patients referred for lower GI endoscopy. Patients with colonic polyps are more anxious and depressed than other patients referred for lower GI endoscopy. There is no difference in anxiety nor depression between patients with an organic cause for their symptoms and patients with functional GI disease.

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