Chronic dyspepsia in general practice. Tapering the use of acid suppressant drugs
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Psychological disorders and health status in chronic dyspeptic patients in general practice: a case control study

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Submitted
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Background
Psychological distress is supposed to be common among dyspeptic patients, however it is not clear whether this is due to major psychiatric disorders like depression, anxiety and phobia. The prevalence of these diseases and their relation with functional health in chronic dyspeptic patients is studied.

Methods
In this cross-sectional, case control study, 318 patients from primary care on long-term use of acid suppressant drugs (ASD) for reasons of ulcer disease, functional dypepsia or mild reflux disease were included. Self-reported symptoms of depression, anxiety and phobia (DSM-III-R), consultation rate, psychopharmacca and health status (COOP / WONCA) were compared between study patients and age and sex matched controls.

Results
In dyspeptic patients, life-time depression, anxiety and phobia disorders were self-reported in 45%, 22% and 24%, respectively. Anxiety (only in males) was more often observed in dyspeptic patients than in controls (p<0.05). Yearly consultation rate in dyspeptic patients (4.9) was 50% higher than in controls (3.2) (p<0.05). The use of psychopharmacca was not different, 17% and 13 %, respectively. Prior psychiatric comorbidity was diagnosed only in 15% of patients with selfreported depression and in 10% of patients with anxiety. Fear of cancer was perceived by 48% of patients, independent of prior investigations. Health status was more negatively perceived in all aspects by dyspeptic patients with self-reported psychiatric disorders than by controls (p<0.05). Neither ulcer disease nor H. pylori status influenced either one of the outcomes.

Conclusions
Depression and anxiety are common in chronic dyspeptic patients. However, it may not always be recognised and is responsible for a more negative view on health status. Treatment strategies of chronic dyspepsia should not only be focussed on repeated ASD prescriptions and H. pylori infection but should also explore and treat psychological diseases and worries of patients.
INTRODUCTION

The prevalence of dyspepsia varies around 30% in a western general population while only approximately one-quarter of dyspeptic patients consult their GP. For relief of dyspeptic symptoms acid suppressant drugs (ASD) are prescribed in 80% of patients as short periods of empirical treatment. If symptoms are relapsing, long-term treatment is prescribed. In the Netherlands 2% of all people uses long-term ASD per year.

Increased prevalence of depression, anxiety and mental distress in dyspeptic patients relative to the general population is suggested in the literature, but there are only few controlled studies available to support this notion. The relationship between psychological disorders and dyspepsia remains complex, since the illness can lead to psychological disorders, but psychological disorders may also generate and influence dyspeptic symptoms perceived by patients. These studies were often secondary care based and included patients with a new episode of dyspepsia not currently controlled by ASD. Although there is general agreement that depression and mental comorbidity are more common in chronic somatically ill subjects than in the general population, it is questionable whether this accounts for chronic dyspepsia.

The relation between dyspepsia and health status has also been the subject of some studies. A recent primary care study showed that in dyspeptic patients presenting to the general practitioner the relationship between dyspeptic symptom severity and health status is limited and that psychological distress may be a major determinant for impaired health. Furthermore, no studies are available on the relation between health status and dyspepsia in long-term ASD users in general practice. Caring for the chronically ill in primary care is challenging; not cure but optimising the quality of life of the individual patient is the task of the GP. Mislabelling psychological symptoms as "side effects" of dyspepsia may lead to repeat prescriptions of ASD and underdetection and undertreatment of psychological disorders in general practice.

Since the role of *H. pylori* as a cause of peptic ulcer disease is clarified, the interest in an infectious i.e. organic cause of dyspeptic symptoms is highlighted. Test and treat strategies are advised. However, most of the investigated dyspeptic patients haven’t got peptic ulcer disease but symptomatic or erosive gastro esophageal disease (GERD) or functional dyspepsia. In reflux disease no etiological role of *H. pylori* is found. Until now only a minority (if any) of patients with functional dyspepsia benefit of a *H. pylori* infection eradication treatment. Even in patients with peptic ulcer disease one might challenge the infection as a moncausal explanation since most infected people do not develop ulcer disease.
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The aim of our study is to examine in general practice in chronic dyspeptic patients compared to controls the relation between dyspepsia and psychological disorders with instruments commonly used in general practice with respect to depression, anxiety, phobia, the use of psychopharmaca, the frequency of GP consultation and the health status.

METHODS

Subjects
This study which forms a part of a larger study on ‘Chronic dyspepsia in General Practice’ which was conducted in the period April 1997-October 1999 in Amsterdam. Patients, aged 18-85 years, were enrolled into a study on the management of chronic dyspepsia and long-term use of acid suppressant drugs (ASD) in primary care. From fifty-four general practices, 434 of 1083 eligible patients (40%) on long-term ASD (H$_2$-Receptor Antagonist (H$_2$RA) or proton pump inhibitor (PPI)) for chronic upper abdominal pain/discomfort or reflux disease (symptomatic or oesophagitis grade 1) participated in the study and volunteered for upper intestinal endoscopy. All patients who entered this larger study in the period April ‘97-October ‘98 (n=337) were included for this study. Patients were identified by means of computerised medication data of all pharmacists co-operating with the participating GPs. Excluded were patients with a documented history of gastro esophageal reflux disease grade II,III,IV, patients with severe comorbidity; lactating women; patients requiring an interpreter; patients taking antibiotics or bismuth containing compounds during the previous month, patients taking NSAIDs; patients with any condition associated with poor compliance (e.g. drug or alcohol abuse, dementia). To patients eligible for inclusion an invitation letter to participate in the study was sent by their GP. In hospital, after endoscopy, demographic and other questionnaires were filled out.

The study was approved by the Institutional Ethics Committee of the Academic Medical Center and a written informed consent was obtained at the time of endoscopy.

Instruments

Endoscopy and H. pylori assessment
After an overnight fasting period, the patients underwent GI endoscopy with biopsies for H. pylori infection. These were assessed according standard protocols as described before.\textsuperscript{19}

Questionnaires
The GP-investigator (G.H.) investigated in the general practice the psychopharmaca prescribed in the previous half year, the frequency of GP consultations in the year prior to entry the study and psychiatric comorbidity.
In hospital at the appointment day patients answered several questionnaires:

*Psychiatric morbidity and Health status*

The most common psychiatric conditions in general practice, i.e. depressive-, anxiety- and simple phobia disorder were assessed by questions referring to the DSM-III-R symptoms of these conditions, which are also used in the Dutch GP Guidelines for these disorders. Selfreported depression was considered as a period of at least two weeks in which daily activities (nearly) couldn’t be performed due to either depressed mood or markedly diminished interest or pleasure in all, or almost all, activities, combined with one or more other symptoms of depression as mentioned in the DSM-III-R. A similar operationalisation was used for anxiety disorder. If excessive fears of being in places or situations or exposure to a circumscribed stimulus (object or situation) restricted a patient in his daily activities, it was considered as a phobia. Furthermore, patients were asked for fear of cancer of the upper gastrointestinal tract. Health status was measured by the COOP/Wonca charts, representing the patient’s physical, social and work performance. The patient’s status during the preceding two weeks on six dimensions (physical fitness, feelings, daily activities, social activities, change in health and overall health) was selfreported by the patient on a five point ordinal scale, each point illustrated by a drawing. This instrument is well validated in general practice, easy to handle, clinically accepted and commonly used in many countries.

*Controls*

We used three different control groups.

Prescription of psychiatric medication, consultation rates and psychological comorbidity were compared with non dyspeptic control patients matched for age and sex randomly selected from the electronic medical records of one of the participating health centres servicing 11.500 patients.

For comparison of psychological symptoms, controls were recruited from the computerised data of a GP based prevalence study for psychiatric disorders conducted in the same study area and were randomly chosen matched for age, sex, and ethnicity.

Functional health scores were compared with an age-matched Dutch population, usually used as reference for this measurement.

*Statistics*

Analysis was performed using the SPSS for Windows (version 7.5.3). The odds ratio was used for comparison of groups. Means were compared with the T-test. Significance was set at $\alpha = 0.05$ (two-sided).
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Results

Patients
Eligible for the study were 824 chronic dyspeptic patients of whom 337 (41%) participated. After upper endoscopy 19 patients were excluded due to severe esophagitis or incomplete baseline records. Baseline characteristics of the 318 patients are: male (46%), mean age (53 years (18-83)), natives (76%), \(H_2\)-receptor antagonist use (65%), proton pump inhibitor use (35%), \(H. pylori\) positive (48%), peptic ulcer disease (16%).

Self-reported depression, anxiety and simple phobia
Prevalence of life-time depression and phobia did not differ between dyspeptic patients and controls (table 1). In total 53% patients (169/318) reported either one or more of the three psychiatric diagnoses. Dyspeptic patients reported significantly more often to have sought professional help than controls for depression 67% (96/143) versus 21% (33/156) (OR=3.2;95% CI 2.0-5.0). Although the prevalence of anxiety differed significantly between dyspeptic patients and controls (22% and 14%, respectively), the professional help seeking didn’t. Significant prevalence differences for selfreported anxiety between dyspeptic patients and controls were only seen in males, not in females.

GPs had diagnosed depression in 15% of patients with a selfreported depression period (22/143) and anxiety in 10% of patients with such a selfreported diagnosis (7/70). Of patients with a major depressive episod (n=66) 52% reported their last major depressive period less than one month ago, 26% between 2-12 months ago and 22% more than a year ago. Of patients aged 18-65 years 23% (57/243) reported a major depression and 81% (46/57) reported their last major depressive period less than one year ago. Of patients with a selfreported period of anxiety (n=70) 36%, 33% and 31% had such a period less than one month, between 2-12 months ago and more than one year ago, respectively. For patients with phobia (n=77) these figures were 31%, 31% and 38% respectively.

Fear of cancer of the upper gastrointestinal tract was perceived by 48% (152/314). No significant difference in this aspect was observed between patients with a history of investigations and patients without, 46% vs 52%.

Prescription of psychopharmaca and consultation rates
Antidepressants and benzodiazepines were all more commonly prescribed in dyspeptic patients than in controls. However, differences were small and not significant (table 1). Dyspeptic patients had consulted their GP 50% more often than controls in the year prior to study entry; 4.9 and 3.2, respectively.
Table 1. Results of self-reported psychiatric comorbidity, use of psychofarmaca, consultation rate, psychiatric diagnosis, stratified for dyspeptic patients (n=318) and controls (n=318).

<table>
<thead>
<tr>
<th>selfreported psychiatric comorbidity in life-time</th>
<th>Dyspepsia % (n)</th>
<th>Controls % (n)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>depression (1-10 symptoms)</td>
<td>45 (143)</td>
<td>49 (156)</td>
<td>0.9 (0.6-1.2)</td>
</tr>
<tr>
<td>seeking professional help</td>
<td>67 (96)</td>
<td>21 (33)</td>
<td>3.2 (2.0-5.0)</td>
</tr>
<tr>
<td>depression (≥ 5 symptoms)</td>
<td>21 (66)</td>
<td>25 (78)</td>
<td>0.8 (0.6-1.2)</td>
</tr>
<tr>
<td>seeking professional help</td>
<td>77 (51)</td>
<td>32 (25)</td>
<td>2.4 (1.4-4.3)</td>
</tr>
<tr>
<td>anxiety</td>
<td>22 (70)</td>
<td>14 (46)</td>
<td>1.7 (1.1-2.5)</td>
</tr>
<tr>
<td>seeking professional help</td>
<td>79 (55)</td>
<td>65 (30)</td>
<td>1.2 (0.7-2.2)</td>
</tr>
<tr>
<td>phobia</td>
<td>24 (77)</td>
<td>20 (63)</td>
<td>1.3 (0.9-1.9)</td>
</tr>
<tr>
<td>seeking professional help</td>
<td>55 (42)</td>
<td>38 (24)</td>
<td>1.4 (0.8-2.6)</td>
</tr>
<tr>
<td>psychopharmaca</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>psychopharmaca</td>
<td>17 (54)</td>
<td>13 (42)</td>
<td>1.3 (0.9-2.1)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>5 (17)</td>
<td>4 (12)</td>
<td>1.2 (0.5-2.7)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>13 (40)</td>
<td>11 (35)</td>
<td>0.6 (0.2-1.6)</td>
</tr>
<tr>
<td>registered psychiatric comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>depressive disorder</td>
<td>7 (21)</td>
<td>2.1 (7)</td>
<td>3.1 (1.3-7.5)</td>
</tr>
<tr>
<td>anxiety</td>
<td>2 (13)</td>
<td>1.3 (4)</td>
<td>3.4 (1.1-10.4)</td>
</tr>
<tr>
<td>consultation rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>4.9</td>
<td>3.2</td>
<td>1.1-2.3*</td>
</tr>
</tbody>
</table>

* 95%CI of the difference

Functional health
Dyspeptic patients < 65 years of age perceived their health status more negative than controls (table 2) in all aspects.
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Table 2. Functional health status of chronic dyspeptic patients (n=318) and controls

<table>
<thead>
<tr>
<th>functional status**</th>
<th>dyspepsia &lt;65y</th>
<th>≥65y</th>
<th>control &lt;65y</th>
<th>≥65y</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>3.5</td>
<td>3.3</td>
<td>2.4*</td>
<td>2.9*</td>
</tr>
<tr>
<td>Daily activities</td>
<td>2.2</td>
<td>2.1</td>
<td>1.5*</td>
<td>1.9</td>
</tr>
<tr>
<td>Social activities</td>
<td>1.8</td>
<td>1.5</td>
<td>1.5*</td>
<td>1.6</td>
</tr>
<tr>
<td>Physical fitness</td>
<td>2.5</td>
<td>3.2</td>
<td>1.9*</td>
<td>3.5*</td>
</tr>
<tr>
<td>Feelings</td>
<td>2.2</td>
<td>1.8</td>
<td>1.6*</td>
<td>1.7</td>
</tr>
<tr>
<td>Health Change</td>
<td>3.0</td>
<td>2.9</td>
<td>3.0</td>
<td>2.9</td>
</tr>
</tbody>
</table>

* significant difference (p<0.05) between dyspeptic patients and controls
** (score: 1-5; the higher the worse)

Except for the aspect of general health, these differences with controls were not more observed in dyspeptic patients without selfreported psychiatric diagnoses (table 3).

Table 3. Functional health status of chronic dyspeptic patients stratified for self-reported psychiatric diagnosis

<table>
<thead>
<tr>
<th>selfreported psychiatric diagnosis</th>
<th>Yes (n=169)</th>
<th>No (n=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>functional status**</td>
<td>&lt;65y ≥65y</td>
<td>&lt;65y ≥65y</td>
</tr>
<tr>
<td>General health</td>
<td>3.6 3.4</td>
<td>3.3* 3.2</td>
</tr>
<tr>
<td>Daily activities</td>
<td>2.5 2.6</td>
<td>1.7* 1.9†</td>
</tr>
<tr>
<td>Social activities</td>
<td>2.1 2.0</td>
<td>1.5* 1.3†</td>
</tr>
<tr>
<td>Physical fitness</td>
<td>2.6 3.4</td>
<td>2.2* 3.1</td>
</tr>
<tr>
<td>Feelings</td>
<td>2.6 2.5</td>
<td>1.7* 1.5†</td>
</tr>
<tr>
<td>Health Change</td>
<td>3.0 2.8</td>
<td>2.9 3.0</td>
</tr>
</tbody>
</table>

* † p<0.05 between dyspeptic patients with and without a selfreported psychiatric diagnosis
** score: 1-5; the higher the worse
However, dyspeptic patients with such a self-reported psychiatric diagnosis were significantly more negative in all aspects about their health status than dyspeptic patients without and than controls. Dyspeptic patients ≥ 65 years had in general equal results in health status as controls, however, also for this age group, the subgroup of patients with self-reported psychiatric diagnoses were significantly more negative than the group of dyspeptic patients without self-reported psychiatric diagnoses and than controls.

**Patients with ulcer disease versus patients with non-ulcer disease**

The percentages of listed items in table 1 and 2 were equal between patients with or without ulcer disease except for consultation rate. Patients with non-ulcer dyspepsia consulted more often their GP than patients with ulcer disease; 5.1 consultations / year and 4.1, respectively (p<0.05) (data not shown).

**Patients with H. pylori infection versus patients without H. pylori infection**

The percentages of listed items in table 1 and 2 were equal between patients with or without H. pylori infection (data not shown) (p<0.05). H. pylori positive patients scored significantly higher than H. pylori negative patients with respect to one of the charts of functional health (perceived general health) 3.6 and 3.3, respectively.

**Discussion**

Patients who present with dyspeptic symptoms, such as abdominal pain or discomfort or heartburn are common in general practice. They are a selection of patients from the open population with same symptoms not consulting a general practitioner (GP), the so-called iceberg phenomenon. Patients who finally, after empirical treatments and further investigations, reach the stage of long-term treatment with ASD are again a selection. The long-term users which we have studied had in majority minor or no abnormalities at endoscopy. They represent about half the population of long-term ASD users in primary care. We have tried to elucidate by several instruments, commonly used in primary care daily practice and research, whether there is an association between psychiatric disorders and chronic dyspeptic complaints. Our symptom questionnaire for psychiatric disorders is not formally validated; however it has a high concordance with the list of symptoms of psychiatric diagnoses according the DSM-IIIR (20). The COOP/Wonca charts are of proven value for assessment of functional health status in research and clinical practice at many different locations. The choice of control groups and the cross-sectional design make strong causal interferences impossible. Firstly, we do not know the dyspeptic status of two of our control groups. Secondly the nature of the association between dyspepsia and the psycho-
social determinants (cause or effect) is impossible to determine. Finally, not all potential confounders have been considered in the analyses.

Overall, there is no substantial difference in prevalence of life-time self-reported depression and phobia between chronic dyspeptic patients and healthy controls. However, the 19% of patients aged 18-64 reporting a major depressive episode less than one year ago (46/243) is three times higher than the "past twelve month" prevalence of 5.8% observed in a recent large community survey in the Netherlands. Depressive dyspeptic patients sought more often help for these symptoms than controls. Perhaps, therefore the diagnosis was more often made than in controls. Anxiety was more often reported among dyspeptic patients, which is in line with Haugh et al. It was striking that this difference in our study population was observed only in men and not in women. An important difference was observed in the self-report of depressions, anxiety or phobia and detection by the GP. This under-detection is a well-known phenomenon in primary care. Maybe the focus was too much on dyspeptic symptoms at the time of consultation or the GP didn't reach in the specific patient all DSM criteria for a psychiatric diagnosis.

The use of psychopharmaca was not different compared to controls. The consultation rate was clearly higher in the dyspepsia group. Lydeard and Jones found that patients who choose to consult a physician for dyspeptic complaints were people more concerned about the fear of serious disease and that the decision to consult didn't depend on the severity or frequency of symptoms. Our population of chronic dyspeptic patients may be a selection of people more worried than others. In line with this hypothesis is the fact that about half of the patients had fear of cancer of the upper gastrointestinal tract. A similar rational for consulting behaviour has been observed in patients with irritable bowel syndrome. This belief can not easily be altered in many of the patients, since even half of the patients with investigations in the past still had such a believe at entry of this study.

Functional status in all aspects was judged more negative by dyspeptic patients in the age group < 65 years. This negative judgement was not caused by the stop with ASD before entry of the study since general health had not changed within the period two weeks prior to study entry, when patients were still on long-term ASD, as reported by the patients in the COOP/Wonca charts. A decrease in health status in dyspeptic patients has been described before. Not dyspepsia but the psychiatric comorbidity seems to be responsible for the perceived negative functional health status in chronic dyspeptic patients long-term on ASD. Patients who did not report such comorbidity had an almost equal functional health as the control population. Since patients with other severe somatic comorbidity were excluded, we assume that psychiatric comorbidity is the most important effect modifier determining the relation we found in the subgroup in our study. It is remarkable that the age group of > 65 years without psychiatric disorders seem to be healthier than controls of that age. This could be caused by a selection-bias as a result of strict inclusion criteria for the dyspepsia patients:
patients had to be able to attend the hospital and patients with serious diseases were excluded, while these could be present in the control group.

We didn’t observe any differences between ulcer and non-ulcer dyspeptic patients, except for the higher consultation rate for non-ulcer patients, nor between \textit{H. pylori} positive patients and negative patients.

In general, not chronic dyspepsia but the reported psychiatric co-morbidity seems to make chronic dyspeptic patients assess their functional health in a negative light. Psychiatric co-morbidity, although not more present than in control populations, may not always be recognised by the GP. Quite a high percentage of these patients suffered from active depression. Based on our findings, it is clear that more attention on the worries of patients and psychiatric disorders may improve the health of chronic dyspeptic patients long-term on ASD and may thereby be a better option than the prescription of ASD on a long-term basis.

\textbf{References}


