Research

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Psychiatric comorbidity among terminally ill patients in general practice in the Netherlands:

a comparison between patients with cancer and heart failure

Abstract

Background
It is unclear whether psychiatric disorders are specifically related to the terminal phase of cancer, or independent of the underlying disease.

Aim
To investigate the rate of psychiatric comorbidity and psychotropic drugs prescription in terminally ill patients in the GP setting, comparing both patients with terminal cancer and heart failure.

Design and setting
Retrospective cohort study using the Utrecht General Practitioner Research Network.

Method
Equally-sized groups of patients with terminal cancer and heart failure were randomly selected from the database of four general practices over the years 2005–2009. Psychiatric comorbidities were determined using the International Classification for Primary Care (ICPC) codes and psychotropic drugs prescriptions using the Anatomical Therapeutic Chemical (ATC) Classification System codes.

Results
A total of 191 terminally ill patients were included in the study (111 with cancer and 80 with heart failure). The mean age for patients with terminal cancer (70.8 years, standard deviation [SD] = 12.8) was 15 years younger than that of patients with heart failure (85.6 years, SD = 9.2). Half of the terminally ill patients (50.3 %) were prescribed psychotropics, but only 13.6% of them had obtained a psychiatric diagnosis. There were no significant differences in prevalence of psychiatric disease and psychotropic drug prescription between patients with terminal cancer and heart failure.

Conclusion
The results demonstrate a high use of psychotropic drugs in terminally ill patients, often in the absence of a formal diagnosis of a psychiatric disorder. The absence of differences between patients with cancer and heart failure suggests that psychiatric diagnoses and increased psychotropic prescriptions are primarily related to the terminal stage of the disease and not to the background of cancer or heart failure.

Keywords
cancer; heart failure; general practitioners; psychiatry; psychotropic drugs; terminal care.

INTRODUCTION

Cancer is a leading cause of morbidity and mortality in the Netherlands.[1] In 2010, 30% of the population mortality was related to cancer.[2] The incidence of cancer is still rising, mainly because of the ageing of the population. Mortality rates are declining due to advances in treatment and early detection of disease.[1–3]

The GP's role as gatekeeper in the Dutch healthcare system means that most patients will consult their GP on initial symptoms. As most patients with cancer die at home, GPs also coordinate the palliative care for these patients and their families in their final phase of life.[4–8] Previous research demonstrated that GPs in the Netherlands provide palliative care to, on average, four patients with cancer per year.[9] The growing number of patients with cancer will further increase the palliative care workload in general practice in the future.

Patients with end-stage cancer experience a wide range of somatic symptoms.[10] Most common symptoms are pain, fatigue, reduced appetite, breathlessness and vomiting.[9–12] In addition to somatic complaints, many terminally ill patients experience psychological distress.[13,14]

Previous reports demonstrate that the prevalence of psychiatric disorders among patients with cancer ranges from 20% to 60%.[15–17] Most patients suffer from adjustment disorders or major depressive disorders. Diagnosing psychiatric comorbidity in terminally ill patients is challenging. Somatic symptoms, physical deterioration, and accompanying mood changes often mask psychiatric symptoms, leading to under-reporting in primary care registration data.[18–20] To bypass the potential problem of systematic under-reporting, this study examined prescriptions of psychotropic drugs as a proxy indicator of psychiatric comorbidity in the study of terminally ill patients.[21–23] However, it is possible that the significant increase in the use of psychotropic drugs in the terminal stage may also indicate the high prevalence of psychological and somatic symptoms experienced by the patients that do not fulfil the diagnosis of psychiatric disorder but warrant intervention.[24,25]

To date, it is unclear if the increased incidence of psychiatric symptoms in the last phase of life is unique to cancer or related to the terminal disease stage in general. Recent studies report an increased incidence of psychiatric symptoms for other chronic conditions as well.[26,27] A meta-analysis reported that also in patients with heart failure the incidence of depression is increased, ranging from 10% to 40% depending on the diagnostic methods and the disease stage.[28] Therefore, the study compared the prevalence of psychiatric comorbidity in the terminal disease phase in primary care patients with cancer and heart failure to assess whether the increased

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How this fits in

Psychiatric comorbidity is a major burden in cancer patients, certainly in the terminal phase. This study investigated the rate of psychiatric comorbidity and psychotropic drugs prescription in terminally ill patients, comparing patients with terminal cancer and heart failure, to determine whether psychiatric disorders are related to the terminal phase of cancer, or specifically to the underlying disease. The results showed there were no significant differences between patients with terminal cancer and heart failure and increased psychotropic prescriptions are primarily related to the terminal stage of the disease.

psychiatric comorbidity is disease specific or related to the terminal disease stage.

METHOD

Patients and setting

Data were extracted from the database of six general practices participating in the Utrecht General Practitioner Research Network (GPRNU). The network represents a cross section of the urban and rural GP practices in the region of the middle Netherlands. In the GPRNU database routine primary care data of approximately 60 000 patients have been recorded from 1994 onwards, collecting standardised medical registration data, including diagnostic codes according to the International Classification for Primary Care (ICPC), and prescription codes according to the Anatomical Therapeutic Chemical (ATC) Classification System.

All patients in the database diagnosed with cancer (based on the relevant ICPC codes for cancer) between 1 January 2005 and 31 December 2009 were identified. The study aimed to select at random 200 patients with cancer who died during this time period, and an equally sized group of patients with heart failure (ICPC code K77) who died in the same time period in the GPRNU database. In the records of the practices the accuracy of coding was examined, and it was confirmed that the patient had cancer or heart failure. Patients with both cancer and heart failure were excluded from this study.

Somatic and psychiatric comorbidity

The prevalence of somatic and psychiatric comorbidity in the two groups was determined using both the ICPC diagnostic codes as well as prescription data in the GPRNU database. Psychiatric diagnoses were identified using the ICPC codes depression (P76), affective psychosis (P73), anxiety disorder (P74), other neurosis (P79), schizophrenia (P72), and other organic psychosis (P71). For somatic comorbidities the following codes were selected: diabetes mellitus (T90), angina pectoris (K74), acute myocardial infarction (K75), other chronic/ischaemic heart disease (K76), transient ischaemic attack (K89), and cerebrovascular accident (K90). Of all patients, demographic data was collected (date of birth, sex). The presence of somatic comorbidities is defined as the presence of one or more of the above medical illnesses.

Psychotropic drug prescription

Psychotropic drugs prescribed to the patients with cancer or heart failure were identified in the GPRNU data using the corresponding ATC codes (antipsychotic = N05A, antidepressant = N06A, benzodiazepine derivatives = N05CD and methylphenidate = N06BA04).

Analysis

Pearson's χ^2 test or Fisher's exact test was used to compare the presence of comorbidity and the rate of psychotropic drugs use. The rate of each type of psychotropic drugs prescription in the patients with cancer and heart failure were calculated. The differences between the two groups of subjects were analysed using χ^2 test, differences reported with 95% confidence interval (CI). The psychiatric comorbidities were categorised into depression, neurosis (fear disorder and other neurosis) and psychosis (schizophrenia, affective psychosis, and organic psychosis). Logistic regression analysis was used to examine the association of age, sex, somatic comorbidities, psychiatric comorbidities, and disease category with psychotropic prescriptions (categorised as prescription of one or any psychotropic drugs versus none), and reported in odds ratio (OR) with 95% CI. Further subgroup analysis of the association for each category of patients (cancer or heart failure) was conducted. All analysis was done in SPSS (version 13).

RESULTS

Characteristics of the patients

Due to the change of computer system during the study period data could not be extracted in two of the six GPRNU practices. In the four remaining GP practices with 29 GPs and 44 030 patients, 162 terminal cancer cases and 116 terminal heart failure cases were identified in the study period. After excluding cases with inaccurate

Table 1. Baseline characteristics of the study subjects

	Terminal patients (*N* = 191)		
	Cancer (*n* = 111)	Heart failure (*n* = 80)	Mean difference (95% CI)
Mean age, years[a] (SD)	70.77 (12.76)	85.75 (9.24)	−14.98 (−18.12 to −11.84)
Female sex *n* (%)	52 (46.8)	48 (60.0)	*P* = 0.07

[a]Age at death.

coding of diagnoses and incomplete data (*n* = 78), a total of 191 patients were eligible for analysis (111 with cancer and 80 with heart failure). There was no significant difference in age and sex between those included or excluded from the study. For those included in the study, there were more female patients in the terminal heart failure group (60.0%) as compared to the terminal cancer group (46.8%) but the difference was not statistically significant (OR = 1.702, 95% CI = 0.951 to 3.047). The average age at death for patients with terminal cancer was 70.8 years (standard deviation [SD] = 12.8), and for patients with heart failure was 85.75 years (SD = 9.24) (Table 1). The most common types of cancer were: gastrointestinal (rectal, colon and pancreas, stomach) (43.2%) followed by pulmonary (23.4%), haematological (9.9%), breast (9.0%), genital-urinary (5.4%), and others/unknown (9.1%).

Somatic comorbidity
The prevalence of somatic comorbidity in the complete study group was 43.5%. Somatic comorbidities were significantly more common in patients with terminal heart failure (65.0%) compared to patients with terminal cancer (27.9%) (OR = 4.793, 95% CI = 2.581 to 8.899). Diabetes mellitus (20.9%) was the most common comorbidity followed by chronic obstructive pulmonary disease (COPD) (13.1%) and ischaemic heart disease (IHD; 11.5%). Chronic disease comorbidity was also more common among patients with terminal heart failure than patients with cancer (diabetes mellitus, 32.5% versus 12.6%, OR = 3.336, 95% CI = 1.608 to 6.922; COPD, 26.2% versus 3.6%, OR = 9.521, 95% CI = 3.121 to 29.050 and IHD, 21.2% versus 4.5%, OR = 5.721, 95% CI = 2.012 to 16.262).

Psychiatric comorbidity and psychotropic prescription
The overall prevalence of psychiatric diagnoses in the study group was 13.6% (Table 1). The most prevalent psychiatric comorbidities were other organic psychosis (6.3%) and depression (4.7%). There was no statistical significance in the prevalence of psychiatric diagnoses between patients with cancer and heart failure.

Based on the prescription data, half of the terminally ill patients were prescribed at least one type of psychotropic drugs (Table 2). Benzodiazepines were the most common followed by antipsychotics and antidepressants.

There was no significant difference in the prevalence of psychotropic drugs prescribed to the patients with cancer or heart failure, except for methylphenidate that was only used by patients with cancer. Some patients in the terminal phase used more than one drug; 9.4% used two psychotropic drugs and 5.2% used three types. There was no significant difference between patients with cancer and heart failure in the frequency of multiple psychotropic drug prescription.

Association of psychotropic drugs prescription
Logistic regression analysis showed that the presence of a psychiatric diagnosis was the only factor significantly associated with psychotropic drug prescription in the terminal phase of life, after adjustment for sex, age, presence of physical comorbidities and type of terminal illness (Table 3).

DISCUSSION
Summary
In patients with terminal cancer and heart failure the study found no difference in the prevalence of psychiatric diagnoses or in the prescription of psychotropic drugs. Half of the patients were prescribed at least one type of psychotropic drug,

Table 2. Comparison of psychiatric diagnosis and psychotropic drug prescription in the study population

	Total,% (*n* = 191)	Cancer,% (*n* = 111)	Heart failure,% (*n* = 80)	*P*-value
Psychiatric diagnosis				
Depression	4.7	5.4	3.8	0.594
Affective neurosis	0.5	0	1.2	0.419[a]
Anxiety disorder	1.6	1.8	1.2	1.000[a]
Other neurosis	0.5	0	1.2	0.419[a]
Schizophrenia	1.0	0.9	1.2	1.000[a]
Other organic psychosis	6.3	6.3	6.2	0.987
Any psychiatric morbidities[b]	13.6	13.5	13.8	0.962
Psychotropic prescription[c]				
Antipsychotic	19.9	23.4	15.0	0.150
Antidepressant	14.1	11.7	17.5	0.257
Benzodiazepine derivatives	34.6	35.1	33.8	0.843
Methylphenidate	1.6	2.7	0	0.138
Any psychotropic drug	50.3	54.1	45.0	0.217

[a]Fisher's exact test. [b]Patients could have more than one psychiatric morbidities. [c]Patients could use more than one type of psychotropic drugs.

Table 3. Logistic regression analysis of the associated factors for psychotropic prescription in the study subjects (*N* = 191)

	n (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Age, years			
≤75	43 (53.1)	1.217 (0.685 to 2.162)	1.184 (0.590 to 2.378)
>75	53 (48.2)		
Sex			
Male	40 (44.0)	0.616 (0.348 to 1.092)	0.541 (0.288 to 1.017)
Female	56 (56.0)		
Terminal patient			
Cancer	60 (54.1)	1.438 (0.807 to 2.651)	1.941 (0.923 to 4.079)
Heart failure	36 (45.0)		
Somatic comorbidities			
Yes	45 (54.2)	1.324 (0.746 to 2.349)	1.914 (0.974 to 3.763)
No	51 (47.2)		
Psychiatric morbidities			
Yes	22 (84.6)	6.764 (2.232 to 20.495)	6.993 (2.256 to 21.680)
No	74 (44.8)		

OR = odds ratio. [a]Adjusted OR = adjusted for all other variables.

mostly benzodiazepines and antipsychotics. Although psychotropic drug prescription was associated with psychiatric comorbidity, only 13.6% of the patients actually had a psychiatric diagnosis, mostly psychosis and depression.

Strength and limitations

The study used the patient data from the GPRNU database, which is a representative sample of the Dutch primary care population.[29] The patient sample studied is most probably an adequate representation of the patients with cancer and heart failure in the terminal phase of life.

Patient data came from GPs from four different primary care centres only, which may have hampered the representativeness of the results. The fact that they work closely together may have affected the registration routine of these GPs for psychiatric disorders.

In general, routine registration data do have limitations when used for research. In the review of the records it was noticed that GPs often identified different psychiatric complaints within each cancer episode, but did not use separate ICPC codes for each of these symptoms. In addition, the ICPC coding structure does not allow all complaints to be registered specifically.

In addition, the focus of palliative care in general practice is primarily on maintaining the best quality of life and not on accurate diagnosis and registration. GPs are probably more concerned about relieving the pain and anguish at the end of life, including the use of psychotropic prescriptions, than to diagnose difficult

-to-distinguish psychiatric symptoms and classify them.

In this study, patients with cancer and heart failure were compared, but patients in these two groups differed in many respects. Patients with heart failure were on average 10–15 years older than patients with cancer when they died. Also, unexpectedly, there was no difference in sex in the heart failure group. Age and sex may have biased the presence of psychiatric symptoms. Furthermore, the cancer group was heterogeneous, taking different cancer types with different disease progression together. As distress levels of patients in different age and disease groups differ *a priori*, this may have affected the comparison between the two groups.

Comparison with existing literature

This study found that a psychiatric diagnosis among terminally ill patients in a primary care setting, either patients with cancer or heart failure, was relatively infrequent. The prevalence of depression was 5.4% for patients with cancer. This is in line with an earlier report of Reeve *et al*, who found a prevalence of 4.1% in patients with cancer.[30] However, in a previous meta-analysis the study found a prevalence of 10.8% depression in patients with cancer.[31] Differences in patient selection between studies may play a role in this discrepancy. Particularly, more severely depressed patients may not stay in the GP setting.

In this study the prevalence of depression in patients with heart failure was 3.8%. An earlier meta-analysis showed that the prevalence of depression in patients with heart failure was 21%.[26] The overall prevalence of psychiatric comorbidity in patients with terminal cancer in the study was 13.6%, which is strikingly low compared to other studies which reported prevalence up to 50% in patients with cancer.[15–17] The main reason for this under-reporting of psychiatric comorbidity by GPs is probably the difficult diagnostic process in terminally ill patients. The various somatic complaints in patients with cancer, resulting from both disease progression and treatment side effects, overlap with and may even mask psychiatric symptoms.[18,19,20,32] Although in the past, there were many studies on diagnostic validity or case-finding tools in palliative and cancer patients, their reliability and validity were never demonstrated.[32,33] Therefore GPs who suspect psychiatric symptoms in terminally ill patients, lack evidence-based criteria to adequately diagnose psychiatric disease. In addition, depression may be

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underdiagnosed because a depressed mood is considered as a physiological phenomenon in the terminal phase of life.

The psychotropic drug prescription rate of 50.3% seems relatively high and in sharp contrast with the low prevalence of psychiatric diagnoses. This contrast is also visible for separate drug subclasses. The antidepressant rate was 14.1%, while only 4.7% of patients were diagnosed with a depression. The same dissociation was demonstrated for benzodiazepines and antipsychotics. This may be explained by the fact that psychotropic drugs are also prescribed for many non-psychiatric complaints.[34] For instance, antidepressants are used for fatigue, insomnia, and pain, while antipsychotics are used in case of vomiting, agitation, and confusion in terminal phase patients.[35] The finding is in line with the generalist approach adopted by GPs; they recognise the needs of patients and treat the symptoms accordingly. In the terminal stage of disease with complex psychiatric comorbidity an individually-tailored model prevails and a disease oriented model according to diagnostic criteria is abandoned.[36–38] This also suggests that psychotropic drug prescription is not the optimal proxy indicator of psychiatric disease in patients with terminal stage cancer.

Regarding the main objective of this study, it was demonstrated that psychiatric symptoms are frequent both in patients with terminal cancer and heart failure. In this study neither the prevalence of psychiatric comorbidity nor the use of psychotropic drugs differed between the two patient groups, despite the difference in mean age. In both groups it was found that there was a similar discrepancy between the frequency of psychiatric diagnoses and that of psychotropic drug prescription. Patients from different age classes and distinctive illnesses used the same amount of psychotropic drugs in the terminal stage before dying. A previous study showed that shortly before dying the chances for prescription of a new psychotropic drug increase.[39] It can now be added that the increased incidence of psychiatric comorbidity and the use of psychotropic drugs are related to the terminal disease phase and are not disease specific.

Implications for practice and research

Psychological symptoms and psychiatric comorbidity are common in terminally ill patients, as indicated by the high use of psychotropic drugs. The study demonstrated that this is primarily related to the terminal disease stage and not to the type of illness. This warrants more attention for psychiatric morbidity, not only in patients with cancer, but in the terminal phase of all chronic diseases. The findings in this study should be replicated in a prospective cohort study to examine the experience of psychological suffering in patients at terminal stage. In addition, intervention studies may address the cost-effectiveness of psychotropic drug use in the terminal stage. Alternative therapeutic intervention with rapid responses like psychostimulants or less adverse effects like mindfulness-based psychotherapy need to be explored.

The rate of formally registered psychiatric diagnoses in the terminally ill patients reported by the GP was relatively low. In contrast, the frequency of psychotropic drugs prescription was much higher. The study observed no differences in psychiatric diagnoses and prescriptions between patients with cancer and heart failure, regardless of the age differences. These findings suggest that psychiatric disorders in terminal patients in the general GP practice are primarily related to the terminal disease phase, and not disease specific.

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