Title: Suicidal thoughts in patients with cancer and comorbid major depression: findings from a depression screening program.

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ABSTRACT

Background

Major depression is found in around ten percent of patients attending cancer clinics. One of the symptoms of major depression, defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM), is 'thoughts of death or suicide'. In order to implement depression screening programs for patients with cancer, we need to know the prevalence not only of this broadly defined symptom, but also of more specific suicidal thoughts, as only the latter clearly indicates the need for specialist psychiatric assessment and management of suicide risk.

Methods

We analyzed data from a routine two-stage depression screening program that operated in three UK cancer centers, linked with demographic and clinical data obtained from a national cancer registry. We included data on 2,217 patients with common cancers and comorbid, interview-diagnosed, major depression. We determined the percentage of patients with: (a) the DSM-IV symptom 'thoughts of death or suicide' and (b) suicidal thoughts, defined as an affirmative response to the question 'have you had thoughts of ending your life?' We investigated the associations of patients' demographic and clinical characteristics with each of these using logistic regression models.

Results

We found that 29% (641/2,217) of patients had the DSM symptom 'thoughts of death or suicide' and 9% (207/2,217) had suicidal thoughts. Of the demographic and clinical characteristics that we studied, none had statistically significant associations with having the

DSM symptom. Only younger age and primary cancer were associated with having suicidal thoughts.

Conclusions

We found that almost one third of patients with cancer and comorbid major depression, have the DSM symptom 'thoughts of death or suicide'. However, only a third of the patients with this symptom report suicidal thoughts. These findings suggest that around one in ten patients found by a screening program to have major depression will have suicidal thoughts requiring a psychiatric assessment. The staffing of depression screening programs should be designed with these data in mind.

KEYWORDS

Cancer; major depression; suicidal thoughts; screening

INTRODUCTION

Major depression is common in people with cancer, affecting approximately 10% of patients attending cancer clinics (1). This comorbid depression substantially worsens patients' quality of life, reduces their ability to tolerate anticancer treatments and is associated with worse survival (2-4). However, it is often unrecognized and consequently untreated (1). Screening programs, linked to treatment provision, have been recommended as a way to improve the recognition and outcome of comorbid major depression in patients attending cancer services (5, 6).

'Thoughts of death or suicide' is a symptom of major depression as defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM), where it is diagnostic criterion A9 (7, 8). This DSM symptom is broadly defined and encompasses a spectrum of thoughts, ranging from a passive wish to die to active plans to die by suicide.

It is important for clinicians to unpack this broadly defined DSM symptom in order to identify the subset of patients with suicidal thoughts, as it is these that predict suicidal behavior (9). This unpacking is particularly important for depression screening programs in cancer services. In patients with a life-threatening illness such as cancer, a preoccupation with death may be distressing and require treatment, especially in the context of comorbid depression. However, only suicidal thoughts will typically prompt an urgent psychiatric risk assessment. The prevalence of suicidal thoughts is therefore an important indicator of the amount of specialist psychiatric time that will be required for risk assessment and management.

We currently lack this information because previous studies have: (a) only described the prevalence of the DSM symptom 'thoughts of death or suicide' and (b) have only described this within the subgroup of depressed cancer patients who have been referred to psychiatric services (10, 11).

We therefore aimed to determine, in a sample of patients with cancer and comorbid major depression diagnosed by a two-stage routine depression screening program: (a) the percentage who report the DSM symptom 'thoughts of death or suicide'; (b) the percentage who have suicidal thoughts, defined as an affirmative response to the question 'have you had thoughts of ending your life'; (c) and whether any demographic and clinical characteristics are associated with having the DSM symptom and with having suicidal thoughts.

METHODS

Setting

We analyzed data from a routine depression screening program which operated in clinics of the Edinburgh, Glasgow and Dundee National Health Service (NHS) cancer centers in Scotland, UK. Most (80%) patients attending the clinics completed depression screening (the main reason that patients did not complete screening was that their oncology appointment had begun before they could complete the first stage).

The screening program used a conventional two-stage procedure, which has been described in detail in previous publications (1, 12). In brief, the first stage of screening used the Hospital Anxiety and Depression Scale (HADS) self-rated questionnaire to identify those patients who required a diagnostic interview (those with a HADS total score ≥ 15) (13, 14). In the second stage, patients with a high score on the HADS were assessed using the depression section of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID for DSM-IV) to determine whether they met criteria for major depression (7, 15).

The diagnosis of major depression was made using the standard inclusive approach (all relevant symptoms counted towards the diagnosis of depression without attempting to establish whether they should be attributed to depression or to cancer) as this is the most reliable method and has been found to not significantly overestimate depression in the medically ill (16). To minimise the misdiagnosis of adjustment disorder as a depressive disorder, major depression was only diagnosed if the patient described relevant symptoms of at least four weeks' duration rather than the minimum of two required by DSM (if they

reported symptoms between two weeks and four weeks they were re-interviewed two weeks later). The diagnostic interviews were conducted by specially trained psychology graduates and nurses with regular supervision of the interviews provided by consultation-liaison psychiatrists.

Patients

We included a patient's data in this analysis if: (a) they had attended an outpatient oncology clinic between May 12, 2008 and August 24, 2011 and taken part in routine depression screening; (b) they had received an interview-based diagnosis of major depression (if a patient was diagnosed with major depression more than once by the screening program, we used data from the earliest occasion on which this diagnosis was made); (c) full data were available from the notes of the diagnostic interview; (d) they had given consent for their relevant clinical data to be used for research; (e) we could obtain their matched demographic and clinical data from the Scottish National Cancer Registry; and (f) they had a diagnosis of primary breast, colorectal, gynecological, lung or prostate cancer.

Measures

DSM symptom 'thoughts of death or suicide'

The DSM-IV criteria for major depression include the following symptom: "*recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide*" (7). As part of the diagnostic interview for major depression the presence of this symptom in the preceding two weeks was determined. This was done by asking patients: '*Were things so bad that you were thinking a lot about death or that you would be better off dead?*', if necessary followed by

one or more of these prompts: '*Sometimes when people are feeling stressed or low they can think it's not worth carrying on – is that something that you've thought?'; 'Do you ever feel that it would be better if you didn't wake up in the morning?'; 'Have things been so bad you've wished you were dead?'*

Suicidal thoughts

Patients who were found to have the DSM symptom 'thoughts of death or suicide' as described above, were then asked the standard clinical question '*Have you had thoughts about ending your life?*' We defined suicidal thoughts as an affirmative response to this question. If the patient reported suicidal thoughts during depression screening a risk assessment was conducted by a consultation-liaison psychiatrist.

Demographic and cancer data

We obtained the following data from the NHS Scotland Cancer Registry (which systematically collects information from hospitals throughout Scotland for all recorded cases of cancer): sex, age, date of cancer diagnosis (the date on which the cancer was first diagnosed, whether by histopathological, radiological or other clinical methods), socioeconomic status (defined by the Scottish Index of Multiple Deprivation [SIMD], which provides a relative measure of deprivation, based on area of residence at the time of cancer diagnosis; see appendix for details), primary cancer (see appendix for details) and initial cancer treatment objective (curative or palliative). We used initial cancer treatment objective as a proxy for cancer severity because it could be applied across all the cancers studied, whereas staging systems differ between and within the cancers.

We obtained pain scores reported by patients at the time of depression screening (patients were asked to rate how much they had been bothered by pain over the last week on a 0-10 scale, where 0 is 'not at all' and 10 is 'extremely').

We also obtained data on dates and recorded causes of death from the National Records of Scotland (NRS) database (up to April 30, 2012) in order to determine whether any patients included in the sample had died by suicide.

Data linkage

To ensure data security and confidentiality, the depression screening and pain data were sent to the Information Services Division of NHS Scotland for linkage using unique patient identification numbers (Community Health Index numbers) and dates of birth. All identifying data were then removed in a one-way linkage to produce the anonymized dataset that was used for analysis. The study was approved by the South East Scotland Research Ethics Committee, the NHS Scotland Caldicott Guardian Forum and the NHS Scotland Privacy Advisory Committee.

Statistical analysis

We calculated the percentage of depressed patients who had the DSM symptom 'thoughts of death or suicide' and the percentage who had suicidal thoughts as defined above. We used logistic regression models to separately estimate the unadjusted and adjusted effects of sex, age (categorized as ≤54, 55-64 and ≥65 years), socioeconomic status (SIMD quintiles), primary cancer, time since cancer diagnosis, initial cancer treatment objective and pain score on having the DSM symptom 'thoughts of death or suicide' and on having suicidal

thoughts. We assigned patients with multiple primary cancer diagnoses to the diagnosis that most closely preceded their diagnosis of major depression. We included age, sex and primary cancer as covariates when fitting models that estimated the adjusted effects of each of the variables listed above. We examined the effects of each predictor on a particular outcome using Wald tests, with joint tests used for categorical predictors with more than two levels. All analyses were carried out in Stata 16.

RESULTS

We analyzed data on 2,217 patients with cancer and comorbid major depression. These patients had a median age of 60 years and 80% were female (see Table 1). The median time from cancer diagnosis to depression diagnosis was eight months (interquartile range two to 31 months).

[Table 1 about here]

DSM symptom 'thoughts of death or suicide'

29% (641/2,217) of patients had 'thoughts of death or suicide' as defined in DSM-IV. We found no evidence that sex, age, socioeconomic status, cancer, time since cancer diagnosis, initial cancer treatment objective or pain score were associated with this symptom in either unadjusted or adjusted analyses (see Table 2).

[Table 2 about here]

Suicidal thoughts

9% (207/2,217) of our sample of depressed cancer patients (32% of those with the DSM symptom 'thoughts of death or suicide') had suicidal thoughts as defined above. We found that younger age was associated with greater odds of suicidal thoughts in both unadjusted and adjusted analyses (see Table 3). The estimated odds of having suicidal thoughts also varied by primary cancer in both unadjusted and adjusted analyses; the highest odds was in patients with prostate cancer. We found no evidence that sex, socioeconomic status, time

since cancer diagnosis, initial cancer treatment objective or pain score were associated with suicidal thoughts.

[Table 3 about here]

750 patient deaths had occurred by April 30, 2012. None of these deaths were recorded as due to suicide (the majority were due to cancer).

DISCUSSION

Main findings

We found that, in a large representative sample of patients who were attending cancer clinics and who were found by screening to have comorbid major depression, 29% had the DSM symptom 'thoughts of death or suicide'. We also found that 9% (32% of those with the broader DSM symptom 'thoughts of death or suicide') had suicidal thoughts, defined as an affirmative answer to the question ''have you had thoughts of ending your life?' Of the demographic and clinical characteristics that we studied, none were associated with having the DSM symptom 'thoughts of death or suicide'. Only younger age and primary cancer were significantly associated with suicidal thoughts.

Discussion of findings

Our findings indicate that the DSM symptom 'thoughts of death or suicide' is common in cancer outpatients with major depression, but that suicidal thoughts are much less common. These findings underscore the ambiguity of the DSM symptom 'thoughts of death or suicide' and show that, unless unpacked by asking supplementary questions, the prevalence of suicidal thoughts may be markedly overestimated. The complex question that comprises the ninth item of the Patient Health Questionnaire (PHQ-9) self-report depression scale ('how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?') raises similar issues (17). The use of either the DSM symptom or the ninth item of the PHQ-9 as an indicator of the need for a psychiatric assessment has the potential to waste resources. Our findings do, however, suggest that about ten percent of all cancer outpatients found to have major depression will have suicidal thoughts that merit a psychiatric assessment.

Our finding that younger patients were more likely to report suicidal thoughts is perhaps unsurprising as it is consistent with studies of depressed patients in primary care and in psychiatric settings (18, 19). Our analysis also suggested that the risk of having suicidal thoughts varies with primary cancer, with this being highest in patients with prostate cancer. Whilst there is some evidence from other studies that suicide is more common in patients diagnosed with prostate cancer than in patients with other cancers (20, 21), our finding should be interpreted with caution, given the small number of patients with prostate cancer in our sample.

We found no evidence that sex, socioeconomic status, time from diagnosis, initial treatment objective or pain score were associated with suicidal thoughts. Whilst the absence of statistically significant associations with these variables may reflect in part our sample size and other limitations of our study, as described below, it is likely that these characteristics are less relevant in the subpopulation of cancer patients with major depression, than in the wider cancer population.

Other literature

The only relevant previous studies of the prevalence of the DSM symptom 'thoughts of death or suicide', that we are aware of, have been of the highly selected population of depressed cancer patients referred to psychiatric services. These studies have found that this symptom is present in approximately half of these patients and may be associated, in this population, with more severe depression, worse functioning and more advanced cancer (10, 11, 22). We are not aware of any previous published studies of the prevalence of

suicidal thoughts, defined as 'thoughts of ending your life' or similar, in representative samples of patients with cancer and interview-diagnosed comorbid major depression.

A systematic review of the prevalence of 'suicidal ideation' in the whole population of patients with cancer, not specifically those with comorbid depression, found that the prevalence varied greatly (from less than 1% to 46%) in the different populations studied (for example, one study was of women awaiting surgery for breast cancer, another was of elderly patients admitted to palliative care units) and in studies that used different methods to assess suicidal ideation (for example, some studies used the ninth item of the PHQ-9 whereas others used questions like 'have you had any thoughts of killing yourself?') (23). Similarly, studies of the prevalence of 'desire for hastened death' in patients with cancer have reported a range of prevalence estimates that vary with the sample characteristics and the measures used (24). By way of comparison, it has been estimated that approximately 3% of the general population have thought seriously about killing themselves in the last year and that 58% of psychiatric patients with major depression have suicidal ideation (25, 26).

Strengths and limitations

This study has a number of strengths: (a) we analyzed data from a large representative sample of patients with relatively recent cancer diagnoses and interview-diagnosed comorbid major depression; (b) we used clear definitions of both the broader symptom 'thoughts of death or suicide' and the more specific 'suicidal thoughts'; and (c) the presence of these thoughts was determined during an interview, rather than relying on items from a questionnaire.

It also has limitations: (a) we did not have available data to test whether variables such as depression severity, a past history of suicide attempts, alcohol misuse, unemployment, performance status or symptoms other than pain were associated with having thoughts of death or thoughts of suicide (27); (b) we were limited to the use of initial treatment objective as a proxy for cancer severity; (c) patients in our sample were all within a limited range of time since their cancer diagnoses; (d) there is a possibility that, although the interviewers were trained to ask sensitive questions, patients may have underreported suicidal thoughts in a diagnostic interview; and (e) it is uncertain whether our findings generalize to other populations (such as patients attending different healthcare settings).

Clinical implications

Depression screening programs are now commonplace in many medical settings, and in cancer centers in particular. These programs are usually staffed by nurses, social workers and other healthcare professionals along with experts, such as consultation-liaison psychiatrists, who carry out assessments of complex cases, especially where there is potential risk of suicide. We found that nearly a third of patients with major depression met criteria for the DSM symptom 'thoughts of death or suicide' but around one in ten (a third of those with the DSM symptom) reported suicidal thoughts. These data are useful in indicating the amount of specialist psychiatric time required by depression screening programs for suicide risk assessment and management.

Research implications

There is currently considerable debate about how best to reduce the rate of suicide in the medically ill, including in those with cancer. One frequently proposed approach, given the

strong association between suicide and depression, is to use a depression screening program, such as the one we describe here (21). Another approach is to screen specifically for suicidal thoughts and other risk factors, such as a history of suicide attempts. Whilst depression screening will likely identify most patients at risk of suicide, some medically ill patients with suicidal thoughts do not meet criteria for major depression (28). These different approaches, used either separately or together, each have advantages and disadvantages; studies are needed to evaluate their effects on suicide rates, the full cost of implementing them and their acceptability to patients.

CONCLUSIONS

We conclude that, of the patients attending cancer clinics who have comorbid major depression, almost one third have the DSM symptom 'thoughts of death or suicide' and around one in ten (a third of those with the DSM symptom) have suicidal thoughts. Only younger age and primary cancer are associated with having suicidal thoughts. These findings suggest that around one in ten patients found by a screening program to have major depression will have suicidal thoughts requiring a psychiatric assessment. The staffing of depression screening programs should be designed with these data in mind.

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DISCLOSURE

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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