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Mutuality and specificity of mental disorders in advanced cancer patients and caregivers

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Abstract

Background—We sought to determine mutuality and specificity in rates of mental disorders between advanced cancer patients and their caregivers.

Method—Data from 168 non-genetically related patient–caregiver dyads participating in the multi-site Coping with Cancer (CWC) study were included in this analysis. Multivariate logistic regression analyses were conducted to examine associations between diagnoses of a psychiatric disorder in patients with diagnoses of psychiatric disorders in caregivers, and vice versa, controlling for confounders.

Results—When patients met criteria for any psychiatric diagnosis, then caregivers were 7.9 times ($P < 0.0001$) more likely to meet criteria for any psychiatric diagnosis, and vice versa. Caregiver Panic Disorder (PD) diagnosis was associated with patient Generalized Anxiety Disorder (GAD).

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Patient GAD was also associated with caregiver PD. Finally, patient PD was associated with caregiver GAD and caregiver Post-Traumatic Stress Disorder (PTSD).

Conclusions—To our knowledge, this is the first study that demonstrates the mutuality of psychiatric disorders in both advanced cancer patients and their informal caregivers. Specifically, the presence of anxiety disorders in one partner (either caregiver or patient) was associated with a greater likelihood of anxiety disorders in the other. Results suggest that psychiatric distress should be assessed in both patients and their caregivers, and that mental illness in one should raise concern about the possibility of a psychiatric disorder in the other. Results also suggest that targeted interventions to address shared fears and concerns of patients and caregivers might reduce anxiety in the end phases of the patient's illness.

Keywords

major depressive disorder; generalized anxiety disorder; panic disorder; post-traumatic stress disorder; caregivers; oncology; end-of-life

Introduction

A total of 40–70% of dying cancer patients experience psychological distress at the end-of-life [1]. Caregiving and bereavement can also adversely affect the mental health of loved ones of cancer patients [2–4]. Mental disorders among advanced cancer patients and their caregivers diminish their respective quality of life in a variety of ways (e.g., impair relationships, and exacerbate pain and other physical symptoms) [5,6]. Both partners in a dyad in which one person has a terminal illness confront many sources of anxiety and sadness. However, little is known about the impact of mental disorders in one member of the patient–caregiver dyad on the likelihood of psychiatric illness in the other member of the dyad. We hypothesize that psychiatric illness in one member of the dyad contributes to and exacerbates distress in the other member, compromising well-being and functioning [7,8].

In 1995, Kurtz et al. [9] examined 150 cancer patients and their caregivers using the Center for Epidemiologic Studies Depression (CES-D) Scale and found that higher levels of depressive symptoms in patients were associated with higher levels depressive symptoms in caregivers. Kornblith et al. [10] found that spouses or partners of men with prostate cancer report even higher levels of psychological distress than the patients themselves on the European Organisation for Research and Treatment of Cancer (EO-RTC) Psychological Distress subscale. Limited information regarding the actual prevalence of psychiatric disorders in advanced cancer patients and their caregivers exists, and virtually nothing has been published on the co-occurrence of psychiatric disorders between the two partners. Existing literature, which primarily derives from studies on breast cancer, usually examines the presence of anxiety and depression (rarely PTSD and PD) in patients or in caregivers [11–13]. However, such papers focus on how patient cancer and health-related characteristics influence caregiver emotional health, or how the presence of a supportive caregiver can influence patient psychological health. No research specifically examines the presence of concurrent and multiple psychiatric disorders in both patients and in caregivers.

Two exceptions to the dearth of literature on mutuality of psychiatric disorders in these dyads are recent reports from our multi-site NCI/NIMH study establishing separate rates of psychiatric illness in advanced cancer patients and their caregivers using structured clinical interviews based on criteria from the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) [14,15]. The present report uses these data to examine mutuality in rates of mental disorders between advanced cancer patients and their caregivers.

The identification of patients and caregivers at highest risk of emotional distress will enhance clinical understanding of vulnerable groups and suggest opportunities to develop interventions that target shared concerns and sources of psychological distress. Understanding the reciprocal influence of psychiatric illness in patient–caregiver dyads requires: (a) determination whether a mental disorder in one member of the dyad influences the likelihood of the other member will also have a mental disorder, and (b) assessment of the specificity of the association of elevated rates of any particular form of mental illness (e.g., Major Depressive Disorder) with heightened likelihood that the other member of the dyad will experience that same mental disorder. The aims of this study are to test for mutuality and specificity in rates of mental disorders in advanced cancer patients and their informal caregivers.

Methods

Subjects and data source

Patients and caregivers were recruited from 8/1/2002 to 8/25/2005, as part of an ongoing multi-institutional longitudinal evaluation (MH63892, CA106370) of advanced cancer patients and their primary, informal (non-paid) caregivers in the Coping With Cancer (CWC) study. A primary aim of the CWC study was to determine the prevalence of and concordance between psychiatric disorders in advanced cancer patients and their informal or family caregivers. Participating sites included the Yale Cancer Center (New Haven, CT), the Veterans Affairs Connecticut Healthcare System Comprehensive Cancer Clinics (West Haven, CT), Memorial Sloan-Kettering Cancer Center (New York, NY), Simmons Comprehensive Cancer Center (Dallas, TX), Parkland Hospital Palliative Care Service (Dallas, TX), the Dana-Farber Cancer Institute and Brigham and Women's Hospital (Boston, MA). Approval was obtained from the human subjects committees of all participating centers; all enrolled patients provided written informed consent. Additional details about the CWC study are provided elsewhere [8,9].

Inclusion criteria

(1) diagnosis of advanced cancer (presence of distant metastases and failure of first-line chemotherapy); (2) age $\geq$ 20 years; (3) identified unpaid, informal caregiver; and (4) adequate stamina to complete the interview. Patient–caregiver dyads in which either the patient or caregiver met criteria for dementia or delirium (by neuro-behavioral cognitive status exam), or did not speak either English or Spanish were excluded. Only patients and caregivers that were not genetically related were included to remove the confounding influence of shared genetic predisposition toward developing a psychiatric disorder.

Measures

Participant data obtained in the baseline interview included information on the respondent's age, race, gender, and education level. Patients and caregivers were assessed for psychiatric disorders using the Structured Clinical Interview for DSM-IV (SCID) [16]. The SCID is a widely used instrument with proven reliability and validity (e.g., $K = 0.56$ for Generalized Anxiety Disorder (GAD); $K = 0.58$ for Panic Disorder) [17]. Participants were administered SCID modules to assess the presence of current diagnosis for the following psychiatric disorders: (1) any psychiatric diagnosis, (2) Major Depressive Disorder (MDD), (3) Generalized Anxiety Disorder, (4) Post-Traumatic Stress Disorder (PTSD), and (5) Panic Disorder (PD). They were also assessed for any lifetime psychiatric disorder using the SCID.

Statistical analysis

First, contingency tables produced the percentages of patients and caregivers who met criteria for any examined current psychiatric disorder using the SCID, with the chi-square statistic determining the significance of the association between the rates of patient and caregiver

psychiatric illness. Next, multivariate logistic regression analyses were conducted to examine associations between diagnosis of one specific psychiatric disorder in caregivers or patients and diagnoses of psychiatric disorders in patients or caregivers. We tested for significant associations between confounding factors and each current psychiatric disorder. Only variables that were found to be significantly associated with the outcome were retained in the model as control variables. Significant confounders varied based on the outcome variable and were selected from age, education, race, sex, and caregiver or patient's lifetime psychiatric diagnosis. Controlling for significant demographic characteristics and lifetime psychiatric disorder in patients, we also examined whether those patients who met current criteria for any psychiatric disorder (i.e., current MDD, GAD, PTSD, or PD) were more likely to have caregivers who met criteria for any current psychiatric disorder, and vice versa. For example, we examined whether the presence of MDD in patients predicted the presence of GAD in caregivers, adjusting for significant demographic covariates and lifetime psychiatric disorders in caregivers. Given quasi-complete separation of the data (i.e., for small to medium-sized samples, the responses and non-responses can be almost perfectly separated by a single predictor or by a linear combination of predictors, so that at least one parameter estimate becomes infinite [18]) penalized maximum likelihood estimation was used. In the penalized maximum likelihood estimate, the core function of maximum likelihood was modified so that the estimates were obtained by splitting each original observation into two new observations—a response and non-response—with iteratively updated weights to guarantee finite estimates [18]. Firth's odds ratio estimates and penalized likelihood confidence limits are reported in Table 1. To adjust for possible false positive associations (Type 1 error inflation) resulting from multiple comparisons, we used a Bonferroni corrected alpha level, where $P = 0.0087$ (i.e., 0.05/10 tests, and adjusted by the average correlation among the outcomes, which was $r = 0.24$).

Results

Our sample consisted of 168 patient–caregiver dyads. The mean age of patients was 58.2 (SD = 11.7) and the mean patient education level was 13.9 years (SD = 3.5). The mean age of caregivers was 54.8 (SD = 12.2) and the mean caregiver education level was 14.0 years (SD = 3.5). A total of 127 (76%) patients were white and 106 (63%) were male, 128 (76%) of caregivers were white and 117 (70%) were female, 126 (75%) of caregivers were spouses of the patient and 124 (74%) patients had metastatic cancer, with a mean time to death from baseline of 5.6 months (SD = 4.8).

Contingency table analyses revealed that of the 27 (16.1%) patients who met current criteria for a psychiatric disorder, 40.7% of the caregivers met criteria for any current psychiatric disorder. Of the 22 (13.1%) caregivers who met criteria for a current psychiatric disorder, 50% (11) of the patients also met criteria for a current psychiatric disorder ($\chi^2 = 21.60$; df = 1; $P < 0.0001$).

Results of logistic regression analyses are presented in Tables 1 and 2. Patients who met criteria for any psychiatric diagnosis were 7.9 times more likely to meet criteria for any psychiatric diagnosis if the caregiver met criteria for any psychiatric disorder, and vice versa. Caregiver PD was associated with GAD in the patient. Patient GAD also was associated with an elevated risk of caregiver PD. Finally, patient PD was associated with caregiver GAD and caregiver PTSD. All reports of PTSD from both caregivers and patients referred to the patient's diagnosis as the primary stressor associated with their PTSD.

Discussion

The findings from this study indicate mutuality in rates of patient and caregiver psychiatric illness such that if one member of the dyad met criteria for a mental disorder, the other member

of the dyad was significantly more likely to do so. In particular, there was specificity such that anxiety disorder in one member of the dyad increased the likelihood of an anxiety disorder in the partner. Patient PD was the disorder associated with the most specific types of other anxiety disorders (namely PTSD and GAD) in the caregivers, highlighting the need to specifically target patient PD.

The concept of mutuality of anxiety in cancer patients and their caregivers is a unique finding from this research. Sullivan discusses in his (1953) text the notion that anxiety passes between mothers and infants through “empathy” [19]. A similar phenomenon might be taking place between patients and caregivers. Since the present study only included non-genetically related caregivers, it may provide an example of empathic anxiety in unrelated persons. A next step in this line of research, we have shown now that (a) mutuality and (b) specificity with respect to anxiety disorders, is to identify whether there are sources of shared anxiety, such as patient–caregiver concerns related to impending death. Additional research is also needed to determine whether the increased likelihood of co-occurring anxiety disorders in patients and their caregivers or partners holds in contexts other than advanced cancer.

Counter to the findings of Kurtz et al. [8], MDD neither had general nor specific associations with partner psychiatric morbidity. The Kurtz et al. [8] study, however, examined depressive symptom severity rather than DSM-IV psychiatric diagnoses. Future research using diagnostic criteria for MDD is needed to confirm the lack of association between MDD in one member of the cancer patient and caregiver dyad and the other. Although we are unaware of data that explicitly test this hypothesis, it appears that depressive disorders may be more internally experienced whereas anxiety disorders are externally expressed and this contributes to the greater rates of shared distress in patients with anxiety disorders but not with depressive disorder. Depressed persons tend to withdraw from social interactions and have blunted affect. Persons with anxiety disorders tend to make more outward emotional demands on others, especially their partners relative to persons with depressive disorders. Perhaps these differences in expression of psychological distress account for the presence of shared anxiety disorders but not depressive disorder. Among anxiety disorders, panic is the most noticeable given it is an acute anxiety state with observable manifestations such as sweating and flushing. GAD is a much less easily detectable state of worry and PTSD is also less obvious, with intrusive thoughts and avoidance, which are primarily internalized processes.

Although the presence of a psychiatric disorder in one person appears to influence the development of a psychiatric disorder in the other person, there may be a few other possible explanations for the results found in this study. It is possible that individuals may select partners who react similarly to stressful situations such as serious medical illness and the health care crises associated with caring for a critically ill person. Longitudinal analyses are needed to determine whether such factors as pairing of anxiety-prone individuals (e.g., those with a history of anxiety disorders) better account for anxiety disorder onset in the partner than does contagion (i.e., the spread of anxiety disorders from patient to caregiver, and vice versa). Longitudinal studies will be able to determine whether the heightened risk of anxiety disorders among dyads is more a function of: (a) a pre-existing shared vulnerability to anxiety disorders, (b) the effect of the onset of an anxiety disorder, per se, in one partner that contributes to the onset of anxiety disorder in the other member of the dyad (potentially a form of “empathic” anxiety), or (c) that an anxiety disorder in the partner proves an additional stressor (particularly given its apparent outward expression) that heightens risk for anxiety disorder onset in the other member of the dyad. Whatever the answer, determining the major factors contributing to the onset of anxiety disorders in advanced cancer patients and their caregivers is needed to develop interventions to target these sources of anxiety and, thereby, improve the quality of life of patients and caregivers.

These findings, taken together, have important implications for policy as well as for the development of future interventions and research. Interventions could explore the greatest fears reported by advanced cancer patients and their caregivers (e.g., that the patient will suffer; die in pain; that the caregiver will not be available when the patient needs him or her; that the caregiver will not know what to do if a medical crisis occurs with the patient; that the patient's treatment preferences will not be honored). Interventions that target concerns about these anxieties, such as assurances of proper symptom management, respect for treatment preferences, training in how to respond effectively to potential medical crises, might minimize these fears. Stress inoculation techniques could be taught to reduce fears associated with the threatening experiences of coping with advanced cancer. Lastly, given the results pointing to PD as having the greatest association with shared psychiatric morbidity between patients and caregivers, this indicates that PD should be the primary focus of treatments to minimize rates of shared mental distress.

As informal caregivers contribute substantial time and resources to the health system by providing care to patient, policymakers should develop systems of care that recognize the interdependence of patient and caregiver mental health. Strategies to identify “at risk” dyads, as well as clinical interventions targeted at vulnerable patients and caregivers are needed to reduce rates of psychiatric illness and its concomitant suffering.

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Table 1

Significant associations of psychiatric disorders or diagnosis between caregiver and patient[a,b]

Patient	**Caregiver**									
Independent variables in model[c]	**Dependent variables**									
	MDD OR (95% CI)	***P*-value**	**PTSD OR (95% CI)**	***P*-value**	**GAD OR (95% CI)**	***P*-value**	**PD OR (95% CI)**	***P*-value**	**Psych Dx OR (95% CI)**	***P*-value**
MDD (*N* = 13 7.74%)	ns	ns	ns	ns	ns	ns	ns	ns		
PTSD (*N* = 3 1.79%)	ns	ns	ns	ns	ns	ns	ns	ns		
GAD (*N* = 8 4.76%)	ns	ns	ns	ns	ns	ns	**15.49 (2.59 −91.31)**[d]	**0.0036**		
PD (*N* = 11 6.55%)	8.22 (1.3342.09)[d]	0.0263	**16.09 (2.25 −142.95)**[d]	**0.0066**	**20.77 (2.77 −238.16)**[d]	**0.0035**	ns	ns		
Psych Dx (*N* = 27 16.07%)									**7.9 (2.79−23.47)**[d]	**0.0001**

[a] All the models tested were controlled for significant confounders which varied based on the outcome variable and were selected from age, education, race, sex, and Caregiver or Patient's Lifetime Psychiatric Diagnosis

[b] Bold numbers indicate significant associations after Bonferroni's adjustment

[c] Partial Associations of Caregiver or Patient's Current Psychiatric Disorders with Patient's or Caregiver's Current Psychiatric Disorders with other psychiatric disorders being included in the model simultaneously

[d] Due to quasi-complete separation in our data, Firth's odds ratio and the profile penalized likelihood confidence limits were reported;[10] otherwise, some of the parameters in the model could not be estimated

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Table 2

Significant associations of psychiatric disorders or diagnosis between patient and caregiver[a,b]

Caregiver	**Patient**									
Independent variables in model[c]	**Dependent variables**									
	MDD OR (95% CI)	***P*-value**	**PTSD OR (95% CI)**	***P*-value**	**GAD OR (95% CI)**	***P*-value**	**PD OR (95% CI)**	***P*-value**	**Psych Dx OR (95% CI)**	***P*-value**
MDD (*N* = 6 3.57%)	ns	ns	ns	ns	ns	ns	ns	ns		
PTSD (*N* = 7 4.17%)	ns	ns	98.16 (2.45 −14389.97)[d]	0.0173	17.82 (1.45 −227.36)[d]	0.024	9.98 (1.56 −65.02)[d]	0.0169		
GAD (*N* = 8 4.76%)	ns	ns	ns	ns	ns	ns	ns	ns		
PD (*N* = 11 6.55%)	ns	ns	ns	ns	**24.73 (4.49 −148.04)[d]**	**0.0004**	ns	ns		
Psych Dx (*N* = 22 13.10%)									**7.91 (3.02 −21.11)[d]**	**<0.0001**

[a] All of the models tested were controlled for significant confounders which varied based on the outcome variable and were selected from age, education, race, sex, and Caregiver or Patient's Lifetime Psychiatric Diagnosis

[b] Bold numbers indicate significant associations after Bonferroni's adjustment

[c] Partial Associations of Caregiver or Patient's Current Psychiatric Disorders with Patient's or Caregiver's Current Psychiatric Disorders with other psychiatric disorders being included in the model simultaneously

[d] Due to quasi-complete separation in our data, Firth's odds ratio and the profile penalized likelihood confidence limits were reported;[10] otherwise, some of the parameters in the model could not be estimated