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Associations between cognitive impairment in advanced cancer patients and psychiatric disorders in their caregivers

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Abstract

Objective—This study examined whether cognitive impairment in advanced cancer patients is associated with a heightened frequency of psychiatric disorders in their primary caregivers.

Methods—356 patient-caregiver dyads were interviewed and administered the SPMSQ (Short Portable Mental Status Questionnaire) and the Structured Clinical Interview of the Diagnostic and Statistical Manual of Mental Disorder Fourth Edition (SCID) approximately 3.4 months before the patient's death. The SCID was administered to caregivers again approximately 6 months after the patient's death.

Results—46 (12.9%) patients displayed signs of mild cognitive impairment at the baseline interview. After adjustment for relevant confounders, patient cognitive impairment was significantly associated with caregiver pre-loss major depressive disorder (MDD) [OR 6.88 (95% CI 1.32–35.92); $p=0.02$], without associated increases in suicidality. There were no significant associations between patient cognitive impairment and caregiver pre-loss generalized anxiety disorder, posttraumatic stress disorder, panic disorder, or grief. Likewise, there were no significant associations between patient cognitive impairment and caregiver post-loss psychiatric disorders, but caregivers of cognitively impaired patients appeared to be less satisfied with the patient's manner of death ($p=0.01$).

Conclusions—Caregivers of cognitively impaired advanced cancer patients appear at heightened risk of major depression that resolves after the patient's death. Further study with a larger sample and more sensitive longitudinal cognitive measures is indicated.

Keywords

cancer; oncology; caregiver; cognitive impairment; depression; psychiatric disorder

Caregiving for a terminally ill loved one has emerged as a public health concern given its association with increased rates of depression and other psychiatric disorders, cardiovascular morbidity, and economic hardship. Previous research suggests that 13% of the caregivers of advanced cancer patients may meet criteria for an axis I psychiatric disorder, of whom less than half accessed mental health services after the patient's diagnosis [1]. Predictors of increased risk for post-loss psychiatric disorders in caregivers of advanced cancer patients

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may include hospital or ICU-based deaths, pessimistic thinking, limited social support, and stressful life events in addition to the loved one's illness [2, 3].

Delirium is a common complication of cancer, affecting 25%–50% of hospitalized cancer patients; up to 80% of cancer patients develop delirium in their final days. Prior research among cancer patients suggests that caregivers are more distressed than patients in response to delirium [4], and that caregiver-perceived delirium may be associated with generalized anxiety in caregivers [5]. In non-oncology settings, independent risk factors for distress and depression in caregivers of patients with dementia include younger age, white or Hispanic race/ethnicity, low income, and extent of impairment in ADLs [6, 7]. Caregivers of patients with mild cognitive impairment display variability in cortisol secretion and distress levels which correlate with daily stressors including patient behavioral disturbances [8]. However, no prior research has examined the relationship between milder forms of patient cognitive impairment and caregiver psychiatric disorders specifically in an advanced cancer patient population.

The objective of this study was to assess whether the cognitive status of advanced cancer patients is associated with psychiatric disorders of their primary caregivers. We hypothesized that, under the strains of caregiver burden, anticipatory grief, and increased decisional responsibility, caregivers of cognitively impaired patients would be at higher risk for pre-loss psychiatric disorders than the caregivers of cognitively intact patients.

Methods

Sample

Study participants were recruited as part of the Coping with Cancer (CwC) study, a prospective, multi-institutional cohort study of advanced cancer patients and their caregivers funded by the National Cancer Institute and the National Institute of Mental Health. Participants were recruited between September 2002 and February 2008 at six comprehensive cancer centers across the United States: Yale Cancer Center (New Haven, CT), Veterans Affairs Connecticut Healthcare System Comprehensive Cancer Clinics (West Haven, CT), Parkland Hospital (Dallas, TX), Simmons Comprehensive Cancer Center (Dallas, TX), Dana-Farber Cancer Institute (Boston, MA), and New Hampshire Oncology-Hematology (Hooksett, NH). The review boards of all participating institutions approved the study procedures, and all participants provided written, informed consent. Criteria for patient eligibility included diagnosis of advanced cancer (presence of distant metastases and disease refractory to first-line chemotherapy); age ≥ 20 years; presence of an informal caregiver; adequate stamina to complete the interview; and fluency in English or Spanish. Patients and caregivers also completed the Short Portable Mental Status Questionnaire (SPMSQ; Table 1), a validated screen for cognitive impairment in elderly and cancer patients [9]. Patients with SPMSQ scores ≤ 6 (indicating equal to or greater than 6 errors) were excluded because their responses to the detailed self-report measures utilized in the parent study were considered unlikely to be reliable or valid. Of 939 eligible patients, 661 (70.4%) participated in the survey. Patients who declined to participate were more likely to be white ($p=0.04$) and report greater distress ($p<.001$).

The sample for the present study ($N=356$) was restricted to deceased patient participants with complete baseline assessments of the patient's and caregiver's mental status. Patients included in the present study did not differ significantly from those excluded with respect to age, gender, race/ethnicity, and education.

Measures and Timing of Assessments

At the baseline interview, which occurred at a median of 4.5 months before the patient's death, patient-caregiver dyads provided information regarding age, gender, race/ethnicity, education, marital status, primary cancer diagnosis, health insurance status, and relationship with each other. Patients' functional status and comorbidities were determined by the Karnofsky score, Zubrod score, and the Charlson Comorbidity Index. Patients and caregivers also completed quality of life measures (SF-36; McGill Quality of Life Questionnaire); the Structured Clinical Interview for DSM disorders (SCID) was administered to both patients and caregivers by a trained interviewer. Two weeks after the patient's death, caregivers completed a post-mortem debriefing questionnaire about the manner of death. At a median of 6 months after the patient's death, the SCID was administered again to caregivers.

Patient Cognitive Impairment

At the screening interview, both patients and caregivers completed the SPMSQ. Because patients with moderate to severe cognitive impairment were excluded from the CwC study, the vast majority (87.1%) of patients in the present study had no more than 2 errors and would be considered cognitively intact. The remaining minority (12.9%) had 3–5 errors, indicating mild impairment according to SPMSQ. Notably, MCI (mild cognitive impairment) is a heterogeneous clinical syndrome for which various definitions have been proposed including amnesic and nonamnesic subtypes. Lacking a single consensus definition, we defined mild cognitive impairment in this study as greater than or equal to 2 errors based on prior studies using SPMSQ [10, 11], as well as on our clinical judgment that making more than one error on these relatively basic cognitive screening questions reflects subtle but meaningful deficits in awareness.

Statistical Analyses

Means (standard deviations) and frequencies (percentages) were used to describe patient and caregiver baseline characteristics. The associations between participant characteristics and patient cognitive impairment were assessed using t tests or Fisher's exact tests. The associations between patient cognitive status and caregiver mental health were evaluated as odds ratios estimated using logistic regression. Each model was adjusted for relevant confounders, which were screened using correlation analysis, with ultimate retention of variables significantly associated with both patient cognitive status and caregiver baseline mental health outcome ($p < 0.10$). The variables that remained significant at a p -value < 0.05 were controlled for in the final regression model. All analyses were performed using the SAS statistical package, version 9.2 (SAS Institute, Cary, NC).

Results

Participant Characteristics

A total of 46 (12.9%) patients displayed signs of mild cognitive impairment at the baseline interview. Patients who were Hispanic, less educated, and uninsured were more likely to be cognitively impaired (all $p < 0.001$). Patients on pain medications ($p = 0.005$) and patients with higher levels of religious coping ($p < 0.001$) were also more likely to display cognitive impairment. Patients with mild cognitive impairment were more likely to meet criteria for MDD ($p = 0.04$), panic disorder ($p = 0.04$), and for any SCID disorder ($p = 0.002$). Poor functional status as assessed by the Karnofsky score was associated with cognitive impairment ($p = 0.013$). Patient cognitive impairment was not significantly associated with shorter overall survival.

Caregivers of cognitively impaired patients were more likely to be Hispanic ($p<0.001$), less educated ($p=0.001$), and less likely to be the spouse ($p<0.002$). Patient cognitive impairment was not significantly associated with caregiver cognitive impairment.

Caregiver Pre-Loss Mental Health

There were no significant associations between patient cognitive impairment and caregiver pre-loss generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), panic disorder, or grief in adjusted analyses (Table 2). However, after adjustment for the identified confounders of White race and patient self-efficacy, patient cognitive impairment was significantly associated with caregiver pre-loss major depressive disorder (MDD) [OR 6.88 (95% CI 1.32–35.92); $p=0.02$], without associated increases in suicidality (and in fact a trend toward reduced suicidality).

Bereaved Caregivers' Mental Health Outcomes

There were no significant associations between patient cognitive impairment and caregiver post-loss MDD, GAD, PTSD, panic disorder, or grief in adjusted analyses. Even in analyses unadjusted for pre-loss disorders, there was no significant association between patient cognitive impairment and caregiver post-loss MDD. Caregivers of cognitively impaired patients appeared to be less satisfied with the patient's manner of death ($t=-2.53$, $p=0.01$).

Discussion

The data suggest that caregivers of cognitively impaired patients may be at higher risk of MDD pre-loss, without significant increases in suicidality. There were no significant increases in lifetime rates of MDD in these caregivers, suggesting that the effect occurs specifically in association with caregiving stress. Major depressive disorder may be an episodic, relapsing-recurring psychiatric condition in comparison to anxiety disorders, which are often static/chronic over many years, and involve months rather than weeks of continuous symptoms [12]. Therefore, it is plausible that the strain of caring for a cognitively impaired advanced cancer patient is more likely to lead to a major depressive episode than a new presentation of an anxiety disorder, and that the depression might resolve after the situational strain is removed. Furthermore, anxiety disorders in caregivers of advanced cancer patients are closely associated with anxiety disorders in their loved ones (rather than with other forms of distress), suggesting specificity and mutuality among psychiatric disorders [13]. The depression findings are consistent with prior studies in caregivers of dementia patients, who displayed pre-loss elevations in depressive symptoms that mostly resolved post-loss after the stressor of caregiving for a terminally ill significant other was removed [14]. However, patient cognitive impairment was notably associated with less caregiver satisfaction with the patient's quality of life just prior to death. This may be explained by mildly cognitively impaired patients becoming more physically and mentally impaired than patients who were not mildly cognitively impaired at our baseline assessment, resulting in caregiver recollections of a more stressful, burdensome, and “depressing” situation near death.

Because of the limitations of this study, our results must be considered preliminary. The fact that patients who declined to participate in the study tended to be more distressed introduced selection bias, which may result in underestimation of caregiver psychiatric disorders. In addition, the study excluded patients who were obviously grossly impaired, limiting our ability to study the effects of frank dementia or delirium on caregiver distress. Highly sensitive longitudinal measures of cognitive function were not available; the SPMSQ was administered only at baseline, and given its focus on orientation, attention, and biographical information, it cannot detect subtle deficits in short-term memory or executive function. The

definition of mild cognitive impairment (MCI) according to SPMSQ is not a universally accepted approach, and it is possible that some of the MCI patients in this study in fact had mild dementia or a prodromal/subsyndromal delirium. Finally, SCID disorders were relatively rare outcomes in this study, and only a small number of caregivers met criteria for MDD, contributing to limited statistical power. Adjustment disorders were not measured in this study, raising the possibility that some caregivers actually had adjustment disorders rather than MDD, given that their symptoms resolved after the death of the patient. Most importantly, the data merely indicate correlation, rather than causation, between patient cognitive impairment and caregiver pre-loss MDD.

Despite these limitations, the findings underscore the need to screen and monitor for depression in caregivers of advanced cancer patients, particularly in the setting of patient cognitive impairment. In busy oncology practices, caregiver depression may be missed, particularly since depressed caregivers do not appear to demonstrate florid symptoms such as suicidality. At the same time, our results hint at post-loss caregiver resilience, suggesting that interventions for caregivers of cognitively impaired patients might be short-term and best targeted to the pre-loss period. Further research with larger samples and sensitive longitudinal measures of cognitive function is indicated to confirm these findings.

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Table 1**SHORT PORTABLE MENTAL STATUS QUESTIONNAIRE (SPMSQ)**

Question
1. What are the date, month, and year?
2. What is the day of the week?
3. What is the name of this place?
4. What is your phone number?
5. How old are you?
6. When were you born?
7. Who is the current president?
8. Who was the president before him?
9. What was your mother's maiden name?
10. Can you count backward from 20 by 3's?

SCORING:

0–2 errors: normal mental functioning

3–4 errors: mild cognitive impairment

5–7 errors: moderate cognitive impairment

8 or more errors: severe cognitive impairment

* One more error is allowed if the patient had a grade school education or less.

* One less error is allowed if the patient had education beyond high school.

Table 2

Bereaved Caregiver Pre-Loss Mental Health by Patient Cognitive Status

Caregiver's Pre-Loss Characteristics	Significant Confounders	Total (N=356)	Patients With Mild Cognitive Impairment		Adjusted Result	p-value
			Yes (N=46; 12.9%)	No (N=310; 87.1%)	Adjusted OR/HR (95% CI)	
Mental Health Status						
MDD life	---	55 (16.87%)	9 (19.6%)	46 (14.8%)	1.32 (0.59–2.93)	0.496
MDD		13 (3.99%)	4 (8.7%)	9 (2.9%)	6.88 (1.32–35.92)	0.022
	Patient White Race; N (%)	225 (63.20%)	15 (32.6%)	210 (68.0%)	10.69 (1.14–100.61)	0.038
	Self-Efficacy; Mean±SD	33.3±4.8 (328)	34.4±4.5 (43)	33.1 ±4.8 (285)	0.79 (0.68–0.92)	0.003
GAD		17 (5.26%)	4 (8.7%)	13 (4.2%)	2.39 (0.58–9.81)	0.226
	Patient Age; Mean±SD	58.4±12.6 (355)	61.6±13.3 (46)	57.9±12.4 (309)	0.95 (0.90–0.99)	0.024
	McGill Symptoms; Mean±SD	5.3±2.1 (354)	4.8±2.1 (46)	5.4±2.1 (308)	0.77(0.57–1.03)	0.078
	Self-Efficacy; Mean±SD	33.3±4.8 (328)	34.4±4.5 (43)	33.1 ±4.8 (285)	0.83 (0.73–0.94)	0.003
PD		15 (4.64%)	3 (6.5%)	12 (3.9%)	1.52 (0.39–5.94)	0.544
	Had Living will or DPA; N (%)	183 (55.62%)	16 (37.2%)	167 (58.4%)	0.23(0.06–0.86)	0.029
PTSD	---	11 (3.37%)	2 (4.3%)	9 (2.9%)	1.44 (0.30–6.92)	0.645
Any SCID		37 (11.35%)	7 (15.2%)	30 (9.7%)	1.44 (0.50–4.16)	0.499
	Patient Worried; Mean±SD	3.1 ±3.2 (353)	4.0±3.6 (46)	3.0±3.1 (307)	1.15 (1.03–1.29)	0.014
	Self-Efficacy; Mean±SD	33.3±4.8 (328)	34.4±4.5 (43)	33.1 ±4.8 (285)	0.84 (0.77–0.91)	<0.001
Continuous Measure of Grief						
Suicidality Sum Score		5.3±4.5 (340)	4.3±0.7	5.5±0.3	t-value	p-value
	Patient on Pain Meds; N (%)	237 (66.57%)	39 (84.8%)	198 (63.9%)	–1.69	0.090
	Caregiver Education; Mean±SD	13.0±3.5 (346)	10.9±4.7	13.3±3.1	–5.16	<.001
	McGill Symptoms; Mean±SD	12.9±5.4 (323)	14.5±0.9	13.2±0.3	–3.20	0.002
	Patient Worried; Mean±SD	5.3±2.1 (354)	4.8±2.1 (46)	5.4±2.1 (308)	1.41	0.160
	Self-Efficacy; Mean±SD	33.3±4.8 (328)	34.4±4.5 (43)	33.1 ±4.8 (285)	–2.87	0.004
	Caregiver Being Spouse of Patient; N (%)	208 (60.47%)	14 (31.1%)	194 (64.9%)	2.26	0.025
	Caregiver Being Spouse of Patient; N (%)	153 (50.00%)	13 (28.9%)	140 (53.6%)	–2.49	0.014
					–2.74	0.007
					3.07	0.002

Note:

* No confounders were significant.