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Elizabeth R. Goy
Portland Veterans Affairs Medical Center

Linda Ganzini
Oregon Health and Science University

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Original Article

Prevalence and Natural History of Neuropsychiatric Syndromes in Veteran Hospice Patients

Elizabeth R. Goy, PhD, and Linda Ganzini, MD, MPH
Mental Health Division and Health Services Research and Development Program, Portland Veterans Affairs Medical Center; and the Department of Psychiatry, Oregon Health and Science University, Portland, Oregon, USA

Abstract

Context. Prospective studies are needed to adequately describe the overall impact of neuropsychiatric syndromes on the course of hospice enrollment in outpatient settings.

Objectives. To determine the prevalence and natural history of delirium, cognitive impairment, alcohol abuse, anxiety, depression, and suicidal ideation (SI) in community-dwelling veteran hospice patients.

Methods. Home hospice patients were visited regularly from enrollment until their deaths, study withdrawal, or discharge from hospice. Family caregivers gave consent for those with Mini-Mental State Examination (MMSE) scores less than or equal to 23. Measures included the Structured Clinical Interview for DSM-IV for depression (past and current) and alcohol abuse; the Hospital Anxiety and Depression Scale; MMSE; and Confusion Assessment Method (CAM). A clinician-rated CAM item documented sleep disturbance, and participants were asked about SI at each visit.

Results. The median length of hospice enrollment was 81 days. Of 88 participants, 77 (88%) experienced at least one neuropsychiatric syndrome. Cognitive impairment was prevalent, with 60 (68%) registering MMSE less than or equal to 23 at least once. More than half of the participants developed delirium; the proportion with delirium, any cognitive impairment, sleep disturbance, or any neuropsychiatric syndrome increased significantly from first to last study visit. Twelve (14%) participants had SI during the study, and 30 (34%) participants were affected by depression overall. Sixteen patients who were not depressed on admission subsequently developed depression. Anxiety was present in 14 (16%) on at least one study visit. Active alcohol abuse remained relatively stable (8%) across visits.

Conclusions. Psychiatric syndromes are highly prevalent in hospice patients. Systematic case finding of psychiatric disorders may be necessary to improve

Address correspondence to: Linda Ganzini, MD, MPH, Mental Health Division and Health Services Research and Development Program, R&D 66, Portland Veterans Affairs Medical Center, P.O. Box 1034, Portland, OR 97207, USA. E-mail: linda.ganzini@va.gov

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Key Words
Hospice, veterans, mental disorders, anxiety, depression, suicide, delirium, alcohol abuse, insomnia

Introduction

The passage through the final months of life is marked by accumulating physical challenges that can be complicated by distressing mental disorders, including depression, anxiety, delirium, alcohol abuse, sleep disturbance, and cognitive impairment. Although the hospice treatment model is ideally guided by a holistic biopsychosocial approach, studies have repeatedly shown that health care providers tend to underrecognize or undertreat both depression and delirium in their hospice patients, and very little is known about the prevalence and course of substance abuse, anxiety, and sleep difficulties in this setting.[1] Documentation of the incidence, prevalence, and natural history of neuropsychiatric syndromes during hospice enrollment is essential to alert care providers to the full range of palliative needs of community-dwelling hospice patients.

In the United States, most hospice treatment is provided outside of medical settings, with at least two-thirds of hospice patient deaths occurring at home.[2] The prevalence of individual neuropsychiatric syndromes, however, has been examined rigorously in inpatient cancer palliative care units, mostly outside of the United States.[1,3–9] These samples may not be representative of community hospice if only patients with particularly difficult management problems or poor social support are admitted. Studies of outpatient, community-dwelling palliative care, and hospice populations have shed some light on specific mental disorders; however, much of the research is either retrospective or cross-sectional.[10] Prospective studies are needed to adequately describe the overall impact of neuropsychiatric syndromes on the course of hospice enrollment in outpatient settings. The goal of this study was to determine the prevalence, severity, and natural history of neuropsychiatric syndromes in terminally ill veterans enrolled in community hospice.

Methods

The protocol and recruitment methods were approved by the Portland Veterans Affairs Medical Center (PVAMC) Institutional Review Board. This longitudinal study used repeated in-home visits by the study psychologist or psychology doctoral candidates trained by the psychologist. Eligible participants were veterans who had been referred for hospice care and survived long enough to be contacted by the study (within two weeks of study referral), lived within a 50-mile radius of the PVAMC, and had speech and hearing adequate to complete a structured clinical interview. Participants who were approved for study participation by their primary care provider at the PVAMC were recruited by mail and follow-up telephone call. Those enrolled were seen an average of six days after referral to hospice, for three weekly visits and then every other week continuing until their deaths, withdrawal from the study, or discharge from hospice because of improved medical or functional status. Data were analyzed from participants who were evaluated within 90 days of death. All participants with Mini-Mental State Examination (MMSE) score greater than 23 gave written informed consent; those with scores less than or equal to 23 were consented by proxy through their primary caregivers, usually a family member, and additionally gave their assent to participate.

Measures

Measures were chosen to determine the prevalence and incidence of mental disorders and, more broadly, neuropsychiatric syndromes, including alcohol abuse; suicidal ideation (SI); and the prevalence and severity of depression, delirium, anxiety, sleep disturbance, and cognitive impairment. We obtained demographic information through interview and electronic medical record review, including the participant's age, sex, educational

attainment, race, marital status, past psychiatric diagnoses from the medical record, and medical reason for hospice referral. Confusion, cognitive impairment, and delirium were assessed using 1) the MMSE, with a cutoff of 23 or lower out of 30 possible points, indicating possible delirium or dementia, and 2) the observer-rated Confusion Assessment Method (CAM). The CAM documents the presence or absence of hallmark symptoms of delirium (e.g., inattention, disorientation, sleep disturbance) and results in a positive score for delirium if both acute onset and inattention are observed and either disorganized thinking or altered level of consciousness is present. The clinician-rated CAM item, "presence or absence of sleep disturbance," was based on direct observation and patient/caregiver report and used to calculate point prevalence of sleep disturbance. In all subjects, we also rated the presence or absence of SI by asking,[11,12] "During the past week/two weeks, were things so bad that you were thinking that you would be better off dead, or thinking a lot about harming yourself?"

Additional measures were completed in participants whose CAM was negative and MMSE greater than 23. A one-time Structured Clinical Interview for DSM-IV (SCID) was conducted at the first visit to document history of past depression and alcohol abuse/dependence. The SCID interview for current depression and current alcohol abuse was then administered at each subsequent visit. The severity of depression and anxiety also was assessed with the 14-item Hospital Anxiety and Depression Scale (HADS), where each item score ranged from 0 = none to 3 = severe. Anxiety and depression severity scores each ranged from 0 to 21. Subjects were categorized as depressed if either the SCID or the HADS (using a cutpoint of 11 or higher) met the criteria for depression for two or more weeks. A HADS anxiety score of 10 or higher was used to identify presence of anxiety.

Statistical Analysis

Demographic variables are represented as frequencies and proportions. Continuous variables are described by means if normally distributed or by medians for skewed data. We report demographic characteristics and whether participants ever endorsed SI for the full sample of eligible participants. We excluded those whose last study visit occurred more than 90 days before the date of death when determining the presence of a disorder at first visit, last visit, or whether a disorder was ever present during the course of the study. Anxiety, depression, and alcohol dependence were recorded as not present on study visits when patients were delirious. Categorical data were evaluated using the Chi-squared statistic, and means with standard deviations (SDs) were compared with Student's *t*-test. McNemar's statistic for within-subjects comparisons was used to test whether there were differences between two study visits (e.g., first and last).

Results

Study Demographics

Of 795 veterans referred to hospice care, 467 were not eligible to participate—270 were referred to out-of-range facilities, 153 died within two weeks of hospice referral, 32 declined hospice, and 12 were not eligible for other reasons. Of the 328 eligible subjects, we enrolled 106 subjects. Those not enrolled included 41 whose physicians did not approve their participation, 107 who declined participation for themselves, and 74 who could not be contacted. Excluding two survivors at the close of the study and one person whose consent form was incomplete, we analyzed 103 hospice patient participants. The study participants ($n = 103$) were comparable to the eligible nonparticipants ($n = 222$) with respect to demographic and diagnostic characteristics, except for the mean survival span from referral to death (186 days for the participants and 115 days for the nonparticipants, $t = -2.8$, $P = 0.005$). Fifteen participants eventually withdrew from the study because of fatigue ($n = 1$), discharge from hospice ($n = 13$), or loss to further follow-up ($n = 1$); all 15 died over 90 days later. These veterans are not included in some analyses.

The 103 veterans studied were predominantly male and Caucasian (Table 1), reflecting the demographics of the PVAMC. The participants ranged in age from 45 to 93 years and had completed a mean of 12.6 years of education. About half were married (Table 1).

Table 1
Personal and Clinical Characteristics of Study Subjects at Entry to Hospice Care ($n = 103$)

Personal Characteristics	*n*	%
Sex		
Male	97	94.2
Female	6	5.8
Race		
White	96	93.2
Black	5	4.9
Asian	2	1.9
Marital status		
Married	51	49.5
Not married	49	47.6
Unknown	3	2.9
Diagnosis for hospice referral		
Cancer	66	64.1
Cardiopulmonary disease	18	17.5
End-stage kidney disease	3	2.9
End-stage liver disease	6	5.8
Neurological disease (stroke)	3	2.9
Amyotrophic lateral sclerosis	1	1.0
Dementia	6	5.8
Any past history of psychiatric diagnoses	56	54.4
Past depression by medical record or structured clinical interview for DSM-IV ($n = 99$)	41	41.4
Past alcohol abuse ($n = 100$)	45	45.0
History of dementia by medical record diagnosis	21	20.4
Age in years, mean (SD)	70 (11.8)	
Education in years, mean (SD, $n = 93$)	12.6 (2.7)	
Median (IQR) length of hospice care in days[a]	81 (43–157)	

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, fourth edition; IQR = interquartile range.
[a]Includes 88 participants under hospice care within 90 days of the date of death; the 15 patients whose last study visit was more than 90 days before death were excluded from this analysis.

The most common terminal diagnosis was cancer. For those 88 veterans who remained in the study from enrollment to within 90 days of the date of death, the median length of hospice care received was 81 days, with 32 (36%) receiving less than two months of hospice care.

Mental Disorders Before Hospice Enrollment

Medical record review and historical interviewing with the SCID revealed that more than half of the 103 participants had a past history of Axis I psychiatric diagnoses, including major depressive disorder in 41%, alcohol abuse/dependence in 45%, and/or a medical record diagnosis of dementia in 20% (Table 1).

Cognitive Impairment, Sleep Disturbance, and Delirium

Seventy-seven (88%) participants were diagnosed with at least one neuropsychiatric syndrome during study enrollment (Table 2). Cognitive impairment, identified by MMSE score less than or equal to 23, was the most common problem, with 68% falling at or below this threshold at least once during the study. More than half developed frank delirium and/or sleep disturbance. Comparison

Table 2
Prevalence of Neuropsychiatric Syndromes at Any Time During Hospice Care ($n = 88$)

Disorder	*n*(%)
Depression[a,b]	30 (34.1)
Alcohol dependence[a,c]	9 (10.2)
Cognitive impairment[d]	60 (68.2)
Delirium[e]	48 (54.5)
Sleep disturbance[f]	47 (53.4)
Anxiety[a,g]	14 (15.9)
Suicidal ideation[h]	12 (13.6)
Any of the aforementioned syndromes	77 (87.5)

Analysis restricted to patients enrolled in hospice, evaluated within 90 days of death.
[a]Coded as not present when patient was delirious (CAM).
[b]Either positive on SCID or HADS depression score ≥ 11.
[c]SCID screening question for current alcohol abuse.
[d]MMSE score ≤ 23.
[e]Based on CAM algorithm: Must have both acute onset with fluctuating course *and* inattention, plus *either* disorganized thinking *or* altered level of consciousness.
[f]Based on yes/no CAM item: "Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?"
[g]HADS anxiety score ≥ 10.
[h]Based on SCID item "During the past week/two weeks, were things so bad that you were thinking that you would be better off dead, or thinking a lot about harming yourself?"

Table 3
Prevalence of Neuropsychiatric Syndromes at First and Last Study Visits ($n = 73$)

	At First Visit	At Last Visit	
Disorder	n(%)	n(%)	P-value
Depression[a,b]	14 (19.2)	11 (15.1)	0.61
Alcohol dependence[a,c]	7 (9.6)	5 (6.8)	0.62
Cognitive impairment[d]	25 (34.2)	36 (49.3)	0.03
Delirium[e]	3 (4.1)	31 (42.5)	<0.01
Sleep disturbance[f]	14 (19.2)	28 (38.4)	0.01
Anxiety[a,g]	5 (6.8)	2 (2.7)	0.19
Suicidal ideation[h]	3 (4.1)	1 (1.4)	0.62
Any of the aforementioned syndromes	42 (57.5)	58 (79.5)	<0.01

Analysis restricted to patient enrolled in hospice care within 90 days of death, who had at least two study visits. Compared with McNemar's Test.
[a]Coded as not present when patient was delirious (CAM) is positive.
[b]Either positive on SCID or HADS depression score ≥ 11.
[c]SCID screening question for current alcohol abuse.
[d]MMSE score ≤ 23.
[e]Based on CAM algorithm: must have both acute onset with fluctuating course *and* inattention, plus *either* disorganized thinking *or* altered level of consciousness.
[f]Based on yes/no CAM item: "Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?"
[g]HADS anxiety score ≥ 10.
[h]Based on SCID item "During the past week/two weeks, were things so bad that you were thinking that you would be better off dead, or thinking a lot about harming yourself?"

of point prevalence at first and last study visits revealed that sleep disturbance, cognitive impairment, and delirium increased significantly in the final weeks of life compared with those at entry (Table 3).

Depression

Of the 34 subjects with pre-existing major depressive disorder who were assessed within 90 days of death, 27 (79%) were on antidepressant medication at the time they were referred for hospice care. More than one-third of the participants met the criteria for depression on at least one study visit (Table 2). The prevalence of depression remained relatively constant across the span of study enrollment (Table 3). Fourteen individuals were depressed at first study visit, whereas 16 developed a new episode of depression after the initial study visit. Half (15 out of 30) of the patients who developed major depression during hospice enrollment had no previous history of depression. Depression during hospice was unrelated to any demographic grouping or hospice-qualifying diagnosis.

Suicidal Ideation

SI was acknowledged over the course of the study by 12 (14%) participants. On the visit date that SI was endorsed, half also reported sleep disturbance, and 58% met our depression criteria (Table 4). Four of the 12 participants who expressed SI also were clinically anxious (Table 4). For the eight with SI who also completed the HADS on the same date, the average anxiety score was 11.4 (SD = 4.7), whereas the average depression score was 11.1 (SD = 5.1).

Anxiety

Over the course of study participation, 16% of the participants experienced substantial anxiety (Table 2), with point prevalence at entry of 7% and of last visit at or less than 3% (Table 3). Experience of depression during hospice was associated with greater likelihood that anxiety ($P = 0.01$) would develop at any point in the study.

Table 4
Concurrent Neuropsychiatric Disorders Among Patients Who Indicated SI ($n = 12$)

Disorder	n(%)
Depression[a,b]	7 (58.3)
Anxiety[a,c]	4/8 (50)
Sleep disturbance[d]	6 (50.0)
Alcohol abuse[a,e]	1 (8.3)

[a]Coded as not present when patient was delirious (CAM) is positive.
[b]Based on positive SCID or HADS depression ≥ 11.
[c]HADS anxiety score ≥ 10.
[d]Based on CAM item, "Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?"
[e]SCID screening question for current alcohol abuse.

Alcohol Abuse

In structured interview, more than 45% of the participants met the criteria for history of alcohol abuse or dependence (Table 1), and 10% abused alcohol at some point during hospice enrollment. Four continued to abuse alcohol until the final study visit (Table 3); only one new case of alcohol abuse occurred after hospice enrollment.

Discussion

The main finding of our study is that community-dwelling veteran hospice patients experience a sizable burden of neuropsychiatric syndromes during the final months of life; in this study, 88% of the participants were diagnosed with at least one neuropsychiatric syndrome during the course of hospice care. This longitudinal study also demonstrates that psychiatric distress mounts as the final weeks of life approach. Across the median three months of hospice care delivered to our participants, the likelihood of having any of the measured problems rose from more than half at first visit to more than three-quarters at last visit, with significant increases in the prevalence of delirium, cognitive impairment, and sleep disturbance close to the end of life. Clearly, psychosocial and psychiatric issues should be a high priority when assessing for palliative needs at the end of life.

Studies set in inpatient palliative cancer units that use rigorous criteria report that the prevalence of major depressive disorder is between 9% and 14%,[3,5] and one with a mixed population of inpatients and home-care palliative cancer patients found major depressive disorder in 21%.[8] Our measures of point prevalence at first (19%) and last (15%) study visits were comparable. Although the prevalence of depression appears relatively stable across the span of hospice enrollment, more than half (16 out of 30) of the veterans who did not have depression at first study visit subsequently developed depression. Our longitudinal design revealed that over the course of hospice enrollment, an individual has nearly a one-in-three chance of experiencing a depressive episode. This suggests that ongoing surveillance for depression is necessary for optimal treatment; simply screening on hospice admission will not suffice.

Interestingly, a lifetime history of depression did not necessarily predict a depressive episode during hospice enrollment. In contrast, Akechi et al. demonstrated a relationship between past and current depression in terminally ill Japanese cancer patients.[6] We found that 79% of individuals with a history of depression entered hospice on an antidepressant medication. It seems likely that medication and possible psychosocial support linked to recognition and treatment of depression reduced their vulnerability for subsequent episodes. Health care providers should be aware that most of those who succumb to depression at the very end of life have had a life history of relative resilience that cannot necessarily be sustained through the challenges of the dying process.

Not surprisingly, the prevalence of delirium and sleep disturbance rose significantly from the first to the last visit. A Taiwanese study of delirium presence in terminal cancer inpatients reported a prevalence of 47%, very similar to our overall finding that 54.5% ever experienced delirium during the course of the study, although other inpatient studies report prevalence greater than 90%.[7] However, at entry, only 4.1% of our participants were assessed as delirious. Studies of inpatient populations may reflect circumstances most comparable with those experienced by our community participants at the end of the study, in the final weeks of life. However, our monitoring may have missed some delirious episodes in the one- to two-week span between study visits. At a minimum, informing family members that delirium and sleep disturbance increase significantly over entry to hospice may help them feel better prepared.

SI was found in 12% of our sample, based on the SCID single item, but seven of the 12 with SI also were rated as depressed at the same study visit. Kelly et al. measured interest in hastening death in terminally ill cancer patients, using a six-item questionnaire, and reported that 14% of the respondents had high levels of wish to hasten death.[13] Despite differences in measures and populations, these findings suggest that about one in 10 hospice patients wish for death to be hastened.

The hospice trajectory might place people at risk of turning or returning to alcohol abuse as a means of coping, particularly as they lose access to other hobbies and activities that may

have enhanced coping; however, this was not the case in our study. The prevalence remained at 10% overall, and only one new patient relapsed into alcohol abuse by the final visit. On the other hand, our study found that some patients who abused alcohol on admission were not likely to stop before the final study visit. More work is needed to increase our understanding of the impact of alcohol abuse on treatments and quality of life in hospice; access to substance abuse treatment services in hospice; and views of hospice providers toward alcohol abuse in this population.

There are many difficulties inherent in studying palliative care and hospice populations, and this study has related limitations. Our participation proportion of 33% reflects that it is difficult to represent the dying population in research when the most debilitated patients often feel too ill to participate. Although systematic reviews of research on advanced disease[10] critique the literature based on poor participation rates, it is questionable whether longitudinal studies in hospice care are able to meet standards of recruitment necessary to assure confidence in generalizability.[14] Recruitment for this study certainly reflected that the most moribund were less likely to participate. We intentionally included diseases other than cancer to represent a typical hospice roster; however, the heterogeneity of illnesses and varying length of enrollment across subjects prevented us from systematically examining comorbidities. Other limitations include that the population was a veteran, mostly male, Caucasian group from the northwest United States, and the overall number of study participants was small. Our veterans may enter hospice earlier than other groups as they have the option of continuing to receive VA and hospice care.

In conclusion, the final months of life are complicated by increasing burden of neuropsychiatric syndromes for the vast majority of community-dwelling veteran hospice patients. Care plans in hospices should include periodic reassessment for new-onset depression and SI, and knowledge that delirium and sleep disturbance accelerate in the final weeks may help family members be better prepared to cope with their loved one's experience at the end of life.

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