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High anxiety is associated with an increased risk of death in an older tri-ethnic population

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Abstract

Background and Objectives— The health consequences of anxiety in late life have not been adequately investigated. We sought to examine the association between anxiety and death in an older tri-ethnic population.

Methods— A longitudinal population-based study of 506 older noninstitutionalized non-Hispanic Whites, non-Hispanic Blacks, and Hispanics aged 75 years or older from Galveston County.

Results— Average age was 80.8 (SD 4.4) and 50.8% were women. Older non-Hispanic Whites (21.6%) reported the highest prevalence of anxiety, followed by Hispanics (12.4%) and non-Hispanic blacks (11.3%) ($P = .0001$). High anxiety was significantly associated with an increased hazard of all cause death (HR 1.52; 95% CI 1.02, 2.28) and cardiovascular death (HR 1.90; 95% CI 1.06, 3.36); and was associated with an increased hazard of cancer death (HR 2.38; 95% CI 0.88, 6.45) during 5-years of follow-up.

Conclusion— There is a high prevalence of anxiety in late life. Our results indicate an association between anxiety and increased risk of death in persons aged 75 and older.

Keywords

Anxiety; Death; Aged; Ethnic groups; Longitudinal studies

1. Introduction

Symptoms of anxiety occur in relation to some event, whether social, financial, medical, or personal, where the individual experiences increased or excessive uncertainty or worry [1]. In late life up to 20% of the population may experience symptoms of anxiety [2], although most research suggests the prevalence ranges from 10–15% [3]. Despite the high occurrence in late life, anxiety remains a poorly studied problem [4].

Several explanations have been offered to explain the lack of information. There is some suggestion that because anxiety occurs less frequently in older than younger persons, research efforts are better placed with this later group [5,6]. More recently, this view has been challenged [7]. Data indicate that the incidence of anxiety does not change with age to a statistically

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significant degree. Robins et al. [8] also points out that because anxiety can occur throughout adult life, one would expect a rising lifetime prevalence, because older persons would have lived through a larger portion of years of risk; and would have been exposed to more threatening-life events. Other explanations for lack of study include under recognition or misdiagnosis by health care professionals, an older person's reluctance to report symptoms to his or her clinician [9], and lack of reliable instruments for use in older populations [4] as most anxiety instruments were developed for use in younger populations [10].

Because anxiety research has been limited in older populations, studies that show a linkage with health outcomes also has been limited [11]. Available empirical data does, however, point to an association between anxiety and poor psychologic and physical health. Massion and colleagues [12], using data from the National Comorbidity Survey, found increasing levels of anxiety significantly impaired role functioning and social life, and lowered life satisfaction and emotional well-being. Data from The Normative Aging Study, which included 1,759 middle-aged and older adults initially free of coronary heart disease, reported a dose-response association between worry and nonfatal myocardial infarction and total coronary heart disease [13]. Anxiety symptoms also have been shown to predict incidence of hypertension [14] and higher cholesterol levels [15]. Fava et al. [15] concluded that anxious persons may be at an increased risk of death due to the presence of anxiety.

Given the high prevalence of anxiety and limited research in older populations, the current study was interested in examining relations between anxiety measured at baseline and risk of death for persons 75 and older over the subsequent 5-year period. We hypothesized that high anxiety would be associated with an increased risk of death independent of other risk factors. Data are from a tri-ethnic sample of non-Hispanic Whites, non-Hispanic Blacks, and Hispanics living in the community.

2. Methods

2.1. Subjects

Data are from the Health of the Public (HoP) Study [16], a population-based needs assessment study of the 75 and older population of Galveston County, Texas. A detailed description of the sampling methods has been published elsewhere [16]. Briefly, differential sampling techniques were used to ensure equal numbers of each major ethnic group (non-Hispanic White, non-Hispanic Black, and Hispanic) and equal numbers of men and women in each ethnic group. Sample subjects were identified from a master enrollment file of Medicare beneficiaries obtained from the Health Care Finance Administration (HCFA).

Data were initially collected in 1995 by in-home interviews with the subject or proxy by trained bilingual interviewers. The sample consisted of 200 non-Hispanic Whites, 200 non-Hispanic Blacks, and 200 Hispanics, for a total of 600 subjects [16]. The overall participation rate was 85.6%, and did not vary significantly among the three ethnic groups. The majority of Hispanics interviewed were Mexican Americans (87%) [16].

In the current study only non-Hispanic Whites ($n = 176$), non-Hispanic Blacks ($n = 177$), and Hispanics ($n = 153$) who had complete information on the key variables of interest were included in the analysis ($N = 506$). Excluded individuals did not significantly differ by age, gender, or ethnicity with the study sample. Consent for research participation was obtained prior to the interview. The Institutional Review Board of University of Texas Medical Branch at Galveston, TX, approved the study.

2.2. Measures

2.2.1. Generalized anxiety—Generalized anxiety was measured using the Zung self-rating anxiety scale [17]. The self-rating anxiety scale, based on DSM-II, consisted of 20 items [17]. Responses were scored on a four-point scale ranging from “none of the time” to “most or all of the time.” The 20 items were summed for a raw scale score (range 20 to 80), and then converted to an index scale score (with a possible range of 25 to 100) by multiplying the raw score by 1.25 [17]. For the current study the anxiety scale was used as a continuous (range 26 to 72) and categoric variable with a score of <45 indicating low anxiety, 45–49 minimal anxiety, and a score ≥ 50 indicating high anxiety [2,17]. Cronbach’s alpha was reported as 0.81; and test–retest reliability over a period ranging from 1 to 16 weeks was 0.81 to 0.84 [18]. The scale has been validated in English and Spanish for use in older populations [19].

2.2.2. Mortality—Death of a subject was determined by crossreferencing the study sample to the National Death Index (NDI) for the years 1995 through 1999. A total of 179 (36%) subjects died during the 5-year period including 53 non-Hispanic Whites, 70 non-Hispanic Blacks, and 56 Hispanics. Underlying cause of death included: cardiovascular ($n = 85$), cancer ($n = 36$), influenza/pneumonia ($n = 15$), and other causes (e.g., diabetes, dementia, renal, accidents, and so on) ($n = 43$).

2.2.3. Sociodemographic—Sociodemographic characteristics included age, sex, race, marital status (married vs. unmarried), years of education (less than high school vs. high school or more), alcohol use (yes vs. no), and smoking status (current vs. former or never).

2.2.4. Medical and functional health—Medical conditions were assessed by asking subjects if they ever had a physician diagnosis of stroke, cancer, diabetes, or myocardial infarction. A medical conditions summary scale was created with a range of 0–4. Self-rated health was included as a subjective indicator of health because of its strong linkages with mortality risk even after number and severity of medical conditions are accounted for [20–24]. Self-rated health was assessed by asking subjects to rate their general health. Responses were coded on a four-level ordinal scale ranging from poor to excellent. The self-rated health measure was used as a four-level ordinal variable and as a categoric variable (excellent/good vs. poor/fair). Equivalent coding of items have been used in other studies [22]. Functional health, measured by the Activities of Daily Living scale (ADLs), included the following seven items: bathing, using the toilet, transferring from bed to chair, walking across a small room, personal grooming, dressing, and eating [25]. The ADL scale was used as a continuous variable (range 0–7) and as a categoric variable (no ADL limitations vs. one or more ADL limitations) [25].

2.3. Statistical analysis

Sociodemographic characteristics, medical conditions, and functional health were examined for all subjects using descriptive and univariate statistics for continuous variables and contingency tables (chi-square) for categoric variables. Chi-square analyses were used to test for differences between the categoric anxiety variable and sociodemographic characteristics, medical, and functional health.

The Kaplan-Meier method was used to assess the survivor function between anxiety and death including all-cause, cardiovascular, and cancer during the 5-year follow-up period (1995–1999). A Cox proportional hazard model was used to estimate associations between the continuous and categoric (≤ 44 , 45–49, and ≥ 50) anxiety score and death (all-cause, cardiovascular and cancer) adjusting for socio-demographic characteristics, medical conditions, and functional health during the same 5-year period. An alpha level of .05 was

chosen to determine statistical significance in the above analysis. All analyses were performed using SAS software, version 9.0 (SAS Institute, Inc. Cary, NC).

3. Results

Table 1 shows the baseline sociodemographic characteristics, medical conditions, and functional health of the total sample, and stratified by survival status (alive and dead) at the end of the 5-year follow-up. The mean age at baseline interview was 80.8 years (SD = 4.4, range = 75–100); 50.8% were women, 41.5% were married, and 33.0% had 12 or more years of formal schooling (mean 8.5 years, SD = 4.3). Approximately equal percentages of non-Hispanic Whites (34.8%), non-Hispanic Blacks (34.0%), and Hispanics (30.2%) were included in the study. Most reported no ADL limitations (91.5%), and 42.9% reported no prior medical condition. As expected older age, men, lower education, being a current smoker, reporting one or more medical conditions, fair or poor self-rated health, and one or more ADL limitations were all significantly associated with an increased risk of death.

Next, we examined associations for sociodemographic characteristics, medical conditions, and functional health and anxiety (categorized as <44, 45–49, and ≥50) (Table 2). Significant associations were found between anxiety and ethnicity ($P = .0001$), where older non-Hispanic Whites (21.6%) reported the greatest percentage of high anxiety (score ≥50) with non-Hispanic Blacks and Hispanics reporting similar lower percentages. High anxiety was also significantly associated with ≥2 medical conditions (31.8%), poor self-rated health (35.3%), and with ≥1 ADL limitation (30.2%).

Figure 1 shows the survival curves for the three anxiety categories (<45, 45–49, and ≥50). Older persons with high anxiety (scores ≥50) were significantly more likely to die (all-cause) during the 5 years of follow-up compared with those who scored <50 ($\chi^2 = 7.5$; $P = 0.02$). Similar patterns of increased death (all-cause) in those with high anxiety were seen in men and women and in each ethnic group. Also, increased cardiovascular and cancer death were seen in those with high anxiety.

Multivariate Cox Proportional Hazard models assessed the independent association between anxiety and hazard of all-cause death during a 5-year period, adjusting for relevant risk factors (Table 3). High anxiety (score ≥50) was significantly associated with an increased hazard of all-cause death. In model 1 with adjustment for age and sex the HR was 1.66 (95% CI: 1.14, 2.42) for subjects categorized with high anxiety. In Model 2, with further adjustment for race, education, marital status, current smoking status, alcohol use, and number of medical conditions the HR of death for subjects categorized with high anxiety was 1.56 (95% CI: 1.05, 2.32). Because severity of the medical condition could influence the reporting of anxiety and is associated with increased mortality risk we added self-rated health and number of ADLs to the model. Model 3 shows, with the addition of self-rated health and number of ADLs, that high anxiety remained significantly associated with death (HR 1.52; 95% CI: 1.02, 2.28). Model 3 was also reanalyzed using anxiety score as a continuous variable. The analysis showed each one-point increase in anxiety score was significantly associated with a 2% increased risk of death (HR 1.02; 95% CI: 1.00, 1.05).

Similar multivariate models were assessed for deaths associated with cardiovascular and cancer events. With adjustment for the variables listed in Table 3 (Model 3), high anxiety was significantly associated with an increased hazard of cardiovascular death (HR 1.90; 95% CI: 1.06, 3.38); and associated with an increased hazard of cancer death (HR 2.38; 95% CI: 0.88, 6.45). When the continuous anxiety variable was included in the model each one-point increase was significantly associated with an increased hazard of cardiovascular death (HR 1.03; 95% CI: 1.00, 1.07) and associated with cancer death (HR 1.03; 95% CI: 0.99, 1.09).

4. Discussion

Because limited research has considered health outcomes associated with anxiety in late life, we examined linkages between anxiety and risk of death (all cause, cardiovascular, and cancer) in a tri-ethnic sample of persons aged 75 and older. To increase the clinical applicability of our findings, death was crossreferenced to the National Death Index (NDI). Our findings can be summarized as follows. Approximately one-third of older adults reported anxiety (score ≥ 45), with 15.2% reporting high anxiety (score ≥ 50). This result is in accord with other reported anxiety studies in older populations [2]. The finding of a nonstatistical difference between older men and women and anxiety, however, differs from studies of middle-aged persons, where women typically report greater anxiety than men [26]. One possible explanation is that age may significantly interact with gender producing a strong association in middle age, but a weaker association in late life. The prevalence of anxiety was about twofold greater in older non-Hispanic Whites compared with older non-Hispanic Blacks and Hispanics. The explanation of ethnic differences is not evident from our data. Because non-Hispanic blacks and Hispanics reported similar rates of anxiety, it is reasonable to suggest that social and cultural differences may influence the reporting of anxiety symptoms in minority groups. Understanding unique factors associated with anxiety within an ethnic group are clearly an area in need of further investigation.

The current study also showed that high anxiety was significantly associated with an increased risk of all-cause death and cardiovascular death during the 5-year follow-up independent of other risk factors. Analysis further revealed an association between anxiety and cancer death. The basis of the association between anxiety and death is uncertain. However, research investigating the body's stress response to negative affective states suggests that anxiety may adversely alter levels of certain hormones such as cortisol, epinephrine, and norepinephrine required for effective physiologic functioning [27]. From an epidemiologic perspective, anxiety may affect health by discouraging persons from receiving medical attention, complying with treatments or engaging in healthy lifestyles or behaviors. Anxiety may also increase the likelihood of reengaging in anxiety-reducing behaviors such as smoking or excessive alcohol use [28].

Our result linking anxiety and increased risk of death is consistent with a growing literature in older populations that connect psychologic health and well-being with important health outcomes including death. Penninx et al. [29] in a large prospective study of subjects aged >70 years reported that men newly diagnosed with depressive symptoms had a significantly increased risk of CVD death. Barefoot et al. [30] reported about a 60% increased risk of all-cause death associated with high levels of depressive symptoms. Our results also extend findings from middle-aged to older adults with anxiety. To date, most of the information about anxiety in older persons comes from those aged 65 and younger. However, because older persons are more vulnerable to comorbid illness, low socioeconomic status, social isolation, and other stressors, findings from middle-aged and younger population samples should be interpreted with some caution [31].

As previously noted, anxiety research in older populations has been limited for a combination of reasons including issues related to frequency of occurrence, lack of appropriate measurement instruments, and misdiagnosis, which have contributed to the underreporting of the condition. In the clinical setting, anxiety may be spuriously low because of lack of recognition or misdiagnosis by the clinician. Because anxiety frequently co-occurs with other psychiatric complaints [32], clinicians assessing older persons with anxiety need to obtain enough information to make an appropriate diagnosis or at least a differential diagnosis. In the overall population an estimated 75% of patients with generalized anxiety have a comorbid psychiatric diagnosis [33]. In older populations, rates of comorbidity vary depending on the psychiatric

disorder. For example, in a study of older adults hospitalized for depression 67% also reported symptoms of anxiety [34]. In older persons with major depression living in the community, Beekman et al. [35] reported an anxiety prevalence rate of 47.5%. The clinical presentation of anxiety in older persons can also be complicated by somatic complaints including Parkinson's disease [36], heart disease [37], diabetes [38], and chronic obstructive pulmonary disease [39]. Although most of the available evidence is cross-sectional, and does not provide information on temporal associations between anxiety and onset of the medical condition.

Once diagnosed, anxiety can be successfully treated with either pharmacologic or non-pharmacologic interventions [40–42]. In older adults nonpharmacologic interventions such as cognitive-behavioral therapy may be preferable to pharmacologic interventions as a first-line treatment [4]. There is some indication that pharmacologic intervention may complicate the management of anxiety in older adults because of comorbid medical conditions, poly-pharmacy, and vulnerability to adverse drug reactions [43]. In a meta-analysis, Gould et al. [41] reported an overall effect size for cognitive-behavioral therapy of .70, a figure that was statistically equivalent to the effect size for pharmacologic interventions (.60). Available data also indicate that cognitive-behavioral therapy results in maintenance of gains for periods of up to 1 year [41], and decreases the use of antianxiety medications [42].

There are limitations to our study. First, because this study was conducted in Galveston County, TX, it may not be generalizable to other older populations in the United States. Second, because the anxiety instrument was based on self-ratings, the possibility exists for misclassification. However, the instrument is based on diagnostic conceptualizations in DSM-II, and has been validated for use in older ethnically diverse populations. Third, the occurrences of the medical conditions were obtained by self-report, although a recent report by Horner et al., using the Veterans Health Administration hospital discharge database, found strong agreement between the self-reported and actual medical condition [44]. A final limitation, common to all observational studies, is that the finding of an association between high anxiety and increased subsequent mortality does not prove that these two findings are causally related. It may be that an underlying disorder was responsible both for the elevated anxiety and subsequent mortality, and although we controlled for comorbidity in a number of ways (ADLs, self-rated health, medical diseases), unmeasured comorbidity may still confound the results. Strengths of the study include the large tri-ethnic sample size of persons aged 75 and older and deaths were crossreferenced to the National Death Index (NDI).

Overall, the number of persons aged 65 years or older is expected to increase from approximately 35 million in 2000 to an estimated 71 million in 2030 [45], and the number of persons aged 80 years or older is expected to more than double, increasing from 9.3 million in 2000 to 19.5 million in 2030 [45]. Within this context, the number of older persons with anxiety will increase. Anxiety has been shown to impair an older person's quality of life, and is associated with poor health outcomes. Because effective intervention is available, improved screening techniques might have an important impact on the long-term health consequences of the older person.

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Fig. 1. Survival curve of subjects by categorical anxiety score at baseline interview (1995–1999).

Table 1

Baseline sociodemographic and health characteristics of subjects who survived and died over a 5-year follow-up ($n = 506$)

Characteristic	Total <i>n</i>	Alive <i>n</i> (%)	Died <i>n</i> (%)	<i>P</i> -value
Age				
75–79	227	164 (72.3)	63 (27.8)	.001
≥80	279	163 (58.4)	116 (41.6)	
Sex				
Men	249	139 (55.8)	110 (44.2)	<.0001
Women	257	188 (73.2)	69 (26.9)	
Ethnicity				
Non-Hispanic White	176	122 (69.3)	54 (30.7)	.21
Non-Hispanic Black	177	107 (60.5)	70 (40.0)	
Hispanic	153	98 (64.1)	55 (36.0)	
Marital status				
Unmarried	296	195 (65.9)	101 (34.1)	.48
Married	210	132 (62.9)	78 (37.1)	
Years of schooling				
<high school	339	205 (60.5)	134 (39.5)	.005
≥high school	167	122 (73.1)	45 (27.0)	
Smoking status				
Current	69	35 (50.7)	34 (49.3)	.01
Former/never	437	292 (66.7)	145 (33.3)	
Current alcohol use				
No	404	252 (62.4)	152 (37.6)	.04
Yes	102	75 (73.5)	27 (26.5)	
Medical conditions				
0	217	157 (72.4)	60 (27.7)	<.0001
1	182	118 (64.8)	64 (35.2)	
≥2	107	52 (48.6)	55 (51.4)	
Self-rated health				
Poor	68	31 (45.6)	37 (54.4)	<.0001
Fair	209	126 (60.3)	83 (39.7)	
Good	186	135 (72.6)	51 (27.6)	
Excellent	43	36 (83.7)	7 (16.3)	
ADLs				
0	463	315 (68.0)	148 (32.0)	<.0001
≥1	43	12 (27.9)	31 (72.1)	

Table 2
Sociodemographic and health characteristics stratified by anxiety score ($n = 506$)

Characteristic	Anxiety score			P-value
	0–44	45–49	≥50	
Age				
75–79	160 (70.5)	34 (15.0)	33 (14.5)	.49
≥80	187 (67.0)	48 (17.2)	44 (15.8)	
Sex				
Men	173 (69.5)	42 (16.9)	34 (13.7)	.46
Women	174 (67.7)	40 (15.6)	43 (16.7)	
Ethnicity				
Non-Hispanic White	98 (55.7)	40 (22.7)	38 (21.6)	.0001
Non-Hispanic Black	130 (73.5)	27 (15.3)	20 (11.3)	
Hispanic	119 (77.8)	15 (9.8)	19 (12.4)	
Marital status				
Unmarried	211 (71.3)	41 (13.9)	44 (14.9)	.27
Married	136 (64.8)	41 (19.5)	33 (15.7)	
Years of schooling				
<high school	238 (70.2)	50 (14.8)	51 (15.0)	.44
≥high school	109 (65.3)	32 (19.2)	26 (15.5)	
Smoking status				
Former/never	291 (66.6)	73 (16.7)	73 (16.7)	.008
Current	56 (81.2)	9 (13.0)	4 (5.8)	
Current alcohol use				
No	275 (68.1)	63 (15.6)	66 (16.3)	.33
Yes	72 (70.6)	19 (18.6)	11 (10.8)	
Medical conditions				
0	161 (74.2)	31 (14.3)	25 (11.5)	.0001
1	131 (72.0)	33 (18.1)	18 (9.9)	
≥2	55 (51.4)	18 (16.8)	34 (31.8)	
Self-rated health				
Poor	27 (39.7)	17 (25.0)	24 (35.3)	.0001
Fair	142 (67.9)	35 (16.8)	32 (15.3)	
Good	143 (76.9)	24 (12.9)	19 (10.2)	
Excellent	36 (83.7)	6 (14.0)	1 (2.3)	
ADLs				
0	323 (69.8)	76 (16.4)	64 (13.8)	.01
≥1	24 (55.8)	6 (14.0)	13 (30.2)	

Table 3Survival models assessing the association between anxiety and death over 5-years ($n = 506$)

	Death		
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 2 HR (95% CI)
Anxiety score			
<45	1.00	1.00	1.00
45–49	0.98 (0.64, 1.48)	0.94 (0.61, 1.44)	0.93 (0.60, 1.43)
≥50	1.66 (1.14, 2.42)	1.56 (1.05, 2.32)	1.52 (1.02, 2.28)
Age (75–100)	1.08 (1.04, 1.11)	1.08 (1.04, 1.11)	1.07 (1.15, 2.14)
Women (vs. men)	0.51 (0.38, 0.70)	0.50 (0.35, 0.72)	0.49 (0.35, 0.70)
Ethnicity			
Non-Hispanic White		1.00	1.00
Non-Hispanic Black		1.04 (0.68, 1.58)	1.07 (0.70, 1.63)
Hispanic		1.13 (0.73, 1.75)	1.00 (0.64, 1.56)
Years of schooling			
≥high school (vs. high school)		0.83 (0.56, 1.23)	0.83 (0.56, 1.24)
Married (vs. unmarried)		0.92 (0.65, 1.30)	0.94 (0.66, 1.32)
Smoking status			
Current (vs. former/never)		1.82 (1.22, 2.07)	1.70 (1.14, 2.53)
Alcohol use (Yes vs. No)		0.56 (0.36, 0.86)	0.63 (0.41, 0.98)
Medical conditions (0–4)		1.47 (1.26, 1.71)	1.35 (1.15, 1.58)
Self-rated health			0.64 (0.45, 0.89)
ADLs (0–7)			1.45 (1.27, 1.66)

Abbreviations: CI, confidence interval; HR, hazards ratio.