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R1: Effects of Functional Disability and Depressive Symptoms on Mortality in Older Mexican American Adults with Diabetes

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Abstract

Objectives—To examine the effect of co-occurring depressive symptoms and functional disability on mortality in older Mexican American adults with diabetes.

Design—Longitudinal Cohort Study

Setting—Hispanic Established Population for the Epidemiological Study of the Elderly (HEPESE) survey conducted in the southwestern of United States (Texas, Colorado, Arizona, New Mexico, and California).

Participants—Community dwelling Mexican Americans with self-reported diabetes participating in the HEPESE survey.

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Conflict of Interest Checklist:

Element	Financial / Personal Conflicts	Miriam Mutambudzi		Nai-wei Chen		Kyriakos S. Markides		Soham Al Snih	
		Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation			X		X		X		X
Grants			X		X		X		X
Honoraria			X		X		X		X
Speaker's Bureau			X		X		X		X
Consulting			X		X		X		X
Stocks			X		X		X		X
Royalty			X		X		X		X
Expert testimony			X		X		X		X
Board member			X		X		X		X
Patent			X		X		X		X
Personal relationship			X		X		X		X

Author Contributions: Study concept and design: Mutambudzi, Al Snih, and Markides. Acquisition of data: Markides. Data Analysis: Mutambudzi, Chen. Interpretation of data: All authors. Preparation of manuscript: All authors

Measurements—Functional disability was assessed using a modified version of the Katz activities of daily living (ADL) scale. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CES-D). Mortality was determined by death certificate lookup, and reports from relatives. Cox proportional hazards regression analyses were used to examine the hazard of mortality as a function of co-occurring depressive symptoms and functional disability.

Results—Over a 9.2 year follow-up, 391 of the 624 participants died. Co-occurring high depressive symptoms and functional disability increased risk of mortality (HR=3.02, 95%CI=2.11-4.34). Risk was greater in men (HR=8.11, 95%CI=4.34-16.31) when compared to women (HR=2.21, 95%CI=1.42-3.43).

Conclusion—Co-occurring depressive symptoms and functional disability in older Mexican American diabetics increases mortality risk especially in men. These findings hold important implications for research, practice, and public health interventions.

Keywords

Mexican Americans; functional disability; depressive symptoms; diabetes; mortality

Introduction

Diabetes mellitus is one of the leading causes of morbidity and mortality in the US, with greater incidence and prevalence among the elderly and minorities. According to the Center for Disease Control (CDC), prevalence of diabetes continues to increase among minority subpopulations, particularly Hispanics,[1] thereby increasing concerns about further exacerbation of racial and social disparities in diabetes-related morbidity and mortality. Adults diagnosed with diabetes are at greater risk of mortality in comparison to their diabetes free counterparts.[2] Risk of mortality is further exacerbated by co-occurring pathological conditions.[3] Co-occurring conditions such as depressive symptoms and functional disability have been shown to be detrimental to health.[4] Mexican Americans are reported to have the highest rates of diabetes, and are at greater risk for high depressive symptoms and functional disability as they age.[3]

Research indicates that high depressive symptoms and functional disability are independently associated with increased risk of mortality in older Hispanic adults with diabetes.[3, 5] Studies assessing the effects of depression on diabetes have reported an increased risk in participants with major depression and depressive symptoms, with women exhibiting greater risk.[6, 7]

Research further indicates that adults with diabetes are at greater risk of functional disability.[8, 9] In one study, older Mexican American diabetics reported 74% more disability than their nondiabetic counterparts in activities of daily living (ADL).[9] Another study found that ADLs were associated with mortality, showing a negative gradient effect in median life expectancy with disability severity.[10]

While research has shown that diabetics with either high depressive symptoms or functional disability exhibit poorer health outcomes, lower quality of life, and increased mortality risk,

[3, 11] little is known of how the effects of co-occurring functional disability and depressive symptoms may impact mortality in diabetic older adults. Given the burden of diabetes in the Mexican American community, and the high prevalence of depressive symptoms and functional disability in older adults, we were interested in assessing the effects of co-occurring depressive symptoms and functional disability on mortality in older Mexican American adults with a self-report of diagnosed diabetes. Specifically, our goal was to examine the independent, and co-occurring effect of depressive symptoms and functional disability on mortality in diabetic Mexican Americans 75 years of age and older. A second goal was to assess gender differences in the effects of co-occurring functional disability and high depressive symptoms on mortality in this cohort.

Methods

We used data from the Hispanic Established Population for the Epidemiological Studies of the Elderly (EPESE) cohort study. The Hispanic EPESE is an ongoing community-based study of older Mexican Americans residing in five southwestern states (Texas, California, Arizona, Colorado, and New Mexico) which was initiated in 1993/94. At baseline 3,050 participants 65 years of age and older were enrolled in the study, with an additional cohort of 902 participants added at Wave 5 (2004-2005), and followed-up approximately every two or three years for 8 Waves (2012-2013). Interviews were conducted in Spanish or English, depending on the participant's preference. Sampling procedures of the Hispanic EPESE were previously described and are available elsewhere.[12] Wave 5 was treated as the baseline for the current study.

Inclusion and Exclusion Criteria

The inclusion criteria required participants to have been diagnosed with diabetes at Wave 5 conducted during 2004-5 when the subjects were 75 years old and over. Participants were asked if they had been told by a doctor that they had diabetes, sugar in their urine, or high blood glucose. There were 690 participants who responded affirmatively, and of these 16 were lost to follow-up, leaving 674 eligible men and women.

Variables of Interest

All-cause mortality was our outcome of interest. Mortality was determined by death certificate lookup (National Death Index), and reports from relatives. Follow-up time was calculated as the difference between the interview date in Wave 5 and most recent wave participation, or date of death until December 31, 2013.

The primary predictor variables of interest were the Center for Epidemiologic Studies Depression Scale (CES-D) and ADL functional disability at baseline (Wave 5). The CES-D is a validated and reliable instrument that has been used extensively to measure depressive symptoms.[13] The scale consists of 20 questions with possible scores ranging from 0-60. Participants rate the frequency of specific symptoms experienced in the past week on a 4-point Likert scale that ranges from “rarely/none of the time (< 1day)” to “most or all of the time (5-7days)”. Using the sum of scores, an ordinal variable was created with 2 discrete categories, low depressive symptoms (CES-D scores 0-15), and high depressive symptoms

which indicate clinical relevance (CES-D scores ≥ 16). We defined functional disability using a modified version of the Katz ADL scale[14] with a 0 to 7 scale of dependencies in ADLs. These included walking across a small room, moving from a bed to a chair, bathing, grooming, dressing, eating, and using the toilet. Participants unable to perform the task or requiring assistance with one or more ADLs were considered to have functional disability. The CES-D has been validated as a measure of depressive symptoms in English and Spanish speaking Mexican Americans,[15] and the Katz ADL scale has been widely used in studies of community dwelling older Mexican Americans with much success.[16, 17]

Additional covariates included age (treated as a continuous variable), gender, education (no education, $< 6^{\text{th}}$ grade, and 7^{th} grade), marital status (married, not married), visit to a doctor in the previous year (yes, no), diabetes medication (insulin and oral hypoglycemic, insulin only, oral hypoglycemic only), duration of years with diabetes (<15 , ≥ 15), diabetes complications (no complications, 1 or more complications [eyes, amputations, circulation or kidney]), physician-diagnosed hypertension (yes, no), ever had heart attack (yes, no), ever had a stroke (yes, no), and body mass index (BMI) based on measured height and weight. BMI was treated as an ordinal variable with 3 discrete categories underweight/normal (<24.9 Kg/m²), overweight (25.0-29.9 Kg/m²) and obese (≥ 30.0 -34.9 Kg/m²) and morbidly obese (≥ 35 Kg/m²). Underweight and normal weight categories were combined due to the small number of participants with a BMI below 18.5 (n=11).

Missing Data

There were 50 participants (7.4%), with missing data on depressive symptoms. These participants were older, less educated and were more likely to have had diabetes for longer than 15 years. Additional variables with missing data included diabetes medications (n=59 cases, 8.8%), doctor visits (n=10, 1.5%), and hypertension, stroke and heart attack (n=5 cases). Further our study sample had 85 (12.6%) participants for whom BMI data were unavailable, raising concerns of nonresponse bias. To address this we included participants with missing BMI observations by creating a BMI category for missing values to see if their association with mortality would differ from other participants for whom BMI data were available. Our analytic sample therefore consisted of 624 participants.

Statistical analysis

Participants were categorized into 4 groups based on prevalent depressive symptoms and functional status at baseline: (1) No functional disability and low depressive symptoms, (2) functional disability and low depressive symptoms, (3) co-occurring functional disability and high depressive symptoms, (4) no functional disability and high depressive symptoms. Descriptive analyses of the sample were summarized using means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Comparisons of functional disability and depressive symptoms status were made using ANOVA tests and chi-square tests for continuous and categorical variables, respectively. The association between the 4 baseline depressive symptoms and functional disability groups, and mortality were displayed and assessed using the unadjusted Kaplan–Meier survival curves.

Cox proportional hazards regression analyses were used to examine the hazard of mortality as a function of depressive symptoms and functional disability groups in 3 models. Analysis was first conducted separately by depressive symptoms (model 1) and functional disability (model 2) to show the independent effect of each on mortality. Further analyses were performed by the 4 groups of depressive symptoms and functional status (model 3) to assess their co-occurring effect on mortality. All 3 models controlled for the aforementioned covariates. To examine how the co-occurrence of depressive symptoms and functional disability differentially influence mortality in diabetic men and women, gender stratified analysis was conducted where an interaction of gender and predictor variables of interest were significant. All tests of statistical significance were two-sided with significance being $P < 0.05$. Analyses were performed with Stata version 12.0 (StataCorp, College Station, TX) and SAS version 9.3 (SAS Inc., Cary, NC).

Results

The average age at baseline (2004-2005) was 80.97 years. Female participants accounted for 63.6%, 248 participants (42.20%) reported at least one functional disability, and 132 participants (21.19%) had high depressive symptoms. Of the 624 study participants at baseline, 51.4% (n=321) had no functional disability and low depressive symptoms, 27.4% (n=171) had functional disability and low depressive symptoms, 11.4% (n=71) had co-occurring functional disability and high depressive symptoms, and approximately 10% (n=61) had no functional disability and high depressive symptoms (Table 1). Approximately 9% of men compared to almost 13% of women reported co-occurring high depressive symptoms and functional disability. Co-occurring high depressive symptoms and functional disability were more commonly reported by participants who were not married (12.4%), less educated (18.1%), had a history of stroke (23.5%) or heart attack (14.3%), were taking both insulin and oral hypoglycemic (21.4%), and those who reported disease duration of 15 years or greater (12.9%). Approximately 40% of participants with missing BMI, had co-occurring high depressive symptoms and functional disability.

The study follow-up period was 9.2 years. Overall mean follow-up was 5.2 years, with 391 of 624 participants experiencing mortality. The unadjusted Kaplan-Meier curves (Figure 1) indicated the most favorable survival among participants who had no functional disability and low depressive symptoms, and intermediate for those with no functional disability and high depressive symptoms. The differences in survival between the groups was statistically significant (log-rank test, $p < .001$). Participants with both conditions fared worst. Similar trends were noted by gender (Figure 1).

Table 2 shows the fully adjusted HR for the association of depressive symptoms (model 1) functional disability (model 2), and co-occurring functional disability and depressive symptoms (model 3) with mortality. In model 1, when compared to low depressive symptoms, high depressive symptoms were associated with a HR of 1.9 (95%CI=1.48-2.48). In model 2 an approximately 74% increase in mortality hazard (95%CI=1.38-2.19) was evident for participants reporting functional disability. A significant interaction between gender and functional disability led us to conduct stratified analysis by gender, which

indicated greater risk of mortality for older men (HR= 2.27, 95%CI=1.55-3.31) when compared to women (HR=1.47, 95%CI=1.09-1.97).

Model 3 shows the HR for the association of the co-occurrence of functional disability and depressive symptoms with mortality. Co-occurring high depressive symptoms and functional disability significantly increased risk of mortality 3-fold (HR=3.02, 95%CI= 2.11-4.34). Covariates age, disease duration, diabetes complications, doctor visits in the past year, and history of stroke were significantly associated with mortality. Further, participants with co-occurring functional disability and depressive symptoms whose BMI information was missing had a significant 73% increased risk of mortality.

Attenuation of risk for female participants (HR=0.58, 95%CI=.45-.75), and a significant interaction term led us to conduct gender stratified analysis, which indicated that women were over twice as likely (HR=2.21, 95%CI=1.42-3.43), while men were 8 times as likely (HR=8.11, 95%CI=4.34-16.31) to have died during the study interval. Visiting a doctor in the past year and diabetes complications significantly increased the risk of mortality in men only, while history of stroke significantly increased the risk of mortality in women only (HR=1.76, 95%CI=1.21-2.57). Obesity showed a significant, protective effect for men but not women.

Discussion

Similar to previous studies we found that high depressive symptoms and functional disability were independently associated with mortality in older adults with diabetes.[10, 18] Our study further contributes to current literature by demonstrating that among elderly Mexican Americans with diabetes, risk of mortality is compounded with co-occurring high depressive symptoms and functional disability, particularly among men.

Previous research has shown that women are more vulnerable to incident diabetes, high depressive symptoms, functional disability, and co-occurring high depressive symptoms and functional disability.[19–21] Despite being more vulnerable to these conditions, women in our study had a reduced risk of mortality compared to men. A similar survival disadvantage in elderly men has been previously reported.[10] We found that men who had visited a doctor in the past year had greater risk of mortality. Research has shown that men are less likely to utilize health care such as visits to doctor's offices or preventive care visits.[22] However a greater propensity for healthcare utilization among individuals with poor or deteriorating health has been reported in the literature.[23]

A paradoxical BMI–mortality risk association in individuals with chronic conditions has been reported in the literature.[24–25] The obesity paradox was evident in men but not women in our study. We found overweight and obesity among women had a decreased though non-significant inverse association with mortality, while obese men had a significantly reduced risk of mortality.

Missing data on BMI raised concerns of nonresponse bias in the data as it is well established that obesity is independently associated with diabetes, functional disability, and high depressive symptoms.[1, 26] Inclusion of participants with missing BMI data allowed us to

assess if their outcomes differed from those with BMI data. We observed the highest rates co-occurring functional disability and high depressive symptoms in participants with missing data, who also exhibited a significantly increased risk of mortality. We further found that women with missing BMI data were more vulnerable to mortality, particularly if they had high depressive symptomatology. These findings suggest that exclusion of the participants with missing data on BMI may potentially lead to systematic underestimation. [27]

Our findings should be viewed in light of several limitations. The diabetes variable was based on self-report, which may affect results due to recall bias, misinterpretation or simplification.[28] Further, the use of CES-D to measure depressive symptoms in lieu of formal depression diagnosis through structured clinical interviews warrants caution in the interpretation of our results. It has been noted that CES-D scores may be influenced by latent cross-cultural factors which may affect its diagnostic accuracy.[29-30] According to Kim and colleagues (2009), in using standard screening tools such as the CES-D, Mexican American older adults corroborated depressive symptoms more than other cultural groups exhibiting similar levels of depressive symptomatology,[29] resulting in response bias and over diagnosis among older adults.

Despite these shortcomings, our findings are strengthened by use of a large, representative, longitudinal cohort of community dwelling older Mexican Americans from the South Western United States. Studies assessing how co-occurring conditions such as high depressive symptoms and functional disability impact mortality in diabetic adults are lacking particularly in this population, and we were able to partially address this gap in the literature. Further investigation into effects of co-occurring depression and functional status in diabetics is warranted. As diabetes prevalence, functional disability, and high depressive symptoms continue to be a major public health burden in the Mexican American community, the findings of this study as well as additional related studies will increasingly become more important and hold important implications for research, practice, and public health interventions.

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Figure 1. Kaplan-Meier survival curve by baseline functional decline and depressive symptoms for overall sample (N=624) and by gender (N=224 men and N=400 women)

Table 1
Baseline characteristics of older Mexican American adults by functional disability and depressive symptoms status at baseline ^{a,b}

	No Functional Disability-Low Depressive Symptoms	Functional Disability-Low Depressive Symptoms	Functional Disability-High Depressive Symptoms	No Functional Disability – High Depressive Symptoms
	N (%)	N (%)	N (%)	N (%)
Total Participants	321 (51.44)	171 (27.40)	71 (11.38)	61 (9.78)
Age, mean (SD)	80.42 (3.80)	81.68 (4.94)	81.08 (4.62)	79.95 (3.37)
Gender				
Male	130(58.04)	56 (25.00)	20 (8.93)	18 (8.04)
Female	191 (47.75)	115 (28.75)	51 (12.75)	43 (10.75)
Marital status				
Married	161 (58.97)	68 (24.91)	28 (10.26)	16 (5.86)
Not married	158 (45.40)	102 (29.31)	43 (12.36)	45 (12.93)
Diabetes complications				
1 or more	148 (43.66)	97 (28.61)	58 (17.11)	36 (10.62)
No complications	172 (60.56)	74 (26.06)	13 (4.58)	25 (8.80)
Educational level				
None	47 (45.19)	29 (27.62)	19 (18.10)	10 (9.52)
<6	172 (50.74)	92 (27.14)	40 (11.80)	35 (10.32)
7+	102 (56.67)	50 (27.78)	12 (6.67)	16 (8.89)
BMI				
Under and Normal	82 (59.42)	31 (22.46)	8 (5.80)	17 (12.32)
Overweight	131 (59.55)	48 (21.82)	16 (7.27)	25 (11.36)
Obese	74 (53.62)	37 (26.81)	15 (10.87)	12 (8.70)
Severely obese	27 (41.54)	25 (38.46)	7 (10.77)	6 (9.23)
Diabetes medication				
Insulin and oral hypoglycemic	36 (40.45)	28 (31.46)	19 (21.35)	6 (6.74)
Insulin only	11 (21.57)	24 (47.06)	10 (19.61)	6 (11.76)
Oral hypoglycemic only	240 (55.94)	110 (25.64)	36 (8.39)	43 (10.02)
Duration (years)				
<15	189 (60.00)	64 (20.32)	31 (9.84)	31 (9.84)
15	132 (42.72)	107 (34.63)	40 (12.94)	30 (9.71)
Visited doctor in past year				
No	21 (72.41)	3 (10.34)	1 (3.45)	4 (13.79)
Yes	297 (50.42)	167 (28.35)	68 (11.54)	57 (9.68)
Stroke				
No	283 (54.11)	137 (26.20)	47 (8.99)	56 (10.71)
Yes	37 (37.76)	33 (33.67)	23 (23.47)	5 (5.10)

	No Functional Disability-Low Depressive Symptoms	Functional Disability-Low Depressive Symptoms	Functional Disability-High Depressive Symptoms	No Functional Disability – High Depressive Symptoms
	N (%)	N (%)	N (%)	N (%)
Heart attack				
No	264 (52.69)	134 (26.75)	53 (10.58)	50 (9.98)
Yes	56 (47.06)	35 (29.41)	17 (14.29)	11 (9.24)
Hypertension				
No	76 (51.01)	47 (31.54)	13 (8.72)	13 (8.72)
Yes	242 (51.49)	124 (26.38)	57 (12.13)	47 (10.00)
Total CES-D scores, mean (SD)	5.58 (4.67)	7.43 (4.71)	25.51 (4.27)	23.66 (5.87)
Total number of ADL requiring assistance, mean (SD)	NA	3.18 (2.04)	4.27 (2.04)	NA

^a Only 624 participants who had the complete information to identify the status of the co-occurrence of functional disability and depressive symptoms were included in this analysis.

^b With the exception of education, heart attack, and hypertension all participant characteristics were statistically significant across the 4 groups of prevalent depressive symptoms and functional status at baseline. Gender was marginally statistically significant.

Table 2
Multivariable analysis predicting hazard of death over a 9.2-year period as a function of baseline functional disability and depressive symptoms in diabetics ^{a,b,c}

Functional Disability and Depressive Symptoms	Male and Female	Male	Female
	HR (95%CI)	HR (95%CI)	HR (95%CI)
Depressive Symptoms (model 1)			
Low Depressive Symptoms	Ref.		
High Depressive Symptoms	1.92 (1.48-2.48)		
Functional disability (model 2)			
No	Ref.		
Yes	1.74 (1.38-2.19)	2.27 (1.55-3.31)	1.47 (1.47-1.97)
Co-occurring Functional Disability and Depressive Symptoms (model 3)			
No functional disability – Low depressive symptoms	Ref.		
Functional disability- Low depressive symptoms	1.59 (1.22-2.08)	2.18 (1.41-3.35)	1.27 (0.89- 1.8)
Functional disability- High depressive symptoms	3.02 (2.11-4.34)	8.11 (4.04-16.31)	2.21 (1.42-3.43)
No Functional disability- High depressive symptoms	1.81 (1.23-2.66)	3.77 (1.84-7.73)	1.44 (0.90-2.31)

^a In Cox regression analysis, there was no violation of the proportionality assumption assessed by the significance of a term of the predictor associated with the logarithm of survival time.

^b For all modeling analyses, a BMI category for missing values was included. The results for missing category are not shown.

^c Adjusted for age education, gender, marital status, BMI, diabetes complications, duration with diabetes (in years), diabetes medication, hypertension, heart attack, stroke, visited doctor in past year.