Frailty Transitions in the San Antonio Longitudinal Study of Aging

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OBJECTIVES: To examine frailty transitions in Mexican American (MA) and European American (EA) older adults.

DESIGN: Longitudinal, observational cohort study.

SETTING: Socioeconomically diverse neighborhoods in San Antonio, Texas.

PARTICIPANTS: Three hundred twelve MA and 285 EA community-dwelling older adults (≥ 65) with frailty information at baseline (1992–1996) and transition information at follow-up (2000/01) in the San Antonio Longitudinal Study of Aging.

MEASUREMENTS: Five frailty characteristics (weight loss, exhaustion, weakness, slowness, and low physical activity), frailty score (0–5), and overall frailty state (nonfrail = 0 characteristics, prefrail = 1 or 2, frail = ≥ 3) were assessed at baseline. Transitions (progressed, regressed, or no change) were assessed for frailty score and state. Odds ratios (ORs) of progression and regression in individual characteristics were estimated using generalized estimating equations adjusted for age, sex, ethnic group, socioeconomic status, comorbidity, diabetes, and follow-up interval.

RESULTS: Diabetes mellitus with macrovascular complications (OR = 1.84, 95% confidence interval (CI) = 1.02–3.33), fewer years of education (OR = 0.96, 95% CI = 0.93–1.0) and follow-up interval (OR = 1.3, 95% CI = 1.17–1.46) were significant predictors of progression in any frailty characteristic. Mortality increased with greater frailty state, and prefrail individuals were more likely than frail individuals to regress.

CONCLUSION: Diabetes mellitus with macrovascular complications and fewer years of education are important predictors of progression in any frailty characteristic. Because of greater risk of death than for the nonfrail state and greater likelihood of regression than for the frail state, the prefrail state may be an optimal target for intervention. **J Am Geriatr Soc 60:652–660, 2012.**

Key words: frailty; older adults; transitions

It has been hypothesized that frailty is a geriatric syndrome that clinicians recognize in clinical settings and that is characterized by decreased resilience to stressors, causing increased risk for age-related complications and outcomes.[1] Validated criteria developed in the Cardiovascular Health Study (CHS) and defined as the presence of three or more of five characteristics (weight loss, exhaustion, low physical activity, weakness, and slowness) have operationalized the syndrome as a research construct.[2] Frail individuals have been shown to be at risk for adverse outcomes, such as falls, disability, institutionalization, and death.[2,3] A prefrail state is defined as the presence of one or two of these characteristics, and individuals who are prefrail are at higher risk of adverse outcomes than those who are nonfrail.[2]

Previous studies have reported that transitions between frailty states (nonfrail, prefrail, frail) are fairly common, with individuals worsening or improving over time.[4,5] One study of frailty transitions over 4.5 years in 754 predominantly European-American (EA) participants reported that 57% of participants had at least one transition over approximately 4.5 years (although the most common pattern was to remain in the baseline frailty state).[4] In addition, although it was more common for individuals to worsen in frailty state (rates up to 43%), improvement to a less-frail state occurred (rates up to 23%). Frail individuals were more likely to remain frail than to improve. In contrast, another study that followed Mexican-American (MA) participants for 10 years in the Hispanic Established Populations for the Epidemiologic Study of the

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Elderly (H-EPESE) found that the majority of frail individuals died during follow-up.[5] Transitions in individual frailty characteristics were not the primary focus of these prior studies, and neither study was able to make direct comparisons between MAs and EAs.

The purpose of the current study was to characterize change in individual frailty characteristics and overall frailty state in a longitudinal, biethnic cohort of community-dwelling older adults. The San Antonio Longitudinal Study of Aging (SALSA) cohort, comprising approximately equal numbers of MAs and EAs, allows for direct ethnic comparisons. Thus, study results may help to identify not only frailty states and individual frailty characteristics that are optimal targets for intervention to prevent or delay worsening across frailty states, but also potential health disparities in frailty transitions.

METHODS

Sample

Subjects were 597 participants in the SALSA baseline examination (1992–1996) for whom data were available to characterize change in at least one frailty characteristic from baseline to follow-up. Follow-up examinations occurred in 2000/01. This sample has been described previously.[6,7] Ethnic groups were classified using a validated, standardized algorithm.[8] Seven hundred forty-nine participants completed the baseline examination (70.5% response rate). At the follow-up examination, 474 of 599 surviving participants completed the study (79.1% response rate).

The SALSA baseline and follow-up examinations consisted of a comprehensive home-based assessment conducted in the participant's home and a performance-based assessment conducted at a clinical research center. Trained bilingual staff administered assessments in English or Spanish according to participants' preference. The institutional review board of the University of Texas Health Science Center San Antonio approved the study, and all subjects gave informed consent.

Frailty Characterization

Validated CHS criteria and standardization procedures[2] were applied to the pooled SALSA sample; standardized cutpoints have been published previously.[6]

Walking Speed

Subjects were timed in seconds as they walked 10 feet at their usual pace starting from a standing position. Walking speed was standardized based on median height and sex. Participants in the slowest quintile for each sex group were considered slow. If a participant was unable to walk, he or she was considered slow.

Grip Strength

Grip strength was measured in kilograms using a handheld dynamometer in the dominant hand and was standardized based on body mass index (BMI) quartiles and sex. Participants in the lowest quintile for each sex group were considered weak.

Physical Activity

Self-reported physical activity over the previous year was assessed using the Minnesota Leisure Time Physical Activity Questionnaire, which yields average energy expenditure in kilocalories per week[9] and was standardized based on sex. Participants in the lowest quintile for each sex group were considered to have low energy expenditure.

Exhaustion

Exhaustion was measured according to the Geriatric Depression Scale[10] question, "Do you feel full of energy?" Subjects who responded "no" were considered exhausted.

Weight Loss

Weight loss was assessed according to the response to the question, "In the last year have you gained or lost more than 10 pounds?" Response choices were gained only, lost only, gained and lost, and neither. Intentionality was not assessed. Only participants who reported that they had lost but not gained weight were considered to have lost weight.

Frailty state was classified as an ordinal trichotomous variable (nonfrail = 0 characteristics, prefrail = 1 or 2, frail = ≥ 3). Frailty score was calculated as the total number of frailty characteristics, ranging from 0 to 5 at the baseline examination and 0 to 6 at follow-up, with a score of 6 indicating death.

Worsening in frailty state from baseline to follow-up was defined as change from nonfrail to prefrail or frail or from prefrail to frail. Improvement in frailty status was defined as change from frail to prefrail or nonfrail or from prefrail to nonfrail. Worsening and improvement were also measured for individual frailty characteristics. For example, worsening in walking speed was defined as being classified as slow at follow-up if the baseline classification was not slow. Improvement was defined as being classified as not slow at follow-up if the baseline classification was slow.

Missing Data

The analytical cohort excluded individuals who had missing data for all five frailty characteristics at baseline or at follow-up and those whose change (worsened, improved, or unchanged) in at least one frailty characteristic from baseline to follow-up could not be determined. Individuals whose change in all frailty characteristics could not be determined because of missing information were excluded. Some data for individual frailty characteristics was missing in the analytical cohort at baseline and follow-up for each frailty characteristic. At baseline, 92.3% of the analytical cohort had no missing frailty data, 6.4% were missing data for one characteristic, and the remaining 1.3% were missing data for two or three characteristics. At follow-up, 83.6% had no missing frailty information, 15.1% were missing information for one characteristic, and 1.3% were missing information for two or three characteristics.

Vital Status

Death was ascertained according to regular review of local newspaper obituaries, San Antonio Metropolitan Health

District vital statistics records, search of the Social Security Death Index, and search of the National Death Index.

Covariates

Chronic Diseases

Chronic diseases measured at baseline were used as covariates in the longitudinal analyses. Diabetes mellitus was assessed using the American Diabetes Association criteria based on a fasting plasma glucose level of 126 mg/dL or greater or currently taking antidiabetic medication(s).[11] Blood pressure was measured using a random-zero sphygmomanometer with the participant seated after a 5-minute rest. Three measures were taken, and blood pressure was calculated as the average of the second and third readings. Hypertension was assessed using guidelines from the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure six guidelines.[12] Ischemic heart disease (IHD) was assessed by evaluation of a 12-lead electrocardiograph (ECG) for the presence of ischemic ECG abnormalities. These included presence of Q-waves of at least 0.04 seconds in duration in leads II, III, and aVF or Q-waves in the precordial leads (V_1 V_6).[13] Self-reported IHD, or angina pectoris, was assessed using the validated and standardized Rose questionnaire.[14] Diabetes mellitus with macrovascular complications was defined as the presence of diabetes mellitus with IHD or stroke. For the purposes of this article, uncomplicated diabetes mellitus was defined as presence of diabetes mellitus without IHD or stroke.

Chronic obstructive pulmonary disease was assessed according to Global Initiative for Chronic Obstructive Lung Disease criteria.[15] Arthritis, cancer (nonskin), congestive heart failure, and stroke were assessed according to self-report of physician-diagnosed disease. Comorbid disease was calculated as the presence of two or more of the above diseases, excluding diabetes mellitus, which was considered separately because of its three times greater prevalence in MAs than EAs and prior evidence that diabetes mellitus is a risk factor for frailty.[3,5]

Cognitive Impairment

Cognitive impairment was assessed using the Folstein Mini-Mental State Examination.[16] Those with a score of less than 18 were classified as cognitively impaired.

Socioeconomic Status

Monthly household income and number of years of formal education were assessed according to self-report.

Follow-Up Interval

Years to follow-up or death was included as a covariate in the analyses. The average follow-up period in the overall frailty analytic cohort was 6.4 years (range 0.2–9.7 years). For participants who completed the follow-up examination, the average follow-up interval was 7.0 years (range 4.4–9.7 years). For those who died, the average follow-up interval was 4.4 years (range 0.2–9. years 4).

Statistical Analysis

Ethnic differences in demographic, socioeconomic status (SES), disease variables, and frailty characteristics were compared using the chi-square statistic for categorical variables and two-sample *t*-tests for continuous variables that follow a normal distribution. The Wilcoxon two-sample test was used for continuous variables that followed a nonnormal distribution.

A generalized estimating equation (GEE) approach for logistic regression for correlated outcomes was used to estimate the odds of worsening in individual frailty characteristics at follow-up, with death at follow-up considered to be worsening in all five characteristics. GEE accounts for correlations between different frailty characteristics within an individual and uses all available data points to model the marginal probability of worsening of each characteristic. Three models were estimated, adding pertinent covariates in each subsequent model. Model 1 was an unadjusted model; Model 2 was adjusted for ethnic group, age, sex, and follow-up interval; and Model 3 additionally adjusted for SES (income, education), comorbid disease, and diabetes mellitus. To further analyze the role of diabetes mellitus in frailty worsening, Model 4 included the covariates from the previous model except that diabetes mellitus with macrovascular complications and uncomplicated diabetes mellitus were entered as separate variables. Diabetes mellitus with and without macrovascular complications were each compared with no diabetes mellitus as the reference group. Analyses for Tables 1, 2, 3, and 4 were performed using STATA version 10.1 (Stata Corp., College Station, TX), and analyses for Table 5 were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

Figure 1 provides a flowchart of the sample included in the analysis. Five hundred ninety-seven individuals had information to determine change in at least one frailty characteristic from baseline to follow-up. Individuals who had died at follow-up were considered to have progressed in all frailty characteristics. Baseline sample characteristics are shown in Table 1. MAs were older and had lower SES than EAs. Although there were no significant ethnic differences in comorbidity, MAs had a higher prevalence of diabetes mellitus and diabetes mellitus with complications. There was no significant ethnic difference in the presence of hypertension, ischemic heart disease, chronic obstructive pulmonary disease, stroke, arthritis, or comorbidity. MAs were more likely to have cognitive impairment, although the overall prevalence of cognitive impairment in the cohort was low, at approximately 2%. More EAs (44.9%) than MAs (36.8%) had comorbid disease ($P = .049$), and the overall prevalence of comorbidity in the cohort was 40.6%. More MAs (12.1%) than EAs (6.3%) were frail, but approximately equal proportions of both ethnic groups were prefrail, and more EAs than MAs were nonfrail, but ethnic differences in overall frailty state were not statistically significant.

Frailty score and frailty state at follow-up (including death) are shown in Tables 2 and 3 according to baseline

Table 1. Study Sample Characteristics: Individuals for Whom Transition Data, Including Death, Were Obtained at Follow-Up 1

Characteristic	Mexican American (n = 312)	European American (n = 285)	Total (N = 597)*	*P*-Value for Ethnic Difference
Baseline				
Age, mean ± SD (range 65–80)	69.1 (3.2)	70.2 (3.5)	69.6 (3.4)	<.001
Female, n (%)	172 (55.1)	157 (55.1)	329 (55.1)	.99
Hypertension, n (%)	148 (47.4)	144 (50.5)	292 (48.9)	.45
Stroke, n (%)	34 (11.0)	18 (6.4)	52 (8.8)	.046
Arthritis, n (%)	134 (43.1)	135 (47.7)	269 (45.3)	.26
Self-reported ischemic heart disease, n (%)	23 (7.4)	20 (7.0)	43 (7.3)	.85
ECG-defined ischemic heart disease, n (%)	45 (14.5)	46 (16.1)	91 (15.3)	.57
Congestive heart failure, n (%)	0 (0.0)	1 (0.4)	1 (0.2)	.29
Chronic obstructive pulmonary disease, n (%) (n = 583)	93 (30.7)	104 (37.1)	197 (33.8)	.10
Diabetes mellitus, n (%) (n = 532)	99 (33.9)	25 (10.4)	124 (23.3)	<.001
Diabetes with complications, n (%) (n = 449)†	34 (15.0)	7 (3.2)	41 (9.1)	<.001
Cognitive impairment, n (%)‡	9 (2.9)	1 (0.4)	10 (1.7)	.02
Comorbidity, n (%) (n = 571)§	112 (36.8)	120 (44.9)	232 (40.6)	.049
Comorbidity, score, mean ± SD (range 0–5)	1.3 (1.0)	1.4 (1.0)	1.3 (1.0)	.12
Income, category, mean ± SD (range 1–15)‖	10.7 (3.1)	12.9 (2.3)	11.8 (2.9)	<.001
Education, years, mean ± SD (range 0–23)	9.4 (4.5)	13.4 (2.6)	11.3 (4.2)	<.001
Frailty, n (%)				
Weakness (n = 592)	78 (25.2)	39 (13.8)	117 (19.8)	.001
Slowness (n = 596)	71 (22.8)	44 (15.5)	115 (19.3)	.02
Exhaustion (n = 582)	71 (23.4)	100 (36.0)	171 (29.4)	.001
Weight loss (n = 568)	45 (15.5)	35 (12.6)	80 (13.4)	.33
Low physical activity (n=590)	70 (22.7)	43 (15.3)	113 (19.2)	.02
Frailty, ordinal trichotomous, n (%) (n = 559)				
Nonfrail	102 (35.3)	107 (52.6)	209 (37.4)	.05
Prefrail	152 (52.6)	146 (54.1)	298 (53.3)	
Frail	35 (12.1)	17 (6.3)	52 (9.3)	

* Sample size of 597 includes individuals for whom information was available for all five frailty characteristics at baseline or follow-up and whose transition could be classified in at least one frailty characteristic at baseline and follow-up. Sample size may be lower for individual baseline characteristics because missing data in which case, sample size is listed next to the characteristic.

† Defined as the presence of diabetes mellitus (defined by American Diabetes Association criteria) and of stroke (according to self-report of physician-diagnosed disease) or self-reported (assessed according to the Rose questionnaire) or electrocardiogram (ECG)-defined ischemic heart disease.

‡ Defined as a Mini Mental State Examination score of less than 18.

§ Defined as presence of two or more of seven chronic conditions, including angina pectoris, hypertension, myocardial infarction, stroke, arthritis, and cancer (non-skin). Comorbidity score is a sum of the number of these chronic diseases present.

‖ Monthly household income categories: 1 = $0–49, 2 = $50–99, 3 = $100–149, 4 = $150–199, 5 = $200–299, 6 = $300–399, 7 = $400–499, 8 = $500–749, 9 = $750–999, 10 = $1,000–1,249, 11 = $1,250–1,499, 12 = $1,500–1,999, 13 = $2,000–2,499, 14 = $2,500–2,999, 15 = ≥$3,000. Dollar equivalents of annual household incomes are: 10 = $13,500, 11 = $16,500, 12 = $21,000, 13 = $27,000.

SD = standard deviation.

frailty score and frailty state. Of those who were prefrail at baseline, 36.9% remained prefrail. Individuals with two frailty characteristics were almost twice as likely to progress to frail as those with only one (24.3% vs 13.6%), and those with only one characteristic were almost twice as likely to regress as those with two (17.9% vs 10.5%). The death rate was similar for frailty scores of 1 and 2 and was approximately 10% higher than among nonfrail participants. Of those who were frail at baseline, whether they had a frailty score of 3, 4, or 5, the dominant transition was to death. The transition to death for those who were frail was more than twice that for those who were prefrail. Nonetheless, of participants with only three frailty characteristics, 32.4% regressed, whereas few individuals with four or five characteristics regressed.

Table 4 shows the presence or absence of each frailty characteristic (or death) at follow-up, stratified according to presence of that characteristic at baseline. Transition to death was almost twice as high for individuals with frailty characteristics at baseline that were classified using performance-based measures and low physical activity than for those classified using self-report measures.

Adjusted and unadjusted odds of worsening in individual frailty characteristics are shown in Table 5. Weight

Table 2. Follow-Up Frailty Score and Death Status According to Baseline Frailty Score for Total Sample (N = 597)

	N (%)					
	Baseline Frailty Score					
	Nonfrail	Prefrail		Frail		
Follow-Up Frailty Score (n)	0 (n = 228)	1 (n = 212)	2 (n = 105)	3 (n = 37)	4 (n = 12)	5 (n = 3)
0 (145)	94 (41.2)	38 (17.9)	11 (10.5)	2 (5.4)	0 (0.0)	0 (0.0)
1 (159)	68 (29.8)	67 (31.6)	20 (19.1)	3 (8.1)	1 (8.3)	0 (0.0)
2 (93)	26 (11.4)	34 (16.0)	24 (22.9)	7 (18.9)	1 (8.3)	1 (33.3)
3 (59)	9 (4.0)	27 (12.7)	16 (15.2)	6 (16.2)	1 (8.3)	0 (0.0)
4 (14)	1 (0.4)	2 (0.9)	9 (8.6)	2 (5.4)	0 (0.0)	0 (0.0)
5 (3)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Dead (124)	30 (13.2)	43 (20.3)	24 (22.9)	17 (46.0)	8 (66.7)	2 (66.7)

Analysis includes individuals for whom information was available for all five frailty characteristics and whose transition could be classified in at least one frailty characteristic at baseline and follow-up.

Table 3. Follow-Up Frailty Category and Death Status According to Baseline Frailty Category for Total Sample (N = 597)

	n (%)			
	Baseline Frailty Category			
Follow-Up Frailty Category (n)	Nonfrail (n = 209)	Prefrail (n = 298)	Frail (n = 52)	Cannot Classify (n = 38)
Nonfrail (121)	79 (37.8)	37 (12.4)	1 (1.9)	4 (10.5)
Prefrail (201)	70 (33.5)	110 (36.9)	6 (11.5)	15 (39.5)
Frail (76)	6 (2.9)	49 (16.4)	10 (19.2)	11 (29.0)
Deceased (124)	30 (14.4)	67 (22.5)	27 (51.9)	0 (0.0)
Cannot classify (75)	24 (11.5)	35 (11.7)	8 (15.4)	8 (21.1)

Analysis includes individuals for whom information was available for all five frailty characteristics and whose transition could be classified in at least one frailty characteristic at baseline and follow-up.

loss was used as the reference category in all models because it had the highest rate of progression and regression of the five frailty characteristics. As indicated in Table 5, the dependent variable for the GEE analysis was worsening in any of the five frailty characteristics. The predictor variables were age, sex, ethnic group, household income, education, diabetes mellitus without complications, diabetes mellitus with complications, and comorbid diseases excluding diabetes mellitus. In the unadjusted model for worsening, the odds of worsening relative to weight loss were lowest for grip strength, followed by physical activity, walking speed, and exhaustion. In Model 2, age and follow-up interval were significant predictors of worsening in any frailty characteristic, with a 4% greater risk of worsening for each year of age and a 39% greater risk of worsening in frailty for each year of follow-up. In Model 3, diabetes mellitus and fewer years of education were significant predictors of worsening. Diabetes mellitus was associated with an approximately 40% greater risk of worsening (OR = 1.38, 95% CI = 1.0–1.91), whereas each year of education was associated with a 4% lower risk of worsening (OR = 0.96, 95% CI = 0.92–1.0). In Model 4, diabetes mellitus with macrovascular complications— but not uncomplicated diabetes mellitus—was a significant predictor of worsening (OR = 1.84, 95% CI = 1.02–3.33). The magnitude of the effect was higher for diabetes mellitus with macrovascular complications than for undifferentiated diabetes mellitus in Model 3 (OR = 1.38).

DISCUSSION

This study of frailty transitions over an average 6.4 years in community-dwelling older MA and EA participants in SALSA found that prefrail individuals with two baseline frailty characteristics were more likely than those with only one to worsen in frailty state. Similarly, those with only one baseline characteristic were more likely to improve than those with two. Follow-up death rates increased according to poorer baseline frailty state, and the rate was higher for frailty characteristics classified based on performance-based measures and low physical activity than for those classified based on self-reported frailty measures. In GEE analyses of frailty worsening, significant predictors were diabetes mellitus with macrovascu-

Table 4. Follow-Up (F/U) Status, Including Death, for Individual Frailty Characteristics According to Corresponding Baseline Status

	n (%)			
Individual Frailty Characteristic	**Exhibited Characteristic at Baseline**		**Did Not Exhibit Characteristic at Baseline**	
Grip strength	Weakness at baseline (n = 84)		No weakness at baseline (n = 382)	
	Weakness at F/U	26 (30.9)	Weakness at F/U	27 (7.1)
	No weakness at F/U	24 (28.6)	No weakness at F/U	271 (70.9)
	Dead at F/U	34 (40.5)	Dead at F/U	84 (22.0)
Walking speed	Slowness at baseline (n = 82)		No slowness at baseline (n = 384)	
	Slowness at F/U	28 (34.2)	Slowness at F/U	37 (9.6)
	No slowness at F/U	21 (25.6)	No slowness at F/U	262 (68.2)
	Dead at F/U	33 (40.2)	Dead at F/U	85 (22.1)
Exhaustion	Exhaustion at baseline (n = 138)		No exhaustion at baseline (n = 328)	
	Exhaustion at F/U	71 (51.5)	Exhaustion at F/U	50 (15.2)
	No exhaustion at F/U	25 (18.1)	No exhaustion at F/U	202 (61.6)
	Dead at F/U	42 (30.4)	Dead at F/U	76 (23.2)
Weight loss	Weight loss at baseline (n = 65)		No weight loss at baseline (n = 401)	
	Weight loss at F/U	21 (32.3)	Weight loss at F/U	91 (22.7)
	No weight loss at F/U	24 (36.9)	No weight loss at F/U	212 (52.9)
	Dead at F/U	20 (30.8)	Dead at F/U	98 (24.4)
Physical activity	Low physical activity at baseline (n = 84)		No low physical activity at baseline (n = 382)	
	Low physical activity at F/U	22 (26.2)	Low physical activity at F/U	24 (6.3)
	No low physical activity at F/U	27 (32.1)	No low physical activity at F/U	275 (72.0)
	Dead at F/U	35 (41.7)	Dead at F/U	83 (21.7)

lar complications, fewer years of education, and follow-up interval. Individuals with undifferentiated diabetes mellitus were approximately 40% more likely to progress in any frailty characteristic. In Model 4, those who had diabetes mellitus with macrovascular complications were 84% more likely to worsen in any frailty characteristic than those without diabetes mellitus. These findings suggest that diabetes mellitus plays a pervasive role in worsening of frailty, affecting all five frailty characteristics.

Previous studies have shown that diabetes mellitus is associated with prevalent[2] and incident[3,5] frailty, and fasting hyperglycemia is associated with frailty in individuals without diabetes mellitus.[17] Several studies support associations between frailty and insulin resistance and diabetes mellitus.[18] In particular, insulin resistance has been shown to be predictive of incident frailty, and higher levels of glycosylated hemoglobin is also associated with frailty.[19] Frailty has also been linked with other diseases, such as cardiovascular disease, congestive heart failure, peripheral vascular disease, and stroke.[20,21] Although more research is needed to develop agreed-upon clinical criteria for identifying frailty in the clinical setting, in the future, performing a clinical frailty assessment at the onset of diabetes mellitus in older adults may help identify those at risk of frailty and lead to early initiation of preventive interventions.

To the knowledge of the authors, this is the first study to examine diabetes mellitus as a predictor of worsening in individual frailty characteristics. In spite of the fact that diabetes mellitus is two to three times as prevalent in MAs as in EAs, no ethnic differences were found in worsening in any frailty characteristic. It has previously been reported that MAs are 60% less likely than EAs to develop incident frailty (OR = 0.40, 95% CI = 0.23–0.72) after covariate adjustment for relevant covariates,[22] but the present findings suggest that MAs and EAs may be equally likely to transition in individual frailty characteristics and that factors predicting worsening of any frailty characteristic, including diabetes mellitus, may operate similarly in both ethnic groups.

This study also showed that fewer years of education, an important indicator of SES, is also a significant predictor of worsening in any individual frailty characteristic (OR = 0.96, 95% CI = 0.93–1.0). Previous studies have shown that low SES is associated with prevalent and incident frailty.[2,3,23] A potential mechanism explaining this association between low SES and frailty is inflammation, which is thought to be a major physiological alteration operant in frailty[24] and which may result from poorer nutritional status, less access to medical care, and higher prevalence of chronic disease in individuals with lower SES.[25] The current study extends these findings by showing that education is a predictor of worsening in any frailty characteristic. In combination with the findings relative to diabetes mellitus, there may be a greater burden of frailty in older individuals with diabetes mellitus with lower education. More research is needed, although it is possible that education interventions in the area of diabetes mellitus management for older adults could indirectly reduce frailty progression by lowering the incidence of diabetes mellitus with complications.

Mortality was higher for individual frailty characteristics classified using objective or quasi-objective measures than for those that were self-reported. One possibility for this finding is that individual perceptions or self-report bias may affect more-objective measures of frailty, which may be more reflective of underlying physiological deficits than self-reported measures, less. Prior studies have shown that individual frailty measures are predictive of mortality,[26,27] although previous reports of which individual frailty

Table 5. Likelihood of Frailty Worsening (vs Remaining Unchanged or Improving) in Multivariate Models Using Generalized Estimating Equations (GEEs) (N = 597)

Variable	Odds Ratio (95% Confidence Interval) P-Value			
	Model 1	Model 2	Model 3	Model 4
Dependent variable				
Grip strength	0.56 (0.47–0.66) <.001	0.3 (0.21–0.43) <.001	0.28 (0.19–0.41) <.001	0.28 (0.19–0.41) <.001
Walking speed	0.65 (0.55–0.77) <.001	0.39 (0.27–0.56) <.001	0.40 (0.27–0.58) <.001	0.4 (0.27–0.58) <.001
Exhaustion	0.73 (0.61–0.88) .001	0.57 (0.41–0.81) .001	0.54 (0.37–0.78) .001	0.54 (0.37–0.78) .001
Physical activity	0.59 (0.49–0.70) <.001	0.36 (0.25–0.51) <.001	0.36 (0.25–0.52) <.001	0.36 (0.25–0.52) <.001
Weight loss	1	1	1	1
Predictor variable				
Ethnicity (Mexican American vs European American)		1.05 (0.82–1.36) .68	0.78 (0.56–1.07) .09	0.76 (0.56–1.05) .09
Age		1.04 (1.00–1.08) .05	1.04 (1.00–1.08) .06	1.04 (1.00–1.08) .06
Sex (male vs female)		1.11 (0.86–1.42) .42	1.21 (0.92–1.59) .23	1.20 (0.91–1.58) .19
Follow-up interval, years		1.39 (1.26–1.54) <.001	1.30 (1.17–1.46) <.001	1.30 (1.17–1.46) <.001
Income (1-category increment)*	–	–	0.95 (0.90–1.01) .09	0.96 (0.91–1.01) .11
Education (1-year increment)	–	–	0.96 (0.93–1.0) .04	0.96 (0.93–1.0) .04
Comorbidity (not including diabetes mellitus)	–	–	1.30 (0.99–1.71) .06	1.26 (0.95–1.67) .11
Diabetes mellitus (yes vs no)	–	–	1.38 (1.00–1.91) .05	
Diabetes mellitus without complications (vs no diabetes mellitus)	–	–		1.25 (0.88–1.79) .21
Diabetes mellitus with complications (vs no diabetes mellitus)†	–	–		1.84 (1.02–3.33) .04

The GEE analysis includes all subjects whose change in at least one of the five frailty characteristics can be determined.

* Monthly household income categories: 1 = $0–49, 2 = $50–99, 3 = $100–149, 4 = $150–199, 5 = $200–299, 6 = $300–399, 7 = $400–499, 8 = $500–749, 9 = $750–999, 10 = $1,000–1,249, 11 = $1,250–1,499, 12 = $1,500–1,999, 13 = $2,000–2,499, 14 = $2,500–2,999, 15 = ≥$3,000.

† Defined as the presence of diabetes mellitus (defined by American Diabetes Association criteria) and the presence of stroke (defined according to self-report of physician-diagnosed disease) or self-reported (assessed by Rose questionnaire) or electrocardiogram-defined ischemic heart disease.

characteristics predict mortality vary between study populations and have included objective and self-reported characteristics as the strongest mortality predictor.[26–28] Because prefrail individuals may have only one frailty characteristic but still be at significant risk of death and incident frailty,[2,6] the potential ability of individual frailty characteristics to predict these outcomes in diverse populations should continue to be examined to identify appropriate targets for intervention in different population subgroups.

The SALSA cohort was aged 69.6 ± 3.4 at baseline, an average of 8.8 years younger than the cohort in a previous study[4] (78.4 ± 5.3) and 12.9 years younger than the H-EPESE cohort (82.5 ± 4.5).[5] Despite these age differences, all studies found that frail individuals were unlikely to regress. The SALSA and H-EPESE studies found that frail individuals were more likely to die than remain frail, whereas the other study,[4] which followed participants for a shorter time, found that frail individuals were more likely to remain frail than die. The advanced age of the H-EPESE cohort and slightly longer follow-up interval probably account for the greater proportion of frail individuals who died in that study than in SALSA (84% vs 52%).

The present study has several limitations. There were minor modifications of the CHS criteria. Results obtained for MAs living in a single major urban area in south Texas may not be generalizable to MAs living in other urban areas in the United States or those living in rural areas. The sample size was small, and only approximately 7% of the analytical cohort regressed in overall frailty status. Bias could have been introduced if the individuals lost to follow-up differed systematically from those who completed the follow-up examination. To address this concern, baseline frailty information for those included in the analytical cohort was compared with that of non-completers (data not shown); no differences were found in individual frailty characteristics or frailty state between the two groups. Disease ascertainment is also a potential limitation. Although diabetes mellitus, hypertension, and IHD were measured according to clinical criteria or validated measures, many were ascertained according to self-report of physician-diagnosed disease and were not adjudicated. Finally, the varying length of follow-up among SALSA participants was by design. Interval lengths were varied across individuals by reversing the order of enrollment at baseline to maximize information from the assessment. Interval length was included as a covariate in the GEE analyses.

The findings of greater mortality in prefrail than non-frail individuals, approximately equivalent death rates in prefrail individuals with one or two frailty characteristics, and a substantially lower death rate in prefrail than frail individuals provides further validation of the trichotomous frailty classification proposed by Fried in the CHS,[2] high-

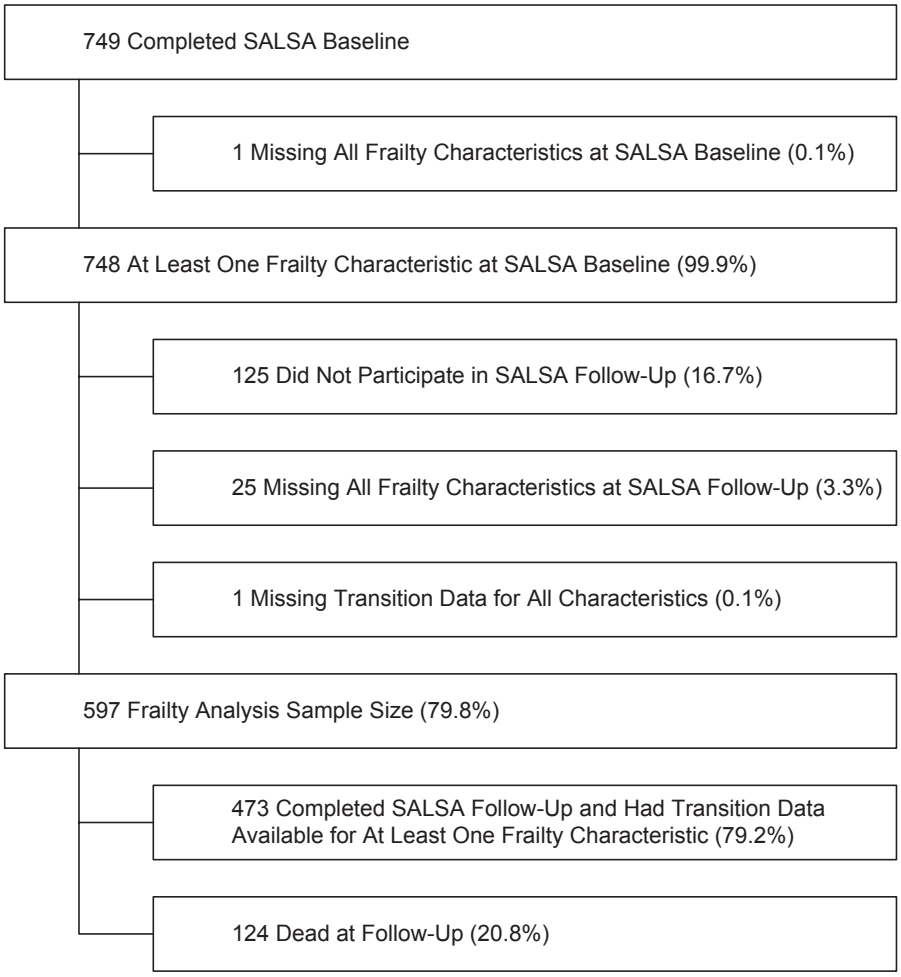

Figure 1. Sample size. SALSA = San Antonio Longitudinal Study of Aging.

lighting the significance of prefrailty as a separate risk state. Furthermore, the finding that prefrail individuals were more likely than frail individuals to improve in frailty state suggests that this group of individuals is capable of significant improvement over time and may be responsive to clinical and behavioral interventions to slow or reverse worsening of frailty.

Although there is no established clinical intervention for frailty per se, characteristics of the frailty phenotype include physical activity, muscle strength, and nutrition. One study has shown that physical activity, in the form of strength training, is more effective than a nutritional intervention in improving muscle strength and gait speed in older adults and that it is safe, even in nursing home residents.[29] Other studies have shown that exercise interventions can ameliorate frailty and prevent disability in frail older adults,[30] but there are conflicting findings regarding the effectiveness of therapeutic exercise, as well as the specific type of exercise that should be recommended to older adults.[31] Future research should focus on translating exercise and strength training interventions into clinical prescriptions for therapeutic exercise in older adults and testing and translating into clinical practice various approaches to frailty screening in the clinical setting. Given the increasing rates of diabetes mellitus in the U.S. population, including older adults, the role of diabetes mellitus in the development of frailty is an important concern and should be considered when developing methods and interventions for improving the health of older adults in the future.

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