

ORIGINAL RESEARCH

THE ASSOCIATION OF FRAILITY WITH HOSPITALIZATIONS AND MORTALITY AMONG COMMUNITY DWELLING OLDER ADULTS WITH DIABETES

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Abstract: *Background:* Diabetes (DM) is associated with an accelerated aging that promotes frailty, a state of vulnerability to stressors, characterized by multisystem decline that results in diminished intrinsic reserve and is associated with morbidity, mortality and utilization. Research suggests a bidirectional relationship between frailty and diabetes. Frailty is associated with mortality in patients with diabetes, but its prevalence and impact on hospitalizations are not well known. *Objectives:* Determine the association of frailty with all-cause hospitalizations and mortality in older Veterans with diabetes. *Design:* Retrospective cohort. *Setting:* Outpatient. *Participants:* Veterans 65 years and older with diabetes who were identified as frail through calculation of a 44-item frailty index. *Measurements:* The FI was constructed as a proportion of healthcare variables (demographics, comorbidities, medications, laboratory tests, and ADLs) at the time of the screening. At the end of follow up, data was aggregated on all-cause hospitalizations and mortality and compared non-frail (robust, $FI \leq .10$ and prefrail $FI = .10, < .21$) and frail ($FI \geq .21$) patients. After adjusting for age, race, ethnicity, median income, history of hospitalizations, comorbidities, duration of DM and glycemic control, the association of frailty with all-cause hospitalizations was carried out according to the Andersen-Gill model, accounting for repeated hospitalizations and the association with all-cause mortality using a multivariate Cox proportional hazards regression model. *Results:* We identified 763 patients with diabetes, mean age 72.9 (SD=6.8) years, 50.5% were frail. After a median follow-up of 561 days (IQR=172), 37.0% they had 673 hospitalizations. After adjustment for covariates, frailty was associated with higher all-cause hospitalizations, hazard ratio (HR)=1.71 (95%CI:1.31-2.24), $p < .0001$, and greater mortality, HR=2.05 (95%CI:1.16-3.64), $p = .014$. *Conclusions:* Frailty was independently associated with all-cause hospitalizations and mortality in older Veterans with diabetes. Interventions to reduce the burden of frailty may be helpful to improve outcomes in older patients with diabetes.

Key words: Frailty, diabetes mellitus, hospitalizations, mortality, older adults.

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Introduction

Frailty is a state of vulnerability to stressors, characterized by multisystem decline that results in a diminished intrinsic reserve (1). Frailty is associated with higher morbidity, mortality and healthcare utilization. Research evidence suggests bidirectional relationship between diabetes and frailty (2). Older adults with frailty demonstrate a high prevalence of risk factors associated with diabetes including obesity, inactivity, declining renal function (3, 4). On the other hand, diabetes may contribute to a higher risk for frailty as a result of the high prevalence of cardiovascular risk factors (5). The bidirectional association between frailty and diabetes and their combined effects may be particularly deleterious for older persons (2, 5).

Several explanations for the relationship between frailty and diabetes mellitus have been proposed. Frailty and diabetes share some of the same mechanisms: insulin resistance, low grade inflammation, oxidative stress, stem cell dysfunction, mitochondrial dysfunction, and sarcopenia (6-8). Comorbid medical and mental health conditions often coexist in both

frailty and diabetes including but not limited to obesity, cardiovascular disease, sleep apnea, depression and cognitive impairment (5, 9, 10). Hypoglycemia in older people with diabetes may be a particularly important contributor to frailty risk and similarly frailty may predispose older people with diabetes to hypoglycemia (8).

Both frailty (11) and diabetes (12) are prevalent in the Veteran than the general US population. Diabetes (13) and frailty (14) are both independently associated with a higher risk for all-cause hospitalizations in older adults. Furthermore, mortality is also higher in frailty and diabetes. In these patients, the concurrence of frailty and diabetes may further increase the effects of individual conditions on clinical outcomes that may lead to higher healthcare utilization and mortality. Previous studies have shown that older adults with either frailty (14) or diabetes (15) are high utilizers of healthcare including hospitalizations. Although Veterans receiving care at Department of Veterans Affairs (VA) Medical Centers have an increased risk for hospitalizations, there is, however, no data regarding the effects on hospitalizations in Veterans with

coexistent frailty and diabetes. Thus, the aim of this study was to determine the effects of frailty on all-cause hospitalization and mortality in older adults with diabetes at a VA medical center.

Methods

Study Setting

This research is a retrospective cohort study that was conducted at a tertiary care VA Medical Center, a US government-run healthcare institution. The study is part of a clinical demonstration quality improvement project looking at identifying Veterans with frailty.

Identification of Patients

Our project team identified community-dwelling Veterans 65 years and older with diabetes coming to the VA Medical Center outpatient clinics from January 2016 to August 2017, and patients were follow-up until October 2018. We identified patients with diabetes, diagnosed between October 2, 1996, and July 17, 2017. Trained research associates collected patient data from the electronic health record and the VA Corporate Data Warehouse (CDW) including demographic information; vital signs and BMI, physical and mental health conditions; laboratory data, sensory problems and functional status. We used the zip code and race to obtain the patients annual median household income based on 2014 Census tract data as a parameter for social status classification. Information on physical health conditions was used to calculate an age-adjusted Charlson comorbidity index (CCI) (16).

Frailty Assessment

Data collected for each patient from reviews of the VA electronic health record and the VA Corporate Data Warehouse (CDW) was used to calculate a frailty index (FI) which included 44 items. Each patient's FI had a minimum of 30 of the 44 items. The 44 items in the FI belonged to 7 major categories (supplementary materials): socio-demographic (4 items), vital signs and other measurements (3 items), physical and mental health conditions (20 items), laboratory data (10 items), sensory problem (1 item) and functional status (6 items). The 44-item frailty index used in this study is based on the deficit accumulation conceptual framework that assumes that frailty is the result of interacting physical, functional psychological, and social factors (17). Unlike the frailty phenotype, which is the most widely used conceptual model in the field, the deficit accumulation approach does not rely on predetermined variables (18). Each patient's FI was calculated by dividing the number of items present (19). We chose the cut-off of 0.21, which was most recently used by Orkaby et al. as part of a large VA study on the prevalence of frailty in the VA (11). This resulted in a score between 0-1, where higher scores represent higher frailty. The patients were stratified as non-frail (FI is <0.21) and frail (FI is \geq 0.21).

Hospitalization Ascertainment

Patients were followed from January 2016 to August 2017 until October 2018 for VA all-cause hospitalizations following the initial assessment of frailty. We recorded the total number of hospital admissions during the previous one year and for the follow up period. The primary reasons for hospitalizations were assessed using ICD 9 and 10 codes assigned by trained staff after discharge.

Mortality

All-cause mortality was identified through official sources including VHA facilities, death certificates, and National Cemetery Administration data available from the VA CDW. There is high agreement (91-99%) between dates of death recorded in the CDW and dates of death recorded in external sources that feed the VHA Vital Status File (20). The last day of follow-up was October 31st, 2018.

Data Analysis

Baseline characteristics are presented as frequency (percent) for categorical variables, and as mean+SD for continuous variables. We report descriptive statistics of age, race, ethnicity, median income, marital status, body-mass index (BMI), and age-adjusted CCI, duration of diabetes, DM with complication, number of medications, use of insulin or sulfonylureas, metformin, level of glycemia control, previous and during follow-up hospitalizations. All variables were checked for normality of distribution using the Kolmogorov-Smirnov test. All values showed no-normal distribution. Mann-Whitney U and Kruskal-Wallis test (for non-normally distributed variables) and Chi-Square were run to evaluate the differences between non-frail and frail. The association of frailty with all-cause hospitalizations in older adults with diabetes was determined with the Andersen-Gill model, accounting for repeated hospitalizations. Patients were censored if they died without having a hospital admission. Univariate and multivariate analyses were conducted adjusting for age, race, ethnicity, median household income, BMI, age-adjusted CCI, diabetes complications, duration of diabetes, use of insulin or sulfonylureas, metformin, level of glycemia control, and all-cause hospitalizations in the previous year. Four models were constructed to assess the role of the covariates in the association between frailty and all-cause hospitalization: Model 1 was adjusted for age, race, ethnicity, BMI and Median Household Income. Model 2 was adjusted for the covariates in Model 1 and age-adjusted CCI. Model 3 was adjusted for the covariates in Models 1-2 and diabetes complications, duration of diabetes, use of insulin or sulfonylureas, metformin and level of glycemia control. Model 4 was adjusted for the covariates in the previous models and for hospitalizations in the previous year. The proportional hazard assumption was tested using scaled Schoenfeld residuals and was found to be valid. Cox regression analysis was performed to calculate the hazard ratios and 95% confidence intervals (CIs) of survival for frailty on all-cause

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Table 1
Participant Characteristics

Variable	Non-frail (n=378, 49.5%)	Frail (n=385, 50.5%)	Total (n=763, 100%)	p value
Age, mean (SD)	72.40 (6.23)	73.33 (7.26)	72.87 (6.78)	.190
Male, n (%)	372 (98.4)	378 (98.2)	750 (98.3)	.805
Married, n (%)	210 (55.5)	158 (41.0)	368 (48.2)	<.0001
Caucasian n (%)	219 (57.9)	214 (55.6)	433 (56.7)	.512
Non-Hispanic, n (%)	284 (75.1)	304 (79.0)	588 (77.1)	.208
Median Household Income, \$ (SD)	54,004 (25,068)	50,877 (22,883)	52,426 (24,026)	.100
BMI, mean (SD)	29.82 (5.15)	30.07 (6.00)	29.95 (5.60)	.542
Diabetes with end organ damage, n (%)*	107 (28.3)	140 (36.4)	247 (32.4)	.017
Duration of Diabetes, y (SD)	8.46 (5.36)	9.48 (5.21)	8.97 (5.60)	.009
More than 5 Medications, n (%)	344 (91.0)	380 (98.7)	724 (94.9)	<.0001
Metformin, n (%)	225 (59.5)	161 (41.8)	386 (50.6)	<.0001
Insulin or Sulfonylurea, n (%)	189 (50.0)	221 (57.4)	410 (53.7)	.040
Glycemic Control				
Tight (HbA1c≤7), n (%)	219 (57.9)	202 (52.5)	421 (55.2)	.146
Intermediate (HbA1c>7, <9), n (%)	128 (33.9)	137 (35.6)	265 (34.7)	
Poor (HbA1c≥9), n (%)	31 (8.2)	46 (11.9)	77 (10.1)	
Frailty Index, mean (SD)	.16 (.03)	.28 (.06)	0.22 (0.07)	<.0001
Charlson CI, mean (SD)	5.75 (1.65)	6.91 (2.00)	6.33 (1.93)	<.0001
Hospitalization in Previous Year, mean (SD)	0.27 (.74)	1.11 (1.74)	0.69 (1.40)	<.0001
Hospitalization during FU, mean (SD)	0.50 (1.18)	1.26 (1.95)	0.88 (1.66)	<.0001
Mortality, n (%)	19 (5.0)	62 (16.1)	81 (10.6)	<.0001

*Diabetes with End organ damage: patients diagnosed with one or more of the following diagnosis: retinopathy, neuropathy and nephropathy. SD = standard deviation; n = number of participants. BMI= body mass index; FU= follow-up; Mann-Whitney U and Kruskal-Wallis test (for non-normally distributed variables) and Chi-Square for continuous variables and categorical variables, respectively. Significant differences between frailty groups are in bold (p<.05).

mortality. We built 4 models to assess the role of the covariates in the association between frailty and all-cause mortality as described for all-cause hospitalizations. To assess the robustness of our results, sensitivity analyses were performed in which we dichotomized subgroups of older Veterans with frailty by age (<75 and ≥ 75 years old), race (White vs. African American), and with history of hospitalizations in the previous year (Yes vs. No). We did not have to exclude variables having a high collinearity among themselves. Associations were considered significant if p<0.05. Follow up duration was calculated as follows: (October 31th, 2018 – frailty assessment date)/365. All analyses were performed using the SPSS 25.0 for Windows (SPSS, Inc., Chicago, Illinois) and SAS for Windows version 3.71 (SAS Institute Inc., Cary, North Carolina). All statistical tests were two-tailed, and statistical significance was assumed for a p-value <0.05.

Results

Patient Characteristics

Table 1 shows participant characteristics. 763 participants were included in the study. Patients were 98.3% male, 56.7% White, 77.1% non-Hispanic and the mean age was 72.9 (SD= 6.8) years. Compared with the non-frail, older adults with diabetes were less likely to be married, have more end-organ damage, longer duration of diabetes, more multimorbidity and use of medications, more likely to be taking insulin or sulfonylureas, less likely to be on metformin and have more hospitalizations in the previous year (Table 1).

Hospitalizations

There were 673 all-cause hospitalizations over a median follow-up period of 561 days (IQR= 172) with the range between 0 and 12 hospitalizations. The leading causes for hospitalization were cardiovascular, infectious and renal diagnoses representing 137 (21%), 71 (11%) and 69 (10%)

Table 2
Association of Frailty with All-Cause Hospitalizations and Mortality in Older Veterans with Diabetes (n = 763)

Hospitalizations										
	Unadjusted HR (95% CI)	p value	Model 1 HR (95% CI)	p value	Model 2 HR (95% CI)	p value	Model 3 HR (95% CI)	p value	Model 4 HR (95% CI)	p value
Non-Frail					1 (reference)					
Frail	2.77 (2.08-3.69)	<.0001	2.94 (2.23-3.87)	<.0001	2.52 (1.88-3.38)	<.0001	2.36 (1.77-3.14)	<.0001	1.71 (1.31-2.24)	<.0001
Mortality										
	Unadjusted HR (95% CI)	p value	Model 1 HR (95% CI)	p value	Model 2 HR (95% CI)	p value	Model 3 HR (95% CI)	p value	Model 4 HR (95% CI)	p value
Non-Frail					1 (reference)					
Frail	3.85 (2.25-6.56)	<.0001	3.77 (2.20-6.47)	<.0001	2.89 (1.68-5.04)	<.0001	2.65 (1.52-4.64)	.001	2.05 (1.16-3.638)	0.014

Model 1 was adjusted for age, race, ethnicity, BMI and Median Household Income. Model 2 was adjusted for the covariates in Model 1 and Charlson Comorbidity Index. Model 3 was adjusted for the covariates in Models 1-2 and diabetes complications, duration of diabetes, use of insulin or sulfonylureas, metformin and level of glycemia control. Model 4 was adjusted for the covariates in the previous models and for hospitalizations in the previous year. Significant associations are in bold (p< .05).

Table 3
Association of All-Cause Hospitalizations with Age Group (<75 y (n=261) vs. ≥75 y (n=124)), Race (White (n=220) vs. African American (n=165) and Prior Hospitalizations (No (n=207) vs. Yes (n=178)) in Patients with Frailty and Diabetes (n = 385)

	Unadjusted HR (95% CI)	p value	Model 1 HR (95% CI)	p value	Model 2 HR (95% CI)	p value	Model 3 HR (95% CI)	p value	Model 4 HR (95% CI)	p value
<75 y					1 (reference)					
≥ 75y	.78 (.55-1.11)	.1732	.84 (.59-1.21)	.346	.74 (.51-1.06)	.099	.74 (.5041-.09)	.130	.86 (.59-1.23)	.399
White					1 (reference)					
African American	.73 (.53-1.02)	.063	.63 (.42-.97)	.035	.63 (.41-.97)	.036	.64 (.42-.98)	.042	.61 (.41-.91)	.015
No Prior Hosp					1 (reference)					
Prior Hosp	3.57 (2.59-4.91)	<.0001	3.59 (2.61-4.95)	<.0001	3.45 (2.49-4.79)	<.0001	3.37 (2.43-4.66)	<.0001	-	-

Model 1 was adjusted for age, (except age group: <75y and ≥75y), race (except for race group: White vs African American), ethnicity, BMI and Median Household Income. Model 2 was adjusted for the covariates in Model 1 and Charlson Comorbidity Index. Model 3 was adjusted for the covariates in Models 1-2 and diabetes complications, duration of diabetes, use of insulin or sulfonylureas, metformin and level of glycemia control. Model 4 was adjusted for the covariates in the previous models and for hospitalizations in the previous year (except for Prior hospitalizations: Yes Prior and No prior). Significant associations are in bold (p< .05).

of the total respectively. The year before evaluation of frailty, 239 patients (31.3%) had at least one hospitalization and 524 (68.7%) did not have any hospitalizations. Over the follow up period, 481 participants (63.0%) did not have any hospitalizations; whereas, 282 (37.0%) had at least 1 hospitalization (data are not shown).

As shown in Table 2, using the Andersen-Gill model fully adjusted for covariates, frailty was significantly associated with higher risk for hospitalizations compared to non-frail patients, adjusted HR=1.71 (95%CI:1.31–2.24), p<.0001. There were some differences appeared after conducting sensitivity analysis in the subgroup of older Veterans with diabetes and frailty. In terms of age, there were no associations between frailty and all-cause hospitalizations in participants 75 years of age and older after adjustment for all covariates (Table 3), HR=.86 (95%CI:.59-1.23), p=.399. There were significant associations of frailty with lower risk for all-cause hospitalizations in African American participants after adjusting for covariates: HR=.61 (95%CI:.41-.91), p=.015 (Table 3). After dividing the groups into those with and those without hospitalizations

in the previous year, there were significant differences in those participants with previous hospitalizations HR=3.37 (95%CI:2.43-4.66), p<.0001 (Table 3).

Mortality

Over the follow-up period, 81 deaths occurred. Table 2 displays the association between mortality and frailty in older Veterans with diabetes. After adjusting for all covariates, (Model 4), frailty increased the risk of all-cause mortality during follow up, HR=2.05 (95%CI:1.16-3.64), p=.014. During sensitivity analyses, frailty did not show association with all-cause mortality in participants 75 years of age and older after adjustment for covariates HR=1.39 (95%CI:.79-2.46), p=.248 (Table 3). There was not association of frailty with all-cause mortality in African Americans after adjustment for covariates: HR=.67 (95%CI:.34 - 1.32), p=.244. Furthermore, frailty was significantly associated with higher all-cause mortality in those with previous hospitalizations after adjustment: HR=3.36 (95%CI:1.87-6.06), p<.0001 (Table 3).

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Table 4

Association of All-Cause Mortality with Age Group (<75 y (n=261) vs. ≥75 y (n=124)), Race (White (n=220) vs. African American (n=165) and Prior Hospitalizations (No (n=207) vs. Yes (n=178)) in Patients with Frailty and Diabetes (n = 385)

	Unadjusted HR (95% CI)	p value	Model 1 HR (95% CI)	p value	Model 2 HR (95% CI)	p value	Model 3 HR (95% CI)	p value	Model 4 HR (95% CI)	p value
<75 y					1 (reference)					
≥ 75y	2.19 (1.33-3.61)	.002	1.66 (.98-2.78)	.058	1.33 (.78-2.27)	.294	1.18 (0.67-2.08)	.557	1.39 (.79-2.46)	.248
White					1 (reference)					
African American	.66 (.39-1.11)	.119	.72 (.37-1.38)	.320	.773 (.39-1.50)	.448	.78 (.40-1.52)	.467	.67 (.34-1.32)	.244
No Prior Hosp					1 (reference)					
Prior Hosp	3.70 (2.09-6.53)	<.0001	3.86 (2.18-6.85)	<.0001	3.55 (1.98-6.34)	<.0001	3.36 (1.86-6.06)	<.0001	-	-

Model 1 was adjusted for age, (except age group: <75y and ≥75y), race (except for race group: White vs African American), ethnicity, BMI and Median Household Income. Model 2 was adjusted for the covariates in Model 1 and Charlson Comorbidity Index. Model 3 was adjusted for the covariates in Models 1-2 and diabetes complications, duration of diabetes, use of insulin or sulfonylureas, metformin and level of glycemia control. Model 4 was adjusted for the covariates in the previous models and for hospitalizations in the previous year (except for Prior hospitalizations: Yes Prior and No prior). Significant associations are in bold (p< .05).

Discussion

In this study, we investigated whether frailty was associated with risk for either all-cause hospitalizations or mortality in older adults with diabetes. The overall analysis showed an association between frailty in older adults with diabetes and a higher risk for all-cause hospitalization and mortality after adjustment for known confounders. There were, however, differences between subgroups of participants with frailty. African Americans with frailty had a lower risk for all-cause hospitalizations than whites. Older adults with frailty and history of hospitalizations in the previous year demonstrated a higher risk for both all-cause hospitalizations and mortality.

The independent contribution of frailty to a higher risk for all-cause hospitalizations and mortality in older people with diabetes may be related to several factors associated with this syndrome. Frailty may shape the presentation of type 2 diabetes by increasing the risk of hypoglycemia (8). Weight loss and sarcopenia which are often part of the frailty syndrome, may be further exacerbated by concurrent anorexia of aging potentially leading to the normalization of glycemic control and an increased risk for recurrent and sometimes severe hypoglycemia (21), which may lead to cardiovascular complications. Cardiovascular diagnoses represented the leading cause of hospitalization in our sample of older Veterans with diabetes. Older individuals with diabetes and frailty may be especially susceptible to the physiological effects of hypoglycemia on the cardiovascular system potentially contributing to a higher rate of hospitalizations. It has been proposed that older adults with diabetes and frailty may benefit from less aggressive targets for glycemic control (21). The increased inflammatory and coagulation abnormalities characteristic of frailty may also worsen the microvascular effects of diabetes (22) resulting in a higher rate of complications and in turn a risk for higher rate of subsequent hospitalizations and poor clinical outcomes including death. In our study complications of renal disease were amongst the leading causes of hospitalization. In older

adults, frailty may mediate the link between diabetes and disability which in itself is associated with a higher risk for all-cause hospitalization (23) and mortality (24). Falls, delirium, dementia and other geriatric syndromes often coexist with frailty sharing mechanisms that may also jointly contribute to an increase risk for hospitalizations and mortality (25). Cognitive impairment, which is often underrecognized, often occurs and coexists patients with both diabetes and frailty, and is a known risk factor for hospital admissions and readmissions (26) and mortality in in patients with diabetes (27). That frailty has an additive effect to that of diabetes on all-cause hospitalizations and mortality in older adults with an already increased risk for healthcare utilization and decreased survival is particularly noteworthy. Identifying frailty could facilitate clinical decision making and potentially contribute to the implementation of clinical interventions aimed at reducing poor clinical outcomes and hospitalization risk in older patients with diabetes.

Although some studies have addressed the issue of previous hospitalizations in older adults with frailty, none has specifically looked at the coexistence of both frailty and diabetes in subgroups of older adults with frailty. This analysis reveals some evidence of the level of heterogeneity in all-cause hospitalizations and mortality older people with diabetes and frailty. The lack of differences in hospitalizations between the two age subgroups may just be function of the smaller sample size. However, another explanation may be related to the characteristics of the subgroups (supplementary materials). The over 75 years old group shows characteristics that may explain the lower rate of hospitalizations we observed namely a higher proportion of Whites, a higher median household income, and a lower rate of diabetes complications. On the other hand, factors that may offset such advantages in the older group include a longer duration of diabetes and higher levels of multimorbidity. African American race is independently associated with frailty (28) but differences in all-cause hospitalizations suggest that all things being equal, African Americans with frailty are less

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likely to be hospitalized. More research is needed regarding race-based differences in clinical and healthcare utilization outcomes of individuals with frailty and the specific factors that may contribute to this differential. Older adults with diabetes and a history of hospitalizations represent a high risk group for future hospitalizations (29). In hospitalized older adults, frailty was independently associated with a higher rate of complications and mortality risk (30). In frail older adults with diabetes hospitalization may further compromise their medical condition as they may be particularly vulnerable to the effects of hospitalization. In terms of mortality, our results are consistent with previous studies showing that African Americans with diabetes have similar (31) or even lower mortality than Caucasians (32, 33). The explanations vary and may include reporting bias, lack of adjustment for socio-economic status (lower for African Americans), better access to care in an integrated healthcare system such as the VA (33) and differences in the prevalence of diabetes-related complications between these two groups (32-34). Although several studies have shown that African Americans have higher rates of kidney disease related mortality (32), Whites have higher rates of coronary heart disease than African Americans (33, 34) potentially leading to competing risks that may offset the effects of ESRD-related mortality on African Americans effectively canceling out any possible mortality differences.

Strengths of this study include a relatively large sample of older adults with documented diabetes diagnoses, complete evaluation of frailty, inclusion of complete healthcare data from electronic health records, adjustment for multiple covariates associated with increased risk for all-cause hospitalization and mortality, and a long period of follow up. There are a few limitations. We used a convenience sample of predominantly male Veterans at one medical center, and the ethnic, racial, educational, and socio-economic composition as well as the structure of the healthcare system may be different from other healthcare settings in the US. Future cohort studies should include larger, more diverse and randomly selected samples from varied geographic locations and healthcare systems.

This study indicated overall associations of frailty with higher risk for all-cause hospitalization and mortality in older adults with diabetes. Frailty appears to have an additive effect beyond that of diabetes on hospitalizations and mortality. Developing interventions aimed at reducing hospitalization risk in older adults with diabetes may start with the identification of frailty followed by the management of this syndrome in these individuals. Further research is needed with random sampling in a broader spectrum of healthcare settings to better understand what roles frailty might play in healthcare utilization, mortality and other clinical outcomes of older adults with diabetes.

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Ethical standards: A protocol of this study was submitted to

and approved by the Institutional Review Board as a VA quality improvement project.

References

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56(3):M146-56.
2. Sinclair AJ, Abdelhafiz A, Dunning T, Izquierdo M, Rodriguez Manas L, Bourdel-Marchasson I, et al. An International Position Statement on the Management of Frailty in Diabetes Mellitus: Summary of Recommendations 2017. *J Frailty Aging.* 2018;7(1):10-20.
3. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K. Frailty, body mass index, and abdominal obesity in older people. *J Gerontol A Biol Sci Med Sci.* 2010;65(4):377-81.
4. Veronese N, Stubbs B, Fontana L, Trevisan C, Bolzetta F, De Rui M, et al. Frailty Is Associated with an Increased Risk of Incident Type 2 Diabetes in the Elderly. *J Am Med Dir Assoc.* 2016;17(10):902-7.
5. Bouillon K, Kivimaki M, Hamer M, Shipley MJ, Akbaraly TN, Tabak A, et al. Diabetes risk factors, diabetes risk algorithms, and the prediction of future frailty: the Whitehall II prospective cohort study. *J Am Med Dir Assoc.* 2013;14(11):851 e1-6.
6. Morley JE, Malmstrom TK, Rodriguez-Manas L, Sinclair AJ. Frailty, sarcopenia and diabetes. *J Am Med Dir Assoc.* 2014;15(12):853-9.
7. Garcia-Esquinas E, Graciani A, Guallar-Castillon P, Lopez-Garcia E, Rodriguez-Manas L, Rodriguez-Artalejo F. Diabetes and risk of frailty and its potential mechanisms: a prospective cohort study of older adults. *J Am Med Dir Assoc.* 2015;16(9):748-54.
8. Abdelhafiz AH, Koay L, Sinclair AJ. The effect of frailty should be considered in the management plan of older people with Type 2 diabetes. *Future Sci OA.* 2016;2(1):FSO102.
9. Garcia-Esquinas E, Jose Garcia-Garcia F, Leon-Munoz LM, Carnicero JA, Guallar-Castillon P, Gonzalez-Colaco Harmand M, et al. Obesity, fat distribution, and risk of frailty in two population-based cohorts of older adults in Spain. *Obesity (Silver Spring).* 2015;23(4):847-55.
10. Adame Perez SI, Senior PA, Field CJ, Jindal K, Mager DR. Frailty, Health-Related Quality of Life, Cognition, Depression, Vitamin D and Health-Care Utilization in an Ambulatory Adult Population With Type 1 or Type 2 Diabetes Mellitus and Chronic Kidney Disease: A Cross-Sectional Analysis. *Can J Diabetes.* 2019;43(2):90-7.
11. Orkaby AR, Nussbaum L, Ho YL, Gagnon D, Quach L, Ward R, et al. The Burden of Frailty Among U.S. Veterans and Its Association With Mortality, 2002-2012. *J Gerontol A Biol Sci Med Sci.* 2018.
12. Liu Y, Sayam S, Shao X, Wang K, Zheng S, Li Y, et al. Prevalence of and Trends in Diabetes Among Veterans, United States, 2005-2014. *Prev Chronic Dis.* 2017; 14:170230.
13. Benjamin SM, Wang J, Geiss LS, Thompson TJ, Gregg EW. The Impact of Repeat Hospitalizations on Hospitalization Rates for Selected Conditions Among Adults With and Without Diabetes, 12 US States, 2011. *Prev Chronic Dis.* 2015; 12:150274.
14. Chang SF, Lin HC, Cheng CL. The Relationship of Frailty and Hospitalization Among Older People: Evidence From a Meta-Analysis. *J Nurs Scholarsh.* 2018;50(4):383-91.
15. De Berardis G, D'Ettore A, Graziano G, Lucisano G, Pellegrini F, Cammarota S, et al. The burden of hospitalization related to diabetes mellitus: a population-based study. *Nutr Metab Cardiovasc Dis.* 2012;22(7):605-12.
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-83.
17. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ.* 2005;173(5):489-95.
18. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. *Age Ageing.* 2014;43(1):10-2.
19. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr.* 2008;8:24.
20. Maynard C. Ascertain Veterans' Vital Status: VA Data Sources for Mortality Ascertainment and Cause of Death. [Internet]. Washington, DC: VA Health Services Research & Development (HSRD); 2017 [updated March 6, 2017; cited 2019. Available from: https://www.hsrdr.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=1242.
21. American Diabetes Association. 11. Older Adults: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018;41(Suppl 1):S119-S125.
22. Walston J, McBurnie MA, Newman A, Tracy RP, Kop WJ, Hirsch CH, et al. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. *Arch Intern Med.* 2002;162(20):2333-41.
23. Miller EA, Weissert WG. Predicting elderly people's risk for nursing home placement, hospitalization, functional impairment, and mortality: a synthesis. *Med Care Res Rev.* 2000;57(3):259-97.
24. Torisson G, Stavenow L, Minthon L, Londos E. Importance and added value of

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- functional impairment to predict mortality: a cohort study in Swedish medical inpatients. *BMJ Open*. 2017;7(5):e014464.
25. Romero-Ortuno R, Forsyth DR, Wilson KJ, Cameron E, Wallis S, Biram R, et al. The Association of Geriatric Syndromes with Hospital Outcomes. *J Hosp Med*. 2017;12(2):83-9.
 26. Callahan KE, Lovato JF, Miller ME, Easterling D, Snitz B, Williamson JD. Associations Between Mild Cognitive Impairment and Hospitalization and Readmission. *J Am Geriatr Soc*. 2015;63(9):1880-5.
 27. McGuire LC, Ford ES, Ajani UA. The impact of cognitive functioning on mortality and the development of functional disability in older adults with diabetes: the second longitudinal study on aging. *BMC Geriatr*. 2006;6:8.
 28. Hirsch C, Anderson ML, Newman A, Kop W, Jackson S, Gottdiener J, et al. The association of race with frailty: the cardiovascular health study. *Ann Epidemiol*. 2006;16(7):545-53.
 29. Rubin DJ. Hospital readmission of patients with diabetes. *Curr Diab Rep*. 2015;15(4):17.
 30. Evans SJ, Sayers M, Mitnitski A, Rockwood K. The risk of adverse outcomes in hospitalized older patients in relation to a frailty index based on a comprehensive.
 31. Conway BN, May ME, Blot WJ. Mortality among low-income African Americans and whites with diabetes. *Diabetes care*. 2012;35(11):2293-9.
 32. Conway BN, May ME, Fischl A, Frisbee J, Han X, Blot WJ. Cause-specific mortality by race in low-income Black and White people with Type 2 diabetes. *Diabet Med*. 2015;32(1):33-41.
 33. Lynch CP, Gebregziabher M, Echols C, Gilbert GE, Zhao Y, Egede LE. Racial disparities in all-cause mortality among veterans with type 2 diabetes. *J Gen Intern Med*. 2010;25(10):1051-6.
 34. DeStefano F, Newman J. Comparison of coronary heart disease mortality risk between black and white people with diabetes. *Ethn Dis*. 1993;3(2):145-51.