Frailty risk in hospitalised older adults with and without diabetes mellitus

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Abstract:

Background: Research indicates that diabetes mellitus (DM) may be a risk factor for frailty and individuals with DM are more likely to be frail than individuals without DM; however, there is limited research in hospitalised older adults.

Objectives: To determine the extent of frailty in hospitalised older adults with and without DM using a 16-item Frailty Risk Score (FRS) and assess the role of frailty in predicting 30-day rehospitalisation, discharge to an institution and in-hospital mortality.

Methods: The study was a retrospective, cohort, correlational design and secondary analysis of a data set consisting of electronic health record data. The sample was older adults hospitalised on medicine units. Logistic regression was performed for 30-day rehospitalisation and discharge location. Cox proportional hazards regression was used to analyse time to in-hospital death and weighted using propensity scores.

Results: Of 278 hospitalised older adults, 49% had DM, and the mean FRS was not significantly different by DM status (9.6 vs. 9.1, $p = 0.07$). For 30-day rehospitalisation, increased FRS was associated with significantly increased odds of rehospitalisation (AOR = 1.24, 95% CI [1.01, 1.51], $p = 0.04$). Although 81% were admitted from home, 57% were discharged home and 43% to an institution. An increased FRS was associated with increased odds of discharge to an institution (AOR = 1.48, 95% CI [1.26, 1.74], $p < 0.001$). The FRS was not significantly associated with increased risk of in-hospital death ($p = 0.17$), but DM was associated with a 484% increase in the instantaneous risk of death (AHR = 5.84, 95% CI [1.71, 19.9], $p = 0.005$).

Conclusion: Diabetes mellitus and frailty were highly prevalent; the mean FRS was not significantly different by DM status. Although increased frailty was significantly associated with rehospitalisation and discharge to an institution, only DM was significantly associated with in-hospital mortality.

Relevance to clinical practice: Frailty assessment may augment clinical assessment and facilitate tailoring care and determining optimal outcomes in patients with and without DM.

Keywords: adult | diabetes mellitus | electronic health records | frailty | hospital mortality | hospitalisation | human | logistic models | patient discharge | propensity score | retrospective studies | risk factors

Article:

1 INTRODUCTION

The world population is ageing rapidly, and accelerated growth in older age groups will continue to outpace that of younger populations. Currently, older adults over 65 years of age comprise 14.9% of the USA (He, Goodkind, & Kowal, 2016). Projections indicate that population ageing will continue, and there is concern that increasing longevity will be accompanied by the burden of morbidity that includes diabetes mellitus (DM) and frailty. Although DM and frailty are different syndromes with multifactorial aetiologies and variable clinical manifestations, evidence suggests that DM may be a risk factor for frailty and that individuals with DM are more likely to be frail than individuals without DM (Chen, Chen, Lin, Peng, & Hwang, 2010). The purpose of this study was to: (a) determine the extent of frailty in hospitalised older adults with DM using a Frailty Risk Score (FRS) and (b) assess the role of frailty in predicting outcomes including 30-day rehospitalisation, discharge to an institution and in-hospital mortality in older adults with and without DM.

2 BACKGROUND

Diabetes mellitus is one of the most common chronic diseases in older adults. In the USA, the overall prevalence of DM is estimated at 9.4%; however, among individuals over 65 years of age, DM prevalence is 25.2% (Centers for Disease Control and Prevention [CDC], 2017). Of those with diagnosed DM, about 5% are diagnosed with type 1 DM (CDC, 2017). The rising prevalence of DM is attributed, in part, to population ageing and increasing numbers of individuals with type 1 DM living into old age as well as increasing rates of type 2 DM due to age-related pancreatic islet dysfunction and insulin resistance and lifestyle factors such as increased sedentary behaviour, unhealthy eating patterns and obesity (American Diabetes Association [ADA], 2016). DM is listed as the seventh leading cause of death; individuals with DM have a significantly reduced life expectancy and about twice the risk of death compared to with people without DM (Centers for Disease Control and Prevention (CDC), 2017). With advancing age, individuals with DM experience higher rates of comorbidity and disability compared with other age groups (ADA, 2017). The estimated USA total direct and indirect costs of DM for 2012 exceeded $245 billion, and average medical expenditures for people with DM are 2.3 times higher than expenditures for people without DM (ADA, 2016; Centers for Disease Control and Prevention (CDC), 2017).

Frailty is a clinical syndrome of impaired homoeostasis and decreased physiologic capacity resulting in diminished ability to resist and recover from physiologic or psychosocial stressors (Rodríguez-Mañas & Sinclair, 2014). Frailty has been operationalised in a variety of ways, but two frameworks are applied most often. The frailty phenotype framework developed by Fried et al. (2001) identifies five indicators that include weight loss, exhaustion, low physical activity,

slow walking speed and weakness. Frailty is determined by the presence of at least three of the five indicators, and prefrailty, by two of them. The deficit accumulation framework represents frailty by the cumulative effects of age-related deficits that include diseases, signs and symptoms, laboratory tests and functional and cognitive impairments that are analysed as an index consisting of 30–70 deficits (Mitnitski & Rockwood, 2015). Estimates of the prevalence of frailty range from 7.9% to 59.1%, depending on which instruments are applied (Collard, Boter, Shoevers, & Oude Voshaar, 2012). In the hospital setting, these frailty prevalence estimates are considerably higher and range from 50% to 94% (Basic & Shanley, 2015; Dent, Chapman, Howell, Piantadosi, & Visvanathan, 2014; Forti et al., 2014). Frailty is significantly associated with numerous adverse outcomes including functional decline, disability, morbidity, institutionalisation and early mortality (Collard et al., 2012; Forti et al., 2014).

Research indicates that the prevalence of DM increases in the context of frailty, and frailty prevalence is higher in individuals with DM. In one systematic review of community-living older adults, the prevalence of frailty ranged from 5% to 10.7%, whereas in older adults with DM, frailty prevalence ranged from 32% to 48% (Cobo, Vázquez, Reviriego, & Rodríguez-Mañas, 2016). In other evidence, DM was associated with an increased risk of frailty among community-living adults 60 years and older (N = 1,750) over 3.5 years of follow-up (OR = 2.18, 95% CI = [1.42, 3.37]) compared with those without DM (García-Esquinas et al., 2015). Similarly, in a study of 1,754 older adults without DM at baseline, frail individuals (N = 1,754) had significantly more DM risk factors (higher haemoglobin A1c and fasting blood glucose, lower glomerular filtration rate) than prefrail or nonfrail individuals, and frailty and prefrailty were significant independent predictors of DM at 4.4-year follow-up (Veronese et al., 2016). These findings highlight that frailty and DM often co-occur, as they are both age-related conditions with multifactorial aetiology (Cobo et al., 2016). Also, underlying pathophysiological processes for both DM and frailty involve derangements in neurohormonal, endocrine, haematologic, and metabolic function, muscle loss and sarcopenia, and chronic inflammation or "inflammaging" (Hunt, Walsh, Voegeli, & Roberts, 2010; Perkisas & Vandewoude, 2016). Shared risk factors for frailty and DM include glucose dysregulation, impaired insulin secretion, nutrient deficiencies, physical inactivity and obesity (Veronese et al., 2016). Owing to the complexity and morbidity associated with DM in older adults, the added vulnerability of frailty may identify a higher risk group that requires more intensive evaluation and treatment to prevent or mitigate more serious adverse outcomes. While the significance of frailty and DM has been established in several community-living populations, there is only limited research in the acutely ill hospitalised older adult. In a study of older hospitalised medical inpatients, Khandelwal et al. (2012) found that patients with DM were more not significantly more likely to be frail, but did not examine frailty and DM prevalence, associations and outcomes in hospitalised older adults with and without DM. Thus, considering the high prevalence and consequences of both DM and frailty and the gap in research, there is a need for research to investigate relationships between these conditions and outcomes in the acutely ill hospitalised population.

3 METHODS

3.1 Study design and sample

The study was a retrospective, cohort, correlational design and secondary analysis of a data set consisting of electronic health record (EHR) clinical data. The sample consisted of 278 adults 55 years and older who were admitted from 1 June 2010 through 31 August 2011 to medicine units at a 938-bed, not-for-profit, academic-affiliated hospital located in the Southeastern USA. The age threshold was determined based on evidence that frailty risk factors and manifestations emerge in middle age in some populations (Collard et al., 2012; Morley, Malmstrom, & Miller, 2012). The study was originally powered a priori to detect a Cohen's f^2 of 0.10 in a multiple regression with 20 independent variables with a sample size of 278 patients with 90% statistical power, assuming a two-sided type I error rate of 0.05. Inclusion criteria were an overnight stay and laboratory data for four serum biomarkers: albumin, C-reactive protein (CRP), haemoglobin and white blood cell count (WBC). Exclusions were a diagnosis of cancer with active treatment.

3.2 Data access

Study data were retrieved from the EHR. The study sample was constructed using a proprietary data query tool to access the data storage repository of archived health system clinical data (Horvath et al., 2011). The data query tool randomly assigned a unique identifier for construction of a deidentified dataset. The data query tool searched the data storage repository with delimitations defined by the study inclusion and exclusion criteria. The sampling strategy first involved identifying unique hospital admissions of patients 55 years and older during the study 15-month time frame. This query yielded 690 total patient hospital admissions. For patients with two or more encounters (n = 354; 51%), the first encounter was selected for inclusion in the data set. Then, the inclusion criteria of laboratory data for four serum biomarkers (albumin, haemoglobin, C-reactive protein, white blood cell count) were applied, yielding a sample of 281 unique hospital admissions. These biomarkers are associated systemic inflammation and with frailty (Hunt et al., 2010; Soysal et al., 2016). Exclusion criteria were then applied using manual search of the record, and three records were excluded. The final sample included 278 hospital first encounters.

3.3 Data collection

Data extraction was by manual search of clinical data in the EHR by the first author and two registered nurses trained in study procedures. The EHR data sources were electronic PDF files of structured information and unstructured narrative physician and nursing notes. Data were recorded on a code sheet and then entered into an electronic spreadsheet. Data verification was performed by the first author for the entire sample and by a second investigator in 10% of the sample.

Table 1. The frailty risk factors and indicators, prevalence on admission in hospitalised older adults with and without diabetes mellitus (DM; N = 278)

	Risk factor	***n*(%)**	**Indicator**	**No DM (*n* = 142; 51%)**	**Has DM (*n* = 136; 49%)**	***p*-value**
1.	Nutrition issues	222 (80)	Weight loss of 15 pounds past 6 months; unplanned weight loss; poor appetite; BMI <18.5 or >30 kg/m^2	112 (79)	110 (81)	1.00
2.	Falls	80 (29)	Fall admission diagnosis; history of falls	36 (25)	44 (32)	1.00

	Risk factor	*n*(%)	Indicator	No DM (*n* = 142; 51%)	Has DM (*n* = 136; 49%)	*p*-value
3.	Weakness	227 (82)	Weakness	118 (83)	109 (80)	1.00
4.	Vision impairment	100 (36)	ICD-9/10 diagnosis (cataracts [corrected, uncorrected], glaucoma, macular degeneration, retinopathy, blind)	38 (27)	62 (46)	0.019
5.	Dyspnoea	104 (37)	Dyspnoea or shortness of breath	46 (32)	58 (43)	1.00
6.	Fatigue	249 (90)	Fatigue; sleep problems, CPAP at night	125 (88)	124 (91)	1.00
7.	Chronic pain	173 (62)	Chronic pain	95 (67)	78 (57)	1.00
8.	Urinary incontinence	66 (24)	Urinary incontinence	33 (23)	33 (24)	1.00
9.	Smoking	45 (16)	Current smoker	23 (16)	22 (16)	1.00
10.	Depression	97 (35)	ICD-9/10 diagnosis of depression	51 (36)	46 (34)	1.00
11.	Cognition problems	88 (32)	ICD-9/10 diagnosis of dementia, any type, Alzheimer's disease, any memory problems; abnormal mental status/delirium	43 (30)	45 (33)	1.00
12.	Social support issues	176 (63)	Living alone; single; caregiver concerns; older adult, disabled, live alone, & clergy visit	87 (61)	89 (65)	1.00
13.	CRP or hs-CRP	246 (89)	Abnormal flag, high	127 (89)	119 (88)	1.00
14.	Albumin	258 (93)	Abnormal flag, low, <3.6 g/dl	130 (92)	128 (94)	1.00
15.	Haemoglobin	267 (96)	Abnormal flag, low. Women, <12.0 g/dl; Men, 13.7 g/dl	134 (94)	133 (98)	1.00
16.	WBC count	206 (74)	Abnormal flag, abnormal-high or low, <3.2 or >9.8 × 10^9/mcL	98 (69)	108 (79)	0.77
	Frailty risk Score (0–16)	9.4 (2.2)	Unweighted sum of 16 0/1 indicators for risk factors above	9.1 (2.0)	9.6 (2.3)	0.072
	Frailty risk Score ≥ 9	189 (68)		89 (63)	100 (74)	0.063
	Frailty risk Score ≥ 10	135 (49)		65 (46)	70 (51)	0.37

Nutritional issues = any of BMI ≤18.5 kg/m^2, ≥30 kg/m^2; unplanned weight loss, or poor appetite. Vision problems = any of cataracts, glaucoma, macular degeneration, retinopathy or blind. Cognition problems = any of delirium, dementia or impaired memory. Social support issues = any of caregiver concerns, aged/disabled/lives alone or clergy visit. Laboratory assay equipment: Albumin (Beckman-Colter Unicel DXC 600–800, Bromocresol Purple [dcp] Timetest Endpoint); CRP and hs-CRP (Beckman Synchron Systems Neon Infrared Particle immunoassay rate methodology); WBC and haemoglobin (Electronic Impedance Differential Lysis Fluorescent Flow Cytometry and Colorimetric Measurement). Numbers for Frailty Risk Score are mean (*SD*). *p*-value for 16 individual Risk Factors given after Bonferroni correction. Chi-square tests are performed for all analyses except for Frailty Risk Score (0–16), where *t* test results are presented.

A FRS was previously investigated by this author and others (Lekan, Wallace, McCoy, Hu, Silva, & Whitson, 2017). The FRS included 16 variables that were identified as frailty risk factors based on a conceptual framework derived from theories on biopsychosocial function, chronic stress, inflammation, and allostatic load (Beckie, 2012; Cesari, 2011; Hunt et al., 2010; Steptoe et al., 2014), the empirical literature on frailty, and variables available in the EHR. The biological variables/risk factors included eight symptoms, syndromes and conditions and four serum biomarkers. Six of the risk factors were operationally defined by more than one subfactor, in which the presence of at least one subfactor resulted in counting the overall risk factor as present. The biomarker risk factors were operationalised by the categorical abnormal flag, which indicated that the laboratory value fell outside the reference range (see Table 1). The frailty risk

factors (and subfactors) included fatigue, weakness, dyspnoea, chronic pain, falls (history or admission diagnosis), vision impairment (glaucoma, cataracts, macular degeneration, retinopathy and blindness), urinary incontinence and nutrition issues (low or high BMI, weight loss and poor appetite); the four serum biomarkers that included albumin, C-reactive protein (CRP), haemoglobin and white blood cell count (WBC); three psychological risk factors that included cognition problems (delirium, dementia), depression and current smoking; and one social support risk factor (single, live alone, and nurse ratings indicating caregiver concerns, and being older, disabled, and living alone).

Frailty risk factors were derived from the EHR and counted as "yes = 1" if present and "no = 0" if not present. A FRS was created as the unweighted count of the presence of indicators for risk factors (theoretical range = 0–16), where higher scores were indicative of increased frailty and was calculated for each patient. Based on decision trees from recursive partitioning, a cut-off score of ≥10 was most salient for in-hospital mortality (area under the ROC curve [AUC] = 0.662 (95% CI = [0.568, 0.755], $p = 0.003$) and a similar cut-off score of ≥9 was most salient for rehospitalisation among those alive at discharge (Lekan et al., 2017). The FRS was used to model the outcome variables rehospitalisation within 30 days of discharge, discharge location and time to in-hospital mortality for patients with and without DM.

3.4 Other variables

The diagnosis of DM was determined from the physician admission note listing ICD 9/10 diagnoses, where DM was identified; determination of type 1 (T1DM) or type 2 (T2DM) classification of DM was not available in the EHR. Other variables that were included in analyses were age, gender, marital status, race/ethnicity, comorbidity, serum creatinine, impaired activities of daily living (ADL), medication count, hyperlipidemia, serum creatinine, unplanned surgery, living arrangement, preadmission location and discharge location. Comorbidity was the count of ten ICD 9–10 medical diagnoses that were listed on admission. Medication count was the number of prescription and nonprescription medications on the admission medication list. All data recorded reflected the patient's health status on admission.

3.5 Ethical considerations

Study procedures were approved by the Institutional Review Boards of Duke University Medical Center and the University of North Carolina at Greensboro.

3.6 Data analyses

Descriptive statistics using cross-tabulation tables and chi-square tests were performed by DM groups for individual frailty indicators after Bonferroni multiplicity adjustment. Demographic and clinical characteristics were compared by DM groups using similar descriptive statistics or within-group means (*M*), standard deviations (*SD*) and ranges for continuous variables. Chi-square (if all expected cell counts ≥5) or Fisher's exact tests were performed for categorical characteristics and *t* tests (if normally distributed within group, no extreme outliers and equal variances) or Wilcoxon rank-sum tests for continuous measures. For those still alive at discharge, logistic regression was separately performed for 30-day rehospitalisation and discharge location

to somewhere other than home. Cox proportional hazards regression was used to analyse time to in-hospital death, which was defined as the length of time between date of admission to discharge (considered censored) or death. The proportional hazards assumption was satisfied in all Cox regression modelling ($p \geq 0.10$). All nonmediation modelling was weighted using inverse probability weighting (IPW) based on propensity scores and best practices (Austin & Stuart, 2015). The propensity scores were created for DM groups based off of demographic and clinical characteristics (except for comorbidity count since presence of individual comorbidities was included) to afford better group equivalence, and standardised differences before and after weighting were assessed to evaluate whether balance between DM groups had been adequately achieved (Austin & Stuart, 2015). For propensity score modelling, race/ethnicity was coded as 1 = Non-White and 0 = White, marital status was coded with three indicator variables with "married" as the referent group, and all other categorical variables were coded as 1 = present and 0 = absent. For mediation, the approach and macros by Valeri and VanderWeele (2015) were performed. The natural indirect effect was estimated at the median FRS value of 9.0 for patients without DM. Here, modelling for these indirect effects of FRS was performed with and without covariates in sensitivity analyses and conveyed the same conclusions about mediation. All analyses were performed using SAS v9.4 (SAS Institute, Cary, NC). A two-sided p-value <0.05 was considered statistically significant.

4 RESULTS

A total of 278 patients comprised this study. Table 1 describes prevalence of the 16 individual FRS indicators by DM status groups, where 49% had DM. The FRS subfactor that had notably higher prevalence in the DM group compared with the group without DM was vision impairment (46% vs. 27%, Bonferroni $p = 0.02$). Dyspnoea (43% vs. 32%, Bonferroni $p = 1.00$), falls (32% vs. 25%, Bonferroni $p = 1.00$) and WBC count abnormally high or low (79% vs. 69%, Bonferroni $p = 0.77$) were greater in prevalence for the DM group versus non-DM group, but were not statistically significant. Mean FRS were close to being significantly different by DM groups (DM 9.6 [$SD = 2.3$] vs. no DM 9.1 [$SD = 2.0$], $p = 0.07$). Here, 74% of those with DM had FRS ≥9 relative to 63% without DM ($p = 0.06$). For FRS ≥10, the groups were more evenly split (51% for DM vs. 46% for no DM, $p = 0.37$).

Table 2 provides distributions of demographic and clinical characteristics of the patients with and without DM. Here, groups were significantly different on: race/ethnicity (43% Black, 55% White for DM vs. 23% Black, 73% White for no DM), BMI ($M = 29.7$ kg/m^2 for DM vs. 27.5 kg/m^2 for no DM on average) and total number of medications (DM $M = 13.0$ vs. no DM $M = 10.4$). Groups were also significantly different in common cardiovascular morbidity of: hypertension (DM 90% vs. no DM 75%), angina (DM 26% vs. no DM 13%), myocardial infarction (DM 32% vs. no DM 18%), heart failure (DM 46% vs. no DM 20%), having a vascular/pressure ulcer (38% for DM vs. 20% for no DM). Additionally, groups were significantly different in other comorbidities including: rheumatoid arthritis (DM 6% vs. no DM 17%), stroke/transient ischaemic attack (DM 26% vs. no DM 15%), having renal disease (renal insufficiency, end-stage renal disease, dialysis or transplant; DM 64% vs. no DM 42%), hyperlipidemia (DM 59% vs. no DM 32%) and typical creatinine levels (DM mean 2.2 mg/dl [$SD = 2.7$] vs. non-DM 1.8 mg/dl [$SD = 1.8$]). Propensity score weighting incorporating these characteristics were performed when assessing associations of FRS and DM status with

outcomes besides mediation. Here, 17 of 20 covariates had absolute standardised differences (ASDs) below 10% after propensity score weighting (median ASD before weighting = 30%). Of those with ASDs 10% or above, COPD had ASD = 14% (before weighting was 1%), CVA/TIA had ASD = 12% (before weighting was 29%), and creatinine had ASD = 45% (before weighting was 47%).

Table 2. Demographic and clinical characteristics of the hospitalised older adults with and without diabetes mellitusa ($N = 278$)

Characteristics	**Overall ($N = 278$)**	**No DM ($n = 142$; 51%)**	**Has DM ($n = 136$; 49%)**	**Test**	***p*-value**
Age (years)	70.1 (10.3) [55, 98]	70.8 (11.0) [55, 96]	69.4 (9.5) [55, 98]	Rank-sum	0.34
Gender					
Female	146 (53)	81 (57)	65 (48)	Chi-square	0.12
Male	132 (47)	61 (43)	71 (52)		
Race/Ethnicity					
Native American	2 (<1)	0	2 (1)	Fisher's	<0.001
Asian	2 (<1)	2 (1)	0		
African American	92 (33)	33 (23)	59 (43)		
Other	4 (1)	4 (3)	0		
Caucasian	178 (64)	103 (73)	75 (55)		
Marital status					
Divorced	26 (9)	13 (9)	13 (10)	Fisher's	0.99
Married	142 (51)	72 (51)	70 (51)		
Single/Separated	49 (18)	25 (18)	24 (18)		
Widowed	61 (22)	32 (23)	29 (21)		
BMI (kg/m^2)	28.6 (7.6) [13.3, 65.4]	27.5 (7.9) [13.3, 61.5]	29.7 (7.2) [14.1, 65.4]	Rank-sum	0.002
≤18.5 kg/m^2	16 (6)	12 (8)	4 (3)	Chi-square	0.049
≥30.0 kg/m^2	98 (35)	41 (29)	57 (42)	Chi-square	0.023
ADL impairment	183 (66)	89 (63)	94 (69)	Chi-square	0.26
Vascular/pressure ulcer	81 (29)	29 (20)	52 (38)	Chi-square	0.011
Medication count	11.7 (5.2) [0, 31]	10.4 (5.0) [0, 27]	13.0 (5.1) [3, 31]	Rank-sum	<0.001
Comorbidity count	3.4 (1.7) [0, 7]	3.1 (1.7) [0, 7]	3.8 (1.7) [0, 7]	*t* test	0.002
Unplanned surgery	95 (34)	43 (30)	52 (38)	Chi-square	0.16
Hypertension	229 (82)	107 (75)	122 (90)	Chi-square	0.002
Angina	55 (20)	19 (13)	36 (26)	Chi-square	0.006
Myocardial infarction	69 (25)	26 (18)	43 (32)	Chi-square	0.010
Heart failure	91 (33)	29 (20)	62 (46)	Chi-square	<0.001
COPD/Asthma	70 (25)	36 (25)	34 (25)	Chi-square	0.95
Rheumatoid arthritis	32 (12)	24 (17)	8 (6)	Chi-square	0.004
CVA/TIA	57 (21)	21 (15)	36 (26)	Chi-square	0.016
Osteoarthritis	137 (49)	78 (55)	59 (43)	Chi-square	0.054
Renal problem	147 (53)	60 (42)	87 (64)	Chi-square	<0.001
Cancer	63 (23)	37 (26)	26 (19)	Chi-square	0.17

Characteristics	Overall (*N* = 278)	No DM (*n* = 142; 51%)	Has DM (*n* = 136; 49%)	Test	*p*-value
Creatinine (mg/dl)	2.2 (2.3) [0, 17]	1.8 (1.8) [0, 11]	2.6 (2.7) [0, 17]	Rank-sum	0.003

ADL: activities of daily living; BMI: body mass index; Comorbidity count: the count of ICD 9/10 medical diagnoses documented on admission; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident (stroke); DM: diabetes mellitus; Renal problem: any one of: renal disease, renal insufficiency, end-stage renal disease (ESRD), dialysis or transplant; TIA: transient ischaemic attack.

[a] Numbers are *n* (%) or mean (*SD*) [Min, Max].

Table 3. Regression modelling of study outcomes[a]

Outcomes	FRS interaction	FRS mediation	FRS independent variable	DM vs. no DM
30-day rehospitalisation	0.73 (0.51, 1.05) 0.09	1.10 (0.93, 1.30) 0.28	1.24 (1.01, 1.51) 0.037	0.87 (0.37, 2.04) 0.75
Discharge location	0.97 (0.70, 1.35) 0.86	1.05 (0.95, 1.16) 0.32	1.48 (1.26, 1.74) <0.001	0.85 (0.44, 1.66) 0.64
In-hospital mortality	0.97 (0.48, 1.96) 0.93	1.00 (0.93, 1.08) 0.97	1.20 (0.92, 1.56) 0.17	5.84 (1.71, 19.9) 0.005

FRS: Frailty Risk Score; DM: diabetes mellitus.

[a] Numbers are adjusted odds ratio (AOR), 95% for AOR, *p*-value from multivariable logistic regression for 30-day rehospitalisation and discharge location or adjusted hazard ratio (adj. HR), 95% for adj. HR, *p*-value from multivariable Cox proportional hazards regression for in-hospital mortality, except for FRS mediation results are estimated, 95% CI, and *p*-value based on results from macros provided from Valeri and VanderWeele (2015). Analysis of 30-day rehospitalisation and discharge location exclude participants who died in-hospital (*n* = 13 excluded). All analyses are adjusted for propensity score weighting based on characteristics in Table 2 except for FRS mediation, which included these as covariates. FRS Interaction = moderation analysis where results are presented for the pairwise interaction of FRS after centring on mean value of 9.38 and 0/1 indicator variable for diabetes (1 = DM). For FRS mediation for in-hospital mortality, convergence warnings were presented for in-hospital mortality and results for the (natural) indirect effect without covariates were as follows: 0.96, (0.88, 1.06), $p = 0.45$. DM vs. no DM group are main effects from a model with FRS as an independent variable, as no statistically significant interaction or mediation effects were present.

Table 3 presents the results of regression modelling for study outcomes. Among the 265 patients alive at discharge, 33 (12.5%) were readmitted within 30 days of discharge. For 30-day rehospitalisation, the effects of the FRS did not depend upon whether the patient had DM (interaction $p = 0.09$). After removing the nonsignificant interaction and as an independent variable, increased FRS was associated with significantly increased odds of rehospitalisation (AOR = 1.24, 95% CI = [1.01, 1.51], $p = 0.04$), accounting for propensity score weighting. There were no significant differences in odds of rehospitalisation between DM groups in this modelling with main effects ($p = 0.75$). The FRS did not statistically significantly mediate the effect of DM status on 30-day rehospitalisation ($p = 0.28$). Thus, the FRS only played the role of an independent risk factor for 30-day rehospitalisation and not a mediator of DM effects or a moderator.

Regarding discharge disposition, about four-fifths (81%) of patients were admitted from home relative to 19% from another location (e.g. nursing home, another hospital) while among those alive at discharge 57% were discharged to home and 43% to another location (e.g. nursing home, hospice). For those patients who remained alive at discharge, the effects of the FRS on other

discharge location did not depend upon whether the patient had DM (interaction $p = 0.86$). After removing the nonsignificant interaction and as an independent variable, increased frailty was associated with significantly increased odds of discharge location to an institution (AOR = 1.48, 95% CI = [1.26, 1.74], $p < 0.001$), accounting for propensity score weighting and DM status. There were no significant differences in odds of other discharge location between DM groups ($p = 0.64$), adjusting for FRS and propensity score weighting. The FRS did not statistically significantly mediate the effect of DM status on discharge location ($p = 0.32$). Again, the FRS only played the role of an independent risk factor also for discharge location and not a mediator of DM effects or a moderator.

There was a total of 13 in-hospital deaths. For time to in-hospital mortality, the effect of the FRS did not depend upon whether or not the patient had DM (interaction $p = 0.93$). After removing the nonsignificant interaction and as an independent variable, the FRS was not significantly associated with increased risk of death ($p = 0.17$) after controlling for DM status and propensity score weighting. DM was associated with a 484% increase in the instantaneous risk of in-hospital death (adjusted *HR* = 5.84, 95% CI = [1.71, 19.9], $p = 0.005$), controlling for FRS and propensity score weighting. Additionally, the FRS did not statistically significantly mediate the effect of DM status on in-hospital mortality ($p = 0.97$). Thus, the FRS was not a moderator, mediator or independent risk factor for in-hospital mortality in these analyses.

5 DISCUSSION

There is growing research on frailty in hospitalised populations, and several review articles have addressed DM and frailty, but to our knowledge, this is the first study to examine frailty prevalence, associations and outcomes in hospitalised medical inpatients with and without DM. In the present study, we found that both frailty and DM are highly prevalent in the hospitalised older population.

5.1 Frailty prevalence

To assess the extent of frailty in the sample of hospitalised older adults with and without DM, we determined that the prevalence of frailty was similarly high and not significantly different in patients with and without DM (74% with DM, 63% without DM). This figure falls at the upper limit of prevalence rates reported in other studies in medical inpatients, with ranges from 32% to 94% (Basic & Shanley, 2015; Forti et al., 2014; Joosten, Demuynck, Detroyer, & Milisen, 2014; Khandelwal et al., 2012; Wou et al., 2013). Similar findings were noted in a study that investigated frailty in older adults admitted to a geriatric medicine unit ($N = 427$; 30% with DM), where thirteen different frailty and functional decline instruments were applied and the prevalence of frailty ranged from 24% to 75% (Dent et al., 2014). The variability in frailty prevalence is attributed to the use of different frailty assessment methodologies. The lack of consensus for frailty assessment is well documented in the literature and is explained by opinions that different frailty assessments have different purposes and are applicable in different contexts and populations (Cesari, 2011; Rodríguez-Mañas & Sinclair, 2014). The utilisation of diverse frameworks and methodologies in research poses challenges to interpreting and generalising research findings.

In the present study, the mean FRS was not significantly different in patients with and without DM, a finding that is in concordance with Khandelwal et al. (2012) who found that among 250 hospitalised older adults, in which 33.2% were classified as frail based on the frailty phenotype and about 20% reported DM. The lack of significance between DM groups in the present study may be potentially explained by higher comorbidity in the study sample. Higher comorbidity is demonstrated in frail hospitalised medical patients (Joosten et al., 2014) and in patients with DM (Chen et al., 2010; Khandelwal et al., 2012). In community-living populations, frail older adults with and without DM have greater comorbidity compared with individuals who are not frail (Cacciatore et al., 2013; Singh et al., 2012). Findings from a longitudinal cohort study that examined DM-related lifestyle, anthropometric and cardiometabolic risk factors and frailty indicate that a one standard deviation in the DM risk score was associated with future frailty (Bouillon et al., 2013). Another consideration is the way that DM was measured in the present study. We relied on the accuracy of documentation of DM in the medical diagnosis admission list in the EHR, but did not have data about DM type, duration or severity. Many reports in the literature do not differentiate T1DM from T2DM due to methodological issues and because T2DM accounts for 90%–95% of all DM cases (American Diabetes Association, 2016). However, T2DM is associated with greater cardiovascular morbidity (stroke, heart attack and microvascular complications [retinopathy, nephropathy]), and increased mortality despite a shorter duration of disease (American Diabetes Association, 2016). Classifying DM type, duration and severity may reveal different frailty levels and risk of outcomes.

Race/ethnicity may have been influential in the higher frailty prevalence in our study and insignificant associations in frailty in patients with and without DM. Approximately one-third of the sample was African American, almost twice the number of African Americans had DM compared to Caucasians, and there were no significant differences in frailty in African American patients with and without DM. Research indicates that the prevalence of both DM and frailty is higher in African Americans compared with Caucasians; 13.2% of African Americans over 20 years of age have DM and are 1.7 times more likely to have DM as non-Hispanic Caucasians, where the proportion with DM is 7.4% (American Diabetes Association, 2017). Few studies have examined race/ethnicity in DM and frailty. Data from the Cardiovascular Health Study indicate that African American older adults were four times more likely to be frail compared with Caucasian older adults (Hirsch et al., 2006). In a study of 998 African Americans enroled in the African American Health Study, Chode, Malmstrom, Miller, and Morley (2016) found that African Americans with DM were more likely to be frail based on any of four frailty assessment tools used compared with those without DM. In contrast to the literature, that there were no differences in level of frailty by race in the present study, suggests that other factors were potentially influential in the study sample, such as comorbidity, as well as factors associated with acute illness and hospitalisation.

5.2 30-day rehospitalisation

The overall 30-day rehospitalisation rate in the present study (12.5%) is lower than national US estimates which range from 18% to 20% among Medicare recipients (Dungan, 2012; Oates et al., 2013). We found that frailty, and not DM, was significantly associated with 30-day rehospitalisation, a finding that has been similarly noted in other research (Forti et al., 2014; Wou et al., 2013). Increasing healthcare costs are partly attributable to a small subset of patients,

particularly those with chronic conditions such as DM, who are prone to disease exacerbation and repeated hospitalisations for treatment (Centers for Disease Control and Prevention (CDC), 2017); however, our study found that frailty was a better predictor of rehospitalisation than DM, and that disease state was not a driver of rehospitalisation. Factors associated with rehospitalisation may include unstable health status at discharge, poor understanding of chronic disease management, discharge instructions, and medications, and inadequate posthospital care or resources (Rubin, Donnell-Jackson, Jhingan, Golden, & Paranjape, 2014).

5.3 Discharge to institution

In the present study, although the majority of patients were admitted from home, slightly over half were discharged home (among those alive at discharge), and frailty (and not DM) was significantly associated with increased odds of discharge to an institution. Although discerning factors contributing to discharge disposition were outside the scope our study, certain patient characteristics may be influential in repeat hospitalisation. For example, in a study of 265 older patients on a geriatric ward where 97% were admitted from home, 78% were discharged home (Singh et al., 2012). In the study, in which frailty was measured by a 40-item frailty index, low serum albumin, cognitive impairment and functional status were significantly associated with discharge status (Singh et al., 2012). In our study, the sample was characterised by higher comorbidity, physical impairment and symptom burden (e.g. FRS risk factors: fatigue, weakness, dyspnoea, etc.). These factors combined with the stress associated with hospitalisation can contribute to prolonged recovery and the need for postdischarge supportive care or rehabilitation in an institution (Dent et al., 2014; Rubin et al., 2014). Our findings agree with other research in which older medical inpatients were also characterised by poor physical function, high comorbidity and high proportion of frailty (Basic & Shanley, 2015; Evans, Sayers, Mitnitski, & Rockwood, 2014; Hunt, Walsh, Voegeli, & Roberts, 2013; Wou et al., 2013). We found, as have other investigators, that patients with DM had significantly greater comorbidity compared with patients without DM (Holman, Hillson, & Young, 2013); however, in our study, propensity score weighting was adjusted for the potential impact of confounder imbalances such as comorbidity on study outcomes (Schroeder, Jia, & Smaldone, 2016). Moreover, discharge to an institution may not always signal a poor outcome since hospitalisation duration has decreased as a cost containment strategy, and continuing care in rehabilitation settings may provide more optimal transition for the patient and family. The present study was not designed to examine contextual factors in discharge disposition.

5.4 In-hospital mortality

Research indicates that in community-living older adults, frail patients with DM have a higher mortality than nonfrail patients, and the presence of frailty was an independent risk factor for mortality even when controlling for comorbidity and disability (Cacciatore et al., 2013; Castro-Rodríguez et al., 2016; Jang, 2016; Morley et al., 2012). In the acute care hospital setting, limited research indicates that frailty is a significant predictor of mortality; however, in the present study, DM, but not frailty, was significantly associated with increased risk of in-hospital death. Using a 55-item frailty index based on comprehensive geriatric assessment, Evans et al. (2014) demonstrated that frailty was independently associated with higher risk of death in 752 medical inpatients. Similarly, in a study of 2,125 hospitalised older patients, frailty, as measured by a

seven-level frailty scale determined by clinical assessment, predicted in-hospital mortality (Basic & Shanley, 2015). Forti et al. (2014) also found that frailty was significantly associated with in-hospital mortality in 685 hospitalised older patients based on the frailty phenotype plus measures for cognition and serum albumin. One study of 250 hospitalised medical patients where 20.4% had reported DM and 21.7% were frail, frailty was significantly associated with in-hospital mortality but frailty and DM were not examined simultaneously (Khandelwal et al., 2012). Limitations of predictive properties of frailty instruments for mortality have been examined. In a study that tested five different frailty instruments in older adults admitted to a medical unit ($N = 677$), only four of five instruments significantly but poorly predicted mortality (Wou et al., 2013). DM is a recognised independent predictor of in-hospital mortality (American Diabetes Association, 2016; Kirkman et al., 2012). In a study of over 10 million hospital admissions, Holman et al. (2013) reported excess mortality among patients with DM; 11.2% of admissions had a diagnosis of DM, but 21.5% of in-hospital mortality occurred in this group. Possible explanations for the lack of significance of the FRS for in-hospital mortality include the small number of events, the timing and circumstances of the frailty assessment (on admission), and unknown factors associated with cause of death. Frailty is recognised as a dynamic state with transitions between levels of frailty (Lee, Auyeung, Leung, Kwok, & Woo, 2014), and frailty status in our study sample may have changed with some patients becoming more frail during hospitalisation. As the majority of the deaths in our study were in patients with DM, factors related to DM may have been influential. For example, life-threatening alterations in serum glucose levels and cardiovascular morbidity are more common in DM (Abdelhafiz, Rodriguez-Manas, Morley, & Sinclair, 2015; Chen et al., 2010; Cobo et al., 2016). The context of care may also be influential. Clinical and organisational factors such as health professional standards and practices, nurse staffing mix and ratios, organisational culture, medical errors and healthcare-acquired complications, and other factors may impact quality of care and mortality. Investigation of these complex issues was outside the scope of this study.

6 STRENGTHS AND LIMITATIONS

Our study has several strengths. The sample was racially diverse, sample size was sufficient for our analysis, and a range of risk factors and confounders were available to inform analyses. The retrospective, correlational study design limits generalisability of the findings. Secondary data analysis can be problematic as the available data were collected for clinical purposes and not to address a particular research question. Clinical data may be subject to provider bias and diligence in recording of accurate information. Frailty level may have changed during hospitalisation and may be affected by factors other than frailty. Medical acuity could not be determined from the available data; illness severity may be a confounding factor in frailty and DM that impact outcomes. The study setting was a single institution in the USA, and provider practices may vary from those of hospitals without academic affiliations and in other geographic locations. The study sample may differ from other populations as biomarkers examined in this study may not be routinely ordered. Propensity score weighting was employed to improve balance between DM groups on nonfrailty-related clinical characteristics; however, some slight imbalance remained in the proportions of patients with COPD, CVA/TIA, and more than slight imbalance remained in creatinine levels. Given the few analyses conducted for outcomes, the false positive rate was left at the nominal 0.05 significance level (Westfall, Tobias, & Wolfinger, 2011).

7 CONCLUSION

Both frailty and DM were highly prevalent in a sample of older hospitalised adults, and the mean FRS was not significantly different by DM status. Although increased frailty was associated with significantly increased odds of rehospitalisation and discharge to an institution, only DM was significantly associated with in-hospital mortality. To our knowledge, this is the first study to investigate prevalence, associations and outcomes of DM and frailty in hospitalised medical inpatients. These findings contribute to new knowledge about relationships between DM and frailty in the acutely ill hospitalised older adult and add to the growing body of evidence that supports the clinical relevance of frailty assessment in risk stratification and prediction. Further research should explore clinical application of frailty assessment using the FRS and investigate the pathophysiological interrelationships between frailty and DM in larger diverse samples and settings to help differentiate vulnerable patients and identify primary prevention and intervention strategies to reduce risk and mitigate adverse consequences of these often co-occurring conditions.

8 RELEVANCE TO CLINICAL PRACTICE

Adoption of frailty assessment in medical and surgical specialties has increased because of research demonstrating its utility in risk stratification and clinical decision-making to prevent rehospitalisation and discharge planning to prevent discharge planning to prevent worsening morbidity and functional decline requiring long term institutionalisation. Our study findings suggest that frailty assessment may be a useful adjunct to clinical judgement to identify more vulnerable patients that may require more nurse-intensive interventions and interdisciplinary care coordination. Indeed, frailty assessment has been advocated for all patients with DM and all older people should be screened for DM (Cobo et al., 2016). Frailty assessment can not only distinguish patients who are at higher risk and more likely to deteriorate and allow clinicians to focus on the highest risk of early intensive interventions, but also identify patients who are at a lower risk and more likely to benefit from more invasive or hazardous treatments or interventions (Singh et al., 2012). Recent reviews indicate a plethora of frailty assessment tools; however, many involve extra data collection and complex analyses that are burdensome to the patient and clinician, and lack clinical utility (Rodríguez-Mañas & Sinclair, 2014). The FRS aggregates empirically based biopsychosocial risk factors for a clinically relevant approach that may facilitate care planning and be easy for nurses to understand and use. Using readily available data from the EHR as demonstrated here for the FRS may expedite adoption of frailty assessment into nursing practice through efficiencies gained from using existing data sources.

Recommended approaches to frailty assessment advocate a two-part strategy with a frailty screening measure (such as the FRS used in the present study) followed by comprehensive geriatric assessment (Evans et al., 2014). In clinical practice, it may also be important to consider frailty as a biometric like blood pressure and pulse that changes based on a constellation of other dynamic factors. Thus, frailty assessment during hospitalisation may provide an early alert to providers of significant changes in condition that require immediate attention. Information technology can be applied to calculate and track a patient's frailty score throughout hospitalisation and could aid in evaluating patient response to interventions. Further research can investigate feasibility and implementation in nursing practice.

One of the greatest hazards of hospitalisation that increases risk of both frailty and DM and contribute to numerous poor outcomes is preventable functional decline. The risk of progressive muscle atrophy, weakness and sarcopenia leading to irreversible functional decline and disability is magnified in DM and frailty (Cobo et al., 2016; Dent, Visvanathan, Piantadosi, & Chapman, 2012). Thus, the FRS on admission can target the higher risk frail patients for interventions to promote mobility and function (e.g. graduated muscle strengthening programmes, range of motion, early mobilisation and prehabilitation) in order to mitigate the muscle atrophy and sarcopenia that is central to both frailty and DM (Chen et al., 2010; Cobo et al., 2016).

The FRS used in the present study included several nutritional indicators that were present on admission (BMI, weight loss and poor appetite). However, nutritional inadequacy is a significant problem during hospitalisation. In a study of 100 hospitalised older adults, where 40% were malnourished and 44% were at risk of malnutrition, poor nutritional status significantly predicted frailty (Dent et al., 2012). Weight loss that occurs in both frailty and DM is associated with loss of muscle and bone resulting in a decrease in muscle strength and function. In DM, weight loss may due to poorly controlled hyperglycaemia or to antidiabetic medications, whereas in frailty, loss of appetite is an underlying aetiology (Chen et al., 2010; Jang, 2016). Thus, carefully assessing nutritional indicators on admission and ongoing would be central to person-centred care and coordinated interdisciplinary efforts for optimal nutritional outcomes.

The use of biomarkers in frailty assessment provides physiologic data that can further characterise frailty risk. The biomarkers used in our study can be further investigated to determine the optimal timing, cut-point and the panel of biomarkers for risk stratification (Beckie, 2012; Perkisas & Vandewoude, 2016). Additional biomarkers may also be considered, for example, haemoglobin A1c and fasting serum glucose levels (which were not available in our study) may help differentiate risk in both DM and frailty (Bouillon et al., 2013; Castro-Rodríguez et al., 2016). The availability of biomarkers in the EHR and inclusion of biomarkers as part of the frailty assessment is an important consideration as there may be additional costs and burdens to patients and clinicians that would impact feasibility.

Diabetes mellitus management guidelines have undergone revision in recent years to address the older adult with DM and frailty. Healthcare providers should understand that management of DM must take into account the heterogeneity of older adults and the influence of frailty. The principles of DM management in healthy older adults are similar to those in younger persons, but special considerations address comorbidity, cognitive disorders, and disability in older adults, and frailty (American Diabetes Association, 2016; Jang, 2016; Veronese et al., 2016). Stricter glycemic control is associated with increased risk of hypoglycaemia, falls, cognitive decline and mortality in frail older persons with DM (Abdelhafiz et al.,2015; Chen et al., 2010); thus, recent recommendations liberalise the metabolic target range of haemoglobin A1c to <8.5% in the context of multimorbidity, poor health and frailty (American Diabetes Association, 2016; Chen et al., 2010; Cobo et al., 2016; Kirkman et al., 2012). The American Diabetic Association (2016) recommends a standardised hospital-wide, surveillance programme hypoglycaemia prevention bundle to prevent iatrogenic hypoglycaemia and nurse-initiated hypoglycaemia treatment protocol to immediately address hypoglycaemia.

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