

# **Predictors associated with prefrailty in older Taiwanese individuals with type 2 diabetes**

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## Abstract

Type 2 diabetes (T2DM) is one of the most well-studied and important factors that increase the risk of prefrailty in older people in Taiwan. This study was conducted to examine whether metabolic biomarkers, lifestyle behaviors, body composition, and chronic diseases are associated with frailty in older people with T2DM. We also observed how people manage their T2DM related to prefrailty. This study investigated a total of 201 participants diagnosed with T2DM who received care in our hospital from September 2018 to February 2019. Patients were divided into 3 groups (not frail, prefrail, and frail), and frailty was measured with the 5-item FRAIL scale. Socioeconomic characteristics, metabolic biomarkers, lifestyle behaviors, body composition, and chronic diseases were assessed at enrollment. No participants who we tested met the criteria for frailty. Based on the results of chi-square tests, prefrailty was associated with female sex, middle school education, unemployment, alcohol use, high body fat percentage, above-normal waist circumference, obesity, cardiovascular disease, and hypertension. Logistic regression analyses identified a significant correlation of prefrailty with the type of job from which they retired, cardiovascular disease, and hypertension. An important and surprising finding of this study was that the unemployed group was at high risk for prefrailty, which was not observed in previous research. The groups engaged in manual and professional jobs had better hand grip strength, a slower walking speed, and less risk of prefrailty than the unemployed group.

**Abbreviations:** ADL = activities of daily living, BMI = body mass index, CIs = confidence intervals, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, IPAQ = International Physical Activity Questionnaire, IRB = Institutional Review Board, LAC = Latin American and Caribbean, LDL-C = low-density lipoprotein cholesterol, ORs = odds ratios, SABE = Salud Bienestary Envejecimiento; Spanish for Health, Well-being and Aging, T2DM = type 2 diabetes.

Keywords: frailty, older people, pre-frailty, type 2 diabetes

## 1. Introduction

It is well known that type 2 diabetes (T2DM) is a common chronic disease in the general and older adult populations.<sup>[1]</sup> T2DM is one of the most important factors that increases the risk of frailty in older people.<sup>[2-4]</sup> Frailty is defined as a condition characterized by 3 or more of the following phenotypes: weight loss, weakness, decreased physical activity, slow walking speed, and exhaustion.<sup>[5-7]</sup> Frailty is an important predictive risk factor for hip fracture, sarcopenia, falls, and poor health outcomes.<sup>[8-10]</sup> In the past, several studies have reported findings on the relationship between frailty and T2DM in older people. One pilot study used the FRAIL scale to predict the health

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article by the National Science Council, Taiwan (MOST 107-2314-B-469-001).

We Shu-Fen Lee, Chih-Ping Li, Yen-Lin Chen, and Dee Pei give our consent for information about ourselves to be published in the Medicine. We understand that the information will be published without our name attached, but that full anonymity cannot be guaranteed. We understand that the text and any pictures or videos published in the article will be freely available on the internet and may be seen by the general public. The pictures, videos and text may also appear on other websites or in print, may be translated into other languages or used for commercial purposes. We have been offered the opportunity to read the manuscript.

The authors have no conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

<sup>a</sup> Department of Nursing, Cardinal Tien College of Healthcare and Management, New Taipei City, Taiwan, <sup>b</sup> Department of Health Industry Management, Kainan outcomes of older T2DM patients at the Center of Gerontology and Geriatrics at West China Hospital. The findings suggested that frailty is an independent risk factor for poor health outcomes in older Chinese people with T2DM.<sup>[11]</sup> Liccini and Malmstrom<sup>[8]</sup> also found that frailty and sarcopenia are highly prevalent and are predictive of disability with regard to activities of daily living (ADL) among middle-aged and older adults (50–90 years) with T2DM in the USA. Some reports have indicated that frailty in patients with T2DM may be due to reduced physical quality of life and is mainly determined by underlying musculoskeletal and cardiovascular disorders.<sup>[12]</sup> In addition, Abdelhafiz et al<sup>[13]</sup> suggested that hypoglycemia is a less well-recognized risk factor for frailty in older people. Frailty

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How to cite this article: Lee S-F, Li C-P, Chen Y-L, Pei D. Predictors associated with prefrailty in older Taiwanese individuals with type 2 diabetes. Medicine 2022;101:38(e30432).

Received: 25 November 2021 / Received in final form: 10 June 2022 / Accepted: 17 June 2022

http://dx.doi.org/10.1097/MD.000000000030432

and optimal glucose control are adversely influenced by undernutrition, as inadequate caloric intake prevents muscle mass retention and physical activity.

Life events, socioeconomic status, functional health, and behaviors can all contribute to frailty in old age.<sup>[14-16]</sup> The SABE project (Salud Bienestar y Envejecimiento; Spanish for Health, Well-being and Aging) carried out a cross-sectional study in 7 Latin American and Caribbean (LAC) cities. Their research showed that frailty in women was associated with a lack of education, a manual occupation, being a housewife, having 2 or more chronic medical conditions, and inadequate financial resources in late life.<sup>[14]</sup> The Seniors-ENRICA study examined 2614 noninstitutionalized residents of Spain aged ≥60 years. They found that women with lower levels of education and having or having had a manual occupation, were relatively more likely to be frail or obese and frail, indicating that these outcomes are the result of complex processes beginning in early life.<sup>[15,16]</sup> Therefore, many potential predictors may go unrecognized in older T2DM patients. Our study examined metabolic biomarkers, lifestyle behaviors, body composition, and chronic diseases that may be associated with prefrailty or frailty in older T2DM patients. In addition, we also measured T2DM self-management as it relates to frailty.

#### 2. Methods

#### 2.1. Participant's enrollment

A total of 206 participants diagnosed with T2DM were recruited at one hospital in Northern Taiwan from September 2018 to February 2019. This study was approved by the Institutional Review Board (IRB) of the Cardinal Tien Hospital (IRB No. CTH-107-3-1-008). Participants were informed about the study's purpose and the confidentiality of their individual data and advised of their right to withdraw from the research study by simply failing to complete the questionnaire.

The inclusion criteria for participants were age 65 years or older, willingness to participate in this study, and a diagnosis of T2DM. We excluded from our study any patient who reported a physician-diagnosed mental illness, stroke, hemiplegia, acute angina, Alzheimer's disease, severe cognitive impairment, active drug or alcohol addiction, need for insulin injections, or liver or renal function test results greater than 1.5 times the upper limit of normal. We also excluded any person who was unable to communicate in Mandarin or Taiwanese or was unable to complete the questionnaire for any other reason.

#### 2.2. Anthropometric measurements and general data

Participants had fasted for 8 to 10 hours before the physical examination, and blood samples were taken from the median cubital vein by a registered nurse. All participants completed the self-rated health questionnaire, physical measurements (e.g., body fat percentage, waist-hip ratio, waist circumference, BMI), health management questions, lifestyle behavior questions, chronic disease questions and clinical indicators including fasting blood glucose, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (HDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels.

All the following variables were recorded for analysis: age, sex, marital status (married vs others), education (less than primary, secondary, and university and above), and occupation (no work, manual, and professional). Lifestyle behaviors included smoking status (never, former, and current) and alcohol consumption (never and current). Body composition parameters were body fat percentage, waist circumference, and body mass index (BMI). Clinical indicators were fasting blood glucose, HbA1c, LDL-C, HDL-C, and triglyceride levels. T2DM-associated chronic diseases, including cardiovascular disease,

hypertension, hyperlipidemia, asthma or chronic bronchitis, and osteoarthritis/arthritis were recorded. Self-management of T2DM was assessed with 3 questions (e.g., Do you know the values indicating well-controlled glycosylated hemoglobin levels in T2DM? Do you adjust the dose of your medication on your own or do you follow your doctor's advice? Do you regularly measure your blood sugar at home?) that were answered as yes or no.

#### 2.3. Definition of frailty

In this study, the outcome variable of frailty was measured by examining 5 phenotypic factors based on a slight modification of the Fried et al proposal: unintentional weight loss of at least 3 kg or at least 5% of their body weight in the prior year<sup>[6]</sup>; lowest quintile grip strength in their dominant hand as measured with a hand-held dynamometer and adjusted for sex and BMI<sup>[6]</sup>; slow walking speed, which was defined as a score in the worst cohort-specific quintile of a 15-foot timed walk, adjusted for sex and standing height<sup>[6]</sup>; self-reported exhaustion, which was based on at least 2 positive responses on the SF-36 scale asking whether they had felt fatigue or exhaustion<sup>[17]</sup>; and low levels of physical activity, as defined by the Taiwan International Physical Activity Questionnaire (IPAQ) short form for the elderly population and the weighted score of kilocalories expended per week that was calculated at baseline.<sup>[18]</sup>

Frailty was defined as a positive score of 3 or more on our slightly modified Fried et al phenotypic criteria.<sup>[6]</sup> Prefrail was defined as a score of 1 or 2. Not frail was defined as a score of 0. However, we recruited a sample population that did not have any frail T2DM patients. Thus, frail was an outcome variable dummy compared to the not frail vs prefrail groups.

#### 2.4. Statistical analysis

The data in this study are presented as the means  $\pm$  standard deviations. All data were tested for a normal distribution with the Kolmogorov–Smirnov test and for homogeneity of variance with Levene's test. The *t*-test was used to evaluate the differences between the 2 groups. Descriptive and chi-square analyses were used to examine all predictor variables. Multivariate logistic regression analyses were carried out to examine the significant variables selected by chi-square tests to determine which variables were significant in the model analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were reported for the logistic regression analyses. Data were analyzed using SPSS v18 (PASW Statistics for Windows, Version 18.0. Chicago, IL).<sup>[19]</sup> All *P* values were 2-tailed, and those <.05 indicated statistical significance.

#### 3. Results

A total of 206 participants were enrolled in the current study. However, only 5 subjects met the criteria for frailty, rendering further analysis of that subgroup difficult. Therefore, we focused on the analysis of prefrail subjects. There were only 201 subjects left for analysis, with a mean age of 72.9 years (SD 5.95). There were 104 (51.7%) males and 97 females (48.3%), as shown in Table 1.

Participants with T2DM were more likely to be male, married, obese, hypertensive, and prefrail and to have a professional occupation. Table 2 shows that compared with the not frail group, the prefrail group had significantly higher proportions of females ( $\chi^2 = 8.58$ ; P = .003), people who had only completed a secondary school education ( $\chi^2 = 9.96$ ; P = .007), professionals ( $\chi^2 = 15.29$ ; P < .001), people who never consumed alcohol ( $\chi^2 =$ 6.36; P-0.012), people who were obese as defined by BMI ( $\chi^2 =$ 17.26; P = .001), people with cardiovascular disease ( $\chi^2 = 9.72$ ; P = .002), and people with hypertension ( $\chi^2 = 8.73$ ; P = .003);

# Table 1

Five phenotypic criteria of measured variables with frailty levels (N = 201).

			-		
Variables	Non-frail (%)	Pre-frail (%)	Total (%)	χ²	<i>P</i> value
Unintentional weight l	OSS				
No	52 (76.5)	110 (82.7)	162 (80.6)	1.12	.290
Yes	16 (23.5)	23 (17.3)	39 (19.4)		
Hand grip strength					
Good	68 (100)	46 (34.6)	114 (56.7)	78.43	<.001
Worse	0 (0)	87 (65.4)	87 (43.3)		
Slow speed					
Good	68 (100)	114 (85.7)	182 (90.5)	10.73	.001
Worse	0 (0)	19 (14.3)	19 (9.5)		
Self-reported exhaust	ion				
No	63 (92.6)	118 (88.7)	181 (90.0)	0.77	.379
Yes	5 (7.4)	15 (11.3)	20 (10.0)		
Low physical activity (	using IPAQ)				
Good	68 (100)	126 (94.7)	194 (96.5)	3.71	.054
Worse	0 (0)	7 (5.3)	7 (3.5)		

Mean age of 72.9 years (SD 5.95), 104 (51.7%) males and 97 females (48.3%). IPAQ = International Physical Activity Questionnaire.

Table 2	
Multivariate association of measured variables with pre-frailty (N = 201).	

Age $65-74$ 48 (70.6) 77 (57.9) 125 (62.2) $\geq 74$ 20 (29.4) 56 (42.1) 76 (37.8)   Gender Male 45 (66.2) 59 (44.4) 104 (51.7)   Female 23 (33.8) 74 (55.6) 97 (48.3)   Marital status Married 57 (83.3) 101 (75.9) 158 (78.6)   Others 11 (16.2) 32 (24.1) 43 (21.4)   Education = \$3 (32.3) 53 (26.4) $\leq Primary$ 10 (14.7) 43 (32.3) 53 (26.4)   Secondary 25 (36.8) 51 (38.3) 76 (37.8) $\geq$ University 33 (48.5) 39 (29.3) 72 (35.8)	3.08 8.58 1.66 9.96	.079 <b>.003**</b> .197 <b>.007**</b>
65–7448 (70.6)77 (57.9)125 (62.2)≥7420 (29.4)56 (42.1)76 (37.8)Gender $Wale$ 45 (66.2)59 (44.4)104 (51.7)Female23 (33.8)74 (55.6)97 (48.3)Marital status $Warried$ 57 (83.3)101 (75.9)158 (78.6)Others11 (16.2)32 (24.1)43 (21.4)Education $V$ $V$ $V$ $V$ Secondary25 (36.8)51 (38.3)76 (37.8)≥University33 (48.5)39 (29.3)72 (35.8)	3.08 8.58 1.66 9.96	.079 <b>.003**</b> .197 <b>.007**</b>
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GenderTotalTotalMale45 (66.2)59 (44.4)104 (51.7)Female23 (33.8)74 (55.6)97 (48.3)Marital status $Married$ 57 (83.3)101 (75.9)158 (78.6)Others11 (16.2)32 (24.1)43 (21.4)Education $=$ $=$ $=$ $\leq Primary$ 10 (14.7)43 (32.3)53 (26.4)Secondary25 (36.8)51 (38.3)76 (37.8) $\geq$ University33 (48.5)39 (29.3)72 (35.8)	8.58 1.66 9.96	<b>.003</b> ** .197 <b>.007</b> **
	8.58 1.66 9.96	<b>.003</b> ** .197 <b>.007</b> **
Female   23 (33.8)   74 (55.6)   97 (48.3)     Marital status	1.66 9.96	.197 <b>.007</b> **
Marital status101 (75.9)158 (78.6)Married57 (83.3)101 (75.9)158 (78.6)Others11 (16.2)32 (24.1)43 (21.4)Education $\sim$ $\sim$ $\sim$ $\leq$ Primary10 (14.7)43 (32.3)53 (26.4)Secondary25 (36.8)51 (38.3)76 (37.8) $\geq$ University33 (48.5)39 (29.3)72 (35.8)	1.66 9.96	.197 <b>.007</b> **
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	1.66 9.96	.197 <b>.007</b> **
Others   11 (16.2)   32 (24.1)   43 (21.4)     Education	9.96	.007**
Education   ≤Primary   10 (14.7)   43 (32.3)   53 (26.4)     Secondary   25 (36.8)   51 (38.3)   76 (37.8)     ≥University   33 (48.5)   39 (29.3)   72 (35.8)	9.96	.007**
≤Primary   10 (14.7)   43 (32.3)   53 (26.4)     Secondary   25 (36.8)   51 (38.3)   76 (37.8)     ≥University   33 (48.5)   39 (29.3)   72 (35.8)	9.96	.007**
Secondary   25 (36.8)   51 (38.3)   76 (37.8)     ≥University   33 (48.5)   39 (29.3)   72 (35.8)		
≥University 33 (48.5) 39 (29.3) 72 (35.8)		
Patiromont ich		
וזפנוופוונ וטט		
Unemployed 2 (2.9) 31 (23.3) 33 (16.4)	15.29	<.001***
Manual 19 (27.9) 39 (29.3) 58 (28.9)		
Professional 47 (69.1) 63 (47.4) 110 (54.7)		
Lifestyle behaviors		
Smoking status		
Never 43 (63.2) 99 (74.4) 142 (70.6)	3.77	.152
Former 12 (17.6) 12 (9.0) 24 (11.9)		
Current 13 (19.1) 22 (16.5) 35 (17.4)		
Alcohol use		
Never 43 (63.2) 106 (79.7) 149 (74.1)	6.36	.012*
Current 25 (36.8) 27 (20.3) 52 (25.9)		
Body composition		
Body fat*		
Normal 29 (42.6) 25 (18.8) 54 (26.9)	13.03	<.001***
High 39 (57.4) 108 (81.2) 147 (73.1)		
Waist circumferencet		
Normal 25 (36.8) 26 (19.5) 51 (25.4)	7.04	.008**
High 43 (63.2) 107 (80.5) 150 (74.6)	1101	
Waist-hin ratio		
Normal 17 (25 0) 24 (18 0) 41 (20 4)	1.34	.247
High 51 (75.0) 109 (82.0) 160 (79.6)		
BMIS		
Normal 20 (29.4) 17 (12.8) 37 (18.4)	17.26	.001**
10  der 4 (5.9) 1 (0.8) 5 (2.5)		
0 verweight 14 (20.6) 21 (15.6) 35 (17.4)		
Obesity   30 (44 1)   94 (70 7)   124 (61 7)		
Clinical indicators		
Easting blood alucose		
>100 mp/dl 38 (55 9) 80 (60 2) 118 (58 7)	0.34	561
<100 mg/dl 30 (44.1) 53 (39.8) 83 (41.3)	0.01	.001

(Continued)

(Continued)					
Variables	Non-frail (%)	Pre-frail (%)	Total (%)	χ²	<i>P</i> value
HbA1c					
>7.5%	25 (36.8)	55 (41.4)	80 (39.8)	0.40	.529
<7.5%	43 (63.2)	78 (58.6)	121 (60.2)		
Triglyceride					
>150 mg/dL	7 (10.3)	28 (21.1)	35 (17.4)	3.62	.057
<150 mg/dL	61 (89.7)	105 (78.9)	166 (82.6)		
LDL-C					
>100 mg/dL	28 (41.2)	43 (32.3)	71 (35.3)	1.54	.214
<100 mg/dL	40 (58.8)	90 (67.7)	130 (64.7)		
HDL-C					
<40 mg/dL	11 (10.2)	31 (23.3)	42 (20.9)	1.39	.239
>40mg/dL	57 (83.8)	102 (76.7)	159 (79.1)		
Morbidity					
Cardiovascular disease					
No	59 (86.8)	88 (66.2)	147 (73.1)	9.72	.002**
Yes	9 (13.2)	45 (33.8)	54 (26.9)		
Hypertension					
No	41 (60.3)	51 (38.3)	92 (45.8)	8.73	.003**
Yes	27 (39.7)	82 (61.7)	109 (54.2)		
Hyperlipidemia					
No	39 (57.4)	62 (46.6)	101 (50.2)	2.08	.150
Yes	29 (42.6)	71 (53.4)	100 (49.8)		
Asthma or chronic bronchiti	is				
No	62 (91.2)	124 (93.2)	186 (92.5)	1.59	.600
Yes	6 (8.8)	9 (6.8)	15 (7.5)		
Osteoarthritis/arthritis					
No	49 (72.1)	84 (63.2)	133 (66.2)	0.28	.207
Yes	19 (27.9)	49 (36.8)	68 (33.8)		
Diabetes-related health manage	gement				
Do you know the values of v	well controlled glycosylated hemog	plobin for T2DM?			
No	10 (14.7)	22 (16.5)	32 (15.9)	0.11	.736
Yes	58 (85.3)	111 (83.5)	169 (84.1)		
Do you adjust the dose of y	our medication on your own or do	you follow your doctor's advice?			
No	56 (82.4)	105 (78.9)	161 (80.1)	0.33	.567
Yes	12 (17.6)	28 (21.2)	40 (19.9)		
Do you regularly measure y	our blood sugar at home?				
No	32 (47.1)	61 (45.9)	93 (46.3)	0.03	.872
Yes	36 (52.9)	72 (54.1)	108 (53.7)		

BMI = body mass index, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, T2DM = type 2 diabetes.

\*Body fat percentage presented to be normal (<25% in men and <30% in women). \*P < .05, \*\*P < .01, \*\*\*P < .001.

 $\pm$  +Waist circumference presented to be normal (<90 cm in men and <80 cm in women).

 $\pm$ Waist-hip ratio presented to be normal (<0.9 in men and < 0.85 in women).

\$BMI grouped to be <18.5 (underweight), 18.5–24.9 (normal weight), 25.0–29.9 (overweight), and 30.0 or above (obesity).

the prefrail group also had higher body fat percentages ( $\chi^2 = 13.03$ ; *P* < .001) and waist circumferences ( $\chi^2 = 7.04$ ; *P* = .008),.

Logistic regression analysis was carried out to examine the selected significant variable from the Chi-square tests to understand which variables were significant in multivariate analysis. Table 3 lists the factors that predicted frailty (not frail vs prefrail) by logistic regression. In the model, people who were retired from manual occupations (OR = 0.12; P= .012) and professional occupations (OR = 0.10; P = .007) had a lower risk of being prefrail than unemployed individuals with T2DM.

We examined 5 phenotypic criteria based on measured variables that were significant in logistic regression: the type of job from which they retired, body fat, cardiovascular disease, and hypertension. Table 4 shows that the relationship between the type of job from which they retired and hand grip strength (manual 31.6% and professional 57.9%,  $\chi^2 = 6.73$ ; P = .035) and slow walking speed (manual 28.6% and professional 57.7%,  $\chi^2 = 11.58$ ; P = .003) suggested that most people were in relatively good condition. When examining the relationship between the type of job from which they retired and low physical activity (professional 97.5%,  $\chi^2 = 6.65$ ; P = .036), this trend was reversed, with most people in worse condition.

# Table 3

The model of significant correlates of non-frailty vs pre	e-frailty
from binary logistic regression.	

Variable (reference)	Category	OR (CI 95%)	P value
Gender (Male) Education (≤ Primary)	Female	0.91 (0.41-2.02)	.806 .449
	Secondary	0.60 (0.22-1.59)	.300
	≥University	0.50 (0.17-1.50)	.216
Retirement job (Unemployed)			.025*
	Manual	0.12 (0.02-0.63)	.012*
	Professional	0.10 (0.02-0.53)	.007**
Alcohol use (Never)	Current	0.62 (0.27-1.39)	.245
Body fat (Normal)	High	0.43 (0.21-0.89)	.024*
Cardiovascular disease (No)	Yes	3.29 (1.39-7.79)	.007**
Hypertension (No)	Yes	2.42 (1.22-4.77)	.011*

CI = confidence interval, OR = odds ratio.

\*P < .05, \*\*P < .01.

When we examined the association between body fat and hand grip strength, we observed that people with higher body fat percentages (high body fat 81.6%,  $\chi^2 = 5.61$ ; P = .018)

	Uninte	entional we	sight los	ş	Ĥ	and grip str	ength			Slow sp(	ed		Self-	reported ex	haustio	=	Low phys	ical activil	y (usin	I IPAQ)
Variables	No (%)	Yes (%)	X²	<i>P</i> value	Good (%)	Worse (%)	×2	<i>P</i> value	Good (%)	Worse (%)	X²	<i>P</i> value	No (%)	Yes (%)	χ²	<i>P</i> value	Good (%)	Worse (%)	×2	P value
Retirement job																				
Unemployed	24 (14.8)	9 (23.1)	2.50	.287	12 (10.5)	21 (24.1)	6.73	.035*	25 (13.7)	8 (42.1)	11.58	.003**	27 (14.9)	6 (30.0)	3.39	.184	33 (17.0)	0 (0.0)	6.65	.036*
Manual	50 (30.9)	8 (20.5)			36 (31.6)	22 (25.3)			52 (28.6)	6 (31.6)			52 (28.7)	6 (30.0)			53 (27.3)	5 (71.4)		
Professional Bodv fat	88 (54.3)	22 (56.4)			66 (57.9)	44 (50.6)			105 (57.5)	5 (26.3)			102 (56.4)	8 (40.4)			108 (55.7)	2 (28.6)		
Normal	40 (24.7)	14 (35.9)	2.01	.156	38 (33.3)	16 (18.4)	5.61	.018*	52 (28.6)	2 (10.5)	2.85	.091	50 (27.6)	4 (20.0)	0.53	.465	53 (27.3)	1 (14.3)	0.58	.445
High	122 (75.3)	25 (64.1)			76 (66.7)	71 (81.6)			130 (71.4)	17 (89.5)			131 (72.4)	16 (80.0)			141 (72.7)	6 (85.7)		
Cardiovascular disease																				
No	119 (73.5)	28 (71.8)	0.04	.834	89 (78.1)	58 (66.7)	3.27	.071	135 (74.2)	12 (63.2)	1.06	.303	133 (73.5)	14 (70.0)	0.11	.739	140 (72.2)	7 (100)	2.66	.103
Yes	43 (26.5)	11 (28.2)			25 (21.9)	29 (33.3)			47 (25.8)	7 (36.8)			48 (26.5)	6 (30.0)			54 (27.8)	0 (0.0)		
Hypertension																				
No	73 (45.1)	19 (48.7)	0.17	.681	57 (50.0)	35 (40.2)	1.90	.168	87 (47.8)	5 (26.3)	3.20	.074	81 (44.8)	11 (55.0)	0.76	.383	87 (44.8)	5 (71.4)	1.92	.165
Yes	89 (54.9)	20 (51.3)			57 (50.0)	52 (59.8)			95 (52.2)	14 (73.7)			100 (55.2)	9 (45.0)			107 (55.2)	2 (28.6)		

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had worse hand grip strength than those with lower body fat percentages.

#### 4. Discussion

This is a pilot study with a very small sample size conducted to identify predictors of prefrailty in older people with T2DM among community-dwelling residents in Taiwan. Based on the results of the chi-square tests, prefrailty was associated with female sex, middle school education, unemployment, alcohol use, high body fat percentage, above-normal waist circumference, obesity, cardiovascular disease, and hypertension. These findings are consistent with prior studies and the accumulating evidence of the impact of frailty on life processes, such as lifespan, chronic disease, and health behaviors, among older people with T2DM.<sup>[14–16,20]</sup> However, none of the clinical biomarkers (e.g., fasting blood glucose, HbA1c, LDL-C, HDL-C, and triglyceride) had a significant association with prefrailty in this study.

Logistic regression analyses identified a significant correlation of prefrailty with the type of job from which they retired, cardiovascular disease, and hypertension. An important new finding arising from this study is that the type of job from which they retired is associated with prefrailty. To the best of our knowledge, this discovery differs from all previous findings. Participants who had held manual or professional jobs had a lower risk of being prefrail than diabetic patients who had been unemployed. The association of the type of job from which they retired with prefrailty persisted even after we adjusted for alcohol use, body fat percentage, waist circumference, BMI, cardiovascular disease, and hypertension.

We also examined the 5 phenotypic factors that were the criteria for prefrailty (unintentional weight loss, reduced hand grip strength, slow speed, self-reported exhaustion, and low level of physical activity). Although people who had held manual or professorial jobs had greater hand grip strength and faster speed than those who had been unemployed, they had lower levels of physical activity. In this study, we observed that people who had technical or professional jobs had a relatively lower risk of being prefrail. In contrast, a large number of prior articles from the Seniors-ENRICA study reported that a current or prior manual occupation caused health problems and led to frailty.<sup>[16]</sup> In Taiwan, no studies have been performed to provide evidence clarifying the relationship between the type of job from which they retired and frailty. This is a new finding, indicating that unemployed individuals are more likely to develop frailty because they engage in less physical activity. One possible reason is that the type of job from which they retired may reduce risk factors for frailty (e.g., sedentary, obesity, depression) that are more common in women than in men. This in turn may lead to a larger social gap in the risk of frailty among women. Further research is needed to confirm this finding and investigate causal processes in Taiwan.

Rising levels of frailty and associated cardiovascular disease and hypertension present a large threat to older people with T2DM and are also consistent with previous studies.<sup>[12,20]</sup> A previous study identified that congestive heart failure was related to a lack of achievement of cholesterol management goals. Obesity was related to poor HbA1c and blood pressure control.<sup>[21]</sup> The T2DM care guidelines now highlight the concepts of individualized goal setting and treatment plans, as well as the optimization of the quality of everyday life.<sup>[20]</sup>

There are several limitations of this study. First, the sample in this study was recruited from only one hospital and is extremely unlikely to be representative of all older adults with T2DM in Taiwan. Second, our analysis and conclusions are based on self-reported data. Self-reported data may be affected by recall bias. Some study participants may not have felt comfortable being absolutely truthful about answering questions concerning their alcohol consumption, cigarette use or compliance with medication instructions. Third, this study was unable to explore predictors of falls or hip fractures in prefrail older people, although these risk factors could lead to frailty, hospitalization, and mortality. Fourth, we did not examine sarcopenia, which is also highly prevalent among older adults with T2DM.

# 5. Conclusions

Prefrailty is a common condition among older people that is associated with many component factors, such as personal characteristics, lifestyle behaviors, health conditions, and comorbidities. We suggest that clinicians screen for and identify those in need of interventions to optimize the health management programs of older people with T2DM.

Further studies are needed to explore frailty and sarcopenia in older Taiwanese individuals with T2DM. There were only 5 patients who met the criteria for frailty, and they were excluded from further analysis. However, the identification of prefrailty-related predictors in this study was still valuable.

## **Author contributions**

SFL had research idea, study design, analysis and interpretation. PD and YLC were performed data analysis, interpretation, supervision and mentorship. CPL was a major contributor in writing the manuscript and data analysis. All authors read and approved the final manuscript.

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