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Original Article

Short Term Structured, Multimodal, Interdisciplinary, Home-Based, Self-Help Program is Effective in Improving Frailty Status among Elderly T2DM Patients

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SUMMARY

Background: This short term structured, multimodal, home-based, self-help program was designed to reduce frailty of elderly type 2 diabetes mellitus (T2DM) patients, and detect the major predictors of frailty status improvement.
Method: This study recruited T2DM patients aged 65 years and older from the DM shared care center in a regional hospital who were frail or prefrail according to Fried Frailty Phenotype. Short term (12 weeks) home-based intervention including an elastic band low resistance exercise, a smart bracelet monitored walking exercise, and nutrition consultation was conducted. Change of frailty status, functional outcomes, body composition and metabolic indices after intervention were analyzed. A logistic regression was applied to determine the predictive factors associated with frailty status improvement.
Results: 81 participants were enrolled after they were fully consented. After 12 weeks' intervention, 60 participants completed the program. Since two participants with incomplete data were excluded, there were 58 remaining in the analysis. They were on average 71.7 ± 4.9 years old and 22 persons (36.7%) were male. 46 (79.3%) of them were prefrail and 12 (20.7%) were frail. The average duration between the pre-test and the post-test was 107.1 ± 25.6 days. The average incidence of home-based exercise was 1.4 ± 1.1 times a week. Fried Frailty Phenotype, handgrip strength, muscle quality, HbA1c, and symptomatic hypoglycemic episodes significantly improved. Initial poorer frailty status was the major predictor (OR = 104.446, 95% CI = 7.551–1444.726, $p = 0.001$) of frailty status improvement.
Conclusions: Short term structured, multimodal, interdisciplinary, home-based, self-help program is effective in reducing frailty status among elderly T2DM patients.

1. Introduction

Frailty in old people is not just a decline in physical strength, but a gradual decline in physiological function of multiple systems, including loss of physiologic reserve, and increased vulnerability to disease and death.[1,2] The incidence of frailty gradually increases along with aging process. On average, the prevalence of frailty among 65 years and older is 10.7% (95% CI 10.5–10.9%). Most seniors have a period of frailty before their functional status falling below disability (frailty window). So, frailty can be regarded as a state of pre-disability, a dynamic process with recoverable potential. Early detection and intervention to reverse frailty can prevent the elderly from disability and restore daily life independency.[3]

There are many etiologies like decline in metabolism, inflammation, hormone dysregulation, etc., being correlated with frailty.[4] Multiple-comorbidity is also an important factor especially diabetes mellitus. A Chinese study showed that prevalence of frailty (19.32%) of community-dwelling elderly diabetes patients were higher than those without (11.92%).[5] A Spanish study showed that for every 10 points increase in the Frailty Trait Score, the hazard ratio of mortality for the elderly diabetes patients will rise to 1.51 (95% CI 1.28–1.77).[6] So, it is important to screen and early intervene to old diabetes mellitus (DM) patients with frailty to minimize disaster sequels.

A previous study demonstrated that dietary and exercise interventions could prevent and reverse sarcopenia in the elderly.[7] Exercise intervention alone or exercise combined with diet intervention, both had significant effects in increasing limbs muscle mass, handgrip strength, and walking speed in a meta-analysis study of interventional therapy for sarcopenic obesity of the elderly.[8] Also, according to 2019 MID-Frail study, a 12-month structured multimodal intervention program led to a clinically relevant and cost-effective improvement in functional status of older frail participants with type 2 DM (T2DM).[9,10]

Regarding exercise intervention, resistance training is effective in improving muscle strength and size, as well of physical function of the elderly.[11] In comparison with traditional resistance exercise, elastic band had higher acceptance among elderly for its simplicity, portability, less space requirements and relatively low costs.[12] It is effective in reducing fat mass, improving blood glucose control, and

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physical function in elderly women with T2DM.[13] However, all the above studies were designed to be on-site grouped or one-on-one training programs. In comparison with home-based, self-help programs, on-site grouped or one-on-one programs possess a better patient motivation and compliance so that the effect is more obvious, but it is costly and requires more human resources.[14] Furthermore, the effect of home-based, self-help program for the elderly T2DM patients was still not well investigated. For further investigate the effectiveness in reducing frailty status, we launch this 12 weeks, structured, multimodal, interdisciplinary, home-based, self-help intervention for the frail elder T2DM patients.

2. Materials and methods

2.1. Study design and study participants

This study is designed as a single arm study to determine whether a short term multimodal, home-based intervention can improve the frailty status of the elderly T2DM patients. The local ethics committee of Feng-Yuan Hospital approved the study (No. 108009) and all the participants were fully consented. We recruited participants from the DM shared-care center in a regional hospital in Taiwan. Inclusion criteria included: (1) aged 65 years and older patients with T2DM (definition was according to Clinical Practice Guidelines for Diabetes Care-2018, Taiwan),[15] (2) regular attendance to the DM shared care center for at least 6 months, (3) physically frail or pre-frail according to the Fried 's Frailty Phenotype (FFP),[1] (4) intact communication capacity, (5) able to grant the informed consent. Besides, patients with the following conditions were excluded: (1) Partial or total Activity of Daily Living (ADL) dependency (Barthel score lower than 60 points), (2) Mini-Mental State Examination (MMSE) less than 20 points, (3) subject is unwilling to consent or unable to participate safely, (4) previous history of severe cardiovascular disease within 6 months, or congestive heart failure at stage III to IV of the NYHA classification, (5) terminal illness with life expectancy less than 6 months, (6) concurrent participation in other clinical trials.

2.2. Demography, functional assessment and laboratory measurements

For all the participants, the research staff completed the questionnaire of demographic characteristics, past medical history, and personal health behavior. The body mass index (BMI) was calculated as the weight divided by the square of height (kg/m^2). Monthly symptomatic hypoglycemia episodes were assessed by a self-report questionnaire, and the daily protein intake was estimated base on the 24-hour diet recall by the dietitians of the DM shared care center.

Functional assessments were performed before and after intervention by well-trained research nurses for all participants, including MMSE, Geriatric Depression Scale-5 (GDS-5),[16] Barthel score, Instrumental Activities of Daily Living (Lawton-Brody IADL Scale).[17] Besides, blood test to measure fasting blood sugar and hemoglobin A1c (HbA1c) was also performed at the enrollment and the end of intervention for further analysis.

2.3. Measurement of body composition

Body composition of all participants were measured by the dual-energy X-ray absorptiometry (Horizon, Hologic, Bedford, Massachusetts, USA). Appendicular lean mass (ASM) was estimated as the sum of fat-free mass of the four limbs, and the relative appendicular muscle mass (RASM) was calculated as the ASM divided by height square (kg/m^2).

Definitions of weakness, slowness and sarcopenia were made based on the consensus report of the 2019 Asian Working Group for Sarcopenia,[18] weakness as handgrip strength < 28.0 kg in men and < 18.0 kg in women; slowness as the 6-meter usual walking speed < 1.0 m/s; low muscle mass as the RASM < 7.0 kg/m^2 in men and < 5.4 kg/m^2 in women; and sarcopenia as low muscle mass with weakness and/or slowness. Meanwhile, muscle quality was estimated as the muscle strength per unit of the muscle mass, i.e., handgrip strength dived by RASM.[19]

2.4. Multimodel, interdisciplinary intervention

The intervention consists of a multimodal, interdisciplinary program comprising a 12-week structured, home-based exercise program including anelastic band (Thera-Band®, the Hygenic Corporation, Akron, OH, USA) low resistance exercise and a smart bracelet pedometer monitored daily walking exercise, and a nutritional education intervention. Glycemia and other metabolic disorders control still depended upon original caregiving physician's expertise without pre-defined targets. All subjects will follow the program. Details about the program was shown in Appendix 1.

2.4.1. Exercise program

The enrollees would receive at least once an hour of group class. Following, they must carry out 12-week, home-based, self-help practice. Details about the exercise program were described in Appendix 2. The group class attendance was defined as total number of group classes attended, and the program adherence was defined as average number of times per week to practice at home recorded by enrollees themselves.

2.4.2. Nutrition intervention

Nutrition intervention schedule was designed to accommodate monthly group classes schedule. The content of the nutrition intervention was described in Appendix 2.

2.5. Sample size estimation

According to 2019 MID-Frail study, the mean difference and standard deviation of the primary outcome Short Physical Performance Battery of the intervention group were 0.66 ± 0.44.[9,10] This study would require a sample size of 34 at least to achieve a power of 80% and a level of significance of 5% (two sided). The analysis was performed by statistical software G*power 3.1.

2.6. Statistical methods

In this study, Kolmogorov-Smirnov or Shapiro-Wilk test were used to evaluate the normality of all continuous variables. In normal distributed variables ($p \geq 0.05$), mean ± standard deviation would be used to express the value, and paired-t test or Student-t test would be used to investigate the significance of difference when appropriate. In non-normal distributed variables ($p < 0.05$), median (interquartile range) would be used to express the value, and Wilcoxon Signed Rank test or Mann-Whitney U test would be used when appropriate. Categorical data were expressed as frequency and percentage and McNemar or Chi-squared test were used when appropriate.

Logistic regression was used to assess the association between predicting factors and frailty status improvement after intervention among frail elderly T2DM patients (Table 4). The frailty status improvement was defined as subjects whose frailty status improved from frail to prefrail, prefrail to robust, or frail to robust according to FFP. Potentially associated factors with $p < 0.10$ showed in Table 3 were used for logistic regression analysis and a forward stepwise selection procedure was used to fit the multivariate model. The odds ratio (OR) with 95% confidence interval (95% CI) was calculated.

For all tests, the two-tailed p value less than 0.05 was considered as statistically significant. All statistical analyses were performed by statistical software SPSS 26.0 (SPSS, Chicago, IL).

3. Results

During the study period (6th February to 22th October, 2020), 81 participants fulfilled the inclusion/exclusion criteria were enrolled after they were fully consented. After 12 weeks' intervention, 60 participants completed the program. Because two participants with incomplete data were excluded, only 58 remained in the analysis (Figure 1). They were on average 71.7 ± 4.9 years old and 22 persons (36.7%) were male. 46 (79.3%) of them were prefrail and 12 (20.7%) were frail. The average duration between the pre-test and post-test was 107.1 ± 25.6 days. The average incidence of home-based, self-help exercise was 1.4 ± 1.1 times a week. But there were only 20 people had a record of using the bracelet.

Table 1 showed functional status, body composition, and metabolic indices change before and after interventions of frail elderly T2DM patients. After 12-week intervention, FFP, handgrip strength, muscle quality, Hba1c, and symptomatic hypoglycemic episodes significantly improved, although RASM, walking speed, and daily protein intake per kg body weight revealed no significant change.

Table 2 revealed changes of the prevalence of frailty status, sarcopenia and its components before and after intervention. The prevalence of frail status significantly reduced from 20.7% to 3.4% (p = 0.006) but one person had regressed from pre-frail to frail status among them. The prevalence of sarcopenia and its components revealed no significant change except handgrip strength weakness reduced significantly from 27.6% to 13.8%, p = 0.039.

Table 3 showed the baseline characteristics between frailty status improvement responders and non-responders. There were 11 responders fulfilled the definition of frailty status improvement. FFP, muscle quality, and MMSE showed significantly correlated with frailty status improvement. Program adherence and daily protein intake per kg body weight revealed borderline significance.

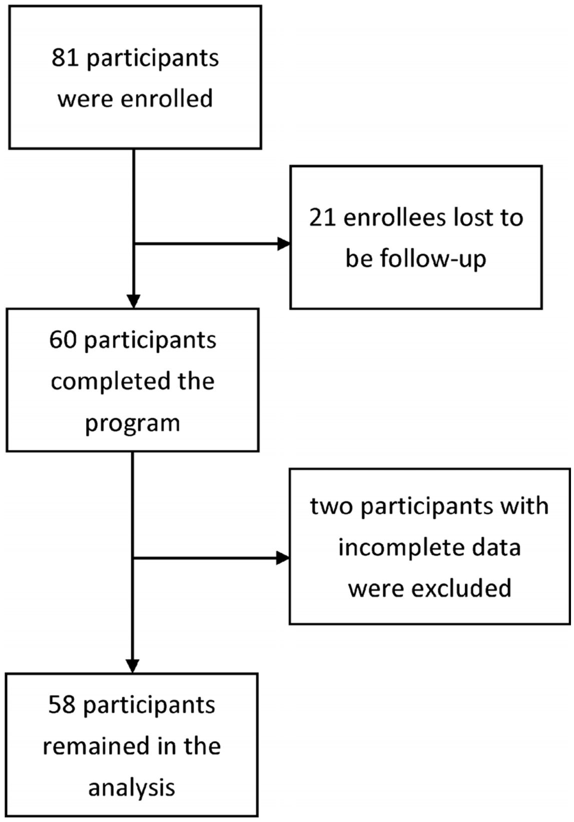

Figure 1. The flowchart of the study process.

Table 1
Functional status, body composition, and metabolic indices change before and after intervention of frail elderly T2DM patients (N = 58).

	Normality [a]	Before	After	p
Body Mass Index (kg/m^2)	Y [b]	24.1 ± 3.8 [c]	24.2 ± 3.7	0.724
Fried Frailty Phenotype	N	1.8 (1.0–2.7) [d]	1.3 (0.8–1.8)	< 0.001**
Walking speed (m/s)	Y	0.86 ± 0.19	0.88 ± 0.20	0.351
Handgrip strength (kg)				
Male	Y	31.7 ± 5.4	34.6 ± 6.8	0.014*
Female	Y	20.1 ± 3.8	22.0 ± 4.3	< 0.001**
Relative appendicular muscle mass (kg/m^2)				
Male	Y	7.3 ± 0.8	7.2 ± 0.7	0.475
Female	Y	5.87 ± 0.73	5.80 ± 0.77	0.095
Muscle quality (kg/kg/m^2)	Y	3.80 ± 0.11	4.21 ± 1.13	< 0.001**
Sarcopenia (%)	NA	13 (22.4%)	14 (24.1%)	0.568
Mini-Mental State Examination	N	29.8 (28.6–30)	30.0 (29.7–30)	0.223
Geriatric Depression Scale-5	N	0.2 (0–0.6)	0.1 (0–0.9)	0.713
Barthel score	NA	100	100	
Instrumental Activities of Daily Living	N	7.9 (7.6–8.0)	7.9 (7.6–8.0)	1.000
Fasting blood sugar (mg/dl)	N	128.0 (111.8–159.3)	130.5 (113.5–144.3)	0.253
Hemoglobin A1c (%)	N	7.1 (6.6–7.7)	6.9 (6.4–7.4)	0.023*
Symptomatic hypoglycemic episodes (times/month)	N	0.5 (0–1.9)	0.2 (0–0.8)	0.011*
Daily protein intake per kg body weight (g/kg/day)	Y	1.07 ± 0.25	1.11 ± 0.25	0.138

[a] Normality tested by Kolmogorov-Smirnov or Shapiro-Wilk test. The detailed results were shown in Supplementary Materials Appendix 3.
[b] Y = normal distributed, N = non-normal distributed, NA = not available.
[c] Mean ± standard deviation.
[d] Median (interquartile range).
* $p < 0.05$, ** $p < 0.01$.

Table 4 showed the result of uni- and multivariate logistic regression analysis for predicting factors correlated with frailty status improvement after intervention. In the univariate analysis, initial FFP and muscle quality were significantly correlated with frailty status improvement. But in the multivariate analysis, initial FFP was the only significant predicting factor after adjustment for age and gender with positive correlation with responders (OR = 104.446, 95% CI = 7.551–1444.726, p = 0.001). The collinearity between initial FFP with muscle quality was moderate (variance inflation factor = 1.387).

4. Discussions

This study revealed that short term (12 weeks) home-based, self-help multimodal, interdisciplinary intervention may improve frailty status, improve hand grip strength and muscle quality of frail and pre-frail elderly T2DM patients. Furthermore, this intervention program could also improve glycemic control without increasing symptomatic hypoglycemic episodes.

As mentioned in previous section, elderly patients with T2DM committed to a higher incidence of frailty and mortality.[5,6] According to 2019 MID-Frail study, a 12-month structured multimodal intervention program led to functional status improvement of frail elderly T2DM participants.[9,10] Our study revealed similar results in a short term (12 weeks) home-based program.

Frailty is a dynamic process with recoverable potential.[3] Initial poorer frailty status itself is the predictor of frailty status improvement found in this study. This may propose that the frailty of the elderly T2DM patients was a transient condition and could have even a higher chance to be reversed. A recent intervention study revealed that community-dwelling elderly who had the frailty phenotype of exhaustion, are more prone to improve in their frail severity. The author regarded frailty phenotype of exhaustion sharing some similarities with chronic fatigue syndrome, and could be reversed by graded exercise therapy and cognitive behavioral therapy.[20]

On the other hand, poorer muscle quality was significantly correlated with frailty status improvement shown in Table 3 and univariate analysis of Table 4, although not left in the multivariate

Table 2
Change of prevalence of frailty status, sarcopenia and its components before and after intervention.

	Before	After	p
Prefrail	46 (79.3%)	56 (96.6%)	0.006**
Frail	12 (20.7%)	2 (3.4%)	
Sarcopenia	13 (22.4%)	14 (24.1%)	0.568
Slowness	44 (75.9%)	46 (79.3%)	0.687
Weakness	16 (27.6%)	8 (13.8%)	0.039*
Low muscle mass	19 (32.8%)	18 (31.0%)	0.568

* $p < 0.05$, ** $p < 0.01$.

Table 3
Baseline characteristics between frailty status improvement responders and non-responders.

	Normality [a]	Responders (N = 11)	Non-responders (N = 47)	p
Age (years-old)	N[b]	69.0 (67.0–79.0) [c]	71.0 (68.0–74.0)	0.976
Male gender (%)	NA	3 (27.3%)	18 (38.2%)	0.493
Group class attendance (times) [d]	N	2.1 (1.4–2.8)	2.6 (2.4–2.8)	0.149
Program adherence (times/week) [e]	N	0.8 (0.4–1.6)	1.6 (0.8–1.9)	0.05
Body Mass Index (kg/m^2)	Y	24.6 ± 2.5 [f]	24.0 ± 4.0	0.658
Fried Frailty Phenotype	N	3.1 (2.9–3.3)	1.5 (1.4–1.7)	< 0.001**
Walking speed (m/s)	Y	0.82 ± 0.23	0.87 ± 0.19	0.373
Muscle quality (kg/kg/m^2)	N	3.14 ± 0.64	4.00 ± 0.85	0.004**
Sarcopenia (%)	NA	2 (18.2%)	11 (23.4%)	0.708
Mini-Mental State Examination	N	29.4 (28.3–30)	29.9 (29.6–30)	0.036*
Geriatric Depression Scale-5	N	0 (0-0)	0.2 (0.0–0.4)	0.215
Barthel score	NA	100	100	
Instrumental Activities of Daily Living	N	7.8 (7.4–8.0)	8.0 (7.9–8.0)	0.259
Fasting blood sugar (mg/dl)	N	123.0 (105.0–178.0)	129.0 (112.0–159.0)	0.882
Hemoglobin A1c (%)	N	7.3 (6.7–7.7)	7.0 (6.6–7.7)	0.773
Symptomatic hypoglycemic episodes (times/month)	N	0.3 (0–0.7)	0.6 (0.1–1.0)	0.768
Daily protein intake per kg body weight (g/kg/day)	Y	0.95 ± 0.20	1.10 ± 0.26	0.085

[a] Normality tested by Kolmogorov-Smirnov or Shapiro-Wilk test. The detailed results were shown in Supplementary Materials Appendix 4.
[b] Y = normal distributed, N = non-normal distributed, NA = not available.
[c] Median (interquartile range).
[d] Total number of group classes attended.
[e] Average number of times per week to practice at home.
[f] Mean ± standard deviation.
* $p < 0.05$, ** $p < 0.01$.

Table 4
Uni- and multi-variate logistic regression analysis for predicting factors correlated with frailty status improvement after intervention among frail and pre-frail elderly T2DM patients.

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	P
Age (y/o)	1.044	(0.920–1.185)	0.501	0.942	(0.761–1.165)	0.579
Gender (male)	0.604	(0.142–2.579)	0.496	1.730	(0.107–27.879)	0.699
Fried Frailty Phenotype	88.086	(7.435–1043.582)	< 0.001**	104.446	(7.551–1444.726)	0.001**
Muscle quality (kg/kg/m^2)	0.252	(0.088–0.720)	0.01*			
Mini-Mental State Examination	0.759	(0.475–1.212)	0.248			
Daily protein intake per kg body weight (g/kg/day)	0.074	(0.004–1.493)	0.089			
Program adherence (times/week)	0.407	(0.154–1.073)	0.069			

* $p < 0.05$, ** $p < 0.01$.

analysis. A cohort study stated that physical activity improvement, self-reported exhaustion, and handgrip strength improvement at the 1-year follow-up, but none of weight loss and gait speed improvement, were significantly associated with improved frailty at the 2-year follow-up. This may imply that handgrip strength is a more sensitive indicator for frailty status improvement and prone to be facilitated than that of gait speed.[21]

The walking speed did not improve in this study. In a single-blinded, randomized-controlled intervention trial among elderly, with or without DM, the gait speed was relatively faster in intervention group after 2 years of follow-up, but still deteriorated in comparison with initial gait speed measurement.[22] DM patients have more than two-fold higher prevalence of peripheral arterial disease compared with general population, and it remained largely undiagnosed because of asymptomatic.[23] A study showed that 30% of elderly T2DM patients had asymptomatic diabetic neuropathy and thus decreased physical function.[24] A cross-sectional study revealed that suffering from diabetes and arthritis concomitantly resulted in more gait speed loss than either disease alone.[25] All these hidden etiologies may contribute to the non-response of walking speed in this intervention study.

Considering the implementation of training program, on-site grouped program seemed to be superior to home-based program in improving muscle mass among sarcopenic elderly;[14] one-on-one program is effective in terms of patient motivation and for securing compliance. However, they were costly and requires more human resources.[26] Home-based program is more accessible and also effective. In comparison with the group-based program, a home-based multicomponent program conducted in Northern Thailand revealed effective in reducing frailty and improving physical performance in community-dwelling elderly.[27] A randomized controlled trial performed in Austria revealed that home-based program led by lay-volunteers could significantly improve handgrip strength and frailty status.[28,29] Our study also revealed that home-based program is feasible and effective in improving muscle strength and frailty status among elder T2DM patients.

Despite all the efforts went into this study, there were still some limitations. First, this was a single arm, self-controlled study without a control group, and with also rather small sample size, which could affect the interpretation of the study results. Second, quite an amount of lost to be follow-up rate (25.9%), lower program adherence, and only 20 participants with record of the bracelet were considered. Poor program adherence is a universal problem in such a home-based program.[30] This could be facilitated to include patients in the decision-making process about exercise selection.[31] The staff of this study had done their best to work together with the enrollees to accommodate the program content to their daily life and the improved outcomes were still achieved after all the efforts contributed.

In conclusion, this first short term structured, multimodal, interdisciplinary, home-based, self-help program may improve frailty status, handgrip strength and muscle quality, glycemic control, without increasing symptomatic hypoglycemic episodes, among frail and pre-frail elderly T2DM patients. Poor frailty status itself predicted frailty status improvement further highlight the dynamic process and reversable potential of frailty in the elderly diabetic patients and may be reversed through an adequate intervention. Home-based, self-help program is effective in improving functional status of community-dwelling elder DM patients and a higher accessibility in comparison with on-site grouped or one-on-one training programs, although the program adherence may be lower than that of aforementioned ones. At last, the long-term effect of this program is still in need of further investigation and follow-up.

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Supplementary materials

Supplementary materials for this article can be found at http://www.sgecm.org.tw/ijge/journal/view.asp?id=24.

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