Accepted Article

Journal of Frailty, Sarcopenia and Falls

Short Communication

Examining the Cycle of Physical Frailty in Falls Clinic Attendees Through Structural Equation Modeling

Román Romero Ortuño[1,2], Eoin Duggan[1,2]

[1]FRAILMatics research group, Discipline of Medical Gerontology, School of Medicine, Trinity College Dublin, Ireland; [2]Falls and Syncope Unit, Mercer's Institute for Successful Ageing, St James's Hospital, Dublin, Ireland

Abstract

In 1998, Fried and Walston introduced the Cycle of Frailty (CF) as a foundational concept for defining the physical frailty phenotype (FP). While the FP has been extensively validated, the CF hypothesis lacks equivalent support. This study aimed to internally validate the CF using structural equation modeling (SEM) in a clinical dataset of adults aged 50 or older attending an outpatient falls clinic. Measures included: age, morbidity, nutrition, sarcopenia by bioelectrical impedance, VO_2max, handgrip strength, basal metabolic rate (BMR), 5-times chair stand test (5CST), physical activity, and total energy expenditure (TEE). The SEM, incorporating CF hypothesized causal pathways, was tested using IBM® SPSS® Amos 27.0.0 (maximum likelihood method) with a sample of 102 adults (mean age 69.8 years, 58.8% women). Overall, the SEM was supported by the data (χ^2 = 44.4, df = 37, p = 0.189), with significant (p < 0.05) regression weights for morbidity→sarcopenia, age→sarcopenia, sarcopenia→VO_2max, sarcopenia→handgrip strength, handgrip strength→5CST, physical activity→TEE, TEE→nutrition, and BMR→TEE. However, nutrition→sarcopenia, sarcopenia→BMR, VO_2max→5CST, and 5CST→physical activity were not significant. Although the SEM was limited by inclusion of surrogate CF measures (e.g., 5CST instead of gait speed, VO_2max based on age-predicted maximal/resting heart rate), it provided some internal support for the CF hypothesis.

Keywords: Falls clinic, Physical frailty phenotype, Sarcopenia, Structural equation modeling, Validation studies

In 1998, Linda P. Fried and Jeremy Walston proposed the Cycle of Frailty (CF) as the conceptual foundation for defining the physical frailty phenotype (FP)[1]. While the FP has undergone extensive validation and utilisation[2,3], the CF hypothesis lacks comparable support. This study aimed to internally and cross-sectionally validate the CF using a structural equation model (SEM) in a clinical dataset of patients attending a falls clinic.

Adults aged 50 years or older attending an outpatient falls and syncope unit (FASU) in St. James's Hospital, Dublin, Ireland, were recruited between January and November 2022. The clinical setting has been described elsewhere[4,5].

Measures collected in the clinic included: age in years; sex (male vs. female); disease burden (morbidity) as per Cumulative Illness Rating Scale-Geriatric (CIRS-G)[6] score; nutritional status as per Mini Nutritional Assessment® Short-Form (MNA®-SF)[7] ordinal classification (0: normal; 1: at risk of malnutrition; 2: malnourished); sarcopenia status (0: robust; 1: probable sarcopenia; 2: sarcopenia) determined by bioelectrical impedance using TANITA® DC-430 MAP Body Composition Analyser following European Working Group on Sarcopenia in Older People guidelines, as described elsewere4,5; VO_2max calculation (ml/kg/min) as per the following formula: 15.3 x [208 - (0.7 x age)] / resting heart rate[8,9], where resting heart rate was obtained using a Finapres® Nova (Finapres Medical Systems, Amsterdam, The Netherlands) by averaging the mean heart rate from 60 to 30 seconds while lying down supine before an active stand

The authors have no conflict of interest.

Corresponding author: *Román Romero Ortuño, Discipline of Medical Gerontology, Mercer's Institute for Successful Ageing (MISA), St James's Hospital, James's Street, Dublin 8, Ireland*

E-mail: *romeroor@tcd.ie*

ORCID: *0000-0002-3882-7447*

Edited by: *George Lyritis*

Accepted *1 July 2024*

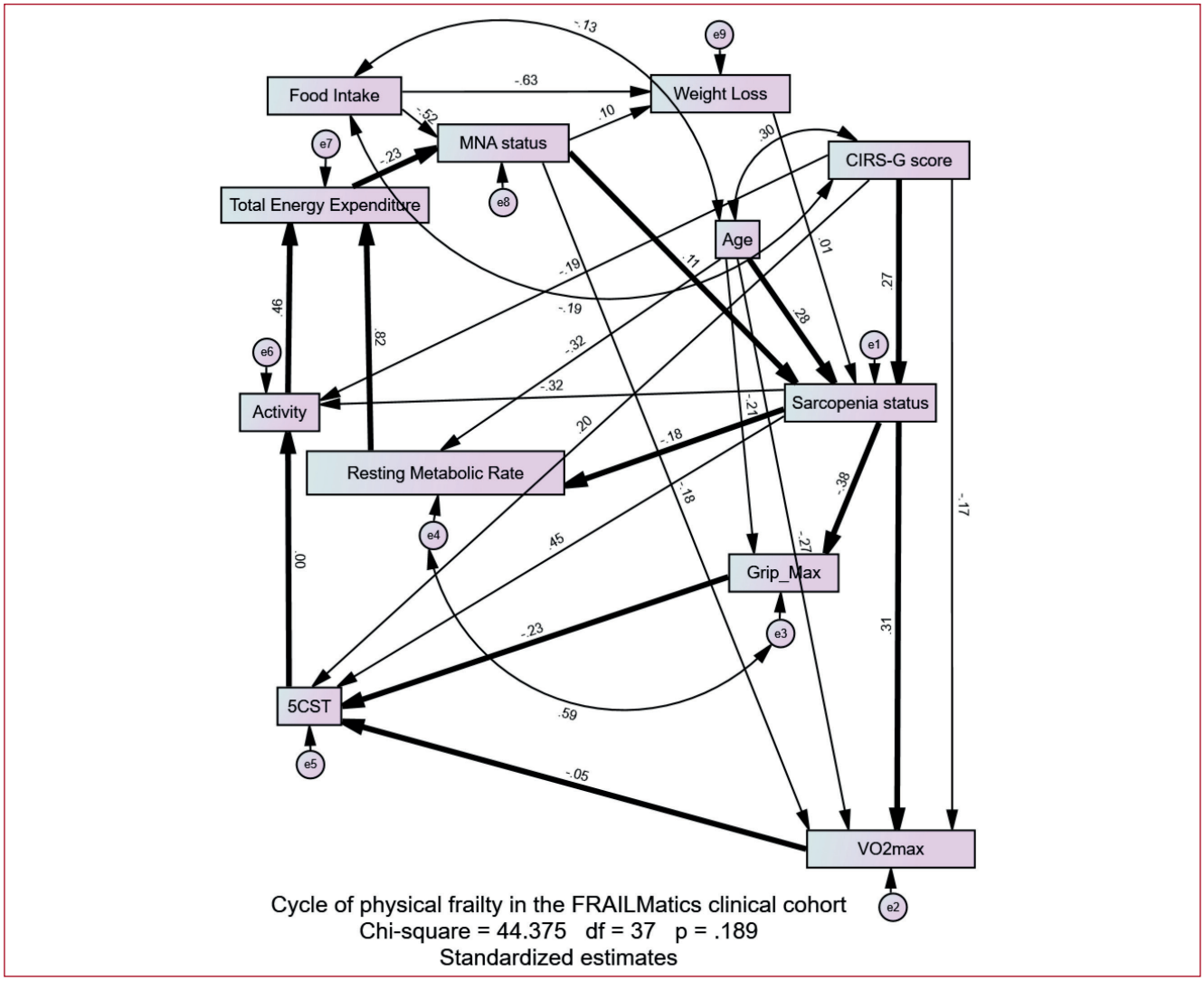

Figure 1. Structural equation model depicting the cycle of physical frailty incorporating data from 102 falls clinic attendees. The cycle of frailty main hypothesized pathways1 are depicted by bold arrows. MNA status: MNA®-SF status; CIRS-G: Cumulative Illness Rating Scale-Geriatric; Grip_Max: maximum handgrip strength; 5CST: 5-times chair stand test; Activity: physical activity; e: error term; df: degrees of freedom.

test[5]; maximum handgrip strength (kg) defined as the highest value obtained from four consecutive measurements while seated, two from the right hand and two from the left hand, using a Jamar Hydraulic Hand Dynamometer (Performance Health, Wisconsin, USA)[5]; basal (resting) metabolic rate (BMR, kcal/day), measured by the TANITA® device[4]; time in seconds to complete a 5-times chair stand test (5CST)5; self-reported physical activity assessed by the question: "*How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or doing a walk?*" (1: Hardly ever or never; 2: One to three times a month; 3: Once a week; 4: More than once a week)[10]; total energy expenditure (TEE) (kcal/day), defined as BMR x activity factor, where the following activity factors were assigned to the four aforementioned physical activity categories: 1.2 (hardly ever/never); 1.375 (one to three times/month); 1.55 (once a week); 1.725 (more than once a week)[11]; self-reported food intake in the last month (0: diminution in desire for food and/or eating less than usual; 1: no change in desire for food and/or eating the same as usual; 2: increase in desire for food and/or eating more than usual)[10]; and self-reported weight loss in the past month (0: no; 1: yes).

IBM® SPSS® Statistics version 27 was used to compute descriptive statistics in the included sample of 102 adults. The mean age was 69.8 years (standard deviation [SD]

Hypothesized effect	Unstandardized Estimate	Standard Error	p
VO_2max ← age	-0.161	0.061	**0.008**
Sarcopenia status ← CIRS-G score	0.053	0.018	**0.003**
Physical activity ← CIRS-G score	-0.055	0.029	0.061
Sarcopenia status ← age	0.020	0.006	**0.002**
BMR ← age	-9.783	3.018	**0.001**
Weight loss ← food intake	-0.554	0.076	**<0.001**
VO_2max ← CIRS-G score	-0.283	0.167	0.090
MNA®-SF status ← food intake	-0.772	0.118	**<0.001**
5CST ← CIRS-G score	0.338	0.132	**0.011**
Handgrip strength ← age	-0.206	0.089	**0.021**
5CST ← Handgrip strength	-0.144	0.052	**0.005**
TEE ← Physical activity	258.959	6.242	**<0.001**
VO_2max ← sarcopenia status	2.631	0.905	**0.004**
TEE ← BMR	1.592	0.022	**<0.001**
5CST ← VO_2max	-0.053	0.075	0.477
Sarcopenia status ← weight loss	0.013	0.193	0.947
Weight loss ← MNA®-SF status	0.058	0.051	0.260
Sarcopenia status ← MNA®-SF status	0.136	0.121	0.260
MNA®-SF status ← TEE	<0.001	<0.001	**0.006**
Handgrip strength ← sarcopenia status	-5.189	1.271	**<0.001**
Physical activity ← sarcopenia status	-0.494	0.177	**0.005**
VO_2max ← MNA®-SF status	-1.869	0.966	0.053
BMR ← sarcopenia status	-77.651	43.261	0.073
5CST ← sarcopenia status	3.840	0.755	**<0.001**
Physical activity ← 5CST	<0.001	0.021	0.998
Age ←→ CIRS-G score	11.456	3.968	**0.004**
CIRS-G score ←→ food intake	-0.289	0.157	0.065
Age ←→ food intake	-0.547	0.425	0.197
e4 ←→ e3	1429.013	280.688	**<0.001**

CIRS-G: Cumulative Illness Rating Scale-Geriatric; BMR: basal (resting) metabolic rate; 5CST: 5-times chair stand test; TEE: total energy expenditure; MNA®-SF: Mini Nutritional Assessment® Short-Form; ←: regression; ←→: covariance. Main CF hypothesized effects 1 are highlighted in bold; statistically significant (p < 0.05) values are highlighted in bold.

Table 1. Structural equation model estimates.

10.3; minimum 50; maximum 93), and 58.8% were women. The median CIRS-G score was 6 (interquartile range [IQR]: 5). According to the MNA®-SF, 39.2% were at risk of malnutrition and 5.9% were malnourished. As per TANITA® assessment, 30.4% had probable sarcopenia and 13.7% were sarcopenic. The mean VO_2max was 35.6 ml/kg/min (SD 6.2), and the mean maximum handgrip strength was 25.8 kg (SD 9.9). Mean BMR was 1487.7 kcal/day (SD 317.4) and mean 5CST time was 16.0 seconds (SD 6.2). In terms of engagement in physical activities, 15.7% reported hardly ever or never; 1.0% one to three times a month; 5.9% once a week; and 77.5% more than once a week. In terms of self-reported food intake, 2.0% reported diminution in desire for food and/or eating less than usual; 11.8% no change in desire for food and/or eating the same as usual; 86.3% increase in desire for food and/or eating

more than usual; and 15.7% self-reported weight loss.

The SEM was tested using IBM® SPSS® Amos 27.0.0 (maximum likelihood method). Overall, the SEM was supported by the data (χ^2 = 44.4, df = 37, p = 0.189). In terms of model fit, the root mean square error of approximation (RMSEA) was 0.044 (95% confidence interval: <0.001 – 0.087, p = 0.546). Figure 1 displays the SEM results with standardized estimates (SE), illustrating the main CF hypothesized causal pathways[1] depicted by bold arrows. Table 1 shows the full model estimates.

In terms of the main CF hypothesized causal pathways 1, we observed significant (p < 0.05) regression weights for CIRS-G score → sarcopenia status (SE = 0.27, p = 0.003), age → sarcopenia status (SE = 0.28, p = 0.002), sarcopenia status → VO_2max (SE = 0.31, p = 0.004), sarcopenia status → handgrip strength (SE = -0.38, p < 0.001), handgrip strength → 5CST (SE = -0.23, p = 0.005), physical activity → TEE (SE = 0.46, p < 0.001), BMR → TEE (SE = 0.82, p < 0.001), and TEE → MNA®-SF status (SE = -0.23, p = 0.006).

However, MNA®-SF status → sarcopenia status (SE = 0.11, p = 0.260), sarcopenia status → BMR (SE = -0.18, p = 0.073), VO_2max → 5CST (SE = -0.05, p = 0.477), and 5CST → physical activity (SE < 0.01, p = 0.998) were not significant in the SEM. In this same clinical cohort, consistent with the SEM analysis presented herein, we previously demonstrated using multiple binary logistic regression that bioimpedance-measured appendicular skeletal muscle mass was not significantly associated with abnormal MNA®-SF but with frailty status measured by the frailty phenotype-based SHARE-FI tool[4]. Regarding sarcopenia status → BMR, the SEM regression approached significance (SE = -0.18, p = 0.073), suggesting potential statistical underpower in the SEM, especially considering that other larger studies previously reported a significant association between sarcopenia and BMR[12,13]. Furthermore, the lack of significance observed in the relationships VO_2max → 5CST and 5CST → physical activity could be attributed to the fact that in this analysis, 5CST served as a surrogate for usual gait speed, with the latter originally included in the CF hypothesis[1]. Although it has been previously proposed that 5CST might be useful as a substitute for gait speed when diagnosing sarcopenia[14], this modification could impact on its predictive ability in the context of the FP operationalisation[15].

In terms of additional CF hypothesized effects in the SEM, significant results were as expected: older age causing a reduction in VO_2max[16] (SE = -0.27, p = 0.008), BMR[17] (SE = -0.32, p = 0.001), and handgrip strength[18] (SE = -0.21, p = 0.021); reduced food intake leading to weight loss (SE = -0.63, p < 0.001) and worse MNA®-SF status (SE = -0.52, p < 0.001); higher CIRS-G score prolonging 5CST time (SE = 0.20, p = 0.011); and sarcopenia impairing 5CST time (SE = 0.45, p < 0.001) and physical activity (SE = -0.32, p = 0.005). The direct covariance between age and CIRS-G score (SE = 0.30, p = 0.004) was also as expected; and the covariance of error terms between maximum handgrip strength and RMR highlights that both these measures are influenced by anthropometric factors such as weight and/or height, age, and sex[17,18].

The proximity to statistical significance (p < 0.100) of certain anticipated effects might indicate statistical underpower within the SEM. This scenario is likely applicable to hypothesized effects, such as higher CIRS-G score leading to decreased physical activity (SE = -0.19, p = 0.061) and VO_2max (SE = -0.17, p = 0.090), along with a correlation with reduced food intake (SE = -0.13, p = 0.065). Similarly, it may pertain to worse nutrition status causing a decrease in VO_2max (SE = -0.18, p = 0.053). Notably, the exclusion of adults aged 50 to 64 from the sample, considering that the original FP was validated in adults aged 65 or over[3], would have further compromised the power of the SEM.

In terms of the remaining SEM effects (p ≥ 0.100), statistical underpower may have also been implicated in the non-significant inverse association between age and food intake[19] (SE = -0.13, p = 0.197). Additionally, limitations inherent in self-reporting, particularly in subjective weight loss, may have contributed to the lack of significance in hypothesized effects with sarcopenia and MNA®-SF status.

Further limitations include that our calculation of VO_2max was based on age-predicted maximal heart rate, which can be less accurate in non-healthy adults[9]; furthermore, while resting heart rate serves as a valid biomarker of cardiorespiratory fitness at the population level, the relationship between resting heart rate and fitness may be weakened by factors such as physical activity and adiposity[20]. Indeed, even though sarcopenia status → VO_2max was significant (SE = 0.31, p = 0.004), the direction of the association (sarcopenia increasing VO_2max) was counterintuitive[21], even if VO_2max in older subjects may be less influenced by muscle mass than in younger subjects[22]. Uth and colleagues observed that the ratio of maximal heart rate to resting heart rate could serve as a potential indicator for estimating VO_2max in well-trained men, but applicability to other groups was less certain[8]. Interestingly, no other standardized estimates in the SEM displayed an unexpected direction. Finally, the standard activity factors derived from the Harris-Benedict Equation, which were utilized to estimate Total Energy Expenditure (TEE) in our sample, may not accurately reflect the energy requirements of this clinical sample[23].

In conclusion, this study's primary strength lies in offering some empirical support for the CF hypothesis through SEM analysis of a clinical dataset comprising adult patients from a falls clinic, representing a novel methodological contribution to the literature. Nonetheless, limitations include the relatively small sample size, utilization of surrogate CF measures, and the lack of an independent sample for external validation of the model. Further research addressing these limitations is encouraged.

Ethics approval

The study received ethical approval from the Tallaght University Hospital (TUH)/ St. James's Hospital (SJH) Joint Research Ethics Committee (Project ID: 0221; approval date: 4 May 2021). Approval was also granted by St. James's Hospital Research & Innovation Office (Reference: 6567, approval date: 26 July 2021). The study adhered to the World Medical Association Declaration of Helsinki on ethical principles for medical research involving human subjects.

Consent to participate

All participants provided written informed consent for inclusion in the study.

Funding

This research was funded by Science Foundation Ireland (SFI), grant number 18/FRL/6188.

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