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Original Article

Frailty predicts short-term survival even in older adults without multimorbidity

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ABSTRACT

Background: Frailty and multimorbidity are both strongly associated with poor health-related outcomes, including mortality. Being multimorbidity one of the major determinants of frailty, we aimed to explore whether, and to what extent, frailty without multimorbidity plays an independent role in shortening life.

Methods: We used data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). Among the 3363 adults aged 60+ enrolled at baseline, those without multimorbidity (i.e.: less than two chronic diseases) (N = 1115) have been characterized according to Fried's frailty phenotype (i.e. robust, prefrail, and frail). The association between frailty and mortality was estimated using piecewise proportional hazard regression models in three five-year time periods.

Results: Among participants without multimorbidity, 424 (38%) were prefrail and 19 (2%) were frail. During the 15-year follow-up, 263 (24%) participants died: 19%, 29%, and 63% of those who were robust, prefrail, and frail at baseline, respectively. Within the first 5 years of follow-up, prefrail and frail participants had more than doubled mortality risk in comparison to robust ones (HR for pre-frailty 2.08, 95% CI 1.15–3.76; HR for frailty 2.69, 95% CI 1.22–5.97). Beyond 5 years, a trend of increased mortality rate was still detectable for prefrail and frail subjects in comparison to robust ones.

Conclusions: Physical frailty and pre-frailty are associated with short-term mortality in a cohort of older adults free from multimorbidity. Frailty could be a clinical indicator of increased risk of negative health outcomes even among subjects without multiple chronic conditions.

1. Introduction

Frailty is defined as a status of increased vulnerability to internal and external stressors due to the loss of homeostasis in several organs and systems. This condition can be detected in about 10% of the general old population and may be thought as a summary measure of clinical and subclinical alterations conferring such vulnerability [1]. Frailty is strongly associated with higher risk of mortality, hospitalization, poor quality of life, and health-related costs [2].

Notably, up to 70% of frail individuals are affected by two or more chronic diseases [3], a condition called multimorbidity. Multimorbidity per se is a strong determinant of several negative health outcomes and can be considered as a major contributor to the onset and worsening of frailty [4, 5]. Still, little is known about the relationship between multimorbidity and frailty [6, 7]. Few studies [8, 9] indirectly showed that frailty predicts mortality, mainly among those affected by multiple chronic conditions. Their findings support the hypothesis that multimorbidity might be the main driver of the association between frailty and mortality [10]. Anyhow, to the best of our knowledge, no study formally addressed the question of the prognostic ability of frailty in the absence of multimorbidity.

As multimorbidity is one of the major determinants of frailty, we aimed to explore whether and to what extent frailty without multimorbidity predicts shorter survival.

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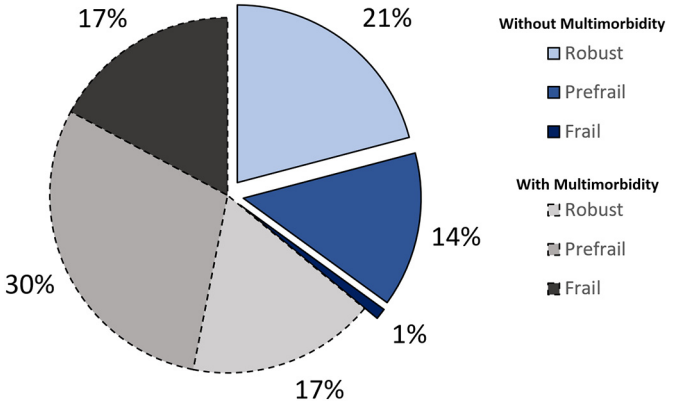

Fig. 1. Distribution of frailty and multimorbidity in SNAC-K, based on imputed data.

2. Methods

2.1. Study population

We analyzed data from the Swedish National study on Aging and Care in Kungsholmen (SNAC-K). SNAC-K is an ongoing population-based study established in 2001, whose population was randomly sampled among people aged 60+ living in a central area of Stockholm, Sweden. The Regional Ethical Review Board in Stockholm approved every phase of the study. Written informed consent was collected from participants or from a proxy in case of cognitive impairment. SNAC-K includes 3363 participants at baseline (73.3% participation rate). Out of these, we excluded 2153 (64%) subjects affected by multimorbidity. Of the remaining 1210 subjects, 95 (8%) had missing data for frailty, leaving a final sample of 1115 individual free from multimorbidity. Fig. 1 shows the distribution of multimorbidity and frailty in the SNAC-K study, based on imputed data. This study was reported in keeping with the STROBE recommendations. Demographic, clinical and functional information was gathered via standard questionnaires, medical examinations and interviews, neuropsychological assessments, and blood tests, as described elsewhere [11].

2.2. Frailty assessment

Physical frailty was operationalized according to the Cardiovascular Health Study criteria as reported by Fried et al. [3]. Briefly, the following domains were evaluated: gait speed, grip strength, exhaustion, weight loss, low activity (Table S1 shows the assessment used in this study). Participants were defined frail if they met at least three out of the five criteria, prefrail if they met one or two criteria, and robust otherwise.

2.3. Covariates

Diseases were coded according to the International Classification of Diseases 10th edition and multimorbidity was operationalized as the coexistence of at least two chronic diseases according to Calderón-Larrañaga et al. [12]. Cardiovascular risk factors (i.e. hypertension, obesity and dyslipidemia) were excluded from the count of chronic illnesses. Data on education, smoking and alcohol intake of participants were gathered. C-reactive protein (CRP) serum concentration was considered high when > 5 mg/dL. Malnutrition was defined as having a body-mass-index < 18.5 kg/m^2. Lower cognitive performance was defined as a Mini Mental State Examination (MMSE) score below 27.

Table 1
Characteristics of the study population according to physical frailty status.

	Robust	Prefrail	Frail	Total	P
	N = 672	N = 424	N = 19	N = 1115	
Demographics					
Age; years; mean ± SD	66.3 ± 6.9	68.0 ± 8.2	74.2 ± 10.3	67.1 ± 7.6	< 0.001
Female sex; n. (%)	393 (58)	239 (56)	10 (53)	642 (58)	0.723
Education					
Elementary; n. (%)	62 (9)	45 (11)	7 (36)	114 (10)	0.002
High school; n. (%)	294 (44)	197 (46)	6 (32)	497 (45)	
University; n. (%)	316 (47)	182 (43)	6 (32)	504 (45)	
Smoking habit					
Never; n. (%)	296 (44)	173 (41)	9 (47)	478 (43)	0.055
Former; n. (%)	274 (41)	158 (37)	8 (42)	440 (40)	
Current; n. (%)	99 (15)	92 (22)	2 (11)	193 (17)	
Alcohol consumption					
Never/occasional; n. (%)	116 (17)	91 (21)	11 (58)	218 (20)	0.001
Light/moderate; n. (%)	428 (64)	255 (60)	7 (37)	690 (62)	
Heavy; n. (%)	128 (19)	78 (18)	1 (5)	207 (19)	
Diseases					
Malnutrition; n. (%)	1 (0)	5 (1)	1 (5)	7 (1)	0.010
One of any cardio-metabolic diseases; n. (%)	32 (5)	35 (8)	1 (5)	68 (6)	0.060
One of any neuropsychiatric diseases; n. (%)	31 (5)	9 (2)	0 (0)	40 (4)	0.081
One of any musculo-skeletal diseases; n. (%)	36 (5)	36 (8)	1 (5)	73 (7)	0.106
Biomarkers					
CRP > 5 mg/dL; n. (%)	76 (12)	60 (15)	3 (17)	139 (13)	0.308
Functional assessment					
Lower cognitive performance; MMSE < 27; n. (%)	15 (2)	15 (4)	4 (27)	34 (3)	< 0.001
Disability; ≥1 ADL limitations; n. (%)	2 (0)	1 (0)	0 (0)	3 (0)	1.000

Missing data: 4 for smoking habit; 1 for malnutrition (based on BMI < 18.5); 37 for CRP; and 25 for cognitive impairment. Abbreviations: CRP – C-reactive protein; MMSE – MiniMental State Examination; ADL – Activities of Daily Living. SD - standard deviation; Cardio-metabolic diseases: diabetes, heart failure, atrial fibrillation, ischemic heart disease. Neuropsychiatric diseases: dementia, depression and mood disorder, Parkinson's disease. Musculo-skeletal diseases: osteoarthritis, osteoporosis, dorsopathies, inflammatory arthropathies.