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The ability of three different models of frailty to predict all-cause mortality: Results from the European Male Aging Study (EMAS)

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ABSTRACT

Few studies have directly compared the ability of the most commonly used models of frailty to predict mortality among community-dwelling individuals. Here, we used a frailty index (FI), frailty phenotype (FP), and FRAIL scale (FS) to predict mortality in the EMAS. Participants were aged 40–79 years (n = 2929) at baseline and 6.6% (n = 193) died over a median 4.3 years of follow-up. The FI was generated from 39 deficits, including self-reported health, morbidities, functional performance and psychological assessments. The FP and FS consisted of five phenotypic criteria and both categorized individuals as *robust* when they had 0 criteria, *prefrail* as 1–2 criteria and *frail* as 3+ criteria. The mean FI increased linearly with age (r^2 = 0.21) and in Cox regression models adjusted for age, center, smoking and partner status the hazard ratio (HR) for death for each unit increase of the FI was 1.49. Men who were *prefrail* or *frail* by either the FP or FS definitions, had a significantly increased risk of death compared to their *robust* counterparts. Compared to robust men, those who were FP *frail* at baseline had a HR for death of 3.84, while those who were FS *frail* had a HR of 3.87. All three frailty models significantly predicted future mortality among community-dwelling, middle-aged and older European men after adjusting for potential confounders. Our data suggest that the choice of frailty model may not be of paramount importance when predicting future risk of death, enabling flexibility in the approach used.

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1. Introduction

Although specific definitions and models of frailty remain contested there is broad agreement that it describes a non-specific state reflecting age-related declines in multiple physiological systems, which in turn lead to an increased risk of adverse outcomes including morbidity, hospitalization, institutionalization and mortality (Rockwood, Mitnitski, Song, Steen, & Skoog, 2006). Frailty may be conceptualized as a state characterizing the broad health of individuals, facilitating risk classification across a wide range of people and conditions (Rockwood & Mitnitski, 2007). While this implies that frailty need not be operationalized as a clinical syndrome, extensive research has focused on identifying those older people with and without a frailty syndrome, defined in terms of specific criteria such as exhaustion, slowness, low or decreased activity, weakness and unintentional weight loss (Fried et al., 2001; Kuh & New Dynamics of Ageing Preparatory, 2007). An alternative approach has been to construct an index of frailty by summing the number of accumulated age-related symptoms or deficits a person has to derive a score to predict future risk of adverse outcomes (Rockwood & Mitnitski, 2007).

Currently, the most commonly used approaches to characterize frailty include the FI of Rockwood and colleagues (Mitnitski et al., 2005; Rockwood & Mitnitski, 2007), the FP described by Fried and colleagues (Fried et al., 2001), and the FS proposed by the International Academy of Nutrition, Health and Aging (IANA) (Abellan van Kan, Rolland, Bergman, et al., 2008; Abellan van Kan, Rolland, Morley, & Vellas, 2008), but its utility has not been fully explored. The phenotypic approach has the advantage of being relatively simple to administer, although the relatively restrictive set of criteria may not be applicable to all individuals. Conversely, while frailty indices may offer a broader coverage of deficits than simpler models and also allow identification of high functioning individuals, they are more time consuming in terms of data collection and may be less practical to apply in a clinical setting.

Although index based and phenotypic definitions of frailty have proved useful in predicting a range of deleterious health outcomes (Sternberg, Wershof Schwartz, Karunananthan, Bergman, & Mark Clarfield, 2011), there are few data describing how well the most commonly used frailty models predict mortality in older men living in different regions of the European Union. In this study we utilized the cohort of men participating in the European Male Aging Study to examine and compare the utility of three frailty models adapted from existing index and phenotypic approaches to predict all-cause mortality. A secondary aim was to investigate which of the individual component criteria of our frailty models were associated with mortality.

2. Methods

2.1. Participants and study design

Details concerning the study design and recruitment for the EMAS have been described previously (Lee et al., 2009). Briefly, an age-stratified probability sample of 3369 men aged 40–79 (mean ± *SD*: 60 ± 11) years were recruited from population registers in eight European centers (Florence, Italy; Leuven, Belgium; Malmö, Sweden; Manchester, UK; Santiago de Compostela, Spain; Łódź, Poland; Szeged, Hungary; Tartu, Estonia). Participants completed a postal questionnaire and then attended a research clinic for further assessments. The men were subsequently invited to attend a follow-up assessment and completed another postal questionnaire a median of 4.3 years later (range 3.0–5.7 years). Ethical approval for the study was obtained in accordance with local institutional requirements in each center, with all participants providing written informed consent.

2.2. Assessments

The postal questionnaire included questions concerning general health and lifestyle, including age leaving education, smoking and alcohol consumption. Participants were asked whether they were currently being treated for various morbidities including heart conditions, hypertension, bronchitis, asthma, diabetes, liver disease, kidney conditions, prostate disease and thyroid disorders, and if they had ever been treated for cancer or had suffered a stroke.

The assisted questionnaire which men completed when they attended for assessment included the Medical Outcomes Study 36-item Short Form survey (SF-36) (Ware & Sherbourne, 1992), Beck's Depression Inventory-II (BDI-II) (Beck, Steer, & Brown, 1996), International Prostate Symptom Score (IPPS) (Bosch, Hop, Kirkels, & Schroder, 1995), the Physical Activity Scale for the Elderly (PASE) (Washburn, Smith, Jette, & Janney, 1993), Reuben's Physical Performance test (PPT) (Reuben & Siu, 1990) and Tinetti's balance and postural stability index (Tinetti, Williams, & Mayewski, 1986). Cognitive function was assessed using three neuropsychological tests; the Rey–Osterrieth Complex Figure test (Osterrieth, 1944), the Camden Topographical Recognition Memory test (Warrington, 1996) and the Digit-Symbol Substitution test (Uiterwijk, 2001). Anthropometric measurements included height, weight, mid-upper arm circumference, and triceps skin fold thickness. Body mass index (BMI) was calculated as body weight (kg) divided by the square of height (m^2).

2.3. Frailty

Frailty was characterized using three commonly used approaches: a FI, FP and FS. The FI is based on the number of health deficits present in an individual divided by the total number of deficits considered (range 0–1) (Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008). Thirty-nine deficits were included in the EMAS FI, representing symptoms, signs, or functional impairments that accumulate with age and are individually related to adverse outcomes. The EMAS FI has been described previously (Tajar et al., 2011) and includes items from the Medical Outcomes Study 36-item Short Form survey, Beck's Depression Inventory-II, Reuben's Physical Performance test, Tinetti scale, in addition to morbidities and cognitive function (Appendix A). Binary variables were recoded such that 0 indicated the absence and 1 the presence of a deficit. For categorical variables with an intermediate response (e.g., sometimes/maybe), an additional value of 0.5 was used. Continuous variables were dichotomized based on the distribution of participants' scores; cut points were the worst-performing 10th centile. We have previously shown that the EMAS FI is linked with poorer sexual health (Lee, Tajar, et al., 2013), low levels of serum vitamin D (Tajar et al., 2012), and disruption in hormones of the hypothalamic–pituitary–testicular axis (Tajar et al., 2011).

Frailty was also assessed using a phenotypic definition adapted from the Cardiovascular Health Study (Fried et al., 2001) based on five criteria: sarcopenia, exhaustion, slowness, weakness, and low activity. The EMAS FP has been described previously (O'Connell et al., 2013), and details of the EMAS criteria alongside the Cardiovascular Health Study original are shown in Appendix B. The FP variable was categorized as follows: 0 criteria = *robust*, 1–2 criteria = *prefrail*, and 3+ criteria = *frail*. The EMAS FP has been shown to be linked with increasing age, falls, and impaired quality of life (O'Connell et al., 2013).

Finally, we used an adaption of the IANA frailty scale (FRAIL) (Abellan van Kan, Rolland, Bergman, et al., 2008) to derive the FS categories. The original FRAIL scale is a simple 5-question instrument and has been validated in a number of population groups including older, community-dwelling men. The adapted