European Geriatric Medicine 7 (2016) 531–537

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Research paper

Factors associated with frailty in community-dwelling elderly population. A cross-sectional study

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ARTICLE INFO

Article history:
Received 18 July 2016
Accepted 26 September 2016
Available online 25 October 2016

Keywords:
Frailty
Elderly
Prevention
Functional capacity
Nutritional status
Comorbidities
Pain
Medication

ABSTRACT

Background: Frailty is a major public health problem. Designing effective preventive measures requires an understanding of frailty mechanisms and risk factors.
Objective: To identify the main social, clinical and analytical factors associated with frailty.
Methods: An observational cross-sectional study of community-dwelling individuals aged 75 years and older was performed.
Results: One hundred and seventy men and 154 women were recruited (mean age 80.1 years). Frailty was associated with age, female sex, educational level, certain comorbidities (osteoarthritis, peripheral vascular disease, stroke, depression, cancer, diabetes, dyspepsia and hypertension), geriatric syndromes, previous falls, pain, number of medications, anorexia, nutritional status, physical activity, muscle mass, obesity, anaemia, kidney function and C-reactive protein. Frailty was not associated with serum levels of ghrelin, testosterone, insulin or IGF-1.
Conclusions: Factors identified as associated with frailty may alert healthcare professionals and help them to identify subjects at risk fragilization. Good control over underlying diseases and pain, rationalizing use of medications, optimizing nutritional status and body weight, promoting physical activity and improving social support may contribute to preventing or even reverting frailty. However, these hypotheses need to be tested.

1. Introduction

Frailty is a geriatric syndrome defined as a state of increased vulnerability to stressors associated with age-related declines in physiological reserves across different organs and systems [1]. Although prevalence varies significantly according to different studies due to the lack of a common operational definition, one systematic review reported a rate of 11% for community-dwelling people aged 65 years and older [2]. Prevalence increases with age and is slightly higher for women than for men. Several studies show that frail people are at greater risk of falls, functional decline, disability, dependence, and institutionalization [3,4]. Frailty, by its negative effect on physical and psychological functions and social relationships, represents a significant burden on healthcare and social resources [5]. Moreover, the ageing of the population means that frailty and its consequences are becoming a major public health problem and a challenge that needs to be urgently addressed by healthcare systems [6]. There is evidence suggesting that frailty can be prevented and reverted, however, the causes of frailty are not well understood. Designing effective preventive measures requires understanding frailty mechanisms and risk factors. The aim of this study was to identify main social, clinical and biochemical factors associated with frailty in community-dwelling elderly individuals and to assess possible differences according to sex.

2. Material and methods

2.1. Study design and population

An observational cross-sectional study was performed of community-dwelling subjects aged 75 years and older. A sample was pre-selected from the database of 3 primary care centres, two in the city of Mataró (“Mataró-Centre” and “Cirera-Molins”) and one in the nearby village of Argentona, both municipalities in the province of Barcelona (Spain). These databases register more than 99% of the population assigned to these primary care centres.

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http://dx.doi.org/10.1016/j.eurger.2016.09.005
1878-7649/

Mataró is an industrial city with 124,280 inhabitants in the west Mediterranean coast. "Mataró-centre" provides primary care health services in an aged population in the centre of the city, and Cirera-Molins in a peripheral working class neighborhood. Argentona is a rural and residential village with 11,963 inhabitants. Sampling was stratified by gender. Pre-selected subjects were invited by telephone to an appointment at the physician's office to be informed about the study. Individuals were excluded if they had active malignancy, dementia or serious mental illness, had a life expectancy of less than 6 months, were in a palliative care programme or were institutionalized. Of the individuals contacted, 49% refused to participate and 15% were excluded as not fulfilling selection criteria. The 36% who agreed to participate, representing 324 individuals, signed the informed consent form. Recruitment took place from January to July 2014. The hospital research ethics committee approved the study protocol (code 64/13).

2.2. Frailty definition

Subjects were classified as robust, pre-frail or frail according to the following 5 Fried criteria [7]:

- unintentional weight loss of $\geq$ 4.5 kg in the last 12 months;
- exhaustion, considered to be the case if the subject answered 3 days or more to either or both of 2 questions: "How often in the last week did you feel you could not get going?" and "How often in the last week did you feel that everything you did was an effort?
- low physical activity, measured as total weekly kcal of physical activity expenditure of $<$ 383 kcal in men/ $<$ 270 kcal in women;
- slow walking speed, measured as $<$ 0.65 m/s for a height of $\leq$ 173 cm in men/$\leq$ 159 cm in women or $<$ 0.76 m/s for a height of $>$ 173 cm in men/ $>$ 159 cm in women;
- poor grip strength, measured (using a hand-held JAMAR dynamometer), as $\leq$ 29 kg for body mass index (BMI) $\leq$ 24, $\leq$ 30 kg for BMI 24.1–28 and $\leq$ 32 kg for BMI $>$ 28 in men/ $\leq$ 17 kg for BMI $\leq$ 23, $\leq$ 17.3 kg for BMI 23.1–26, $\leq$ 18 kg for BMI 26.1–29 and $\leq$ 21 kg for BMI $>$ 29 in women.

Persons were classified as follows: robust if they fulfilled none of the above criteria; pre-frail if they fulfilled 1 or 2 criteria; and frail if they fulfilled 3 or more criteria. Gait speed was measured as the time it took for the patient to travel 4.57 m at its usual speed step. The patient was positioned approximately 2 m behind the starting line and then he/she was asked to start normally walking. The time since the first foot crossed the starting line until the first foot crossed the finish line was measures by a chronometer (in seconds). The exercise was repeated twice and the best score was considered. Hand-grip was measured in the dominant hand by a hand-held JAMAR dynamometer. The patient had to stand with the dominant arm 15° separate from the body and the elbow slightly flexed. He/she was asked to press with full force three times with a rest of 30 seconds between them. The best result was registered.

2.3. Study factors and data collection

Study factors included:

- nutritional status: assessed by anthropometric measurements (weight, height, BMI), recent weight loss and the short-form Mini Nutritional Assessment (MNA-sf) questionnaire;
- hormone levels: fasting plasma levels of total ghrelin, IGF-1, testosterone and insulin were determined using validated commercial kits;
- inflammatory markers: fasting plasma levels of interleukin-6 (IL-6) and C-reactive protein (CRP) were determined using validated commercial kits;
- physical exercise: assessed by the International Physical Activity Questionnaire (IPAC) and daily outdoors walking hours;
- body composition: fat mass, lean mass and muscle mass as a percentage of total body weight were assessed by bioimpedance analysis (Bioelectrical Impedance Analyser, EFG3Elecrtofluidgraph®, AkernSRL) and fat distribution was assessed by triceps skin fold, waist and hip circumferences and waist-hip circumference ratio;
- hand-grip strength: assessed in kg by the hand-held JAMAR dynamometer.

Other study variables included sociodemographic characteristics (age, sex, education level, family support); comorbidities; geriatric syndromes; chronic medication; appetite and satiety assessed by the visual analogue scale (VAS); functional capacity assessed by the Barthel Index, Timed Up-and-Go Test (TUG), unipodal stand test, falls and gait speed; and, finally, a complete blood count (CBC) and basic blood biochemical analyses for glucose, creatinine, albumin and lipid profile. Information on comorbidities and medications was obtained from the electronic medical records held by the corresponding centres. All other information was obtained directly from the patient by trained healthcare professionals.

2.4. Statistical analysis

All data were coded and recorded in an electronic database for scrubbing and analysis. Continuous variables were described using means and standard deviations and categorical variables were described using percentages. Comparisons across the 3 study groups (robust, pre-frail and frail) were made using the χ^2 test or the Fisher's exact test for categorical variables and ANOVA or the Kruskal–Wallis test for numerical ones. To assess factors associated with frailty, the robust and pre-frail groups were pooled together in a non-frail group so that frail versus non-frail subjects could be compared. The odds ratios (OR) and their 95% confidence intervals (CI) were used as a measure of association between studied factors and frailty and were calculated using logistic regression. All variables first underwent bivariate analysis; only those significantly associated with frailty (for $P < 0.10$) were used to fit multivariate models using the stepwise method. When multicollinearity was detected for the different variables, the most generic variable was selected. Initially, three partial multivariate models were fitted: one for sociodemographic and life style variables, another for pathologies and medication and a third for analytical parameters. A final multivariate model was fitted with variables that showed a $P < 0.10$ in these partial models. Bivariate analyses were performed on the overall sample and separately for men and women.

3. Theory/calculation

Many physiological changes that appear with age, such as the activation of certain inflammatory processes, changes in body composition (such as loss of lean body mass), hormonal imbalances (such as those caused by menopause, andropause, corticopause and somatopause), loss of appetite, insulin resistance, etc. may play a role in triggering the onset of the frailty process [8]. Ghrelin is a gastrointestinal peptide that increases appetite and food intake, regulates the energy balance, stimulates the anabolic growth hormone (GH)/insulin-like growth factor 1 (IGF-1) axis and inhibits certain inflammatory cytokines that have negative effects on appetite and anabolism [9]. Some studies have noted a decline in ghrelin levels with age [10,11], suggesting that this peptide may play a role in the pathogenesis of sarcopenia and frailty. Frailty is