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ORIGINAL ARTICLE

# Prevalence of frailty and its associated factors in patients with rheumatoid arthritis: a cross-sectional analysis

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## Abstract

**Objectives** The aims of the present research were to assess the prevalence of frailty and its potential associated factors in a cohort of adult patients with rheumatoid arthritis (RA).

**Methods** Consecutive RA patients and healthy controls were assessed according to the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI), and classified as frail, pre-frail, or non-frail. Chi-square, analysis of variance (ANOVA), and multinomial logistic regression analyses were used to test the prognostic value of frailty for the outcomes of interest.

**Results** Two hundred and ten consecutive RA patients (65.7% female, mean age 60.4 years) and 100 healthy controls (63% female, mean age 59.1 years) were included. According to SHARE-FI criteria, 35 RA patients (16.6%) were categorized as frail, 68 (32.4%) as pre-frail, and 107 (51%) as non-frail, while 8 control subjects were categorized as frail, (8%), 17 as pre-frail (17%), and 75 as non-frail (75%) (chi-squared 12.8; $P = 0.0016$). The results from logistic regression analysis revealed that age (odds ratio [OR] = 1.12, 95% confidence interval [CI] = 1.07–1.17; $P < 0.0001$), comorbidities (OR = 1.51, 95% CI = 1.01–2.27; $P = 0.0446$), and high disease activity (OR = 1.10, 95% CI = 1.04–1.16; $P = 0.0006$) were independently associated with frailty in RA.

**Conclusions** Frailty or pre-frailty are common in RA. The SHARE-FI may be a useful tool for the screening of frailty in RA and may summarize the results of a comprehensive RA assessment providing a marker of deficits accumulation.

**Keywords** Comorbidities · Frailty syndrome · Grip strength · Rheumatoid arthritis · SHARE-FI

## Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic synovial joint inflammation, which determines restriction of the joint mobility and deformities leading to cartilage destruction, bone erosion, and impairment in joint integrity and, consequently, may reduce physical function and patient's quality of life [1]. RA may predispose patients to different factors that can induce frailty, including sarcopenia, fatigue, and low activity [2–6]. Frailty is defined as a syndrome with multiple causes and contributors characterized by decrease of strength, endurance, and reduced physiological function. This condition enhances the individual's vulnerability for developing increased dependency and/or death [7, 8].

In terms of prevalence, about half of older adults have to deal with frailty. In a systematic review, Collard and colleagues reported an average prevalence rate of 10.7% of frailty in community-dwelling older persons and 41.6% for pre-frailty [9].

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Until now, the accepted definition of frailty is that proposed by Fried et al. which encompasses phenotypic criteria suggestive of compromised energetics: low grip strength, low energy, slowed walking speed, low physical activity, and/or unintentional weight loss. When a subject meets three of the five criteria, the subject can be defined as frail [8]. Among RA patients, the prevalence of frailty is comparable to, or even greater, that of older geriatric cohorts and pre-frailty, a condition including a major health vulnerability between robust and frail, is much more prevalent in RA than in geriatric cohorts [10].

The concept of frailty is a recent issue in the rheumatologic field; by now, the prevalence of frailty among individuals with RA has not been extensively examined and few studies on frailty in RA adults have been conducted. Moreover, the relationship between frailty and sociodemographic or disease characteristics in RA is unknown.

The present study aims to address this gap in the literature by assessing the prevalence of frailty in a cohort of adult patients with RA and examining its associations with sociodemographic and disease characteristics.

## Materials and methods

### Study population

Between March 2016 and June 2018, the cross-sectional evaluation involved consecutive RA patients from the outpatient clinic of an Italian tertiary rheumatology center (Rheumatological Clinic, Università Politecnica delle Marche, "Carlo Urbani" Hospital, Jesi, Ancona). All the patients with an adult-onset RA, as defined by the American College of Rheumatology (ACR)/European League Against Rheumatism classification criteria (EULAR), have been involved [11].

The exclusion criteria were the presence of severe comorbidities that interfere with the evaluation of disease activity (i.e., Parkinson's disease, severe depression, Alzheimer's disease or other dementia, or that contraindicate treatment with conventional or biological disease-modifying antirheumatic drugs (c- or bDMARDs) (i.e., severe ongoing infections or ongoing malignancies)). Pregnant women were also excluded.

All patients were receiving at least one cDMARD (methotrexate, sulphasalazine, or hydroxychloroquine), or a bDMARD (infliximab, etanercept, adalimumab, certolizumab pegol, golimumab, abatacept, or tocilizumab). The cross-sectional cohort reflected a wide range of arthritis states/severity found in routine practice. The control group consisting of 100 healthy subjects was also enrolled.

Local ethical review board (Comitato Unico Regionale) approved the study, and patients provided written informed consent for the anonymous analysis of the data.

### Evaluation parameters

**Clinical assessment** The clinical evaluation included the following items: the Swollen Joint Count 28-joints (SJC) and the Tender Joint Count 28-joints (TJC), the 0–10 pain Numerical Rating Scale (NRS), and the Physician and Patient Global Assessments of disease activity (PhGA and PaGA, respectively) by 0–10 NRS.

**Evaluation of disease activity was performed with the Simple Disease Activity Index (SDAI)** SDAI employs the linear sum of five untransformed and unweighted variables (SJC+TJC+PaGA+PhGA+C-reactive protein (CRP) in mg/dl) with a range from 0 to 86. Patients were categorized in disease activity states according to the SDAI definition: remission (REM) $>0$ and $\leq 3.3$, low disease activity (LDA) $>3.3$ and $\leq 11$, moderate disease activity (MDA) $>11$ and $\leq 26$, and high disease activity (HDA) $>26$ [12].

**Evaluation of functional capacity was performed through the Health Assessment Questionnaires Disability Index (HAQ-DI)** The HAQ-DI evaluates the degree of difficulty in accomplishing tasks in eight functional areas of daily life actions: dressing and grooming, arising, eating, walking, hygiene, reach, grip, activities. For each question, patients are asked to rate level of difficulty over the past week on a four-point scale (from 0—no difficulty to 3—unable to perform), with higher scores indicating more disability. In each functional area is considered the greater value. The HAQ-DI final score is given by the mean of the eight scales [13].

**Evaluation of articular damage was evaluated according to the Simple Erosion Narrowing Score (SENS)** An experienced musculoskeletal radiologist (MC) scored the radiographs of the hands, wrists, and feet according to SENS. A detailed description of SENS is beyond the purpose of this paper and the reader can rely on the original article [14].

**Evaluation of the comorbidities burden was performed with the modified Rheumatic Disease Comorbidity Index (mRDCI)** The mRDCI formula is: 1* lung disease and [2* (myocardial infarction, other cardiovascular diseases, or stroke) or 1* hypertension] and 1* (ulcer or other gastrointestinal diseases) and 2* kidney disease and 1* if body mass index (BMI) is $>30$ kg/m$^2$ or 2* if BMI is $>35$ kg/m$^2$, and 1 for each of diabetes, fracture, depression, and cancer [15].

### Frailty definition

For frailty definition, the Survey of Health, Ageing and Retirement in Europe (SHARE) variables previously selected by Santos-Eggimann and colleagues were used [16].

In particular, exhaustion was identified with the question: "In the last month, have you had too little energy to do the things you wanted to do?". A positive answer coded as 1, a negative answer as 0.

The weight loss criterion was identified by reporting a "Diminution in desire for food" in response to the question: "What has your appetite been like?" or, in the case of a non-specific or uncodeable response to this question, by responding "Less" to the question: "So, have you been eating more or less than usual?". The presence of the criterion was coded as 1, its absence as 0.

Weakness was assessed by handgrip strength using an electronic grip device (a five-force sensor (FSR-402) manufactured by Interlink Electronics connected to an Arduino Mega 2560). Two consecutive measurements were taken from the left and right hands. The highest of the four was selected (this variable was considered as continuous).

Slowness was defined as a positive answer to either of the following two items: "Because of a health problem, do you have difficulty [expected to last more than 3 months] walking 100 metres?" or "... climbing one flight of stairs without resting?". One or two positive answers were scored 1, and two negative answers were scored 0.

The low activity criterion was evaluated 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?". This variable was kept ordinal: 1 = "More than once a week"; 2 = "Once a week"; 3 = "One to three times a month"; and 4 = "Hardly ever or never."

The parameters abovementioned allowed the calculation of the SHARE Frailty Instrument (SHARE-FI); its calculators (one for each sex) are freely accessible on the Web [18]. Entering the data into the calculator, the tool provides a continuous frailty score (i.e., the predicted discrete factor score, whose formulae are in the paper) and enables automatic classification into phenotypic frailty categories: non-frail, pre-frail, and frail. SHARE-FI represents the first European research effort towards a common frailty language at the community level [17, 18].

### Statistical analysis

Data were stored in a Microsoft Excel database and have been processed with MedCalc 18.0.0 (statistical software packages for Windows XP). Data are presented as median and interquartile ranges (IQR) as well as means and standard deviations (SD), where appropriate. The Kolmogorov–Smirnov test was used to verify the normal distribution (our data were generally normally distributed).

The frailty phenotype comparison (dependent variable) was tested with the chi-square test or Fisher's exact test for comparison with categorical variables. The non-parametric Spearman's rank correlation coefficient was used to assess relationships between clinical, functional, and radiological measures and SHARE-FI scores. Differences in characteristics among frailty categories were tested with one-way analysis of variance (ANOVA), or Kruskal-Wallis analysis as appropriate. In order to assess the relative contribution of the individual determinants (age, sex, disease duration, mRDCI, BMI, PhGA, PaGA, NRS pain, SDAI, HAQ-DI, and SENS) on the SHARE-FI score (as the dependent variable), multivariate logistic regression models procedure was used. Analysis with backward elimination included variables that yielded $P$ values of 0.1 or lower in the initial univariate analysis. $P$ values < 0.05 were considered statistically significant.

## Results

A total of 210 RA patients have been enrolled, 138 (65.7%) were women. The mean ± SD age was 60.4 ± 13.5 years, the mean ± SD disease duration was 7.5 ± 2.7 years, and the mean ± SD BMI was 26.3 ± 4.3 kg/m$^2$. One hundred and fifty (71.4%) subjects were positive for rheumatoid factor. With regard to treatment, 178 (84.7%) patients were assuming cDMARDs (178 [70.9%] methotrexate, 18 [8.6%] sulphasalazine, and 11 [5.2%] hydroxychloroquine), while 78 (37.1%) patients were taking bDMARDs (18 [8.6%] adalimumab, 16 [7.6%] etanercept, 15 [7.1%] abatacept, 12 [5.7%] tocilizumab, nine [4.2%] certolizumab pegol, five [2.4%] golimumab, and three [1.4%] infliximab). Forty-seven (22.4%) patients were treated with oral steroids.

The 100 healthy controls were represented by 63 females and 47 males, with mean age of 59.1 ± 14.5 years.

Of the 210 RA patients, 101 (48.1%) reported one or more medical comorbidities. The more frequent conditions were arterial hypertension (10.4%), cardiovascular diseases (9.0%), gastrointestinal diseases (7.6%), and diabetes mellitus (6.6%). The mean mRDCI was 1.94 ± 2.03.

According to the SDAI definition, 22 patients (10.5%) were in REM, 38 subjects (18.1%) in LDA, 65 patients (30.9%) in MDA, and 85 subjects (40.5%) in HDA. The mean SDAI was 29.7 ± 11.0.

The mean score of SHARE-FI was 2.22 (SD = 2.65), showing a high level of adverse health outcomes of the participants. According to SHARE criteria, 103 participants (49%) fulfilled the frailty criteria. In particular, 35 (16.6%) patients were categorized as frail, 68 (32.4%) as pre-frail, and 107 (51%) as non-frail, whereas eight control subjects were categorized as frail, (8%), 17 as pre-frail (17%), and 75 as non-frail (75%). The difference between groups was significant (chi-squared 12.8; $P = 0.0016$). Focusing on grip strength, patients with rheumatoid arthritis showed significantly lower mean values than healthy controls (17.24 vs. 20.38 kg; $P < 0.001$).

**Table 1** Demographic and disease-related characteristics of the whole cohort (210 patients)

| | Mean | SD | Median | 25–75 percentiles |
|---|---|---|---|---|
| Gender | | | | |
| Male *n* (%) | 72 (34.3%) | | | |
| Female *n* (%) | 138 (65.7%) | | | |
| Age (years) | 60.36 | 13.45 | 60.00 | 49.00–72.00 |
| Disease duration (years) | 7.47 | 2.74 | 7.00 | 5.00–10.00 |
| BMI (kg/m$^2$) | 26.24 | 4.28 | 25.45 | 23.03–28.71 |
| RF (%) | 150 (71.4%) | | | |
| Educational level (years) | 12.17 | 3.69 | 13.00 | 8.00–16.00 |
| Patient with comorbidities, *n* (%) | 101 (48.1%) | | | |
| mRDCI (0–13) | 1.94 | 2.03 | 1.00 | 0.00–3.00 |
| HAQ-DI (0–3) | 1.21 | 0.61 | 1.00 | 0.87–1.50 |
| SDAI (0–86) | 29.68 | 11.03 | 29.06 | 22.88–37.33 |
| SENS (0–86) | 15.20 | 14.02 | 12.00 | 3.00–23.00 |
| PhGA (NRS 0–10) | 4.81 | 1.80 | 5.00 | 3.00–6.00 |
| PaGA (NRS 0–10) | 6.46 | 1.74 | 7.00 | 6.00–8.00 |
| Pain (NRS 0–10) | 4.72 | 2.56 | 4.00 | 3.00–7.00 |
| SHARE-FI | 2.22 | 2.65 | 1.11 | 1.08–1.36 |

*BMI* body mass index, *RF* Positivity of Rheumatoid Factor, *mRDCI* modified Rheumatic Disease Comorbidity Index, *HAQ-DI* Health Assessment Questionnaire – Disability Index, *SDAI* Simplified Disease Activity Index, *SENS* Simple Erosion Narrowing Score, *PhGA* physician global assessment of disease activity, *PaGA* patient global assessment of disease activity, *NRS* numerical rating scale, *SHARE-FI* Survey of Health, Ageing and Retirement in Europe Frailty Instrument

Table 1 summarizes the demographic and disease-related characteristics of the RA cohort.

Stratifying the patients according to the frailty categories, frail subjects were older ($P < 0.001$), with a low educational level ($P = 0.041$), and with a longer disease duration ($P = 0.008$), compared to non-frail participants. Frail patients showed higher SDAI scores ($P < 0.001$), HAQ-DI scores ($P = 0.002$), pain levels ($P = 0.01$), and higher radiographic damage ($P = 0.045$).

**Table 2** Participant characteristics and comparison according to the frailty group

| | Frail ($n = 35$ patients) | | | | Pre-frail ($n = 68$ patients) | | | | Non-frail ($n = 107$ patients) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Median | 25–75 P | Mean | SD | Median | 25–75 P | Mean | SD | Median | 25–75 P | *P* values |
| Age (years) | 75.34 | 9.12 | 77.00 | 73.25–80.00 | 68.01 | 9.55 | 70.00 | 66.00–75.00 | 50.60 | 8.06 | 50.00 | 45.00–56.00 | < 0.001 |
| Disease duration (years) | 8.17 | 2.80 | 9.00 | 6.00–11.00 | 8.01 | 2.62 | 9.00 | 5.50–10.00 | 6.89 | 2.69 | 6.00 | 5.00–9.00 | 0.008 |
| Educational level (years) | 9.77 | 3.91 | 8.00 | 7.25–13.00 | 11.55 | 3.40 | 13.00 | 8.00–13.00 | 13.34 | 3.33 | 13.00 | 13.00–16.00 | 0.041 |
| BMI (kg/m$^2$) | 25.02 | 3.62 | 24.26 | 22.39–26.64 | 26.38 | 4.73 | 26.77 | 26.68–29.89 | 26.24 | 4.13 | 25.39 | 23.38 28.86 | 0.112 |
| mRDCI (0–13) | 5.11 | 1.99 | 6.00 | 5.00–6.00 | 1.94 | 1.49 | 2.00 | 1.00–3.00 | 0.91 | 1.05 | 1.00 | 0.00–1.00 | < 0.001 |
| HAQ-DI (0–3) | 1.41 | 0.61 | 1.32 | 1.00–1.90 | 1.33 | 0.62 | 1.12 | 0.92–1.62 | 1.06 | 0.58 | 1.00 | 0.62–1.32 | 0.002 |
| SDAI (0–86) | 40.64 | 9.00 | 41.40 | 37.91–45.37 | 32.90 | 9.40 | 32.99 | 26.95–39.02 | 24.04 | 8.93 | 25.17 | 20.40–29.80 | < 0.001 |
| SENS (0–86) | 19.00 | 15.95 | 16.00 | 4.25–28.00 | 14.86 | 13.60 | 11.00 | 4.00–22.50 | 14.17 | 13.54 | 12.00 | 3.00–22.00 | 0.045 |
| PhGA (NRS 0–10) | 5.25 | 1.85 | 5.00 | 4.00–7.00 | 5.23 | 1.54 | 5.00 | 4.00–6.00 | 4.40 | 1.89 | 4.00 | 3.00–6.00 | 0.040 |
| PaGA (NRS 0–10) | 6.94 | 1.16 | 7.00 | 6.00–8.00 | 6.66 | 1.21 | 7.00 | 6.00–7.00 | 6.17 | 2.10 | 7.00 | 5.00–8.00 | 0.003 |
| Pain (NRS 0–10) | 5.62 | 2.72 | 6.00 | 3.25–8.00 | 5.02 | 2.48 | 5.00 | 3.00–7.00 | 4.24 | 2.48 | 4.00 | 3.00–5.75 | 0.010 |
| SHARE-FI | 7.69 | 0.73 | 7.65 | 6.98–8.43 | 2.13 | 1.06 | 1.80 | 1.41–2.50 | 0.49 | 0.37 | 0.30 | 0.25–0.98 | < 0.001 |

*BMI* body mass index, *mRDCI* modified Rheumatic Disease Comorbidity Index, *HAQ-DI* Health Assessment Questionnaire – Disability Index, *SDAI* Simplified Disease Activity Index, *SENS* Simple Erosion Narrowing Score, *PhGA* physician global assessment of disease activity, *PaGA* patient global assessment of disease activity, *NRS* numerical rating scale, *SHARE-FI* Survey of Health, Ageing and Retirement in Europe Frailty Instrument

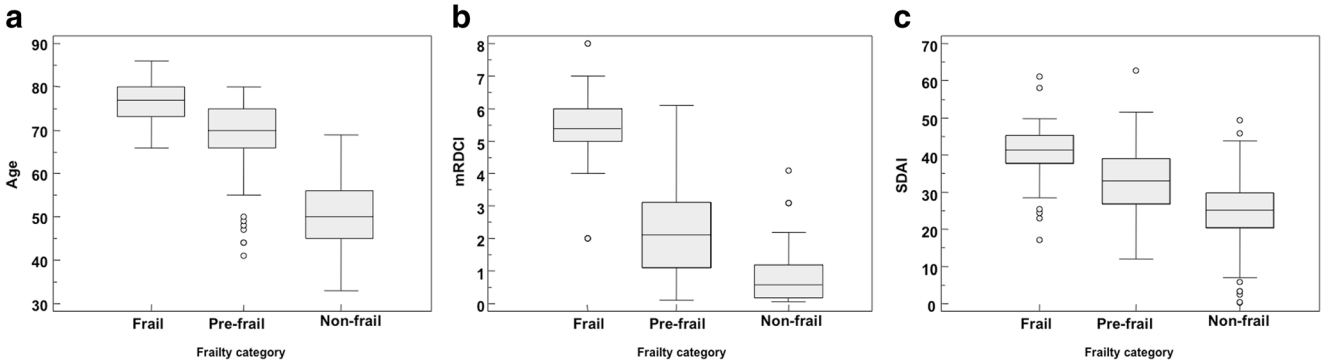


**Fig. 1** Box-and-Whisker plots of age (**a**), modified Rheumatic Disease Comorbidity Index (mRDCI) (**b**), and Simplified Disease Activity Index (SDAI) (**c**) for each frailty category. The boxes include the values from 25th to 75th percentiles; the lines inside the boxes are the medians

Moreover, as expected, mRDCI differed significantly between patients classified as frail, pre-frail, and non-frail ($P < 0.001$) (Table 2). Thus, age, disease activity (SDAI score), and comorbidities (mRDCI score) represented the three principal variables linked to frailty (Fig. 1a–c). No significant differences were found in treatment (bDMARDs, cDMARDs, or corticosteroid) through the frailty categories.

The logistic regression analysis confirmed that age (odds ratio [OR] = 1.12, 95% CI = 1.07–1.17; $P < 0.0001$), coexistence of comorbidities (OR = 1.51, 95% CI = 1.01–2.27; $p = 0.0446$), and high disease activity (OR = 1.10, 95% CI = 1.04–1.16; $P = 0.0006$) were independently associated with frailty in RA patients (Table 3).

The strong correlations between SHARE-FI and age, mRDCI, and SDAI were corroborated also by two-tailed Spearman's rank correlation coefficient (respectively, rho = 0.634; rho = 0.501; rho = 0.504; all $P < 0.001$) (Fig. 2a–c).

Analyzing frailty according to age (grouping together patients over and under 65 years), substantial differences have been found. Respectively, the percentage of frail in RA was 2.5% in younger patients, and 36.4% in elderly patients ($P < 0.001$). Pre-frailty was detected in 11.5% of the younger patients, and in 57.9% of the elderly ($P < 0.001$) (Fig. 3). Similarly, the percentage of frail in healthy subjects was 1% in younger patients, and 7% in elderly patients ($P < 0.001$), whereas pre-frailty was detected in 2% of the younger subjects, and in the 15% of the elderly ($P < 0.001$).

## Discussion

In this study, we revealed that frailty or pre-frailty are common conditions in RA patients. To the best of our knowledge, this is the first study showing that a validated definition of the frailty phenotype can be applied to an adult RA cohort and that this definition of frailty identifies potential factors causing severe impairment [8, 19, 20]. The main factors associated with frailty were age, disease activity, and comorbidity burden.

The aging of the population is a general problem for Western countries [21]. It is even more so when aging is associated with chronic and disabling diseases such as RA. Although RA can occur in individuals of any age, its incidence continues to increase with age at least into the seventh decade of life and possibly beyond [22]. Crowson and colleagues reported that the cumulative lifetime risk of developing RA is < 1% before 50 years of age, but greatly increases for both genders starting at approximately 60 years of age and then plateaus after 80 years of age [23].

The prevalence of frailty in geriatric cohorts is variable in different studies around the world. However, age is a major risk factor for developing frailty: the 26.1% of the subjects over 85 years is frail [9]. In a systematic review considering the Fried phenotype, the prevalence of frail individuals aged 65 years and over was 9.9%, and 44.2% the pre-frails [9]. The variability can be attributed to differences in the definition of frailty in the population studied. Findings from the SHARE

**Table 3** Logistic regression analysis showing the variables independently associated with frailty in rheumatoid arthritis patients

| Variable | Coefficient | Standard error | Odds ratio | 95% CI | *P* value |
|---|---|---|---|---|---|
| Age (years) | 0.1168 | 0.0240 | 1.12 | 1.07–1.17 | < 0.0001 |
| mRDCI (0–13) | 0.4154 | 0.2068 | 1.51 | 1.01–2.27 | 0.0446 |
| SDAI (0–86) | 0.0987 | 0.0289 | 1.10 | 1.04–1.16 | 0.0006 |
| Constant | − 10.1751 | | | | |

*mRDCI* modified Rheumatic Disease Comorbidity Index, *SDAI* Simplified Disease Activity Index

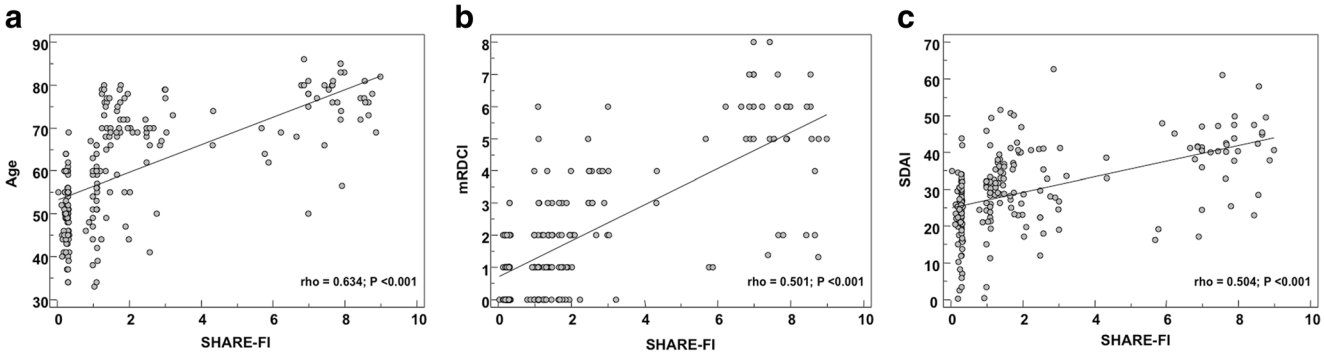


**Fig. 2** Correlations (Spearman's rho) between the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) and age (**a**), modified Rheumatic Disease Comorbidity Index (mRDCI) (**b**), and Simplified Disease Activity Index (SDAI) (**c**)

cohort estimated 12.1% of people aged 65 years as frail in Germany [16], and a cross-sectional study in Italian community-dwelling older adults estimated that 14% of participants were frail and 55% pre-frail [24].

The prevalence of frailty observed in our RA cohort is greater than those observed in a cohort of elderly patients with osteoarthritis (OA) (10%) [25], and is comparable to those observed in patients with chronic obstructive lung disease (COPD) [26]. Recently, Andrews and colleagues investigated frailty in a RA cohort, finding a prevalence of 13% [10]; this percentage is comparable to the average prevalence of 4–11% in geriatric cohorts that are at least 10 years older [27, 28].

RA belongs to those chronic inflammatory conditions (i.e., cancer, heart failure, COPD, chronic kidney disease, Crohn's disease, systemic lupus erythematosus) and musculoskeletal disorders (i.e., OA) associated with muscle loss [29, 30].

These prerequisites make RA a condition closely linked to the sarcopenia. Sarcopenia has been suggested as a human model of physical frailty, and it is defined as a condition characterized by progressive and generalized loss of skeletal muscle mass and strength, with the risk of adverse outcomes such as physical disability, poor quality of life, and death [31]. In this study, we assessed weakness evaluating the muscular performance through grip strength. In the SHARE-FI definition, grip strength is the only objective parameter. Grip strength testing is likely to be increasingly used in clinical settings, for example in the assessment of sarcopenia in the elderly, and has already been used as an outcome measure in RA clinical trials [32]. There are several different instruments available for measuring grip strength [33]: we measured it using an electronic grip device. In a RA clinical setting, grip strength showed to be a major aspect in the assessment of both disability and hand function [34], predicting functional ability in both cross-sectional and longitudinal studies [35].

The presence of comorbidities, common in older age, can lead to a minor strength altering the individual performance. Comorbid conditions are disproportionately increased in RA, and adversely affect quality of life, disability, and other outcomes [36]. Advancing age over the long course of the disease may also considerably contribute to increase levels of comorbidity, while age itself is associated with a decrease in physical function.

We found a clear incremental association between the comorbidity burden and pre-frailty and frailty. At baseline, 48.1% of our patients reported at least one comorbid condition. This prevalence is in accordance with previous findings [37]. However, to date, there is no consensus on which comorbidity index is optimal for rheumatic health outcomes research. We used the mRDCI which is an excellent index employed in RA and also in other inflammatory joint diseases [38, 39].

We found also a significant relationship between disease activity and frailty. The finding that systemic high-level inflammation is strongly associated with frailty is consistent with the consensus that inflammation is associated with aging

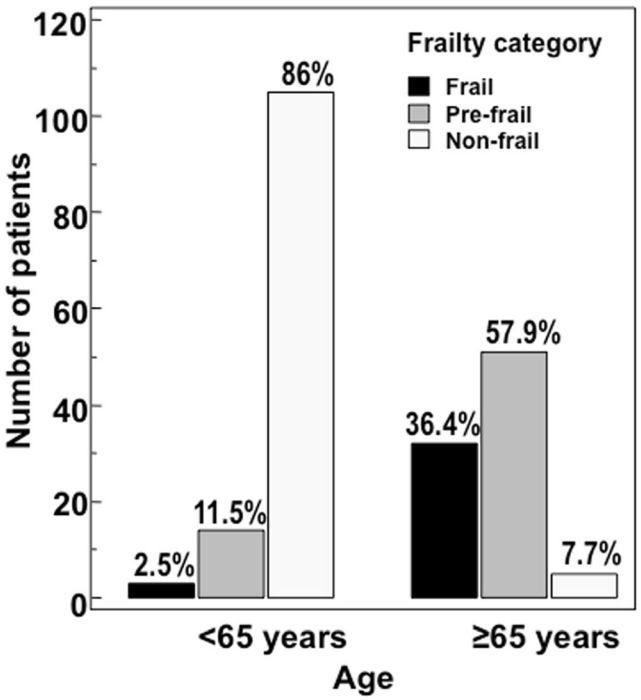


**Fig. 3** Histograms showing the frailty distribution according to age (dichotomous distinction over and under 65 years)

and chronic age-related diseases too [40]. Cross-sectional studies demonstrated both an association of high levels of interleukin-6 and tumor necrosis factor α with low muscle mass and strength [41, 42], while low levels of CRP are related to higher grip strength [43].

The results of the present study should be interpreted in light of different limitations. First of all, the absolute numbers of RA participants with frailty was low and restricted analyses. Secondly, the participants were representative of a relatively small area of Italy: although included according to rigorous criteria, it is impossible to generalize the results to the entire aged population. Thirdly, some potential clinical confounder determinants for frailty, like cognitive decline or major depressive disorder, were not included. Finally, the absence of a wider set of geriatric clinical outcomes (i.e., hospitalization, institutionalization, falls, use of health services) did not allow the evaluation of the impact of psychosocial factors and physical frailty in a more exhaustive and complete way.

In conclusion, our results support the use of SHARE-FI criteria to measure frailty in patients with RA. The prevalence of frailty among this RA cohort is greater than that of older geriatric cohorts. Clinically oriented prospective studies of frailty are needed to evaluate the importance of diagnosing pre-frailty or frailty and to study potential interventions to decrease risks and poor health outcomes.

**Author's contribution** FS and MC contributed to the study conception and design. MDC, EDD, and SF contributed to the acquisition of data. FS and MDC contributed to the analysis and interpretation of data. FS and MDC drafted the article. FS, MDC, SF, EDD, and MC contributed to the revision of the manuscript. SF, EDD, and MC revised it critically for important intellectual content. All authors approved the final version of the manuscript to be published.

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## Compliance with ethical standards

The local ethical review board (Comitato Unico Regionale) approved the study, and patients provided written informed consent for the anonymous analysis of the data.

**Disclosure** None.



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