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Editorial

Frailty in Inflammatory Arthritis: A Fragile Construct

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Due to the exponential growth of the aging population, the concept of frailty cannot be ignored anymore in the field of rheumatology.[1] Frailty is a common geriatric syndrome and although no consensus definition has been developed, frailty is generally characterized as a "decline in functioning across multiple organs systems accompanied by an increased vulnerability to stressors."[2] In older patients, seemingly minor stressors (eg, change in medication, minor balance disturbances) may already increase the risk for adverse outcomes, such as mobility impairment.[1,3] This cycle of events further increases the vulnerability to new stressors, such as a fall. Ultimately, the threshold to permanent disability is crossed.[3] Frailty is closely linked to resilience. Resilience represents the capability of a person to recover from a stressor and maintain homeostasis.[4]

Frailty is rarely an isolated phenomenon, as frailty often accumulates in older patients together with other geriatric syndromes, multimorbidity, and polypharmacy. Frailty can be both an outcome and a predictor of other health issues.[1,3]

The presence of frailty inevitably complicates the management of older patients with rheumatic diseases (RDs) as frail patients have an increased likelihood of adverse outcomes such as iatrogenic complications, hospitalization, and mortality.[3] The concept of frailty and its operationalization therefore deserves a closer look. In this editorial, we discuss the promises, nuances, and pitfalls of frailty assessment approaches, so that rheumatologists can critically appraise and appropriately use the concept to improve patient care.

Although the concept of frailty is widely recognized nowadays, there is still much debate about how to practically translate this concept for use in clinical and research settings.[5] A gold standard to measure frailty is not available. Correct identification of frailty may, however, help to guide prognosis and individualized care planning.[6] Since 2001, many researchers have therefore tried to operationalize definitions of frailty.[7] This has resulted in the development of more than 60 assessment instruments that attempt to measure frailty and distinguish frail from nonfrail older persons.[5] These instruments most likely measure different constructs of frailty, as Aguayo et al found, with only 10.4% of the possible 595 paired comparisons among 35 frailty assessment instruments achieving better than fair agreement by κ statistics.[8] It also seems that several of these instruments do not exclusively measure frailty but assess related constructs such as disability, resulting in a potentially invalid assessment of frailty as well as misclassification.[5]

Generally speaking, frailty assessment instruments can be categorized under 3 groups: the (1) phenotypic, (2) multidimensional, and (3) cumulative deficits approach (Figure).[3,6] The frailty phenotype proposed by Fried and colleagues is one of the most widely accepted phenotypic models and is based on the co-occurrence of at least 3 of 5 physical criteria, including unintentional weight loss, self-reported exhaustion, low physical activity, slow gait speed, and weak grip strength.[2] Next to the purely physical criteria of the phenotypic approach, the multidimensional approach also incorporates cognitive, psychosocial, and/or environmental items, such as memory loss, anxiety, loneliness, and social isolation.[3,6] Rockwood and colleagues developed the cumulative deficits approach or Frailty Index.[9] It examines a number of predefined possible deficits in an individual (ie, stroke, mobility impairment, difficulty with cooking, laboratory abnormalities) and the more deficits are counted in an individual patient, the more likely the individual is to be frail (Figure).[9]

Both the absence of a clear frailty definition and the abundance of available assessment instruments may explain the broad

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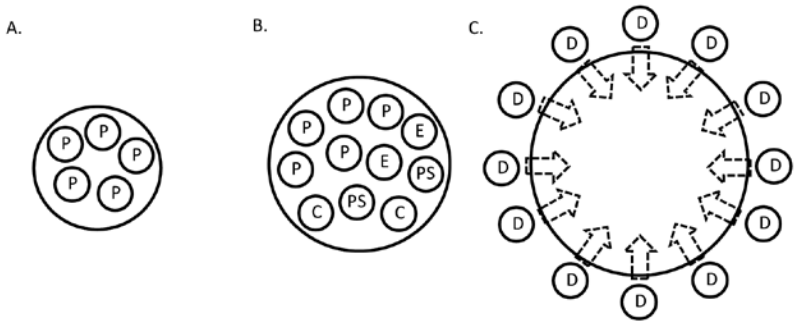

Figure. Abstract representation of 3 groups of frailty assessment instruments. (A) Phenotypic approach: based on physical criteria to define frailty. (B) Multidimensional approach: next to physical criteria, cognitive, psychosocial, and/or environmental items are also included to define frailty. (C) Cumulative deficits approach: a predefined number of deficits are assessed (signs, symptoms, impairments, diseases) and included in the Frailty Index. C: cognitive items; D: deficits; E: environmental items; P: physical items; PS: psychosocial items.

frailty prevalence range found in the literature. A recent meta-analysis of 240 population-based studies from 62 countries showed that the pooled prevalence of frailty when using the Fried physical phenotype approach was 12% (95% CI 11-13), compared to 24% (95% CI 22-26) for the cumulative deficits approach.[10] Overall prevalence rates increased with age in this latter study[10] and ranged from 11% (95% CI 8-14), when the minimum age for study inclusion was 50 to 59 years, to 31% (95% CI 29-34), when the minimum age for study inclusion was 80 to 89 years.[10] Prevalence rates were also generally higher in females (15-29%) compared to males (11-20%).[10] Another study that analyzed frailty prevalence trends in the United States found that prevalence rates were higher among ethnic minorities, nursing home residents, and persons from lower socioeconomic groups, pointing to the role of context and associated confounders.[11]

Reflecting further on variations between subgroups, it is even more challenging to estimate the true frailty prevalence in patients who also have RDs. Clearly, symptoms of frailty and symptoms of RDs can overlap importantly, further complicating measurement of both constructs.[1] For example, weak grip strength and slow gait speed are 2 of the Fried criteria, but they are also part of the disease symptomatology of most RDs.[1,2] Further, depression and anxiety are frequently seen both in patients with RDs and in frailty.[12] Most research about frailty prevalence in RDs focuses on patients with rheumatoid arthritis (RA), and rates depend on the chosen instrument and study characteristics, generally ranging between 15% and 65%, which are substantially higher than reported in the general population.[13,14]

Several prevalence studies in patients with RA also concluded that disease activity levels and Health Assessment Questionnaire scores are higher in frail patients. In a study of Salaffi et al, 210 patients with RA (65.7% female, mean age 60.4 yrs) and 100 controls (63% female, mean age 59.1 yrs) were included.[15] In total, 16.6% of the patients with RA vs 8% of the controls were frail on the Survey of Health, Ageing and Retirement in Europe (SHARE) frailty instrument. The logistic regression analysis revealed that high disease activity, as defined by a Simplified Disease Activity Index > 26, was independently associated with frailty in RA (odds ratio 1.10, 95% CI 1.04-1.16).[15] The association of disease activity and physical function with frailty points to the difficulty of the frailty concept in general in older patients with RA. Patients might seem frail when, in fact, they simply have active disease. On the other hand, presence of frailty might also distort scores of disease-specific instruments.[1]

Currently, only 1 frailty instrument has been specifically designed for patients with RA, the Comprehensive Rheumatologic Assessment of Frailty (CRAF).[14] The multidimensional CRAF investigates 10 health domains (nutritional status, weakness, falls, comorbidity, polypharmacy, social activity, pain, fatigue, physical function, and depression). Each domain is given a score of between 0 and 1 by using predefined cut-offs; the average of the 10 domains is calculated and the final score ranges from 0 (no deficits present) to 1 (all deficits present).[14] During the development phase of the CRAF, it was found that among 219 patients with RA (mean age 58.5 [SD 13.3] yrs), 36.1% were classified as nonfrail (CRAF ≤ 0.12), 28.8% as mild frail (CRAF 0.12 to ≤ 0.24), 15.5% as moderate frail (CRAF 0.24 to ≤ 0.36), and 19.6% as severe frail (CRAF > 0.36).[14] Further validation studies need to follow, however, as no data are available from a control population and cut-offs of many of the domains included in the CRAF were arbitrarily defined.[14]

Despite all abovementioned limitations, rheumatologists are beginning to see usefulness of frailty identification. It can be seen as a starting point to risk-stratify older persons facing potential stressors and to subsequently adapt treatment strategies in high-risk patients or refer these patients for geriatric care. Although the associations between frailty, adverse health outcomes, and inefficient care utilization have invariably been demonstrated, there is unfortunately no solid evidence base for a beneficial effect of care interventions specifically designed to manage frailty.[16] An important reason for failure of these care interventions is that patients are not properly selected for the intervention, most likely because of the unresolved issues with frailty identification.[1]

Nonetheless, the best available evidence to tackle frailty and its related outcomes seems to be a comprehensive geriatric assessment (CGA).[17,18] A CGA is "a multidisciplinary diagnostic

and treatment process that identifies medical, psychosocial, and functional limitations of a frail older person in order to develop a coordinated plan to maximize overall health with aging."[19] Following the CGA, additional interventions can be arranged, such as nutritional support, a physical exercise program, or social worker consultation, preferably coordinated by a multidisciplinary medical care team. When a CGA is applied on admission in specialist geriatric wards, older frail patients are more likely to be alive and in their own homes at follow-up.[17] There is low-certainty evidence that community-dwelling, older frail people who receive a CGA may have a reduced risk of unplanned hospital admission.[18] Reports on the effect of a CGA specifically in older frail patients with inflammatory RDs are not available at this moment.

In conclusion, the number of older frail persons with inflammatory RDs will increase inevitably over the next years due to population aging. Rheumatologists must therefore be prepared for tomorrow's complex longevity challenges.[1] Realizing progress in efficient and reliable frailty assessment would be a sensible starting point. It is therefore essential to first reach consensus about how to define frailty, undertake appropriate efforts to standardize its measurement, and validate the most promising instruments.[5] Researchers and clinicians should base their final choice for a frailty instrument on the intended purpose, domains covered, and context (eg, use in patients with RDs).[5] Specifically for the rheumatology field, the predictive validity of frailty instruments for progressive disability, mortality, and care utilization, independent of disease activity and physical function, should also be assessed.[20] Once this all has been realized, we can investigate which geriatric care interventions are (cost-)effective, feasible, and in line with the preferences of older persons with RDs and should become part of the management armamentarium of health professionals in rheumatology.[16]

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