Validation of two frailty questionnaires in older patients with rheumatoid arthritis: a cross-sectional study

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Abstract

Objective

Several questionnaires exist to assess frailty, a geriatric syndrome. None of these has been validated in older patients with rheumatoid arthritis (RA). Our objective was to assess aspects of validity of two frailty questionnaires: Groningen Frailty Indicator (GFI) and Geriatric 8 (G8) among RA patients.

Methods

In a cross-sectional study among patients ≥65 years information was collected on socio-demographics, disease characteristics including comorbidities and physical function and on frailty using the GFI and G8. Content validity was assessed by linking items of the GFI and G8 to the International Classification of Functioning, Disability and Health (ICF). Classic psychometric methods were used to test hypotheses on construct validity and interpretability.

Results

Eighty patients (74.6 years (SD 5.9); 66% female) participated. The GFI has more items on social and mental functions; the G8 more on functions of the digestive system (e.g. nutritional status). As hypothesised, correlations (r) with physical function (R_{GFI}=0.54; R_{G8}=0.56) and disease activity (R_{GFI}=0.24; R_{G8}=0.36) were moderate to weak. However, correlations with age (R_{GFI}=0.20; R_{G8}=0.11) or comorbidities (R_{GFI}=0.30; R_{G8}=0.16) were lower than expected. Instrument-specific thresholds classified 43 (54%) of participants as frail on the GFI and 44 (55%) on the G8; 33 (41%) were frail on both instruments.

Conclusion

The GFI and G8 differ in content with more emphasis on nutritional status for the G8. Both instruments are insensitive to age and comorbidities. Before deciding on their usefulness in RA, their predictive validity for mortality and resource utilisation independent of disease activity and physical function should be further evaluated.

Key words

ageing, frailty, rheumatoid arthritis, comorbidity

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Introduction

Over the next decades, the incidence and prevalence of rheumatoid arthritis (RA) will likely increase due to population ageing (1, 2). Because of the chronic inflammation inherent to RA, patients are also at increased risk of (accelerated) development of co- and multimorbidity (3). In addition, ageing is often accompanied by the development of frailty, a geriatric syndrome. Fried *et al*. defined the 'frailty phenotype' in 2001 as a 'physiologic syndrome of decline in physiological reserve and function on a multi-organ level', which may ultimately lead to increased vulnerability to stressors and adverse health outcomes, including mortality, falls and hospitalisation (4). Fried *et al*. defines frailty as a purely physical condition and uses several criteria to define a frail patient: low grip strength (adjusted for sex and body mass index (BMI)), unintentional weight loss (more than 4.5 kg over the last year), self-reported exhaustion, low physical activity and slower walking speed (adjusted for sex and height) (4). When at least three of these five Fried criteria are present, the patient is classified as being frail. Other, more practical frailty questionnaires, such as the self-reported Groningen Frailty Indicator (GFI) and the professional administered Geriatric-8 (G8) also include psychosocial aspects of frailty (*e.g*. loneliness) (5, 6). The reliability, feasibility and construct validity of the broadly used GFI in relation to daily functioning was supported in multiple studies with home-dwelling and institutionalised older people (7, 8). The Geriatric 8 (G8) was originally developed for vulnerable oncology patients who would benefit from a comprehensive geriatric assessment (CGA) before the start of chemotherapy and shows good screening properties (6, 9).

The average pooled prevalence of frailty, as defined by a variety of approaches, was 10.7% in a systematic review in community-dwelling adults aged >65 years (10). In chronic diseases, such as heart failure, the overall prevalence of frailty, defined by a variety of approaches, was estimated to be 44.5% (95% confidence interval, 36.2–52.8%) in a systematic review (11). Similar results were observed in patients with end-stage renal disease (12). Measurement of frailty in RA patients, however, is complicated, since several frailty criteria are part of the RA disease construct, for instance lower grip strength and slower walking speed due to sarcopenia. Using the Fried criteria among 124 RA patients with a mean age of 58 years who were selected and included in a longitudinal cohort study, 12.8% was already considered frail (13). Other instruments have never been applied in RA.

The GFI and G8 seem promising for use in RA. Both instruments are feasible for clinical studies and daily care, but have a different focus with GFI focussing on the role of ageing on functioning and the G8 on treatment intensification. Therefore, both can be of interest in management of RA and research on aging. The objective of our study is to explore the content and construct validity of two frailty questionnaires, the GFI and G8 in a cross-sectional setting among older RA patients.

Materials and methods

Study design, participants and assessments

The current cross-sectional study was conducted in one academic and one large non-academic clinic in the south of The Netherlands. Patients ≥65 years with RA according to the rheumatologist were consecutively recruited during a visit to the rheumatology outpatient clinic between January and April 2018. Patients who were unable to understand the study information were excluded. The institutional review board of the Maastricht University Medical Center approved the study and judged it could be exempted from formal evaluation. All participants provided written informed consent. In the information letter, patients received information on the frailty construct, the frailty questionnaires and that data will be used to improve patient care.

Data collection

In addition to demographic characteristics (*e.g*. age, marital status, educational level), information on disease duration and general medical history

was collected. Educational level was categorised in three categories: low (seven years of primary school or shorter to middle school/junior high school); intermediate (1 year of high school to high school degree); high (1 year of college / university to college / university degree). A researcher (SO) administered the GFI and G8 questionnaires, to ensure participation of older participants with visual impairment, mild cognitive impairment or illiteracy.

The 15-item GFI questionnaire assesses self-reported limitations over the last month in four domains: (1) physical (mobility, presence of comorbidity, fatigue, vision, hearing), (2) cognition, (3) social (emotional isolation) and (4) psychological (depressed mood and feelings of anxiety). All answer categories are dichotomised and a score of 1 indicates a problem or dependency. GFI takes less than 15 minutes to complete and a patient with a sum score of ≥4 (score range 0–15) is considered frail (5).

The 8-item G8 screens for important impairments in several health domains: nutritional status, weight loss, body mass index, motor skills, psychological status, number of medications, self-perception of health and an indication of age. The G8 takes 5 minutes to complete by the administrator, items have 2-4 answer categories (score 0–3) and scores of ≤14 (score range 0–17) indicates presence of frailty (6).

In addition, functional and disability status was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI) (14). The Rheumatic Disease Comorbidity Index (RDCI) was used to measure the comorbidity burden (15). The 28-joint Disease Activity Score erythrocyte sedimentation rate (DAS28-ESR and -CRP) was computed by the treating rheumatologist on the same day.

Analysis

The COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) was followed to assess and report the measurement properties of the GFI and G8 (16).

Content validity was defined as the degree to which the GFI and G8 adequately reflect the construct (*i.e.* frailty) to be measured. It was assessed by linking the content of the GFI and G8 to the International Classification of Functioning, Disability and Health (ICF), using the ICF linking rules of Cieza *et al.* (17). Further, participants in the cross-sectional survey are described with regard to limitations in each domain of the instruments.

Finally, internal consistency of both instruments was assessed using the Cronbach's alpha.

To investigate construct validity, five hypotheses were formulated on constructs with external constructs (14), and assessed through spearman correlations. Coefficients (r) of ≤0.40 were considered as weak, between 0.41 and 0.75 as moderate and ≥0.75 as strong (18).

We pre-specified that the GFI and G8:

- Hypothesis 1: have a strong mutual correlation.
- Hypothesis 2: correlated strongly with age.
- Hypothesis 3: correlated moderately with physical functioning / disability, as measured by the HAQ-DI.
- Hypothesis 4: correlated moderately with the comorbid burden, as measured by the RDCI.
- Hypothesis 5: correlated weakly with disease activity, as measured by DAS28-ESR.

Lastly, interpretability of the GFI and G8 was explored. First, using established thresholds to classify patients as frail, we hypothesised that higher scores on the GFI and G8 would be observed in older people who were: female, living alone, have a low educational level, using multiple medications and have higher levels of comorbidity and worse physical function. These characteristics are known to be highly prevalent in community-dwelling adults who suffer from frailty (19). Data for continuous variables were analysed using one-way ANOVA. Second, the possible presence of floor and ceiling effects was assessed, by analysing the percentage of patients who achieved each possible score on the GFI and G8. The commonly used 15% threshold for patients achieving the highest and lowest total score to define a ceiling and floor effect, respectively, was adopted (20). IBM SPSS Statistics 25 was used to analyse data.

Table I. Baseline characteristics of all patients included in the study.

	All patients (n=80)
Age in years (SD)	74.6 (5.9)
Age 65-75 years	42 (52.5)
Age 75+ years	38 (47.5)
Female sex	53 (66)
Living alone	24 (30)
Educational level	
Low	52 (65)
Intermediate	14 (18)
High	14 (18)
Smoking status	
Current smoker	8 (10)
Ex-smoker	55 (69)
Never smoked	17 (21)
GFI: mean (SD); n (%) frail	3.9 (2.2); 43 (54)
G8: mean (SD); n (%) frail	13.8 (1.9); 44 (55)
Frail on both GFI and G8	33 (41)
HAQ-DI score (SD)	0.84 (0.65)
RDCI (SD)	2.8 (1.6)
Disease duration in years (SD)	16.4 (10.6)
DAS-28 ESR score (SD) (total n=59)	2.7 (1.1)
DAS-28 CRP score (SD) (total n=16)	2.5 (0.7)
Number of prescribed drugs (SD)	6.6 (3.1)
Methotrexate	50 (63)
Other csDMARDs	15 (19)
NSAIDs	23 (29)
Glucocorticoids	23 (29)
bDMARDs	16 (20)

The values are expressed as number (percentage) of patients unless stated otherwise.
SD: standard deviation; HAQ-DI: Health Assessment Questionnaire Disability Index; RDCI: Rheumatic Disease Comorbidity Index; DAS28: Disease Activity Score of 28 joints; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; VAS: visual analogue scale; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; NSAIDs: non-steroidal anti-inflammatory drugs; bDMARDs: biological disease-modifying anti-rheumatic drugs; GFI: Groningen Frailty Index; G8: Geriatric-8.
Numbers may not add up due to rounding.

Results

In total, 80 RA patients (mean age 74.6 years (SD 5.9), age range 65-87 years; 66% female; mean disease duration 16.4 years (SD 10.6)) participated in this study. For the GFI, the average score was 3.8 (SD 2.2), with a score range of 0–8 (higher scores indicate a higher level of frailty). For the G8, the average score was 13.8 (SD 1.8), with a score range of 8–17 (higher scores indicate a lower level of frailty). Baseline

Table II. Linkage of the Groningen Frailty Index and Geriatric-8 to the International Classification of Functioning, Disability and Health.

ICF components	ICF category	Item GFI	Item G8
Body functions	Specific mental functions, memory functions (b144)	Complaints about memory	
	Specific mental functions, emotional functions (b152)	- Feeling down or depressed - Feeling nervous or anxious - Experience of emptiness - Missing people around - Feeling abandoned	
	Seeing an related functions, seeing functions (b210)	Impaired vision	
	Hearing and vestibular functions, hearing functions (b230)	Impaired hearing	
	Mark physical fitness (b455)	Mark global health status when compared to other people of same age	
	Functions related to the digestive system, ingestion functions (b510)		Decline in food intake due to issues with ingestion
	Functions related to the digestive system, weight maintenance functions (b530)		Lost weight
Activities and participation	Walking and moving, moving around in different locations (d460)	Walking around outside	Moving around within the home or goes out
	Self-care, toileting (d530)	Going to the toilet	
	Self-care, dressing (d540)	Dressing and undressing	
	Acquiring of necessities, acquisition of goods and services (d620)	Shopping	
Environmental factors	Products of substances for personal consumption (e110)	Polypharmacy	Polypharmacy
Personal factors			Age Body mass index
Not in ICF			Neuropsychological problems, dementia or depression (hc)

ICF: International Classification of Functioning, Disability and Health; GFI: Groningen Frailty Index; G8: Geriatric-8; hc: health condition.

characteristics can be found in Table I.

Content validity

In Table II, the content of the GFI and G8 is assessed by linking the categories of the questionnaire to ICF codes.

Information about sensory functions (seeing and hearing) are only part of the GFI. Items related to mental and emotional functions are more elaborately present in the GFI (six out of 15 items). Compared to the GFI, the G8 has more items on functions of the digestive system (*e.g.* nutritional status), health conditions (depression and dementia) and several personal factors (*e.g.* BMI). Items about polypharmacy and self-perceived health are present in both questionnaires (Table II).

Using the GFI, patients participating in the study were typically characterised by depressive feelings (54%), anxiety (40%) and polypharmacy (81%). For the G8, patients were characterised by limitations in maintaining body weight (20%) and presence of polypharmacy (81%). In the Supplementary material a complete list of all items of the GFI and G8 is provided (Suppl. Table S1).

The reliability or internal consistency of both the GFI (Cronbach's alpha 0.59) and G8 (Cronbach's alpha 0.32) indicated low average inter-item correlation.

Construct validity

Pre-specified hypothesis of correlation between the GFI or G8 and HAQ-DI (hypothesis 3) and DAS-28-ESR (hypothesis 5) were confirmed (Table III). Hypothesis 1, 2 and 4 were rejected, since there was only a moderate correlation between the GFI and G8 (r=0.51) and a weak correlation between age and the GFI (r=0.20) and G8 (r=0.11). There was also a weak correlation between the RDCI and the GFI (r=0.30) and G8 (r=0.16).

Interpretability

Scores differed between subgroups as hypothesised, except for age for both questionnaires and educational level and RDCI for the G8 only (Table IV). Applying the threshold for frailty of the GFI, 43 (54%) patients were classified as frail, the G8 classified 44 (55%) participants as frail; 54 (68%) were frail on either questionnaire; 33 (41%) on both questionnaires. Frail participants were more often female, more fre-

Table III. Hypothesis-testing of construct validity of GFI and G8 using Spearman correlations.

Hypothesis	Strength correlation	Correlation coefficient		Hypothesis confirmed
GFI and G8	Strong	0.51		No
	Strength correlation with either GFI or G8	Correlation coefficient, GFI	Correlation coefficient, G8	Hypothesis confirmed
Age	Strong	0.20	0.11	No
HAQ-DI	Moderate	0.54	0.56	Yes
RDCI	Moderate	0.30	0.16	No
DAS28-ESR	Weak	0.24	0.36	Yes

HAQ-DI: Health Assessment Questionnaire Disability Index; RDCI: Rheumatic Disease Comorbidity Index; DAS28: Disease Activity Score of 28 joints; ESR: erythrocyte sedimentation rate; GFI: Groningen Frailty Index; G8: Geriatric-8.

quently lived alone and suffered from polypharmacy. Depression was the only comorbidity that was significantly more present in frail participants. No signs of a floor or ceiling effects were present.

Discussion

Over the last few decades frailty has emerged as an important syndrome in geriatric medicine and multiple tools to screen for frailty have been developed (19). To the best of our knowledge, the first study investigating the measurement properties of two frailty questionnaires in older RA patients.

After linking to the ICF, differences in the content of the GFI and G8 was found. This indicates that general consensus about what frailty actually constitutes, is lacking. All together, the GFI has more items on mental and emotional functions and the G8 more on functions related to the digestive system (ingestion, weight control). These differences probably explain the moderate correlation between the GFI and G8 and why 21 (26%) patients were considered frail on either the GFI or G8, whereas only 33 (41%) patients were frail on both questionnaires. However, both the GFI and G8 were able to select a subgroup of older patients who were more often female, more frequently lived alone and characterised by polypharmacy. These characteristics are generally considered as important hallmarks of frailty (19). However, age and the comorbidity burden (except depression) did not differ between frail and non-frail patients and the corresponding correlation coefficients were low. Previous research suggests that frailty, age, comorbidity and disability are distinct entities, but that there is a complex interplay between them (21). For instance, frailty and comorbidity predict disability and vice versa. Comorbidity may also add to the development of frailty (12).

The considerable overlap that exists between frailty and consequences of RA itself, is likely due to a shared common ground. As an example, sarcopenia is an important hallmark of both frailty and RA. Since the interplay between RA and frailty is complex, we therefore need to be cautious when interpreting frailty questionnaires as screening instrument in older RA patients. It is important that we first define what frailty actually encompasses in the older RA population. Until that moment, on a daily practice level, selecting RA patients who also fulfil the frailty phenotype may be used to optimally allocate intervention resources to those who are most likely to benefit (22). As an example, in 173 older patients with chronic heart failure, who were randomised to either usual care or a multidisciplinary management, the mild-to-moderately frail patients experienced a significantly reduced risk of hospitalisation and mortality (23).

This study has several limitations. The design is cross-sectional which means there is no information on the role of frailty in predicting future relevant

Table IV. Discrimination between frail and non-frail RA patients.

	GFI Frail (n=43)	GFI Non-frail (n=37)	*p*-value	G8 Frail (n=44)	G8 Non-frail (n=36)	*p*-value
Age in years (SD)	75.7 (± 6.1)	73.2 (± 5.6)	0.07	75.2 (± 6.6)	73.7 (± 5.0)	0.26
Age 65-69 years	7 (16)	12 (32)	0.19	9 (20)	10 (28)	0.10
Age 70-74 years	11 (26)	12 (32)		12 (27)	11 (31)	
Age 75-79 years	12 (28)	7 (19)		8 (18)	11 (31)	
Age > 80 years	13 (30)	6 (16)		15 (34)	4 (11)	
Female	35 (81)	18 (49)	*<0.01*	35 (79)	18 (50)	<0.01
Living alone	19 (44)	5 (14)	*<0.01*	18 (41)	6 (17)	0.02
Low educational level	33 (77)	19 (51)	*0.04*	30 (68)	22 (61)	0.06
Intermediate educational level	6 (14)	8 (22)		10 (23)	4 (11)	
High educational level	4 (9)	10 (27)		4 (9)	10 (28)	
Polypharmacy	37 (86)	21 (57)	*<0.01*	38 (86)	20 (56)	<0.01
HAQ-DI	1.16 (±0.65)	0.48 (± 0.44)	*<0.01*	1.16 (±0.69)	0.46 (±0.45)	<0.01
RDCI (SD)	3.16 (±1.36)	2.35 (± 1.69)	*0.02*	3.00 (±1.41)	2.53 (±1.72)	0.18

The values are expressed as number (percentage) of patients unless stated otherwise.
SD: standard deviation; HAQ-DI: Health Assessment Questionnaire Disability Index; RDCI: Rheumatic Disease Comorbidity Index.

outcomes, such as falls and hospitalisation. The population consists mostly of patients with a low educational level. To ensure participation of patients with visual impairment, mild cognitive impairment or illiteracy, the researcher filled out the questionnaires together with the patient. However, by doing this, we might have introduced social desirability response bias. In addition, before signing informed consent, patients received information on the construct of frailty, the frailty questionnaires and that we wanted to use these data to ultimately improve patient care. In theory, the latter indeed may have stimulated patients to highlight needs. Patients with RA living in nursing homes or severely disabled patients who are not visiting outpatient clinics are not included and could be underrepresented. Reasons for non-participation were not documented, as rheumatologists recruited patients during their daily outpatient clinics.

In conclusion, frailty in RA patients needs further investigation, due to a significant overlap between both constructs. Future studies in RA patients should therefore first focus on (1) how to define frailty and (2) the best measurement method to screen for frailty. Before deciding on the usefulness of frailty questionnaires in RA, their predictive validity for mortality and resource utilisation independent of disease activity and physical function should first be evaluated.

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