

BRIEF REPORT

Prevalence of Frailty in Ankylosing Spondylitis, Psoriatic Arthritis, and Rheumatoid Arthritis: Data from a National Claims Dataset

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Objective. Frailty is associated with disability and mortality independent of age. Although studies have evaluated frailty in rheumatoid arthritis (RA), information on the prevalence of frailty in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) is limited. We aimed to determine the prevalence of frailty in AS and PsA and to evaluate whether characteristics known to be associated with frailty, including anxiety, differ among these three types of inflammatory arthritis.

Methods. We performed a cross sectional study of Centers for Medicare & Medicaid Services (CMS) beneficiaries aged 65 years or older with AS, PsA, or RA enrolled in 2014. We operationalized frailty using a validated claims-based frailty index. We also explored the prevalence of frailty among CMS beneficiaries younger than age 65 years with work disability, a younger population that also may be at risk of frailty.

Results. The prevalence of frailty in beneficiaries aged 65 years or older with AS and PsA was 45.2% and 46.7%, respectively, significantly lower than in RA (65.9%, $P < 0.05$). The prevalence of frailty in beneficiaries less than 65 years old was much lower overall, though still highest in RA; 11.7%, 4.4%, and 7.0% in RA, AS, and PsA, respectively ($P < 0.05$). Anxiety was significantly associated with frailty in subjects of all ages, particularly among those less than 65 years old ($P < 0.05$).

Conclusion. Almost half of beneficiaries with AS or PsA aged 65 years old or older were frail, higher than in younger disabled beneficiaries. Further studies are needed to understand the risks of developing frailty in these diseases. Frailty was associated with anxiety, particularly in the younger age groups.

Frailty, a state of decreased homeostatic reserve, is known to be associated with morbidity and mortality in the elderly (1) and has been associated with other adverse health outcomes, as well as increased healthcare utilization (2). Frailty is an important independent risk factor for disability in rheumatoid arthritis (RA) (3).

Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are types of spondyloarthritis (SpA) that preferentially affect younger

people and, when poorly controlled, lead to increased disability and worse health-related quality of life (4). AS and PsA often lead to impairment during prime working years and have been associated with decreased workplace productivity and early retirement (4). Limited preliminary data from a single-center cross-sectional study of patients with multiple types of SpA (including AS, PsA, undifferentiated SpA, and SpA associated with inflammatory

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bowel disease) compared with RA suggest that the prevalence of frailty is similar in both conditions (5). This study defined frailty according to the Fried frailty phenotype (1), which is measured at point of care and therefore cannot be applied retrospectively to large population-based cohorts. However, a claims-based frailty index (CFI) has been developed and validated for use in administrative datasets (6)

The aim of this study was to determine prevalence of frailty in Centers for Medicare & Medicaid Services (CMS) beneficiaries with AS or PsA compared with those with RA. We also evaluated differences in anxiety and fibromyalgia among frail and non-frail patients with RA, AS, and PsA. Anxiety and fibromyalgia are known to be associated with frailty and may help provide face validity for the CFI in patients with inflammatory arthritis (7,8). We also explored frailty prevalence and these associated characteristics among patients with AS, PsA, or RA enrolled in CMS Social Security Disability Insurance (SSDI). SSDI provides Medicare benefits to individuals less than 65 years old who have been deemed to have a work disability. This dataset provides the opportunity to evaluate whether work-disabled patients with inflammatory arthritis are similarly frail and whether frailty differs by disease.

PATIENTS AND METHODS

Study design. This is a cross-sectional study of CMS beneficiaries who were enrolled in 2014.

Inclusion criteria. We included individuals 18 years of age or older with International Classification of Diseases, Ninth Revision (ICD-9) codes for AS (ICD-9-CM 720.0x), PsA (ICD-9-CM 696.0x, 696.1x [only if another code for 696.0x available]), or RA (ICD-9-CM 714.xx), coded by a rheumatologist on at least 2 occasions at least 7 days apart (9). All participants were continuously

enrolled in Medicare Part A and B and not in Part C (Medicare Advantage) for the entire 12 months of 2014.

Exclusion criteria. We excluded individuals who had an ICD-9 code for systemic lupus erythematosus, inflammatory bowel disease (IBD), cancer, human immunodeficiency virus, end stage renal disease, or organ transplantation or who were coded as having met inclusion criteria for more than one of AS, PsA, or RA.

Frailty definition. Frailty was operationalized using a validated ICD-9 CFI (6). This index includes variables such as age, impaired mobility, recent admission, falls, and comorbid conditions and has been shown to identify individuals with the Fried frailty phenotype, a widely accepted frailty metric (1,6) (Table S1). The CFI incorporates a weighted arthritis component, which includes ICD-9 codes for RA; a weighted Charlson-Deyo comorbidity index (CCI) component, which includes ICD-9 codes for RA (10); and a weighted musculoskeletal problems component, which includes ICD-9 codes for AS (6). We excluded ICD-9 codes for RA, AS, and PsA when calculating the CFI and CCI for this study. We chose a CFI cut point of 0.12 to identify frailty as suggested by Segal et al to maximize sensitivity and specificity at 66% and 73%, respectively (6).

Sociodemographic and comorbid variables. Age, sex, and race/ethnicity were extracted from the CMS files. We used the CCI as a measure of disease burden (10). The CCI is a weighted index originally designed to predict risk of death within 1 year of hospitalization for patients with specific comorbid conditions, including RA and osteoarthritis, but not AS or PsA. We also evaluated whether anxiety and fibromyalgia differed between frail and non-frail beneficiaries, as both have been associated with frailty in other populations (7,8). Anxiety and fibromyalgia are found neither in the CCI nor in the

Table 1. Characteristics of study participants

Characteristic	<65 Years Old (N = 59,087)				≥65 Years Old (N = 238,090)			
	AS (N = 2,490)	PsA (N = 6,950)	RA (N = 49,647)	P Value	AS (N = 2,750)	PsA (N = 17,779)	RA (N = 217,561)	P Value
Age (y), Mean ± SD	50.3 ± 9.4	52.8 ± 8.6	54.9 ± 7.9	<0.05	71.9 ± 5.4	72.5 ± 5.8	74.7 ± 6.7	<0.05
Female, %	31.6	60.5	78.1	<0.05	34.5	60.7	76.1	<0.05
Race/Ethnicity, %				<0.05				<0.05
African American	9.0	3.4	15.7		3.5	1.7	7.4	
White	75.8	85.3	68.9		88.1	91.7	84.0	
Hispanic	8.9	7.6	15.7		3.9	5.1	5.1	
Other	6.3	3.7	4.2		4.5	3.4	3.5	
CCI Score, %				<0.05				<0.05
0	43.8	31.0	0		31.6	26.8	0	
1-4	53.9	64.8	94.1		62.2	66.0	89.8	
≥5	2.3	4.2	5.9		6.2	7.2	10.2	
Frail, %	4.4	7.0	11.7	<0.05	45.2	46.7	65.9	<0.05

Abbreviations: AS, ankylosing spondylitis; CCI, Charlson-Deyo comorbidity index; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

Table 2. Frailty components and associated characteristics of participants*

Characteristic	<65 Years Old (N = 59,087)						≥65 Years Old (N = 238,090)					
	AS		PsA		RA		AS		PsA		RA	
	Frail (109)	Non-Frail	Frail (489)	Non-Frail	Frail (5,811)	Non-Frail	Frail (1,244)	Non-Frail	Frail (8,296)	Non-Frail	Frail (143,435)	Non-Frail
Frailty Components (%)												
Impaired mobility	2.8	0.1	2.5	0.1	2.3	0.1	0.3	0.0	0.2	0.0	0.4	0.0
Depression	56.0	26.0	64.2	35.2	61.6	28.1	23.2	5.9	27.8	8.2	22.3	5.1
Congestive heart failure	46.8	2.7	43.2	3.1	36.4	2.3	19.9	0.9	18.4	0.6	16.6	0.3
Parkinson's disease	4.6	0.4	2.3	0.3	1.7	0.2	3.4	0.3	2.3	0.2	1.6	0.2
Cognitive impairment	7.3	0.9	8.0	1.7	8.2	1.0	6.8	0.6	7.7	0.6	8.4	0.4
Stroke	19.3	1.8	17.2	2.1	16.0	1.9	8.3	1.5	9.3	0.8	8.5	0.7
Paranoia	12.8	4.0	11.5	3.9	8.8	2.3	3.2	0.3	3.4	0.3	3.1	0.3
Chronic skin ulcer	16.5	2.1	21.1	3.2	16.6	3.1	7.9	1.3	8.6	1.4	9.5	1.4
Pneumonia	18.4	2.5	19.2	4.1	21.4	4.5	10.8	1.7	9.7	2.1	11.0	2.4
Skin/soft tissue infection	23.9	9.7	38.5	14.5	30.2	11.3	16.7	6.0	19.4	8.1	16.8	6.0
Mycoses	31.2	10.1	43.2	14.3	33.5	11.7	26.1	11.6	28.5	10.6	25.8	7.9
Recent admission	35.8	5.8	33.7	6.6	31.9	6.9	14.4	3.5	15.1	3.5	15.2	3.2
Crystalline arthropathy	11.0	4.8	15.3	5.7	12.3	3.8	13.5	6.6	14.0	7.2	9.6	4.1
Falls	11.9	3.8	13.7	3.8	11.5	3.6	8.0	1.9	8.4	1.9	8.8	2.3
Urinary tract infection	27.5	9.4	35.0	14.1	33.2	14.6	22.8	8.7	26.2	11.6	27.5	12.1
Associated Characteristics (%)												
Anxiety	39.5	19.8	41.5	27.5	37.4	22.1	14.3	5.7	17.8	8.1	15.3	7.6
Fibromyalgia	61.5	40.8	56.9	41.7	58.4	41.8	32.6	18.5	28.4	17.6	27.2	18.0

Abbreviations: AS, ankylosing spondylitis; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

* $P < 0.05$ for all comparisons between frail and non-frail participants by age and disease classification.

CFI, and a high prevalence of these conditions would provide face validity for the CFI in this patient population.

Statistical methods. We used descriptive statistics to describe our cohort. We compared the frailty prevalence among individuals with AS, PsA, or RA, separately for CMS beneficiaries 65 years of age and older and CMS SSDI beneficiaries less than 65 years old. For each rheumatic condition, we also compared the prevalence of variables included in the CFI, as well as the prevalence of anxiety and fibromyalgia between frail and non-frail beneficiaries. We used Chi-Square tests and analysis of variance to determine differences in frailty components among AS, PsA, and RA. Within each age group, we used logistic regression to determine the odds of frailty in patients with AS and PsA compared with patients with RA. As multiple sociodemographic features and comorbid conditions were included in the frailty index, we chose not to adjust for potential confounding factors to avoid overfitting. All analysis was done using SAS 9.4 (Cary, NC).

Ethical oversight. This study was approved by the Institutional Review Board of Weill Cornell Medicine.

RESULTS

Study sample

A total of 297,177 Medicare enrollees were included in this analysis; 5,240 (1.8%) with AS, 24,729 (8.3%) with PsA, and 267,208 (90%) with RA (Figure S1).

Medicare beneficiaries less than 65 years old

Sociodemographic characteristics. Individuals with AS or PsA were younger (mean age: 71.9 ± 5.4 and 72.5 ± 5.8 years, respectively) than those with RA (mean age: 74.7 ± 6.7 years, $P < 0.05$) and were less often female (34.5% and 60.7%, respectively, vs. 76.1%, $P < 0.05$) (Table 1). Most individuals were White. Individuals with AS or PsA had significantly less comorbidity than those with RA ($P < 0.05$).

Frailty and associated characteristics. Frailty was common in all three rheumatic diseases, but significantly less prevalent in those with AS (45.2%) or PsA (46.7%) compared with those with RA (65.9%) ($P < 0.05$) (Table 1). Urinary tract

Table 3. Unadjusted odds of frailty in PsA and AS relative to RA

Condition	Odds Ratio (95% Confidence Interval)	
	<65 Years Old	≥65 Years Old
RA	1.00 (referent)	1.00 (referent)
PsA	0.57 (0.52-0.63)	0.45 (0.44-0.47)
AS	0.35 (0.29-0.42)	0.43 (0.40-0.46)

Abbreviations: AS, ankylosing spondylitis; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

infections, mycoses, and depression were the most common frailty components (Table 2).

Anxiety and fibromyalgia were significantly more common among frail versus non-frail beneficiaries in all three rheumatic conditions (Table 2): Prevalence of anxiety was 14.3% versus 5.7% in AS, 17.8% versus 8.1% in PsA, and 15.3% versus 7.6% in RA ($P < 0.05$ for all comparisons) (Table 2). The prevalence of fibromyalgia was 32.6% versus 18.5% in AS, 28.4% versus 17.6% in PsA, and 27.2% versus 18.0% in RA ($P < 0.05$ for all comparisons). The likelihood of frailty was lower in beneficiaries with AS (odds ratio [OR] 0.43; 95% confidence interval [CI] 0.40-0.46) and PsA (OR 0.45, 95% CI 0.44-0.47) relative to beneficiaries with RA (Table 3).

SSDI beneficiaries less than 65 years old

Sociodemographic characteristics. SSDI beneficiaries less than 65 years old with AS or PsA were significantly younger (mean age: 50.3 ± 9.4 and 52.8 ± 8.6 years, respectively) than those with RA (mean age: 54.9 ± 7.9 years, $P < 0.05$) and were less often female (31.6% and 60.5% vs. 78.1%, $P < 0.05$) (Table 1). Likewise, most individuals were White, and those with AS or PsA had a significantly lower comorbidity burden than those with RA ($P < 0.05$).

Frailty and associated characteristics. Frailty was much less common in this younger cohort with work disability. Similar to the older cohort, frailty was significantly more prevalent in beneficiaries with RA compared with AS and PsA (11.7%, 4.4%, and 7.0%, respectively; $P < 0.05$; Table 1). In contrast to those aged 65 or older, the most prevalent frailty component in those less than 65 years old was depression in all rheumatic conditions (56.0% in AS, 64.2% in PsA, and 61.6% in RA) (Table 2).

Similar to the older cohort, anxiety and fibromyalgia were also more common in frail versus non-frail individuals in all three conditions (anxiety: 39.5% vs. 19.8% in AS, 41.5% vs. 27.5% in PsA, and 37.4% vs. 22.1% in RA; fibromyalgia: 61.5% vs. 40.8% in AS, 56.9% vs. 41.7% in PsA, and 58.4% vs. 41.8% in RA; $P < 0.05$ for all comparisons) (Table 2). Odds of frailty were lower in AS (OR 0.35, 95% CI 0.29-0.42) and PsA (OR 0.57, 95% CI 0.52-0.63) relative to RA, a similar trend as seen in those 65 years of age or older (Table 3).

DISCUSSION

In this large cross-sectional sample of Medicare beneficiaries, patients with AS or PsA were less likely to be frail than those with RA, whether they were aged 65 years or older or less than 65 and work disabled. However, Medicare enrollees with AS and PsA had a greater than 4-fold higher frailty prevalence compared with the 11% prevalence of frailty in Medicare enrollees participating in the Cardiovascular Health Study, which determined frailty using the same CFI (6). This suggests that frail patients with AS and PsA could have similar increased risk of death, time to death, number of hospital admissions, and number of nursing home admissions as other frail Medicare enrollees 65 years of age or older [6].

To our knowledge, the prevalence of frailty in patients with SpA has been assessed in only one prior cross-sectional cohort (5). That study included a mix of 523 subjects with a heterogeneous group of patients with SpA (AS, PsA, undifferentiated SpA, and IBD-associated SpA); frailty was defined according to the Fried frailty phenotype. In that study, 37% of the subset of patients with SpA 65 years of age or older were frail, similar to our estimates of 45.2% and 46.7% for patients with AS and PsA, respectively (5). The prior study also evaluated frailty in RA, but the authors reported a much lower prevalence of frailty in their subset of individuals with RA who were 65 years of age or older (42% vs. 65.9% in our study) (5). Why there is a divergence in the proportion of patients with RA categorized as frail using the Fried definition versus the CFI in older beneficiaries, compared with estimates in patients with SpA, requires further study.

Prior cohort studies have evaluated younger patients with RA, and most have found similar ranges of frailty as the 11.7% found in our cohort of beneficiaries with RA less than 65 years of age. For instance, one cohort with a mean age of 58.0 years found a prevalence of 13% using the Fried frailty phenotype (3). In a second cohort with a mean age of 59.2 years among patients with RA, 18.6% of participants were frail according to the Fried frailty phenotype (11). A third study using the Survey of Health, Aging and Retirement in Europe Frailty Index, another phenotypic definition of frailty based on the Fried frailty phenotype, had a mean age of 50.9 years and found a frailty prevalence of 15% (12). In a fourth study—in which frailty was determined using the Comprehensive Rheumatologic Assessment of Frailty, an RA-specific cumulative deficits index, and for which the mean age was 58.5 years—moderate to severe frailty was present in 35.1% of participants (13). Further study is needed to evaluate relative performance of frailty metrics in subjects with RA less than 65 years old in association with clinical outcomes.

The prevalence of anxiety was 1.5 to 2 times higher in frail Medicare enrollees with RA, SpA, and PsA compared with those who were not frail. In another recent study of patients with RA who were aged less than 40 years, anxiety was similarly greater

among frail participants, defined according to a 5-item frailty scale, than non-frail participants (14). In an additional study of patients with RA who were at least 55 years old, symptoms of anxiety were more often reported by frail than non-frail participants, with frailty classified by the Groningen Frailty Indicator (15). To our knowledge, the higher prevalence of anxiety among frail as compared with non-frail patients with inflammatory arthritis other than RA has not been previously observed. The prevalence of anxiety in frail enrollees in this study, particularly work-disabled beneficiaries aged less than 65 years, exceeded the 8.3% prevalence of anxiety reported in Medicare enrollees in 2012 (16). The association between frailty and anxiety in patients with inflammatory arthritis needs to be explored in longitudinal studies. Whether or not the presence of mental health comorbidity may accelerate the development of frailty is unknown.

Our results should be viewed in light of several limitations. We were unable to validate the CFI directly against the Fried frailty phenotype in this specific rheumatic disease sample. However, we used a CFI that has been validated in general CMS beneficiaries 65 years of age or older (6). Furthermore, it is unknown which frailty construct is best suited for measurement of frailty in patients with inflammatory arthritis. We also were unable to account for the effect of disease activity or medication use, including polypharmacy. Given its inclusion in the CFI, the CCI was used as a measure of disease burden; however, other comorbidity indices, such as the Rheumatic Disease Comorbidity Index, may be more highly predictive of adverse outcomes in patients with inflammatory arthritis (17). Depression is often correlated with anxiety (18), and since depression is a component of the CFI, patients classified as frail using the CFI may appear to have higher levels of anxiety than frail patients classified using other frailty metrics, though our findings are consistent with those of other studies of frail patients with RA. Likewise, age (as a component of the CFI) may impact frailty prevalence in patients 65 years of age or older versus those younger than 65 in our study. This is in addition to the risks of misclassification inherent in working with administrative data.

Our study has several strengths. We analyzed a large sample of patients with AS, PsA, and RA from the CMS, capturing a large subset of the United States population 65 years of age or older. We used a CFI that has been validated against the Fried frailty phenotype in CMS data. When calculating the CFI and CCI, we excluded inflammatory arthritis ICD-9 codes describing our target population to prevent systematic inflation of frailty prevalence in these groups. Although work-disabled SSDI beneficiaries aged less than 65 years are often removed from studies of administrative datasets due to limited generalizability, we were able to describe frailty prevalence and associated characteristics of enrollees in this population—recognizing its unique characteristics—and, to our knowledge, document for the first time important differences between frail CMS enrollees with inflammatory arthritis less than and more than 65 years old.

Being able to identify frail Medicare beneficiaries is important, because frailty increases risk of adverse outcomes, including increased mortality and healthcare use (1,2). Inclusion of the CFI in risk stratification algorithms may improve risk assessment in large claim-based datasets. As frailty has been associated with other inflammatory conditions (19), this may be particularly true for frail patients with AS and PsA, who are already at an increased risk owing to their underlying disease. Further study is needed to determine the longitudinal association of frailty with adverse health outcomes in AS and PsA, including mortality, functional disability, and healthcare use.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

Study conception and design. Lieber, Navarro-Millán, Rajan, Curtis, Sattui, Lui, Mandl.

Analysis and interpretation of data. Lieber, Navarro-Millán, Rajan, Curtis, Sattui, Lui, Schwartzman, Mandl.

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