Published in final edited form as:

Mayo Clin Proc. 2019 June ; 94(6): 1035–1039. doi:10.1016/j.mayocp.2019.01.002.

Trends in Prevalence of Functional Disability in Rheumatoid Arthritis Compared to the General Population

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Abstract

The objective of the study was to assess trends in functional disability (FD) in rheumatoid arthritis (RA) versus non-RA subjects. This retrospective population-based study included patients with RA (n=586) and non-RA subjects (n=531). Activities of Daily Living (ADL) were obtained from self-report questionnaires. The prevalence of FD was higher in RA (26%) versus non-RA subjects (11%) at RA incidence/index date ($p<0.001$), with persistent excess over the follow-up and calendar time. RA patients had 15%-higher prevalence of FD than the non-RA subjects in most age-groups. Patients with RA have higher prevalence of FD across RA duration, age and calendar time than non-RA subjects.

Keywords

Rheumatoid arthritis; functional disability; trends

Introduction

Rheumatoid arthritis (RA) is an aggressive and disabling disease with significant impact on quality of life and well-being. Despite recent advances in treatment of RA, functional disability (FD) in patients with RA is still common. In fact, RA remains one of the most common chronic conditions associated with FD¹. However, it remains unclear whether the excess in FD in RA is universal for all age groups, how serologic status impacts FD and how trends in FD in RA compare to the general population.

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The authors declare no conflict of interest.

We aimed to assess the prevalence of patient-reported FD in RA versus subjects without RA within 3 years prior to RA incidence/ index date and over RA disease duration, age, sex and calendar time, and to define the effect of rheumatoid factor/anti-cyclic citrullinated peptide (RF/CCP) positivity on the prevalence of FD in patients with RA.

Materials and Methods

The study comprised a population-based inception cohort of Olmsted County, Minnesota residents aged ≥ 18 years who fulfilled the 1987 American College of Rheumatology (ACR) criteria for RA between 1/1/1999 and 12/31/2013. Patient ascertainment was performed using the Rochester Epidemiology Project (REP), a population-based records-linkage system with access to the complete (in-patient and outpatient) medical records from all providers in the community²⁻⁵. The RA incidence date was defined as the earliest date of fulfillment of ≥ 4 1987 ACR criteria for RA. The comparison cohort included randomly selected Olmsted County residents without RA of similar age, sex and calendar year of index for each RA patient. The index date for each non-RA subject corresponded to the incidence date of the patient with RA.

Information on smoking (never, current or former) and obesity (body mass index [BMI] ≥ 30 kg/m²) was collected from the medical records for all patients. Use of antidepressants within one year prior to index date was collected for subjects with an index year ≥ 2005 . For patients with RA, information on RA disease duration and RF/CCP positivity was also gathered.

Activities of Daily Living (ADL) were part of the self-report questionnaire administered annually to all patients during routine outpatient appointments at Mayo Clinic for the past 20 years. The completion of the questionnaires was independent of patients' rheumatologic care. Patients provided information about their ability to perform six ADLs without assistance, including feeding oneself, dressing, using the toilet, bathing, walking and housekeeping. FD was defined as having difficulty with either 1 or ≥ 2 of the six ADLs. Subjects who returned 1 questionnaire on or following RA incidence/index date were included in the analysis. Last follow-up date was defined as date of the most recent questionnaire before 1/5/2018. This study was approved by institutional review boards of Mayo Clinic (IRB #675-99) and Olmsted Medical Center (IRB #018-OMC-06).

Statistical Methods:

Analyses were performed using age-, sex- and disease duration-adjusted logistic regression models of FD with random subject effects to account for multiple measures per patient. Smoothing splines were used to examine non-linear effects. Two-way interactions between cohort and variables of interest were examined. FD within the 3 years prior to RA incidence/ index date was examined in 1-year intervals: the odds ratio (OR) and 95% confidence interval (95%CI) for FD in RA vs non-RA patients within each 1-year period was calculated. SAS version 9.4 (SAS Institute, Cary, NC, USA) and R 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analyses.

Results

Out of the total cohort of 609 patients with RA diagnosed between 1/1/1999 and 12/31/2013, there were 586 patients with RA who completed at least one questionnaire on or following RA incidence/index date and were included in the study. The comparison cohort included 531 non-RA subjects. RA patients and non-RA subjects completed 7,446 questionnaires (4,301 RA and 3,145 non-RA) from 1/5/1999 to 1/5/2018 at or following their RA incidence/index date. There was no apparent reduction in number of completed questionnaires over time. An additional 975 RA and 916 non-RA questionnaires in the 3 years prior to RA incidence/index were included in the analyses of disease duration. The RA and non-RA cohorts were similar in demographics, length of follow-up, smoking habits, obesity rates and antidepressant use (Table 1).

The prevalence of any FD (i.e., difficulty with 1 ADL) was significantly higher in RA vs. non-RA subjects at the RA incidence/index date (26% vs 11%, respectively, $p<0.001$) with persistent excess in prevalence over the follow-up time (Figure 1, Panel A). Comparisons for FD defined as difficulty with 2 ADLs at incidence/index date were similar, but the prevalences were smaller (13% in RA vs 5% in non-RA; $p<0.001$).

In the period from three to two years prior to RA incidence/index, there was no statistically significant difference between cohorts: OR:1.50; 95%CI:0.74–3.05. However, in the periods from two to one years prior and within one year prior to RA incidence/index date, patients with RA had significantly higher prevalence of FD than comparators: OR:2.07; 95%CI: 1.66–3.64 and OR:2.78; 95%CI:1.63–4.72, respectively.

Patients with RA had persistent excess in prevalence of FD over calendar time, and there was no evidence of a difference in the pace of increase of FD between the RA (regardless of RF/CCP-positivity) and non-RA cohort (interaction $p=0.51$, Figure 1, Panel B).

Relative to comparators, patients with RA had 15%-excess in the proportion of FD at any age <80 years (Figure 1, Panel C). Starting at age 80, the proportions of patients with FD were similarly high between the cohorts, potentially reflecting growing comorbidity burden with age. Results were similar for FD defined as difficulty with 2 ADLs, with RA subjects having at least a 10%-increase in FD versus non-RA subjects prior to age 60 with no differences thereafter.

Compared to the non-RA subjects, patients with RA had higher prevalence of FD in men ($p<0.001$) and women ($p<0.001$). The prevalence of FD was higher in women than in men in both RA ($p<0.001$) and non-RA subjects ($p=0.039$).

The prevalence of FD overall was similar in RF/CCP positive vs negative patients with RA ($p=0.67$). However, there was a significant interaction between RF/CCP positivity and disease duration ($p=0.027$; Figure 2), reflecting an increase in prevalence of FD over disease duration in patients with RF/CCP and a decline in FD prevalence in those without RF/CCP. For FD defined as difficulty with 2 ADLs, the results were similar (interaction $p=0.040$).

Discussion

This study is the first to report persistent excess in self-reported FD in a US population of RA patients compared to the general population across RA disease duration, calendar time, sex and age. This study uniquely shows that excess in prevalence of FD in RA predates the RA incidence date defined by fulfillment of 1987 ACR criteria for RA by 1–2 years. These findings suggest that the burden of FD affects most groups of RA patients, begins early in the disease course and may precede RA diagnosis.

Two large cohort studies from Europe recently reported lack of improvement in physical functioning based on HAQ score in patients with inflammatory arthritis in the new millennium versus those diagnosed in previous decades^{6–7}. While higher disease activity and delayed RA diagnosis has been linked to increased likelihood of disability^{8–9}, the persistent FD excess appears to be despite the improvements in RA disease activity and RA management^{6–7, 10}. The growing burden of mental and somatic comorbidity and pain, use of glucocorticoids and antidepressants, and increasing expectations for optimal physical functioning are possible reasons for the lack of improvement in FD in RA^{6–7, 11–13}.

Female sex was associated with worse disability in this study, which is consistent with the prior studies^{6, 11}. Not unexpectedly, patients with RF/CCP-positive status as a marker of severe disease experienced increasing FD over the RA duration, a finding consistent with previous observations in some studies^{14–15}, but not in others⁸.

The implications of this persistent burden of FD in RA are broad, including the substantial financial and societal burden associated with work disability, extensive use of healthcare resources and suboptimal quality of life. Timely evaluation and management of physical impairments in the context of comorbidity, pain and disease activity in patients with RA can be expected to improve their disability profile. Further advances in treatment, earlier disease recognition with the 2010 ACR criteria¹⁶, and more aggressive treatment may also lessen this burden. Further understanding of the underpinnings of the trends in FD in RA may help with healthcare planning and resource utilization.

Strengths of this study include its population-based design, standardized case ascertainment and a comparison cohort from the same underlying population. The availability of information on ADL in both cohorts for two decades, including prior to the RA incidence/index date, and good questionnaire response rates of 60–70% each year further strengthens the study.

There are some potential limitations. In this retrospective study, objective assessment of FD was not available. Possible fluctuations in physical functioning and related worsening/improvement in FD over time were not accounted for in this study. However, further studies are underway to understand the pattern of change in FD in RA patients. Changing approaches to RA treatment were not considered. Investigation of antirheumatic therapy-related risk factors for persistent and worsening FD is ongoing. Finally, the population of Olmsted County, Minnesota is predominately white, so the results may not be generalizable to more diverse populations.

Conclusion

In summary, patients with RA have a significantly higher prevalence of FD over RA disease duration, calendar time, sex and age compared to their non-RA counterparts. This excess in FD prevalence predates the RA incidence date. RF/CCP-positive patients are disadvantaged with an increasing burden of FD over their disease duration, suggesting that additional vigilance may be needed to help improve their functional outcomes.

Acknowledgments

Financial support: This work was funded by a grant from the National Institutes of Health, NIAMS (R01 AR46849). Research reported in this publication was supported by the National Institute of Aging of the National Institutes of Health under Award Number R01AG034676. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Figure 1.

Trends in prevalence of functional disability* in patients with (solid line) and without (dashed line) rheumatoid arthritis across disease duration (Panel A), calendar time (Panel B), and age (Panel C).

Footnote:* Functional disability, % on Y-axis shows % of patients who had any FD defined as difficulty with performing 1 ADL

Figure 2.
Trends in prevalence of functional disability in patients with rheumatoid arthritis who are RF/CCP positive (solid line) vs. RF/CCP negative (dashed line).

Table 1.

Characteristics of patients with and without rheumatoid arthritis (RA).

Characteristics	RA (n=586)	Non-RA (n=531)
Age at index date, years, mean (SD)	55.4 (15.3)	56.2 (15.0)
Sex, female, N (%)	412 (70)	374 (70)
Length of follow up, years, mean (SD)	8.3 (4.6)	8.5 (4.6)
Number of completed questionnaires after index date	4,301	3,145
Smoking, N (%)		
- Never	307 (52)	304 (57)
- Current	90 (15)	78 (15)
- Former	189 (32)	149 (28)
Obesity, N (%)	235 (40)	209 (39)
RF/ CCP positive, N (%)	374 (64)	-
Use of antidepressants within 1 year prior to index date *, N (%)	102/367 (28)	82/317 (26)

* Available for patients with RA incidence/ index date in 2005–2013.

Abbreviations: N = number; RF/CCP = rheumatoid factor/ cyclic citrullinated peptide; SD = standard deviation.