Age and Gender Differences in Comorbidities among Patients with Rheumatoid Arthritis in a Large US-Based Real World Cohort

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Background

- Treatment decisions for rheumatoid arthritis (RA) are complex due to underlying disease conditions driven by patient characteristics.
- The prevalence of RA is well known to be higher in women than in men, and studies have suggested that the incidence of disease, disease course, and prognosis differ between men and women.
- RA generally begins to affect people between the ages of 30 and 60 years old. The average person doesn't develop symptoms of RA until they reach their 60's[1].
- The extent of the differences in disease course between men and women are not fully agreed upon in the literature. Generally, women report more severe symptoms and disability, while men are more likely to achieve remission in early RA but report more adverse effects of biologic treatments[2].
- Studies have found differences in males and females in disease activity measures and remission rates[3], however radiographic disease progression has consistently been found to be similar between males and females[4].
- Further research is needed to better describe the role that gender and age play in RA

Objective

To characterize key patient characteristics that influence treatment decisions and outcomes.

Methods

- The OM1 Data Cloud (OM1, Boston, MA) collects, links and leverages additional structured and unstructured data from electronic medical records (EMR), claims and other sources in an ongoing and continuously updating manner. These linkages provide ongoing data from rheumatologists, primary care and other specialties, which is important in understanding the multi-systemic burden of the disease.
- For a subset of these patients in the curated OM1 RA Registry, more than 120,000 patients are followed longitudinally by rheumatologists with deep clinical data, including laboratory, symptom, patient-reported and disease activity information.
- For this analysis, patients were required to be at least 16 years and have at least 1 of the following: 2+ RA diagnosis codes from a rheumatologist at least 30 days apart, 1+ inpatient RA diagnosis code, 2+ outpatient RA diagnosis codes at least 30 days but less than 1 year apart, or 1+ outpatient RA diagnosis code and at least one disease-modifying anti-rheumatic drug (DMARD) medication record (and <2 diagnosis codes for other conditions for which DMARDs may be prescribed).
- Patients meeting cohort entry criteria starting from January 2013 through February 2019 were included in analyses.

Methods (continued)

- Comorbid conditions recorded at any time during follow-up are included. Charlson score calculated at the time of entry into the cohort is reported. Categorical extra-articular manifestations evaluated were: hematologic, oral, pulmonary, ocular, neurologic, cardiac.
- RA disease activity measures, such as the RAPID3, and symptom scores, such as fatigue score, were evaluated as reported during routine clinical practice and therefore were not available for all patients in the cohort.
- RAPID3 values at the time of first observed biologic DMARD (bDMARD) treatment start are included. Fatigue scores and MDHAQ VAS pain scores at the time each DMARD was started for the first time were included; multiple scores per patient may be included.

Results

- Overall, **1,074,695 prevalent RA patients** were identified, with an average observation time in the cohort of 4.9 years (standard deviation [SD] 1.2). Average age at cohort entry was 64.1 years (SD=14.5) for women (n=818, 967) and 66.5 years (SD =13.2) for men (n=255,728) (**Figure 1 and 2**).
- Men had higher Charlson scores (2.2 vs. 2.0), more hypertension (61.5% vs. 55%), more diabetes (27.4% vs. 22.7%) (**Figure 3**), higher mean C-reactive protein (1.3 vs. 1.0), but were less likely to have extra-articular oral manifestations (2.3% vs. 7.3%), had lower mean fatigue score (4.6 vs. 5.6), and lower multidimensional health assessment questionnaire visual analog scale (MDHAQ VAS) pain scores (5.1 vs. 5.6).
- Older patients had more cardiovascular and respiratory comorbidities (**Figure 4,5,6**), and higher Charlson scores (2.3 vs. 1.8), but lower fatigue scores (5.0 vs. 5.7) and MDHAQ VAS pain scores (5.2 vs. 5.7).
- Although a similar proportion had joint exam data available (n=82,453), 55.% of men with scores had a tender joint count = 0-4, compared to 48.7% for women (**Figure 7**). A larger proportion of younger patients had tender joint counts (0-4), (**Figure 8**).
- Similar proportions of patients were treated with bDMARDs during follow-up (n=260,105, 22% male, 25% for females). At bDMARD baseline, a smaller proportion of men (51.7% vs. 58.6%) had high RAPID3 disease activity scores (**Figure 9**). This difference was consistent across age groups, but was more pronounced among patients aged >= 65 (47.5% vs. 56.0%, **Figure 12**) compared to patients aged 16-64 (55.7% vs. 60.3%, **Figure 11**).
- At bDMARD baseline, a smaller proportion of older patients (54.0% vs 59.5%) had high RAPID3 scores (**Figure 10**).
- In comparisons across age groups (16-64 vs. 65+ years), older patients had higher ESR scores (67.1% of older males had <= 20 vs. 77.0% for younger male, and 74.3% of older women had <=30 vs. 81.2% for younger women).

Figure 1. Gender Distribution

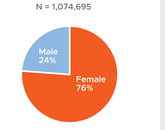


Figure 2. Age Distribution by Gender

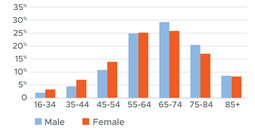


Figure 3. Distribution of Common Comorbidities by Gender

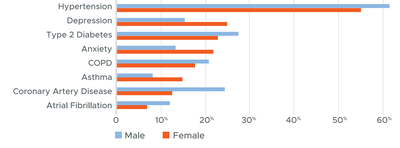


Figure 4. Distribution of Common Comorbidities by Age (years)

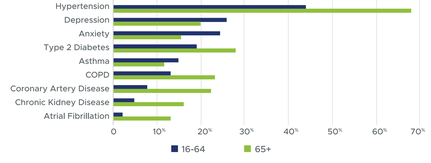


Figure 5. Distribution of Comorbidities by Gender, Patients Aged 16-64

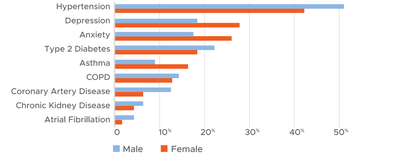


Figure 6. Distribution of Comorbidities by Gender, Patients Aged 65+

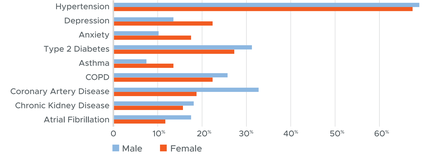


Figure 7. Distribution of Tender Joint Counts by Gender

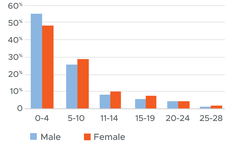


Figure 8. Distribution of Tender Joint Counts by Age (years)

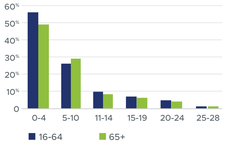


Figure 9. RAPID3 Scores at bDMARD Treatment Baseline by Gender

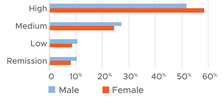


Figure 10. RAPID3 Scores at bDMARD Treatment Baseline by Age (years)

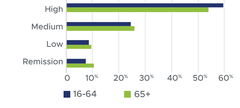


Figure 11. RAPID3 Scores at bDMARD Treatment Baseline by Gender, Age 16-64

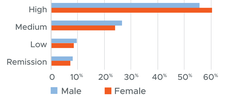
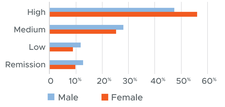


Figure 12. RAPID3 Scores at bDMARD Treatment Baseline by Gender, Age 65+



RAPID3 score categories: 0-3 remission, 3-6 low, 6-12 medium, 12-30 high

Conclusions

- The proportion of female RA patients in this cohort is 76%, which is consistent with estimates in the US (74-76%)[3]. The age distribution is generally consistent with estimates from the literature for prevalent RA, however, this registry reports a higher proportion of patients over the age of 65.
- Patterns of differences in comorbidities by gender generally follow that in the general US population, with more cardiovascular disease in men, and more anxiety, depression, and asthma in women. However, this cohort shows a higher proportion of men with type 2 diabetes, whereas in the general US population the prevalence is slightly higher in women. The substantial differences seen between genders in cardiovascular disease may have an important impact on cardiovascular disease risk management.
- The lower pain scores observed in men in this registry may be an artifact of the widely reported phenomena of women being more likely in general to report pain than men, both in experimental and clinical settings for many conditions[6].
- Given the high cost and complexity of RA treatments such as bDMARDS, full assessment of the impact of patient age and gender on comorbidities should be part of the evaluation of treatment choice and outcomes to maximize treatment effect.

[1]www.rheumatoidarthritis.org/ra/facts-and-statistics.

[2]Sokka, Tuulikki et al. "Women, men, and rheumatoid arthritis: analyses of disease activity, disease characteristics, and treatments in the QUEST-RA study" Arthritis research & therapy vol. 11,1 (2009): R7.

[3]Forslind K, Hafstrom I, Ahlmen M, Svensson B. Sex: a major predictor of remission in early rheumatoid arthritis? Ann Rheum Dis. 2007;66:46–52.

[4]Tengstrand B, Ahlmen M, Hafstrom I. The influence of sex on rheumatoid arthritis: a prospective study of onset and outcome after 2 years. J Rheumatol. 2004;31:214–222.

[5]Hunter, T.M., et al., Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014. Rheumatol Int, 2017. 37(9): p. 1551-1557.

[6]Bartley, E.J. and R.B. Fillingim, Sex differences in pain: a brief review of clinical and experimental findings. Br J Anaesth, 2013. 111(1): p. 52-8.