ORIGINAL RESEARCH

Prevalence of Renal Impairment in a US Commercially Insured Rheumatoid Arthritis Population: A Retrospective Analysis

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ABSTRACT

Introduction: Global prevalence estimates for chronic kidney disease (CKD) in rheumatoid arthritis (RA) vary. This study assessed real-world prevalence estimates of renal impairment, based on estimated glomerular filtration rate (eGFR), among commercially insured patients with RA in the United States (US).

Methods: In this retrospective cohort study, we used administrative claims data from the HealthCore Integrated Research Database (HIRD®) between January 2013 and December

2018. Adult patients with ≥ 2 claims for RA and ≥ 2 serum creatinine (SCr) measurements ≥ 90 days apart on or after the index date were included. eGFR was calculated per the Modification of Diet in Renal Disease equation. Prevalence of eGFR-based renal impairment was estimated for the overall RA population and for two subgroups: patients on advanced therapies (biologic disease-modifying antirheumatic drugs/tofacitinib) and patients stratified based on health plan types.

Results: Among 128,062 patients with ≥ 2 RA claims, 42,173 had qualifying SCr measurements, 16,197 were on advanced RA therapies, and 4911 had Medicare Advantage or Supplemental plus Part D coverage. For the overall population and the subgroup on advanced therapies, mild renal impairment was observed in 52% and 51%, moderate renal impairment in 9% and 7%, and severe renal impairment in 0.5% and 0.3% of patients, respectively. Moderate and severe renal impairment was more prevalent in the Medicare Advantage/Supplemental plus Part D population compared to the commercial coverage population.

Conclusions: Approximately 7–10% of commercially insured adult patients in the US with RA had moderate or severe renal impairment. Assessment of renal function is an important consideration for safe treatment.

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Summary Slide

Why carry out this study?

Renal impairment in rheumatoid arthritis (RA) may influence treatment choice and increase mortality.

Reports citing prevalence of renal impairment among patients with RA in the United States (US) vary widely due to different assessment techniques, geographic restrictions, and/or small sample size.

This study assessed prevalence of estimated glomerular filtration rate-based renal impairment among adult patients with RA in the US. The aim was to provide a more contemporary view using a large, nationally representative US cohort, treated in the community.

What was learned from the study?

Prevalence of moderate or severe renal impairment was estimated to be ~ 10% among commercially insured patients with RA, and ~ 7% in a subgroup of patients on advanced therapies; prevalence was higher among managed Medicare compared to commercial coverage patients.

Assessment of renal function is an important consideration for safe treatment for RA.

The outcomes of the study underpin the importance of renal function assessment among patients with RA for appropriate selection and dosing of medications.

INTRODUCTION

Renal dysfunction in rheumatoid arthritis (RA) may influence treatment and increase mortality [1]. It may result from comorbidities, chronic inflammation, aging, or medication effects [1, 2]. Regular assessment of renal function is important to inform dosage adjustment of medications, such as methotrexate, nonsteroidal anti-inflammatory drugs (NSAIDs), and Janus kinase inhibitors (JAKi) [3, 4]. These commonly used medications in RA have the potential to affect renal function and can result in toxicity even in mild renal dysfunction [3].

Chronic kidney disease (CKD) is characterized by decreases in glomerular filtration rate (GFR) or presence of ≥ 1 markers of kidney damage for > 3 months [5]. The prevalence of CKD in RA has been reported in frequencies ranging from 5 to 50% [3, 6–8]. Methods for quantifying renal impairment differed in these studies, and there were potential limitations such as geographic restriction, and/or small sample sizes [1, 7, 9, 10].

This study aimed to assess the prevalence of estimated GFR (eGFR)-based renal impairment among adult patients with RA in the United States (US). We have conducted this study to provide a more contemporary view of renal impairment in RA using a large, nationally representative US cohort, treated in the community.

METHODS

In this retrospective cohort study, we used claims data from the HealthCore Integrated Research Database (HIRD®) between January 1, 2013 and December 31, 2018. The HIRD® encompasses a diverse spectrum of longitudinal medical and pharmacy claims data, and laboratory data from health plan members across the US.

Patient Population

Patients were required to have ≥ 2 claims ≥ 7 days apart with diagnosis codes for

RA (714.0×, 714.1×, 714.2× [International Classification of Diseases, Ninth Revision, Clinical Modification/ ICD-9-CM] and M05.%, M06.0%, M06.8% [International Classification of Diseases, Tenth Revision, Clinical Modification/ICD-10-CM]) and ≥ 2 serum creatinine (SCr) measurements ≥ 90 days apart. For patients with > 2 measurements, the first two measurements were used. The index was the date of the earliest RA claim. Characteristics of patients with and without SCr measurements are shown in Table 1. Patients aged ≥ 18 years on index date with ≥ 1 day of enrollment during the study period were identified. No minimum enrollment before or after the index date

was required. Patients with a claim during the study period for juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, or lupus were excluded.

Researchers' access to claims data was limited to data stripped of identifiers to ensure confidentiality. HealthCore maintains data use agreements with the covered entities in compliance with the Health Insurance Portability and Accountability Act. Permission was obtained from HealthCore to access the database. An Institutional Review Board did not review the study since only this limited data set was accessed.

Table 1 Characteristics of patients with and without ≥ 2 serum creatinine lab results

Characteristics	All RA patients, <i>n</i> = 128,062	RA patients with ≥ 2 SCr lab results, <i>n</i> = 42,173
Age, mean (SD)	58.0 (14.1)	55.5 (12.3)
Females	74.8	75.9
Plan type		
Commercial coverage	81.3	88.4
Medicare Advantage	9.3	7.6
Medicare Supplemental/Part D	9.4	4.0
Region		
Northeast	15.0	15.9
Midwest	26.3	13.9
South	33.2	40.1
West	21.2	25.5
Comorbidities ^a		
≥ 1 medical claim for hypertension	42.4	40.1
≥ 1 pharmacy claim for antihypertensives	42.5	42.2
≥ 1 medical claim for heart failure	4.8	3.2
≥ 1 medical claim for diabetes	15.8	15.8
≥ 1 pharmacy claim for antidiabetics	10.2	10.7

All values are % unless otherwise indicated

n number of patients in each group, *RA* rheumatoid arthritis, *SCr* serum creatinine, *SD* standard deviation

^a Within a window of -90 days to $+90$ days around the index date

Assessment of Renal Function

eGFR was estimated using the Modification of Diet in Renal Disease (MDRD) equation, where eGFR is expressed in ml/min/1.73m², serum creatinine in mg/dl, and age in years [11]. This method, proposed by the Food and Drug Administration, is employed in package inserts for recently approved medications for RA [12].

$$\begin{aligned} \text{eGFR} = & 175 \times \text{standardized SCr}^{(-1.154)} \\ & \times \text{age}^{(-0.203)} \times 0.742 \text{ (if female)} \\ & \times 1.212 \text{ (if black)}. \end{aligned}$$

Race information was unavailable, and individuals were designated non-black for calculation.

Prevalence Assessment

In this descriptive analysis, prevalence of eGFR-based renal impairment by severity (classifications based on Kidney Disease Improving Global Outcomes guidelines 2012, see Table 2) was calculated [13]. Grades 4 and 5 were combined given the low frequency (i.e., < 1% in aggregate). Patients falling into > 1 severity category were classified into the less severe category. Prevalence was calculated overall and for commercial and Medicare Advantage/Supplemental/Part D (Medicare) populations; for a subset of patients with ≥ 1 claim for advanced therapies (abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab,

tofacitinib citrate) on or after the index date; and on an annual basis among patients who had ≥ 2 SCr measurements in the year of interest.

RESULTS

A sample of 128,062 RA patients was identified from the HIRD®. Among them, 42,173 had ≥ 2 SCr measurements and 16,197 had ≥ 1 claim for advanced therapies. Mean (standard deviation) age was 56 (12) years and 76% were female (Table 3). Patients were stratified by health plan type (commercial plan: *n* = 37,262; Medicare: *n* = 4911). Assessed comorbidities (hypertension, heart failure, and diabetes) were more frequent in the Medicare population (Table 3).

Prevalence of Renal Impairment by Severity

Renal impairment was observed in 62% of patients in the overall population, and 58% of patients treated with advanced therapies; the majority had mild impairment, 7–9% had moderate impairment, and < 1% had severe impairment (Table 4). Prevalence estimates were consistent over time (Fig. 1).

Prevalence of Renal Impairment by Health Plan

The proportion of patients with moderate renal impairment was higher in the Medicare group

Table 2 Classification of renal impairment based on estimated glomerular filtration rates

	Grade ^a	eGFR (ml/min/1.73 m ²)
Normal GFR	G1	≥ 90
Mild decrease in GFR	G2	60–89
Moderate decrease in GFR	G3	30–59
Severe decrease in GFR	G4	15–29
End-stage renal disease	G5	< 15

^a Thresholds for the severity group definitions are based on existing guidance. Thomas et al. 2008 [13]
eGFR estimated glomerular filtration rate

Table 3 Patient demographic and clinical characteristics

Variable	All patients ^a (<i>n</i> = 42,173)	Patients treated with advanced therapies ^b (<i>n</i> = 16,197)	Patients with Medicare Advantage or Supplemental plus Part D coverage (<i>n</i> = 4911)	Patients with commercial insurance coverage (<i>n</i> = 37,262)
Age in years, mean (SD)	55.5 (12.3)	53.1 (11.3)	72.1 (8.9)	53.4 (10.9)
Female	75.9	77.1	74.9	76.0
Medicare Advantage or Supplemental plus Part D	11.6	6.7	–	–
Region of residence				
Northeast	15.9	12.8	33.3	13.6
Midwest	13.9	12.9	22.0	12.8
South	40.1	43.1	25.1	42.1
West	25.5	26.4	19.6	26.2
Comorbidities				
Hypertension ^c	40.1	33.1	68.4	36.3
Heart failure ^c	3.2	1.8	10.6	2.2
Diabetes ^c	15.8	12.2	27.0	14.3

All values are % unless otherwise indicated

RA rheumatoid arthritis, SD standard deviation

^a With at least two SCr laboratory test results available

^b Advanced therapies included abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab, and tofacitinib citrate

^c Based on presence of ≥ 1 medical claim with ICD-9/10-CM codes for the disease of interest, in a window ± 90 days around the index date (first diagnosis of RA)

Table 4 Prevalence of renal impairment by severity category

Severity of renal impairment ^a (%) (95% confidence interval)	All patients ^b (<i>n</i> = 42,173)	Patients treated with advanced therapies ^c (<i>n</i> = 16,197)
Mild (grade 2)	52.1 (51.6, 52.6)	50.9 (50.1, 51.6)
Moderate (grade 3)	9.3 (9.0, 9.6)	7.0 (6.6, 7.4)
Severe (grade 4–5)	0.5 (0.4, 0.6)	0.3 (0.2, 0.4)
Overall (any impairment level)	61.9 (61.4, 62.3)	58.2 (57.4, 58.9)

^a Mild: eGFR = 60–90 ml/min/1.73 m²; moderate: eGFR = 30–59 ml/min/1.73 m²; severe: eGFR = < 30 ml/min/1.73 m²

^b With at least two SCr laboratory test results available

^c Advanced therapies included abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab, and tofacitinib citrate

eGFR estimated glomerular filtration rate, *n* number of patients in each group, SCr serum creatinine

Number of patients by year (%)	2013	2014	2015	2016	2017	2018
Mild renal impairment	5,093 (53.4)	1,682 (51.9)	898 (54.2)	846 (49.8)	844 (48.1)	585 (51.0)
Moderate renal impairment	1,051 (11.0)	373 (11.5)	121 (7.3)	104 (6.1)	118 (6.7)	89 (7.8)
Severe renal impairment	66 (0.7)	16 (0.5)	7 (0.4)	7 (0.4)	6 (0.3)	4 (0.4)
Total number of eligible patients ^a	9,531	3,239	1,658	1,700	1,754	1,148
Thresholds for the severity group definitions are based on existing guidance. Mild: eGFR = 60–90 mL/min/1.73m ² ; Moderate: eGFR = 30–59 mL/min/1.73m ² ; Severe: eGFR = <30 mL/min/1.73m ² [13]. eGFR=estimated glomerular filtration rate.						
^a The total number of eligible patients across all years listed here is ~19,000. This differs from the ~42,000 patients listed in Table 1 and elsewhere because the annual analysis required the index date (RA claim) and both SCr values to occur within each specified year. In the full population the SCr values could also occur in years following the index RA claim.						

Fig. 1 Annual prevalence of renal impairment in patients with RA and ≥ 2 SCr measurements. Mild: eGFR = 60–90 mL/min/1.73 m²; moderate: eGFR = 30–59 mL/min/1.73 m²; severe: eGFR = < 30 mL/min/1.73 m²; and any renal impairment: sum of mild, moderate, and severe. RA rheumatoid arthritis, SCr serum creatinine

min/1.73 m²; severe: eGFR = < 30 mL/min/1.73 m²; and any renal impairment: sum of mild, moderate, and severe. RA rheumatoid arthritis, SCr serum creatinine

(21–26%), who were on average 20 years older than the commercial group (with prevalence of 6–7%). For severe impairment, corresponding values were 0.9–1.3 and 0.2–0.4%, respectively (Table 5).

DISCUSSION

In this study, prevalence of moderate or severe renal impairment by MDRD was estimated to be ~ 10% among privately insured US patients

Table 5 Prevalence of renal impairment by health plan type

Severity of renal impairment ^a (%)	Commercial plan coverage		Medicare advantage or supplemental plus part D coverage	
	All patients ^b (<i>n</i> = 37,262)	Patients treated with advanced therapies ^c (<i>n</i> = 15,107)	All patients ^b (<i>n</i> = 4911)	Patients treated with advanced therapies ^c (<i>n</i> = 1090)
Mild (grade 2)	51.9	50.6	53.6	55.0
Moderate (grade 3)	7.2	6.0	25.5	20.6
Severe (grade 4–5)	0.4	0.2	1.3	0.9
Overall (any impairment level)	59.4	56.8	80.5	76.5

^a Mild: eGFR = 60–90 ml/min/1.73 m²; moderate: eGFR = 30–59 ml/min/1.73 m²; and severe: eGFR = < 30 ml/min/1.73 m²

^b With at least two SCr laboratory test results available

^c Advanced therapies included abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab, and tofacitinib citrate

eGFR estimated glomerular filtration rate, *n* number of patients in each group, SCr serum creatinine

with RA and ~ 7% in a subgroup of patients on advanced therapies. The prevalence was higher among Medicare compared to commercial coverage patients.

Renal impairment in RA is relevant to inform drug treatment (e.g., avoidance of NSAIDs) and dose selection (e.g., methotrexate), as patients can accumulate multiple treatments undergoing renal elimination. The MDRD equation for eGFR incorporates age, sex, and SCr and is a validated tool to assess renal function [3, 12].

Earlier studies estimating eGFR by MDRD were limited to single centers, small populations, and did not include US patients with RA. Prevalence rates of renal impairment (eGFR < 60 ml/min/1.73m²) ranged from 8 to 19% across these studies [3, 6–8].

Our study included a large cohort of US patients with available SCr laboratory measurements. This claims-based study also has limitations. Some patients with severe renal impairment are not commercially insured and would not appear in the HIRD®. While MDRD is the method presently employed in US package inserts and associated dosage adjustments, newer methods (e.g., Chronic Kidney Disease

Epidemiology Collaboration [CKD-EPI]) may be employed in practice [14]. Some literature suggests that MDRD may estimate a slightly higher proportion with CKD compared to CKD-EPI [15]. SCr measurements were available for ~ 46% of patients with RA in the database, potentially limiting generalizability. Because race is not captured, patients were designated non-black for purposes of eGFR calculation. As patients were required to have two RA claims, there is the possibility for underestimation of cases in the event of death or transition from commercial coverage before the second claim. RA diagnosis claims were used for identification irrespective of associated provider specialty and claims for renal impairment were not examined; different approaches may help quantify uncertainty around the CKD prevalence estimates. The association between renal impairment and factors such as patient demographics (e.g., gender and geographical area of residence), comorbidities, or concomitant medications (e.g., methotrexate, NSAIDs, etc.) or for specific medication classes (e.g., JAKi) was not assessed in this project; however, it should be considered in future research.

CONCLUSIONS

In summary, moderate or severe renal impairment was present in ~ 10% of insured patients with RA in the US. These findings support assessment of renal function in patients with RA to enable appropriate selection and dosing of medications.

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Compliance with Ethics Guidelines. Researchers' access to claims data was limited to data stripped of identifiers to ensure confidentiality. HealthCore maintains data use agreements with the covered entities in compliance with the Health Insurance Portability and Accountability Act. Permission was obtained from HealthCore to access the database. An Institutional Review Board did not review the study since only this limited/deidentified data set was accessed.

Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to their proprietary nature and the associated restrictions that apply to their availability to external sources. Data may be made available through the corresponding author upon reasonable request and with permission of HealthCore.

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