The 3-Year Incidence of Gout in Elderly Patients with CKD

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Abstract

Background and objectives The risk of gout across CKD stages is not well described.

Design, setting, participants, & measurements We performed a retrospective cohort study using linked health care databases from Ontario, Canada from 2002 to 2010. The primary outcome was the 3-year cumulative incidence of gout, on the basis of diagnostic codes. We presented our results by level of kidney function (eGFR≥90 ml/min per 1.73 m^2, 60–89, 45–59, 30–44, 15–29, and chronic dialysis) and by sex. Additional analyses examined the risk of gout adjusting for clinical characteristics, incidence of gout defined by the receipt of allopurinol or colchicine, and gout risk in a subpopulation stratified by the level of eGFR and albuminuria.

Results Of the 282,925 adults aged ≥66 years, the mean age was 75 years and 57.9% were women. The 3-year cumulative incidence of gout was higher in older adults with a lower level of eGFR. In women, the 3-year cumulative incidence of gout was 0.6%, 0.7%, 1.3%, 2.2%, and 3.4%, and in men the values were 0.8%, 1.2%, 2.5%, 3.7%, and 4.6%, respectively. However, patients on chronic dialysis had a lower 3-year cumulative incidence of gout (women 2.0%, men 2.9%) than those with more moderate reductions in kidney function (*i.e.*, eGFR 15–44 ml/min per 1.73 m^2). The association between a greater loss of kidney function and a higher risk of diagnosed gout was also evident after adjustment for clinical characteristics and in all additional analyses.

Conclusions Patients with a lower level of eGFR had a higher 3-year cumulative incidence of gout, with the exception of patients receiving dialysis. Results can be used for risk stratification.

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Introduction

Gout is associated with decreased quality of life, increased morbidity, and increased health care costs and utilization (1–4). In 2013, the economic burden in the United States was estimated at $6 billion (5). Individuals with CKD may be at an increased risk of gout (6–9). Krishnan reported that men with nondialysis CKD (defined as an eGFR<60 ml/min per 1.73 m^2) have almost a two-fold higher risk of gout compared with individuals with normal kidney function (9). Patients with CKD may be predisposed to gout due to decreased uric acid excretion resulting in hyperuricemia (10).

We performed a comprehensive search of PubMed and other major bibliographic databases on May 7, 2016 and identified no previous studies that have characterized the incidence of gout according to level of kidney function and sex. Previous studies have been limited to individuals on chronic dialysis or have not grouped individuals according to the CKD stages defined by modern Kidney Disease Improving Global Outcomes (KDIGO) guidelines, preventing a comprehensive understanding of the risk of gout in CKD (9,11–14). Moreover, there are conflicting results regarding whether individuals on dialysis have a higher risk of gout compared with individuals with more moderate declines in kidney function (12–14).

A better understanding of the incidence of gout across the stages of CKD is important for risk stratification. Therefore, we examined the 3-year cumulative incidence of diagnosed gout in adults according to level of kidney function (eGFR) and sex. To further understand this relationship, we assessed the time to first gout event (expressed as hazard ratios), incidence rate of receipt of a gout medication (allopurinol or colchicine) per 1000 person-years, and in a subpopulation, presented by level of eGFR and albuminuria.

Materials and Methods

Design and Setting

We conducted a population-based cohort study using health care databases held at the Institute for Clinical Evaluative Sciences (ICES) in Ontario, Canada. These datasets were linked using unique encoded identifiers and analyzed at ICES Western. Universal access to physician and hospital services is provided to all Ontario residents. We conducted this study according to a prespecified protocol that was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre (Toronto, Ontario, Canada).

Data Sources

We used eight linked databases to determine patient baseline and outcome characteristics. To determine kidney function, we obtained serum creatinine values from Dynacare which contains outpatient laboratory data from 148 sites in Ontario, and Cerner, which contains laboratory data from 11 hospitals in Southwestern Ontario. We used the Ontario Registered Persons Database for demographic and vital status information. Information on health claims for inpatient and outpatient physician services was obtained from the Ontario Health Insurance Plan database. The Canadian Institute for Health Information Discharge Abstract Database contained diagnostic and procedural information for hospitalizations, whereas information on emergency room visits was obtained from the National Ambulatory Care Reporting System. We used the Ontario Drug Benefit database to identify prescription drug use. This database captures all outpatient prescriptions dispensed to individuals aged ≥65 years with an error rate of <1% (15). Lastly, we used the Canadian Organ Replacement Register to identify kidney transplant recipients for exclusion. Data were complete with the exception of income and rurality (<0.5% missing). The only reason for loss to follow-up was emigration from the province (<0.5% annually) (16).

Primary Cohort

We included individuals if they had evidence of at least two serum creatinine values from April 1, 2002 to March 31, 2010. The CKD Epidemiology Collaboration equation was used to calculate eGFR (ml/min per 1.73 m^2) (17). To ensure stability of kidney function, we required the two eGFR values to be separated by ≥90 days to <1 year and to also be within 5 ml/min per 1.73 m^2 or ≤5% of each other. We presented eGFR according to the KDIGO recommendations: ≥90 ml/min per 1.73 m^2, 60–89, 45–59, 30–44, 15–29, and chronic dialysis (11,17). When there were multiple eligible inclusion dates, we designated the most recent serum creatinine value before cohort entry as the index date (cohort entry date). We defined chronic dialysis as two chronic dialysis billing codes separated by ≥90 days but <180 days with the date of the second chronic dialysis code considered the index date. To ensure we had prescription drug information on all Ontario individuals, we restricted our analysis to individuals aged ≥66 years to allow for a minimum of 1 year of drug coverage. We excluded individuals who received a kidney transplant or chronic dialysis before index date to ensure only individuals with incident ESRD were included. We also excluded individuals with an eGFR<15 ml/min per 1.73 m^2 who had no evidence of chronic dialysis (n=457) from the primary analysis. The rationale for this included: (*1*) small sample size and number of events precluded us from reporting the results of this group (ICES privacy policy requires small cell sizes <6 to be suppressed); and (2) we did not combine this group with the dialysis group as *a priori* we hypothesized that the filtering of uric acid during dialysis may reduce the incidence of gout; however, in an additional analysis we combined these individuals with the eGFR 15–29 ml/min per 1.73 m^2 group. To ensure we only included *de novo* gout cases, we excluded all individuals with prior evidence of gout (on the basis of diagnostic codes or prescription for allopurinol and colchicine before the index date).

Subpopulation

Using the KDIGO recommendations, for a subpopulation with at least one available eGFR and albumin-to-creatinine ratio (ACR) measurement, we categorized individuals by CKD prognosis (low risk, moderate risk, high risk, or very high risk) (Supplemental Table 1) (11). We required the eGFR and the urine ACR measurements to be within 6 months of each other and the date of the most recent test before cohort entry was considered the index date. We excluded individuals who received dialysis before or at cohort entry; however, we included individuals with an eGFR<15 ml/min per 1.73 m^2 with no evidence of chronic dialysis (11).

Outcomes

Our primary outcome was gout defined by evidence of a diagnostic code from a physician visit, emergency room visit, or hospitalization (Supplemental Table 2). We followed all individuals for a maximum of 3 years after cohort entry for a gout event. To ensure we were accurately capturing gout, in an additional analysis, we defined gout solely by evidence of dispensing of a medication typically used to treat gout (allopurinol or colchicine).

Statistical Analyses

We used standardized differences (with a standardized difference >10% considered to be a meaningful difference) to compare baseline characteristics between individuals with an eGFR≥90 ml/min per 1.73 m^2 and those with a lower eGFR (18). Compared with traditional hypothesis tests, standardized differences are less sensitive to sample size (18). We estimated the 3-year cumulative incidence of gout using the cumulative incidence function, accounting for the competing risk of death, and using the exponential function on the basis of the incidence rate (noncompeting risk method) (19). Because it is known that death is common in patients with CKD, particularly in dialysis, it is important to account for the competing risk of death to avoid potentially overestimating the risk of gout (20). We also estimated the incidence rate of gout, defined as the rate per 1000 person-years of follow-up, censoring at death, the first diagnosis of gout in follow-up, or 3-years postindex date. We also calculated hazard ratios using Cox proportional hazard regression and we calculated subdistribution hazard ratios using the Fine and Gray method to account for the competing risk of death (21,22); the proportional hazard assumption was satisfied. We adjusted for the following potential confounders which were selected on the basis of a literature review and clinical expertise: age, diabetes mellitus, diuretic use (including loop diuretics, potassium sparing diuretics, and thiazide diuretics), hypertension, and additional comorbidities using the Charlson comorbidity index (23). For the Cox proportional hazard analysis, the reference group for the primary cohort was an eGFR>90 ml/min per 1.73 m^2 and for the subpopulation with ACR measurements the reference group was an eGFR≥60 ml/min per 1.73 m^2 and

ACR<30 mg/g (low risk group). To help guide prognostication we presented all results by level of eGFR and sex at cohort entry. We tested the trend of a higher incidence of gout with declining eGFR using the Cochran–Armitage test for trend. We used the chi-squared test to compare differences in gout risk between men and women at each level of eGFR. We considered a two-sided P value <0.05 as statistically significant and conducted all analyses with statistical analysis system (SAS) software, version 9.3 (www.sas.com).

Results

Baseline Characteristics

In the primary cohort, we included 282,925 elderly Ontario residents (Supplemental Figure 1). Approximately 87% (n=246,109) of the cohort had an eGFR<90 ml/min per 1.73 m^2 and 1.6% (n=4528) were on dialysis (Table 1). Patients with an eGFR<90 versus ≥90 ml/min per 1.73 m^2 were older (75.5 versus 68.8 years) and were more likely to have hypertension (68.3% versus 58.8%). Regarding medication use, patients with an eGFR<90 versus ≥90 ml/min per 1.73 m^2 were more likely to be prescribed loop diuretics (10.3% versus 3.9%) and thiazide diuretics (19.7% versus 15.5%).

The total person-years of follow-up over 3 years across the six eGFR (ml/min per 1.73 m^2) levels was 107,060 person-years (≥90), 486,362 (60–89), 135,625 (45–59), 54,493 (30–44), 12,893 (15–29), and 9958 (dialysis), respectively. During the 3 years of follow-up, we censored 25,980 (9.2%) patients at death (5.6%, 6.7%, 11.0%, 18.3%, 29.4%, and 47.5% with an eGFR ≥90 ml/min per 1.73 m^2, 60–89, 45–59, 30–44, 15–29, and chronic dialysis, respectively) and 3559 (1.3%) had at least one gout event in follow-up.

Gout Risk

Presented in Table 2 is the 3-year cumulative incidence of diagnosed gout presented by level of kidney function and sex, accounting for the competing risk of death, corresponding values of the 3-year incidence rate of gout per 1000 person-years, and the relative association (hazard ratio [HR] and subdistribution hazard ratio [sHR]) between level of kidney function and gout adjusted for other baseline characteristics. The 3-year cumulative incidence of diagnosed gout, accounting for the competing risk of death, was higher across five groups of older adults defined by progressively lower levels of eGFR (P for trend <0.001) (Figure 1); in women, the 3-year cumulative incidence ranged from 0.6% to 3.4% and in men from 0.8% to 4.6% (Table 2). However, persons on chronic dialysis had a lower 3-year cumulative incidence of diagnosed gout (women: 2.0%; men: 2.9%) than those with more moderate reductions in kidney function (*i.e.*, eGFR 15–44 ml/min per 1.73 m^2). Women and men with an eGFR 15–29 ml/min per 1.73 m^2 had the highest 3-year cumulative incidence of gout among all of the eGFR levels. The association between a lower eGFR and a higher risk of gout persisted after adjustment for clinical characteristics (Table 2). For example, in both women and men, an eGFR between 15 and 29 ml/min per 1.73 m^2 was associated with over a five-fold higher risk of diagnosed gout compared with persons with an eGFR≥90 ml/min per 1.73 m^2. Similar results were found when we used a noncompeting risk method to estimate the cumulative incidence and when we combined the previously excluded eGFR<15 ml/min per 1.73 m^2 with no evidence of dialysis group into the eGFR 15–29 ml/min per 1.73 m^2 group (P for trend <0.001). When comparing men to women, men had a significantly higher incidence of gout across all levels of kidney function (P for chi-squared test <0.05), except for the chronic dialysis group which did not reach statistical significance (P for chi-squared test=0.07).

Similar trends were found when gout was defined by the receipt of medications (Table 3) (P for trend <0.001), although the 3-year cumulative incidence estimates were lower and the HR and sHRs were higher compared with the primary gout definition. It is important to note that this trend did not hold in the unadjusted Cox proportional hazard analysis where the HR for gout was highest in patients receiving dialysis; however, the wide confidence intervals in this analysis point to a lack of precision in the effect estimates.

When we performed a sensitivity analysis defining gout by evidence of one hospitalization or emergency room visit with a gout diagnostic code or two provincial billing diagnostic codes of gout, we still found a strong gradient between decreasing eGFR and a higher incidence of gout (P for trend <0.001 for both men and women). To ensure our results were not spurious we performed a test of specificity which, as expected, revealed there was no statistically significant increase in the incidence of rheumatoid arthritis across the eGFR levels (P for trend men 0.57, women 0.06).

Sensitivity Analysis

Presented in Supplemental Tables 3 and 4 for the subpopulation with eGFR and ACR values are the baseline characteristics, the 3-year cumulative incidence of diagnosed gout presented by level of kidney function and sex accounting for the competing risk of death, corresponding values of the 3-year incidence rate of gout per 1000 person-years, and the relative association (HR and sHR) between level of kidney function and gout adjusted for other baseline characteristics. The 3-year cumulative incidence of diagnosed gout was higher in individuals with a lower eGFR and higher albuminuria (P for trend <0.001).

Discussion

In this population-based study we found that adults ≥66 years of age with a lower level of eGFR had a higher 3-year cumulative incidence of diagnosed gout; however, persons on chronic dialysis had a lower incidence of gout compared with those with more moderate reductions in kidney function. Men and women with an eGFR 15–29 ml/min per 1.73 m^2 had the highest incidence of gout, with 1 in 30 older women and 1 in 20 older men ≥66 years experiencing diagnosed gout within 3 years. The association between gout and kidney function persisted even after adjustment for clinical characteristics and when defining kidney function by eGFR and albuminuria.

The incidence of gout in patients with CKD found in this study is similar to previous studies (9,12–14,24). However, limitations of previous studies prevented an accurate and

Table 1. Baseline characteristics of 282,925 individuals in the primary cohort[a]

Characteristic	eGFR ml/min per 1.73 m^2					
	≥90 (*n*=36,816)	60–89 (*n*=168,115)	45–59 (*n*=48,024)	30–44 (*n*=20,240)	15–29 (*n*=5202)	Dialysis (*n*=4528)
Age, yr	68.8±3.5	74.2±6.5[b]	77.5±7.2[b]	79.8±7.5[b]	80.5±7.9[b]	75.7±6.4[b]
Women, *n* (%)	21,498 (58.4)	93,576 (55.7)	29,780 (62.0)	13,424 (66.3)[b]	3378 (64.9)[b]	2104 (46.5)[b]
Income, lowest quintile, *n* (%)	6894 (18.7)	31,460 (18.7)	9662 (20.1)	4497 (22.2)	1222 (23.5)[b]	1095 (24.2)[b]
Rural residence,[c] *n* (%)	3163 (8.6)	16,729 (10.0)	5499 (11.5)	2529 (12.5)[b]	758 (14.6)[b]	593 (13.1)[b]
eGFR, ml/min per 1.73 m^2	93.6±3.4	76.3±8.8[b]	53.4±4.2[b]	38.9±4.2[b]	24.7±3.9[b]	
Comorbidities						
Charlson comorbidity index[d]	0 (0–0)	0 (0–0)	2 (2–2)[b]	2 (2–2)[b]	2 (2–3)[b]	3 (2–5)[b]
Coronary artery disease, *n* (%)	10,296 (28.0)	58,468 (34.8)[b]	20,544 (42.8)[b]	10,089 (49.8)[b]	2856 (54.9)[b]	2641 (58.3)[b]
Diabetes mellitus, *n* (%)	13,938 (37.9)	53,460 (31.8)[b]	15,893 (33.1)	7604 (37.6)	2272 (43.7)[b]	2474 (54.6)[b]
Heart failure, *n* (%)	2060 (5.6)	14,513 (8.6)[b]	7524 (15.7)[b]	4987 (24.6)[b]	1810 (34.8)[b]	2128 (47.0)[b]
Hypertension, *n* (%)	21,638 (58.8)	107,756 (64.1)[b]	35,789 (74.5)[b]	16,400 (81.0)[b]	4342 (83.5)[b]	3768 (83.2)[b]
Peripheral vascular disease, *n* (%)	336 (0.9)	1933 (1.1)	1011 (2.1)	672 (3.3)[b]	274 (5.3)[b]	484 (10.7)[b]
Medications						
Loop diuretics, *n* (%)	1442 (3.9)	10,158 (6.0)	6038 (12.6)[b]	4645 (22.9)[b]	2045 (39.3)[b]	2526 (55.8)[b]
Potassium-sparing diuretics, *n* (%)	979 (2.7)	6006 (3.6)	3546 (7.4)[b]	2305 (11.4)[b]	610 (11.7)[b]	257 (5.7)[b]
Thiazide diuretics, *n* (%)	5703 (15.5)	30,034 (17.9)	11,043 (23.0)[b]	5262 (26.0)[b]	1257 (24.2)[b]	960 (21.2)[b]

Data are presented as number (%) except for age and eGFR which are presented as mean±SD. The Charlson comorbidity index is presented as a median (interquartile range).

[a]Standardized differences were used to compare baseline characteristics between the referent group (eGFR≥90 ml/min per 1.73 m^2) and the other five groups (eGFR 60–89 ml/min per 1.73 m^2, 45–59, 30–44, 15–29, and chronic dialysis). Standardized differences are less sensitive to sample size than traditional hypothesis tests. They provide a measure of the difference between groups divided by the pooled SD; a value >10% is interpreted as a meaningful difference between groups.

[b]Denotes a meaningful difference (>10%).

[c]Refers to location of residence with a population size <10,000 persons.

[d]All individuals with an eGFR<60 ml/min per 1.73 m^2 with a Charlson comorbidity index of 0 were given a score of 2 and those with a score of 1 were given a score of 3; one of the variables in the Charlson comorbidity index is presence of kidney disease which automatically results in these individuals receiving a score of 2.

Table 2. Three-year cumulative incidence, incidence rate, hazard ratios, and subdistribution hazard ratios of a gout diagnosis presented by level of kidney function and sex

eGFR, ml/min per 1.73 m^2	3-Year Cumulative Incidence[a], % (95% CI)	Incidence Rate per 1000 Person-Years (95% CI)	Hazard Ratio (95% CI)		Subdistribution Hazard Ratio (95% CI)[a]	
			Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
Women						
≥90 (*n*=21,498)	0.6 (0.5 to 0.7)	2.0 (1.7 to 2.4)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
60–89 (*n*=93,576)	0.7 (0.7 to 0.8)	2.6 (2.4 to 2.8)	1.3 (1.1 to 1.6)	1.4 (1.1 to 1.7)	1.3 (1.1 to 1.6)	1.4 (1.2 to 1.7)
45–59 (*n*=29,780)	1.3 (1.2 to 1.4)	4.6 (4.2 to 5.1)	2.3 (1.9 to 2.9)	2.1 (1.7 to 2.7)	2.3 (1.9 to 2.8)	2.3 (1.9 to 2.9)
30–44 (*n*=13,424)	2.2 (1.9 to 2.5)	8.0 (7.1 to 8.9)	4.0 (3.3 to 5.0)	3.5 (2.7 to 4.4)	3.8 (3.0 to 4.6)	3.7 (2.9 to 4.7)
15–29 (*n*=3378)	3.4 (2.9 to 4.0)	13.7 (11.3 to 16.3)	7.0 (5.4 to 9.0)	5.6 (4.2 to 7.4)	6.0 (4.6 to 7.7)	5.6 (4.2 to 7.5)
Dialysis (*n*=2104)	2.0 (1.5 to 2.8)	8.9 (6.5 to 12.0)	4.3 (1.8 to 10.5)	3.1 (1.2 to 7.7)	3.5 (2.5 to 4.9)	2.8 (1.9 to 4.2)
Men						
≥90 (*n*=15,318)	0.8 (0.7 to 1.0)	2.9 (2.4 to 3.4)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
60–89 (*n*=74,539)	1.2 (1.1 to 1.3)	4.3 (4.0 to 4.6)	1.5 (1.2 to 1.8)	1.6 (1.3 to 1.9)	1.5 (1.3 to 1.8)	1.6 (1.3 to 1.9)
45–59 (*n*=18,244)	2.5 (2.3 to 2.7)	8.8 (8.0 to 9.7)	3.1 (2.5 to 3.8)	2.9 (2.3 to 3.6)	3.0 (2.5 to 3.7)	3.2 (2.6 to 3.9)
30–44 (*n*=6816)	3.7 (3.3 to 4.3)	14.1 (12.4 to 15.9)	5.0 (4.0 to 6.1)	4.4 (3.5 to 5.5)	4.6 (3.7 to 5.7)	4.7 (3.7 to 5.9)
15–29 (*n*=1824)	4.6 (3.7 to 5.7)	18.8 (15.1 to 23.1)	6.7 (5.1 to 8.8)	5.5 (4.1 to 7.4)	5.7 (4.3 to 7.6)	5.5 (4.1 to 7.4)
Dialysis (*n*=2424)	2.9 (2.3 to 3.6)	13.1 (10.3 to 16.5)	4.9 (2.0 to 12.0)	3.6 (1.5 to 9.1)	3.5 (2.6 to 4.7)	3.1 (2.2 to 4.3)

95% CI, 95% confidence interval.

[a]Estimates derived from the Fine and Gray method to account for the competing risk of death.

[b]Cox regression model looking at kidney function and gout, adjusted for age, diabetes, diuretic use, hypertension, and Charlson comorbidity index.

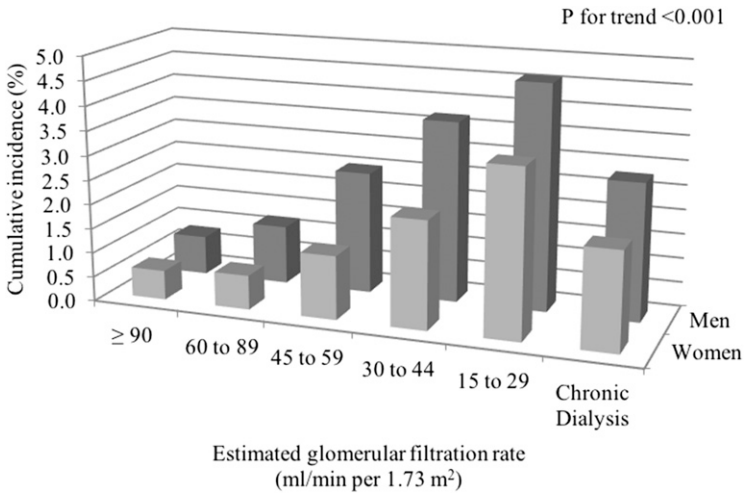

Figure 1. | **Three-year cumulative incidence of a gout diagnosis presented by level of kidney function and sex**. The 3-year cumulative incidence of diagnosed gout was higher across the five groups of older adults defined by progressively lower levels of eGFR for both men and women (*P* for trend <0.001); however, persons on chronic dialysis had a lower incidence of gout than those with a moderate reduction in kidney function.

comprehensive understanding of gout incidence in CKD. For example, many previous studies only included patients on dialysis and no prior studies presented the incidence of gout according to the stages of CKD defined by KDIGO and by eGFR and albuminuria (12–14).

Our study supports that gout incidence is higher in patients with CKD compared with the general population (6). For example, our study found even persons with mild-to-moderate declines in kidney function (eGFR 45–59 ml/min per 1.73 m^2) had more than a two-fold increased risk of gout compared with persons with normal kidney function. With our results, physicians who care for patients with CKD may wish to avoid medications that increase the risk of gout (*e.g.*, thiazide diuretics) as well as suggest lifestyle modifications such as reduced red meat and alcohol consumption (25,26).

Similar to previous studies, we found that patients on dialysis had a lower incidence of gout compared with those with more moderate CKD, not on dialysis (13,14). For example, the risk of gout in our study was close to two-fold higher in women with an eGFR between 15 and 29 ml/min per 1.73 m^2 compared with women on dialysis. There are two potential explanations for this finding. First, uric acid is filtered during dialysis with uric acid levels being reduced by 54%–66% after dialysis treatment (27–29). Second, uric acid is contained in many foods; dialysis patients often have decreased nutritional intake along with dietary restrictions (30).

The high incidence of gout in this unique patient population is concerning as it is a condition associated with morbidity and high health care utilization costs (2,4). Moreover, many standard medications used to treat gout in the general population are contraindicated or have unproven efficacy in CKD. Thus, there may be value in conducting clinical trials on gout prevention in patients with CKD (31).

Limitations of our study are recognized. First, we were unable to obtain serum uric acid values from our databases, therefore, we used administrative database codes to define gout; however, we have successfully used these codes in a previous study assessing gout in living kidney donors (32). Moreover, to ensure these database codes were accurate we defined gout in several different ways and found similar results for each definition; we also performed a test of specificity, finding no association between level of kidney function and the risk of rheumatoid arthritis. Second, we were unable to control for gout risk factors not in our data sources (*e.g.*, body mass index) (26,30). Third, our findings may not be generalizable to the entire Ontario population (Dynacare and Cerner do not include all labs in Ontario) and to the younger population. Fourth, approximately 75% of the Ontario population is of white race, and caution should be exercised when extrapolating our results to other races (*i.e.*, blacks have been found to have a higher incidence of gout compared with whites) (33–35).

In conclusion, patients with a lower level of eGFR had a higher risk of gout, with the exception of patients receiving dialysis. These results suggest strategies to reduce the risk of gout in patients with moderate-to-severe CKD might be beneficial.

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Table 3. Three-year cumulative incidence, incidence rate, hazard ratios, and subdistribution hazard ratios of receipt of a gout medication (allopurinol or colchicine) presented by level of kidney function and sex

eGFR, ml/min per 1.73 m^2	3-Year Cumulative Incidence,[a] % (95% CI)	Incidence Rate per 1000 Person-Years (95% CI)	Hazard Ratio (95% CI)		Subdistribution Hazard Ratio (95% CI)[a]	
			Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
Women						
≥90 (*n*=21,498)	0.3 (0.2 to 0.4)	1.1 (0.9 to 1.4)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
60–89 (*n*=93,576)	0.4 (0.4 to 0.5)	1.6 (1.4 to 1.7)	1.4 (1.1 to 1.9)	1.6 (1.2 to 2.1)	1.4 (1.1 to 1.8)	1.7 (1.3 to 2.2)
45–59 (*n*=29,780)	0.9 (0.8 to 1.1)	3.6 (3.2 to 4.0)	3.3 (2.5 to 4.3)	3.3 (2.5 to 4.4)	3.2 (2.4 to 4.2)	4.1 (3.0 to 5.5)
30–44 (*n*=13,424)	1.8 (1.6 to 2.0)	7.5 (6.7 to 8.5)	6.9 (5.3 to 9.0)	6.7 (5.0 to 8.9)	6.0 (4.6 to 7.9)	7.7 (5.6 to 10.5)
15–29 (*n*=3378)	2.8 (2.2 to 3.4)	13.4 (11.1 to 16.1)	12.3 (9.1 to 16.6)	11.1 (8.0 to 15.5)	9.4 (6.8 to 12.9)	11.6 (8.2 to 16.6)
Dialysis (*n*=2104)	1.2 (0.7 to 1.8)	7.7 (5.5 to 10.5)	13.8 (6.9 to 27.6)	10.7 (5.2 to 22.1)	3.9 (2.4 to 6.2)	3.9 (2.3 to 6.6)
Men						
≥90 (*n*=15,318)	0.4 (0.3 to 0.5)	1.6 (1.3 to 2.0)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
60–89 (*n*=74,539)	0.7 (0.7 to 0.8)	2.6 (2.4 to 2.8)	1.6 (1.3 to 2.1)	1.8 (1.4 to 2.3)	1.8 (1.4 to 2.3)	2.1 (1.6 to 2.7)
45–59 (*n*=18,244)	1.7 (1.6 to 1.9)	6.7 (6.0 to 7.4)	4.2 (3.2 to 5.4)	4.1 (3.1 to 5.4)	4.4 (3.3 to 5.8)	5.6 (4.1 to 7.5)
30–44 (*n*=6816)	2.9 (2.6 to 3.3)	12.9 (11.3 to 14.6)	8.0 (6.2 to 10.5)	7.5 (5.9 to 10.0)	7.5 (5.6 to 10.0)	9.4 (6.9 to 13.0)
15–29 (*n*=1824)	3.0 (2.3 to 3.8)	15.6 (12.3 to 19.6)	9.8 (7.0 to 13.6)	8.4 (5.9 to 12.0)	7.6 (5.3 to 10.9)	9.2 (6.1 to 13.7)
Dialysis (*n*=2424)	2.3 (1.7 to 3.0)	15.1 (12.1 to 18.8)	10.4 (4.5 to 24.1)	7.6 (3.2 to 18.1)	5.7 (4.0 to 8.2)	6.0 (3.9 to 9.2)

95% CI, 95% confidence interval.

[a]Estimates derived from Fine and Gray method to account for the competing risk of death.

[b]Cox regression model looking at kidney function and gout, adjusted for age, diabetes, diuretic use, hypertension, and Charlson comorbidity index.

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