Gout Prevalence, Practice Patterns, and Associations with Outcomes in North American Dialysis Patients

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Key Points

- Gout is a common inflammatory arthropathy, and it can be as frequent in patients with ESKD as in the general adult population.
- Patient outcomes and providers' practice patterns for ESKD patients with gout are unknown. We sought to address these gaps in this study.
- We found that gout is not associated with worse clinical or patient-reported outcomes, despite being frequent and possibly under-reported.

Abstract

Introduction Gout occurs frequently in patients with kidney disease and can lead to a significant burden on quality of life. Gout prevalence, and its association with outcomes in hemodialysis (HD) and peritoneal dialysis (PD) populations located in North America, is unknown.

Methods We used data from North America cohorts of 70,297 HD patients (DOPPS, 2012–2020) and 5117 PD patients (PDOPPS, 2014–2020). We used three definitions of gout for this analysis: (1) having an active prescription for colchicine or febuxostat; (2) having an active prescription for colchicine, febuxostat, or allopurinol; or (3) having an active prescription for colchicine, febuxostat, or allopurinol, or prior diagnosis of gout. Propensity score matching was used to compare outcomes among patients with versus without gout. Outcomes included erythropoietin resistance index (ERI=erythropoiesis stimulating agent dose per week/(hemoglobin×weight)), all-cause mortality, hospitalization, and patient-reported outcomes (PROs).

Results The gout prevalence was 13% in HD and 21% in PD; it was highest among incident dialysis patients. Description of previous history of gout was rare, and identification of gout defined by colchicine (2%–3%) or febuxostat (1%) prescription was less frequent than by allopurinol (9%–12%). Both HD and PD patients with gout (versus no gout) were older, were more likely male, had higher body mass index, and had higher prevalence of cardiovascular comorbidities. About half of patients with a gout history were prescribed urate-lowering therapy. After propensity score matching, mean ERI was 3%–6% higher for gout versus non-gout patients while there was minimal evidence of association with clinical outcomes or PROs.

Conclusion In a large cohort of PD and HD patients in North America, we found that gout occurs frequently and is likely under-reported. Gout was not associated with adverse clinical or PROs.

Introduction

Gout is an inflammatory response to monosodium urate crystals in the articular tissue, a frequently chronic and progressive condition driven by serum uric acid (SUA) above its solubility threshold of 6.8 mg/dl. Gout, the most common inflammatory arthropathy in adults, leads to increased health care utilization and poor health-related quality of life in the general population.[1] Since the kidney excretes uric acid, SUA concentration increases as kidney function declines. Thus, the prevalence of both gout and hyperuricemia increases as GFR decreases.[2] Gout inflicts patients with CKD five times more frequently than in age-standardized individuals with normal kidney function.[2]

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Hyperuricemia correlates with increased endothelial cell oxidative stress, greater inflammation, and arterial stiffness and may contribute to accelerated atherosclerosis and poor cardiovascular (CV) outcomes in the general population.[3,4] In observational studies among nondialysis CKD patients, both hyperuricemia and gout are associated with worse kidney outcomes[5] and increased risk of CV mortality.[6,7] In general, xanthine oxidase urate lowering therapy (ULT) agents safely and effectively treat gout in patients with CKD, despite the absence of available data from randomized controlled trials (RCTs) in patients with advanced CKD undergoing KRT.

A paucity of data exists on the prevalence of gout and its associations with clinical outcomes among patients with kidney failure (KF) undergoing KRT. Hemodialysis (HD) easily clears uric acid, a small nonprotein bound molecule. Peritoneal dialysis (PD), particularly continuous cycling PD, also effectively reduces SUA concentrations.[8] Despite the rationale that KRT lowers SUA concentration through dialysis clearance and therefore reduces clinical significance of gout among patients with KF on dialysis, an observational study suggested an increased risk of all-cause mortality among ESKD patients with incident gout episodes.[9] Notably, the cumulative incidence of gout in the dialysis population can be as high as the general population, suggesting that KRT may not reduce gout risk among patients with advanced CKD.[9]

Given the clinical importance of gout in patients with KF on dialysis, there remains an important unmet need to assess its prevalence and impact on key clinical and patient-reported outcomes (PRO), as well as to describe ULT practice patterns in KF populations. We sought to address these objectives to further characterize the clinical impact of gout on individuals living with KF undergoing KRT.

Materials and Methods

Study Design

This multicenter prospective cohort study used data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) and Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS). The DOPPS is a continuous prospective cohort study of adult chronic in-center HD patients in 21 countries since 1996. Maintenance HD patients were randomly selected from HD facilities in each country. The PDOPPS is a continuous prospective cohort study designed to identify optimal practices for individuals treated with maintenance PD in eight countries since 2014. Adult patients were selected randomly for enrollment from stratified national samples of PD facilities.

Patient Population

This analysis uses US DOPPS data from phases 5–7 (2012–2020) and US PDOPPS data from phases 1–2 (2014–2020). The US DOPPS was approved by an independent institutional review board (E&I Study Number 98004-2, latest). The study was conducted according to the Declaration of Helsinki. Patient consent was obtained as required following national and local ethics committee regulations. Patients who did not have data on gout at enrollment were excluded. Details regarding DOPPS[10] and PDOPPS[11] cohorts have been previously published.

Exposure Variable

We used three definitions of gout for this analysis: (1) having an active prescription for colchicine or febuxostat; (2) having an active prescription for colchicine, febuxostat, or allopurinol; or (3) having an active prescription for colchicine, febuxostat, or allopurinol, or prior diagnosis of gout. Data on gout definitions were captured at the date of patient enrollment in PDOPPS or DOPPS.

History of gout was captured differently between PDOPPS and DOPPS. In DOPPS facilities and in large dialysis organization (LDO) PDOPPS clinics, comorbidity was defined by mapping international classification of disease (ICD)-10 codes entered by dialysis providers. In PDOPPS non-LDO facilities, medical history was assessed via a questionnaire completed by a study coordinator, with information on history of gout answered directly by the study coordinator on the basis of review of patient medical records.

Data were analyzed separately for each definition to explore sensitivity of gout prevalence and association with outcomes. Each exposure was represented as a dichotomous variable (reference group: patients without any of these indications of gout). We also used a five-category variable with mutually exclusive groups for (1) colchicine alone; (2) febuxostat; (3) allopurinol; (4) prior diagnosis of gout; and (5) none of the above.

Outcomes

Clinical Outcomes

We explored all-cause mortality, all-cause hospitalization, and CV death, as defined by the composite of CV-related codes for cause of death including acute myocardial infarction, cardiac arrhythmia, and stroke. In addition, we assessed baseline erythropoietin resistance index (ERI), defined as the erythropoiesis stimulating agent (ESA) weekly dose divided by (patient weight×hemoglobin). ERI is a surrogate for inflammatory activity in patients with CKD and has been associated with worse outcomes among patients with ESKD.[12]

Patient-Reported Outcomes

For health-related quality of life, the KDQOL-36 physical component summary (PCS) and mental component summary (MCS) were measured. We used the KDQOL-36, a disease-specific validated instrument in patients with ESKD, to assess symptoms and health-related quality of life among patients undergoing maintenance dialysis.[13,14] The KDQOL-36 kidney-specific domains of burden, effects, and symptoms subscales were also analyzed. On the basis of prior studies of minimally important changes in KDQOL scores, a three- to five-point mean difference in PCS and MCS was considered clinically meaningful.[15]

Depression was assessed using the 10-item questionnaire Center for Epidemiologic Studies Depression Scale (CES-D) score, a validated instrument for depression screening in the general population.[16,17] Functionality was measured by the Katz/Brody scale, which combines two validated measurements of basic and instrumental daily activities. In brief, the Katz/Brody scale assesses the respondent's ability to perform routine basic activities such as bathing, feeding themselves, and toileting, as well as instrumental activities, for example, financial, housekeeping, and shopping tasks. These measurements are strongly associated with health care utilization and are predictors of a poor prognosis in patients with ESKD.[18,19] Finally, self-reported physical

activity was defined by Rapid Assessment Physical Activity (RAPA), also a validated instrument in the general population.[20] In summary, the RAPA allows physical activity categorization into low, moderate, and intense. Low physical activity, as defined by the RAPA, is associated with worse clinical outcomes in patients with CKD.

Among the HD cohort, limited data on PROs and cause of death were collected due to electronic health record (EHR) capture of US HD data, and thus, outcomes for HD were limited to all-cause mortality, hospitalization, and ERI.

Statistical Methods

Gout prevalence was estimated using the three gout definitions as above. For the associations with clinical and PROs, the most inclusive gout definition was used as the primary analysis. Associations between different gout definitions and outcomes were assessed via sensitivity analyses (Supplemental Figure 1).

We used propensity score matching to balance covariates between patients with and without gout. We matched patients with gout to non-gout patients using Proc PSMatch in SAS 9.4 using a 1:1 greedy nearest neighbor match with exact matching on sex, and a caliper of 0.5 for other variables that were used in the full model (listed below). Propensity score matching was done separately for HD and PD and for different outcomes.

Gout and Clinical Outcomes

We estimated the hazard ratio (HR) and 95% confidence interval (CI) of the association of gout with three clinical outcomes—(1) time to all-cause mortality; (2) time to first all-cause hospitalization; and (3) time to CV death—using Cox regression with a robust sandwich estimator to account for facility clustering. Follow-up began at study enrollment (when the exposure was assessed) and continued through the event of interest, namely, death, 7 days after leaving the facility due to transfer or change in modality, loss to follow-up, or administrative censoring at study end. Cox models were stratified by study phase and EHR data source. Propensity score models were fitted with progressive adjustments to demonstrate the impact of adjustment for potentially confounding covariates. Model 1 was unadjusted; model 2 included age; model 3 included sex, Black race, body mass index (BMI), and dialysis vintage; model 4 included comorbidities; model 5 included albumin, creatinine, and phosphorus; and finally, model 6 (HD only) included vascular access type.

Gout and Erythropoietin Resistance Index

To investigate whether patients with gout had greater ESA resistance, we estimated the difference in log (ERI) using linear generalized estimating equations (GEE) and reported the ratio of means (with 95% CI) separately for the HD and PD cohorts. Models have a random facility intercept to account for facility clustering. Progressive covariate adjustment following the models defined above was performed.

Gout and PROs

For continuous measures of health-related quality of life (i.e., PCS, MCS, kidney disease burden, kidney effects, and kidney disease symptoms), we estimated the difference (95% CI) in score using linear GEE, with repeated facility statement to account for facility clustering. For binary outcomes (i.e., CESD-10 score ≥10 [indicative of depressive symptoms], functional status score of <11 [indicative of some functional dependence], and inactive [versus highly active] RAPA score), we estimated the odds ratio (OR; 95%

CI) using logistic regression, with GEE used to account for facility clustering.

Treatment of Missing Data

For missing data, we used the Sequential Regression Multiple Imputation Method implemented by IVEware and analyzed using the MIAnalyze procedure in SAS/STAT 9.4. All analyses used SAS software, version 9.4 (SAS institute, Cary, NC).

Results

Patient Characteristics

There were 70,297 HD patients and 5117 PD patients available in North America for analysis. Figure 1 depicts the inclusion and exclusion processes of this study. Patient characteristics before propensity score matching stratified by gout and by KRT modality are shown in Table 1.

The proportion of patients missing information on prior gout diagnosis was 14% in HD and 1% in PD. The proportion of patients with missing medication information was 5% in HD and 14% in PD. Missingness for most covariates was low (<20%), except for BMI (28%) in PD.

PD patients were younger than HD patients and with a generally lower comorbidity burden. Both HD and PD patients with gout were older, were more likely male, had a higher BMI, had a shorter dialysis vintage, and had a higher prevalence of comorbidities than patients without gout. Levels of serum albumin, serum phosphorus, and hemoglobin varied minimally by gout status. In HD, patients with gout were more likely to dialyze with a fistula than catheter. Patient characteristics stratified by gout medication use are described in Supplemental Tables 1a and 1b. After propensity score matching, all measured covariates were well balanced (Supplemental Table 2).

Gout Prevalence

Gout prevalence varied depending on the exact definition. Considering patients with a current prescription for colchicine or febuxostat, gout prevalence was 2% in HD and 4% in PD. Adding allopurinol prescription to the definition increased the estimates to 11% in HD and 16% in PD. Finally, including history of gout to the definitions above increased gout prevalence to 13% in HD and 21% in PD (Figure 2). Gout prevalence decreased with longer dialysis vintage for both HD and PD patients (Figure 2), whereas it was higher when gout medical history was assessed by medical questionnaire than through ICD-10 mapping (Figure 2). Among HD and PD patients with gout in their medical history, 42% and 48% were prescribed at least one ULT, respectively.

Clinical Outcomes

Among all 70,297 HD patients, 11,739 died (17%) during follow-up (median: 11 months, interquartile range [IQR], 4–23 months). After implementing the propensity score matching, we matched all 9409 HD patients with gout 1:1 to patients with no indication of gout. In this subset of 18,818 patients eligible for analyses of outcomes, 3492 died (19%) during a median follow-up of 11 months. Among all 5117 PD patients, 546 died (11%) during follow-up (median, 9 months; IQR, 4–19 months). After implementing the propensity score matching, we matched all 1060 PD patients
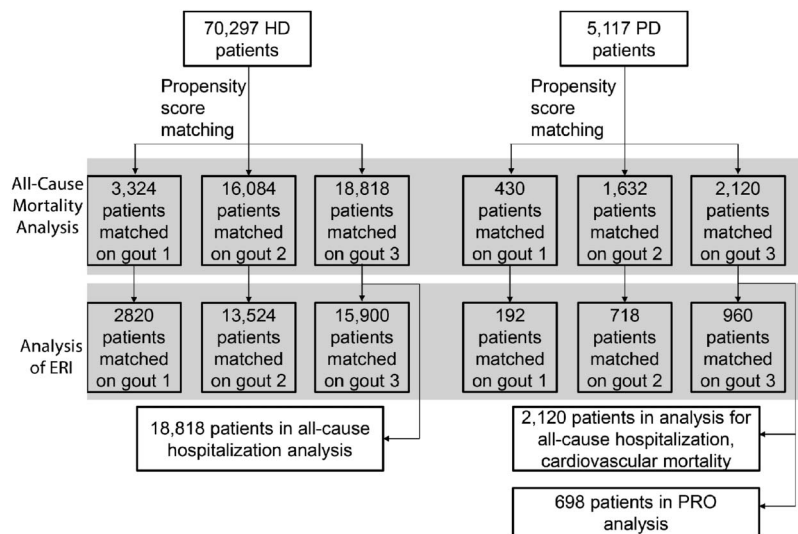
Figure 1. Study flowchart.

with gout 1:1 to patients with no indication of gout. In this subset of 2160 patients eligible for analyses of outcomes, 269 died (13%) during a median follow-up of 9 months.

Figure 3, A and B, illustrates the propensity score-matching analysis by gout definitions on all-cause mortality. In the fully adjusted models, the HR (95% CI) of all-cause mortality for gout (versus non-gout) was 0.94 (0.87 to 1.02) in HD and 0.95 (0.71 to 1.28) in PD (Figure 3).

The adjusted HR (95% CI) of CV-related death for gout versus non-gout was 1.08 (0.60 to 1.96) in PD (no cause of death data for HD). The adjusted HR (95% CI) of all-cause hospitalization for gout versus non-gout was 1.01 (0.96 to 1.06) in HD and 1.06 (0.91 to 1.23) in PD. Results according to distinct gout definitions did not qualitatively change the estimates (Figure 3). Supplemental Figure 1 depicts additional sensitivity analyses by gout definition.

Erythropoietin Resistance Index

The median (IQR) ERI was 13.2 unit/wk per g/dl per kg (7.2–23.1) in HD patients and 8.5 (4.5–15.5) in PD patients. Crude analyses of the HD cohort showed that the median (IQR) ERI was 12.7 (6.8–21.6) among gout patients versus 13.3 (7.3–23.3) among non-gout patients. In PD, the median (IQR) ERI was 8.2 (4.5–14.5) among gout patients versus 8.6 (4.5, 15.8) among non-gout patients. In propensity score–matched models, the ratio of ERI means (95% CI) between gout and non-gout patients was 1.06 (1.03 to 1.09) in HD and 1.03 (0.90 to 1.18) in PD, that is, mean ERI was 6% higher in the HD cohort and 3% higher in the PD cohort in gout versus non-gout patients. Figure 4 depicts stepwise model estimates for the association between gout and ERI.

Patient-Reported Outcomes

Continuous PRO measures are summarized in Table 2. For the physical and mental component summary scores, adjusted models showed that PD patients with gout had 0.7 point lower mean PCS and 0.6 point lower MCS, although estimates were generally imprecise. Null results were similarly observed for other measures of PRO including the burden, effects, and symptoms of kidney disease (Table 2).

Other binary PROs are summarized in Table 3. The adjusted OR (95% CI) comparing gout versus non-gout PD patients was 0.85 (0.57 to 1.27) for CES-D score ≥10 (indicative of depression), 0.94 (0.56 to 1.59) for functional status score <11 (indicative of some functional dependence), 0.91 (0.63 to 1.32) for RAPA-strength/flexibility, and 1.29 (0.78 to 2.14) for RAPA-aerobic (Table 3).

Discussion

In this nationwide cohort study in North America, we found that gout is a common yet under-reported comorbidity among HD and PD patients. Less than half of the patients with gout are prescribed ULT agents. Allopurinol was the most common prescribed ULT agent in this population. Gout prevalence as indicated by medical history or drug therapy was not found to be associated with worse clinical or PROs.

In our study, gout prevalence, despite varying by specific definitions, was 13% for HD and 21% in PD. Gout prevalence was similarly high in a cohort of patients in New Zealand that found a prevalence of 28% among KF on KRT.[21] These estimates are akin to studies in the nondialysis CKD population, wherein prevalence varied between 16% and 36% depending on GFR. We found that gout patients were on average older, had higher BMI, and had greater CV comorbidity burden. These results are consistent with previous reports both in nondialysis CKD[22,23] and in dialysis patients.[24] Also similar in HD and PD populations, longer dialysis vintage was associated with decreasing gout prevalence.[21]

Between KRT modalities and across dialysis vintage, allopurinol was the most prescribed ULT agent, as compared with febuxostat. Although there are few RCTs of xanthine oxidase inhibitors in patients with CKD, both allopurinol and febuxostat are considered safe in the CKD population.[25]

Table 1. Patient characteristics in hemodialysis and peritoneal dialysis patients, with and without gout, before propensity score matching

| Characteristics	HD		PD	
	No Gout	Gout	No Gout	Gout
Number of patients	60,888	9409	4057	1060
Demographics				
Patient age, yr	63.2 (14.9)	69.1 (12.8)	56.2 (15.3)	62.6 (13.7)
Male	55%	64%	53%	69%
Black race	39%	35%	27%	25%
BMI, kg/m^2	28.3 (7.1)	30.0 (7.3)	29.0 (6.5)	30.3 (6.2)
Time on dialysis, years	3.35 (4.04)	2.27 (2.97)	2.63 (3.39)	2.20 (2.83)
Comorbidity history				
Coronary artery disease	19%	26%	18%	25%
Cancer (nonskin)	5%	9%	5%	10%
Other cardiovascular disease	16%	26%	10%	15%
Cerebrovascular disease	6%	7%	4%	6%
Congestive heart failure	24%	32%	12%	16%
Diabetes	66%	64%	52%	48%
Gastrointestinal bleeding	4%	4%	1%	3%
Hypertension	79%	83%	75%	79%
Lung disease	7%	11%	4%	6%
Neurologic disease	5%	6%	2%	3%
Psychiatric disorder	24%	25%	19%	19%
Peripheral vascular disease	12%	14%	9%	10%
Recurrent cellulitis/gangrene	5%	5%	2%	2%
Dialysis treatments				
Vascular access type				
Catheter	41%	37%		
Fistula	47%	51%		
Graft	13%	12%		
Single-pool Kt/V	1.54 (0.28)	1.53 (0.28)		
Laboratory results				
Phosphorus, mg/dl	5.19 (1.64)	5.06 (1.49)	5.31 (1.56)	5.08 (1.44)
Albumin, g/dl	3.63 (0.49)	3.65 (0.46)	3.51 (0.47)	3.54 (0.43)
PTH, pg/ml	322 [188–535]	312 [187–500]	358 [210–556]	346 [206–520]
Creatinine, mg/dl	7.57 (3.07)	7.11 (2.90)	9.04 (4.30)	8.62 (4.14)
Hemoglobin, g/dl	10.5 (1.4)	10.6 (1.4)	11.0 (1.5)	11.1 (1.5)
Ferritin, ng/ml	615 [338–948]	603 [328–941]	582 [300–933]	549 [271–939]
White blood cell count, 10^3 cells/mm^3	6.7 [5.4–8.4]	6.8 [5.4–8.5]	7.2 [5.7–9.2]	7.3 [5.7–9.2]

Gout: active Rx for colchicine or febuxostat or allopurinol; or prior diagnosis of gout (Gout3); mean (SD), median [interquartile range], or % shown. Most variables had missingness <15%, with exception of Black (18%), VA type (16%), and single-pool Kt/V (27%) in HD, and BMI (28%), PTH (17%), and white blood cell count (23%) in PD patients. HD, hemodialysis; PD, peritoneal dialysis; PTH, parathyroid hormone; BMI, body mass index.

A recent RCT in patients with moderate to advanced CKD showed allopurinol safely and effectively reduces SUA levels, but it did not improve clinical outcomes.[26] In our study, approximately half of HD and PD patients with a history of gout were receiving ULTs. Despite the belief that KRT effectively reduces SUA levels and gout flares, observational studies in the HD population estimated a 15% gout incidence[9] over 5 years, a similar rate compared with the general population.[27] Therefore, our results may point to the under prescription of ULT in ESKD patients with gout.[28]

Additional factors may play a role in the relatively low proportion of ULT prescription among patients with KF on dialysis with a gout medical history. Increased uric acid production in CKD results from ingesting high-purine foods or taking medications associated with hyperuricemia. Frequently used medications that cause hyperuricemia include angiotensin converting enzyme inhibitors

(ACEi) and diuretics.[29,30] As KF ensues, deprescription of these drugs may reduce SUA and reduce gout episodes. In fact, we found higher gout prevalence among PD patients, who are often prescribed diuretics for volume control and ACEi for preserving peritoneal membrane and residual kidney function.[31] Finally, it remains possible that KF patients with gout medical history are actively tapered off ULTs over time. Currently, there are no clear recommendations to deprescribe ULT in KF patients with gout who remain free of flares, although individualization balancing patients' preferences are recommended for the general population.[32]

Our results do not support the hypothesis that gout portends worse clinical and PROs in patients with KF on dialysis. A previous gout medical history or its treatment was not associated with worse scores on depression, functionality, general health-related quality of life, or self-
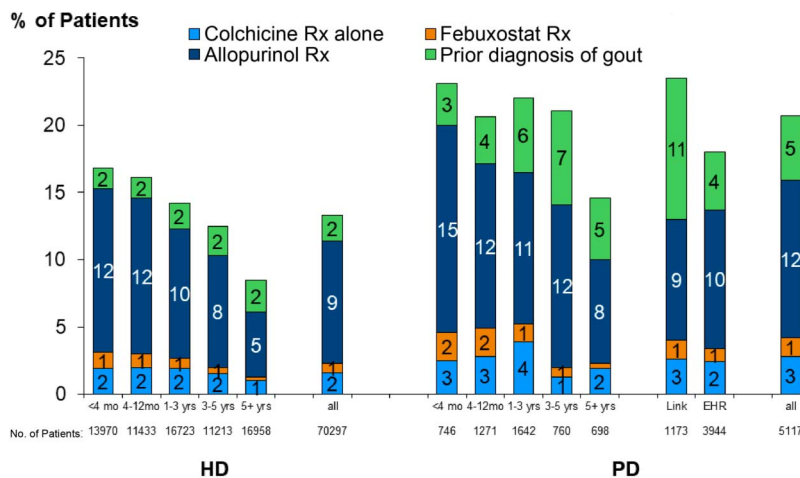
Figure 2. Gout prevalence in US HD and PD patients. DOPPSLink: prior diagnosis of gout on the basis of yes/no question completed by study coordinator; EHR: prior diagnosis of gout on the basis of ICD-10 codes. Mutually exclusive categories were defined hierarchically as (*1*) colchicine Rx alone; (*2*) febuxostat Rx with no colchicine Rx; (*3*) allopurinol Rx with no colchicine or febuxostat Rx; (*4*) prior diagnosis of gout with no colchicine, febuxostat, or allopurinol Rx; and (*5*) none of the above.

reported physical activity. In addition, risks of all-cause mortality and hospitalization were not different across our propensity score–matched cohorts. This finding contrasts with a United States Renal Data System (USRDS) analysis[9] that reported incident gout associated with increased mortality and CV hospitalization risk in HD patients. Of note, the USRDS study did not adjust for important key confounders such as laboratory variables and vascular access. In addition, we analyzed associations

between prevalent gout rather than incident episodes. Specifically, prevalent maintenance dialysis patients are often chronically inflamed and malnourished. This phenotype is associated with lower SUA, and selection bias of CKD patients onto chronic dialysis can affect the associations between SUA, gout, and mortality[33]—similar to the paradox of obesity associated with lower mortality in the dialysis population.

Both asymptomatic hyperuricemia and gout activate inflammatory pathways.[34] As a surrogate outcome, we explored the associations between ERI, which associates with inflammatory states. Our results suggest gout increases ESA resistance in patients with KF, a potential indicator of residual inflammation driving worse anemia outcomes. However, the effect size of this association was small and in PD patients our wide confidence intervals restrict interpretability. The clinical significance of these results, albeit potentially limited, warrants further analyses.

Of note, our study has important limitations. Our prevalence estimates varied according to the definition of gout.
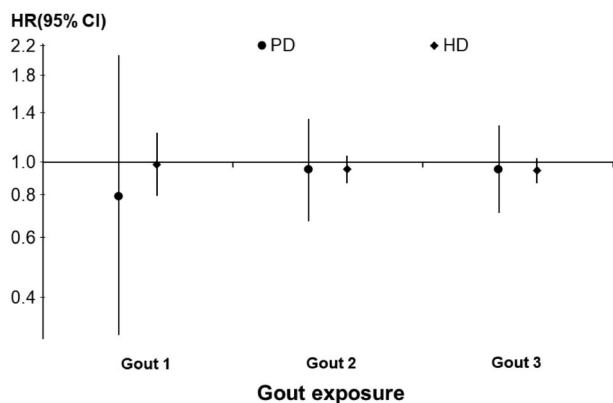
Figure 3. Association between gout and all-cause mortality among HD and PD patients. Binary exposure definitions: (*1*) Gout1: active Rx for colchicine or feboxustat; (*2*) Gout2: active Rx for colchicine or feboxustat or allopurinol; and (*3*) Gout3: active Rx for colchicine or feboxustat or allopurinol; or prior diagnosis of gout. Cox models were stratified by study phase and EHR data source, and propensity-score matched 1:1 with progressive covariate adjustments model 1: unadjusted; model 2: age only; model 3: model 2 + other demographics, including sex, Black race, BMI, and dialysis vintage; model 4: model 3 + 13 comorbidities; model 5: model 4 adjustments+albumin, creatinine, and phosphorus; model 6 (HD only): model 5 adjustments+vascular access type. Estimates from the fully adjusted models are reported. BMI, body mass index.
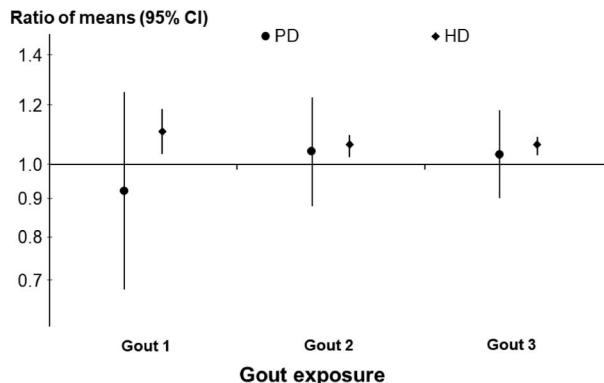
Figure 4. Associations between gout and ERI among HD and PD patients. Estimates from the fully adjusted models are reported.

Table 2. Association between gout and HRQOL in peritoneal dialysis

Outcome	Overall Mean	Among Gout	Among No-Gout	Effect	95% CI
PCS	37.5	37.4	37.5	−0.7	−2.3 to 0.9
MCS	49.0	48.7	49.3	−0.6	−2.2 to 1.1
Kidney disease burden	54.7	55.2	54.3	−0.8	−5.8 to 4.2
Kidney disease effects	72.8	73.4	72.3	1.0	−2.2 to 4.2
Kidney disease symptoms	78.0	77.9	78.1	−0.4	−2.6 to 1.8

Adjusted difference between gout and non-gout patients (Gout3). Propensity score models adjusted for study phase, EHR data source, demographics, including patient age, sex, Black race, BMI, and dialysis vintage, 13 comorbidities, albumin, creatinine, phosphorus, and vascular access type. HRQOL, health-related quality of life; CI, confidence interval; PCS, physical component summary; MCS, mental component summary EHR, electronic health record; BMI, body mass index.

In the most comprehensive gout definition, we used allopurinol, febuxostat, colchicine, and gout medical history as gout indicators. However, colchicine can be prescribed for reasons other than gout flares, despite being used by only up to 3% of our cohort. Albeit contraindicated in advanced CKD, colchicine can be prescribed for other crystal arthropathies, such as calcium pyrophosphate deposition (CPPD)–related disorders, which is also common in CKD.[35] Allopurinol is also often prescribed for other reasons than gout in CKD. Of particular interest is asymptomatic hyperuricemia, a common and frequently treated comorbidity in CKD. Because of such heterogeneity in practice patterns, it is difficult to predict whether our gout estimates on the basis of ULT prescription are underestimated or overestimated.

Other key limitations are noteworthy. Because of the observational design, we cannot rule out residual confounding. Moreover, SUA levels were not routinely measured in this population and were only available in a small subset of patients (<10%) for whom they were measured by indication; thus, we were unable to describe how many patients with gout had SUA levels within clinically recommended targets. We also did not have data on acute gouty arthritis episodes or gout severity, which can limit the interpretation of our findings.

Finally, distinct data extraction mechanisms in our cohorts may have affected our estimates. In facilities where a medical questionnaire was used to define comorbidities, gout was more frequently reported. In our study, medical questionnaires were used by non-LDO and small dialysis facilities, whereas EHR-based ICD-10 mapping was the primary method used to define gout in LDO facilities. We have no reason to believe that gout patients distribute unevenly across LDO versus non-LDOs or small dialysis facilities; therefore, these findings are probably due to under-reporting in EHR data extraction. This issue was previously reported and reflects the challenges in analyzing observational data from EHR sources.[36] To the authors' knowledge, the use of ICD-10 codes has not yet been validated among patients with ESKD. Patients on dialysis are often affected by conditions that can closely mimic gout, such as calcific arthritis, CPPD, and osteoarthritis, all frequent in the context of hyperuricemia. This resulting diagnostic uncertainty can affect the accuracy of prevalence estimates in this population, irrespective of the data capture mechanism. In sum, the combination of gout underreporting, potential misdiagnosis, and the use of active gout treatment to ascertain gout exposure may have shifted our findings toward the null. These results may help inform future study designs leveraging real-world data in populations with gout.

This study also has relevant strengths. This is the first analysis in a representative nationwide cohort of both PD and HD patients to address gout prevalence, practice patterns, and clinical associations in North America. Particularly, we reported a comprehensive set of PROs, key to the outstanding need of exploring factors affecting

Table 3. Association between gout and other patient-reported outcomes in peritoneal dialysis

Outcome	Overall Prevalence, %	Among Gout, %	Among No-Gout, %	OR	95% CI
CESD-10 score ≥10	22	21	22	0.85	0.57 to 1.27
Functional status score of <11	20	19	20	0.94	0.56 to 1.59
RAPA strength/flexibility score, none versus other	65	61	65	0.91	0.63 to 1.32
RAPA aerobic score, not active versus active	18	19	18	1.29	0.78 to 2.14

OR between gout and non-gout patients (Gout3). Propensity score models adjusted for study phase, EHR data source, demographics, including patient age, sex, Black race, BMI, and dialysis vintage, 13 comorbidities, albumin, creatinine, and phosphorus. RAPA strength/flexibility score was dichotomized as none versus other (strength but not flexibility, flexibility but not strength, or both). RAPA aerobic score was dichotomized as not active (never/rarely active or infrequently active) versus active (sometimes active, often active, or very active). OR, odds ratio; CI, confidence interval; CESD-10, Center for Epidemiologic Studies Depression-10; RAPA, Rapid Assessment Physical Activity; EHR, electronic health record; BMI, body mass index.

health-related quality of life to meet the care expectations of patients with KF. Our estimates were robust across many sensitivity analyses, including different exposure definitions and the inclusion of key confounders after propensity score matching.

Our null findings for PROs do not rule out short-term impacts on health related quality of life driven by preventable acute gouty arthritis episodes. Gout is recurrent and progressive, often leading to debilitating pain in a subset of highly burdened patients. The natural history of gout in KF remains elusive as observational studies have shown a high incidence of acute gouty arthritis among patients with ESKD without a prior diagnosis of gout.[9] Efforts should thus be furthered to characterize gout natural history in ESKD, as well as to increase awareness of *de novo* cases after dialysis initiation to prevent short-term morbidity and avoid unnecessary interventions that may expose patients with KF to adverse events.

Finally, in this large cohort of PD and HD patients in North America, we found that gout is a frequent, likely under-reported comorbidity. Yet, a history of gout or its pharmacological treatment is not associated with worse clinical outcomes or PROs. Given its recurrent and progressive nature, there remains a significant gap in the understanding of gout clinical course to guide medical practice in patients with KF undergoing KRT.

Author Contributions

B. Robinson conceptualized the study; R. Pecoits-Filho and B. Robinson were responsible for methodology; V. Domingues, M. Guedes, B. LaMoreaux, S. Lew, B. Marder, R. Pecoits-Filho, M.B. Rivara, and B. Robinson were responsible for investigation; M. Guedes, A. Karaboyas, B. Marder, R. Pecoits-Filho, B. Robinson, and J. Zhao wrote the original draft; and M. Guedes, J. Zhao, B. LaMoreaux, B. Marder, B. Gorlitsky, V. Domingues, M.B. Rivara, S. Lew, B. Robinson, R. Pecoits-Filho, and A. Karaboyas reviewed and edited the manuscript.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/KN9/A236.

Supplemental Table 1A. HD patient characteristics, by gout indications.

Supplemental Table 1B. PD patient characteristics, by gout indications.

Supplemental Table 2. Patient characteristics in HD and PD patients, with and without gout, after propensity score matching.

Supplemental Figure 1. Association between five-category gout exposure and all-cause mortality in HD (A) and PD (B).

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