ANNALS OF TRANSPLANTATION

ORIGINAL PAPER

e-ISSN 2329-0358
© Ann Transplant, 2020; 25: e920553
DOI: 10.12659/AOT.920553

Received: 2019.10.08
Accepted: 2019.12.23
Published: 2020.04.14

A Retrospective Cohort Study of the Effect of Gout on Mortality Among Patients with a History of Kidney Transplantation

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Source of support: Research funding provided by Horizon Pharma

Background: Kidney transplantation is associated with increased prevalence of gout. However, evidence of the effect of gout on long-term kidney transplantation outcomes is mixed. This study examined mortality risk among patients with a history of kidney transplantation with *vs.* without gout.

Material/Methods: A retrospective study was conducted using Medicare Fee-for-Service administrative claims of patients with a history of kidney transplantation. Cox proportional hazards models determined the effect of gout on all-cause mortality, controlling for confounders, including comorbid mortality risk, via the Charlson Comorbidity Index. Because the relationships between gout and components of the Charlson Comorbidity Index are also debated, 3 different model assumptions were used: 1) gout shares a common cause with these comorbidities, 2) gout is upstream of these comorbidities, 3) the effect of gout on mortality is modified by these comorbidities.

Results: Gout increased the risk of all-cause mortality in the unadjusted model (hazard ratio: 1.44, 95% CI 1.27–1.63) and after adjustment for demographics and transplant vintage (hazard ratio: 1.16, 95% CI 1.02–1.32). Gout was not a significant risk after adjustment for baseline Charlson Comorbidity Index (hazard ratio: 1.03, 95% CI 0.90–1.17). Gout was associated with greater mortality among patients without baseline comorbidities (Charlson Comorbidity Index=0; hazard ratio: 3.48, 95% CI 1.27–9.57) in the stratified model.

Conclusions: Among patients with a history of kidney transplantation, gout did not have an independent effect on all-cause mortality. However, gout was a predictor of mortality among patients with no comorbidities, suggesting that gout is an early warning sign of poor health in kidney transplantation patients.

MeSH Keywords: **Comorbidity • Gout • Kidney Transplantation • Medicare • Mortality**

Full-text PDF: https://www.annalsoftransplantation.com/abstract/index/idArt/920553

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Indexed in: [Science Citation Index Expanded] [Index Medicus/MEDLINE] [Chemical Abstracts] [Scopus]

Background

Gout is a common form of inflammatory arthritis, with an estimated lifetime prevalence of 4% in the USA [1].Gout is caused by elevated serum uric acid (sUA) levels that promote deposition of urate crystals in joints and other tissues [2]. Gout has a range of clinical manifestations that can include painful acute joint inflammation (or flares) and visible tophaceous deposits [3]. Left uncontrolled, gout can lead to bone erosions and joint destruction and has been linked to several comorbid conditions, including cardiovascular disease and chronic kidney disease (CKD) [2,4,5].

High rates of gout have been reported among kidney transplantation patients [6]. In a study using data from 2016, the prevalence of gout was 13.1% among kidney transplantation patients [7]. Emerging evidence also suggests that, among nephrology patients with gout, those with a history of kidney transplantation are more likely to experience symptoms of severe, uncontrolled gout [8].

The treatment of gout in the context of kidney transplantation aftercare poses several challenges. Hyperuricemia, as well as new-onset and recurrent gout, can be induced by use of the calcineurin inhibitors, which form the basis of most prophylactic immunosuppressive regimens prescribed to this population [9]. Additionally, xanthine oxidase-inhibiting urate-lowering therapies are contraindicated in patients receiving azathioprine [1], a second-line antiproliferative agent in certain immunosuppressive regimens used to protect against graft loss.

Several recent studies investigated the relationship between hyperuricemia and graft outcomes [11,12]. However, despite evidence of gout contributing an independent risk associated with CKD and end-stage renal disease (ESRD) [13,14], cardiovascular morbidity and mortality [15], and all-cause mortality in other adult populations [16], to the best of our knowledge only 1 study has investigated the risk of gout in kidney transplant recipient populations [6]. Abbott et al. found that development of new-onset gout following kidney transplantations performed in the 1990s was an independent predictor of graft loss and decreased survival (HR 1.26, 95% CI 1.08–1.47) [6].

This study was conducted to examine mortality risk among patients with a history of kidney transplantation with *vs.* without gout. A preliminary abstract of this study was previously presented at the Annual European Congress of Rheumatology, EULAR 2019, Madrid, 12–15 June 2019 [17].

Material and Methods

Study design, data, and population

A retrospective cohort study was conducted using Medicare Fee-for-Service Limited Data Set administrative claims obtained from the Centers for Medicare and Medicaid Services (CMS). This publicly available dataset contains a representative, de-identified 5% sample of beneficiaries enrolled in Medicare Parts A (inpatient care) and B (physician services and outpatient care). Data on patient demographics and enrollment information, as well as on services and procedures provided to the beneficiaries, are available at the claim level. While this dataset captures specific diagnostic and laboratory tests performed, the results of the tests are not available.

To be included in the study, patients must have: 1) been continuously enrolled in Medicare Parts A and B in calendar year 2012; 2) be alive as of January 1, 2013; 3) had a kidney transplant status claim (International Classification of Diseases, Ninth Revision, Clinical Modification code V42.0) in 2012; and 4) not received a solid-organ transplant procedure in 2012. Patients with incomplete information for US Census Bureau region, sex, or race were excluded from the analysis.

All patients were indexed on January 1, 2013 (index date) and tracked forward until end of their Medicare A and B enrollment, death, or end of the study period (December 31, 2016). A look-back period from 2007 to 2011 was used to identify the kidney transplant procedure date, if available. Baseline demographic and clinical characteristics of patients were based on 2012 claims.

Outcome and predictors of interest

The main outcome of interest was time to all-cause mortality. Patients whose death was not observed within the study period were censored on the date that their enrollment ended or the end of the study period, whichever occurred first. The main predictor of interest was gout diagnosis, assessed both in the 2012 look-back year ("baseline gout") and during the follow-up period ("incident gout"). Gout status was defined by the presence of at least 1 gout-related claim identified using International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) code prefixes (274 in ICD-9, M10 and M1A in ICD-10). The high concordance between physician documentation of gout in electronic health records and claims with gout ICD diagnosis codes was previously demonstrated [18]. To adjust for incident gout, gout diagnosis was treated as time-varying for all regression analyses, in which a patient was considered a gout patient starting from the date that the first gout-related service claim was observed. Those who did not have a gout-related claim in 2012 or during follow-up

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were considered non-gout patients. As serum urate levels are not available, patients in the gout and non-gout groups may have had elevated uric acid levels.

Covariates

Baseline demographic covariates included age, sex, race, and US Census Bureau region as of January 1, 2012.

Kidney transplant year was treated as a categorical variable and was determined using 2007–2011 claims. For patients who were continuously enrolled but did not have a kidney transplant reported during the period, transplant year was classified as "Prior to 2007." Patients who were not continuously enrolled and did not report a kidney transplant procedure during the period were coded as having an "Unknown" transplant year.

Baseline (2012) health status of patients was assessed via the Charlson Comorbidity Index (CCI), using claims-coding algorithms as previously described [19]. Although all patients had a history of kidney transplantation, patients were not assigned CCI points for 'moderate to severe renal disease' unless they met corresponding criteria from the claims-coding algorithm published by Deyo et al. [19] Importantly, this algorithm does not consider history of kidney transplant alone to qualify a patient as currently having 'moderate to severe renal disease'. Among patients not meeting the CCI claims-coding algorithm criteria for 'moderate to severe renal disease', it was assumed that successful renal transplantation had mitigated the pre-transplantation renal disease diagnosis as of the study baseline timepoint (i.e., calendar year 2012).

Confounding and effect modification

The presence of confounding distorts the estimated measure of association between gout and time to death. To eliminate any confounding by baseline demographics, analyses were controlled for age, sex, race, and Census Bureau region in all multivariable regression models.

In contrast to patient demographics, the causal relationship between gout and specific comorbidities is less well-established; therefore, 3 analyses were conducted to explore this relationship. Under the assumption that gout and several of the conditions that make up the CCI were associated with one another by way of a common pathogenic root and patients' baseline health status therefore confounded the association between gout and death, regression models were constructed to control for gout, demographics, and CCI score. Alternatively, under the assumption that gout was upstream of these comorbidities and CCI score was therefore an intermediate (mediating) step in the causal pathway between gout and death, regression models were fit without the CCI score.

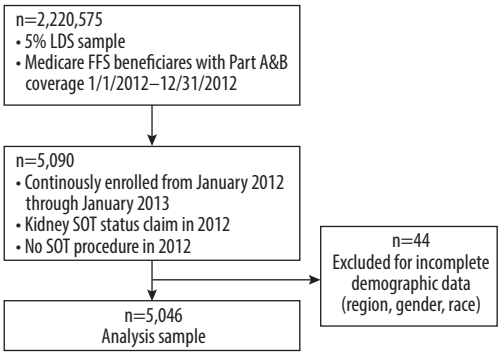

Figure 1. Sample selection diagram.

Lastly, to understand how patients' baseline health modified the effect of gout on death, stratified analyses were performed at various levels of CCI score.

Statistical analyses

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary NC, USA).

The effect of gout on time to death was first examined in a Cox proportional hazards regression model without adjustment for potential confounders (unadjusted). Multivariable models were then constructed, adjusting for age, sex, race, region, and year of kidney transplant procedure, with and without controlling for baseline CCI score.

To explore the possibility that CCI modifies the effect of gout on death, the relationship between gout and other comorbid conditions at baseline was assessed. Mean CCI scores by gout status were compared using the t test and the rates of comorbidities by gout status were compared using the chi-square test. The results suggested the presence of effect modification by baseline CCI score, so stratified multivariable Cox proportional hazards models were constructed based on CCI scores of 0 *vs.* 1–4 *vs.* ≥5.

Results

Of 2 220 575 Medicare beneficiaries contained in the 5% Limited Data Set from January 2012 to January 2013, there were 5046 patients with a history of kidney transplantation who met the eligibility criteria for this study (Figure 1). Of these patients, 1405 (27.8%) either had gout at baseline (13.4%) or developed gout during follow-up (14.4%). Gout patients were older, more likely to be male, and more likely to have received their kidney transplant in earlier years compared to non-gout patients (Table 1). Both among gout and non-gout

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Table 1. Baseline characteristics of the study population.

Variable *n (%) unless noted otherwise*	Overall n=5,046	Gout patients n=1,405	Non-gout patients n=3,641	P-value
Age in years, *mean (standard deviation)*	56.2 (14.1)	60.2 (12.3)	54.6 (14.5)	<0.001
Sex				<0.001
Males	2905 (57.6%)	933 (66.4%)	1972 (54.2%)	
Region				0.019
Northeast	920 (18.2%)	275 (19.6%)	645 (17.7%)	
West	883 (17.5%)	264 (18.8%)	619 (17.0%)	
South	1955 (38.7%)	534 (38.0%)	1421 (39.0%)	
Midwest	1243 (24.6%)	327 (23.3%)	916 (25.2%)	
Other	45 (0.9%)	5 (0.4%)	40 (1.1%)	
Race				<0.001
White	3085 (61.1%)	898 (63.9%)	2187 (60.1%)	
Black	1248 (24.7%)	310 (22.1%)	938 (25.8%)	
Asian	179 (3.5%)	69 (4.9%)	110 (3.0%)	
Other	534 (10.6%)	128 (9.1%)	406 (11.2%)	
Kidney transplant procedure year				<0.001
2011	522 (10.3%)	115 (8.2%)	407 (11.2%)	
2010	471 (9.3%)	93 (6.6%)	378 (10.4%)	
2009	343 (6.8%)	94 (6.7%)	249 (6.8%)	
2008	293 (5.8%)	87 (6.2%)	206 (5.7%)	
2007	254 (5.0%)	74 (5.3%)	180 (4.9%)	
Assume prior to 2007	2522 (50.0%)	764 (54.4%)	1,758 (48.3%)	
Unknown	641 (12.7%)	178 (12.7%)	463 (12.7%)	
Baseline CCI score, *mean (standard deviation)*	4.1 (2.4)	4.5 (2.4)	4.0 (2.4)	<0.001
Baseline Comorbid Conditions (used for CCI scoring)				
AIDS	45 (0.9%)	15 (1.1%)	30 (0.8%)	0.409
Any malignancy	964 (19.1%)	345 (24.6%)	619 (17.0%)	<0.001
Cerebrovascular disease	797 (15.8%)	259 (18.4%)	538 (14.8%)	0.001
Chronic pulmonary disease	1010 (20.0%)	325 (23.1%)	685 (18.8%)	<0.001
Congestive heart failure	1024 (20.3%)	359 (25.6%)	665 (18.3%)	<0.001
Connective tissue disease	262 (5.2%)	80 (5.7%)	182 (5.0%)	0.318
Dementia	56 (1.1%)	17 (1.2%)	39 (1.1%)	0.673
Diabetes w/o complication	2787 (55.2%)	804 (57.2%)	1983 (54.5%)	0.077
Diabetes with complication	1744 (34.6%)	476 (33.9%)	1268 (34.8%)	0.526
Hemiplegia or paraplegia	72 (1.4%)	23 (1.6%)	49 (1.3%)	0.434

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Table 1 continued. Baseline characteristics of the study population.

Variable *n (%) unless noted otherwise*	Overall n=5,046		Gout patients n=1,405		Non-gout patients n=3,641		P-value
Metastatic solid tumor	82	(1.6%)	18	(1.3%)	64	(1.8%)	0.220
Mild liver disease	159	(3.2%)	44	(3.1%)	115	(3.2%)	0.961
Moderate/severe liver disease	94	(1.9%)	26	(1.9%)	68	(1.9%)	0.968
Myocardial infarction	465	(9.2%)	172	(12.2%)	293	(8.0%)	<0.001
Peptic ulcer disease	114	(2.3%)	31	(2.2%)	83	(2.3%)	0.875
Peripheral vascular disease	772	(15.3%)	247	(17.6%)	525	(14.4%)	0.005
Renal disease (moderate to severe)	4246	(84.1%)	1241	(88.3%)	3005	(82.5%)	<0.001

CCI – Charlson comorbidity index.

Table 2. Cox model hazard ratios of all-cause mortality for gout patients versus non-gout patients.

Model	HR (gout *vs.* non-gout)	95% CI	P-value
Unadjusted	1.44	1.27–1.63	<0.001
Adjusted for age, sex, race, region, and year of kidney transplant procedure	1.16	1.02–1.32	0.024
Adjusted for age, sex, race, region, year of kidney transplant procedure, and CCI	1.03	0.90–1.17	0.716

CI – confidence interval; HR – hazard ratio.

Table 3. Prevalence ratios of baseline comorbidities among patients with *vs.* without gout at baseline.

Comorbid condition	Prevalence ratio	P-value
AIDS	1.61	0.195
Any malignancy	1.54	<0.001
Cerebrovascular disease	1.40	<0.001
Chronic pulmonary disease	1.40	<0.001
Congestive heart failure	1.62	<0.001
Connective tissue disease	1.56	0.003
Dementia	0.63	0.320
Diabetes w/o complication	1.14	<0.001
Diabetes with complication	1.05	0.354

Comorbid condition	Prevalence ratio	P-value
Hemiplegia or paraplegia	1.16	0.645
Metastatic solid tumor	1.10	0.749
Mild liver disease	1.03	0.881
Moderate/severe liver disease	1.03	0.910
Myocardial infarction	2.09	<0.001
Peptic ulcer disease	1.54	0.063
Peripheral vascular disease	1.40	<0.001
Renal disease	1.12	<0.001

cohorts, the transplant year was unknown for 12.7% of patients. Furthermore, gout patients' mean baseline CCI score was higher compared to that of non-gout patients. The median follow-up time for the overall cohort was 1461 days, or 4 years.

The unadjusted model revealed that kidney transplant recipients with gout had a 44% greater risk of death from all causes compared to patients without gout (hazard ratio: 1.44, 95% CI: 1.27–1.63) (Table 2). Controlling for age, sex, race, region, and year of kidney transplant procedure, the risk of death was attenuated (hazard ratio: 1.16, 95% CI: 1.02–1.32). When CCI score at baseline was added to the model, gout was no longer a significant predictor of death (hazard ratio: 1.03, 95% CI: 0.90–1.17).

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Table 4. Cox model adjusted hazard ratio of all-cause mortality for gout patients versus non-gout patients, stratified by baseline CCI score.

CCI stratum	n	HR (gout *vs.* non-gout)	95% CI	P-value
CCI 0	248*	3.48	1.27–9.57	0.016
CCI 1–4	2,875**	1.08	0.86–1.36	0.516
CCI ≥5	1,878***	0.99	0.85–1.16	0.914

* Excludes one patient whose region was listed as "Other"; ** Excludes 27 patients whose region was listed as "Other"; *** Excludes 17 patients whose region was listed as "Other". CCI – Charlson comorbidity index; CI – confidence interval; HR – hazard ratio.

There was a strong association between gout status and CCI score at baseline. Kidney transplant patients with gout at baseline had a mean CCI score of 4.9, while those without gout at baseline had a mean score of 4.0 ($p<0.001$) (data not shown). Furthermore, gout patients were characterized by significantly higher rates of 9 out of the 17 comorbidity categories that comprise the CCI score (Table 3). The rate of myocardial infarction was 2.1 times higher among those with gout at baseline compared to those without gout at baseline ($p<0.001$). The rate of congestive heart failure, connective tissue disease (e.g., rheumatoid arthritis and osteoarthrosis), and any malignancy were 62% ($p<0.001$), 56% ($p=0.003$), and 54% ($p\leq0.001$) greater, respectively, among gout patients compared to non-gout patients. Additionally, patients with gout were 40% more likely to have peripheral vascular disease, chronic obstructive pulmonary disease, and cerebrovascular disease (all $p<0.001$) compared to those without gout. Finally, gout patients were also 14% more likely to have diabetes without chronic complication and 12% more likely to have moderate to severe renal disease, despite history of kidney transplantation.

Stratified survival analysis revealed that the CCI score modifies the relationship between gout and risk of death (Table 4). Among 248 healthy patients (CCI=0), the presence of gout increased the risk of death by 3.5-fold (HR: 3.48, 95% CI: 1.27–9.57). However, among patients with CCI=1–4 and CCI ≥5, gout did not appear to increase the risk of death (HR: 1.08, 95% CI: 0.86–1.36; and HR: 0.99, 95% CI: 0.848–1.16, respectively).

Discussion

Our findings are important for physicians involved in renal transplant aftercare. In the present study, there was an association between gout and unadjusted mortality risk among kidney transplantation patients. After adjusting for baseline demographics and time from transplantation, the effect of gout on mortality risk was smaller but still significant after controlling for age, sex, race, region, and time since transplant. When the analysis controlled for these factors as well as CCI, HR risk was not statistically significant. Baseline gout status was strongly associated with higher rates of comorbid conditions, notably cardiovascular diseases, suggesting the potential modifying effect of a composite comorbidity score. To understand the modifying effect of CCI, patient cohorts were stratified by baseline CCI score. Among patients without baseline comorbidities (CCI=0), risk of all-cause mortality increased by 3.5-fold for patients with gout. Among the majority of patients with baseline CCI ≥1 (95%), gout was not an independent risk factor. The CCI algorithm developed by Deyo et al., which does not assign points based on history of kidney transplantation, was used in this study [19]. Given that all patients had a history of kidney transplantation, the Deyo et al. algorithm was used to gain greater insight by identifying, via differential CCI scores, those patients who continue to have a positive diagnosis of moderate to severe renal disease even after transplantation *vs.* those who achieve healthy renal function after transplantation.

In an otherwise healthy cohort of kidney transplantation patients, gout had an independent effect on mortality risk. This suggests that gout can be an early warning sign of poor health in kidney transplantation patients. That gout behaves as an independent predictor of mortality in healthy kidney transplant recipients but not in those with pre-existing comorbidities is a novel finding, but one perhaps indicative of complex pathogenesis and clinical manifestation of gout in populations with significant comorbid disease burden. Gout has long been viewed as a systemic disease whose role as a cause or consequence of the development of certain comorbid diseases has been controversial. Our results may reflect some of these complex relationships between gout, persistent hyperuricemia and uric acid deposition, treatment of gouty flares, the presence of specific comorbidities, and subsequent mortality risk.

Patients having the diagnosis of gout among adjusted cohorts with baseline CCI=0 had a greater risk of all-cause mortality. Patients in the baseline CCI=0 cohort were also predisposed to develop downstream incident comorbidities. For all other CCI strata (CCI >1), comorbid diseases could modify risk, as gout could develop before, after, or co-occur with comorbidities. Taken together, several potential relationships between gout, key comorbidities, and mortality in the renal transplantation population were analyzed.

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Although this study suggests that gout can be an early warning sign of declining health among otherwise healthy (CCI=0) patients, one cannot determine the exact relationship between gout and the potentially downstream diseases that more directly lead to morbidity and death. It is possible that gout plays a causal role in their emergence, or it may be that these other diseases are undiagnosed but sufficiently developed to cause gout and other metabolic dysfunction, or a combination of these relationships may exist across different comorbidities. Either way, one may conclude that a new gout diagnosis should be an indication not only for treatment of the disease itself, but also as an indication of the need for increased awareness of the comorbidities with which it is highly correlated.

The nature of the relationship between gout and comorbid diseases is frequently discussed in the literature. In adult subjects, elevated sUA is causative in gout [2], and both are associated with cardiovascular morbidity [4,20,21], as well as CKD and ESRD [13,14,22–24]. Gout could theoretically have a role in renal and cardiovascular morbidity and mortality as it is a condition that results in a systemic inflammatory response that can even persist between gout attacks ('intercritical gout'). In addition, experimental studies suggest that elevated serum urate can activate processes that result in kidney disease and hypertension [25,26]. Indeed, meta-analyses show dose-response relationships between sUA level (for each 1 mg/dL increase) and risk for incident hypertension (adjusted risk ratio 1.13, 95% CI 1.06–1.20) [27], as well as coronary heart disease mortality (pooled multivariate risk ratio 1.13, 95% CI 1.06–1.20).20 Several studies have found that elevated urate levels in patients with normal kidney function independently predicts development of incident CKD [24,28]. While the causal role of hyperuricemia in these comorbidities remains controversial, pilot clinical studies have reported that lowering serum urate can improve blood pressure [29] and slow progression of kidney disease [30], but the evidence will not be conclusive without studies meeting the highest standards for randomized controlled trials [31].

The specific causative relationship between hyperuricemia and graft outcomes is just as inconclusive in the most recent studies [11,12,32,33]. Kim et al. (2015) observed, in adjusted models for time-varying confounders in sUA concentration and estimated glomerular filtration rate (eGFR), that hyperuricemia – defined as sUA levels >7.0 mg/dL for men and >6.0 mg/dL for women – had no adverse effect on graft outcomes, and in fact they observed a modest protective effect of elevated sUA (HR 0.90, 95% CI 0.85–0.94) [12]. Conversely, a separate study using a similar marginal structural model found that high sUA levels – as measured using the same sUA level thresholds – predicted worse graft outcomes among hyperuricemic patients (HR 2.27, 95% CI 1.33–3.78) [11].

Limitations

This study has several limitations worth noting. As with any study that leverages administrative claims data, medical claims lack detailed clinical information such as sUA levels, a definitive diagnosis for hyperuricemia, and living *vs.* deceased donor status. It is possible that some patients were misdiagnosed with gout. Malik et al. found that, in practice, 33% of patients meeting American College of Rheumatology (ACR) gout clinical diagnostic criteria did not meet the criterion standard for gout diagnosis (i.e., presence of urate crystals in synovial fluid) [34]. Further, data from a medical records study suggests that, considering the criteria of the present study and the distribution of patients with 1 *vs.* 2 or more gout claims from a prior study in the kidney transplantation population, ~43% of patients identified with gout ICD codes would not have evidence meeting ACR criteria in their records [7,35]. However, a similar study, which followed up with additional patient interviews, found that the majority of such errors were due to a lack of documentation in medical records rather than due to an absence of qualifying signs and symptoms [36]. Nonetheless, considering the possibility for misdiagnosis of gout, and given the overlap between gout and hyperuricemia, one might ask whether it would be appropriate to refer to the predictor of interest in this study as "hyperuricemia" rather than "gout". However, the US National Health and Nutrition Examination Survey has consistently found that the proportion of the general population with any history of a gout diagnosis is many times smaller than the population with hyperuricemia – 3.9% *vs.* 20.1% in 2015–2016 [37]. The proportion of patients with hyperuricemia who have a current gout diagnosis (i.e., within a calendar year rather than at any point in the patient's medical history) could be even lower considering a recent study that estimated the prevalence of a current gout diagnosis at 1.1% in the USA [7]. Thus, referring to the predictor of interest in the present study as "hyperuricemia" rather than "gout" would result in the misclassification of a far greater proportion of patients, even in light of the limitations of gout coding and clinical diagnostic criteria.

eGFR values were not available in the dataset. Variability in eGFR is possible even among patients with CCI=0, either because of the wide range of possible values above the threshold for a CKD diagnosis (≥90 mL/min/1.73 m^2) or if the diagnosis coding capture is less consistent for patients with lower severity CKD (e.g., stage 1–2) even after transplantation. If so, it is also possible that lower eGFR values are responsible for the higher rates of gout and the increased mortality among a subset of patients with CCI=0. Data on prescription drugs were not available in this dataset, which meant that the use of urate-lowering therapy to treat gout could not be controlled for in the models. Similarly, because the immunosuppressant regimen used was not available in the dataset, one cannot rule

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out the possibility that the minority of patients treated with cyclosporine had high rates of gout as well as poorer outcomes compared to the rest of the population, most of whom would have received tacrolimus. For patients undergoing transplantation prior to 2007, lack of a specific transplant date limits the model's ability to control for time since transplantation.

Conclusions

In our unadjusted model of gout and mortality among patients with a history of kidney transplantation from the Medicare Fee-for-Service database, greater mortality risk was observed in the cohort of patients with gout. However, gout was not shown to be an independent predictor of mortality after baseline risk-adjustments that included CCI. In stratifying baseline CCI, gout was observed to be an independent predictor among a subset of patients without comorbidities (CCI=0). Given the nuanced pathogenesis and varied clinical manifestations of gout, an independent association of gout in kidney transplant recipients with comorbid disease cannot be ruled out. The possibility that gout behaves similarly in the larger prevalent kidney transplant population with comorbidities as it does in a healthy subset should concern physicians, as the presence of gout can serve as an early indicator of subsequent declining renal function and overall health.

Acknowledgements

The authors thank Sina Aghsaei for database development and programming.

Conflicts of Interest

Justin W. Li, Marissa Suh, Mark D. Brigham, Nandini Hadker, Herman Sanchez, Kevin Francis, and Gavin Miyasato received research funding for this study from Horizon Pharma. JDK and BL are employed by and own stock in Horizon Pharma. RJJ and BFM have consulted for Horizon Pharma outside of the current study.

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