Original Research

Association Between Colchicine and Risk of Diabetes Among the Veterans Affairs Population With Gout

Liya Wang, BS[1]; Monika Sawhney, PhD, MSW[2]; Yingnan Zhao, PhD[3]; Gandahari Rosa Carpio, MD[4]; Vivian Fonseca, MD[1,4]; and Lizheng Shi, PhD[1,4]

[1]Department of Global Health Systems and Development, School of Public Health and Tropic Medicine, Tulane University, New Orleans, Louisiana; [2]Department of Public Health, College of Health Professions, Marshall University, Huntington, West Virginia; [3]College of Pharmacy, Xavier University of Louisiana, New Orleans, Louisiana; and [4]Section of Endocrinology, Tulane University Health Sciences Center, New Orleans, Louisiana

ABSTRACT

Purpose: This study aimed to determine the association between colchicine use and the incidence of diabetes in a cohort of patients with gout.

Methods: This is a retrospective study of 27,876 adults with gout identified via the Veterans Integrated Services Network 16 data warehouse. Patients had up to 11 years of follow-up (January 1999 through December 2010). The final study sample consisted of 1046 pairs of 1:1 propensity score–matched patients from the colchicine treated and control cohorts. Time to first diabetes development since the first gout diagnosis was modeled.

Results: After the propensity score matching, the 12-month baseline variables (eg, age, sex, race, index year, body mass index, serum uric acid, antigout drug use, and health care use) were comparable between the matched cohorts ($P > 0.05$ for all). Among the 1046 matched pairs, 234 patients who had taken colchicine and 224 patients who had never taken colchicine developed diabetes; the incidence rates were 38.95 and 39.02 per 1000 patient-years, respectively. In Poisson and Cox proportional hazards regression, the risk of incident diabetes was reduced with increased duration of colchicine use, but the difference was not statistically significant ($P > 0.05$). In a time-varying Cox proportional hazards model, the hazard ratio for incident diabetes among patients who had taken colchicine was 0.877 (95% CI, 0.662–1.163; $P = 0.362$) compared with those who had not taken colchicine.

Conclusion: This study suggests a possible duration- or dose-related association between colchicine use and reduced risk of diabetes in adults with gout even though the risk reduction was not significant. Further studies are needed to confirm findings from this study. (*Clin Ther*. 2015;37:1206–1215)

Key words: colchicine, diabetes, gout, veterans.

INTRODUCTION

Hyperuricemia is characterized by elevated levels of serum uric acid in blood (6 mg/dL for women and 7 mg/dL for men).[1] Hyperuricemia was present in 21.2% of men and 21.6% of women in data from the US National Health and Nutrition Examination Survey, which was conducted in 2007 and 2008.[2] This condition is often accompanied by comorbidities: metabolic syndrome, including diabetes, hypertension, and renal disease.[3,4]

The most well-known medical manifestation of hyperuricemia is gout, a chronic disease of the joints

Accepted for publication March 11, 2015.
http://dx.doi.org/10.1016/j.clinthera.2015.03.010
0149-2918/$ - see front matter

characterized by recurrent attacks of sudden severe pain[5] in one or more joints and inflammation due to deposition of monosodium urate or uric acid crystals in joints, tendons, and surrounding tissues. A range of comorbidities are often exhibited by patients with gout, including but not limited to hypertension, chronic kidney disease, obesity, and type 2 diabetes.[6,7] A 2007-2008 study based on the US National Health and Nutrition Examination Survey estimated the prevalence of gout as 3.9%.[2] Between 1996 and 2008, a total of 15.1% of the >177,000 US patients with gout were diagnosed as having diabetes. Men with gout were found to have a 34% to 66% higher risk of developing type 2 diabetes compared with those without gout after adjustment for various factors, such as age, body mass index (BMI), smoking, family history of type 2 diabetes, alcohol intake, dietary factors, and presence of individual components of the metabolic syndrome.[8] The standard pharmacologic management of acute attacks of gout involves use of oral colchicine, nonsteroidal anti-inflammatory drugs, or corticosteroids.[9,10]

Colchicine, an antigout and anti-inflammatory drug, is usually used to prevent gout attack and relieve the pain of gout attacks caused by hyperuricemia in adults.[11] Among the unique features of colchicine is its low therapeutic index. Effective steady-state plasma concentrations after short-term treatment range from 0.5 to 3 ng/mL, with toxic effects occurring at a level of approximately 3 ng/mL.[12]

Colchicine has hypoglycemic effects and may reduce the risk of diabetes mellitus.[13] This retrospective study is designed to examine the treatment pattern of colchicine and its association with the risk of incident diabetes in patients with gout. We hypothesized that colchicine use would be associated with a decreased likelihood of the development of type 2 diabetes.

MATERIALS AND METHODS

Data Source

The Veterans Affairs Veterans Integrated Services Network (VISN) 16 data warehouse was used for this research. The VISN 16 data warehouse contains all demographic (age, sex, race, and BMI), service use, and pharmacy data for patients treated in the South Central Veterans Affairs Health Care Network (Arkansas, Louisiana, Mississippi, Oklahoma and parts of Alabama, Florida, Missouri, and Texas), as well as certain clinical data, such as laboratory values and patient vital data. Data also include medical claims (inpatient and outpatient), pharmacy claims, laboratory test results, and vital data (height and weight). Data covering the period January 1999 through December 2010 were used for this study. Appropriate institutional review board approval was obtained before the study initiation.

Study Design

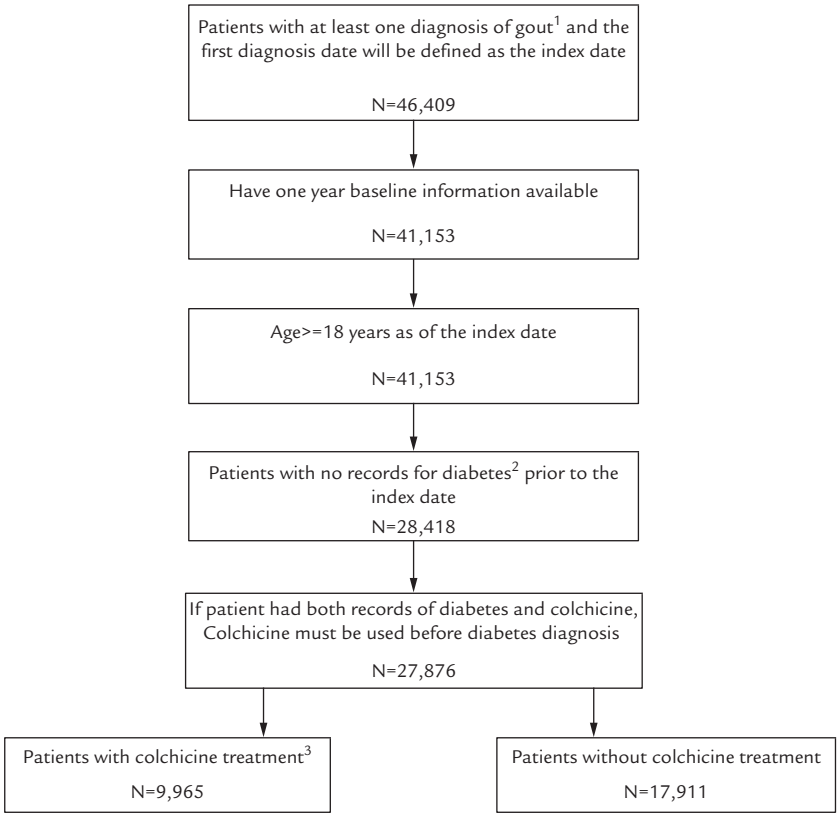
The study sample included adult patients (≥18 years) diagnosed as having gout in the VISN 16 data warehouse. The first diagnosis date of gout was defined as the index date. Patients diagnosed as having diabetes or any antidiabetes drug use before the index date were excluded. Patients were followed up from the index date to the onset of diabetes, the date of death, or the end of data availability, whichever came first. Everyone in this study had 1-year continuous enrollment eligibility before index date.

Variables

Patients with gout were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code 274.xx. Patients with diabetes were identified using *ICD-9-CM* code 250.xx or any antidiabetic medication use. The comorbidities were identified using the following *ICD-9-CM* codes: cardiovascular diseases, 390 through 459 excluding 401-405; coronary artery disease, 410 through 414; angina, 410; myocardial infarction, 411 and 413; stroke, 430 through 438; peripheral artery disorder, 443; congestive heart failure, 398.91 and 428; hypertension, 401 through 405; diabetes, 250; kidney stone, 592, 594, and 274.11; and renal disease, 580 through 588, 250.4, 590, 593, and 791.0. The Charlson comorbidity index (CCI)[14] was also used based on diagnosis codes, such as heart disease, AIDS, or cancer (a total of 22 conditions). Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one.[15]

Subjects

The VISN 16 data warehouse contained records for 46,409 unique veterans with at least one gout diagnosis. Patients had at least baseline information before the first diagnosis of gout and had to be ≥18 years old on the index date. Patients with any records of diabetes before first diagnosis of gout or first use of colchicine were excluded. Study participants were allowed to receive other standard of care medication for gout, including nonsteroidal anti-inflammatory drugs, corticosteroids,



Notes:

1. Patients with gout diagnosis were identified using ICD-9-CM code: 274.xx.

2. Patients with diabetes diagnosis were identified using ICD-9-CM code: 250.xx or use of any anti-diabetic medications

Figure 1. Flowchart of Sample Selection of Patient with Gout Diagnosis.

adrenocorticotropic hormone, allopurinol, probenecid, or sulfinpyrazone. The final sample for data analysis in this study included 9965 gout patients treated with colchicine and 17,911 gout patients who never used colchicine. Figure 1 is a flowchart of patient selection.

Statistical Analysis

Baseline characteristics were compared during the baseline period of 1 year, including patient demographic information, index year, and baseline comorbidities. The comorbidities included the ones commonly associated with gout, such as hypertension, hyperlipidemia, obesity, heart failure, cardiovascular disease, and renal disease. Categorical variables were assessed with χ^2 tests, whereas continuous variables were analyzed with *t* tests or nonparametric Wilcoxon tests. The primary outcome was defined as the incidence of new onset of diabetes as defined by the *ICD-9-CM* codes or antidiabetes medication use, following the index date. Incidence rate of diabetes was measured per 1000 patient-years of observation. A Kaplan-Meier survival curve of the probability of developing diabetes was constructed according to colchicine exposure status (ever or never use).

Patients who never took colchicine were matched (with 1:1 ratio) to the patients who took colchicine via propensity scoring method. The propensity scores were predicted from a logistic regression that estimated the probability of colchicine initiation using the baseline characteristics, including demographic characteristics (BMI, age, sex, and race), index year, comorbidities,

baseline antigout medication, and health care use in the 12-month preindex period. The nearest neighbor method with a caliper of 0.001[16,17] was then used to construct the matched cohorts.

To assess cumulative dose-related effects of colchicine, an ordered categorical variable was established based on approximate quartiles of duration of use in the patients taking colchicine.[18] A Poisson regression model was then constructed to test the association between duration of drug exposure and risk of incident diabetes, providing adjusted relative risks for each category of colchicine use compared with patients who never used colchicine. Incident diabetes rates were calculated for each of the 4 groups for duration of colchicine use and compared with patients who never used colchicine in this study. A Cox proportional hazards model was also fit using the same group of independent variables in a sensitivity analysis.

In time-varying multivariable survival analysis,[18,19] with adjustments for possible confounding factors, the hazard ratio for incident diabetes among patients who had taken colchicine was compared with those who had not. First, time-varying Cox proportional hazards regression models were examined using all the 6-month follow-up data, thus allowing medication use and covariates to change over time. This approach also accounted for changes in standard drug therapy for gout and variations in the threshold for diagnosing and treating diabetes during the observation period. For example, in the Cox time-varying regression analysis, if individuals were not taking colchicine during certain phases of the study (possibly at study entry or if they stopped taking colchicine before censoring or the end of the observation period), they would contribute to the estimates for patients in the never use category during those periods. Thus, the time-varying model took all observations until censoring or dropout into account, even if a participant was not taking colchicine at study entry or if a person stopped taking colchicine later. Diabetes is measured in 6-month cycles from the first gout diagnosis date until the occurrence, death, or the end of eligibility. Statistical significance was set at $P < 0.05$.

RESULTS

A total of 27,876 patients met the study inclusion criteria, including 17,911 patients not treated with colchicine and 9965 patients treated with colchicine. Patients in the colchicine-treated cohort were younger (mean [SD] age, 61.94 [12.71] vs 64.57 [12.68] years; $P < 0.0001$).

Study Using Propensity Score–Matched Sample

After propensity score matching, the final study sample consisted of 1046 pairs of 1:1 matched patients from the colchicine-treated and control cohorts. No significant differences were observed between the matched cohorts in terms of baseline demographic characteristics, comorbidity profiles, gout medication treatment history, and health care use as highlighted in Table I.

After matching, the median follow-up was 5.92 and 5.70 years in the colchicine and noncolchicine cohorts, respectively. Approximately 22.37% developed diabetes in the colchicine cohort during the follow-up period compared with 21.41% in the noncolchicine cohort. The diabetes incidence rate was 38.95 per 1000 person-year among patients treated with colchicine and 39.02 per 1000 person-year among patients without any colchicine use. According to the Kaplan-Meier estimate, the difference in the incidence of diabetes between the 2 cohorts was not significant (log-rank $\chi^2 = 0.05$, $P = 0.829$).

For patients in the colchicine cohort, the median treatment duration was 210 days, and the total mean (SD) dose of colchicine was 332 (852) mg (Table II). Four quartiles were created based on the treatment duration; group 1 patients received colchicine treatment for up to 60 days (n=273), group 2 for up to 200 days (n=252), group 3 for up to 760 days (n=260), and group 4 for >760 days (n=261). The incidence rate of diabetes ranged from 43.74 per 1000 person-year among patients with a median colchicine treatment duration of 60 days to 36.04 among those with a median colchicine treatment duration of 1620 days (Table II).

In Poisson regression with adjustment for possible confounding factors, the strength of association of reduced risk of diabetes increased with duration of colchicine exposure, but the difference was not significant ($P > 0.05$, Table III). Similar results were obtained using the Cox proportional hazard model.

Results of the Cox time-varying multivariable regression analysis reveal a reduction in the risk of diabetes for patients with colchicine use (hazard ratio = 0.877) compared with those with never use at each phase; however, the difference was not significant (95% CI, 0.662–1.163; $P = 0.362$; Table IV). Use of corticosteroids or urate-lowering medications was associated with a significantly higher risk of diabetes ($P = 0.004$ and 0.040, respectively). As for the time invariant variables, higher BMI or CCI were associated with higher risk of diabetes ($P < 0.01$).

Table I. Baseline characteristics of gout patients after propensity score matching.

Characteristic*	Patients Without colchicine (n = 1046)	Patients With Colchicine (n = 1046)	*P* Value
Age at first gout diagnosis, mean (SD), y	62.75 (12.85)	62.21 (12.66)	0.332
Race, No. (%)			
White	606 (57.93)	601 (57.46)	0.825
Others	440 (42.07)	445 (42.54)	
Sex, No. (%)			0.546
Male	1032 (98.66)	1035 (98.95)	
Female	14 (1.34)	11 (1.05)	
Region, No. (%)			
Arkansas	235 (22.47)	244 (23.33)	
Louisiana	119 (11.38)	128 (12.24)	
Mississippi	481 (45.98)	463 (44.26)	
Oklahoma	161 (15.39)	161 (15.39)	
Texas	8 (0.76)	10 (0.96)	
Others	42 (4.02)	40 (3.82)	
Body mass index, mean (SD), kg/m^2	30.10 (5.47)	29.98 (5.67)	0.601
Insurance, No. (%)†			
Medicare	422 (40.34)	409 (39.10)	
Preferred providers	106 (10.00)	106 (10.00)	> 0.99
Other	124 (11.85)	108 (10.33)	0.265
Index year, No. (%)			0.136
2000	175 (16.73)	186 (17.78)	
2001	203 (19.41)	182 (17.4)	
2002	193 (18.45)	199 (19.02)	
2003	134 (12.81)	134 (12.81)	
2004	38 (3.63)	47 (4.49)	
2005	89 (8.51)	90 (8.6)	
2006	45 (4.3)	44 (4.21)	
2007	32 (3.06)	26 (2.49)	
2008	35 (3.35)	34 (3.25)	
2009	48 (4.59)	47 (4.49)	
2010	54 (5.16)	57 (5.45)	
Charlson comorbidity index	0.57 (1.11)	0.52 (1.04)	0.309
Comorbidities, No. (%)‡			
Any cardiovascular disease	337 (32.22)	301 (28.78)	0.087
Coronary artery disease	251 (24.00)	230 (21.99)	0.275
Angina	32 (3.06)	46 (4.4)	0.106
Myocardial infarction	5 (0.48)	3 (0.29)	0.726
Congestive heart failure	79 (7.55)	65 (6.21)	0.227
Peripheral arterial disease	37 (3.54)	32 (3.06)	0.541
Stroke	65 (6.21)	59 (5.64)	0.579

(continued)

Table I. (continued).

Characteristic*	Patients Without colchicine (n = 1046)	Patients With Colchicine (n = 1046)	*P* Value
Valvular heart disease	31 (2.96)	25 (2.39)	0.416
Hyperlipidemia	423 (40.44)	390 (37.28)	0.139
Hypertension	717 (68.55)	712 (68.07)	0.814
Kidney stone	38 (3.63)	27 (2.58)	0.166
Renal disease	108 (10.33)	118 (11.28)	0.481
Smoking	148 (14.15)	134 (12.81)	0.370
Serum uric acid results, No. (%)	1046	1046	0.837
<5 mg/dL	109 (10.42)	93 (8.89)	
5-6 mg/dL	89 (8.51)	97 (9.27)	
6-7 mg/dL	153 (14.63)	161 (15.39)	
7-8 mg/dL	240 (22.94)	243 (23.23)	
8-9 mg/dL	236 (22.56)	227 (21.70)	
>9 mg/dL	219 (20.94)	225 (21.51)	
Medications at baseline, No. (%)			
Nonsteroidal anti-inflammatory drug	492 (47.04)	506 (48.37)	0.540
Naproxen	150 (14.34)	158 (15.11)	0.622
Indomethacin	281 (26.86)	291 (27.82)	0.624
Sulindac	26 (2.49)	17 (1.63)	0.166
Salsalate	30 (2.87)	18 (1.72)	0.080
Ibuprofen	124 (11.85)	139 (13.29)	0.323
Corticosteroids	131 (12.52)	126 (12.05)	0.739
Prednisone	87 (8.32)	83 (7.93)	0.749
Triamcinolone	53 (5.07)	54 (5.16)	0.921
Urate-Lowing Therapy	397 (37.95)	389 (37.19)	0.718
Allopurinol	378 (36.14)	365 (34.89)	0.553
Probenecid	22 (2.10)	29 (2.77)	0.321
Resource use at baseline, mean (SD)			
No. of inpatient stays	0.13 (0.50)	0.13 (0.47)	0.928
No. of emergency department visits	0.19 (0.83)	0.25 (1.19)	0.172
No. of outpatient visits	9.75 (10.95)	9.99 (10.41)	0.606

*Variables are measured during the 12-month baseline period, including index date, unless mentioned otherwise.
†Not exclusive categories.
‡The comorbidities were identified using the following *International Classification of Disorders, Ninth Revision, Clinical Modification* codes: cardiovascular diseases, 390 through 459 excluding 401 through 405; coronary artery disease, 410 through 414; angina, 410; myocardial infarction, 411 and 413; stroke, 430 through 438; peripheral artery disease, 443; congestive heart failure, 398.91 and 428; hypertension, 401-405; diabetes, 250; kidney stone, 592, 594, and 274.11; and renal disease, 580 through 588, 250.4, 590, 593, and 791.0.

Table II. Colchicine duration and diabetes incidences in gout patients.

Variable	Patients Without Colchicine	Patients With Colchicine	Group 1 (n = 273)	Group 2 (n = 252)	Group 3 (n = 260)	Group 4 (n = 261)
Median treatment duration, d*	0.00	210.00	60	120	420	1,620
Total colchicine dose, mean (SD), 100 mg	0.00	3.32 (8.52)	0.62 (0.58)	1.58 (1.03)	4.53 (2.85)	19.90 (15.55)
Follow-up, No. of patient-years	5,741	6,008	1,372	1,325	1,535	1,776
Diabetes incidence, No.	224	234	60	52	58	64
Diabetes incidence rate per 1000 patient-years	39.02	38.95	43.74	39.24	37.78	36.04

*Colchicine use after diabetes does not count; treatment duration was roughly divided into 4 groups based on duration of colchicine use.

DISCUSSION

Findings from this study suggest that the use of colchicine may be associated with a reduced risk of type 2 diabetes in patients with gout after propensity score matching. This reduction in diabetes risk was observed after adjusting for diabetes risk factors and other covariates, such as BMI, CCI, and other antigout medications (eg, corticosteroid use). The reduction in diabetes risk was not statistically significant, indicating that the reduction effect of diabetes incidence may be very weak given the observational study setting.

The decreasing trend of diabetes risk with increased duration of colchicine exposure is apparent. A time-varying regression model was used to assess colchicine effects on risk of diabetes because gout treatment always evolves over time. Use of the time-varying model further enabled us to adjust for variations in these factors and for changes in possible confounders at each 6 months during the 11 years of observation and allowed for a more accurate reflection of total antigout treatment over time. This study also used Poisson regression and Cox proportional hazards regression to examine the effect of ever use of colchicine. Both models reached very similar conclusions that the use of colchicine was associated with reduced risk of diabetes development, but the difference in risk was not significant.

The possible beneficial effect of colchicine in non–insulin-dependent diabetes mellitus has been studied before. One study concluded that colchicine could significantly reduce blood glucose levels, both fasting and postprandial, when given at a dose of 0.5 mg 3 times a day in patients with non–insulin-dependent diabetes mellitus.[13] Furthermore, no adverse effects due to colchicine were observed in that study. Colchicine's hypoglycemic effects in this study suggest an antidiabetic property of colchicine. Meanwhile, colchicine's other properties beyond antigout treatment have been examined in the literature. Colchicine can affect macrophages, neutrophils, and endothelial cells, all of which are implicated in the pathogenesis of cardiovascular disease. Gout patients who took colchicine were reported to have a significantly lower prevalence of myocardial infarction and exhibited trends toward reduced all-cause mortality and lower C-reactive protein level versus those who did not take colchicine.[20] At the same time, cardiovascular diseases have been long linked to diabetes.[21,22] Prospective studies document an increased likelihood of sudden cardiac death and myocardial infarctions in patients with diabetes.[23]

Another finding in this study is that use of corticosteroids is associated with higher risk of diabetes after propensity score matching. This finding was confirmed using both a standard Cox proportional hazards model and a time-varying Cox proportional hazards model, and it was consistent with existing knowledge.[24] The risk of developing diabetes more than doubled in elderly patients

Table III. Colchicine effect on diabetes risks among gout patients using Poisson model.

Variable	Estimate (95% CI)	*P* value
Intercept	−5.307 (−6.974 to −3.641)	<0.001
Colchicine (reference, without colchicine)		
Colchicine group 1	0.160 (−0.127 to 0.447)	0.275
Colchicine group 2	−0.089 (−0.392 to 0.214)	0.565
Colchicine group 3	0.036 (−0.256 to 0.328)	0.808
Colchicine group 4	−0.031 (−0.311 to 0.250)	0.830
Race (reference, white)		
Black	−0.146 (−0.366 to 0.074)	0.193
Other	−0.566 (−0.906 to −0.225)	0.001
Female	−0.688 (−2.086 to 0.710)	0.335
Charlson comorbidity index	0.047 (−0.044 to 0.137)	0.310
Serum uric acid	0.032 (−0.016 to 0.079)	0.190
Age on index date	−0.003 (−0.011 to 0.006)	0.518
Body mass index	0.047 (0.032 to 0.062)	<.001
Index year (reference, 2010)		
2000	2.639 (1.234 to 4.043)	<.001
2001	2.685 (1.282 to 4.087)	<.001
2002	2.635 (1.232 to 4.038)	<.001
2003	2.689 (1.281 to 4.096)	<.001
2004	2.498 (1.032 to 3.963)	<.001
2005	2.564 (1.143 to 3.984)	<.001
2006	2.230 (0.747 to 3.713)	0.003
2007	1.616 (−0.025 to 3.257)	0.054
2008	2.037 (0.503 to 3.571)	0.009
2009	1.321 (−0.280 to 2.922)	0.106
Nonsteroidal anti-inflammatory drugs	−0.091 (−0.283 to 0.101)	0.354
Urate-lowing therapy	−0.181 (−0.368 to 0.006)	0.058
Corticosteroids	−0.040 (−0.319 to 0.239)	0.779

who are newly prescribed an oral corticosteroid.[25] It is known that corticosteroids used to reduce harmful inflammation can lead to diabetes, which is often referred to as steroid diabetes.[26] After considering the fact that gout patients already have a higher risk of diabetes due to hyperuricemia,[27,28] extra caution should be exercised in treating gout patients with corticosteroids because of the competing risks of diabetes and cardiovascular risks. We also observed higher diabetes risks among patients receiving urate-lowering drugs. To our best knowledge, there was no literature suggesting the association between urate-lowering drugs and diabetes risk. Our finding needs to be further explored in other data sets.

This study has its share of strengths and limitations. It has limitations inherent in any observational study. However, the limitation of our study as a retrospective study has been mitigated by the comparability between propensity score–matched cohorts. Admittedly, potential unmeasured confounding variables might still introduce bias into the findings of this study.[17] In addition, we did not examine the cardiovascular comorbidities during the follow-up period, which might be associated with colchicine prescription. Our information on antigout medications taken during the baseline period may be not consistently complete for all patients, especially those with other insurance other than Veterans Health Affairs coverage. Veteran patients are not representative of the

Table IV. Diabetes risks among gout patients with and without colchicine treatment using a time-varying Cox proportional hazards model.

Variable	Hazard Ratio (95% CI)	*P* value
Time-varying variables		
Colchicine	0.877 (0.662–1.163)	0.362
Nonsteroidal anti-inflammatory drug	2.040 (0.681–6.106)	0.203
Urate-lowing therapy	3.659 (1.511–8.859)	0.004
Corticosteroids	2.153 (1.037–4.467)	0.040
Serum uric acid	1.026 (0.976–1.079)	0.316
Time invariant variables		
Age at index date	1.001 (0.994–1.009)	0.705
Race (reference, white)		
Black	0.815 (0.653–1.016)	0.068
Other	0.521 (0.369–0.735)	<.001
Female	0.491 (0.123–1.964)	0.315
Body mass index	1.054 (1.038–1.071)	<.001
Charlson comorbidity index	1.140 (1.047–1.241)	0.003
Index year (reference, 2000)		
2001	1.127 (0.841–1.510)	0.425
2002	1.178 (0.877–1.582)	0.277
2003	1.332 (0.963–1.843)	0.083
2004	1.365 (0.810–2.302)	0.243
2005	1.508 (1.032–2.201)	0.034
2006	1.303 (0.746–2.275)	0.353
2007	0.666 (0.244–1.816)	0.427
2008	1.849 (0.910–3.756)	0.089
2009	1.416 (0.612–3.276)	0.416
2010	1.074 (0.251–4.583)	0.924

US population because the Veterans Health Affairs system is not like other health care systems. The Veterans Health Affairs is a national integrated health care system that provides a set of comprehensive services to a population that is predominantly male and elderly and thus very different from the populations covered by commercial health plans, Medicare, or Medicaid.

CONCLUSIONS

This study suggests a possible duration- or dose-related association between colchicine use and reduced risk of diabetes in adults with gout even though the risk reduction was not significant. Colchicine may have a role in treating gout not only to antiinflame but also to reduce the likelihood of developing diabetes. As quality of life and life expectancy improve for patients with gout, the use of tolerable therapies that have multiple beneficial effects is promoted. Further studies are needed to confirm these findings from this study.

ACKNOWLEDGMENTS

We thank the Department of Veterans Affairs VISN 16 data warehouse for the deidentified data set and the Southeast Louisiana Veterans Health Care System for additional resources. We also thank Takeda Pharmaceuticals USA Inc for their support.

V. Fonseca, L. Shi designed this study, L. Wang conducted the analysis. V. Fonseca, L. Shi, L. Wang interpreted the results. L. Wang and L. Shi drafted the manuscript. M. Sawhney, Y. Zhao, G.R. Carpio provided comments. No body else helped to write or revise this manuscript.

CONFLICTS OF INTEREST

The author has indicated that they have no conflicts of interest with regard to the content of this article.

REFERENCES

1. Luk AJ, Simkin PA. Epidemiology of hyperuricemia and gout. *Am J Managed Care*. 2005;11:S435–S442. quiz S465–S438.
2. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. *Arthritis Rheum*. 2011;63:3136–3141.
3. Sachs L, Batra KL, Zimmermann B. Medical implications of hyperuricemia. *Med Health R I*. 2009;92:353–355.
4. Edwards NL. The role of hyperuricemia in vascular disorders. *Curr Opin Rheumatol*. 2009;21:132–137.
5. Axelrod D, Preston S. Comparison of parenteral adrenocorticotropic hormone with oral indomethacin in the treatment of acute gout. *Arthritis Rheum*. 1988;31:803–805.
6. Pillinger MH, Goldfarb DS, Keenan RT. Gout and its comorbidities. *Bull NYU Hosp Jt Dis*. 2010;68:199–203.
7. Primatesta P, Plana E, Rothenbacher D. Gout treatment and comorbidities: a retrospective cohort study in a large US managed care population. *BMC Musculoskel Disord*. 2011;12:103.
8. Choi HK, De Vera MA, Krishnan E. Gout and the risk of type 2 diabetes among men with a high cardiovascular risk profile. *Rheumatology (Oxford)*. 2008;47:1567–1570.
9. Zhang W, Doherty M, Bardin T, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2006;65:1312–1324.
10. Schlesinger N, Schumacher R, Catton M, Maxwell L. Colchicine for acute gout. *Cochrane Database Syst Rev*. 2006:CD006190.
11. Terkeltaub RA. Gout. *N Engl J Med*. 2003;349:1647–1655.
12. Molad Y. Update on colchicine and its mechanism of action. *Curr Rheumatol Rep*. 2002;4:252–256.
13. Das UN. Colchicine in diabetes mellitus. *J Assoc Physicians India*. 1993;41:213.
14. Kastner C, Armitage J, Kimble A, et al. The Charlson comorbidity score: a superior comorbidity assessment tool for the prostate cancer multidisciplinary meeting. *Prostate Cancer Prostatic Dis*. 2006;9:270–274.
15. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.
16. Heinze G, Juni P. An overview of the objectives of and the approaches to propensity score analyses. *Eur Heart J*. 2011;32:1704–1708.
17. Caliendo M, Kopeinig S. Some practical guidance for the implementation of propensity score matching. *J Econ Surv*. 2008;22:31–72.
18. Wasko MC, Hubert HB, Lingala VB, et al. Hydroxychloroquine and risk of diabetes in patients with rheumatoid arthritis. *JAMA*. 2007;298:187–193.
19. Bellera CA, MacGrogan G, Debled M, et al. Variables with time-varying effects and the Cox model: some statistical concepts illustrated with a prognostic factor study in breast cancer. *BMC Med Res Method*. 2010;10:20.
20. Crittenden DB, Lehmann RA, Schneck L, et al. Colchicine use is associated with decreased prevalence of myocardial infarction in patients with gout. *J Rheumatol*. 2012;39:1458–1464.
21. Kengne AP, Batty GD, Hamer M, et al. Association of C-reactive protein with cardiovascular disease mortality according to diabetes status: pooled analyses of 25,979 participants from four U.K. prospective cohort studies. *Diabetes Care*. 2012;35:396–403.
22. Maahs DM, Snell-Bergeon JK. Current knowledge and future directions on cardiovascular disease in diabetes. *Diabetes Technol Ther*. 2012;14(suppl 1):S75–S76.
23. Nesto RW, Phillips RT. Asymptomatic myocardial ischemia in diabetic patients. *Am J Med*. 1986;80:40–47.
24. Lansang MC, Hustak LK. Glucocorticoid-induced diabetes and adrenal suppression: how to detect and manage them. *Cleve Clin J Med*. 2011;78:748–756.
25. Blackburn D, Hux J, Mamdani M. Quantification of the risk of corticosteroid-induced diabetes mellitus among the elderly. *J Gen Intern Med*. 2002;17:717–720.
26. Hwang JL, RE W. Steroid-induced diabetes: a clinical and molecular approach to understanding and treatment. *Diabetes/Metab Res Rev*. 2014;30:96–102.
27. Chen L-Y, Zhu W-H, Chen Z-W, et al. Relationship between hyperuricemia and metabolic syndrome. *J Zhejiang Univ Sci B*. 2007;8:593–598.
28. Bhole V, Choi JW, Kim SW, et al. Serum uric acid levels and the risk of type 2 diabetes: a prospective study. *Am J Med*. 2010;123:957–961.

Address correspondence to: Lizheng Shi, PhD, Department of Global Health Systems, School of Public Health and Tropic Medicine, Tulane University, 1440 Canal St, New Orleans, LA 70112. E-mail: lshi1@tulane.edu