CLINICAL RESEARCH STUDY

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Prevalence of Contraindications and Prescription of Pharmacologic Therapies for Gout

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ABSTRACT

BACKGROUND: Patients with gout have comorbidities, but the impact of these comorbidities on treatment has not been studied.

METHODS: A total of 575 patients with gout were stratified according to certainty of diagnosis according to International Classification of Diseases, 9th Revision, Clinical Modification code alone (cohort I), American College of Radiology criteria (cohort II), and crystal diagnosis (cohort III). Comorbid conditions were defined according to International Classification of Diseases, 9th Revision, Clinical Modification codes, and stratified as either moderate or severe. Drug contraindications were defined as moderate or strong, based on Food and Drug Administration criteria and severity of disease.

RESULTS: The most common comorbidity was hypertension (prevalence 0.89). The presence of comorbidities resulted in a high frequency of contraindications to approved gout medications. More than 90% of patients had at least 1 contraindication to nonsteroidal anti-inflammatory drugs. Many patients demonstrated multiple contraindications to 1 or more gout medications. Frequently, patients were prescribed medications to which they harbored contraindications. The prevalence of patients prescribed colchicine despite having at least 1 strong contraindication was 30% (cohort I), 37% (cohort II), and 39.6% (cohort III).

CONCLUSION: Patients with gout typically harbor multiple comorbidities that result in contraindications to many of the medications available to treat gout. Frequently, despite contraindications to gout therapies, patients are frequently prescribed these medications.

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KEYWORDS: Comorbidity; Drug contraindication; Gout; Quality of care; Treatment

Gout is the most common inflammatory arthropathy and an increasing public health problem.[1-5] The most important risk factor for developing gout is hyperuricemia. Conditions promoting hyperuricemia (eg, diuretic use, renal failure, obesity) are increasing, posing a challenge for gout management.[4,6-9] Currently, gout treatment options are currently limited.[10-13] Anti-inflammatory therapies (colchicine, nonsteroidal anti-inflammatory drugs, and glucocorticoids) treat and prevent acute gout flares.[14] Allopurinol and febuxostat block urate production, and probenecid stimulates renal urate excretion, to lower serum urate.[15] Use of these agents may be limited by contraindications that commonly manifest in patients with gout. For example, nonsteroidal anti-inflammatory drugs may exacerbate renal failure,[16,17] hypertension,[16,18] and cardiovascular disease,[16,18] all reportedly common in patients with gout. Similarly, glucocorticoids may exacerbate diabetes and hyperlipidemia,[19] also reportedly common in these individuals.[8,20] Because pa-

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tients with gout may simultaneously have multiple comorbidities,[7,21-23] the management of the individual patient can be complex and require a customized approach. However, the extent to which patients with gout harbor therapeutic contraindications to their possible treatments and physician responses to these contraindications have not been studied.

The Department of Veterans Affairs (VA) is the largest health care delivery system in the United States, providing services to a population that includes a large proportion of middle-aged and elderly men[10,24] well suited for the study of patients with gout. The VA also is distinguished by an extensive and searchable electronic medical record system. We used the electronic medical record at the New York Harbor Health Care System, New York campus of the VA (NY VA) to examine contraindications to therapy and physician-prescribing patterns among a cohort of patients with gout.

CLINICAL SIGNIFICANCE

- Patients with gout have multiple comorbid conditions.
- Patients with gout frequently have contraindications to acute and chronic gout medications.
- Therapeutic decisions should be based on individualized risks and benefits.
- Potential adverse effects may be averted with heightened clinician and patient education.

MATERIALS AND METHODS

Patient Enrollment

Patients with gout were identified from all patients in the NY VA electronic medical record, ages 18 to 100 years, as having any International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code (274.xx) for gout. Patients from this initial screen were excluded from further analysis if their records lacked documentation of a clinic or hospital visit during the 18-month period of our review (July 2007 to December 2008) or if the patient had died within the first 6 months of the review period. The resulting group was designated cohort I (Figure 1). Baseline demographic information was collected according to NY VA electronic medical record designation, including patient self-designations for race and ethnicity.

To identify a cohort of patients with gout at a higher level of definitional stringency (cohort II), we individually reviewed the charts of cohort I patients to identify those meeting American College of Rheumatology (ACR) criteria for gout.[25] Patients from cohort I were included in cohort II if their electronic medical record also contained evidence of current use of a gout medication (allopurinol, colchicine, or probenecid); microscopic identification of urate crystals; clinical or radiologic evidence of ≥ 1 tophus; or 6 of 12 clinical criteria for the diagnosis of acute arthritis of primary gout.[25] Patients taking allopurinol for hyperuricemia of malignancy/tumor lysis syndrome or with diagnoses of lymphoma, leukemia, myeloma, or other malignancy were excluded. A third, more rigorously defined group of patients with gout (cohort III) included only cohort II patients whose record included polarizing microscopic documentation of monosodium urate crystals in synovial fluid or tophi.

Comorbidities

Comorbidities were identified by the presence of physician-assigned ICD-9-CM codes and confirmed by chart review. On the basis of a review of the literature and consensus opinion of the authors, clinically relevant gout-associated comorbidities were defined as hypertension (ICD-9-CM code 401.xx), chronic kidney disease (585.xx), coronary artery disease (414.xx), hyperlipidemia (272.xx), chronic hepatitis (571.xx), gastroesophageal disease (530.xx, 533.xx), diabetes (250.xx), osteoporosis (733.xx), chronic infection (011.xx-018.xx, 730.xx), and allopurinol hypersensitivity. Comorbidity severities were determined on the basis of clinical and laboratory results documented in the electronic medical record. Most comorbidities were defined within 2 ranges of disease activity (moderate vs severe) (Table 1), depending on whether the comorbidity was controlled successfully by medical management. Coronary artery disease, osteoporosis, and chronic infection were designated as present or absent only. In addition to ICD-9-CM code, chronic kidney disease was confirmed according to the criteria of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative.[26,27]

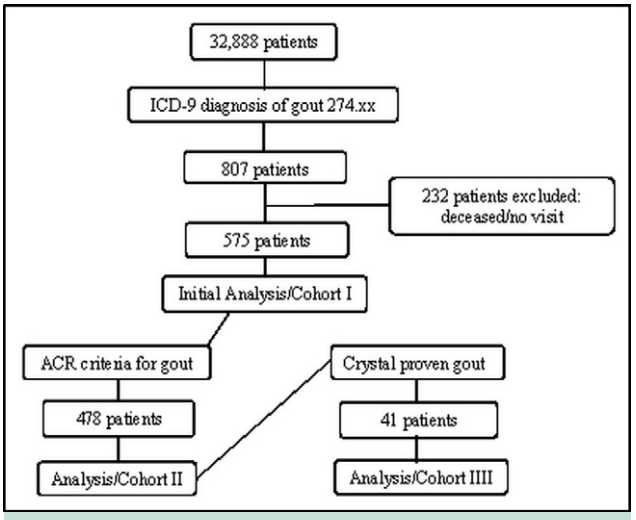

Figure 1 Flow of study design. ACR = American College of Radiology; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification.

Table 1 Comorbidities and Disease Severity Defined

Disease	Mild-to-Moderate or Controlled	Moderate-to-Severe or Uncontrolled
Hypertension	Controlled prescribed anti-HTN medications with SBP $<$ 140 mm Hg or DBP $<$ 90 mm Hg	Uncontrolled with or without prescribed anti-HTN medications and SBP $\geq$ 140 mm Hg or DBP $\geq$ 90 mm Hg
Hyperlipidemia	Documentation of HL controlled with medical therapy (TC $\leq$ 240 mg/dL, TG $\leq$ 150 mg/dL, LDL $\leq$ 150 mg/dL)	Documentation of HL uncontrolled with or without medical therapy (TC $\geq$ 240 mg/dL, TG $\geq$ 150 mg/dL, LDL $\geq$ 150 mg/dL)
Chronic kidney disease*	Creatinine $>$ 1.2 mg/dL and eGFR $\geq$ 60 mL/min/1.73 m^2	eGFR $<$ 60 mL/min/1.73 m^2
Chronic hepatitis	Serologically proven chronic hepatitis with normal LFTs: AST $<$ 42, ALT $<$ 40; and no detectable viral load (hepatitis B and C)	Serologically proven chronic hepatitis with abnormal LFTs or detectable viral load (hepatitis B and C)
Diabetes mellitus	HbA1c $\leq$ 7.0 mg/dL with or without medical therapy	HbA1c $>$ 7.0 mg/dL with or without treatment, or history of DKA/hyperosmolar hyperglycemic state
astroesophageal diseases	GERD with prescribed histamine$_2$ receptor antagonist blocker or proton pump inhibitor	Documented PUD or history of upper GI bleed regardless of prescribed histamine$_2$ receptor antagonist blocker or proton pump inhibitor
	Present	
Coronary artery disease	Documentation of angina, ischemia, positive stress test, or myocardial infarction	
Osteoporosis†	Documentation by DEXA (T-score ≤ -2.5) on medical therapy or osteopenia (T-scores between -2.0 and -2.5) documented by DEXA not on therapy	
Chronic infection	Documented presence of untreated or partially treated osteomyelitis or tuberculosis	

HTN = hypertension; SBP = systolic blood pressure; DBP = diastolic blood pressure; NA = not applicable; HL = hyperlipidemia; TC = total cholesterol; TG = triglycerides; LDL = low-density lipids; eGFR = estimated glomerular filtration rate; LFT = liver function test; AST = aspartate aminotransferase; ALT = alanine transaminase; HgA1c = glycosylated hemoglobin; HbA1c = hemoglobin A1c; GERD = gastroesophageal reflux disease; PUD = peptic ulcer disease; DEXA = dual-energy x-ray absorptiometry; GI = gastrointestinal.

*Calculated by the 4 variable Modification of Diet in Renal Disease equations.

†Per World Health Organization 2000 Prevention and Management of Osteoporosis Technical Report Series 921 World Health Organization, Geneva, Switzerland.

Contraindications

Contraindications to gout medications were defined, wherever possible, using criteria established by the US Food and Drug Administration (FDA).[28] Contraindications included the following:

- to nonsteroidal anti-inflammatory drugs—hypertension, cardiovascular disease, chronic kidney disease, gastroesophageal disease;
- to glucocorticoids—hypertension, diabetes mellitus, cardiovascular disease, hyperlipidemia, gastroesophageal disease, osteoporosis;
- to colchicine—chronic kidney disease, chronic hepatitis;
- to allopurinol—chronic kidney disease, chronic hepatitis, allopurinol hypersensitivity;
- to probenecid—chronic kidney disease, severe gastroesophageal disease.

Categorization of the degree of contraindication was based, wherever possible, on the FDA definitions of "precaution" versus "contraindication,"[29] which were operationalized as indicating that a particular drug was "moderately" or "strongly" contraindicated, respectively, in the setting of a particular comorbidity. In cases in which FDA guidelines did not provide guidance, medications were defined as "moderately" or "strongly" contraindicated based on the severity of the condition in question. For example, use of nonsteroidal anti-inflammatory drugs was defined as moderately contraindicated in patients with moderate chronic kidney disease, but strongly contraindicated in patients with severe chronic kidney disease. Allopurinol hypersensitivity was identified in subjects with a documented allopurinol allergy who had not undergone desensitization.

Statistical Analyses

All statistical analyses, including analysis of variance and Pearson chi-square, were done using R statistical software (version 2.8.1).

Institutional Approval

This study was approved by the Institutional Review Board and Research Committee of the NY Harbor Healthcare System, NY Campus of the Department of VA.

RESULTS

Patients

From among 32,888 patients in the NY Harbor VA Medical Center electronic medical record, 807 individuals age $\geq$ 18 years (2.5%) were identified as having $\geq$ 1 ICD-9-CM code diagnosis of gout. Exclusion of individuals who failed to meet other entry criteria resulted in an initial cohort for

Table 2 Baseline Patient Characteristics

Characteristics	Mean ± SD (95% CI)		
	Cohort 1 (N = 575)	Cohort 2 (N = 478)	Cohort 3 (N = 41)
Serum uric acid level, mg/dL	7.67 ± 2.06 (7.49-7.86)	7.72 ± 2.16 (7.51-7.93)	7.91 ± 2.33 (7.16-8.65)
Body mass index, kg/m^2	28.97 ± 5.45 (28.52-29.42)	29.11 ± 5.60 (28.60-29.61)	28.78 ± 4.93 (27.22-30.34)
Systolic BP, mm Hg	127.47 ± 17.73 (126.01-128.92)	127.26 ± 17.70 (125.67-128.86)	125.75 ± 20.16 (119.39-132.12)
Diastolic BP, mm Hg	71.25 ± 12.68 (70.21-72.29)	71.06 ± 12.81 (69.91-72.22)	69 ± 15.27 (64.17-73.82)
Creatinine, mg/dL	1.45 ± 0.93 (1.37-1.53)	1.45 ± 0.94 (1.37-1.54)	1.55 ± 0.62 (1.35-1.74)
eGFR, mL/min/1.73 m^2	66.64 ± 27.40 (64.32-68.95)	66.43 ± 27.48 (63.91-68.95)	58.79 ± 20.57 (52.12-65.46)
HgA1C, mg/dL	6.44 ± 3.94 (6.04-6.83)	6.33 ± 1.73 (6.14-6.52)	6.43 ± 1.35 (5.96-6.90)
Total cholesterol, mg/dL	169.29 ± 47.67 (165.30-173.27)	168.57 ± 41.57 (164.79-172.35)	158.75 ± 30.63 (149.08-168.42)
Triglycerides, mg/dL	154.73 ± 179.68 (139.71-169.75)	158.35 ± 191.91 (140.89-175.80)	142.68 ± 66.59 (121.66-163.70)
Allopurinol dose, mg	192.18 ± 99.79 (179.90-204.47)	192.18 ± 99.79 (179.90-204.47)	202.63 ± 97.85 (155.46-249.79)
Age, y	71.75 ± 11.64 (70.79-72.70)	71.74 ± 11.78 (70.67-72.79)	71.73 ± 9.96 (68.58-74.87)
Race/ethnicity, %			
Black	33.9	33.3	26.8
White	49.2	49.8	51.2
Hispanic	7.7	7.5	7.3
South East Asian	2.1	2.1	7.3
Pacific Islander	1	1	0
Native American	0.5	0.4	0
Unknown	4.9	4.6	4.9
Sex, %			
Male	99.3	99.2	97.6
Female	0.7	0.8	2.4

SD = standard deviation; CI = confidence interval; BP = blood pressure; eGFR = estimated glomerular filtration rate; HgA1c = hemoglobin A1c.

analysis (cohort I) of 575 patients (1.7%). As expected, this cohort was almost exclusively male. Mean age was 72 ± 11.8 years. Mean and median serum urate levels for cohort I were 7.7 mg/dL and 7.6 mg/dL (range, 3-15.7 mg/dL), respectively (Table 2).

Of the patients in cohort I, 478 fulfilled ACR criteria for gout (cohort II) based on available data and were reanalyzed. Clinical parameters for cohort II were similar to those for cohort I (Table 2). Forty-one patients from cohort II had documentation of crystal-proven gout and were included in cohort III. Parameters were similar across all 3 cohorts (Table 2).

Comorbidities

Patients in cohort I had substantial comorbidity (Figure 2). The most prevalent comorbidity was hypertension (88.7%). Coronary artery disease, chronic kidney disease, and hyperlipidemia affected 37.4%, 47.1%, and 62.6% of patients, respectively. Diabetes was present in 28.9% of the cohort I population. Only 2.4% of the patients in cohort I had no listed comorbidity. Most patients in cohort I had multiple comorbidities: 17.4%, 22.3%, and 25.2% had 2, 3, and 4 comorbidities, respectively (Figure 3). Approximately 1.0% of the patients had ≥ 7 comorbidities.

Trends in cohort II were similar to those observed in cohort I. Patients with 0, 2, 3, and 4 comorbidities comprised 2.7%, 28.2%, 21.8%, and 24.3% of cohort II, respectively; 1.0% of the patients had ≥ 7 comorbidities. All patients in cohort III had ≥ 1 comorbidity, and the majority had ≥ 2 comorbidities. Patients with 3, 4, and 5 comorbidities accounted for 24.0%, 12.2%, and 19.5% of cohort III, respectively. More than 12% of the patients in this cohort had ≥ 7 comorbidities (Figures 2 and 3).

To determine whether comorbidity rates among patients with gout were greater than those seen in patients without gout, we determined the rates of comorbidities in a randomly selected cohort of 190 patients with osteoarthritis but no gout (mean age 71.3 years). Rates of comorbidity in the osteoarthritis group were lower than those in the gout group. In the osteoarthritis group, 63% had hypertension, 12.5% had coronary artery disease, 7.3% had chronic kidney disease, 17.3% had gastroesophageal disease, 4.2% had osteoporosis, and 8.9% had hepatitis.

We further stratified the frequencies of gout comorbidities into moderate versus severe disease (Figure 2). In cohort I, 64.0% of patients had moderate hypertension and 24.7% had severe hypertension. In cohorts II and III, 65.0% and 73.2% had moderate hypertension, respectively, and 21.9% and 17.1% had severe disease, respectively. Hyperlipidemia was moderate in 35.5%, 35.6%, and 39.0% and severe in 27.1%, 27.8%, and 29.3% of the patients in cohorts I, II, and III, respectively. According to our definition, the majority of patients with chronic kidney disease in each cohort had severe disease.

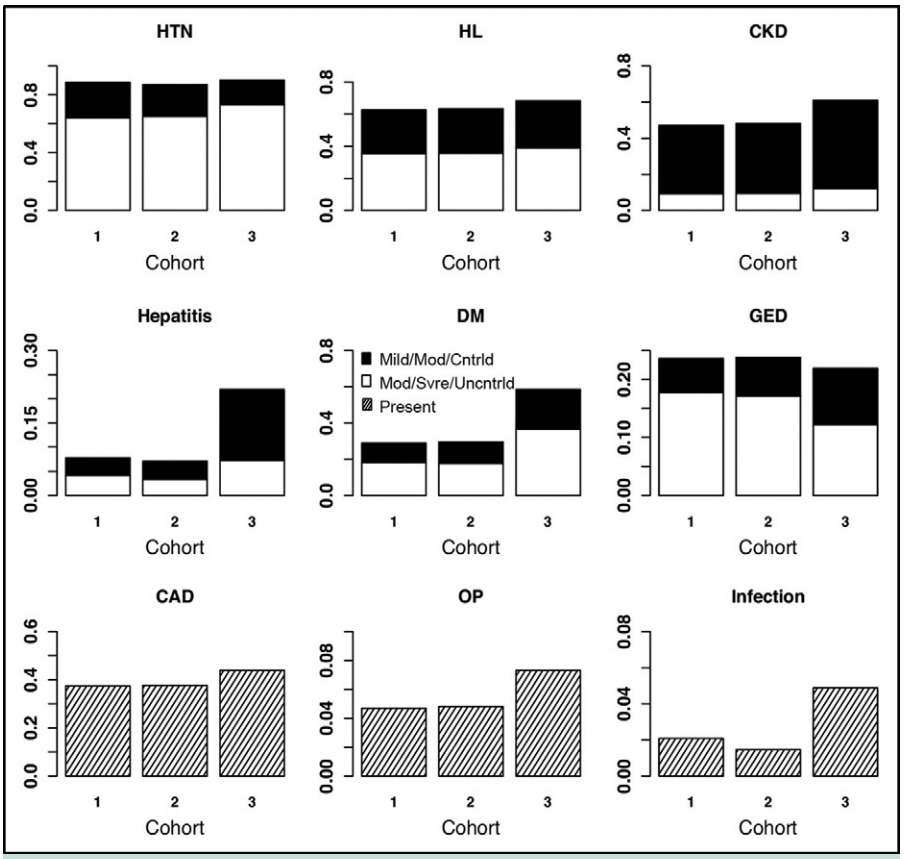

Figure 2 Prevalence of comorbidities in patients with gout. For each cohort defined in Figure 1, the prevalence of specific comorbidities (*y axis*) was redetermined. In some instances, specific comorbidities were further subcategorized as severe (*black bars*) or moderate (*white bars*). In other cases (*hatched bars*), the comorbidities were defined only as absent versus present. HTN = hypertension; HL = hyperlipidemia; CKD = chronic kidney disease: hepatitis = chronic hepatitis; DM = diabetes mellitus; GED = gastroesophageal disease; CAD = coronary artery disease; OP = osteoporosis; infection = chronic infection. See text for additional details.

Prevalence of Contraindications to Gout Medications

Rates of contraindication to approved gout therapies were high. In all 3 cohorts, ≥ 1 contraindications to nonsteroidal anti-inflammatory drug use were present in > 90% of the patients (Figure 4). A similarly high rate of contraindications to glucocorticoids also was observed. Allopurinol was contraindicated in 47.6% of cohort I, 43.0% of cohort II, and 65.9% of cohort III. Large percentages of patients also had contraindications to colchicine and probenecid. Among cohort I patients, approximately 50% had at least 1 contraindication to colchicine; this number increased to 66% in cohort III. The agents with the overall highest rate of contraindications in our study population were glucocorticoids (95.3%, 94.4%, and 97.6% in cohorts I, II, and III, respectively). The mean number of gout drugs to which each patient harbored contraindications was 3.47 (cohort I), 3.49 (cohort II), and 4.00 (cohort III).

Because some contraindications may be more important than others when making therapeutic decisions, we compared the percentage of patients with moderate contraindications with those with strong contraindications to particular medications (Figure 4). In each cohort, a large proportion of the patients had strong contraindications to multiple gout medications. For example, colchicine and probenecid were each strongly contraindicated for approximately 40% of the patients in both cohorts I and II. Similarly, nonsteroidal anti-inflammatory drugs were strongly contraindicated in approximately half of the subjects in the first 2 cohorts and in two thirds of cohort III. Glucocorticoid use was strongly contraindicated for 35.5%, 34.3%, and 39.0% of cohorts I, II, and III, respectively.

Prescription of Gout Medications Despite Contraindications

We next assessed the degree to which patients were being prescribed specific gout medicines in the setting of recognized contraindications (Figure 5). Prescribing of drugs in the presence of contraindications was common. For example, among the 538 patients in cohort I who were identified as having ≥ 1 contraindication to nonsteroidal anti-inflam-

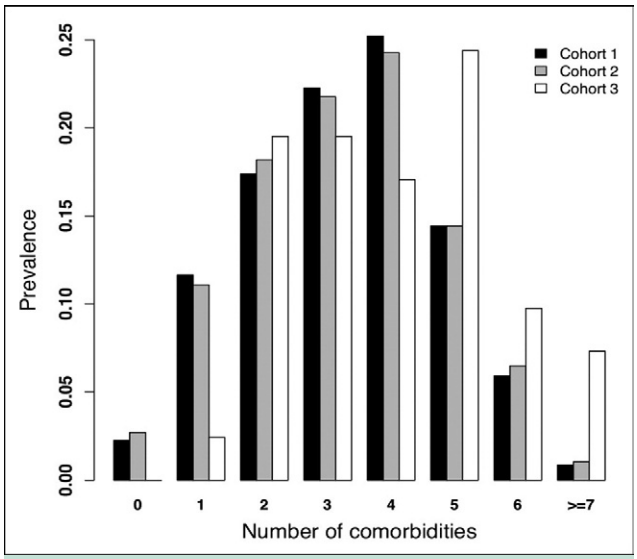

Figure 3 Patients with gout typically harbor multiple comorbidities. The prevalence of having 0 to > 7 associated comorbidities was determined among patients with gout in each of the 3 defined cohorts.

matory drugs, 98 (18.2%) had received 1 of these drugs. Of 293 patients with at ≥ 1 contraindication to colchicine, 119 (40.6%) had received ≥ 1 prescription. In cohort III, 12 of 25 patients (48%) in cohort III had been prescribed allopurinol despite ≥ 1 contraindication to that medication. Notably, glucocorticoids were prescribed relatively rarely in our cohort, in both patients with and without contraindications to these agents.

Prescription of gout medications to patients with moderate versus strong contraindications also was evaluated (Figure 5). Although prescriptions were issued to patients with moderate contraindications to the specific agents in the majority of cases, a significant number of patients received prescriptions despite strong contraindication(s) to the medication prescribed. Among patients possessing ≥ 1 strong contraindication to colchicine use, more than 30% in each of the 3 cohorts were nonetheless prescribed colchicine; 8% to 15% of patients with ≥ 1 strong contraindication to nonsteroidal anti-inflammatory drugs received ≥ 1 prescription for these agents. In cohort II, 17.4% of patients were prescribed allopurinol despite a strong contraindication to the drug.

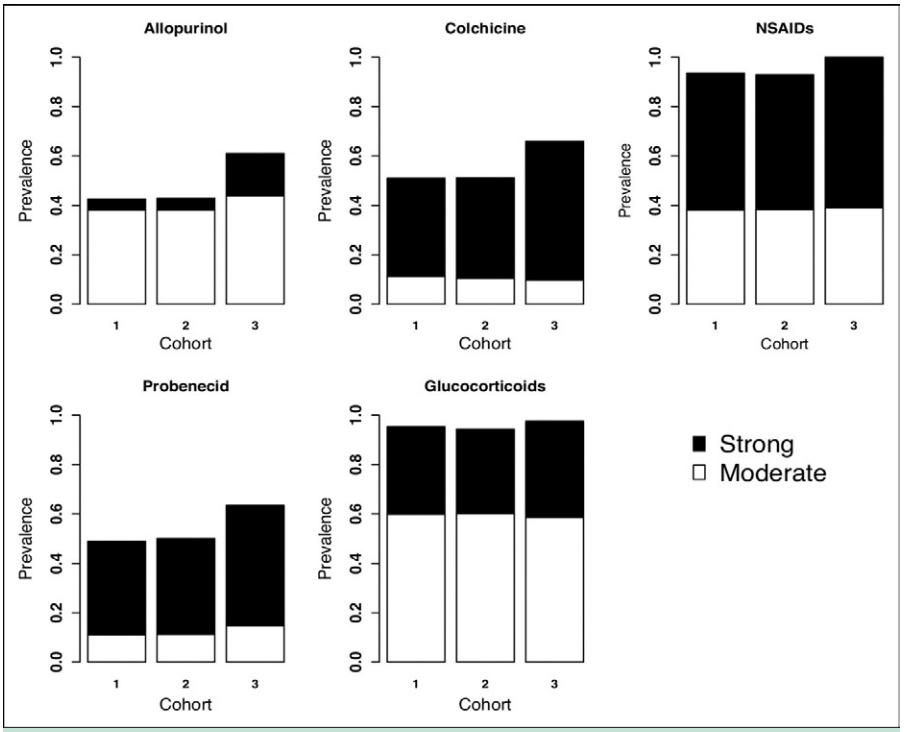

Figure 4 Patients with gout harbor contraindications to multiple gout medications. The prevalence of contraindications to allopurinol, colchicine, nonsteroidal anti-inflammatory drugs, and probenecid are shown among patients from cohorts 1, 2, and 3. The prevalence of contraindications to each drug was further subcategorized according to whether the agents were moderately (*white portions* of the bars) or strongly (*black portions* of the bars) contraindicated in the individual patients. For the purposes of this analysis, in cases in which a patient had multiple contraindications to a single agent, that situation was scored as a single patient contraindication to the drug. NSAID = nonsteroidal anti-inflammatory drug.

Figure 5 Prevalence of patients with gout in each study cohort who were prescribed a contraindicated medication, listed by individual medication. In circumstances in which the patient had multiple contraindications to a particular prescribed medication, the patient was scored as having received a single contraindicated medication. NSAID = nonsteroidal anti-inflammatory drug.

DISCUSSION

To our knowledge, this observational study is the first formal investigation of contraindications to traditional gout medications and of the use of such agents in the setting of such contraindications. Our principal findings were as follows: Patients with gout typically have multiple comorbid conditions; patients with gout frequently harbor multiple, often strong contraindications to the drugs available for gout management; and many patients with gout are prescribed medications for their gout despite contraindications to the agents in question.

Overall, the incidence of comorbidities in our patients with gout was higher than in an age-matched cohort with osteoarthritis but no gout, consistent with several prior reports that patients with gout frequently have chronic comorbid conditions.[8,30-33] Our cohort had a higher rate of comorbidity than patients with gout in some previous studies, probably reflecting the demographic of our VA population. For example, earlier studies typically included a greater representation of female subjects, who may have less severe or chronic gout than male subjects. Moreover, the mean age of our population (72 years) was 15 to 30 years older than that in previous gout comorbidity studies.[8,20,31,33] Given that the population of the United States is currently aging, our study cohort may more accurately reflect future trends in comorbidities than have prior studies.

Medications used to treat acute and chronic gout generally have well-described contraindications.[34,35] Not previously addressed, however, is the prevalence of these contraindications among those with gout. In our study, the majority of patients had ≥ 1 contraindication to at least 1 of the commonly used gout therapies, and many had contraindications to multiple therapies. Moreover, a large proportion of patients had at least 1 strong contraindication to a gout medication. For example, colchicine use was strongly contraindicated in $> 40\%$ of our study population.

Management of gout in patients with multiple comorbidities remains a challenge even for experienced physi-

cians.[28] Clinicians and patients must make therapeutic decisions based on possible risks versus benefits of the individual treatment. Previous studies have evaluated gout medication treatment patterns, but none have addressed the extent to which patients receive gout medications in the face of drug contraindications.[36] We observed a high rate of prescribing medications that were potentially contraindicated. For example, of the 93.6% of patients in cohort I who had at least 1 contraindication to nonsteroidal anti-inflammatory drug use, 18% were nonetheless prescribed these agents, including 9% with strong contraindications to their use. Approximately one fifth of patients in cohorts I, one fourth of patients in cohort II, and one third of patients in cohort III received allopurinol despite contraindications. To some extent, this may reflect the use of allopurinol in renal failure, a strategy with which rheumatologists may be more comfortable than primary care physicians; however (consistent with national trends), most of the patients in our cohort were cared for by primary care physicians.

During chart review, we identified some reasons why physicians prescribed drugs despite contraindications. For example, one physician prescribed prednisone over colchicine or nonsteroidal anti-inflammatory drugs to treat an acute gout attack in a patient with diabetes and renal insufficiency, explicitly risking steroid-induced hyperglycemia rather than nonsteroidal anti-inflammatory drug-induced renal failure or colchicine toxicity. Thus, physicians may feel compelled to make the best drug choice from among a limited palette of available agents, based on clinical scenario. Other reasons why physicians prescribed contraindicated medications may include a failure to recognize the presence, nature, or severity of the contraindication(s). In any event, physician use of these agents in the face of contraindications testifies to a possible need for heightened professional and patient education, and for alternative gout therapies with fewer or different contraindications. In this regard, the recent approval of the non-purine xanthine oxidase inhibitor febuxostat, as well as pegylated uricase and a new dosing schedule for colchicine may provide useful alternative treatments.

The strengths and limitations to our study are worth mentioning. The use of ICD-9-CM codes permitted us to identify a large cohort of patients with gout (cohort I), but may have intrinsic limitations in studying the epidemiology of gout.[37] Pitfalls in basing a diagnosis of gout on physician-designated ICD-9-CM codes may result from several factors, including inadequate and incorrect coding.[37] In addition, a diagnosis of gout based on a syndromic accumulation of features (as in our cohort II) is inherently less definitive than a diagnosis made on an unequivocal test.[37,38] Moreover, gout is episodic and physicians may make presumptive diagnoses during periods when findings are absent, based on patient-reported history alone.[39] Strengths of our study included the rigorous methodology we used to addresses these limitations. We analyzed our enrollment cohort by ICD-9-CM groupings (cohort I), by the ACR's 12 clinical criteria for the diagnosis of gout (cohort II), and by the only universally accepted criterion for gout, a documented crystal diagnosis (cohort III).[37] Patients in cohort III demonstrated a trend toward more comorbidities than those in cohorts I and II, suggesting that the data from the larger cohorts did not overestimate, and may actually have underestimated the frequency of comorbidities among patients with gout. However, in most cases the differences between cohorts I and II versus III did not achieve statistical significance. Thus, our ability to directly review charts allowed us to confirm the validity of our population-based approaches. Another strength of our study was the use of FDA criteria to define drug contraindications, allowing us to assess contraindications according to a rigorous external standard. On the other hand, our studies may have underestimated both the prevalence of drug contraindications and the use of medications in the face of contraindications. For example, in reviewing contraindications to gout medications, we did not address the issue of drug–drug interactions, and in assessing the severity of contraindications, we did not address the extent to which multiple moderate contraindications to a single drug might collectively constitute a strong contraindication to that agent.

CONCLUSIONS

Our study demonstrates that gout is associated with an increased risk for multiple comorbidities, that patients with gout typically harbor contraindications to multiple medications available to treat their condition, and that patients with gout frequently are prescribed medications despite contraindications. Collectively, these data illuminate the limitations of the currently available therapies for gout management.

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