

# Clinical Characteristics of Early-Onset Gout in Outpatient Setting

Yan Li,<sup>1</sup>  Paramarajan Piranavan,<sup>1</sup>  Devi Sundaresan,<sup>2</sup> and Robert Yood<sup>3</sup> 

**Objective.** The objective of this study is to investigate the clinical characteristics and treatment of patients with early-onset gout.

**Methods.** We retrospectively reviewed 327 adult patients with a first diagnosis of gout from 2008 to 2016 using the database of a multispecialty group practice in New England. Patients were classified into the following groups: age 30 years or younger at first diagnosis (group 1), age 31–40 years (group 2), and age over 40 years (group 3). The clinical characteristics and treatment of gout were compared among the three groups.

**Results.** We identified 87 patients in group 1 and 140 patients in group 2. Group 3 included 100 patients randomly chosen from the 7216 patients with a first diagnosis at age over 40 years. Patients within group 1 had significantly higher serum uric acid (sUA) levels at the time of diagnosis and a more prominent family history of gout. Younger patients (groups 1 and 2) had a significantly higher body mass index than patients over 40 years of age (group 3). A substantial number of younger patients also had hypertension or hyperlipidemia. The majority of younger patients met the 2012 American College of Rheumatology (ACR) guidelines for initiating urate-lowering therapy (ULT) on the basis of frequency of gout attacks, whereas the majority of patients over 40 years of age met the guidelines for ULT on the basis of chronic kidney disease. Patients over 40 years of age were more likely to achieve an sUA level less than 6.0 mg/dl.

**Conclusion.** Patients with a first diagnosis of gout at age 40 years or younger frequently had cardiovascular risk factors and were less likely to achieve an sUA level less than 6.0 mg/dl compared with patients over 40 years of age who were treated in routine clinical practice. Clinicians should be aware that patients with early-onset gout may be an undertreated population with poor adherence to ULT and increased risk of recurrent gout and cardiovascular diseases.

## INTRODUCTION

Gout is the most common inflammatory arthritis in adults, affecting primarily men over 45 years of age (1,2). The prevalence of gout among US adults more than doubled between the 1960s and the 1990s (3) and was estimated at 3.9% in a national study in 2007–2008 (4).

In recent decades, data have shown that the first attack of gout occurs at a younger age than previously found (5–7). In 2007–2008, the prevalence of gout was 0.4% among US adults aged 20–29 years and was 1.3% among those aged 30–39 years (4). Similar data for the US population within the past decade are not available. Meanwhile, the distribution of gout varies among different populations; for example, in a retrospective study in Taiwan, Yu and Luo (6) found that 25% of gout patients had their first attack before age 30.

Although, to date, there has been no consensus on the definition of early-onset gout (8–10), distinct features in the

younger patient population have been reported. A cross-sectional French national cohort study (GOSPEL) revealed that patients with gout onset before age 40 years often had polyarticular flares, a family history of gout, longer urate-lowering treatment, higher serum uric acid (sUA) levels, and the metabolic syndrome (10). Chen and Shen (11) found that gout onset before age 20 years was associated with obesity and a positive family history of gout. In a cross-sectional observational study from a Chinese gout clinic, Zhang et al (12) reported that patients with gout onset before 40 years of age had more frequent flares, more joints clinically affected, longer disease duration, and a lower proportion of cardiovascular, cerebrovascular, and renal comorbidities at presentation. However, patients with early-onset gout were at higher risk of severe gout and future cardiovascular events (12).

The clinical characteristics of gout, including comorbidities, concomitant medications, treatment adherence, and outcome,

<sup>1</sup>Yan Li, MD, Paramarajan Piranavan, MD: Saint Vincent Hospital, Worcester, Massachusetts; <sup>2</sup>Devi Sundaresan, MS: Reliant Medical Group, Worcester, Massachusetts; <sup>3</sup>Robert Yood, MD, FACP, MACR: Saint Vincent Hospital and Reliant Medical Group, Worcester, Massachusetts.

No potential conflicts of interest relevant to this article were reported.

Address correspondence to Robert Yood, MD, FACP, MACR, Reliant Medical Group, 5 Neponset Street, Worcester, MA 01606. E-mail: Robert.Yood@reliantmedicalgroup.org.

Submitted for publication March 1, 2018; accepted in revised form June 21, 2019.

have been extensively investigated, mainly in elderly patients. Limited data are available for characterizing early-onset gout (13), especially in the US population. Given the potential aggressiveness of gout progression and the clinical consequences that would warrant early recognition and intervention, we conducted this retrospective study to investigate the clinical characteristics and treatment of young patients with gout.

## PATIENTS AND METHODS

We retrospectively reviewed the medical records of 327 adult patients who received a diagnosis of gout from January 1, 2008, to December 31, 2016, using the database of a multispecialty group practice in New England. The group practice provides care in Central and MetroWest Massachusetts. All medical records are shared within this group.

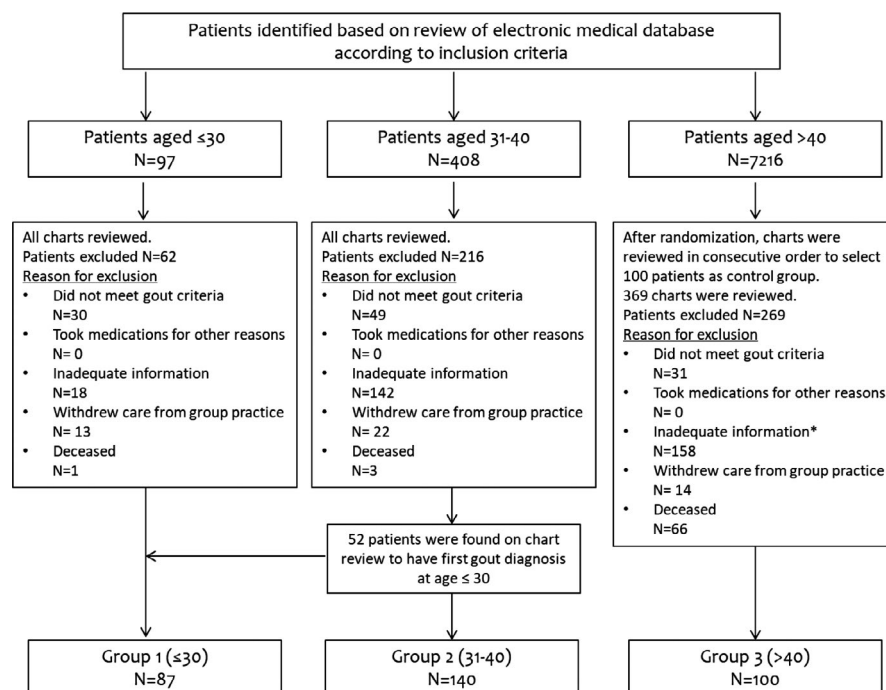
Inclusion criteria included the following: 1) age 18 years or older; 2) patient had 2 or more diagnoses of gout per *International Classification of Diseases, 10th Revision* (ICD-10) code M10.xx or *International Classification of Diseases, Ninth Revision* (ICD-9) code 274.xx recorded on 2 or more dates (office visit only), or patient had 1 diagnosis of gout (office visit only) and 1 or more pharmacy prescriptions of gout-related medication (allopurinol, febuxostat, or colchicine); and 3) patient was treated by the primary care provider or rheumatologist within

the multispecialty group practice at the time of first diagnosis of gout.

Exclusion criteria included the following: 1) patients who did not fulfill the 2015 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) gout classification criteria (14) based on a review of available medical records, 2) patients who took allopurinol, febuxostat, or colchicine for medical conditions other than gout, 3) inadequate information from available medical records to evaluate the validity of the diagnosis of gout or assess treatment, 4) patients who discontinued medical care from the multispecialty group practice prior to the chart review, and 5) patients who were deceased at the time of the chart review.

**Patient groups.** Patients were classified into the following groups: age 30 years or younger at first diagnosis of gout (group 1), age 31-40 years (group 2), and age >40 years (group 3). Age at the first diagnosis of gout was initially determined based on the onset date documented in the problem list in the electronic medical database but was adjusted if needed based on a subsequent chart review.

**Data collection.** All charts of patients age 40 years or younger by the date when gout was first diagnosed were reviewed; 100 of 7216 patients first diagnosed with gout at



**Figure 1.** Patient inclusion flowchart. According to the inclusion criteria, 97, 408, and 7216 patients were identified to have a first diagnosis of gout at age 30 years or younger, at age 31-40 years, and at over 40 years of age, respectively, during the initial review of the electronic medical database based on the age documented when gout was first listed on the problem list. After a detailed chart review and after applying the exclusion criteria, 87 and 140 patients were identified in groups 1 and 2, respectively; 100 patients were randomly selected from patients aged over 40 years and defined as group 3. \*Ten patients were found on the chart review to have a first gout diagnosis at age 40 years and younger; however, all were excluded because of inadequate information.

over 40 years of age were randomly selected and defined as group 3 (Figure 1). All data were extracted from electronic medical records: demographic features, comorbidities, gout diagnosis-related information, and laboratory and radiological findings at the time of diagnosis and follow-up. Assessment of the indication for treatment was based on 2012 ACR guidelines for the management of gout (15,16). We compared the clinical characteristics among the three groups. The study protocol was approved by the local institutional review board.

**Statistical analysis.** Continuous variables were described as the mean and SD. Categorical variables were displayed as the fraction and percentage. Comparisons between any two groups were conducted by one-way analysis of variance, followed by Tukey's honest significant difference test for continuous variables and the  $\chi^2$  tests for categorical variables.  $P < 0.05$  was considered statistically significant. All statistical analyses were performed with IBM SPSS Statistics version 22.0 software (IBM Corporation).

## RESULTS

We identified 87 patients with a first diagnosis of gout at age 30 years or younger (group 1) and 140 patients with a first diagnosis of gout at age 31-40 years (group 2) in addition to the randomly selected 100 patients diagnosed with gout after age 40 years (group 3), as shown in Figure 1.

**Demographic features.** The demographic features of the three groups of patients are summarized in Table 1. The majority of patients were white. The male/female ratio and body mass index (BMI) at the time of diagnosis were similar between groups 1 and 2; the male/female ratio and BMI in both groups were significantly higher than those in group 3. The percentage of patients

with obesity was higher in group 1, although this did not show statistical difference among the three groups. A positive family history of gout was more frequently identified in group 1. More than half of the patients were managed by primary care providers, and about 40% were seen at least once by a rheumatologist within the group practice (Table 1).

In groups 1, 2, and 3, respectively, 16, 17, and 20 patients underwent arthrocentesis; 13, 14, and 7 patients in groups 1, 2, and 3, respectively, were reported to be positive for monosodium urate crystals. One patient in group 1 had concomitant calcium pyrophosphate dehydrate reported. The synovial-fluid white blood cell (WBC) count was not available in all patients given a clinical decision to treat empirically or an inadequate amount of synovial fluid sometimes obtained during arthrocentesis. Twenty-four patients had an available synovial-fluid WBC count ranging from few to 67 020 cells per ml.

**Features of first gout attack.** Patients within group 1 had significantly higher sUA levels at the time of diagnosis ( $9.2 \pm 1.5$  mg/dl) compared with those in Group 2 ( $8.4 \pm 1.3$  mg/dl,  $p=0.001$ ) and Group 3 ( $8.4 \pm 1.6$  mg/dl,  $p=0.002$ ) (Table 2). The most common sites of the first gout attack in all age groups were the first metatarsophalangeal joint, foot, and ankle. X-ray reports at the time of gout diagnosis documented degenerative changes in 31%, 23%, and 47% of patients in groups 1, 2, and 3, respectively; erosive changes consistent with gout were found in only a few patients.

**Medical comorbidities.** The concurrence of coronary artery disease and other cardiovascular risk factors, namely hypertension, hyperlipidemia, and diabetes, were significantly higher in patients over age 40 years (group 3), as shown in Figure 2. It is noteworthy that a substantial number of younger patients (both groups 1 and 2) also had hypertension (41% in both groups) or

**Table 1.** Demographic features of patients in different age groups

	Group 1 (n = 87)	Group 2 (n = 140)	Group 3 (n = 100)	$P_1$ (Group 1 vs 2) <sup>a</sup>	$P_2$ (Group 1 vs 3) <sup>b</sup>	$P_3$ (Group 2 vs 3) <sup>c</sup>
Male, n (%)	86 (99)	136 (97)	71 (71)	0.652	<0.001	<0.001
Race, n (%)				0.911	0.117	0.046
White	69 (79)	107 (76)	89 (89)	...	...	...
Asian	6 (7)	11 (8)	2 (2)	...	...	...
African American	3 (3)	3 (2)	1 (1)	...	...	...
Hispanic	0 (0)	1 (1)	2 (2)	...	...	...
Unknown	9 (10)	180 (13)	6 (6)	...	...	...
Rheumatology consultation, n (%)	34 (39)	44 (31)	49 (49)	0.253	0.187	0.007
BMI, $\bar{x} \pm SD$ <sup>d</sup>	$34.6 \pm 7.2$	$33.6 \pm 7.5$	$31.5 \pm 6.1$	0.530	0.007	0.058
With obesity, n (%)	59 (68)	88 (63)	55 (55)	0.478	0.098	0.233
Alcohol use, n (%)	44 (51)	68 (49)	48 (48)	0.786	0.770	1.000
Family history of gout, n (%)	26 (30)	20 (14)	11 (11)	0.006	0.002	0.559

Abbreviation: BMI, body mass index.

<sup>a</sup> $P_1$  results are from comparisons between group 1 and group 2.

<sup>b</sup> $P_2$  results are from comparisons between group 1 and group 3.

<sup>c</sup> $P_3$  results are from comparisons between group 2 and group 3.

<sup>d</sup>One-way analysis of variance  $P = 0.007$ .

**Table 2.** Clinical characteristics of first gout attack in different age groups

	Group 1 (n = 87)	Group 2 (n = 140)	Group 3 (n = 100)	$P_1$ (Group 1 vs 2) <sup>a</sup>	$P_2$ (Group 1 vs 3) <sup>b</sup>	$P_3$ (Group 2 vs 3) <sup>c</sup>
Age at gout diagnosis, $\bar{x} \pm SD^e$	26 $\pm$ 3	35 $\pm$ 3	61 $\pm$ 12	<0.001	<0.001	<0.001
sUA at gout diagnosis, $\bar{x} \pm SD^e$	9.2 $\pm$ 1.5	8.4 $\pm$ 1.3	8.4 $\pm$ 1.6	0.001	0.002	0.999
sUA >8.0 mg/dl at gout diagnosis, n (%)	75/87 (86)	100/136 (74)	73/99 (74)	0.030	0.045	1.000
Arthrocentesis available, n (%)	16 (18)	17 (12)	20 (20)	0.245	0.853	0.106
Crystal-proven gout, n (%)	13 (15)	14 (10)	7 (7)	1.000	0.008	0.007
Site of first gout attack, n (%)				0.732	0.026	0.207
First MTP joint	49/84 (58) <sup>d</sup>	85/138 (62) <sup>d</sup>	64/100 (64)	...	...	...
Foot and ankle	29/84 (35)	41/138 (30)	20/100 (20)	...	...	...
Knee	5/84 (6)	6/138 (4)	5/100 (5)	...	...	...
Hand	0/84 (0)	2/138 (1)	4/100 (4)	...	...	...
Multiple sites	1/84 (1)	4/138 (3)	7/100 (7)	...	...	...

Abbreviation: MTP, metatarsophalangeal; sUA, serum uric acid.

<sup>a</sup> $P_1$  results are from comparisons between group 1 and group 2.

<sup>b</sup> $P_2$  results are from comparisons between group 1 and group 3.

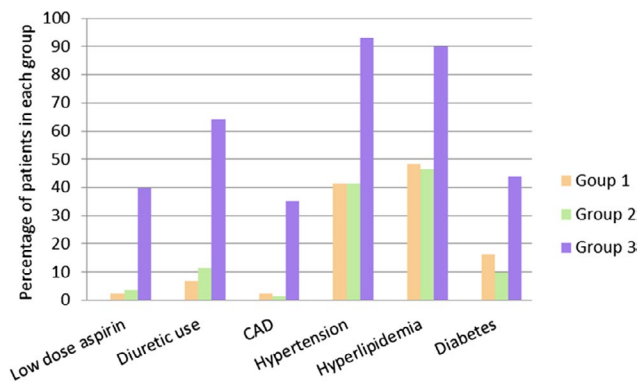
<sup>c</sup> $P_3$  results are from comparisons between group 2 and group 3.

<sup>d</sup>Three and two patients in groups 1 and 2, respectively, did not have detailed information of involved joints during the first gout attack.

<sup>e</sup>One-way analysis of variance  $P < 0.001$ .

hyperlipidemia (48% and 46% in groups 1 and 2, respectively). Two known risk factors for gout, namely low-dose aspirin (81 mg daily) and diuretic use, were more prevalent among patients in group 3.

**Treatment.** In groups 1 and 3, respectively, 74% and 78% of patients met the 2012 ACR guidelines for urate-lowering therapy (ULT); only 48% of patients in group 2 warranted ULT. The majority of patients in groups 1 and 2 met the guidelines for ULT on the basis of frequency of gout attacks, as shown in Table 3. The majority of patients in group 3 met the guidelines for ULT on the basis of chronic kidney disease; one-third of patients had more than one indication for ULT.



**Figure 2.** Medical comorbidities, aspirin, and diuretic use in each group. The y-axis represents the percentage of patients within each age group having each condition.

A higher percentage of patients in group 1 initially received recommended ULT, whereas only 68% of patients in group 3 who met guidelines for ULT initiated treatment. Among patients who started ULT, more than half received prophylaxis in all three groups. Although not consistently tested, the last available sUA during the study time frame (January 1, 2008, to December 31, 2016) was used to assess the achievement of an sUA level less than 6.0 mg/dl. Compared with younger patients (groups 1 and 2), patients in group 3 were more likely to achieve an sUA level less than 6.0 mg/dl.

## DISCUSSION

Our study demonstrated that patients with gout onset at age 30 years or younger had significantly higher sUA levels at the time of diagnosis and a more prominent family history of gout compared with patients with gout onset after age 30 years (groups 2 and 3). Patients in group 2 had similar clinical features to those in group 1, including a significantly higher BMI than that of patients in group 3. The prevalence of cardiovascular risk factors (hypertension and hyperlipidemia) was unexpectedly high among younger patients (both groups 1 and 2; Figure 2).

Although it did not reach statistical significance, we found that the prevalence of obesity was higher in patients with early-onset gout. Obesity has previously been found to be associated with earlier gout onset. In a community-based cohort study, DeMarco et al (17) found that the overall mean age at gout onset was 59.3 years. The onset of gout was 3.1 years earlier in those with obesity

**Table 3.** Indications and performance of ULT in different age groups

	Group 1 (n = 87)	Group 2 (n = 140)	Group 3 (n = 100)	$P_1$ (Group 1 vs 2) <sup>a</sup>	$P_2$ (Group 1 vs 3) <sup>b</sup>	$P_3$ (Group 2 vs 3) <sup>c</sup>
ULT indicated by 2012 ACR guidelines, n (%)	64 (74)	67 (48)	78 (78)	<0.001	0.479	<0.001
Flare: >2 per year	60 (94)	61 (91)	42 (54)	0.745	<0.001	<0.001
Tophi	9 (14)	4 (6)	9 (12)	0.150	0.801	0.383
CKD (≥stage 2 CKD)	4 (6)	7 (10)	58 (74)	0.532	<0.001	<0.001
Nephrolithiasis	2 (3)	8 (12)	8 (10)	0.275	0.185	1.000
Patients who had ≥1 indication for ULT, n (%)	10 (11)	9 (6)	31 (31)	0.220	0.001	<0.001
ULT initiated/ULT indicated, (%)	59/64 (92)	55/67 (82)	53/78 (68)	0.086	<0.001	0.051
Prophylaxis initiated/ULT initiated, (%)	36/59 (61)	33/55 (60)	27/53 (51)	1.000	0.341	0.439
sUA <6.0mg/dl achieved/ULT initiated, (%)	19/59 (32) <sup>d</sup>	21/54 (39) <sup>d</sup>	24/45 (53) <sup>d</sup>	0.555	0.044	0.163

Abbreviation: CKD, chronic kidney disease; sUA, serum uric acid; ULT, urate-lowering therapy.

<sup>a</sup> $P_1$  results are from comparisons between group 1 and group 2.

<sup>b</sup> $P_2$  results are from comparisons between group 1 and group 3.

<sup>c</sup> $P_3$  results are from comparisons between group 2 and group 3.

<sup>d</sup>Zero, one, and eight patients in groups 1, 2, and 3, respectively, did not have follow-up sUA tests.

at baseline and was 11.0 years earlier in participants with obesity at age 21 compared with participants without obesity.

Although the prevalence of cardiovascular risk factors was understandably higher in patients over age 40 years, it was surprising that nearly half of patients under age 30 years had been diagnosed with hypertension or hyperlipidemia and that 30% of patients had both. Similar findings were also seen in patients with gout onset age 31-40 years. The prevalence of cardiovascular risk factors among younger patients with gout is substantially higher than the risk in the general population. Based on Centers for Disease Control and Prevention data from 2015-2016, the prevalence of hypertension in the US general population was 7.5% in those age 18-39 years and 33.2% in those age 40-59 years (18). Sullivan et al (19) reported that the prevalence of hypertension in the general population was 0.4%, 2.2%, and 6.5% in age groups 18-19, 20-29, and 30-39 years, respectively, and the prevalence of hyperlipidemia was 0.1%, 0.4%, and 2.3% in age groups 18-19, 20-29, and 30-39 years, respectively. Along with obesity and hyperuricemia, lifestyle changes in recent decades (20), including sedentary habits, a diet rich in red meat and fructose, and increased alcohol consumption, could play a role in the shift toward a younger population with gout and warrant early intervention.

Gout is an independent risk factor for all-cause and cardiovascular mortality (21). A higher sUA level has been confirmed to pose an increased risk of incident and recurrent gout (22). Hyperuricemia has also been suggested as an integral part of metabolic syndrome and an independent risk factor for both cardiovascular disease and renal disease (23,24). The potential mutual benefit of ULT on gout and cardiovascular disease has been proposed; however, previous studies have not shown consistent results (25-28). Additional studies are warranted to determine whether treatment of

gout or hyperuricemia in patients younger than age 40 decreases the risk of cardiovascular disease.

More than 90% of patients in group 1 met criteria for ULT initiated treatment, but only 32% achieved a target sUA level less than 6.0 mg/dl. By comparison, 68% of patients in group 3 met criteria for ULT initiated treatment, of whom 53% achieved the target sUA level (Table 3). Group 2 had an intermediate percentage of patients who achieved the target sUA level. Previous studies have shown that adherence to ULT is poor; among the treatment of seven common chronic diseases, including hypertension and diabetes, adherence to gout therapy was the lowest (29,30). A lack of education on lifestyle changes and gout-related medications, particularly the risks of gout flares with initiation of ULT (31), likely contributes to poor adherence. Patients with early-onset gout appear to be a particularly high-risk group for poor adherence.

Our study has several limitations. The retrospective chart review was subject to incomplete data and clinical documentation. For example, we could not quantify alcohol consumption, provide details of any family history of gout, and specify reasons ULT or prophylaxis was or was not prescribed or taken. The achievement of an sUA level less than 6.0 mg/dl was based on the last available sUA, which was not consistently tested.

Patients with a first diagnosis of gout at age 40 years or younger frequently had cardiovascular risk factors and were less likely to achieve an sUA level less than 6.0 mg/dl compared with patients over age 40 who were treated in routine clinical practice. Clinicians should be aware that patients with early-onset gout may be an undertreated population with poor adherence to ULT and increased risk for recurrent gout and cardiovascular diseases.

## ACKNOWLEDGMENTS

The authors give special thanks to Joel Popkin, MD, for critical review and interpretation of the study results.

## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Li, Piranavan, Yood.

**Acquisition of data.** Sundaresan.

**Analysis and interpretation of data.** Li, Piranavan, Yood.

## REFERENCES

- Dirken-Heukensfeldt KJ, Teunissen TA, van de Lisdonk H, Lagro-Janssen AL. "Clinical features of women with gout arthritis." A systematic review. *Clin Rheumatol* 2010;29:575–82.
- Singh JA. Research priorities in gout: the patient perspective. *J Rheumatol* 2014;41:615–6.
- Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. *Arthritis Rheum* 2008;58:26–35.
- 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;63:3136–41.
- Lu CC, Wu SK, Chen HY, Chung WS, Lee MC, Yeh CJ. Clinical characteristics of and relationship between metabolic components and renal function among patients with early-onset juvenile tophaceous gout. *J Rheumatol* 2014;41:1878–83.
- Yu KH, Luo SF. Younger age of onset of gout in Taiwan. *Rheumatology (Oxford)* 2003;42:166–70.
- Chen SY, Chen CL, Shen ML, Kamatani N. Trends in the manifestations of gout in Taiwan. *Rheumatology (Oxford)* 2003;42:1529–33.
- Matsuo H, Ichida K, Takada T, Nakayama A, Nakashima H, Nakamura T, et al. Common dysfunctional variants in ABCG2 are a major cause of early-onset gout. *Sci Rep* 2013;3:2014.
- Li QH, Liang JJ, Chen LX, Mo YQ, Wei XN, Zheng DH, et al. Clinical characteristics and renal uric acid excretion in early-onset gout patients. *Zhonghua Nei Ke Za Zhi* 2018;57:185–90. In Chinese.
- Pascart T, Norberciak L, Ea HK, Guggenbuhl P, Liote F. Patients with early-onset gout and development of earlier severe joint involvement and metabolic comorbid conditions: results from a cross-sectional epidemiologic survey. *Arthritis Care Res (Hoboken)* 2019;71:986–92.
- Chen SY, Shen ML. Juvenile gout in Taiwan associated with family history and overweight. *J Rheumatol* 2007;34:2308–11.
- Zhang B, Fang W, Zeng X, Zhang Y, Ma Y, Sheng F, et al. Clinical characteristics of early- and late-onset gout: a cross-sectional observational study from a Chinese gout clinic. *Medicine (Baltimore)* 2016;95:e5425.
- Yamanaka H. Gout and hyperuricemia in young people. *Curr Opin Rheumatol* 2011;23:156–60.
- Neogi T, Jansen TL, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative [published erratum appears in *Arthritis Rheumatol* 2016;68:515]. *Arthritis Rheumatol* 2015;67:2557–68.
- Khanna D, Fitzgerald JD, Khanna PP, Bae S, Singh MK, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1. Systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res (Hoboken)* 2012;64:1431–46.
- Khanna D, Khanna PP, Fitzgerald JD, Singh MK, Bae S, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2. Therapy and antiinflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res (Hoboken)* 2012;64:1447–61.
- DeMarco MA, Maynard JW, Huizinga MM, Baer AN, Kottgen A, Geller AC, et al. Obesity and younger age at gout onset in a community-based cohort. *Arthritis Care Res (Hoboken)* 2011;63:1108–14.
- Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D. Hypertension prevalence and control among adults: United States, 2015–2016. *NCHS Data Brief* 2017;1–8.
- Sullivan PW, Ghushchyan VH, Ben-Joseph R. The impact of obesity on diabetes, hyperlipidemia and hypertension in the United States. *Qual Life Res* 2008;17:1063–71.
- Doherty M. New insights into the epidemiology of gout. *Rheumatology (Oxford)* 2009;48 Suppl 2:ii2–8.
- Kuo CF, See LC, Luo SF, Ko YS, Lin YS, Hwang JS, et al. Gout: an independent risk factor for all-cause and cardiovascular mortality. *Rheumatology (Oxford)* 2010;49:141–6.
- Shiozawa A, Szabo SM, Bolzani A, Cheung A, Choi HK. Serum uric acid and the risk of incident and recurrent gout: a systematic review. *J Rheumatol* 2017;44:388–96.
- Wei CY, Sun CC, Wei JC, Tai HC, Sun CA, Chung CF, et al. Association between hyperuricemia and metabolic syndrome: an epidemiological study of a labor force population in Taiwan. *Biomed Res Int* 2015;2015:369179.
- Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk [published erratum appears. *N Engl J Med* 2010;362:2235]. *N Engl J Med* 2008;359:1811–21.
- Givertz MM, Anstrom KJ, Redfield MM, Deswal A, Haddad H, Butler J, et al. Effects of xanthine oxidase inhibition in hyperuricemic heart failure patients: the Xanthine Oxidase Inhibition for Hyperuricemic Heart Failure Patients (EXACT-HF) Study. *Circulation* 2015;131:1763–71.
- Kim SC, Schneeweiss S, Choudhry N, Liu J, Glynn RJ, Solomon DH. Effects of xanthine oxidase inhibitors on cardiovascular disease in patients with gout: a cohort study. *Am J Med* 2015;128:653.e716.
- Solomon DH, Liu CC, Kuo IH, Zak A, Kim SC. Effects of colchicine on risk of cardiovascular events and mortality among patients with gout: a cohort study using electronic medical records linked with Medicare claims. *Ann Rheum Dis* 2016;75:1674–9.
- Givertz MM. Treating gout in patients with cardiovascular disease: mutual benefit or unintended consequences? [editorial]. *J Am Coll Cardiol* 2018;71:1005–8.
- Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy* 2008;28:437–43.
- Scheepers LE, van Onna M, Stehouwer CD, Singh JA, Arts IC, Boonen A. Medication adherence among patients with gout: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2018;47:689–702.
- Harrold LR, Mazor KM, Peterson D, Naz N, Firreno C, Yood RA. Patients' knowledge and beliefs concerning gout and its treatment: a population based study. *BMC Musculoskelet Disord* 2012;13:180.