Serum Uric Acid Testing Practices Over 5 Years Among Incident Gout Cases

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Introduction

- Gout is a chronic inflammatory disorder associated with elevated levels of serum uric acid (sUA), resulting in urate crystal deposits in soft tissues
- Gout is prevalent in 1%–4% of the adult population in the US and Israel[1,2] with increasing rates over time[3]
- Uncontrolled gout, which is indicated by high uric acid levels (>6 mg/dL), can result in bone erosion, joint destruction, kidney stones, uric acid nephropathy, and other organ damage
- Gout is treatable with medication therapy and lifestyle changes, individualized care and continual monitoring is recommended[4]
  - Long-term sUA monitoring, to confirm that patients are achieving target levels (≤6 mg/dL, or <5 mg/dL in more severe cases), may help to more precisely characterize the patient with gout and control the disease

Objective

- To describe incident cases of gout and characterize these patients by sUA testing during the subsequent 5 consecutive years

Methods

Data Source

- A historical prospective cohort study was conducted using the Clalit Health Services (CHS) database
- CHS is the largest health care maintenance organization (HMO) in Israel, with over 4.2 million insured residents, providing care to >50% of the Israeli population. Annual turnover is <1%
- Since 1998, with increasing comprehensiveness, CHS's electronic medical records have been stored in a centralized data warehouse and include demographic data, clinical diagnoses, laboratory data results, medical treatment, and medications

Study Population

- A total of 15,598 incident cases of gout were identified between 1/1/2003–31/12/2009 among members aged ≥25 years with continuous enrollment in CHS for 1 year prior to and 5 years subsequent to diagnosis (index date)
- Included were patients with ≥1 of the following criteria
  - 1 diagnosis of gout from a hospital or specialist visit
  - ≥2 diagnoses of gout from a general practitioner visit combined with ≥2 elevated sUA test results (>6 mg/dL) or ≥2 purchases of a gout-related prescription medication, such as colchicine or allopurinol, with the first purchase or results within 6 months of the first diagnosis
- Excluded were patients with a concurrent diagnosis of a disease known to affect sUA (eg, renal insufficiency, dialysis, kidney transplantation, cancer, Familial Mediterranean Fever)

Measures

- Grouping variable:
  - Overall sUA testing during the 5-year follow-up period
    - Full (≥1 test per year for all 5 years)
    - Moderate (≥1 test per year for 3 or 4 years)
    - Low (≥1 test per year for 1 or 2 years)
    - No testing (no tests performed)
  - Annual sUA testing during each year of follow up

- Predictor variables:
  - Demographics (baseline): age, sex, and socio-economic status (SES)
  - Clinical characteristics (last recorded prior to baseline): smoking status, body mass index (BMI), systolic and diastolic blood pressure (BP) levels, cholesterol, glucose, creatinine, and the estimated glomerular filtration rate (eGFR)
  - Comorbidities (baseline): cardiovascular disease, diabetes, and hypertension (identified using ICD-9 codes); diuretic use (ATC C03) (as an indicator of comorbidities such as arthritis and hypertension); and Charlson Comorbidity Index (CCI) (to represent multiple comorbid conditions at baseline or when unavailable, for the first year of follow up)
- Outcome variables:
  - Health care utilization frequency: general practitioner visits, specialist visits, hospital admissions, and use of imaging services (x-ray, MRI, ultrasound, CT)
  - Gout control
    - Adequately controlled (sUA ≤6 mg/dL)
    - Inadequately controlled (sUA 6–10 mg/dL)
    - Uncontrolled (sUA ≥10 mg/dL)
- Analysis: Descriptive analyses were performed to characterize the patient population's baseline demographics, medical history, and clinical characteristics of patients. Health care utilization and sUA control were examined according to sUA testing during the 5-year follow-up period. Chi-square testing was used to assess distributional differences between groups

Results

- Baseline sample characteristics
  - A total of 15,598 incident gout cases met the inclusion criteria. Newly diagnosed gout cases were adults aged 45–74 years, men, and of higher SES (~20% of the CHS adult population is of higher SES) (**Table 1**)
  - Clinical indicators showed that 15.2% were current smokers (lower than the national average of 21.6%) and over two-thirds were overweight or obese (**Table 1**)
  - Rates of comorbid conditions at baseline were somewhat higher than expected values, eg, diabetes in the CHS general adult population, 14.4%[5] vs gout, 20.8%) (**Figure 1**). The mean CCI for this cohort was 0.9±1.3. Baseline biochemistry values were available for 77%–95% of the gout cohort (**Table 2**)
- Follow-up sUA testing practice
  - Performance of annual testing practice over the 5-year follow up from initial diagnosis (**Figure 2**):
    - Over the 5 years from diagnosis, the highest annual sUA testing rates occurred during the first year from diagnosis
    - Years 2–5 from diagnosis had similar annual testing rates of approximately 70%
  - Overall 5-year sUA testing practice from initial diagnosis (**Figure 3**):
    - One-third of newly diagnosed patients with gout performed annual sUA testing for all 5 years from diagnosis
    - Less than 2% of newly diagnosed patients with gout were not tested for sUA in the 5 years following diagnosis
- Follow-up health care utilization
  - Patients who visited the general practitioner, rheumatologist, or had a hospital admission in their fifth year of follow up were more likely to have had their sUA tested annually for the 5 years from their gout diagnosis (**Table 3**)

Table 1: Baseline demographic and clinical characteristics of patients with newly diagnosed gout between 2003 and 2009 with 5 years of follow up (N=15,598)

Characteristic	N=15,598
Age (years)	
Mean ± SD	59.3±14.5
Median (IQR25–75)	59.0 (49–71)
Age (categories), n (%)	
25–34 years	909 (5.8)
35–44 years	1631 (10.5)
45–54 years	3236 (20.7)
55–64 years	3744 (24.0)
65–74 years	3489 (22.4)
75–84 years	2211 (14.2)
85+ years	378 (2.4)
Sex, n (%)	
Male	12,435 (79.7)
Female	3163 (20.3)
SES, n (%)	
Low	3058 (19.6)
Medium	6918 (44.4)
High	5573 (35.7)
Missing	49 (0.3)
Smoking habits (adults)[a], n (%)	
Never smoked	9376 (60.1)
Former smoker	3432 (22.0)
Current	2365 (15.2)
Missing	425 (2.7)
BMI (categories) (kg/m²)[a], n (%)	
Underweight	30 (0.2)
Normal	1582 (10.1)
Overweight	5053 (32.4)
Obese	6217 (39.9)
Missing	2716 (17.4)

IQR, interquartile range; SD, standard deviation.
[a]Value for smoking was the closest record to index date through follow up and for BMI was the closest record to index date for up to 3 years follow up.

Figure 1: Baseline comorbidities or medication use of patients with newly diagnosed gout between 2003 and 2009 with 5 years of follow up (N=15,598)
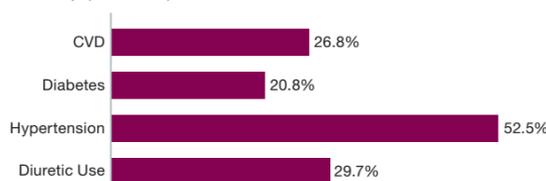
CVD, cardiovascular disease.
Patients were considered positive for CVD, diabetes, or hypertension if they ever received a diagnosis prior to index date and positive for diuretic use if they purchased a diuretic in the year prior to index date.

Table 2: Baseline biochemistry of patients with newly diagnosed gout between 2003 and 2009 with 5 years of follow up (N=15,598)[a]

	N=15,598
Systolic BP (mm Hg) (n)	12,040
Mean ± SD	135.3±16.4
Median (IQR25–75)	133 (124–145)
Diastolic BP (mm Hg) (n)	12,040
Mean ± SD	79.8±9.1
Median (IQR25–75)	80 (74–85)
LDL cholesterol (mg/dL) (n)	13,918
Mean ± SD	115.3±38.2
Median (IQR25–75)	112 (91–136)
Glucose (mg/dL) (n)	14,615
Mean ± SD	107.4±33.1
Median (IQR25–75)	99 (89–115)
Creatinine (mg/dL) (n)	14,777
Mean ± SD	1.05±0.31
Median (IQR25–75)	1.01 (0.9–1.2)
eGFR (mL/min/m²) (n)	14,777
Mean ± SD	78.5±22.6
Median (IQR25–75)	77 (64–92)

LDL, low-density lipoproteins.
[a]Values for systolic and diastolic BP, glucose, creatinine, and eGFR were the closest record to index date for up to 1 year follow up.

Figure 2: Performance of annual sUA testing according to year from diagnosis among newly diagnosed gout between 2003 and 2009 with 5 years of follow up (N=15,598)
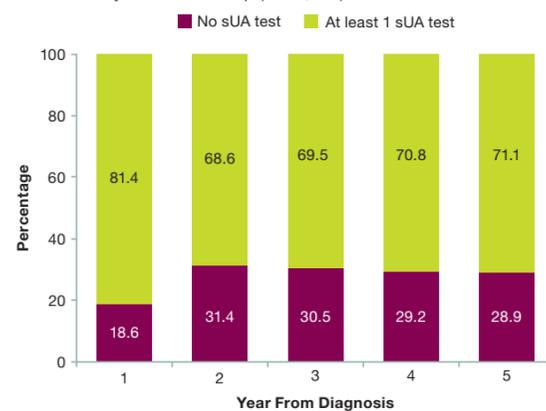
- Follow-up sUA control:
  - Adequate gout control is defined as those patients with sUA levels ≤6.0 mg/dL. At the end of follow up, 25.6% of patients' last documented sUA levels were controlled (≤6 mg/dL) and 4.8% were uncontrolled (≥10 mg/dL)
  - At 5 years of follow up from gout diagnosis, patients who had adequately controlled gout (sUA≤6.0 mg/dL) or uncontrolled gout (sUA≥10 mg/dL) were more likely to have performed sUA testing annually since diagnosis compared to those with inadequate control (sUA levels between 6–10 mg/dL) (**Figure 4**)

Table 3: 5-year annual sUA testing practice for patients with newly diagnosed gout between 2003 and 2009 (n=15,598) by health care visits or admissions in the fifth year of follow up (N=15,598)[a]

| sUA Testing	General practitioner visit in year 5		Rheumatologist visit in year 5		Hospital admission in year 5	
	Yes	No	Yes	No	Yes	No
Full	35.2%	28.4%	44.1%	34.7%	46.0%	31.8%
Moderate	43.4%	31.5%	41.2%	42.9%	40.6%	43.4%
Low	19.8%	34.3%	14.4%	20.6%	12.5%	22.7%
None	1.6%	5.8%	0.3%	1.8%	0.8%	2.1%
Chi-square, P-value	<0.001		<0.001		<0.001	

[a]Utilization is defined as at least 1 visit or admission.

Table 4: 5-year annual sUA testing practice for patients with newly diagnosed gout between 2003 and 2009 by imaging utilization in the fifth year of follow up (N=15,598)[a]

| sUA Testing	X-ray		Ultrasound		MRI		CT	
	Yes	No	Yes	No	Yes	No	Yes	No
Full	41.7%	29.6%	45.6%	28.3%	44.5%	34.7%	46.9%	32.4%
Moderate	41.8%	43.6%	40.6%	44.2%	41.5%	42.8%	40.3%	43.3%
Low	15.6%	24.3%	13.0%	25.1%	13.0%	20.7%	12.3%	22.2%
None	0.9%	2.5%	0.8%	2.4%	1.0%	1.8%	0.6%	2.0%
Chi-square, P-value	<0.001		<0.001		<0.001		<0.001	

[a]Utilization is defined as at least 1 imaging test performed.

Figure 3: Overall 5-year annual sUA testing practice for patients with newly diagnosed gout between 2003 and 2009 (N=15,598)[a]
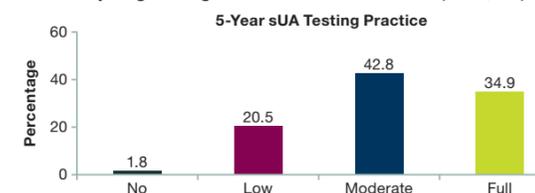
[a]Test practice was determined according to the 5-year follow-up period: full = performed sUA testing during all 5 years of follow up; moderate = performed sUA testing in 3 or 4 of the 5 years of follow up; low = performed sUA testing in 1 or 2 of the 5 years of follow up; and none = no sUA testing was performed during the follow-up period.

Figure 4: 5-year annual sUA testing for patients with newly diagnosed gout between 2003 and 2009 by last sUA level in the last year of follow up (N=15,598)[a]
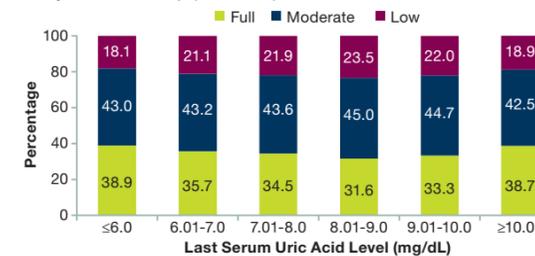
[a]Test practice was determined according to the 5-year follow-up period: full = performed sUA testing during all 5 years of follow up; moderate = performed sUA testing in 3 or 4 of the 5 years of follow up; low = performed sUA testing in 1 or 2 of the 5 years of follow up; and none = no sUA testing was performed during the follow-up period.

Conclusions

- 25.6% of patients' last documented sUA was controlled (≤6 mg/dL)
- 34.9% of patients performed annual sUA testing during the 5 years following diagnosis
- This cohort represents a relatively healthy gout population, for whom gout can be managed and controlled
- Consistent with previous findings, gout patients included in the CHS database were on average, older adults, predominately men, and with concurrent comorbidities
- Gout patients who access the health care system are more likely to perform sUA testing than those with no health care utilization (visits or imaging)
- Further study is required to assess the association between regular testing and health outcomes

References

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