

# The Validity of Gout Diagnosis in Primary Care: Results from a Patient Survey

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**ABSTRACT. Objective.** Validate primary care diagnosis of gout by the Mexico and the Netherlands classification criteria.

**Methods.** Questionnaires on gout characteristics were sent to all individuals aged  $\geq 18$  with  $\geq 1$  International Classification of Diseases, 10th ed. diagnosis of gout at 12 primary care centers.

**Results.** Positive predictive values for gout diagnosis ranged from 71% for the Netherlands criteria to 80% for the Mexico criteria. Maximum inflammation within 24 h was the most common reported symptom (86%).

**Conclusion.** The vast majority of gout cases in primary care fulfill classification criteria and are valid for research purposes. (First Release August 1 2019; J Rheumatol 2019;46:1531–4; doi:10.3899/jrheum.180989)

*Key Indexing Terms:*

GOUT

DIAGNOSTIC CRITERIA

Gout is mainly diagnosed and managed in primary care (PC). The diagnostic gold standard for gout is detection of monosodium urate (MSU) crystals in synovial fluid, a procedure rarely performed in PC<sup>1</sup>. To enable uniform definition of diseases, especially in research, classification criteria have been developed. The first gout classification criteria, Rome 1963<sup>2</sup> and New York 1966<sup>3</sup>, were developed using expert opinion and relied largely on the presence of tophi and MSU crystals. The 1977 American Rheumatism Association (ARA) criteria<sup>4</sup>, the 2010 Mexico criteria<sup>5</sup>, and the 2010 Netherlands criteria<sup>6</sup> incorporated several clinical characteristics of gout and are not primarily based on synovial fluid analysis. Although widely used historically, the ARA criteria are still only preliminary criteria because they have not been extensively validated. It should also be noted that they were developed for acute arthritis of gout. The American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria<sup>7</sup> from 2015 also includes imaging modalities. Of the currently available criteria, only the Rome, New York, and ARA criteria have been validated in PC populations<sup>8,9</sup>. It is of great importance to know how valid a clinical diagnosis of gout in PC is,

especially to facilitate subject recruitment for PC gout researchers. In our study we aimed to validate the PC diagnosis of gout against published classification criteria using self-reported data from patients overall and by sex.

## MATERIALS AND METHODS

All individuals aged  $\geq 18$  years with  $\geq 1$  International Classification of Diseases, 10th ed. (ICD-10) diagnosis of gout (M10) recorded by a physician during a 2-year period (2015–2017) were identified at 12 PC centers in the Western Sweden Health Care Region. Patients were sent a questionnaire with questions on demographics, comorbidities, and gout characteristics. All participants were informed in writing that the reported data would be published, and returning the questionnaire was considered informed consent.

Specifically related to gout, patients were asked about items included in the Mexico<sup>5</sup> and the Netherlands<sup>6</sup> gout classification criteria: knowledge of elevated serum urate, presence of tophi (with illustration), podagra/metatarsophalangeal (MTP)-1 involvement,  $> 1$  attack of acute arthritis, maximum inflammation within 24 h, redness over the joints, unilateral tarsal joint attack, mono- or oligoarticular attacks, male sex, hypertension and/or cardiovascular disease (CVD) defined as previous myocardial infarction, or stroke.

These 2 sets of classification criteria stem from an experienced need for classification and diagnostic tools in a setting where joint fluid is not easily obtained, as in PC. The Mexico criteria are based on items from the ACR<sup>4</sup> and EULAR<sup>10</sup> criteria and were developed in patients seen at rheumatology units. In the Netherlands criteria, a broader array of clinical and laboratory variables were tested for their ability to diagnose MSU crystal-positive versus -negative PC patients with acute monoarthritis, groups that entailed men in 96% and 90%, respectively.

The Netherlands criteria require  $\geq 8$  points for classifying patients as highly likely to have gout. A score of 4–8 calls for further investigation (e.g., joint fluid analysis). Male sex is rewarded with 2 points, demonstrating its importance. In the current setting with 20% postmenopausal women, average age 76 years, we also applied the Netherlands criteria, disregarding sex as an item and requiring only 6 points ( $8 - 2 = 6$ ) for high likelihood of gout diagnosis. The Mexico criteria consists of 8 items and  $\geq 4$  is required for classification as gout.

The ARA<sup>4</sup> and the ACR/EULAR<sup>7</sup> criteria were not used because they are dependent upon imaging and joint fluid analysis. Thus, the ICD-10 gout diagnosis was used as an index test and the Mexico and the Netherlands criteria as reference tests.

Primary nonresponders received a second mailing of the questionnaire.

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Ten percent randomly selected among those still not responding were interviewed by telephone to characterize the group of nonresponders.

Ethical approval was granted from the Ethical Review Board of Gothenburg, Sweden (519-16).

Positive predictive values (PPV) were calculated by dividing the number of patients who met the Mexico/Netherlands classification criteria by the total number of patients who were diagnosed with gout in the medical record. Sex differences regarding fulfillment of classification criteria and frequency of reported gout characteristics were calculated using the chi-square test.

## RESULTS

A total of 1444 individuals with a gout diagnosis were identified and sent the questionnaire. After 1 reminder questionnaire, 784 (54.3%) individuals responded. Nonresponders were overrepresented in young men. Among responders, mean age was 72 years and 80% were men. Ever smoking and history of kidney stone were significantly more common in men ( $p = 0.0003$  and  $p = 0.0007$ , respectively). Women were significantly older ( $p = 0.0001$ ; Table 1). Women reported an insignificantly higher frequency of tophi and lower prescription of urate-lowering therapy (Table 1). A high percentage of respondents (738; 94%) gave valid answers to all classification criteria items. The PPV in the total cohort ranged from 71 to 80% for the different criteria used (Table 2). Applying the criteria sets on men and women separately rendered no difference for the Mexico criteria while for the Netherlands criteria, women had a PPV of only 46% compared to 77% for men (Table 2). When disregarding sex as an item in the Netherlands criteria, the PPV increased to 76% in women (Table 2). Including only subjects who reported knowledge of increased serum urate rendered PPV of 94% and 93% for the Mexico and the Netherlands criteria, respectively. Similar results were found among those interviewed only by telephone (not shown). The 5 most common classification criteria items reported were experienced by the vast majority of respondents. Podagra/MTP-1 involvement was significantly more common in men ( $p = 0.004$ ), whereas CVD and tophi were slightly but not significantly more

common in women (Table 2). Knowledge of increased serum urate was reported by only 42% of the patients (Table 2).

## DISCUSSION

In our present study, we found that the PPV for being classified as having gout ranged from 71 to 80%. The 5 most common classification criteria items reported were maximum inflammation within 24 h, CVD, redness over the joints, podagra/MTP-1 involvement, and > 1 attack of acute arthritis.

These PPV were similar to the results in a previous validation study in the same geographical region, based on medical records<sup>1</sup>, supporting the validity of the current findings.

The Mexico and the Netherlands criteria have been validated in 2 published studies compared to MSU crystal assessment in rheumatology settings. Taylor, *et al*<sup>11</sup> and Jatuworapruk, *et al*<sup>12</sup> collected 983/233 persons in the United States/Thailand with suspected gout/acute arthritis, average age 60/65 years, and 14%/19% women. For the Netherlands criteria, sensitivity was 73–88% for patients with recent-onset symptoms and 92–96% for patients whose symptoms began at least 2 years earlier, with specificities of 75–86% and 47–50%, respectively. The Mexico criteria performed slightly better, with sensitivity of 87–89% for patients with recent-onset symptoms and 99% for patients whose symptoms began at least 2 years earlier, and with specificities of 66–82% and 31–34%, respectively. Thus, both criteria sets displayed high sensitivity, although it should be kept in mind that these studies were performed in rheumatology settings and therefore possibly have included patients with more severe gout, compared to the PC setting in the current study. Many items are similar between the 2 criteria sets, although in the Netherlands criteria the items are weighed from 1 to 3.5 points while all items are weighed equally in the Mexico criteria.

Gout is predominantly a male disease, especially in the

Table 1. Characteristics of the gout questionnaire respondents.

Characteristics	Total, n = 738	Men, n = 598	Women, n = 140	p
Age, mean (SD)	71.9 (11.5)	70.9 (11.4)	75.8 (11.5)	0.0001
BMI, mean (SD)	28.5 (9.8)	28.3 (10.6)	29.0 (5.2)	0.45
Smoking ever	389 (53)	335 (56)	54 (39)	0.0003
Diabetes	173 (23)	141 (24)	32 (23)	0.8
Myocardial infarction	112 (15)	95 (16)	17 (12)	0.2
Stroke	73 (10)	60 (10)	13 (9)	0.7
Kidney disease	57 (8)	42 (7)	15 (11)	0.1
Kidney stone	101 (14)	94 (16)	7 (5)	0.0007
Hypertension	488 (66)	389 (65)	99 (71)	0.18
Dyslipidemia	249 (34)	194 (32)	55 (39)	0.1
Tophus	102 (14)	75 (13)	27 (19)	0.07
ULT ever	497 (67)	408 (68)	89 (64)	0.36

Data are n (%) unless otherwise indicated. BMI: body mass index; ULT: urate-lowering therapy.

Table 2. Positive predictive values (PPV) for gout diagnosis and the 6 most common individual classification criteria items reported with the exception of male sex.

Gout Classification Criteria, n PPV, % (95% CI)	Total, n = 738	Men, n = 598	Women, n = 140	p
Fulfilling Mexico criteria	588, 80 (77–82)	481, 80 (77–83)	107, 76 (69–83)	0.29
Fulfilling the Netherlands criteria	522, 71 (67–74)	458, 77 (73–80)	64, 46 (38–54)	<0.0001
Fulfilling the Netherlands criteria without item “sex”	564, 76 (73–79)	458, 77 (73–80)	106, 76 (68–82)	0.8
Individual classification criteria items, n (%)				
Maximum inflammation developed within 1 day	636 (86)	520 (87)	116 (83)	0.2
Hypertension or ≥ 1 CV disease*	580 (79)	464 (78)	116 (83)	0.19
Redness observed over the joints	564 (76)	459 (77)	105 (75)	0.62
History or observation of podagra/MTP-1 involvement	464 (63)	391 (65)	73 (52)	0.004
> 1 attack of acute arthritis	437 (59)	353 (59)	84 (60)	0.8
High serum urate	309 (42)	251 (42)	58 (41)	0.8

Total no. respondents, and nos. men and women, are the same for each criteria group. \* CV disease here defined as myocardial infarction or stroke. CV: cardiovascular; MTP: metatarsophalangeal.

age spans of premenopausal women. In our study, the women were postmenopausal, average age 76 years, and had a low PPV (46%) for the Netherlands criteria. If on the other hand sex were disregarded as an item in the criteria set, 76% would be classified as gout cases. In the published validation studies<sup>11,12</sup>, subanalysis by sex was not performed.

A minority of the patients in our study were aware of increased urate levels, probably because of gaps in information<sup>13</sup>, lack of recall, and maybe also partly owing to physician nonadherence to guidelines regarding urate monitoring<sup>14</sup>.

A limitation of our study is the response rate at 54.3%, which may have hampered generalizability, particularly because it was slightly skewed with regard to age and sex. It is, however, a common phenomenon in our setting that younger men are poor responders to questionnaires<sup>15,16,17</sup>. Further, the 10% of the nonresponders who were interviewed by telephone reported frequencies for the gout classification items similar to those of the responders. A second possible limitation is the low awareness of increased serum urate among the respondents; however, this could at least partly reflect poor adherence to guidelines. A third limitation to the study is that we were not able to apply the 2015 ACR/EULAR<sup>7</sup> criteria. Finally, some of the items reported by the patients as well as the ICD-10 code are generated by the PC physician and thus are not completely independent from each other.

A strength of our study is the population-based healthcare setting.

The vast majority of patients diagnosed with gout in PC had clinical symptoms compatible with the disease and fulfill the Mexico and the Netherlands classification criteria. A gout diagnosis in PC is valid for identifying patients for research purposes.

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