Diagnosis of Chronic Gout: Evaluating the American College of Rheumatology Proposal, European League Against Rheumatism Recommendations, and Clinical Judgment

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ABSTRACT. ***Objective.*** Observation of monosodium urate (MSU) crystal is the gold standard for diagnosis of gout, but is rarely performed in daily clinical practice, and diagnosis is based on clinical judgment. Our aim was to identify clinical and paraclinical data included in the European League Against Rheumatism recommendations (EULARr) and American College of Rheumatology proposed criteria (ACRp) for diagnosis of gout in patients with chronic gout according to their attending rheumatologists.

Methods. This cross-sectional and multicenter study included consecutive patients from outpatient clinics with a diagnosis of gout by their attending rheumatologists according to their expertise. The frequency of each item from the ACRp and EULARr was determined. Possible combinations of the items that were frequent, clinically relevant, and simple to evaluate in daily practice were determined.

Results. We studied 549 patients (96% men), mean age 50 ± 14 years. Analysis of MSU crystals was performed in 15%. We selected 7 clinical criteria and 1 laboratory measure because of their frequency, importance, and simplicity to obtain: current or past history of: > 1 attack of acute arthritis (93%); mono or oligoarthritis attacks (74%); rapid progression of pain and swelling (< 24 hours; 74%); podagra (70%); erythema (56%); unilateral tarsitis (33%); tophi (52%); and hyperuricemia (93%). The chronic gout diagnosis (CGD) proposal comprised ≥ 4/8 of these; 88% of patients had the criteria of the CGD proposal while 75% had 6/11 ACRp criteria (p = 0.001). When analysis of MSU crystals was added, 90.1% (CGD) and 83.9% (ACRp) met the criteria (p = 0.004).

Conclusion. Current or past history of ≥ 4/8 CGD parameters is highly suggestive of chronic gout. (J Rheumatol First Release June 15 2010; doi:10.3899/jrheum.091385)

Key Indexing Terms:
GOUT HYPERURICEMIA PODAGRA DIAGNOSIS

In 1961, monosodium urate (MSU) crystals were identified using polarized light microscopy for the examination of synovial fluid from patients with gout[1]. Since then, identification of MSU crystals in joints and in tophi have been considered the "gold standard" for the diagnosis of gout[2].

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Unfortunately, demonstration of MSU crystals is not regularly performed in daily outpatient clinics: in the Health Professionals Study, the search for MSU crystals in synovial fluid was performed in only 11% of patients with gout[3,4]. Investigation for MSU crystals was performed in only 70% of patients participating in studies intentionally searching for MSU crystals in synovial fluid[5]. Thus, the diagnosis of gout is frequently made according to clinical data and blood tests.

The American College of Rheumatology's (ACR; formerly the American Rheumatism Association) proposed criteria for the classification of acute arthritis of primary gout[6] are widely used for diagnosis of gout although they were issued as "preliminary" and not validated; they were intended for the diagnosis of acute gout, but also include clinical and radiographic data of chronic disease.

In 2006, an international group of experts published evidence-based recommendations for diagnosis of gout on behalf of the European League Against Rheumatism (denoted the EULARr) Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)[7]. Their proposal derived from a Delphi exercise and evidence-based medicine approaches, and included 10 recommendations, which actually are diagnostic statements that include sensitivity, specificity, and likelihood ratios (LR) for each. Ultimately, the proposal consisted of a diagnostic "ladder" that takes into account the sum of probabilities. To date, there has been no information about the validity of the EULARr in various scenarios including daily clinical practice.

It seems that in patients with gout, 2 different sets of criteria are needed, one for acute attacks and the other for chronic gout. Several proposals for criteria defining acute gout attacks have been published[8,9]; the value of the previous criteria in chronic gout has recently been tested[10,11] in patients treated by 1 rheumatology department[10] and in patients attended by general physicians[11].

We have identified which requirements included in the ACR preliminary criteria (ACRp) for acute gout and in the EULAR recommendations for diagnosis of gout (EULARr) are fulfilled by patients diagnosed as having gout by rheumatologists during their daily practice. Based on previous international proposals and recommendations (ACRp and EULARr), we searched for easily obtained clinical data that would make the diagnosis of chronic gout highly suggestive. These data could be used when the search for MSU crystals was not feasible, particularly in settings such as community studies, general practices, or population studies where "self-reported gout," diagnostic codes, or claims databases had been used.

MATERIALS AND METHODS

This was a cross-sectional database study of demographic and clinical features at baseline of 2 cohorts of consecutive patients with primary gout attending 9 rheumatology departments across Mexico; the data were obtained prospectively during the patient's regular visit to the rheumatologist. The first cohort included the data of patients participating in a multicenter study of the socioeconomic impact of gout as well as rheumatoid arthritis (RA) and ankylosing spondylitis[12]; the second cohort consisted of patients with gout attending the gout clinic at one of our centers. The study protocol was approved by the institutional review board in each participating center and patients agreed to participate by signing an informed consent form.

Before identifying the ACRp and EULARr requirements in the population included in the study, we compared the definitions provided in each set of criteria to determine their equivalence (Table 1): MSU crystal identification, hyperuricemia, tophi, and radiographic findings are items found in both sets of criteria. The 3 following pairs were considered equivalent to each other: (1) maximum inflammation within 1 day (ACRp) and rapid development of pain and swelling (EULARr); (2) first metatarsophalangeal (MTP) joint swelling and/or unilateral first MTP joint attack of arthritis (ACRp) and podagra (EULARr); and (3) redness observed over the joints (ACRp) and erythema (EULARr), in addition to (4) characteristic radiographic findings. In contrast, the following ACRp criteria had no equivalent among the EULARr criteria: > 1 attack of acute arthritis; mono or oligoarthritis attacks; unilateral tarsal joint attack; and negative joint fluid cultures during the attack (EULAR suggests the performance of a gram stain and culture, if septic arthritis is suspected).

We also determined the prevalence of obesity, hypertension, and hyperlipidemia according to the definitions for these entities as part of the metabolic syndrome published in the Adult Treatment Panel III criteria[13]. Ischemic heart disease was considered in patients diagnosed by a cardiologist as having it, and chronic renal failure was defined as patients with glomerular filtration rate < 50 ml/min or serum creatinine concentration > 1.5 mg/dl.

Intra and interobserver rheumatologist agreement. We determined the intra and interobserver rheumatologist degree of agreement for the diagnosis of gout by asking them to diagnose patients randomly selected from the database, as well as 10 patients with RA presented in an electronic format, which included their most important clinical features, but not the diagnosis or findings of MSU crystal test. The task was to diagnose whether the patient had gout.

Statistical analysis. For continuous variables, we have reported the mean and standard deviations; for nominal variables, rates and proportions. A Z-test was used to compare percentages.

RESULTS

Nine rheumatology departments encompassing the different medical care systems in our country participated in this study. Four centers, located in Mexico City, constituted 77% of the patients and 5 centers in 4 different cities formed the rest.

We included 549 patients with gout (96% men) of mean age 50 (SD 14) years, disease duration 12 (SD 10) years, and education level 8 (SD 5) years. Needle-shaped birefringent-negative crystals were demonstrated in all patients under polarized light microscope. Fifty-nine percent had hyperlipidemia, 53% obesity, 46% hypertension, 35% metabolic syndrome, 16% chronic renal failure, and 10% ischemic heart disease.

The clinical data included in both the ACRp and EULARr and found most frequently in our patients were hyperuricemia (93%), rapid onset of pain and swelling (74%), and podagra (70%; Table 2). Although erythema or joint redness is considered in both ACRp and EULARr as an

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Table 1. Gout diagnosis. Items included in the ACR proposal (ACRp)[6] and EULAR recommendations (EULARr)[7].

ACRp	EULARr
MSU crystals in joint fluid or tophi; OR ≥ 6	MSU crystal confirmed in joint fluid or tophi
1. > 1 attack of acute arthritis	
2. Maximum inflammation developed within 1 day	1. Rapid pain and swelling, reaching a maximum in 6–12 h (LR 1.27)
3. Monoarthritis/oligoarthritis attack*	
4. Redness observed over joints	2. Erythema (LR 2.44)
5. 1st MTP joint painful or swollen	3. Podagra (LR 30.64)
6. Unilateral 1st MTP joint attack	
7. Unilateral tarsal joint attack	
8. Tophi (proven or suspected)	4. Definite and possible tophi (LR 39.95 and 33.99)
9. Hyperuricemia	5. Hyperuricemia (LR 7.61)
10. Asymmetric swelling within a joint on radiograph	6. Radiographic asymmetric swelling (LR 4.13)
11. Subcortical cysts without erosions on radiograph	7. Radiographic subcortical cysts, no erosions (LR 6.39)
12. Joint fluid culture-negative*	

* Proposed criteria for acute arthritis of primary gout considers monoarthritis (item 3) and item 12. Proposed survey criteria for acute arthritis of primary gout consider oligoarthritis (item 3), and "Complete termination of an attack" instead of 12. LR: Likelihood ratios reported in the text.

Table 2. Frequency of clinical and paraclinical data in gout patients included in ACRp[6] and this study.

Characteristic	ACRp, n = 178 (%)†	CGD Proposal, n = 549 (%)
Male	86.4	96
Age, mean, yrs	56.2	50 ± 14
Duration of disease, mean, yrs	10.1	12 ± 10
Hyperuricemia*	92.2	93
> 1 attack of acute arthritis*	86.5	90
Mono or oligoarthritis*	71.9	74
Rapid onset of pain and swelling*	85.1	74
Podagra*	78	70
Erythema*	92.2	56
Suspected tophus*	19.5	52
Tarsitis (unilateral)*	21.1	33
Negative synovial fluid culture	95.9§	4
Asymmetric swelling	41.9	58
Subcortical cysts, no erosion	11.9	50

* These correspond to the 8 criteria of the chronic gout diagnosis (CGD) proposal. † Patients with gout included in ACRp, n = 178; clinical data were not available from all; negative synovial fluid was observed in only 49 patients.

important item, it was found in only 56% of patients.

More than 1 attack of acute arthritis and a history of monoarthritis or oligoarthritis were seen in 90% and 74%, respectively, of patients. On the other hand, acute tarsitis, especially unilateral, was found in 33% of the patients. Although ACRp and EULARr emphasize the importance of negative cultures when infection is suspected, this procedure was seldom performed (4%).

Around half the patients had the 2 radiographic abnormalities considered significant in the ACRp and supported by the EULARr: asymmetric swelling within a joint and the presence of subcortical cysts without erosions.

Only 461 (83.9%) patients with gout (according to the opinion of the rheumatologist) met the ACRp criteria (MSU crystals and/or 6/11 ACR proposed criteria); 413 (75%) had only 6/11 criteria without demonstration of MSU crystals and the rest had MSU crystals plus suggestive clinical findings.

The comparison of patients in this study with those included originally in the ACRp[6] is stated in brief in Table 2; our patients more frequently were men, of younger age, less frequently present erythema and synovial fluid-negative cultures, but tophi and radiographic cysts were seen more frequently in them.

Proposal for chronic gout diagnosis. Based on the ACRp and EULARr, we considered the 8 most frequent and important clinical criteria in our population (excluding radiographic changes). Therefore, we propose that when MSU crystal identification in tophi or synovial fluid is not possible, the chronic gout diagnosis (CGD) should be considered when the patient has ≥ 4/8 of the following findings (Figure 1): current or past history of: > 1 attack of acute arthritis; rapid onset of pain and swelling (< 24 hours); mono and/or oligoarthritis attacks; podagra; erythema, possible tophi; unilateral tarsitis; and hyperuricemia.

The CGD criteria (≥ 4/8 findings and/or demonstration of MSU crystals) were observed in 495 patients (90.1%); 88.1% of the patients had ≥ 4/8 CGD criteria ($p = 0.001$ and $p = 0.004$, respectively, compared to ACRp; Figures 2 and 3). When ≥ 3/8 of the criteria were considered, 97% of the patients could be classified as having CGD, and when crystals were taken into account, this increased to 97.8%. Certain demographic characteristics (male sex) and comorbidities (hypertension, obesity, hyperlipidemia, ischemic heart disease, and chronic renal failure) were also analyzed in conjunction with the CGD proposal; 477 patients (86.8%) were male and presented ≥ 4/8 of the proposed criteria. Seventy-five percent were male and had 4/8 criteria and at least one associated disease of those considered as comorbidity.

Seventy-three percent of the patients met both the CGD (4/8) and ACRp (6/11) criteria without demonstration of

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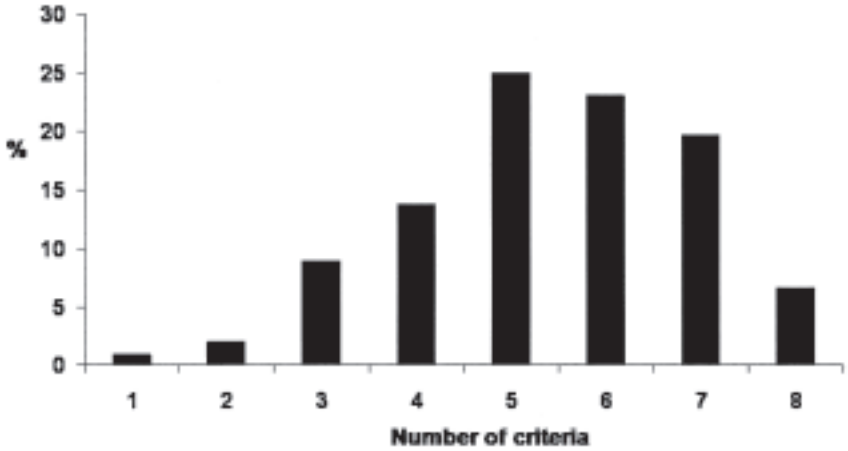

Figure 1. Percentage of patients and number of criteria from the chronic gout diagnosis (CGD) proposal.

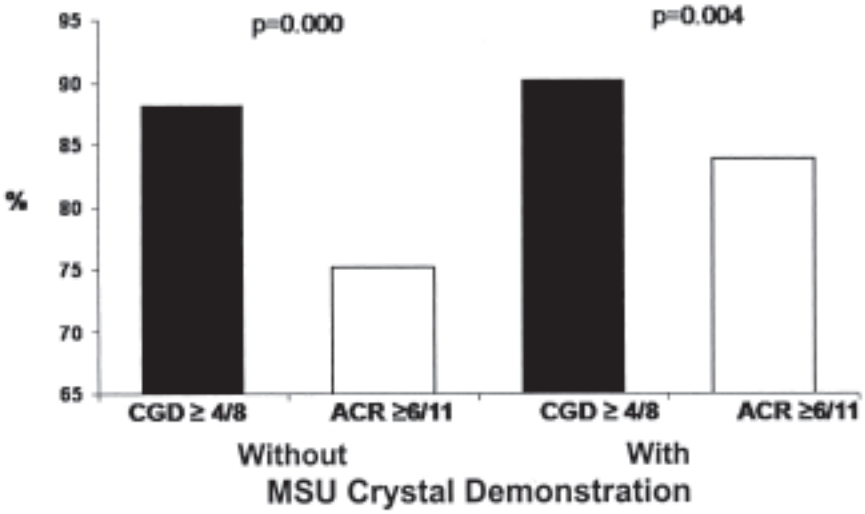

Figure 2. Percentage of patients with diagnosis of gout according to the ACRp (≥ 6/11 criteria)[6] and the CGD proposal (≥ 4/8 criteria) with and without analysis for MSU crystals.

MSU crystals. When MSU crystals were added, 82% of the patients met both criteria sets (Figure 3). Eighty-five patients (15.5%) met the CGD criteria but not the ACRp, 14 patients (2.5%) met the ACRp but not the CGD criteria.

Interestingly, 51 (9.3%) patients with a diagnosis of gout according to their attending rheumatologist did not meet the CGD or ACRp criteria. Thirty-five of them had 3/8 CGD criteria, the most frequent combination, found in 7 patients, being > 1 attack of acute arthritis, mono or oligoarthritis attacks, and hyperuricemia. Twelve patients had 2/8 criteria, podagra plus hyperuricemia and > 1 attack of acute arthritis plus hyperuricemia being the criteria found most frequently in these patients. Four patients had only 1/8 CGD criteria — hyperuricemia in 3; one of them had MSU crystals and the other a possible tophi.

Intraobserver and interobserver agreement, measured in 9/10 rheumatologists assessing paper cases, were 75–95% and 78%, respectively (p = 0.01). One of the participants presented low intraobserver and interobserver agreement in all of the evaluations (40 and 55%, respectively).

DISCUSSION

The proposed CGD criteria are simpler and easier to obtain and detect in the common patient with gout than previously proposed criteria. We maintain that the presence of ≥ 4/8 findings is highly suggestive of a diagnosis of gout when MSU crystals in synovial fluid or tophi cannot be demonstrated. Our CGD proposal comprises a current or past history of ≥ 4/8 of ≥ 1 attack of acute arthritis, mono or oligoarthritis attacks, rapid pain and swelling (< 24 hours), podagra, erythema, unilateral tarsitis, possible tophi, and hyperuricemia.

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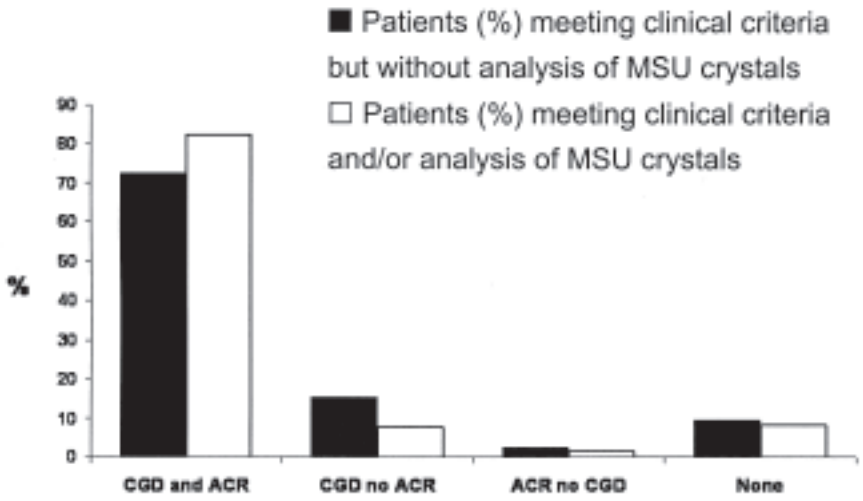

Figure 3. Percentage of patients with diagnosis of gout according to the CGD proposal (≥ 4/8 criteria) and the ACRp criteria[6].

This proposal is based on ACRp and EULARr and also includes data from the Rome and New York criteria for gout[10]. We searched for equivalent items particularly in the ACRp and EULARr, simplified them, and examined their frequency and possible combinations in regular gout patients attended in daily rheumatology outpatient clinics from 9 rheumatology departments. We have a study in progress to determine whether this CGD proposal in patients with other rheumatic diseases is useful to obtain all the relevant data needed for a diagnosis; these data will help us define if 3/8 or 4/8 criteria are better suited to be used in regular patients presenting with gout.

Although a history of erythema in affected joints during acute flares is considered in the ACRp and EULARr, and is a key piece of data (the second one) when using the diagnostic ladder proposed by EULARr, it was seen less frequently in our patients; one should consider that erythema is not easily appreciated in non-whites and most of our patients are Mestizos.

The ACRp considers 2 radiographic abnormalities that are nonspecific and could be observed in several rheumatic conditions. In contrast, large erosions, with sclerosis and overhanging edges, are very typical radiographic abnormalities in gout, but were not considered here because they are late manifestations of the disease[14,15]. For all these reasons, radiographic abnormalities were not included in the CGD proposal. We also did not include the response to colchicine considered by the New York criteria[10]; in our country, physicians prescribe colchicine more frequently as prophylaxis, and during acute attacks the use of nonsteroidal antiinflammatory drugs is preferred.

Crystal analysis should always be performed to confirm the diagnosis of gout, particularly in rheumatology departments; unfortunately, in general practitioner (GP) and non-GP daily practice this tool is not routinely employed for several reasons: limits of time in outpatient clinics, lack of availability of polarized light microscopes, the fact that sometimes patients reject the procedure, and technical difficulties, especially during the intercritical period[16,17]. In daily practice most physicians (75–90% of cases), rheumatologists and nonrheumatologists, establish a diagnosis of gout based only on clinical criteria[18,19,20]. CGD items are simple and easy to obtain and make the diagnosis of chronic gout highly accurate, especially for community studies; the frequency of gout has increased in recent decades, and could be very frequent among some sectors of the population[21].

Two recent articles[10,11] evaluated the performance of the ACR criteria[11] as well as the Rome and NY criteria for gout. Malik, *et al*[10] evaluated the clinical data of 30 patients with demonstrated MSU crystals compared with those in whom non-MSU crystals were reported. In their study, few patients had radiographic data or negative cultures; they found that the ACR criteria had poor diagnostic performance (70% sensitivity, 78% specificity). Janssens, *et al*[11] prospectively investigated for ACR criteria in patients attended by a GP who presented with monoarthritis and the diagnostic suspicion of gout; all were evaluated by one rheumatologist in the 24 hours following the onset of monoarthritis and a sample of synovial fluid was obtained; after MSU crystal analysis they found that the ACR criteria had 80% sensitivity and 64% specificity. Probably both studies included patients with acute gout attacks and, in some cases, it constituted the patient's first attack. In those patients, as in ours, the performance of the ACR criteria was very poor. From the ACRp and EULARr, we selected the items that were more frequent in our population (the same as found by Malik, *et al*[10]) and looked for them in patients with chronic gout.

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One limitation of our study was that the diagnosis of gout was, in most cases, the attending rheumatologist's clinical judgment, and crystal demonstration was performed in 15% of patients, similar to the 11% previously reported[4]. It has recently been shown that among patients with diagnosis of gout according to codes in databases, only 36% complied with ACR criteria when medical records were examined and interviews were done, although the diagnostic accuracy was higher among rheumatologists (72–74%)[17].

As we reported, our patients were younger at onset and at inclusion into our study than gout patients from other countries[22]; most of them were men (96%) and they had "typical gout." In other patients, such as women, older patients, and those with secondary gout associated with organ transplants and chronic renal failure, the CGD proposal could behave differently and would need to be tested.

Our study demonstrates that the CGD proposal, based on clinical data from the ACRp criteria and EULARr, is useful in daily clinical practice. Diagnosis of chronic gout should be considered in patients when ≥ 4 of the following data are present currently or as part of their history: ≥ 1 attack of acute arthritis, mono or oligoarthritis attacks, rapid onset of pain and swelling, podagra, erythema, unilateral tarsitis, possible tophi, and hyperuricemia.

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