OPEN

Performance of the Existing Classification Criteria for Gout in Thai Patients Presenting With Acute Arthritis

Kanon Jatuworapruk, MD, Panomkorn Lhakum, MD, Nuttaya Pattamapaspong, MD, Nuntana Kasitanon, MD, Suparaporn Wangkaew, MD, and Worawit Louthrenoo, MD

Abstract: Currently, there are 5 existing classification criteria for gout: the Rome, New York, American Rheumatism Association (ARA), Mexico, and Netherlands criteria. This study was carried out to determine the performance of these classification criteria in Thai patients presenting with acute arthritis.

All consecutive patients presenting with acute arthritis and being consulted at the Rheumatology Unit, Chiang Mai University Hospital from January 2013 to May 2015 were invited to join the study. Gout was defined by the presence of monosodium urate crystals in the synovial fluid or tissue examined by experienced rheumatologists. The 5 existing gout classification criteria were performed and evaluated in all of the patients, who were divided in subgroups of early disease (≤ 2 years), established disease (> 2 years), and those without tophus.

There were 136 gout and 97 nongout patients. Sensitivity and specificity across all criteria ranged from 75.7% to 97.1% and 68.0% to 84.5%, respectively. Overall, the Mexico criteria had the highest sensitivity (97.1%), and the ARA survey criteria the highest specificity (84.5%), whereas the Mexico criteria performed well in early disease with sensitivity and specificity of 97.1% and 81.7%, respectively. All 5 criteria showed high sensitivity (from 76.4% to 99.1%) but low specificity (from 30.8% to 65.4%) in established disease. In patients without tophus, the sensitivity and specificity ranged from 64.1% to 95.7% and 68.8% to 85.4%, respectively. The ARA survey criteria across all groups showed consistently high specificity for gout.

The 5 existing classification criteria for gout had limited sensitivity and specificity in Thai patients presenting with acute arthritis. The ARA survey criteria are the most suitable for diagnosing gout in Thai people when crystal identification is not available.

(Medicine 95(5):e2730)

This study was partially supported by educational grants from the Thai Rheumatism Association, Thailand.

Abbreviations: ARA = American Rheumatism Association, BCP = Basic calcium phosphate, CPPD = Calcium pyrophosphate dihydrate, MSU = Monosodium urate, SF = Synovial fluid.

INTRODUCTION

out is one of the most common arthritis among men.¹ J Typical clinical presentation is acute arthritis with painful swelling and redness of the joints. Without appropriate treatment, the disease will become more severe, with increasingly frequent and recurrent acute attacks, development of tophus, and joint destruction. However, several diseases can display similar presenting symptoms to gout, including calcium pyrophosphate dihydrate (CPPD) arthritis, septic arthritis, and spondyloarthropathy.^{2–4} Definite diagnosis of gout requires the identification of monosodium urate (MSU) crystals in synovial fluid (SF) or tissue. Unfortunately, arthrocentesis and crystal identification are not performed widely in a primary or an acute care setting, where the majority of gout patients are managed.^{5,6} Furthermore, arthrocentesis is an invasive technique and may cause joint trauma or discomfort for the patients.7

At the time of this study's preparation, there were 5 classification criteria for gout: the Rome, ⁸ New York, ⁹ American Rheumatism Association (ARA), ¹⁰ Mexico, ¹¹ and Netherlands criteria. ¹² Among these, the ARA has been accepted and is used widely, but surprisingly few studies have evaluated the performance of these existing criteria. ¹⁰,¹¹,^{13–17} Recently, Taylor et al¹⁸ performed a large multicenter, multinational study entitled, "The <u>S</u>tudy for <u>U</u>pdated <u>G</u>out ClAssification C<u>R</u>iteria (SUGAR)" in order to set a new classification criteria for gout. They also tested the sensitivity and specificity of the existing gout classification criteria. This study was therefore performed to evaluate the sensitivity and specificity of existing classification criteria for gout in Thai patients presenting with acute arthritis. Additional analyses also were carried out for subgroups of patients with early disease (onset of 2 years), and those without tophus.

METHODS

All consecutive adult patients in this study presented with acute arthritis and had undergone arthrocentesis or subcutaneous nodule aspiration, while being consulted at the Rheumatology Unit, Chiang Mai University Hospital from January 2013 to May 2015. Patients who refused to provide information or were incapable of doing so were excluded. All participants gave their written informed consent before data collection. SF and tissue aspirations were reviewed for the presence of crystals, with an experienced rheumatologist (WL) using compensated polarized light microscopy. SF culture, staining for organisms, and leukocyte count were performed based on the

Editor: Antonio Palazon-Bru.

Received: October 20, 2015; revised: January 12, 2016; accepted: January 15, 2016.

From the Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (KJ, PL, NK, SW, WL); The Division of Rheumatology, Department of Internal Medicine, Thammasat University Hospital, Pathum Thani, Thailand (KJ); The Division of Rheumatology, Department of Internal Medicine, Chiang Rai Hospital, Chiang Rai, Thailand (PL), and The Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (NP).

Correspondence: Worawit Louthrenoo, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (e-mail: worawit.louthrenoo@cmu.ac.th).

The authors have no conflicts of interest to disclose.

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution-NonCommercial License, where it is permissible to download, share and reproduce the work in any medium, provided it is properly cited. The work cannot be used commercially. ISSN: 0025-7974

DOI: 10.1097/MD.000000000002730

clinical judgments of primary physicians. The study was approved by the Ethic Committee of the Faculty of Medicine, Chiang Mai University.

All participating patients were interviewed and physically examined by experienced rheumatologists during a current arthritis episode. Data were collected using a predetermined questionnaire based on the 5 existing classification criteria for gout. Clinical data of the patients included demographics, comorbidities, medications, alcohol consumption, presence of urinary tract stones, presence of tophus, duration of current arthritis attack, duration since first arthritis attack, time to peak inflammation, joint redness, number and pattern of joints involved, and response to colchicine. Serum uric acid and creatinine level were measured within 2 weeks from the onset of the current arthritis episode. Medical records were reviewed for past results of the serum uric acid and creatinine level. Plain radiography on swollen joints or joints with suspected tophus was carried out and read by an experienced musculoskeletal radiologist (NP) who was blinded from clinical diagnosis and SF examination results. Findings on the radiograph, particularly those on the presence of asymmetrical joint swelling, subcortical cyst, and appearance of joint erosion with overhangingedge were recorded.

In this study, gout was defined when MSU crystals were identified in the SF or tissue aspirates. Acute arthritis was defined as the presence of acute painful, swollen, and tender joints for the duration of 2 weeks or less. Early disease was defined as duration of 2 years or less since the first attack of arthritis and established disease as duration of >2 years. Monoarthritis, oligoarthritis, and polyarthritis were defined as the presence of 1, 2 to 4, and >4 swollen and tender joints, respectively. Rapid response to colchicine was defined as patients reporting significant reduction of inflammation or pain of >50% within 48 hours after colchicine initiation. Hyperuricemia was defined as current or past serum uric acid level of >6.8 mg/dL.¹⁹

In the New York, ARA, and Mexico criteria, the patients could be classified as gout with the presence of MSU crystals alone.^{10,11,13} However, this study attempted to determine the performance of the existing classification criteria for gout without relying on crystal identification in SF or tissue. Thus, the patients were considered to satisfy the New York, ARA, and Mexico criteria only when at least 2, 6, and 4 respective items were present in each criterion, excluding the presence of MSU crystals. Similarly, the presence of MSU crystals was not considered in the Rome criteria. The patients were thought to satisfy the Rome criteria only when at least 2 out of 3 clinical criteria were met.^{15,18}

Statistical Analysis

Clinical, laboratory, and radiological data of the patients were described in frequency and percentage for categorical variables, and mean \pm standard deviation (SD) for continuous variables. Comparison between gout and nongout patients was performed using the chi-square or Fisher's exact test for categorical variables, and Student's *t* test or Mann-Whitney U test for continuous variables, where appropriate. By using the presence of MSU crystals as the gold standard in gout diagnosis, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for all classification criteria and each individual item. Subgroup analysis among patients with early disease, established disease, and without tophus was determined as well.

RESULTS

A total of 233 patients participated in this study. One hundred and thirty-six of them were diagnosed as gout by the presence of MSU crystals. Among the 97 nongout patients, 60 were CPPD arthritis, 15 septic arthritis, 5 basic calcium phosphate arthritis (BCP) arthritis, 3 hemathrosis, 3 spondyloarthropathy, 2 rheumatoid arthritis, 2 reactive arthritis, and 1 each with osteoarthritis, neuropathic arthropathy, bacterial endocarditis, acute rheumatic fever, leukemic arthritis, Sweet's syndrome, and unclassified arthritis.

Demographic data of the patients studied are shown in Table 1. Eighty-one percent of gout patients were men, compared to 51.5% of nongout patients. The mean age of gout and nongout patients was 64.5 ± 13.0 and 67.0 ± 17.8 years, respectively. The proportion of patients with no history of alcohol consumption was significantly higher in nongout patients, when compared to gout patients (69.0% vs 44.2%, P < 0.001). Hypertension and hyperlipidemia were significantly more prevalent among gout patients (75.7% vs 55.7%, P = 0.001, and 28.7% vs 16.5%, P = 0.031, respectively). Significantly more patients in the gout group were taking allopurinol, furosemide, and spironolactone (17.6% vs 6.2%, P = 0.010, 16.2% vs 6.2%, P = 0.021, and 7.4% vs 0.0%, P = 0.006, respectively). There was no difference between gout and nongout patients in the prevalence of cardiovascular diseases, chronic kidney disease, urinary tract stone or other medications that might affect the uric acid level.

The mean age at disease onset for gout patients was lower than that of nongout patients $(55.7 \pm 14.6 \text{ vs } 64.4 \pm 17.8 \text{ years},$ P < 0.001). When compared to nongout patients, gout patients had significantly longer duration of disease $(8.8 \pm 7.9 \text{ vs})$ 2.6 ± 6.0 years, P < 0.001), but with less duration of current arthritis attack (3.5 ± 2.1 vs 4.2 ± 3.0 days, P < 0.036). Only 4.4% of gout patients presented with first episode of acute arthritis, compared to 57.7% of nongout patients (P < 0.001). At the time of current attack, monoarticular arthritis in gout patients was significantly less common than that in nongout patients (28.0% vs 53.6%, P < 0.001). Arthritis usually involved the knee joints, but ankle and metatarsophalangeal (MTP) joint involvement were significantly more common in gout patients. Tophus was present in 32.4% of gout patients. Hyperuricemia was found in 73.5% and 28.9% of gout and nongout patients, respectively (P < 0.001). Plain radiographs found that asymmetrical joint swelling, subcortical cyst, and erosion with overhanging edge were more significantly frequent in gout patients.

The sensitivity, specificity, PPV, and NPV of all classification criteria for gout in each subgroup are shown in Table 2. Overall, the Mexico criteria had the highest sensitivity (97.1%), followed by the Netherlands criteria (88.2%), ARA full criteria (85.3%), ARA survey criteria (83.1%), New York criteria (79.4%), and Rome criteria (75.7%). However, the Mexico criteria had the lowest specificity (68.0%), whereas the ARA survey criteria showed the highest specificity (84.5%).

In early disease, sensitivity of the Rome, New York, both ARA full and survey, and Netherlands criteria was low (46.2–73.1%), whereas that of the Mexico criteria remained high (88.5%). All the criteria showed high specificity for the subgroup of early disease (from 81.7% to 91.5%), whereas the New York, Mexico, Netherlands, and both ARA full and survey criteria had high sensitivity in patients with established disease (from 87.3% to 99.1%). Nevertheless, the specificity was low in all criteria (from 30.8% to 65.4%). The sensitivity and

TABLE 1. Demographic and Clinical Data

Variables	Total (n = 233)	Gout (n = 136)	Nongout $(n = 97)$	Р
Age, y, mean \pm SD	65.6 ± 15.2	64.5 ± 13.0	67.0 ± 17.8	
Male	160 (68.7)	110 (80.9)	50 (51.5)	< 0.001
Alcohol consumption				
Current	15 (6.4)	12 (8.8)	3 (3.1)	0.079
Past	58 (24.9)	40 (29.4)	18 (18.6)	0.059
Social	33 (14.2)	24 (17.6)	9 (9.3)	0.071
No consumption	127 (54.5)	60 (44.2)	67 (69.0)	< 0.001
Comorbidities Hypertension	157 (67.4)	103 (75.7)	54 (55.7)	0.001
Coronary artery disease	33 (14.2)	21 (15.4)	12 (12.4)	0.001
Congestive heart failure	11 (4.7)	7 (5.1)	4 (4.1)	
Cerebrovascular disease	24 (10.3)	18 (13.2)	6 (6.2)	0.081
Peripheral vascular disease	3 (1.3)	2 (1.5)	1(1.0)	0.001
Hyperlipidemia	55 (23.6)	39 (28.7)	16 (16.5)	0.031
Diabetes mellitus	49 (21.0)	33 (24.3)	16 (16.5)	
Chronic kidney disease	59 (25.3)	37 (27.2)	22 (22.7)	
Presence of urinary tract stone	36 (15.5)	24 (17.6)	12 (12.4)	
Medications				
Allopurinol	30 (12.9)	24 (17.6)	6 (6.2)	0.010
Uricosuric agent	3 (1.3)	2 (1.5)	1 (1.0)	
Furosemide	28 (12.0)	22 (16.2)	6 (6.2)	0.021
Hydrochlorothiazide	19 (8.2)	14 (10.3)	5 (5.2)	0.158
Spironodactone	10(4.3)	10(7.4)	$ \begin{array}{c} 0 & (0.0) \\ 7 & (7.2) \end{array} $	0.006
Losartan	19(8.2)	12(8.8)	7 (7.2)	0.002
Amlodipine Aspirin (81–300 mg/d)	64 (27.5) 53 (22.7)	43 (31.6) 37 (27.2)	21 (21.6) 16 (16.5)	0.093 0.055
Warfarin	18 (7.7)	11(8.1)	7 (7.2)	0.055
Antituberculosis drugs	3(1.3)	2(1.5)	1(1.0)	
Age at onset of arthritis, y, mean \pm SD	59.5 ± 16.9	55.7 ± 14.6	64.4 ± 17.8	< 0.001
Duration since first arthritis episode, y, mean \pm SD	6.3 ± 7.8	8.8 ± 7.9	2.6 ± 6.0	< 0.001
Duration of current arthritis, d, mean \pm SD	3.8 ± 2.5	3.5 ± 2.1	4.2 ± 3.0	0.036
First arthritis episode	62 (26.6)	6 (4.4)	56 (57.7)	< 0.001
Number of joints currently involved, mean \pm SD	3.9 ± 4.5	4.9 ± 5.3	2.5 ± 2.5	< 0.001
Pattern of current joint involvement				
Monoarthritis	90 (38.6)	38 (28.0)	52 (53.6)	< 0.001
Oligoarthritis	80 (34.4)	49 (36.0)	31 (32.0)	
Polyarthritis	63 (27.0)	49 (36.0)	14 (14.4)	< 0.001
Current joint involvement	156 (67.0)		51 (52.0)	0.007
Knee	156 (67.0)	85 (62.5)	71 (73.2)	0.087
Ankle First metatersonholongool	125 (53.6)	94 (69.1)	31 (32.0) 12 (12.4)	<0.001 <0.001
First metatarsophalangeal 2nd—5th metatarsophalangeal	64 (27.5) 52 (22.3)	52 (38.2) 42 (30.9)	12(12.4) 10(10.3)	< 0.001
Tarsal	14 (6.0)	11 (8.1)	3 (3.1)	0.114
Shoulder	4 (1.7)	0(0.0)	4 (4.1)	0.017
Elbow	27 (11.6)	18 (13.2)	9 (9.3)	01017
Wrist	41 (17.6)	25 (18.4)	16 (16.5)	
Metacarpophalangeal	22 (9.4)	18 (13.2)	4 (4.1)	0.019
Proximal interphalangeal	11 (4.7)	7 (5.1)	4 (4.1)	
Intervertebral	2 (0.9)	0 (0.0)	2 (2.1)	
Sternoclavicular	1 (0.4)	0 (0.0)	1 (1.0)	
Acromioclavicular	2 (0.9)	1 (0.7)	1 (1.0)	
Presence of subcutaneous nodules or tophus	45 (19.3)	44 (32.4)	1 (1.0)	< 0.001
Hyperuricemia	128 (54.9)	100 (73.5)	28 (28.9)	< 0.001
Current serum uric acid, mg/dL, mean \pm SD, [n = 224]	6.6 ± 2.8	7.6 ± 2.8	5.1 ± 2.3	< 0.001
Highest serum uric acid, mg/dL, mean \pm SD, [n = 229]	7.6 ± 3.3	8.9 ± 3.2	5.9 ± 2.6	< 0.001
Current serum creatinine, mg/dL, mean \pm SD	1.7 ± 1.8	1.8 ± 1.6	1.5 ± 2.0	
Highest serum creatinine, mg/dL, mean \pm SD Radiographic findings (n = 228)	2.1 ± 2.6	2.2 ± 2.0	2.1 ± 3.3	
Asymmetrical swelling	82 (36.0)	66 (50.0)	16 (16.7)	< 0.001
Subcortical cyst	58 (25.4)	41 (31.1)	17 (17.7)	0.028
Erosion and overhanging edge	37 (16.2)	30 (22.7)	7 (7.3)	0.0028
	57 (10.2)	50 (22.7)	(1.3)	0.002

Data presented in frequency (percentage) unless specified otherwise. P value was compared between gout and nongout groups. SD = standard devaition.

Criteria	Overall $(n = 233)$	2 Years or Less (n = 97)	More Than 2 Years (n = 136)	Nontophaceou (n = 188)	
Sensitivity					
Rome	75.7	73.1	76.4	64.1	
New York	79.4	46.2	87.3	69.6	
ARA (full)	85.3	57.7	91.8	79.3	
ARA (survey)	83.1	57.7	89.1	75.0	
Mexico	97.1	88.5	99.1	95.7	
Netherlands	88.2	73.1	91.8	82.6	
Specificity					
Rome	81.4	87.3	65.4	82.3	
New York	79.4	84.5	65.4	80.2	
ARA (full)	78.4	85.9	57.7	79.2	
ARA (survey)	84.5	91.5	65.4	85.4	
Mexico	68.0	81.7	30.8	68.8	
Netherlands	76.3	85.9	50.0	77.1	
Positive predictive valu	e				
Rome	85.1	67.9	90.3	77.6	
New York	84.4	52.2	91.4	77.1	
ARA (full)	84.7	60.0	90.2	78.5	
ARA (survey)	88.3	71.4	91.6	83.1	
Mexico	81.0	63.9	85.8	74.6	
Netherlands	83.9	65.5	88.6	77.6	
Negative predictive value	ue				
Rome	70.5	89.9	39.5	70.5	
New York	73.3	81.1	54.8	73.3	
ARA (full)	79.2	84.7	62.5	80.0	
ARA (survey)	78.1	85.5	58.6	78.1	
Mexico	94.3	95.1	88.9	94.3	
Netherlands	82.2	89.7	59.1	82.2	

TABLE 2. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Existing Classification Criteria for Gout

ARA = American Rheumatism Association.

specificity in the subgroup of patients without tophus (mean disease duration 4.7 ± 6.5 years) ranged from 64.1% to 95.7%and 68.8% to 85.4%, respectively.

The sensitivity and specificity for each individual criterion are shown in Table 3. Overall, a history of only having first MTP joint involvement and hyperuricemia (defined as serum uric acid >6.8 mg/dL or >7 mg/dL in men and >6 mg/dL in women) showed a sensitivity and specificity of >65.0%. On the other hand, unilateral tarsal joint involvement, rapid response to colchicine, presence of tophus, asymmetrical joint swelling, and subcortical cyst on plain radiographs were highly specific (from 82.5% to 99.0%), but with low sensitivity (from 14.7% to 48.5%).

DISCUSSION

In this study, performance of the 5 existing classification criteria was evaluated for gout in Thai patients presenting with acute arthritis. Although both the ARA full and survey criteria gave high sensitivity overall, specificity of the ARA survey criteria was higher than that of the full criteria (84.5% vs 78.4%). This could be explained by the higher specificity of "oligoarthritis" and "complete termination of attacks" used in the ARA survey criteria, when compared to "monoarthritis" and "SF culture negative for organisms" used in the ARA full criteria. The Mexico and Netherlands criteria had the highest sensitivity, but also the lowest specificity. This was due to both

4 | www.md-journal.com

criteria accounting for clinical features that were common, but not specific, such as mono and/or oligoarthritis, hypertension, and serum uric acid > 5.88 mg/dL. Despite their simplicity, the Rome and New York criteria had low sensitivity because both of them included features that had low prevalence in this population, such as presence of tophus and rapid response to colchicine.

Previously reported performance of the existing classification criteria for gout in the literature was compared to this study, as shown in Table 4. The sensitivity of both ARA full and survey criteria in this study was similar to that first reported by Wallace et al¹⁰ but the specificity of the ARA criteria in this study was lower (78.4-84.5% vs 94.9-96.0%). This could be due to a large number of patients in their control group having rheumatoid arthritis, which typically presents with chronic arthritis. Sensitivity of the Rome, New York, and ARA full criteria ranged from 66.7% to 70.0% in the study by Malik et al.¹⁵ In comparison, this study found a higher sensitivity ranging from 75.7% to 85.3% for these 3 criteria. This could result from the retrospective nature of Malik's study, leading to missing data. The specificity of the Mexico criteria in this study was much lower than that reported by Vazquez-Mellado et al (68.0% vs 95.6%).¹⁷ However, the control group in their study mainly consisted of patients diagnosed as rheumatoid arthritis, spondyloarthropathies and osteoarthritis, with a tendency of chronic rather than acute arthritis.

	Sensitivity				Specificity			
Criteria	All	≤2 y	>2 yrs	Tophi (–)	All	≤2 y	>2 yrs	Tophi (-)
Painful joint swelling with abrupt onset and resolution within 2 weeks (RM1)	97.8	88.5	100.0	96.7	51.5	69.0	3.9	52.1
At least 2 attacks of painful joint swelling with complete resolution within 2 weeks (NY1)	92.6	61.5	100.0	89.1	63.9	83.1	11.5	64.6
More than one attack of acute arthritis (ARAF1, ARAS1, MEX1, NL2)	95.6	76.9	100.0	93.5	58.8	78.9	3.85	59.4
Maximum inflammation developed within 1 day (ARAF2, ARAS2, MEX2, NL3)	80.9	84.6	80.0	83.7	50.5	57.7	30.8	51.0
Monoarthritis attack (ARAF3)	96.3	88.5	98.2	94.6	25.8	32.4	7.7	26.0
Oligoarthritis attack (ARAS3)	78.7	61.5	82.7	73.9	63.9	70.4	46.2	64.6
Mono and/or oligoarthritis attack (MEX3)	100.0	100.0	100.0	100.0	10.3	12.7	3.9	10.4
First MTP joint involvement (NY2, ARAF5, ARAS5, MEX4, NL5)	74.3	42.3	81.8	66.3	80.4	85.9	65.4	81.3
Unilateral first MTP joint attack (ARAF6, ARAS6)	69.1	34.6	77.3	62.0	85.6	91.5	69.2	86.5
Unilateral tarsal joint attack (ARAF7, ARAS7, MEX6)	14.7	15.4	14.5	15.2	95.9	97.2	92.3	95.8
Joint redness (ARAF4, ARAS4, MEX5, NL4)	89.0	80.8	90.9	85.9	49.5	50.7	46.2	50.0
Rapid response to colchicines (NY4)	30.1	26.9	30.9	26.1	84.5	83.1	88.5	84.4
Complete termination of an attack (ARAS11)	97.8	88.5	100.0	96.7	51.5	69.0	3.9	52.1
Tophus (proven or suspected) (RM3, NY3, ARAF8, ARAS8, MEX7, NL8)	32.4	15.4	36.4	0.0	99.0	100.0	96.2	100.0
Serum uric acid: $> 7 \text{ mg/dL}$ in men, $> 6 \text{ mg/dl}$ in women (RM2)	69.9	73.1	69.1	65.2	68.0	69.0	65.4	68.8
Hyperuricemia (ARAF9, ARAS9, MEX8)	73.5	76.9	72.7	69.6	71.1	70.4	73.1	71.9
Serum uric acid level > 5.88 mg/dl (NL7)	79.4	76.9	80.0	76.1	54.6	54.9	53.8	55.2
Male sex (NL1)	80.9	69.2	83.6	77.2	48.5	49.3	46.2	49.0
Hypertension or at least one cardiovascular disease (NL6)	83.1	80.8	83.6	80.4	37.1	42.3	23.1	37.5
Asymmetrical swelling within a joint on radiograph (ARAF10, ARAS10)	48.5	46.2	49.1	35.9	83.5	80.3	92.3	84.4
Subcortical cysts without erosions on radiograph (ARAF11)	30.1	26.9	30.9	25.0	82.5	83.1	80.8	83.3
Synovial fluid cultures negative for organisms (ARAF12)	100.0	100.0	100.0	100.0	10.3	11.1	8.3	10.3

TABLE 3. Sensitivity and Specificity of Individual Items From Existing Classification Criteria for Gout

Number after abbreviation refers to the item number of the corresponding criteria.

ARAF = American Rheumatism Association full criteria, ARAS = American Rheumatism Association survey criteria, MEX = Mexico criteria, NL = Netherlands criteria, NY = New York criteria, RM = Rome criteria.

Recently, Taylor et al evaluated performance of the 5 existing classification criteria for gout, based on the data of 983 patients worldwide.¹⁸ The sensitivity and specificity of the 5 criteria ranged from 77.6% to 95.3% and 49.5% to 78.4%, respectively. This study found similar sensitivity (from 75.7% to 97.1%) and specificity (from 68.0% to 84.5%) among the 5 existing criteria. It should be noted that 49 patients in Taylor's study received clinical diagnosis of gout without identifiable MSU crystals. These patients were included in the control group, which accounted for ~10% of the participants, and that might have had a negative effect on the specificity reported in their study.

There was no consensus on the disease duration in which early gout was defined. Based on the work of Taylor et al, ¹⁸ this study defined early disease as duration of 2 years or less from the first episode of arthritis. This study demonstrated high sensitivity in this subgroup of the Mexico criteria, which was similar to Taylor's report, ¹⁸ but the specificity was much higher (88.5% vs 66.3%). These differences were parallel to those observed in overall patients. Similar to Taylor's report, this study observed high sensitivity, but low specificity across all criteria in the subgroup of established disease. However, the results for the subgroup of established disease in that study were limited by the small number of nongout patients (110 gout and 26 nongout patients). The low specificity resulted from 22 of the 26 nongout patients having recurrent CPPD or BCP arthritis for >2 years, with clinical manifestations that closely resembled those of patients with established gout.

As the presence of tophus usually indicates chronicity in patients with gout, this study also determined performance of the classification criteria for gout in the subgroup of patients without tophus. The sensitivity and specificity across all criteria in nontophaceous patients were similar to those in the overall patients. This could be the result of relatively long disease duration for gout patients in this subgroup (4.7 years), despite excluding the patients with tophus.

In this study, no individual criterion had high sensitivity or specificity across all subgroups (Table 3). Disease duration clearly affected the specificity of an individual criterion. The longer the disease duration, the more likely nongout patients would develop clinical pictures similar to gout, thus fulfilling the classification criteria.

Authors, y	Rome	NY	ARAF	ARAS	MEX	NL	Comments
O'Sullivan JB, 1972 $(n = 22)^{13}$							
Sensitivity	81.8	63.6	_	_	_	_	
Specificity	_	_	_	_	_	_	
Wallace SL, 1977 $(n = 706)^{10}$							MSU crystal identification not performed in all patients
Sensitivity	_	_	87.6	84.8	_	_	· ·
Specificity	_	_	94.9	96.0	_	_	
Rigby AS, 1994 $(n = 820)^{14}$							MSU crystal identification not performed in all patients
Sensitivity	64.4	79.7	—	—	_	_	
Specificity	99.2	99.5	—	—	-	-	
Malik A, 2009 $(n=82)^{15}$							
Sensitivity	66.7	70.0	70.0	_	-	-	
Specificity	88.5	82.7	78.8	_	-	-	
Janssens HJ, 2010 $(n = 328)^{16}$							
Sensitivity	_	_	_	80.4	_	_	
Specificity	_	_	_	63.9	-	_	
Pelaez-Ballestas I, 2010 $(n = 549)^{11}$							MSU crystal identification not performed in all patients
Sensitivity	_	_	_	75.0	88.1	_	No control group
Specificity	-	-	_	_	-	-	•
Vazquez-Mellado J, 2012 $(n = 167)^{17}$						—	MSU crystal identification not performed in all patients
Sensitivity	-	-	_	_	97.3	-	1 1
Specificity	-	-	_	_	95.6	-	
Taylor WJ, 2014 $(n = 983)^{18}$							
Sensitivity	77.6	78.9	100.0^{*}	85.7	95.3	93.7	
Specificity	74.5	78.4	64.8*	68.1	49.5	60.7	
Current study $(n = 233)$							
Sensitivity	75.7	79.4	85.3	83.1	97.1	88.2	
Specificity	81.4	79.4	78.4	84.5	68.0	76.3	

TABLE 4. Sensitivity and Specificity of Existing Classification Criteria for Gout Reported in the Literature

Data presented in percentage.

ARAF = American Rheumatism Association full criteria, ARAS = American Rheumatism Association survey criteria, MEX = Mexico criteria, MSU = monosodium urate NL = Netherland criteria, NY = New York criteria.

* = patients could be classified as gout in the presence of monosodium urate crystals alone.

Using the presence of MSU crystals in SFs or tissue aspirates, as the gold standard to classify patients with gout, was the strength of this study. All SFs were examined by a certified rheumatologist, who had passed the crystal identification examination in the SUGAR study. The nongout population in this study also was specified clearly by clinical features together with the results of SF examination and appropriate laboratory tests. In addition, patient data collection, according to the predetermined questionnaire during an arthritis episode, ensured the reliability and completeness of the data. However, this study still had some limitations. A large difference in mean disease duration (8.8 vs 2.6 years) and proportion between gout and nongout patients presenting with their first arthritis episode (4.4% vs 57.7%) could create some discrepancy in clinical manifestations. Future study with a larger number of patients with early disease is needed, in order to reflect the population commonly seen in a primary care setting better.

Advanced imaging modalities such as joint ultrasonography and dual energy computed tomography (DECT) are likely to play a major role in future diagnosis and evaluation of gout patients.^{20–22} However, the tool for classifying gout in primary care must be both specific and easy to use. The existing classification criteria for gout are easily applied in clinical practice because they require mostly basic patient history, physical examination, and serum uric acid level. In a situation where MSU crystal identification is not available, the existing classification criteria for gout may still be useful.

At the time of preparing this manuscript, a new 2015 American College of Rheumatology and European League of Association for Rheumatology (ACR/EULAR) criteria for the classification of gout had been published.²³ In this new classification criteria, a summation of ≥ 8 from clinical, laboratory and imaging scores will be able to classify a patient as having gout. It has a sensitivity and specificity of 92.0% and 89.0%, respectively, with 85.0% and 78.0%, respectively, for the clinical only criteria. Advanced imaging modalities, including joint ultrasonography and dual energy computed tomography (DECT), play a major role in the diagnosis in this new classification criteria. In practice, the tool for classifying gout in a primary or an acute care setting must be both easy to use and specific. As a result, the use of advanced imaging modalities in these settings may not be clinically feasible.

The 5 existing classification criteria for gout tested in this study are easily applied in clinical practice because they require mostly basic patient history, physical examination, and serum uric acid level. In a situation where MSU crystal identification or advance imaging modalities is not available, these classification criteria for gout may still be useful. Nevertheless, evaluation of the performance of the newly published 2015 ACR/EULAR classification criteria for gout in Thai patients presenting with acute arthritis is planned for the near future.

CONCLUSIONS

The 5 existing classification criteria for gout had limited sensitivity and specificity in Thai patients presenting with acute arthritis. The limitation was pronounced mostly in the subgroup of established disease. From this study, the ARA survey criteria had consistently high sensitivity and specificity across all groups of patients. When crystal identification is unavailable, the ARA survey classification criteria are the most suitable for diagnosing gout in the Thai population.

ACKNOWLEDGMENTS

The authors thank all participants, including Mrs. Antika Wongthanee for her statistical assistance and Mrs. Waraporn Sukitawut and Mrs. Saowanee Pantana for their secretarial assistance.

REFERENCES

- 1. Roddy E, Doherty M. Epidemiology of gout. Arthritis Res Ther. 2010;12:223.
- Louthrenoo W, Sukitawut W. Calcium pyrophosphate dihydrate crystal deposition: a clinical and laboratory analysis of 91 Thai patients. J Med Assoc Thai. 1999;82:569–576.
- Canhao H, Fonseca JE, Leandro MJ, et al. Cross-sectional study of 50 patients with calcium pyrophosphate dihydrate crystal arthropathy. *Clin Rheumatol.* 2001;20:119–122.
- Margaretten ME, Kohlwes J, Moore D, et al. Does this adult patient have septic arthritis? JAMA. 2007;297:1478–1488.
- Chen LX, Schumacher HR. Current trends in crystal identification. Curr Opin Rheumatol. 2006;18:171–173.
- Pascual E, Sivera F, Andres M. Synovial fluid analysis for crystals. *Curr Opin Rheumatol.* 2011;23:161–169.
- Courtney P, Doherty M. Joint aspiration and injection and synovial fluid analysis. Best Pract Res Clin Rheumatol. 2013;27:137–169.
- Kellgren JH, Jeffery MR, Ball JF. The Epidemiology of Chronic Rheumatism. Oxford: Blackwell Scientific; 1963.
- Decker JL. Report from the subcommittee on diagnostic criteria for gout. In In: Bennett PH, Wood PHN, eds. *Population Studies of* the Rheumatic Diseases—Proceedings of the Third International

Symposium, New York, June 5–10, 1966. Population Studies of the Rheumatic Diseases—Proceedings of the Third International Symposium, New York, June 5–10, 1966 Amsterdam: Excerpta Medica Foundation; 1968:–387.

- Wallace SL, Robinson H, Masi AT, et al. Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum*. 1977;20:895–900.
- Pelaez-Ballestas I, Hernandez Cuevas C, Burgos-Vargas R, et al. Diagnosis of chronic gout: evaluating the American College of Rheumatology Proposal, European league against rheumatism recommendations, and clinical judgment. *J Rheumatol.* 2010;37:1743–1748.
- Janssens HJ, Fransen J, van de Lisdonk EH, et al. A diagnostic rule for acute gouty arthritis in primary care without joint fluid analysis. *Arch Intern Med.* 2010;170:1120–1126.
- O'Sullivan JB. Gout in a New England town. A prevalence study in Sudbury, Massachusetts. Ann Rheum Dis. 1972;31:166–169.
- Rigby AS, Wood PH. Serum uric acid levels and gout: what does this herald for the population? *Clin Exp Rheunatol.* 1994;12: 395–400.
- Malik A, Schumacher HR, Dinnella JE, et al. Clinical diagnostic criteria for gout: comparison with the gold standard of synovial fluid crystal analysis. J Clin Rheumatol. 2009;15:22–24.
- Janssens HJ, Janssen M, van de Lisdonk EH, et al. Limited validity of the American College of Rheumatology criteria for classifying patients with gout in primary care. *Ann Rheum Dis.* 2010;69: 1255–1256.
- Vazquez-Mellado J, Hernandez-Cuevas CB, Alvarez-Hernandez E, et al. The diagnostic value of the proposal for clinical gout diagnosis (CGD). *Clin Rheumatol.* 2012;31:429–434.
- Taylor WJ, Fransen J, Dalbeth N, et al. Performance of classification criteria for gout in early and established disease]. *Ann Rheum Dis.* 2014;75:178–182.
- Loeb JN. The influence of temperature on the solubility of monosodium urate. Arthritis Rheum. 1972;15:189–192.
- Ogdie A, Taylor WJ, Weatherall M, et al. Imaging modalities for the classification of gout: systematic literature review and metaanalysis. *Ann Rheum Dis.* 2015;74:1868–1874.
- Pascal Z, Valcov R, Fabreguet I, et al. A prospective evaluation of ultrasound as a diagnostic tool in acute microcrystalline arthritis. *Arthritis Res Ther.* 2015;17:188.
- Bongartz T, Glazebrook KN, Kavros SJ, et al. Dual-energy CT for the diagnosis of gout: an accuracy and diagnostic yield study. *Ann Rheum Dis.* 2015;74:1072–1077.
- Neogi T, Jansen TL, Dalbeth N, et al. 2015 Gout Classification Criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheumatol.* 2015;67:2557–2568.