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EDITORIAL

The American College of Physicians and the 2017 guideline for the management of acute and recurrent gout: treat to avoiding symptoms versus treat to target

Tim L. Jansen[1] · **Matthijs Janssen**[1]

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Gout is the most common type of arthritis worldwide, and its prevalence varies between 1 and 4% in adults. The prevalence of gout is quite similar to diabetes mellitus. Both of these common disorders clearly deserve our combined clinical attention and our undivided approach. For diabetes, a cooperative effort during the last decades between general practitioners (GP) and general internists produced an effective network in most countries improving the care for diabetics significantly. For gout, a specific effective network between GPs and rheumatologists is lacking.

Gout may become a great bleeder for individual sufferers regarding personally loss of experienced quality of life due to pain, absenteeism from work, skeletal destructions, and ischemic cardiovascular sequelae. These sequelae in gout all bear a serious impact on the financial situation at an individual's level as well as macroeconomically [1]. So an efficient diagnostic and therapeutic phase is really needed for the sake of all our gout patients and for the sake of our societies [2]. Here clearly lies a challenge for us, rheumatologists in cooperation with GPs, for the upcoming years.

Gout is rather well understood pathobiologically as it is a disorder with on the one hand an autoinflammatory syndrome due to an activated inflammasome, and on the other hand, dysmetabolism characterized by a positive urate balance leading to hyperuricemia and articular as well as extra-articular crystallization and chronic subinflammation. Incidentally, this results in a fulminant exacerbation of a classical gout flare. Since 1964, gout was supposed to be an easy medical problem to deal with, as allopurinol became available worldwide. However, things changed. A significant percentage of gout patients does not tolerate allopurinol, which becomes numerically relevant in a growing number of gout patients worldwide; secondly, there are many ways that severe inflammatory gout patients may be presented to us and clearly this complicates an efficient approach as well: patients may be presented to GPs, to internists, First Aid physicians, orthopedic surgeons, general surgeons, and last but not least to rheumatologists. This underscores the need for an efficient network to clear the problems that the gout patients pose to us. A starter for improvement in gout care is a powerful guideline made by primary care physicians and when done so, a need for physicians committing to these guidelines. So, firstly, our compliments for the great efforts by the American College of Physicians (ACP) to fill in the unmet need and update their clinical practice guideline on gout, see Table 1 for a short recapitulation [3–5].

There is some discrepancy between the ACP guidelines and the rheumatologic (ACR/EULAR) guidelines on gout [5, 6]. Partly, this discrepancy can be explained by the predominant picture of gout one has: is gout to be considered a disorder with acute incapacitating attacks, or is it a chronic condition of urate dysmetabolism? For many physicians, it is quite logical to consider gout predominantly as an arthritic attack, such as is done by the ACP. For many rheumatologists, who treat predominantly chronic inflammatory conditions, gout is considered a recurrent autoinflammatory condition with a chronic urate dysmetabolism as driver. This different mindset leads to a

✉ Tim L. Jansen
tjansen@VieCuri.nl

[1] Department of Rheumatology, VieCuri Medical Center, Venlo, The Netherlands

Table 1 ACP core recommendations (recs)

1	ACP recommends that clinicians use synovial fluid analysis when clinical judgment indicates that diagnostic testing is necessary in patients with possible acute gout	Note: 1-not in classical situations with MTP1 involvement 2-to be considered if clinical situation is ambiguous and/or infection is possible
2	ACP recommends that clinicians choose *glucocorticoids/ nonsteroidals/colchicine* to treat patients with acute gout	
3	ACP recommends that clinicians *use low-dose* colchicine when using colchicine to treat acute gout	Note: 1.2 mg colchicine and followed by 0.6 mg after 1 h
4	ACP recommends *against* initiating long-term urate lowering treatment (ULT) in most patients after a first gout attacks or in patients with infrequent attacks	Note: benefits over 12 months duration of ULT have not been studied in patients with single/ infrequent gout attacks
5	ACP recommends that clinicians *discuss* benefits, harms, costs and individual preferences *with patients* before initiating ULT, including concomitant prophylaxis, in patients with recurrent gout attacks	Note: some patients have no or few attacks over many years

ULT urate lowering treatment

different set of recommendations, for a recapitulation see Table 2.

The diagnostic phase of gout

Some controversy has risen on issues within the diagnostic phase, but all agree on one issue: *synovial fluid analysis* is pivotal in cases where clinical judgment indicates that diagnostic testing is necessary whenever a possible gout patient with "clinical ambiguity" is met. This ambiguity reflects to the setting of the potential threat of a septic arthritis, versus a non-tricky situation of inflammatory osteoarthritis, rheumatoid arthritis, or calcium pyrophosphate (CPP) arthritis. Microscopical evaluation of synovial fluid is the gold standard once monosodium urate crystals are seen, but is not 100% perfect, particularly if no crystals are found in the acute phase: ill identifications occurs with false negatives due to ill recognition/microscopisation, or false positives due to artifacts [7]. Further aids for the clinician have been made by the rheumatological societies with updated gout classification criteria, or by GPs in cooperation with a rheumatology centre with a simplified gout calculator [8, 9], the latter being specifically

Table 2 EULAR core recommendations (recs)

Recs		
1	Patients be fully informed on pathophysiology/treatments/ comorbidities/acute attack managing/elimination of urate crystals and lifelong treatment Patients be advised on lifestyle such as regular exercise and weight loss if appropriate/ avoidance of beers/spirits/ heavy meals/excessive intake meat/seafood Patients be screened for associated comorbidities and cardio vascular risk factors/renal impairment	Overarching principles
2	Treat as early as possible Patients should be educated to self-medicate Drug choice should be based on contraindications Consider: colchicine/NSAIDs/ corticosteroid or IL1 blocker	Acute gout management
3	Urate lowering treatment should be adjusted to achieve the uricemia target, should be considered from the first presentation; should aim at <6 mg/dL but even 5 mg/dL to facilitate faster dissolution of crystals in severe gout (tophi/chronic arthropathy/ frequent attacks) Consider: allopurinol or febuxostat monotherapy or benzbromarone monotherapy or add-on therapy with production inhibitor (XOi type) plus a uricosuric	Chronic gout management

XOi xanthine oxidase inhibitor

meant for GPs. One could use the calculator in situations where an arthritis debutes with subdiagnostic scoring on the calculator (below 8 points) as then there is a potential reason for specialist referral. This works best only when a regional network is effective. This may be seen as an essential pillar for effective gout care.

The treatment phase of gout

More interesting is the dispute on the serum urate concentration to be targeted or not to be targeted at all. In hypercholesterolemia as well as in diabetes, all internists know their target. Why not aim for a reasonable serum urate target in gout, which has been shown to be the surrogate marker for most if

Table 3 Concordance between ACP and rheumatologic communities

1	Organize local network to enable a correct diagnosis in acute situations
2	Start inhibitors of auto-inflammation as soon as possible (ASAP)
3	Educate the patient to optimize metabolism from the first attack
4	Initiate available urate lowering treatment (ULT) in
	- cases with a high recurrence risk
	- cases with inappropriate low urate clearance
	As an add-on with prophylaxis for a predefined time period
5	Do not give lifelong therapies if not needed: reconsider your indication of ongoing urate lowering treatment (ULT) at least every 1–5 years

not all outcomes in this patient population? Many papers have discussed the effects of effective treatment (lower serum urate) versus less effective treatment (higher serum urate), and many outcome parameters including outcomes on costs and expenses have been studied. Within the rheumatologist societies, there is some discussion on the exact level of serum urate: should it be 5 mg/dL (=300mcM/L) according to the British, or should it be 6 mg/dL (=360mcM/L) according to the American College of Rheumatology (ACR); the European task force of EULAR formulated a recommendation in between. One could also just treat to the absence of clinical attacks over a predefined time period, a so-called Treat-to-Avoid-Symptoms. There is not much literature on these types of relentless vs pro-active treatment. We clearly need studies to find the best strategy regarding: *treating to (biochemical) target*, i.e., 6 mg/dL (=360mcM/L) (T2T), or perhaps even 5 mg/dL (=300mcM/L) versus Treat-to-Avoid-Symptoms (T2AS). Such studies should be done in both populations of GPs as well as in populations with selection bias that rheumatologists are commonly treating.

Richette et al. previously subdivided gout patients into five distinctive groups [10].: cluster analysis showed a cluster 1 consisting of isolated gout without comorbidity (12%), cluster 2 gout with obesity and often with hypertension (17%), cluster 3 gout in type 2 DM (24%), cluster 4 dyslipidemia in gout (28%), and cluster 5 gout with diuretics and with CardioVascular Disease (18%). Some clusters may be treated more frequently by GPs whereas others may be treated predominantly by cardiologists/internists/rheumatologists. As clinicians, we must realize that we all are biased as we see only a proportion of the whole spectrum of gout patients and that this patient profile may be an important determinant for the outcomes and also for the optimal therapeutic approach [10, 11].

What is the major issue we can learn from these ACP guidelines?

As rheumatologists, we may agree that the ACP may be quite right regarding the approach for patients in cluster 1. The ACP guidelines may not alter significantly the current approach of GPs but they do show that the literature is not as convincing as we, rheumatologists, thought, particularly not on robust clinical endpoints in all the abovementioned patient clusters. Committing to the current ACP guidelines will not result into a T2T approach of GPs. The ACP Guidelines challenge GPs and rheumatologists to study the T2T and theT2AS approaches for safety and (cost-)effectiveness in different subgroups.

The rheumatology community should read and study these ACP guidelines that really point to significant weaknesses. And the rheumatological community has to start empowering networks with GPs to improve the position of all our gout patients, similar as has been done for diabetics before in order to achieve success in over 80% of our gout patients [12]. Leading herein are the following points of concordance, see Table 3.

Compliance with ethical standards

Disclosures None.

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