Reviewer's report

Title: Impact of comorbidities on gout and hyperuricaemia: an update on prevalence and treatment options

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Reviewer: Michael Pillinger

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In this manuscript, Bardin and Richette attempt to digest and summarize a large topic: the interaction between gout and its co-morbidities. This is a challenging topic, both because of the scope of the available data and because in spite of that data, large and important questions remain unanswered, not only about pathophysiology and epidemiology, but about causality and the impact of urate management.

Overall, they do an estimable job. The manuscript is at once condensed but inclusive, and in general, extremely readable.

I have only two minor comments.

The first is that while the authors do a very good job distinguishing between the impacts of hyperuricemia per se and gout, their approach may give a bit of short shrift to the impact of inflammation, in the gouty setting, on comorbid risk or response. This is a bit surprising given the extensive literature on inflammation and vascular disease in general, and on inflammation in rheumatic diseases and its impact on cardiovascular and cerebrovascular disease. They may want to consider addressing this topic a bit more broadly and explicitly.

My second comment is more picayune. Under the section "Hyperuricemia and cardiovascular and renal diseases," we find the sentences,

"Allopurinol was once claimed to protect the kidneys, which led to the hypothesis that hyperuricemia was the cause of renal dysfunction. Genetic studies have now established that the disease has a renal origin, first translating into hyperuricemia, but due to a number of genetic variants, of the uromodulin or hepatocyte-nuclear factor 1 b genes".
This language conveys the clear impression that allopurinol does not protect the kidneys, which may in this context be a reasonable statement. However, later the authors present a more mixed conclusion in the paragraph that begins, "Causality can also be addressed by studying the effect of drugs." In that paragraph, the authors mention that some studies support a renoprotective effect of urate lowering. Thus, the authors may want to make sure that these two discussions do not create any ambiguity for the general reader.

Finally, in discussing cardiovascular disease, the authors may wish to consider including a report potentially linking gout with aortic stenosis. (Chang et al, Am J Med 2017).

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