

Co-Morbidities and Treatment of Gout

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IMPACT PARAGRAPH

This chapter focusses on the societal, scientific and clinical implications of this thesis. Overall, the thesis addressed research gaps in improving quality of care for patients with gout. First, we summarized the literature on efficacy of different types of drugs to treat acute gout flares. We did not find clear difference in efficacy nor safety. Second, we compared outcomes of applying different targets when starting urate-acid lowering therapy (ULT) in gout patients. We revealed that the strategy treating towards a specific serum Uric Acid (sUA) did not result in a statistically significant difference in the number of flares, nor in the achievement of the recommended sUA target, when compared to a patient-centred strategy integrating patient education and a shared decision about adjusting ULT. However, the treat to sUA strategy required more treatment intensifications. Finally, in a literature review and two new cohort studies, we could not find a causal relationship between gout and several co-morbidities. We mainly showed that the strong associations are explained by shared risk factors.

Impact for research

All manuscripts have been published in peer reviewed journals. In addition, our Cochrane Review "NSAIDs for acute gout" was summarized in JAMA as a Clinical Evidence Synopsis following its publication in the Cochrane Database of Systematic Reviews. Results of several articles were presented at national and international meetings.

In our strategy study, the treat to sUA strategy had no undisputable advantages. On this line, treat to target in gout, was selected as one of the II eleven knowledge gaps at the 2019 Research Agenda of the Dutch Society of Rheumatology. Recently, a consortium of three centers – including ours - initiated a randomized-controlled trial to assess cost-effectiveness, of a strict uric acid targeted strategy versus a symptom-controlled approach, hoping to finally resolve this issue.

Despite cumulating epidemiological evidence that hyperuricaemia and gout have no strong causal role in onset or course of comorbidities, some experimental studies cannot be ruled out that causal relationship exists in subgroups of patients. This is relevant, as it would have clinical implications when treating gout patients. Answering those research questions is complex, and requires the long-term data that allow matching of data of persons with treatment according to the different strategies (counterfactual principle). Research in this thesis highlights the need to establish a network of clinician researchers that collect data in clinical practice in an uniform manner, following the earlier mentioned FAIR principles. To improve the value of such real world data, researchers have to agree on a well-defined set of outcomes (benefits and harms) as well as contextual factors (e,g. comorbidities, treatments). Without correctly collected data and well-defined research questions, it is impossible to evaluate the value of care innovations.

Impact for patients

Patients rank control of flares as the most relevant outcome of treatment. Evidence from our studies can reassure patients that the available drug types for treating acute flares are equally effective and safe. Of note, physicians still have to account for comorbidities that preclude the use of certain drug classes in subgroups of patients. Our Cochrane review served as scientific support for the formulation of the European Alliance of Rheumatology recommendation for the treatment of acute gout flares. To prevent (recurrent) flares, urate-lowering therapy can be started or should at least be discussed after a first flare with each patient. In view of the ongoing discussion about the preferred target when treating with ULT, patients should be more involved in decisions to start and intensify ULT, so that the final treatment choice also accounts for the patients' preferences and values. For this reason, we have been developing a decision aid to support patients and their healthcare provider in choosing the best treatment option for the patient, based on available evidence.

Impact for Society

Our observational studies and literature review on comorbidity underlined the importance of lifestyle and especially obesity in the relationship between gout and comorbidity. The obesity epidemic faced by industrialized countries, demands a behavioral change of medical specialists involved in treatment of gout: instead of treating a disease, we should emphasize more the impact of lifestyle on health and motivate the patient to change its behavior. For this reason, we highlighted the role of lifestyle in our ULT decision aid and the ULT adherence tool we developed, as lifestyle – and especially weight control - is a corner stone in the management of our patients, not only to control gout flares but to prevent other comorbidities. Obesity should be recognized as a societal problem and should be addressed as such by policy makers and health insurers.

The association of gout and comorbidity but also the increasing number of patients with gout underlines the importance of collaboration between different specialties but also between the first- and the second-line. Policy makers should stimulate but also facilitate such collaborations between healthcare providers and various researchers.