Re: To Treat or Not to Treat? Effect of Urate-Lowering Therapy on Renal Function, Blood Pressure and Safety in Patients with Asymptomatic Hyperuricemia

To the Editor: Tien et al conducted a network meta-analysis to investigate the effects of different urate-lowering therapies on serum uric acid level, renal function, blood pressure, and safety in patients with asymptomatic hyperuricemia.[1] Regarding safety information, allopurinol had an advantage of reno-protective effect, and febuxostat had a significant impact in lowering diastolic blood pressure. I present additional information on the safety of urate-lowering therapies. Gao et al conducted a meta-analysis to summarize the cardiovascular safety of febuxostat for the treatment of gout,[2] and the pooled odds ratios (95% confidence intervals [CI]) of febuxostat compared with allopurinol for the composite of urgent coronary revascularization and stroke were 0.84 (95% CI: 0.77–0.90) and 0.87 (95% CI: 0.79–0.97). I think that there is an advantage to avoiding cardiovascular side effects by using febuxostat instead of allopurinol. Tien et al handled patients with asymptomatic hyperuricemia, which may relate to the safety of urate-lowering therapies. By the way, there are 2 important clinical trials to compare the safety of allopurinol and febuxostat: "CARES trial" and "FAST trial."[3,4] Choi et al precisely compared 2 studies and concluded that "FAST trial" can be accepted by keeping internal consistency with high rates of follow-up.[5] Fundamentally, there are big differences in the cardiovascular disease (CVD) comorbidities of the target gout patients in 2 trials. Patients with major CVDs within the past 6 months at baseline were excluded in the "FAST trial," and the same exclusion was conducted within the past 60 days at baseline in "CARES trial." Both trials present important information regarding the safety of gout pharmacotherapy, respectively. I think that mortality risk in gout patients with severe CVDs should be conferred to outcomes from "CARES trial," although internal inconsistency exists. In contrast, mortality risk in gout patients with mild-to-moderate CVDs should be conferred to outcomes from the "FAST trial." As there is limited information regarding the safety of urate-lowering therapies in patients with asymptomatic hyperuricemia, more randomized controlled trials should be conducted to specify the risk of pharmacotherapy with special reference to asymptomatic hyperuricemia.

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Response: Re: To Treat or Not to Treat? Effect of Urate-Lowering Therapy on Renal Function, Blood Pressure and Safety in Patients with Asymptomatic Hyperuricemia

To the Editor: We would like to thank Dr. Kawada for his interest in our article. He mentioned the meta-analysis by Gao et al, in which a better safety outcome for febuxostat compared with allopurinol was observed in gout patients in terms of urgent coronary revascularization and stroke.[1] In our network meta-analysis (NMA),[2] trials reporting cardiovascular events all used febuxostat as the treatment, so we could not compare its cardiovascular effect to allopurinol in patients with asymptomatic hyperuricemia. Besides, the cardiovascular events in our analysis included several types of cardiovascular diseases, such as heart failure and non-fatal myocardial infarction. Our study, nevertheless, found that patients using febuxostat had significantly lower diastolic blood pressure than those using placebo, indicating that febuxostat has a cardiovascular protective effect. Similar effects on diastolic blood pressure were not observed in the allopurinol group. We need more randomized controlled trials to clarify this issue.

The safety comparison between allopurinol and febuxostat continues to attract attention. The Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities

(CARES) trial and The Febuxostat versus Allopurinol Streamlined Trial (FAST) are 2 important trials on this issue. However, the CARES trial found increased all-cause mortality and risk of death from cardiovascular causes in gout patients using febuxostat than those using allopurinol. In contrast, the FAST trial demonstrated no increased risk of composite cardiovascular events, cardiovascular disease mortality, or all-cause mortality in gout patients with febuxostat compared with those with allopurinol.[3,4] There are notable differences between these 2 studies: CARES trial recruited patients with a history of major cardiovascular disease; they were likely to have a higher risk of cardiovascular disease during the follow-up than patients in the FAST trial, in which only about one-third had previous major cardiovascular comorbidity. FAST only recruited patients who were already under urate-lowering therapy and might have a lower urate crystal burden, which may relate to a lower cardiovascular risk. As our NMA focused on patients with asymptomatic hyperuricemia, we consider that they may have a lower risk of cardiovascular diseases than symptomatic patients. Consequently, our results may be supplemented by the FAST trial, which reported no association between the long-term use of febuxostat and an increased risk of death or serious cardiovascular events compared with those with allopurinol in asymptomatic patients. However, more randomized controlled trials focusing on asymptomatic hyperuricemia patients are required to provide more evidence on this safety issue.

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Re: Use of Point-of-Care Ultrasonography in Primary Care to Redress Health Inequities

To the Editor: I highly commend the strong take on point-of-care ultrasonography (POCUS) and its attributes in primary care. In the article, POCUS was highlighted for its ability to address health care disparities by enhancing a physician's ability to screen, diagnose, and safely perform procedures in patients who otherwise would not have received that level of care.[5] Imaging is often thought of as the ultimate objective measurement of a patient, defying bias, race, ethnicity, or sexuality and being safe from the disparities that challenge our system. POCUS has the potential to help our skills as diagnosticians, but the multifactorial nature of health disparities demands that we determine whether we have fully addressed the cause of these health disparities in our POCUS physicians.

Health disparities can be defined as differences among specific population groups that affect the attainment of one's full health potential.[2] These disparities can be measured in differences in incidence, prevalence, mortality, the burden of disease, and other adverse health conditions.[1] In the United States, racial/ethnic minority groups are at disproportionate risks of being uninsured, lacking access to care, and experiencing worse health outcomes from preventable and treatable conditions.[2] Furthermore, emergency departments have been plagued by evidence that diagnostic imaging examination orders differ significantly by patient race and ethnicity, commonly known as implicit bias.[4]

POCUS is a powerful tool regarding diagnosis, but implicit bias and subjectivity of perception with minority populations are still prevalent in our health care system.[1] Point of care examinations requires clinical judgment and interpretation of images to determine diagnosis and intervention.[5] There is no evidence that POCUS physicians are not subject to the same bias and subjectivity plaguing our health care system. Until we can address this issue, the benefits from POCUS could still be limited to nonminority populations.

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Response: Re: Use of Point-of-Care Ultrasonography in Primary Care to Redress Health Inequities

To the Editor: I thank Dr. Pierre for his thoughtful engagement with my commentary. He raises the concern that POCUS may not benefit racial/ethnic minority groups due to the implicit bias of clinicians using the technology. He substantiates this concern by citing a study that found that the likelihood of a clinician ordering diagnostic imaging differed by patient race and ethnicity in an emergency departmentsetting. Dr. Pierre's concern acutely reminds POCUS practitioners of the user-dependent nature of the technology. Training and policies that mitigate implicit bias will help ensure all patients maximally experience the benefits of POCUS.

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