

REPLY TO: Serum Uric Acid Still Carries Controversies About Its Role in Endothelial Dysfunction

To the Editor:

Cağar and colleagues suggest that the role of uric acid in endothelial dysfunction and hypertension remains controversial.¹ We agree that the causal role of uric acid remains to be shown in large clinical studies, but short-term pilot studies do suggest that lowering uric acid can reduce blood pressure in hypertensive patients.^{1–3} Likewise, an elevated uric acid strongly predicts the development of hypertension.⁴ Our study also shows a strong relationship between uric acid and type of blood pressure, in this case, the nondipper type.⁵ These studies do not suggest that a patient with an elevated serum uric acid level must have hypertension, or that a patient with a low uric acid level will not have hypertension, as the mechanism by which uric acid is proposed to work involves the induction of oxidative stress and endothelial dysfunction, and there are many variables that can influence these conditions.

While there are small pilot studies that have reported that gout and/or hyperuricemia are not associated with endothelial dysfunction or cardiovascular risk,⁶ these are at odds with 100-year-old literature.⁷ Numerous studies have shown that an elevated serum uric acid level is associated with endothelial dysfunction and that lowering uric acid, especially with allopurinol, can improve endothelial function (reviewed in our paper).⁸ One study did report improvement in endothelial function with xanthine oxidase inhibitors and not with uricosuric agents, suggesting that it was not the uric acid that was responsible for causing the endothelial dysfunction.⁹ While this explanation is possible, it may also relate to the superior ability of xanthine oxidase inhibitors to block uric acid synthesis and thus lower intracellular uric acid, which is responsible for reducing nitric oxide bioavailability. In the clinical trial, probenecid and allopurinol both lowered blood pressure in prehypertensive adolescents, but allopurinol was slightly superior.²

We agree with Cağar and his colleagues that more studies are needed to elucidate the role of uric acid in hypertension; however, our current study provides new information that strengthens the relationship of uric acid with hypertension, and, in this case, with the nondipping form.

Mehmet Kanbay, MD;¹ Osman Turak, MD;²
Richard J. Johnson, MD³

¹From the Department of Medicine, Division of Nephrology, Medeniyet University School of Medicine, Istanbul, Turkey; ²Department of Cardiology, Türkiye Yüksek İhtisas Education and Research Hospital, Ankara, Turkey; ³Division of Renal Diseases and Hypertension, University of Colorado, Denver, CO

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