Is diabetes still a compelling indication for renin-angiotensin-aldosterone system inhibitors?

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TO THE EDITOR: The recent review by Momoniat et al, "ACE inhibitors and ARBs: Managing potassium and renal function," provides a thorough overview of these important medication classes.[1] The authors state, "In general, a renin-angiotensin-aldosterone system inhibitor is recommended if the patient has diabetes; stage 1, 2, or 3 chronic kidney disease; or proteinuria." The sentence suggests that patients with diabetes alone, even without nephropathy, are to receive renin-angiotensin-aldosterone system inhibitors.

We take issue with this statement. The current literature no longer supports the notion that diabetes mellitus is a compelling indication for use of renin-angiotensin-aldosterone system blockers in the absence of associated nephropathy. In a systematic review and meta-analysis of 19 randomized controlled trials that enrolled 25,414 participants with diabetes for a total of 95,910 patient-years of follow-up, we demonstrated that inhibitors of the renin-angiotensin-aldosterone system were not superior to other antihypertensive drug classes in patients with diabetes.[2] Specifically, renin-angiotensin-aldosterone system blockers were not superior to thiazides, calcium channel blockers, or beta-blockers at reducing the risk of hard cardiovascular and renal end points.[2] Current guidelines from the American Diabetes Association,[3] European Society of Cardiology,[4] and Joint National Committee[5] also do not give preference to these drug classes in patients with diabetes without nephropathy.

Perhaps the word "diabetes" could be removed in the above-referenced sentence. Furthermore, heart failure with reduced ejection fraction could be added to the list of conditions that are indications for inhibition of the renin-angiotensin-aldosterone system irrespective of initial blood pressure level.

ROBERT FAKHERI, MD
Weill Cornell Medicine
New York, NY

SRIPAL BANGALORE, MD
NYU Langone Medical Center
New York, NY

FRANZ MESSERLI, MD
University of Bern, Switzerland
Mount Sinai Icahn School of Medicine,
New York, NY
Jagiellonian University Krakow, Poland

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IN REPLY: We would like to thank Dr. Fakheri and colleagues for their extremely helpful comments on our recent review of angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs).[1] We agree entirely with their suggestion on the lack of current data on any superiority of ACE inhibitors or ARBs in patients with diabetes without proteinuria and diabetes with "normal" renal function.[2,3] As mentioned, the sentence perhaps lacks clarity.

In the United Kingdom, ACE inhibitors and ARBs are commonly prescribed for diabetic microalbuminuria, proteinuric renal disease, and hypertension, as well as after myocardial infarction and in heart failure.[4] We therefore also concur that heart failure with reduced ejection fraction could be added

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to the list of conditions that are indications for inhibition of the renin-angiotensin-aldosterone system irrespective of the initial blood pressure level.

Interestingly, chronic kidney disease is associated with significantly increased risk of cardiovascular disease and cardiovascular death.[5,6] Studies of patients with chronic kidney disease have noted an increased relative risk of coronary heart disease, heart failure, and stroke compared with those without chronic kidney disease.[7,8] We recognize that additional randomized controlled studies and a better understanding of these differences in risk are required to guide optimal therapy and improve outcomes, and we wonder if ACE inhibitors and ARBs might be useful in this high-risk population even before proteinuria is established, as alluded in the heart failure group.

Finally, although the data are not available, we wonder if over a longer period of follow-up, one may in the future see a benefit from reduced intraglomerular hyperfiltration, but we concede this is mere speculation, and more recent data have challenged the hyperfiltration model of renal damage.

SUNIL BHANDARI, MBChB, FRCP, PhD, M Clin Edu, FHEA
Hull University Teaching Hospitals
United Kingdom

TASNIM MOMONIAT, MBChB, MRCP (UK)
Hull University Teaching Hospitals
United Kingdom

DUHA ILYAS, MBBS, MRCP (UK)
Hull University Teaching Hospitals
United Kingdom

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