Tissue Inhibition of Angiotensin-Converting Enzyme Activity Stimulates Angiogenesis In Vivo: A Potential Downside

To the Editor:

The study by Fabre et al.,1 which demonstrates that tissue inhibition of angiotensin-converting enzyme (ACE) activity stimulates angiogenesis in the rabbit model of hindlimb ischemia, has profound implications that require investigation. Specifically, should ACE inhibitors be contraindicated in individuals with cancer?

In the study, quinaprilat, an ACE inhibitor with high tissue affinity, promoted angiogenesis as potently as recombinant human vascular endothelial growth factor. Captopril, an ACE inhibitor with low tissue affinity, did not promote angiogenesis.

The proposed mechanism for angiogenesis promotion with ACE inhibition involves the increased availability of endothelial cell nitric oxide, a molecule critical for the mitogenic effect of vascular endothelial growth factor on endothelial cells. Nitric oxide plays a critical role in tumor angiogenesis and spread in individuals with head and neck cancer. It is likely that nitric oxide is involved in the angiogenesis and metastasis of other malignancies as well.1,5

ACE inhibitors are widely used in the treatment of hypertension, congestive heart failure, and coronary artery disease. Studies of their efficacy and safety are typically done in patients without active malignancies. However, in clinical use, ACE inhibitors are given to patients with other comorbidities, including cancer.

It is imperative that the post-marketing surveillance of these drugs specifically looks for adverse outcomes in patients with cancer. Meanwhile, I will have reservations in prescribing ACE inhibitors, particularly those with high tissue affinity, to individuals with cancer.

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