Intrarenal Perfusion and Angiotensin II Levels Regulate In Vivo Angiotensin II Type 1 Receptor Imaging in the Kidney

To the Editor:

In the recent issue of Hypertension, Dr Szabo’s group used novel positron-emission tomographic (PET) \([^{11}C]KR31173\) imaging to study the regulation of intrarenal angiotensin II type 1 (AT1) receptor binding in a swine model of renal artery stenosis in vivo.1 In this study, AT1 receptor binding, as visualized by live \([^{11}C]KR31173\) imaging (L-159 884), was markedly increased in pig kidneys with renal artery stenosis, and pretreatment of the animals with the ACE inhibitor lisinopril for 2 weeks did not alter AT1 receptor binding in vivo.1 The authors interpreted these results as that reduced renal perfusion attributable to renal artery stenosis increases AT1 receptor binding in vivo and that lisinopril should abolish this increase in AT1 receptor binding. The authors further suggest that live PET \([^{11}C]KR31173\) imaging may be a diagnostic biomarker for patients with renovascular disease.

However, renal artery stenosis is well-recognized to increase circulating and intrarenal Ang II levels, which may lead to the downregulation of vascular and intrarenal AT1 receptors.2 Increased \([^{11}C]KR31173\) levels in pig kidneys with stenosis were likely attributable to delayed clearance or increased intrarenal accumulation (or retention) of \([^{11}C]KR31173\), because tissue- or cell-bound and free \([^{11}C]KR31173\) could not be separated before live imaging in the study.1 Indeed, marked decreases in \([^{11}C]KR31173\) levels were clearly observed at 2 minutes, which were followed by marked increases in \([^{11}C]KR31173\) accumulation in the kidneys with stenosis at 30 minutes after injection of the radioligand. By contrast, most injected \([^{11}C]KR31173\) already disappeared from normal kidneys and contralateral kidneys at 30 minutes.1 These images were consistent with >70% reductions in intrarenal perfusion in the kidneys with renal artery stenosis compared with contralateral kidneys.

The finding that long-term lisinopril treatment did not alter intrarenal AT1 receptor binding in pig kidneys with stenosis suggests that angiotensin I–converting enzyme (ACE) might not be adequately inhibited in this study.1 It would be interesting to determine whether plasma renin activities (or concentrations) and circulating and intrarenal Ang II levels in these pigs were altered by long-term lisinopril treatment. These investigators have indeed nicely showed that intrarenal AT1 receptor binding was inversely related to Ang II in dogs treated with high- or low-salt diet.3 We also previously showed that increased renal perfusion by sodium nitroprusside decreased, whereas the ACE inhibitor perindopril increased, intrarenal AT1 receptor binding in rats in vivo.4 Long-term ACE inhibition with captopril also increased receptor-mediated intracellular uptake of \([^{125}I]\)-Val5-Ang II in mice in part because of the upregulation of intrarenal AT1 receptors.5 Thus, long-term lisinopril treatment should increase rather than abolish intrarenal AT1 receptor binding in vivo, as suggested by this study.1

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Disclosures

None.

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