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Endothelium-Dependent and -Independent Vascular Function in Advanced Chronic Kidney Disease

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Abstract

Background and objectives CKD is associated with increased cardiovascular risk not fully attributable to traditional risk factors. We compared endothelium-dependent and -independent vascular function among individuals with advanced CKD with function in those with vascular disease but preserved kidney function.

Design, setting, participants, & measurements Matched cohort analysis randomly selected from 1259 participants at a single center with measurements of brachial artery flow-mediated dilation, an endothelium-dependent process, and nitroglycerin-mediated dilation, an endothelium-independent process. Patients with advanced CKD ($n=70$) were matched 1:1 to controls with preserved kidney function and (1) no overt vascular disease, (2) hypertension, and (3) coronary artery disease.

Results The trend toward lower flow-mediated dilation (mean \pm SEM) in advanced CKD ($5.4\pm 0.5\%$) compared with no overt vascular disease ($7.3\pm 0.6\%$), hypertension ($6.2\pm 0.5\%$), and coronary artery disease ($5.8\pm 0.5\%$) did not reach statistical significance in adjusted analyses ($P=0.05$). Nitroglycerin-mediated dilation was lower in advanced CKD compared with in the other groups (adjusted nitroglycerin-mediated dilation: $6.9\pm 0.8\%$, $11.8\pm 0.9\%$, $11.0\pm 0.7\%$, and $10.5\pm 0.7\%$ in advanced CKD, no overt vascular disease, hypertension, and coronary artery disease groups, respectively; $P<0.001$). Using tertiles generated from the full cohort and no overt vascular disease as the reference, the adjusted odds of flow-mediated dilation falling within the lowest tertile was higher in both the advanced CKD (odds ratio, 4.84; 95% confidence interval, 2.09 to 11.25) and coronary artery disease (odds ratio, 4.17; 95% confidence interval, 1.76 to 9.87) groups. In contrast, the adjusted odds of lowest tertile nitroglycerin-mediated dilation was higher in advanced CKD (odds ratio, 24.25; 95% confidence interval, 7.16 to 82.13) but not in the hypertension (odds ratio, 0.79; 95% confidence interval, 0.23 to 2.77) or coronary artery disease (odds ratio, 2.34; 95% confidence interval, 0.74 to 7.40) group.

Conclusions Impairment in endothelium-dependent vascular function is present in patients with CKD and those with clinically evident vascular disease but preserved kidney function. In contrast, substantial reduction in endothelium-independent function was observed only in the CKD group, suggesting differences in severity and pathophysiology of vascular dysfunction between CKD and other disease states.

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