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Editorial Focus: An ACE Inhibitor Improves Vascular Outcomes in a PKD Model

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An ACE inhibitor improves vascular outcomes in a PKD model

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CARDIOVASCULAR COMPLICATIONS are the most common cause of death in patients with polycystic kidney disease (PKD). Within the context of clinical practice, two possible theories have been reviewed that could help describe the pathogenesis of vascular complications in PKD (7). *Theory 1* points to inherent vascular dysfunctions in solitary cilia as the primary cause of the vascular complications. It has been shown that endothelial cells lining the blood vessels possess primary cilia. In PKD, these primary cilia fail to trigger a biochemical cascade in producing vasodilator nitric oxide (NO) (4, 8), leading to abnormal thickening of the blood vessels (3). Consistent with this view, the plasma concentration of NO is reduced in PKD patients, confirming an association between PKD and endothelial dysfunction (10, 11).

Theory 2 brings about the cystic kidney itself as the origin of vascular complications. The enlarging renal cysts cause structural damage in the nephrons, which leads to distortion of the renal architecture. This distortion compresses the renal vasculature and attenuates the renal vessels, resulting in intrarenal ischemia and activation of the renin-angiotensin-aldosterone system (RAAS). Thus, as cysts enlarge, the RAAS is activated (5), which is known to cause cardiovascular remodeling. Not surprisingly, the angiotensin-converting enzyme inhibitor (ACE-I) and/or the angiotensin receptor blocker (ARB) have remained attractive clinical strategies in managing PKD patients (6).

The most recent work by Phillips et al. (9) in an issue of the *American Journal of Physiology-Renal Physiology* showed that the ACE-I perindopril was beneficial in maintaining proper vascular structure and function in PKD rats. The structural and functional indices of the blood vessels were assessed from the measurements of blood pressure and arterial stiffness in vivo followed by an analysis of calcification and structural integrity of the blood vessels after the rats were euthanized. The authors found that perindopril prevented an age-associated increase in blood pressure. Furthermore, perindopril prevented an age-related increase in arterial stiffness in PKD rats. When blood vessels were isolated and examined more closely, calcium deposits and arterial wall thickening were significantly attenuated with chronic perindopril treatment in PKD rats. Histomorphometric studies further indicated that the elastin-to-collagen ratio within the blood vessels was significantly decreased in PKD rats, but this declined ratio could be ameliorated with chronic perindopril treatment.

Overall, the study suggests that perindopril can improve the structural and functional indices of the vascular system in PKD rats, demonstrating the clinical benefits of the ACE-I in slowing down vascular remodeling in chronic kidney disease. All parameters observed in these PKD rats, including increased collagen, degeneration of elastin, increased wall thickness, and decreased wall distensibility, are part of an arteriosclerotic process and are commonly associated with vascular aging. Consistent with this observation, we have shown that abnormal vascular changes in PKD can be complicated by the aging process (3).

Regardless of whether *theory 1* on ciliopathy or *theory 2* on cystic expansion contributes to vascular complications in PKD, Phillips and colleagues (9) provide an important step forward in delineating vascular death in PKD. There is no doubt that further biomedical research is urgently needed to understand the complex cellular systems in the pathology of PKD. For example, it has been recently shown that activation of ciliary dopamine receptors can improve vascular function in PKD (1, 2). However, because our fundamental knowledge on cilia function and cellular pathology of PKD is still very limited, it remains unclear whether the same mechanism involving dopamine receptors also works in cystic renal cells. Regrettably, we currently have more questions than answers to offer.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author.

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