Letters to the Editor: The Cardiorenal Connection

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Letters to the Editor

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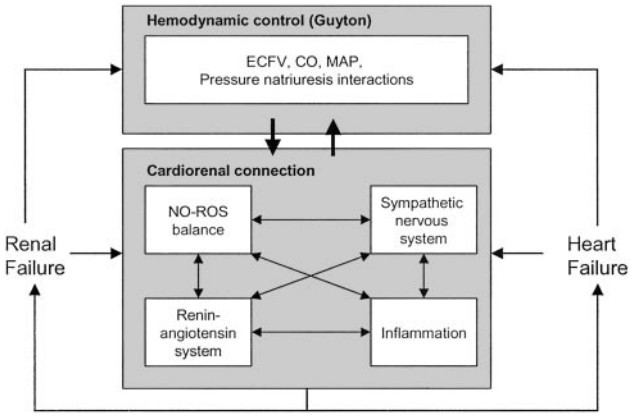
The Cardiorenal Connection

To the Editor:

With much interest we have read the article by Sarnak et al[1] on the risk of kidney disease for the development of cardiovascular disease. Considering the rising prevalence of chronic kidney disease and heart failure, we propose to perceive the reciprocal relationship of heart and kidney failure as a separate disease entity. This severe cardiorenal syndrome (SCRS) can be defined as the accelerated and extensive cardiovascular disease exclusively related to the coexistence of renal failure and heart disease.

In agreement with Sarnak et al, we feel that many questions remain unanswered. However, we would like to underscore the lack of insight in how renal and heart failure-related risk factors interact to lead to the SCRS. This inspired us to attempt to develop a model of heart/kidney interaction. The legacy of the late professor Guyton is a solid model to explain heart/kidney interaction by cardiac output, regulation of the extracellular fluid volume, blood pressure, and renal sodium handling. Central in the model of Guyton is the renin–angiotensin system (RAS), with its corresponding extensions (aldosterone, endothelin), and its antagonists (natriuretic peptides). While the model seems appropriate to explain extracellular fluid volume, blood pressure, and cardiac output in combined heart and renal failure, can it also explain the accelerated atherosclerosis, cardiac hypertrophy, and remodeling and progression of renal disease?



Pathophysiological basis of the severe cardiorenal syndrome. The model of Guyton explains heart/kidney interaction with respect to blood pressure (BP) and extracellular fluid volume (ECFV). When one of the organs fails, a vicious cycle develops in which the renin-angiotensin system, the NO/ROS balance, the sympathetic nervous system and inflammation interact and synergize, called the cardiorenal connection.

To answer these questions, we propose an extension to the Guytonian model for volume and blood pressure control, the cardiorenal connection (CRC) (Figure). At the corners of this model are the RAS, the NO/ROS balance, the sympathetic nervous system, and inflammation. We envision that derangement of one component of the CRC leads to a vicious cycle, so that other factors become disturbed and synergize. Ultimately this induces (irreversible) functional and structural damage in the heart and kidneys, thereby forming a positive feedback loop. In renal failure, oxidative stress[2] and inflammation[3] have been proposed as key factors, and some evidence exists on the interaction of the four corners of the CRC in promoting CVD. In heart failure, evidence is scarce, but recent investigations seem to support our view of the existence of the CRC. For example, increased NADPH-oxidase mediated ROS-release has been identified in both the kidney[4] and the heart[5] in heart failure.

We strongly feel that unraveling the nature of the interactions between the primary forces of the cardiorenal connection will help to understand the severe cardiorenal syndrome. The statement by the American Heart Association strongly stimulates the commencement of a vivid debate by clinical and basic scientists on this intriguing part of pathophysiology.

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