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LETTER TO THE EDITOR

Inferior Vena Cava Diameter and Fontan-Related Nephropathy: Considerations About Clinical Usefulness and Physiology

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We read with interest the study by Patel et al. [1] which found that an indexed inferior cava diameter (iIVC) > 1 cm/m^2 predicted nephropathy in Fontan patients. The authors are to be complimented on their work, as it contributes to the still poorly understood renal implications of the Fontan circulation. However, there are some issues that are worthy of further discussion.

First, the authors used microalbuminuria as a proxy for nephropathy, defining it as a microalbumin/creatinine ratio (MCR) > 20 µg/mg. However, the standard consensus definition is > 30 µg/mg or 3.4 mg/mmol [2]. Based on the data in their article, recalculations with this MCR threshold would show that only 5/39 (12.8%) patients in their population had microalbuminuria. Specificity of iIVC > 1 cm/m^2 would drop from 62 to 47% and positive predictive value from 59% to only 22%. We would be interested to see if the authors would find different results for the remaining analyses when using a MCR threshold of > 30 µg/mg.

Secondly, it could be argued that the goal of any clinically useful measurement of renal injury is to detect patients who are at elevated risk of poor outcomes. In this regard, it is relevant that microalbuminuria has consistently been demonstrated to show no association with outcomes including non-elective cardiovascular hospitalization and death in the Fontan population [3, 4]. On the other hand, several new biomarkers including kidney injury molecule-1 (KIM-1) and *N*-acetyl glucosaminidase (NAG) have been associated with renal dysfunction and poor outcomes, and therefore merit closer investigation [4]. Besides, cystatin C glomerular filtration rate, which is already in clinical use, has also been associated with outcome.

Lastly, while cardiac index did not show an association with microalbuminuria, this was in fact to be expected. The assumption that decreased cardiac index would drive renal dysfunction is based on an oversimplification of physiological principles. However, the kidney displays highly efficient autoregulation so that renal perfusion and filtration can be held constant over a wide range of blood pressures. Indeed, data in heart failure patients included in the ESCAPE trial have similarly been unable to demonstrate a relation between cardiac index and renal dysfunction [5]. In contrast, autoregulatory mechanisms are less effective with sudden drops in systolic blood pressure, such as in the setting of cardiac surgery. Together with the use of nephrotoxic medication, intravenous iodinated contrast agents, long-standing cyanosis, and renal venous congestion, these might constitute the main factors that ultimately lead to renal dysfunction in Fontan patients.

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