

## Editorial



# Increased Urine Albumin-to-Creatinine Ratio-a Harbinger of Renal Dysfunction after Repair of Congenital Heart Disease?

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### Conflict of Interest

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In adults with congenital heart disease (CHD), the prevalence of extracardiac as well as cardiac complications is increasing.<sup>1)</sup> Among these extracardiac complications, renal dysfunction has been reported to be more prevalent in adults with CHD than the general population.<sup>2)</sup> Impaired renal function has been shown in 50% of 1,102 adult patients with CHD, and decreased glomerular filtration rate (GFR) was observed in 65% of cyanotic patients with CHD.<sup>2)</sup> Patients with cyanotic CHD have been shown to be at increased risk for future renal dysfunction as they survive into adulthood.<sup>3)</sup> However, patients with relatively noncomplex defects have demonstrated renal dysfunction as well.<sup>2)</sup>

The association of renal dysfunction with acquired cardiovascular disease, hypertension, and diabetes is well known.<sup>1)</sup> Approximately 63% of adults hospitalized with congestive heart failure present with renal dysfunction (type 2 cardiorenal syndrome).<sup>1,4)</sup> In these patients, left ventricular dysfunction result in low cardiac output, which could cause decreased renal perfusion and activation of the renin-angiotensin-aldosterone system, which lead to sodium and water retention.<sup>2,5,6)</sup> Subsequently, neurohormonal activation could occur, as well as derangement in renal autoregulation.<sup>6)</sup>

Renal dysfunction in patients with CHD may be caused by the common hemodynamic derangements, such as decreased cardiac output and elevated central venous pressure, as well as the abnormal neurohormonal activation observed in the congestive heart failure patients.<sup>1,2)</sup> Atrial natriuretic peptide and norepinephrine levels have been found to be elevated long after surgery in patients with CHD.<sup>2)</sup> However, in addition to these factors, factors unique to patients with CHD that may lead to renal dysfunction are cardiac surgery and cardiopulmonary bypass.<sup>1)</sup> Surgery for repair of CHD could limit renal perfusion and lead to hypoxic ischemic injury and increased secretions of aldosterone and vasopressin.<sup>1,7)</sup> As a result, patients with CHD may experience transient GFR decrease and acute kidney injury, which may lead to the development of future chronic kidney disease.<sup>1)</sup>

Another unique factor in patients with CHD may be that, in congenital syndromes such as VACTERL and CHARGE syndromes, structural renal anomalies may coexist with CHD.<sup>1)</sup> In addition, in Williams syndrome, renal artery stenosis could be present, possibly causing

systemic hypertension.<sup>8)</sup> This may be the reason why screening for renal anomalies in patients with complex CHD is frequently performed in pediatric cardiac centers.<sup>1)</sup>

Cyanosis itself may affect renal function independent of the severity of CHD.<sup>2)</sup> Hypoxia in patients with CHD may directly cause renal tubular injury.<sup>1)</sup> Erythrocytosis and hyperviscosity caused by chronic hypoxia may engorge the glomerular vessels and increase efferent glomerular arteriolar resistance.<sup>1)</sup> With time, glomerular shrinkage and subsequent glomerular sclerosis may develop in patients with cyanotic CHD, increasing postglomerular oncotic pressure and fluid and solute reabsorption in the tubules, resulting in fluid retention.<sup>1,2)</sup> Microalbuminuria or proteinuria with concurrent azotemia may be prevalent in patients with cyanotic CHD due to glomerular sclerosis and osmotic gradient changes.<sup>1)</sup> In a study of 94 patients with cyanotic CHD, the presentation of microalbuminuria has been utilized as a marker for cyanotic nephropathy.<sup>9)</sup> Hongsawong et al.<sup>9)</sup> showed that the risk of significant microalbuminuria increased with hematocrit levels over 40%, platelet counts below 290,000/mm<sup>3</sup>, and longer waiting time for surgical repair in patients with cyanotic CHD.

In this issue of the *Korean Circulation Journal*, Oka et al.<sup>10)</sup> retrospectively investigated fluctuations of biomarkers of renal function in 14 patients with CHD in the remote period after biventricular repair. Of the 14 patients, they report increased urine albumin-to-creatinine ratio (UACR,  $\geq 10$  mg/gCr) in 6 patients (43%) with CHD in the remote period after biventricular repair. They also observed decreased right ventricular ejection fractions, increased right ventricular end diastolic volumes, and increased prevalence of cyanosis in patients with CHD with UACR  $\geq 10$  mg/gCr compared with those who had UACR  $< 10$  mg/gCr. They conclude that measuring UACR may be able to detect renal dysfunction in patients with CHD early in the remote period after biventricular repair.

Common methods of GFR measurement by serum or 24-hour urine creatinine may be applied to patients with CHD to assess renal function.<sup>1)</sup> Alternatively, cystatin C has been suggested as a better predictor of GFR than creatinine.<sup>1)</sup> Currently, it is suggested that cyanotic patients with CHD who have a reduction in GFR be screened for proteinuria by measuring the protein-to-creatinine ratio.<sup>1)</sup>

In addition to the high prevalence, renal dysfunction has been associated with increased morbidity and mortality in adults with CHD.<sup>1)</sup> Higher rehospitalization rates and poor surgical outcomes have been associated with concurrent renal dysfunction in patients with CHD.<sup>1,2)</sup> In addition, patients with CHD who have concomitant renal dysfunction may not receive aggressive medical and surgical treatment because their reduced GFR may escalate their perioperative risk.<sup>2)</sup> Therefore, in adults with CHD, especially those who are cyanotic or have Eisenmenger physiology, regular monitoring of renal function is recommended, with nephrology referral as needed.<sup>1)</sup>

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