Cardiology and nephrology: time for a more integrated approach to patient care?

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This editorial refers to 'Atherosclerotic renovascular disease in chronic heart failure: should we intervene?'† by R. de Silva et al., on page 1596

As the complexity of medicine develops at an exponential rate with an ever-increasing array of investigative and therapeutic strategies, greater subspecialization is inevitable. However, medical problems rarely confine themselves to a single organ and this is particularly apparent in patients with chronic disease of the heart and kidneys. Although cardiology has led the way in terms of establishing an evidence base on which therapeutic strategies can be recommended, conditions such as chronic heart failure (CHF) have increasing prevalence and despite various advances in treatment remain associated with poor outcomes. In addition, patients with significant co-morbidity (particularly nephrological) are generally excluded from clinical trials. There are many lessons to be learnt from specialists within other fields of medicine and this is no more apparent than between the nephrologist and the cardiologist whose patients can manifest many pathophysiological abnormalities that affect both organ systems.

Although there is clearly a pathophysiological overlap between these specialties, to be considered in true clinical context, it is important to establish whether cardiological abnormalities adversely impact on patients presenting with chronic kidney disease (CKD) and vice versa. Furthermore, if an adverse impact is seen, what can we do about it?

Cardiovascular disease is highly prevalent in patients with CKD. In a cohort study of 433 patients starting renal replacement therapy (RRT), 14% had proven coronary artery disease (CAD) and 19% had symptomatic angina. The majority of these patients had abnormal cardiac structure; echocardiographic changes such as left ventricular dilatation and hypertrophy (LVH) were seen in 32 and 74%, respectively, and 31% had clinical heart failure. Cardiac changes are equally apparent in the pre-RRT population and the prevalence of LVH increases sharply with declining glomerular filtration rate (GFR) in patients with CKD. Cardiac disease in patients with CKD also tends to be more severe and to occur at an earlier age than in the general population. In patients with CKD, and RRT patients treated with dialysis or renal transplantation, cardiovascular mortality accounts for >50% of all deaths. In dialysis patients, the adjusted cardiovascular mortality is 10 to 20 times that of the general population (an effect exaggerated in young patients in their second and third decades, with rates greater than 100 times). Mechanisms which underlie this strong association include long-standing hypertension, salt and water overload, and prolonged neurohormonal activation. The renin-angiotensin–aldosterone system (RAAS) is markedly activated and is thought to be a major contributor to the progressive decline in renal function characteristic of many cases of CKD. Here, the effects of angiotensin II are thought to be paramount with resultant intraglomerular hypertension and intrarenal fibrosis (via the upregulation of pro-scarring cytokines such as transforming growth factor β). Angiotensin II also has important direct effects on the heart, such as promoting LVH and an abnormal interstitial matrix, changes which may be fundamental to the increased risk of arrhythmias and heart failure that contribute to the excess cardiovascular mortality seen in CKD.

Disordered calcium and phosphate metabolism increased oxidative stress, dyslipidaemia, and anaemia are all likely to have additional important cardiovascular pathophysiological roles in patients with CKD. Increased vascular calcification in conjunction with activation of the RAAS leads to increased arterial stiffness and progressive atherosclerosis. Although increased arterial stiffness is associated with LVH, they remain independent risk factors for cardiovascular and all cause mortality. As implied previously, the increased cardiovascular mortality is not solely due to CAD, with many deaths believed to be due to worsening heart failure and sudden cardiac death.

Even mild degrees of CKD has been shown to adversely affect outcome in many cardiac conditions, and CKD is a major risk factor for cardiovascular complications following myocardial infarction and will predict both short- and long-term outcomes following percutaneous intervention. Worse lesion characteristics, an increased bleeding risk,
to the management of patients with CKD whether they are therefore symptomatic heart failure. This is now integral itself is a risk factor for left ventricular dysfunction and effective and can result in regression of LVH, which of recombinant erythropoeitin and intravenous iron is safe ventricle. Treating anaemia in these patients with the use strongly linked to development of abnormalities of the left ventricle. Treating anaemia in these patients with the use of recombinant erythropoeitin and intravenous iron is safe and effective and can result in regression of LVH, which itself is a risk factor for left ventricular dysfunction and therefore symptomatic heart failure. This is now integral to the management of patients with CKD whether they are pre-dialysis or receiving RRT.

De Silva et al. provide a comprehensive overview of the often underestimated burden of atherosclerotic renovascular disease (ARVD) in patients with cardiovascular disease. Not only is it common in patients with CAD, but also it has been found in almost one-third of elderly patients with clinical heart failure. A recent echocardiographic study of 79 patients with CKD and ARVD demonstrated LVH in 79%, ventricular dysfunction in 75%, and only 5% were found to have structurally normal hearts.

Patients with CKD secondary to ARVD have a five times greater risk of dying than of requiring dialysis and those on dialysis have a median survival of only 27 months and a 5 year survival of 18%. The excess mortality is thought to be due to cardiovascular disease. In a large epidemiological study of the US Medicare population, incident patients with ARVD had significantly higher rates of CAD and CHF (304 vs.74 and 195 vs. 56 per 1000 patient years, respectively) than patients without the condition during follow-up.

This association of ARVD and cardiac dysfunction might merely reflect shared underlying aetiological risks, in particular prior hypertension and hypercholesterolaemia. Alternatively, ARVD may directly contribute to cardiac abnormalities such as LVH and dilatation via marked RAAS activation, the adverse effects of which we have already alluded to. Intuitively, it is likely that both these mechanisms are influential. Shared risk factors for endothelial abnormalities and atherosclerosis will be manifested on the heart and vasculature (including renal arteries). As ARVD progresses, it is likely that an exaggerated effect on left ventricular remodelling will occur via activation of the RAAS.

ASTRAL is a multi-centre international trial that is currently at an advanced stage of recruitment of 750 patients with significant ARVD. Patients are randomized to treatment with renal revascularization (angioplasty with/ without stent) or conventional medical therapy with the primary aim of assessing the effect of intervention upon renal functional outcome. A cardiac substudy is specifically investigating the effect of renal revascularization upon cardiac structural and functional parameters as determined by echocardiography, cardiac magnetic resonance imaging, and neurohormonal measures, and particular attention is being directed to the clinical effects of this intervention in patients with co-morbid CHF.

As already highlighted, cardiovascular death accounts for the majority of deaths in CKD, and CKD adversely affects prognosis in cardiovascular diseases such as myocardial infarction and CHF. An integrated approach applying the lessons learnt from both renal and cardiovascular studies may lead to improved patient outcomes. Current interest relates particularly to the interaction among CKD, CHF, and anaemia. Even haemoglobin concentrations just below the physiological range appear deleterious in CHF; the vast majority of such patients have evidence of reduced GFR. Initial studies by Silverberg et al. have shown that correction of anaemia is feasible in patients with resistant heart failure and results in improved symptoms and reduced hospitalizations. This experience has originated in a specialized combined cardiology and nephrology clinics and emphasizes the research benefits of integrated care. Utilizing the extensive nephrological experience of treating anaemia in patients with CKD seems logical when considering similar therapies in patients with CHF who have not responded to standard aggressive medical management. Although the results of ongoing randomized studies are awaited, it is conceivable that anaemia may eventually be considered a modifiable risk factor for cardiovascular disease, as is the case for diabetes or hypertension.

The evidence for intervention of ARVD in patients with cardiovascular disease is still incomplete, but hopefully the ASTRAL study will enlighten us. It is also our belief that combined cardio-nephrology clinics (or even nephro-cardiology) will have an important future role in delivering optimal care for those many patients affected by disease in either of these important and closely interacting organ systems.

References
