

## BCRG (Birmingham Cardio-Renal Group)



Group leaders: Dr Jonathan N Townend, Dr Charles J Ferro and Dr Richard P Steeds

### Overview

The broad theme of the current work is to characterise the structural and functional deterioration within the heart and arterial tree affecting patients with early stage CKD and assess pharmacological methods of improving outcomes.

### Our research group

Chronic kidney disease (CKD) as determined by a reduced glomerular filtration rate (GFR - a measure of kidney function) affects up to 15% of the western population, including more than 45% of those aged over 70 years. Studies of patients with even mild CKD show that they are at increased risk of heart failure, stroke and sudden cardiac death with a graded association with reduced GFR. The reasons for these adverse effects on cardiovascular health are not clear. Our research aims to determine what causes these damaging processes and then to establish methods of treatment.



### Current projects

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The original Chronic Renal Impairment in Birmingham (CRIB) study was published in 2003, documenting the relative lack of importance of traditional risk factors in CKD. More recently, the BCRG have demonstrated abnormalities of vascular and ventricular function in patients with early stage CKD and gone on to design potential therapeutic strategies. In the randomised controlled trial CRIB-2, we investigated the effect of treatment with spironolactone, a mineralocorticoid receptor blocker (MRB), in combination with ACE inhibitors and or angiotensin receptor blockers in patients with early stage CKD. Previously considered to be contra-indicated in CKD, spironolactone was shown to improve prognostically important indices including arterial stiffness and left ventricular (LV) mass with improvement in markers of LV diastolic and systolic function. Further work is ongoing using the latest in cardiac MRI sequences to elucidate the role of myocardial fibrosis in the pathogenesis of CKD-related heart failure and sudden death.

The results of CRIB-2 prompted the development of further studies. The SPIRO-CKD trial of spironolactone versus chlorthalidone in early stage CKD has recently been awarded BHF special project grant funding and should demonstrate the effects of MRB therapy on LV mass and arterial stiffness in this population, independent of changes in blood pressure. A further study is now underway in the community with the aim of confirming the safety and efficacy of MRB treatment (STOP-CKD). Team members are also co-investigators in a primary care based NIHR funded clinical end-point trial to determine if MRB therapy might reduce cardiovascular morbidity and mortality in early stage CKD (BARACK-D).

In parallel, we have employed similar methods in a novel randomised controlled clinical study examining the use of a non-calcium based phosphate binder in early stage CKD (CRIB-PHOS). This trial is now due to report.

In a third line of investigation we are assessing the effects of nephrectomy in living kidney donors on cardiovascular structure and function (CRIB-DONOR). Kidney donors provide a unique population without underlying disease and this allows the longitudinal study of an isolated reduction in renal function on the heart and vasculature. A comprehensive pathophysiological study of kidney donors funded by a BHF fellowship is now underway. Meanwhile, a less detailed but larger scale UK multi-centre study (EARNEST) of kidney donors has also recently received funding from the BHF and will involve a number of other UK transplant centres including Cambridge, Glasgow, Bristol, GKT London and Coventry.



### Recent publications

- Chue CD, Edwards NC, Moody WE, Steeds RP, Townend JN and Ferro CJ (2012) Serum phosphate is associated with left ventricular mass in patients with chronic kidney disease: a cardiac magnetic resonance study. *Heart* 98(3):219-24
- Moody WE, Edwards NC, Chue CD, Ferro CJ and Townend JN (2012) Arterial disease in chronic kidney disease. *Heart*; doi:10.1136/heartjnl-2012-302818

- Edwards NC, Steeds RP, Stewart PM, Ferro CJ and Townend JN (2009) Effect of spironolactone on left ventricular mass and aortic stiffness in early-stage chronic kidney disease: a randomized controlled trial. *J Am Coll Cardiol* 54(6):505-12
- Edwards NC, Ferro CJ, Kirkwood H, Chue CD, Young AA, Stewart PM, Steeds RP and Townend JN (2010) Effect of spironolactone on left ventricular systolic and diastolic function in patients with early stage chronic kidney disease. *Am J Cardiol* 106(10):1505-11

## Staff

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- Dr Charles J Ferro, NIHR Fellow and Consultant Nephrologist
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