FINAL PROJECT REPORT

Date: January 24, 2010

Name:

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Project Title:

Renal Impairment in Decompensated Heart Failure

Please copy the "Outcome(s)" statement, entered on your application form, in the space below.

Our proposed study represents an observational study of combined assessments of cardio-renal function over 12 months following hospitalisation with heart failure. The design allows us to explore the severity and evolution of both cardiac and renal function in this clinical setting and to provide information regarding predictors of renal outcome. This in turn will facilitate the identification of those patients particularly at risk of renal failure. If treatment protocols and specific interventions were to be developed for these patients to ameliorate renal impairment the risks of mortality and hospitalisation may be reduced.

The future success of interventions to modify renal dysfunction in heart failure will depend crucially on early real-time detection of declining renal function. Our proposal to establish the clinical utility of urine and plasma biomarkers in decompensated heart failure joins other active ventures. The validation of these tests to predict and measure acute renal failure early may in turn facilitate the development of interventions to prevent or limit kidney injury and morbidity.

Will your work contribute to this outcome(s) in the manner you envisaged? If not, what has changed?

This work has provided detailed evaluation of kidney function in a cohort of people with chronic failure. We have, for the first time, undertaken integrated measurement of kidney blood flow and structure using magnetic resonance imaging combined with neurohormonal and cardiac characterisation. We have established the key determinants of kidney function in these patients, and determined that diastolic cardiac function and renal arterial disease are important factors of kidney function in the setting of heart failure. A manuscript describing this work is nearing completion for submission to a major cardiology journal.

The second part of the project characterised kidney function in patients with acute heart failure using novel plasma and urinary biomarkers of acute kidney injury that have been evaluated in other clinical settings. We identified, in a cohort of individuals requiring hospital admission for acute heart failure that approximately 30% suffered acute kidney injury within the hospital admission. We identified that plasma and urine measures of NGAL were modestly discriminating for acute kidney injury in this setting, but less so that clinical situations where larger changes in kidney function occur.

Please copy the "Specific Objective(s)" statement, entered on your application form, in the space below.

The proposed study has 2 primary aims:

1. *To conduct the first prospective systematic documentation of the prevalence, incidence, severity, nature and evolution of renal function over 12 months in an unselected cohort of patients hospitalised with decompensated (severe)heart failure;*

2. *To determine the diagnostic utility and predictive value of plasma (NGAL, cystatin C) and urinary (cystatin C, ALP, GGT, NGAL, KIM-1, IL-18 and AQP 1, 2) biomarkers of kidney injury in decompensated heart failure compared with standard tests of kidney function (plasma creatinine) and concurrent cardiac function (echocardiography and neurohormonal profile).*

Briefly describe how successful you were in achieving the stated objective(s). If the objective(s) was not achieved, explain why that is the case and describe what you did manage to achieve.

These objectives have been achieved by two separate prospective cohort studies.

First, we have identified the key renal pathologies underlying kidney dysfunction in patients previously admitted to hospital with heart failure. We have established new methods, using magnetic resonance imaging, to measure renal blood flow, and kidney structure in an integrated examination. We will extend these observations in future studies through examination of dynamic changes in kidney function in people with heart failure to evaluate renal autoregulation in the setting of ambulatory heart failure.

Second, we have completed a prospective cohort study of 65 patients admitted acutely to Christchurch Hospital with heart failure. We have characterised the diagnostic utility of a variety of putative biomarkers for acute kidney injury in this setting. About 30% of enrolled patients experienced acute kidney injury; urinary NGAL was the most discriminating biomarker for predicting acute kidney injury. A manuscript describing these results is being written.

Please confirm delivery of the outputs listed on your application form. If these outputs were not to be delivered, please explain why.

We have completed the proposed observational study of combined assessments of cardio-renal function over 12 months following hospitalisation with heart failure. We chose 6 months instead of 12 months as originally planned to avoid bias through loss to follow up at 12 months of the sickest patients. We were able to explore the severity and evolution of both cardiac and renal function in this clinical setting as intended.

We have also evaluated biomarkers that offer real-time detection of declining renal function. Our proposal to establish the clinical utility of urine and plasma biomarkers in decompensated heart failure is achieved. We have also validated magnetic resonance imaging as a method to non-invasively measure kidney structure and function. We will now use this new method to further evaluate dynamic kidney function in people with cardiac disease.

We have also established a collaborative partnership between the Christchurch Cardioendocrine Group and the Christchurch Radiology Group during this work that will enable the conduct of future studies in this field.