Welcome to the sixteenth issue of Heart Failure Research Review.

This issue begins with research showing worse outcomes in patients with HF who also have iron deficiency, regardless of whether they also have anaemia. Research from the US reports that while postdischarge use of spironolactone in patients with HFrEF and advanced chronic kidney disease increases readmissions, all-cause mortality and HF readmission rates are not significantly affected. An analysis of data from three clinical trials has shown that elevated plasma galectin-3 levels can predict early rehospitalisation in patients with HF. This issue concludes with Danish research comparing clinical outcomes associated with the various β-blockers, at differing dose levels, in patients with HF.

I hope you find the articles selected for this issue interesting, and I look forward to hearing from you with your comments and feedback.

Kind Regards,

Prof Peter MacDonald
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Iron deficiency status irrespective of anaemia: a predictor of unfavorable outcome in chronic heart failure patients

Authors: Rangel I et al.

Summary: This prospective study of 127 patients with stable chronic HF and LVEF ≤45% found that iron deficiency, which was present in 46 patients, was significantly more likely in women, patients with plasma BNP levels >400 pg/mL and those with right ventricular systolic dysfunction (p<0.05 for all). The composite endpoint of overall mortality and nonfatal cardiovascular events had occurred significantly more often at 225 ±139 days follow-up in patients with iron deficiency than those without (24% vs. 5% [p=0.001]) and those with versus without anaemia (25% vs. 8% [p=0.014]). A multivariate analysis adjusted for clinical variables including anaemia revealed a significant association between iron deficiency and an increased likelihood of a composite endpoint event (adjusted HR 5.38 [95% CI 1.54–18.87; p=0.009]).

Comment: The findings of this prospective observational study are consistent with similar recently published observational studies and demonstrate that iron deficiency with or without anaemia is common in patients with chronic HF and is associated with increased morbidity and mortality. The definition of iron deficiency used in this and other chronic HF studies is more liberal than that applied in most laboratories, and this may in part explain the high prevalence reported in chronic HF. Other studies have reported improved QOL and exercise performance in chronic HF patients with iron deficiency who are treated with IV iron. These studies have lacked the power to demonstrate an impact of IV iron therapy on mortality; however, iron deficiency is emerging as an important comorbidity in chronic HF and one that should be looked for routinely.

http://www.karger.com/Article/FullText/358377

Independent commentary by Professor Peter MacDonald.

Peter Macdonald is a Conjoint Professor of Medicine in the University of New South Wales, senior staff cardiologist in the Heart & Lung Transplant Unit at St Vincent’s Hospital, Sydney and co-head of the Transplantation Research Laboratory at the Victor Chang Cardiac Research Institute. He is a past President of the Transplantation Society of Australia & New Zealand (TSANZ). His major research interests over the last 20 years have been in the areas of heart failure, pulmonary hypertension, transplant allograft rejection, donor management and organ preservation. He has published six national guidelines, 15 book chapters and over 200 peer-reviewed scientific papers.

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Effect of left ventricular assist device implantation and heart transplantation on habitual physical activity and quality of life

Authors: Jakovljevic DG et al.

Summary: This research involved 14 patients with LVADs implanted, 12 heart transplant recipients, 14 patients with HF and 14 matched healthy controls assessed for physical activity, energy expenditure and QOL. Baseline physical activity levels were 15%, 28% and 51% of that of healthy subjects for the LVAD, heart transplant and HF groups, respectively (p<0.01), and were associated with lower energy expenditure and increased sedentary time (p<0.01). No difference was seen for baseline QOL scores among the LVAD, heart transplant and HF groups (p=0.44). At 3 months, daily physical activity levels had increased by 60% and 52% in the LVAD implantation and heart transplantation groups, respectively, but the activity levels at 6 and 12 months remained unchanged. Similarly, LVAD implantation and heart transplantation were associated with significant improvements in QOL at 3 months (p<0.01) but no further change thereafter. Heart transplantation was associated with significantly higher activity levels than LVAD implantation at the 3-, 6- and 12-month timepoints (p<0.05) and better associated QOL, while patients with HF experienced significant decreases in physical activity and QOL at 12 months (p<0.05).

Comment: This small study demonstrates that patients with advanced HF who receive an LVAD or heart transplant as expected have extremely limited physical activity at the time of surgery. Despite significant improvements in physical activity over the first 3 months postoperatively, their exercise capacity remains very low compared with healthy controls. An important part of the preparative evaluation of LVAD and heart transplant patients includes the assessment of frailty and comorbidities that may prevent or limit postoperative recovery and rehabilitation.

http://www.ajconline.org/article/S0002-9149(14)00964-3/abstract

Fragility is a key determinant of survival in heart failure patients

Authors: Gastelurrutia P et al.

Summary: These researchers assessed the effect of fragility on long-term prognosis in 1314 outpatients with HF. Fragility, defined as ≥1 abnormal evaluation among four standardised geriatric scales ( Barthel Index score ≤30; GARS scale ≤10 and <6 in women and men, respectively; Pfeiffer Test score ≥3.5; and by implication diuretic resistance), renal impairment, prolonged hospitalisation and increased mortality. Similar observations in earlier studies provided the rationale for the development of selective vasopressin antagonists such as tolvaptan and conivaptan; however, clinical trials with these agents have so far proved somewhat disappointing with at best modest symptomatic benefits over conventional therapy and no impact on mortality.

Comment: There is an increasing recognition that there are other determinants of survival in patients with HF beyond the severity of HF and the presence of comorbidities. Some patients with HF lose weight and muscle strength, or become depressed or cognitively impaired. A number of terms are being used by clinicians and researchers to try and characterise this population – cardiac cachexia, frailty or, as in this study, fragility. Similarly, a wide range of diagnostic tools are also being used to identify and quantify this entity. The bottom line is that ‘fragility’ is common, independent of age and associated with a poor prognosis. An important question for future research is the extent to which it is reversible with effective chronic HF therapy.

http://tinyurl.com/qaxa7xl

Spironolactone use and higher hospital readmission for Medicare beneficiaries with heart failure, left ventricular ejection fraction <45%, and estimated glomerular filtration rate <45 ml/min/1.73m²

Authors: Inapudu C et al.

Summary: The relationship between spironolactone use and hospital re-admission was explored in 1140 hospitalised patients with HF with EF <45% and an estimated GFR <45 ml/min/1.73m², 207 of who were prescribed spironolactone at discharge. Propensity score analyses showed that spironolactone use significantly increased the likelihood of re-admission for any cause at 30 days and 1 year (relative risk HRs 1.41 [95% CI 1.04–1.90] and 1.36 [1.13–1.63]), and the 1-year risk was greater among participants with an estimated GFR 15 vs. 15–45 ml/min/1.73m² (4.75 [1.84–12.28] vs. 1.34 [1.11–1.61]; p<0.003 for interaction). Spironolactone use did not impact significantly on re-admission for HF or all-cause mortality.

Comment: This ‘real world’ study of patients with chronic HF highlights the potential hazard of mineralocorticoid use in patients with the combination of HF and advanced renal disease. It is noteworthy that almost half the patients included in this analysis were diabetic, a known risk factor for worsening renal function with the use of mineralocorticoid antagonists. Patients discharged on spironolactone had higher rates of all-cause re-admission although not HF re-admission or mortality. The authors speculated that hyperkalaemia and diuretic resistance were the most likely mechanisms resulting in increased rates of re-admission. The study highlights the importance of close clinical observation and monitoring of electrolyte levels and renal function in chronic HF patients receiving mineralocorticoid antagonists.

Reference: Am J Cardiol 2014;114(1):79–82
http://www.ajconline.org/article/S0002-9149(14)00964-3/abstract

Hyponatraemia is commonly observed in patients with advanced HF and is generally considered to be an indicator of marked neurohormonal activation. Earlier studies have shown that hyponatraemia is a marker of increased sensitivity to and reduced tolerability of ACE (angiotensin converting enzyme) inhibitors and β-blockers. This retrospective review of patients hospitalised with acute decompensated HF demonstrates that hyponatraemia is associated with higher diuretic dosage requirements (and by implication diuretic resistance), renal impairment, prolonged hospitalisation and increased mortality. Similar observations in earlier studies provided the rationale for the development of selective vasopressin antagonists such as tolvaptan and conivaptan; however, clinical trials with these agents have so far proved somewhat disappointing with at best modest symptomatic benefits over conventional therapy and no impact on mortality.

http://www.karger.com/Article/FullText/360604

Reference: Heart Lung and Circulation, the Society’s Journal
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