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Abbreviations used in this issue:

ACE = angiotensin converting enzyme; AF = atrial fibrillation; ARB = angiotensin receptor blocker; BP = blood pressure; CV = cardiovascular; EF = ejection fraction; HF = heart failure; HFPEF = HF with preserved EF; HR = hazard ratio; IV = intravenous; MI = myocardial infarction; OR = odds ratio; QOL = quality of life.

Welcome to issue 33 of Heart Failure Research Review.

This issue begins with research showing that caloric restriction and aerobic exercise have additive positive effects on aerobic capacity in elderly patients with HFPEF, but these don’t appear to be accompanied by improvements in QOL. Other included research identified poor health literacy as an important mediator of the relationship between age and HF outcomes. We also have the findings of an audit of acute HF management conducted in NSW and ACT hospitals. This issue concludes with a large cohort study from Denmark reporting that β-blockers lower mortality in patients with AF both with and without concomitant HF.

I hope the selected papers help you in your everyday practice. I look forward to your feedback and suggestions, so please keep them coming.

Kind Regards

Prof Peter Macdonald
peter.macdonald@researchreview.com.au

Effect of caloric restriction or aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure with preserved ejection fraction

Authors: Kitzman DW et al.

Summary: Older obese patients with chronic, stable HFPEF were randomised to 20 weeks of an exercise programme only (n=26), a dietary programme only (n=24), a combined exercise and diet programme (n=25) or attention control with telephone calls every 2 weeks (n=25); 92 participants completed the trial, the exercise programme attendance rate was 84% and the diet adherence rate was 99%. Both diet and exercise on their own were associated with significant increases in peak VO₂ (1.2 and 1.3 mL/kg/min [p<0.001 for both]), and the effect was additive with the combined exercise and diet programme (2.5 mL/kg/min). Neither exercise nor diet on their own had a significant impact on MLHF (Minnesota Living with Heart Failure) QOL total score. Significant positive correlations were seen between change in peak VO₂ and changes in percent lean body mass (r=0.32 [p=0.003]) and thigh muscle-intermuscular fat ratio (r=0.27 [p=0.02]). No serious adverse events related to study participation were reported. The respective bodyweight decreases in the exercise alone, diet alone, exercise plus diet and control groups were 3%, 7%, 10% and 1%.

Comment: In this carefully conducted study, the authors demonstrate that dietary caloric restriction, structured exercise and the combination significantly improved aerobic exercise capacity in obese older patients with HFPEF, a condition for which there is currently no proven drug therapy. The combination of diet and exercise facilitated weight reduction. Somewhat surprisingly, despite these very clear benefits, there was no significant change in QOL. Nonetheless, this is an important study that provides strong support for these lifestyle interventions in the obese HFPEF patient.


Abstract

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 240 peer-reviewed scientific papers.

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Descriptive epidemiology and short-term outcomes of heart failure hospitalisation in rural Haiti

Authors: Kwan GF et al.

Summary: These authors reported on 311 adults admitted with HF, accounting for 302 of 1049 total admissions, to a rural Haitian tertiary-care hospital during a 12-month period. Sixty percent of the HF admissions were in women, and their mean age was 48.3 years (41% were aged <40 years); the mean age for men was 58.8 years. The median length of stay was 10 days and the in-hospital mortality rate was 12%. Among primary hospitalisation survivors (n=274), 36% were followed as clinic outpatients and 6.6% were readmitted within 30 days of discharge. Increasing distance between a patient’s residence and hospital was associated with reduced follow-up (p<0.01) and readmission (p=0.03). Among patients with echocardiography data (n=81), causes of HF were nonischaemic cardiomyopathy in 64%, right HF in 12%, hypertensive heart disease in 7% and rheumatic heart disease in 5%. Peripartum cardiomyopathy was evident in half of the women with cardiomyopathy on echocardiography.

Comment: This study from Haiti highlights multiple differences in the epidemiology of HF between a poor rural community in a developing country and a high income urban community in the developed world. HF was more common for women, and for non-surgical, non-obstetrical admissions. In contrast to Western communities, women were affected more commonly than men, and on average were younger with 40% being aged <40 years. Interestingly, the most common cause in both sexes was nonischaemic dilated cardiomyopathy with very few cases due to rheumatic heart disease or ischaemic heart disease. The study highlighted the high prevalence of peripartum cardiomyopathy in the rural Haitian community. Although other causes of cardiomyopathy were poorly defined, it is likely that micronutrient deficiencies also played an important role. Not surprisingly given the limited access to advanced healthcare, hospital mortality was high and use of guideline-recommended medication was very low.

Reference: Heart Failure 2016;102(2):140–6
Abstract

The efficacy and safety of iron supplementation in patients with heart failure and iron deficiency

Authors: Qian C et al.

Summary: This was a systematic review and meta-analysis of five clinical trials (n=807) comparing iron therapy with placebo or no treatment in patients with HF. Compared with placebo, no treatments with HF, iron therapy was associated with a significantly reduced likelihood of hospitalisation for HF (OR 0.28 [95% CI 0.16–0.49]), but not all-cause mortality (0.81 [0.42–1.57]). Pooled data from four studies where these endpoints were combined showed lower incidences of HF hospitalisation or death with iron supplementation (OR 0.47 [95% CI 0.29–0.76]). Iron supplementation did not increase the risk of adverse events.

Comment: Iron deficiency is common in chronic HF, and depending on the definition used, affects between one-third and one-half of patients. Several studies have demonstrated improvements in QOL, exercise capacity and hospitalisation rates in patients with iron deficiency and chronic HF following administration of IV iron, but so far studies have lacked the statistical power to determine an effect on mortality. This meta-analysis of five studies involving administration of IV iron strengthens the evidence for a beneficial effect of IV iron on hospitalisation rates (reduced by over 70%) and suggests there may be a substantial benefit with regard to mortality (about 20%); however, the confidence intervals around the point estimate remain wide, and conclusive evidence for a survival benefit is still lacking. Interestingly, there have been no studies examining oral iron supplementation.

Reference: Can J Cardiol 2016;32(2):151–9
Abstract

Psychosocial factors and risk of incident heart failure

Authors: Ogilvie RP et al.

Summary: Relationships between psychological status and incident HF were explored in 6782 MESA (Multi-Ethnic Study of Atherosclerosis) participants, 242 of whom developed incident HF during mean 9.3 years of follow-up. Comparisons between highest and lowest validated scale score quartiles yielded no significant association between the development of HF and anger (HR 1.14 [95% CI 0.81–1.60]), anxiety (0.74 [0.51–1.07]), chronic stress (1.25 [0.90–1.72]), depressive symptoms (1.19 [0.76–1.85]) or hostility (0.95 [0.62–1.42]). An exploratory analysis revealed that among participants self-reporting fair or poor health at baseline, high versus low levels of anxiety, chronic stress and depressive symptoms doubled the risk of incident HF, with no such associations seen in participants self-reporting good, very good or excellent baseline health.

Comment: Earlier studies examining relationships between psychological factors (including depression and anxiety) and incident HF have produced mixed results. This large prospective multi-ethnic cohort study of healthy adults examined relationships between a range of adverse psychological factors assessed at baseline and future incident HF. After adjusting for multiple covariates and after almost a decade of follow-up, there was no significant association between any of the psychological factors and development of HF. With some exploratory analysis (data dredging), three factors – depression, anxiety and chronic stress – could be linked to future development of HF. This is not to be confused with the well-established observation that patients with chronic HF have an increased prevalence of anxiety and depression and that these psychological factors are associated with increased morbidity and mortality in chronic HF patients.

Reference: Circ Heart Fail 2016;9(1):e002243
Abstract

Health literacy mediates the relationship between age and health outcomes in patients with heart failure

Authors: Wu J-R et al.

Summary: This longitudinal research explored the impact of HF severity, evidence-based medication use and health literacy on the relationship between age and health outcomes in 575 rural patients with HF. Health literacy levels and prescriptions for ACE inhibitors, β-blockers and statins were both lower in older patients with HF. Patients aged ≥65 years (57%) and those with low health literacy had significantly worse health outcomes, with age and health literacy both significant predictors on Cox regression analysis (relative p values 0.006 and <0.001). The HR for the association with age decreased from 1.49 to 1.29 and lost statistical significance when health literacy was accounted for in the model; health literacy remained a significant predictor (p<0.001), demonstrating mediation.

Comment: Observational studies in chronic HF invariably demonstrate a significant association between older age and increased mortality in chronic HF. Intuitively it makes sense that, barring accidents, older individuals are closer to death than younger ones. This study suggests that the association between older age and increased mortality in HF may be more complex. The authors found that older chronic HF patients had lower health literacy than younger chronic HF patients, and that after adjusting for health literacy, the relationship between older age and increased mortality was no longer significant. Health literacy refers to the capacity to obtain, read, understand and process health-related information. This begs the question, why do older patients have lower health literacy? One possible explanation is cognitive decline or ‘cognitive frailty’, which is common in older chronic HF patients. Regardless of the mechanism, the clinical implication is that older chronic HF patients should be screened for health literacy, and that those with low or marginal literacy should receive more intensive multidisciplinary care.

Reference: Circ Heart Fail 2016;9(1):e002250
Abstract

Mortality associated with heart failure after myocardial infarction

Authors: Gerber Y et al.

Summary: HF following MI was assessed according to preserved/reduced EF and the timing of its occurrence in 2596 residents from a US county with incident MI diagnosed over a 20-year period. There were 1116 deaths during mean 7.6 years follow-up, with a significantly greater mortality rate among patients who did (n=902) versus did not (n=1694) develop HF (70% vs. 28%; adjusted HR 3.31 [95% CI 2.93–3.75]), particularly CV-related mortality (4.20 [3.50–5.03]). These associations with all-cause and CV-related mortality were attenuated on additional adjustment for MI severity and comorbidity, acute treatment and recurrent MI (2.49 and 2.94, respectively). EF had no significant impact on mortality, but delayed- versus early-onset HF was associated with significantly greater mortality (p=0.002 for heterogeneity). The respective age- and sex-adjusted 5-year survival estimates for 2001–2010 versus 1990–2000 were 82% and 81% among patients without HF and 61% and 54% among patients who developed HF (p=0.05 for heterogeneity of trends).

Comment: HF complicating MI has long been recognised as a major risk factor for increased mortality. This longitudinal study from the mid-West of the US re-evaluated this relationship in a large cohort of MI survivors who were followed for up to 23 years after enrolment. HF remained a major risk factor for premature death with little evidence of improved outcomes in the more recent era.

Reference: Circ Heart Fail 2016;9(1):e002460
Abstract

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Temporal trends and variation in early scheduled follow-up after a hospitalization for heart failure

Authors: DeVore AD et al.

Summary: This US research analysed data from GWTG-HF (Get With The Guidelines–Heart Failure) to explore temporal trends of early follow-up among 52,438 patients discharged following hospitalisation for HF; patient and hospital characteristics associated with early scheduled follow-up were also evaluated. There was a significant increase in scheduled early follow-up at the time of hospital discharge from 51% to 65% over time (p<0.001); a smaller increase from 26% to 30% (p=0.005) in actual follow-up visits was seen over time in a subset of patients with linked Medicare claims data. A multivariable analysis showed that factors associated with an increased likelihood of early scheduled follow-up were older age (adjusted OR 1.04 [95% CI 1.01–1.07]), certain comorbidities (anaemia, diabetes and chronic kidney disease) and anticoagulant use at discharge (1.16 [1.11–1.22]).

Comment: The first few weeks after discharge for acute decompensated HF is a high-risk period for readmission. Current chronic HF guidelines recommend early postdischarge follow-up, ideally in a multidisciplinary clinic within 1 week of discharge. This large contemporary US retrospective survey identified that between half and two-thirds of patients were scheduled for follow-up by early follow-up after admission for acute decompensated HF – with the higher figure observed in the most recent year of the analysis. The figure is similar to the figure of 59% reported in the recently published NSW HF Snapshot. In both jurisdictions, there is clearly room for improvement.

Reference: Circ Heart Fail 2016;9(1):e002344

Abstract

Influence of titration of neurohormonal antagonists and blood pressure reduction on renal function and decongestion in decompensated heart failure

Authors: Kula AJ et al.

Summary: These researchers evaluated the effects of titration of oral neurohormonal antagonists and systolic BP reduction from admission to discharge on diuresis and decongestion in 656 consecutive admissions for acute decompensated HF. Systolic BP decreased by an average 14.4 mm Hg, with 77.6% of the patients having lower systolic BP at discharge than at admission. A strong association was seen between systolic BP reduction and worsening renal function (adjusted OR 2.0 [95% CI 1.3–3.2]), but there was no negative effect of systolic BP reduction on diuresis or decongestion. In more than half of the admissions, neurohormonal antagonists were uptitrated, and this was associated with a modest additional decrease in BP of ≤0.6 mm Hg. Neurohormonal antagonist uptitration improved diuretic efficiency and did not exacerbate worsening renal function.

Comment: A common clinical dilemma is what to do with neurohormonal antagonists when patients with chronic HF are admitted with acute decompensated HF and fluid overload. The concerns are that continued administration of β-blockers may aggravate fluid overload, that ACE inhibitors/ARBs may acutely worsen renal function, that all classes of neurohormonal antagonists may cause excessive BP lowering and that collectively continued administration of neurohormonal antagonists may prevent or delay the response to diuretics. The findings of this observational study suggest that for most patients with acute decompensated HF, these concerns are unwarranted. Indeed, the authors found that uptitration of neurohormonal antagonists during an admission for acute decompensated HF actually facilitated diuresis and the rate of recovery.

Reference: Circ Heart Fail 2016;9(2):e002333

Abstract

Acute heart failure admissions in New South Wales and the Australian Capital Territory

Authors: Newton PJ et al.

Summary: The NSW HF Snapshot study was a prospective audit of 811 consecutive patients admitted with acute HF to 24 participating hospitals in NSW and ACT over a 1-month period in 2013. Left ventricular EF was >50% in 42% of the patients and the median Charlson Comorbidity Index score was 3, with the most common comorbidities being ischaemic heart disease in 56%, renal disease in 55%, diabetes in 38% and chronic lung disease in 32%; in addition, 71% were assessed as frail. The most common precipitants of HF were intercurrent infection in 22% of cases, nonadherence to prescribed medication in 5%, nonadherence to dietary/fluid restrictions in 16% and AF/flutter in 15%. Initial treatments included IV diuretics in 81% of cases, oxygen therapy in 67% and biventricular pacing in 17%. The index admission mortality rate was 6%, and the median length of hospitalisation was 6 days, but this varied between 3 and 12 days across the different hospitals. Referral to a multidisciplinary HF service was made in 59% of cases. Discharge medications included ACE inhibitors/ARBs in 59% of cases, β-blockers in 66% and loop diuretics in 88%.

Comment: The NSW HF Snapshot study was conducted over a 1-month period in mid-2013 across 24 hospitals in NSW and the ACT. Baseline characteristics of 811 consecutive patients admitted with acute decompensated HF are reported in this study. The study highlights the advanced age and high proportion of HFPEF in the study population. Comorbidities were common and physical frailty was highly prevalent. Nonadherence to prescribed treatments accounted for 20% of admissions, while use of guideline-recommended treatments including ACE inhibitors and β-blockers was lower than expected. Also, only 60% of patients were referred to a multidisciplinary HF service – all of which suggests that there is considerable scope for improvement.

Reference: Med J Aust 2016;204(3):113

Abstract

β-blockers in atrial fibrillation patients with or without heart failure

Authors: Nielsen PB et al.

Summary: This nationwide cohort study explored the associations between β-blocker use and CV outcomes and mortality in 205,174 registry patients with nonvalvular AF followed for <5 years, 39,471 of whom also had prevalent HF. β-blocker users were at significantly lower risk of death from any cause over 1 year than nontreated patients in propensity-matched analyses among patients with prevalent HF (HR 0.75 [95% CI 0.71–0.79]) and among those without concomitant HF (0.78 [0.71–0.76]).

Comment: A recent post hoc meta-analysis of ten β-blocker trials in chronic HF suggested that the survival benefit of β-blockers in HF may be limited to those in sinus rhythm with no benefit for β-blockers in chronic HF patients who are also in AF. Given the current regulatory status of β-blockers, it is unlikely that a prospective, randomised, placebo-controlled trial of β-blockers will be conducted in patients with chronic HF and AF in the future. In the absence of such a trial, a nationwide ‘big data’ propensity-matched analysis such as this one from Denmark is probably the next best thing. The authors examined a range of outcomes in over 200,000 subjects with nonvalvular AF, almost 40,000 of who were in chronic HF. β-blocker usage was associated with a 25% reduction in mortality. Interestingly, a similar survival benefit was observed also in patients with nonvalvular HF without HF treated with β-blockers. The findings of this study provide strong supportive evidence for the continued use of β-blockers to treat HF both in the presence and absence of chronic HF.

Reference: Circ Heart Fail 2016;9(2):e002597

Abstract