Heart failure following cancer treatment: characteristics, survival and mortality of a linked health data analysis

Authors: Clark RA et al.

Summary: These authors linked and analysed records from the Queensland Cancer Registry, Death Registry and Hospital Administration to examine HF in 15,887 patients who had received chemotherapy for blood or breast cancer. There were 1062 index admissions for HF, 47% of which occurred within 1 year of cancer diagnosis and 70% within 3 years. Compared with patients without HF, those admitted with HF were older, more likely to be male, more likely to have haematological versus breast cancer (83.1% vs. 16.9%), and be at increased risk of death (adjusted HR 1.67 [95% CI 1.54–1.81]).

Comment: The cardiotoxicity of some anticancer therapies is well recognised, but there is limited information on how this toxicity impacts the survival of cancer patients who develop this complication. This retrospective data-linkage analysis of cancer registry data from Queensland highlights the increased mortality risk associated with the development of HF following anticancer treatment. At present, we have limited ability to predict and prevent the development of cardiotoxicity, but given the data presented in this analysis, these are important areas for research.


Abstract

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Welcome to issue 43 of Heart Failure Research Review.

This final issue for 2016 begins with three papers focussing on the subspecialty of cardio-oncology, including two Australian research papers on HF risk following chemotherapy or RT (radiotherapy), and a review on the topic. The implementation in Queensland of a quality improvement programme designed to increase the utilisation and up-titration of evidence-based therapies in HFREF has been reported. In other included research, the regional and ethnic differences in HF across Asian countries were described. The year concludes with the long-term outcomes of a study, which included Australian participants, of a novel interatrial septal shunt device for reducing left atrial pressure in HFPEF.

I hope you have enjoyed reading your copies of Heart Failure Research Review this year, and I look forward to returning soon with more local and international HF research.

Kind Regards,

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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 250 peer-reviewed scientific papers.

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Meta-analysis of association between mediastinal radiotherapy and long-term heart failure

Authors: Nolan MT et al.

Summary: Six studies (n=45,669) reporting data on the long-term risk of HF following thoracic RT for cancer were included in this meta-analysis; weighted median follow-up was 13.9 years. Pooled data showed a significantly increased risk of HF following thoracic RT (HR 1.83 [95% CI 1.09–3.08]), with significant heterogeneity among the studies (I²=88.47%), approximately 80% of which was explained by age at time of RT and follow-up duration. Significance of the association between thoracic RT and long-term HF was lost when studies of malignancies other than breast cancer or haematological malignancies and those with Newcastle-Ottawa scores <8 were excluded, but the magnitude of the risk remained about the same. An association was seen between earlier publication date and increased HF risk with RT. The study conclusions were not significantly impacted by other variables.

Comment: In another publication relevant to cardio-oncology, Australian authors conducted a meta-analysis of studies (mainly from the Netherlands) examining the risk of adult patients developing symptomatic HF more than 5 years following mediastinal RT for malignancy. They found that the risk of long-term HF is approximately doubled following RT. The risk appeared to be higher in those of younger median age at the time of RT and with longer duration of follow-up. These findings support current guidelines, which recommend echocardiographic screening 5–10 years after completion of RT with repeat echocardiography every 5 years thereafter.


Exercise training effects on elderly and middle-age patients with chronic heart failure after acute decompensation

Authors: Acafora D et al.

Summary: This randomised controlled trial enrolled patients with HF with LVEF <40% within 2 weeks of acute cardiogenic pulmonary oedema, including 40 elderly patients and 32 middle-aged patients, to participate in a 4-week supervised programme of closed-chain resistive activities and abdominal exercises. The exercise programme was associated with significant improvements in exercise duration, peak oxygen consumption and ventilatory threshold in both age groups (p<0.0001). Training significantly influenced previous cardiopulmonary parameters regardless of age, and catecholamine levels were significantly reduced.

Comment: While admission to hospital with acute decompensated HF is a crisis for patients suffering from chronic HF, it also provides an opportunity to review all aspects of the patient’s management and initiate lifestyle interventions if these have not previously been considered. Ideally this should happen in the context of a multidisciplinary team. In this interesting single-centre randomised study, Italian investigators were able to demonstrate a significant benefit of exercise training in both middle-aged and elderly patients with ischaemic heart disease and HFREF 4 weeks after commencing a formal exercise training programme within 2 weeks of presenting to hospital with acute pulmonary oedema. A major limitation of the study was that patients on β-blockers were excluded.

Reference: Int J Cardiol 2016;225:313–23

Management and research in cancer treatment-related cardiovascular toxicity: challenges and perspectives

Authors: Cautela J et al.

Summary: This review paper on cancer therapy-related CV toxicity addressed new challenges, perspectives and research priorities with the aim of identifying strategies for improving the overall prognosis and survival of patients with cancer. The contribution of cardio-oncology in each step of the development and use of cancer therapies were also discussed in detail.

Comment: This is an excellent review of the emerging subspecialty of cardio-oncology. As demonstrated in the study of Clark et al. (see page 1) for some cancers, improvements in cancer survival have come at a cost of increased CV morbidity and even mortality. The authors review the definitions of cancer treatment-induced cardiovascularities, and propose a standardised approach to the baseline CV assessment and monitoring of cancer patients before, during and after treatment. They also review the evidence for the use of concurrent therapies (mainly ACE inhibitors/ARBs and/or β-blockers) to prevent LV dysfunction induced by anthracyclines with or without trastuzumab.

Reference: Int J Cardiol 2016;244:366–75

Improving medication titration in heart failure by embedding a structured medication titration plan

Authors: Hickey, A et al.

Summary: This paper reported on a quality improvement project implemented in three Queensland HF disease management services. It involved the iterative implementation of a structured medication plan that employed methods such as awareness-raising/education, audit/feedback, integration into existing work practice and incentive payments. Compared with a pre-intervention cohort (n=96), two intervention cohorts (n=95 and 89) showed increased use of the titration plan, a shift to greater primary-care responsibility for titration, and more patients achieving target ACE inhibitor/ARB and β-blocker doses. When all three cohorts were combined, patients not on target doses on discharge who received a medication titration plan were significantly more likely to achieve target ACE inhibitor/ARB and β-blocker doses within 6 months.

Comment: This report from Queensland describes the results of a quality improvement programme aimed at increasing utilisation and uptitration of evidence-based therapies, namely ACE inhibitors/ARBs and β-blockers, in HFREF. A major aim of the programme was to improve communication and integration between hospital-based and community-based healthcare providers. An interesting feature of the programme was the use of an incentive payment for each completed uptitration. While the improvement in the proportion of patients achieving target doses of ACE inhibitors/ARBs and β-blockers following the intervention appears modest, the proportions of eligible patients receiving these drugs was more than 95%, which is a remarkable achievement in a real-world elderly chronic HF population.


The healthcare costs of heart failure during the last five years of life

Authors: Hollingworth W et al.

Summary: The health system costs in England associated with HF during the last 5 years of life were estimated using retrospective, linked primary-care and mortality data from a cohort of 1555 adults. The per-patient cost of healthcare cost during the last 3 months of life was £3827, of which >90% was associated with inpatient or critical care. Time spent in hospital during the last 3 months of life averaged 17.8 days per patient, and there was an average of 8.8 primary-care consultations per patient. Most patients (59.9%) died in hospital. Compared with quarters prior to HF diagnosis, the healthcare costs during postdiagnosis quarters were greater by £1439. Costs were lower for older patients and those with lower comorbidity scores.

Comment: The key finding of this UK registry study is that the healthcare costs of patients with HF escalate dramatically in the last 3 months of life, with 90% of these costs related to hospitalisation. More than 60% of HF patients die in hospital. While many interventions (including drugs, devices and multidisciplinary care) improve survival in HF, eventual progression of the HF syndrome means that the costs of care in the last few months of life, as identified in this study, will be postponed but not prevented by these interventions. The most effective way to reduce healthcare costs of terminal HF patients is to provide terminal care in the patient’s home. Use of home-based palliative care services appears logical and has been shown to increase the probability of patients choosing to die at home; however, the cost effectiveness of these services remains inconclusive.

Reference: Int J Cardiol 2016;224:132–8
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Different diuretic dose and response in acute decompensated heart failure: clinical characteristics and prognostic significance

Authors: Palazollo A et al.

Summary: The effects of different diuretic modalities (low versus high dose; cut point 125 mg/day) and diuretic efficiency (bodyweight loss per 40 mg/day of furosemide) on decongestion, worsening renal function and outcomes were explored in this retrospective analysis of data from the DIUR-HF study. Compared with patients on low doses (n=41), those on high doses (n=55) were older and more frequently had diabetes and chronic kidney disease, and greater proportions experienced worsening renal function while in hospital (85% vs. 29% (p<0.001)) and adverse events over 180 days (70% vs. 23% (p<0.001)). Compared with patients with high diuretic efficiency, those with low diuretic efficiency had a greater adverse event rate over 180 days (p=0.02). Univariate and multiviable analyses suggested significant relationships between adverse events and low diuretic efficiency, continuous administration and worsening renal function.

Comment: Intravenous loop diuretics are the most commonly administered drugs for patients admitted with acute decompensated HF. Studies such as the DOSE study published in the N Engl J Med in 2011 reported little difference in outcome comparing continuous versus intermittent administration and high-dose versus low-dose furosemide. In a similar study conducted by Italian investigators, the authors reported higher rates of worsening renal function and more adverse events during 6 months follow-up in patients receiving continuous infusions or higher doses of furosemide. In this post hoc analysis of the trial, they report that reduced diuretic efficiency (or diuretic resistance) was associated with worse outcomes. This could be explained by more advanced HF or renal disease in the group with reduced diuretic efficiency. It is noteworthy that the average age of patients in the Italian study was 80 years compared with 68 years in the DOSE study.

Reference: Int J Cardiol 2016;224:213–9

Abstract

Fluid status telemedicine alerts for heart failure

Authors: Böhm M et al., on behalf of the OptiLink HF Study Investigators

Summary: Patients with a recently implanted cardioverter defibrillator with or without cardiac resynchronisation therapy (n=1002) were randomised to automatic transmission of audible text-message fluid status alerts to the responsible physician or to standard care. A protocol-specified algorithm with remote review of device data and telephone contact was prescribed to assess symptoms and initiate treatment after the alert was transmitted in the intervention arm. The alert transmission failure rate was 24%, and 30% of alerts were followed by medical interventions. There was no significant difference between the intervention and standard care arms for all-cause death or CV-related hospitalisation (composite primary endpoint; 45.0% vs. 48.1%; HR 0.87 [95% CI 0.72–1.04]) or mortality rate (11.7% vs. 12.7%; 0.89 [0.62–1.28]) over average follow-up of 1.9 years.

Comment: The implantation of pacemakers or similar devices capable of determining the fluid status of an individual at risk of worsening HF and then automatically transmitting warnings of fluid overload to the caring physician has intuitive appeal. This large industry-sponsored randomised trial was designed to test the effectiveness of this concept. The results were disappointing, demonstrating that despite physicians receiving automated text messages regarding fluid overload in the intervention group, the overall outcome of the intervention group was no better than usual care. This may be explained in part by the relatively low rate of intervention alerts (30%) following telemedicine alerts, despite intensive physician and patient education prior to trial enrolment.


Abstract

Regional and ethnic differences among patients with heart failure in Asia

Authors: Lam CSP et al.

Summary: These authors reported a prospective study of 5276 registry patients with stable HFREF (LVEF ≤40%) from 11 Asian regions. The patients mean age was 59.6 years, 78.2% were men and their mean body mass index was 24.9 kg/m². Multiple comorbid conditions were present in 64% of the patients, including hypertension in 51.9%, coronary artery disease in 50.2% and diabetes in 40.4%. Compared with patients of Chinese ethnicity, coronary artery disease was more likely in those of Malay and Indian ethnicity (respective adjusted odds ratios 1.97 [95% CI 1.63–2.38] and 1.44 [1.24–1.68]), and less likely in those of Korean and Japanese ethnicity (0.38 [0.29–0.50] and 0.44 [0.36–0.55]). Hypertension and diabetes were more prevalent among Southeast Asian patients. Compared with low-income regions, Indian and Malay patients from high-income regions were more likely to have hypertension (respective adjusted odds ratios 3.95 [95% CI 2.51–6.2] and 2.60 [1.66–4.06]) and hypertension (4.91 [3.07–7.87] and 2.62 [1.73–3.97]).

Comment: There are more people with HF in Asia than in any other continent. This epidemiological study of HFREF across 11 Asian countries highlights the heterogeneous distribution of antecedent causes of HF in different ethnic groups across the region. As expected ischaemic heart disease and hypertension were the most common antecedent causes with most patients having at least two comorbidities. Two striking findings were the relatively young age of Asian HFREF patients compared with their counterparts in Western societies (on average one decade younger) and the high prevalence of diabetes (40%) for the total cohort.

Reference: Eur Heart J 2016;37(41):3141–53

One-year outcomes after transcatheter insertion of an interatrial shunt device for the management of heart failure with preserved ejection fraction

Authors: Kaye DM et al.

Summary: The long-term benefits of a novel interatrial septal shunt device for reducing left atrial pressure in HFREF were investigated in 64 patients with LVEF >40%, NYHA (New York Heart Association) class II–IV and pulmonary capillary wedge pressure ≥15mm Hg at rest or ≥25mm Hg during supine bicycle exercise. Sustained, significant improvements were seen in NYHA class, quality of life and 6-minute walk distance 1 year after device implantation. Echocardiography revealed a small but stable and significant reduction in LV end-diastolic volume index. Invasive haemodynamic data from a subset of patients revealed a sustained, significant reduction in workload-corrected exercise pulmonary capillary wedge pressure. The 1-year survival rate was 95%, with no evidence of device-related complications.

Comment: Creation of an interatrial shunt using an investigational interatrial septal device has been shown to relieve symptoms of pulmonary congestion and improve exercise capacity and haemodynamics in patients with HFREF. The initial publication in the Lancet of this international multicentre trial (including several centres in Australia and New Zealand) reported these outcomes after 6 months follow-up (an early commentary in Issue 35 of Heart Failure Research Review). The current paper examined the 12-month outcomes and confirmed that the benefits observed at 6 months were sustained at 12 months with no device-related complications. Further follow-up and larger trials are needed, but results do suggest that the interatrial septal device is a promising treatment option for patients with HFPEF.

Reference: Circ Heart Fail 2016;9(12):e003662

Abstract

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