Heart Failure Practice Review™

Making Education Easy

Issue 2 - 2024

In this issue:

Abbreviations used in this issue:

ACC = American College of Cardiology;
ACCP = American College of Clinical Pharmacy;
ACS = acute coronary syndrome; **ADHF** = acute decompensated heart failure;
AF = atrial fibrillation; **AHA** = American Heart Association;
CI = confidence interval; **CKD** = chronic kidney disease;
CPD = continuing professional development;
CSANZ = Cardiac Society of Australia and New Zealand;
cSMM = cardiovascular SMM; **ESC** = European Society of Cardiology;
GDMT = guideline-directed medical therapy; **HF** = heart failure;
HFEs = heart failure events; **HFnEF** = heart failure with normal ejection fraction;
HFpEF = heart failure with preserved ejection fraction;
HFRS = heart failure risk score; **HR** = hazard ratio; **HRS** = Heart Rhythm Society;
HT = heart transplant; **ICM** = insertable cardiac monitor; **LV** = left ventricular;
LVAD = left ventricular assist device; **LVEF** = left ventricular ejection fraction;
PBS = Pharmaceutical Benefits Scheme; **sc** = subcutaneous;
SGLT2 = sodium-glucose cotransporter-2; **SMM** = severe maternal morbidity;
T2DM = type 2 diabetes.

Welcome to the 2nd issue of Heart Failure Practice Review.

This Review covers news and issues relevant to clinical practice in heart failure. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. Finally, on the back cover, you will find our COVID-19 resources for Cardiologists and a summary of upcoming local and international educational opportunities, including workshops, webinars, and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne
Editor
janette.tenne@researchreview.com.au

Clinical Practice

Standardised definitions for evaluating acute decompensated heart failure therapies

Acute decompensated heart failure (ADHF) stands as a prevalent cause of hospitalisations and urgent care, marked by considerable morbidity and mortality. Yet, therapeutic options demonstrating efficacy remain limited, prompting a quest for innovation in both pharmacologic and device-based treatments. However, the lack of standardised definitions for ADHF and its trajectory complicates translating clinical trial findings into meaningful clinical care and policy changes.

Addressing this challenge, the Heart Failure Collaboratory, a diverse organisation encompassing clinical investigators, clinicians, patients, government representatives (including bodies like the U.S. Food and Drug Administration and National Institutes of Health), payors, and industry partners, has convened to propose standardised definitions and endpoint considerations for ADHF.

The consensus document produced by the Heart Failure Collaboratory, in conjunction with the Academic Research Consortium, represents a significant step towards establishing clarity in ADHF definitions and endpoint selection. ADHF is defined as the manifestation of heart failure (HF) signs and symptoms resistant to standard treatment, necessitating escalated therapy.

Key considerations highlighted include the complexity of ADHF syndrome, the need for consistent definitions across clinical trials, and the importance of detailed characterisation based on various factors such as coexisting diagnoses, ventricular predominance, and hemodynamic profiling. The proposed reports aim to provide a standardised framework to guide the design of clinical trials for pharmacologic and device-based interventions in ADHF, aiding regulatory decision-making and shaping healthcare policy.

It is recognised that implementing these recommendations requires careful monitoring of their impact, given the intricacies involved in addressing the complexities of ADHF. Through collaborative efforts and ongoing evaluation, these standardised definitions and considerations can significantly enhance clinical trial design and patient care in acute decompensated HF failure.

http://tinyurl.com/3kvvky9j

Optimising evidence-based heart failure medications after an acute heart failure admission

The secondary analysis of the 'Safety, Tolerability, and Efficacy of Rapid Optimization, Helped by N-Terminal Pro–Brain Natriuretic Peptide Testing of HF Therapies (STRONG-HF)' trial sheds light on the variables influencing the success of up-titration of guideline-directed medical therapy (GDMT) post-discharge from acute HF hospitalisation. Among the 515 patients examined, over 90% received medium- to high-dose GDMT within two weeks post-discharge.

The analysis underscores the importance of rapid up-titration to optimal GDMT doses, encompassing renin-angiotensin receptor system inhibitors, β-blockers, mineralocorticoid receptor antagonists, and sodium-glucose transport protein 2 (SGLT2) inhibitors. Patients with lower blood pressure, increased congestion, and higher risk profiles were less likely to undergo up-titration. However, those prescribed more GDMT experienced lower rates of readmission for HF or death within six months and showed improved quality of life.

While the study emphasises the feasibility and safety of up-titrating HF medications, certain limitations merit consideration. The study did not evaluate the individual benefits of each class of HF medication. Further, the effects of angiotensin receptor-neprilysin and SGLT2 inhibitors could not be assessed due to their limited use during the study period.

In clinical practice, identifying patients suitable for rapid up-titration remains crucial. Despite the benefits observed, not all patients achieved maximal GDMT doses, particularly those with less stable clinical profiles. The study suggests that while rapid up-titration is feasible, some patients, especially those with lower blood pressure, increased congestion, and comorbidities, may require more extended titration periods or may not achieve maximal doses.

Ultimately, the analysis highlights the significance of close monitoring and judicious use of decongestion strategies to facilitate GDMT up-titration and improve patient outcomes. To enhance treatment efficacy and safety, efforts should be directed towards optimising HF therapies, focusing on individual patient characteristics and clinical status.

http://tinyurl.com/ye22xzd8

Clinical features of heart failure with normal ejection fraction

Heart failure with normal ejection fraction (HFnEF) is a significant yet understudied condition associated with HF. A recent study aimed to understand the characteristics of patients with HFnEF compared with those with preserved yet below-normal left ventricular ejection fraction (LVEF).

Analysing data from an Asian HF registry, researchers found that 74.4% of patients with HF and preserved LVEF (HFpEF) had HFnEF. Compared with patients with HFpEF and below-normal LVEF, those with HFnEF had less coronary artery disease, thicker LV walls, and higher stroke volumes. However, their mortality rates were similar over two years.

Echocardiographic clustering revealed five distinct groups among patients with HFnEF, each with unique characteristics and survival rates. These clusters included normal LV, restrictive, hypertrophic, high output, and atrial dominant phenotypes. These findings were consistent across different patient populations.

The study underscores the heterogeneity within the HFnEF population and its resemblance to HFpEF with below-normal LVEF, suggesting potential overlaps in their clinical profiles and outcomes. Notably, the study highlights the importance of sex-specific definitions for normal LVEF, which influence the epidemiological estimates of HFnEF.

The study concluded that HFnEF represents a significant portion of HFpEF patients and exhibits diverse clinical and echocardiographic characteristics. Further research is needed to validate these findings and explore their implications for HF management and treatment approaches, potentially redefining HF categories like HF with mildly reduced EF.

http://tinyurl.com/3cfz54br

Aspirin and hemocompatibility events with a left ventricular assist device in advanced heart failure

The ARIES-HM3 randomised trial examined whether aspirin exclusion from the antithrombotic regimen, along with a vitamin K antagonist, in patients supported by a fully magnetically levitated left ventricular assist device (LVAD) reduces bleeding complications without increasing thromboembolic risks. This international study involved 628 patients across 51 centres in 9 countries.

Results revealed that avoiding aspirin led to a significant 34% reduction in major nonsurgical bleeding events without elevating thromboembolic risks. The benefits of aspirin exclusion remained consistent across various patient subgroups, including those with prior vascular diseases, obesity, or diabetes, which are characteristics associated with increased thrombosis risk.

The trial demonstrated that aspirin is not essential for maintaining outcomes in patients with advanced heart failure receiving support from a fully magnetically levitated LVAD. Exclusion of aspirin from the antithrombotic regimen, alongside a vitamin K antagonist, was safe and associated with a notable reduction in bleeding events, thus decreasing hospitalisation rates and the overall cost of care related to bleeding complications.

The study challenges the assumption that aspirin is necessary for antithrombotic therapy in LVAD-supported patients. However, the long-term effects of aspirin withdrawal in patients already on chronic LVAD support remain uncertain.

In conclusion, the ARIES-HM3 trial underscores the safety and efficacy of excluding aspirin from the antithrombotic regimen in LVAD-supported patients with advanced HF. These findings have significant implications for optimising treatment strategies and improving outcomes in this patient population.

http://tinyurl.com/mr2239sh

Maternal and pregnancy outcomes following heart transplantation

A recent study investigated pregnancy outcomes in heart transplant (HT) recipients using national data from 2010-2020. Among 19,399,521 deliveries, 105 were HT recipients. Compared with non-HT recipients, HT recipients had significantly higher rates of severe maternal morbidity (SMM), non-transfusion SMM, cardiovascular SMM (cSMM), and preterm birth ($P < 0.001$). Adjusted analyses revealed HT recipients had 16-fold greater odds of SMM, 28-fold greater odds of non-transfusion SMM, 38-fold greater odds of cSMM, and 7-fold greater odds of preterm birth. Moreover, HT recipients had higher rates of hospital readmission within 1-year post-delivery (26.9% vs 3.8%; adjusted HR: 6.03 [95% CI: 3.73–9.75]).

The study underscores the increased risks associated with pregnancy following HT, including heightened rates of maternal morbidity and preterm birth, alongside elevated readmission rates for HT-related complications. Mortality risk post-pregnancy among HT recipients is noteworthy, with previous studies reporting mortality rates averaging 33% over 9.4 years after the first pregnancy. HT recipients also face increased rates of hypertensive disorders, preterm birth, and neonates who are small for gestational age.

While existing studies provide critical insights, limitations such as data omissions and lack of patient linkage across years necessitate further research for generalisability. There is also a need to explore outcomes across different time frames post-transplantation and to consider patient demographics like race and ethnicity. Counselling patients with HT history on pregnancy risks, coordinating care with high-risk maternal centres and ensuring postpartum follow-up are crucial steps in managing this population.

In conclusion, pregnancy in HT recipients poses substantial risks, necessitating informed decision-making and specialised care to optimise maternal and foetal outcomes. Further research is vital to better understand the complexities and nuances of pregnancy outcomes in this unique patient population.

http://tinyurl.com/ycxwdsvm

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Australian College of Rural and Remote Medicine (ACRRM) Professional Development Program (PDP) participants can claim Educational Activity hours in the self-directed learning category for reading Research Reviews. More info.

GP members of the **Royal Australian College of General Practitioners (RACGP)** are able to include Research Reviews as part of the self-record unaccredited category 2 QI&CPD points by logging onto the RACGP website.

A novel heart failure diagnostic risk score using a minimally invasive subcutaneous insertable cardiac monitor

A recent study aimed to develop an ambulatory heart failure risk score (HFRS) using physiological data from sensors within an insertable cardiac monitor (ICM) to predict worsening heart failure events (HFEs) in patients with NYHA functional class II/III HF, regardless of EF.

Two observational cohorts were analysed, with patients implanted with an ICM measuring parameters like impedance, heart rate, heart rate variability, and activity. An HFRS was created to predict the probability of HFEs within 30 days. Sensitivity and unexplained detection rates were assessed in two independent datasets. HFEs were defined as hospitalisations, observation unit visits, or emergency department visits with HF diagnosis and intravenous diuretic treatment.

Results showed that the ICM-based HFRS accurately predicted HFEs, with a sensitivity of 73.7% in the development dataset and 68.4% in the validation dataset, using a high-risk threshold of 7.5%. The median warning time before HFEs was 47 and 64 days in the respective datasets.

The study's conclusions highlight the ICM-HFRS as a multiparameter diagnostic tool to identify high-risk HF patients, providing early warnings of impending HFEs. Notably, the sensor technology and applications used in ICMs did not significantly affect the accuracy of individual metrics or their ability to predict HFE risk when aggregated.

The data support the use of ICM-derived HFRS in predicting HFEs across EF ranges, emphasising its potential in HF management strategies. It suggests the need for further testing, such as the ALLEVIATE-HF study, to integrate HFRS into patient management and improve outcomes.

Patient selection for device-based risk assessment is crucial, considering factors like EF, symptom status, and comorbidities. The study proposes alert-based and periodic follow-up care models, offering flexibility in managing patients at varying risk levels.

ICM-based management provides additional benefits beyond HFRS, including detecting cardiac arrhythmias and guiding timely interventions. Future iterations may incorporate additional sensor technologies for improved accuracy and efficiency.

Limitations include sample size and follow-up time, necessitating further validation in more extensive studies like the ALLEVIATE-HF trial. However, the study's findings underscore the potential of ICM-derived HFRS in enhancing HF management strategies and improving patient outcomes.

http://tinyurl.com/2hn2xd5r

Regulatory News

Dapagliflozin (Forxiga®) listed on PBS for chronic heart failure

Dapagliflozin (Forxiga®; 10 mg tablet) is now listed on the PBS for the treatment of chronic heart failure where the patient has an LVEF >40%. Dapagliflozin helps protect the heart from weakening further and improves common heart failure symptoms. Thus, it can reduce the risk of hospitalisation for heart failure and cardiovascular death when used alongside standard care. Without subsidy, dapagliflozin would cost patients over $660 annually. Prescriptions for treatment are Authority Required (STREAMLINED).

https://tinyurl.com/3dbhmssp

Expanded access to empagliflozin (Jardiance®)

Starting November 1st, access to empagliflozin (Jardiance®) was extended for use in treating chronic heart failure among patients with an LVEF of ≥40% under the PBS.

Empagliflozin would typically impose a financial burden exceeding $660 annually on patients without subsidy. However, its inclusion in the PBS ensures that eligible patients bear a maximum cost of $30 per prescription, or $7.30 with a concession card.

When used alongside standard care, empagliflozin has the potential to diminish the risk of heart failure-related hospitalisations and cardiovascular mortality. This listing stands to benefit an estimated 98,000 Australians.

Prescriptions for treatment are Authority Required (STREAMLINED).

http://tinyurl.com/2s4pedkx

News in Brief

Correction to focused update of ESC heart failure guidelines

The originally published version of this Guidelines paper has been corrected. In addition to some reference updates, a recommendation in Table 4 has been amended as follows: "In patients with T2DM and CKD, SGLT2 inhibitors are recommended to reduce the risk of HF hospitalisation or cardiovascular death."

http://tinyurl.com/5xsfryzy

Updated guidelines for diagnosing and managing atrial fibrillation

The 2023 ACC/AHA/ACCP/HRS Guideline for Atrial Fibrillation (AF) offers updated recommendations, evolving from a comprehensive literature search spanning May to November 2022. Addressing AF as a continuum, it emphasises risk factor modification, introduces flexibility in risk scoring, and highlights early rhythm control. Key updates include upgraded recommendations for catheter ablation in specific patient groups and enhanced guidance for device-detected AF, left atrial appendage occlusion devices, and AF identified during medical illness or surgery.

http://tinyurl.com/3f4jjnxr

Recognising clinical trajectories using machine learning in hospitalised patients with heart failure

Hospitalised patients with ADHF exhibit diverse clinical paths, impacting length of stay and readmission risks. Early recognition of trajectories, especially non-responsive cases, is vital for successful decongestion. Hemoconcentration, reflecting decongestion success, is monitored using haemoglobin levels. A recent study proposes an AI model predicting hemoconcentration trajectories within 48 hours of admission, utilising data from 190,240 patients. The model shows potential for risk stratification and predicting patient outcomes. Future studies may validate the utility of algorithm-directed care in HF management.

http://tinyurl.com/yc48r5aw

COVID-19 Resources for Cardiologists

CSANZ https://tinyurl.com/y3xp2729
ACC https://tinyurl.com/y68aud3a
ESC https://tinyurl.com/wn3fsts

Conferences, Workshops, and CPD

Please click on the links below for upcoming local and international cardiology meetings, workshops, and CPD.

ACRA, CSANZ, Cardiac Skills Australia, Heart Foundation
Australian Centre for Heart Health, ACC, AHA
ESC Congresses and Events, ESC Education.

Research Review Publications

Cardiology Research Review with Associate Professor John Amerena

Heart Failure Research Review with Professor Andrew Coats, and Dr Mark Nolan

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