

Heart Failure Practice Review™



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Issue 4 - 2024

In this issue:

- > Dietary sodium and fluid intake in HF
- > The tricuspid valve: Pathology, imaging, and current treatment options
- > Chronic RHF and TR
- > IV iron therapy in patients with HF and iron deficiency
- > Diagnosing and managing CS
- > Patient-centred adult cardiovascular care
- > Overcoming clinical inertia with SGLT2 inhibitors
- > Chronic HF treatment
- > Newly diagnosed systemic light chain amyloidosis
- > Changes to the prescription process from 1 July 2024
- > Medicines Repurposing Program established
- > ACHD Workforce Global Survey
- > COVID-19 resources
- > Conferences, workshops and CPD

Abbreviations used in this issue:

ACC = American College of Cardiology; **ACHD** = adult congenital heart disease; **ACRA** = Australian Cardiovascular Health and Rehabilitation Association; **AHA** = American Heart Association; **ANZSVS** = Australian and New Zealand Society for Vascular Surgery; **CMR** = cardiac magnetic resonance; **CPD** = continuing professional development; **CS** = cardiac sarcoidosis; **CSANZ** = Cardiac Society of Australia and New Zealand; **CT** = computed tomography; **ESC** = European Society of Cardiology; **FDG** = fluorine-18 fluorodeoxyglucose; **GDMT** = guideline-directed medical therapy; **HF** = heart failure; **IV** = intravenous; **LGE** = late gadolinium enhancement; **MRI** = magnetic resonance imaging; **NYHA** = New York Heart Association; **PBS** = Pharmaceutical Benefits Scheme; **PET** = positron emission tomography; **RHF** = right-sided heart failure; **RV** = right ventricular; **SGLT** = sodium-glucose cotransporter; **TGA** = Therapeutic Goods Administration; **TR** = tricuspid regurgitation.

Welcome to the 4th 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

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Clinical Practice

Dietary sodium and fluid intake in heart failure

The Heart Failure (HF) Association of the European Society of Cardiology (ESC) has published a clinical consensus statement on dietary sodium and fluid intake in HF. Sodium is an essential element that plays a central role in physiological processes. Approximately 60% of the body's sodium content is dispersed within the extracellular fluid, which includes plasma and interstitial fluid. Fluid homeostasis is controlled by the hypothalamic thirst centre and the renin-angiotensin-aldosterone system, which work to preserve a constant effective circulatory volume.

Gastrointestinal absorption is a highly efficient process that rapidly increases serum sodium and osmolality after oral ingestion. Most sodium absorption occurs in the small intestine through transporters like NHE3 and SGLT1, with water following passively. The interstitium may also act as a sodium storage reservoir.

In the kidneys, sodium undergoes near-complete tubular reabsorption, with only a tiny fraction excreted in urine. Renal blood flow and glomerular filtration rate are tightly regulated to maintain sodium and fluid balance.

Historically, sodium and fluid restriction has been advocated in HF due to these patients' sodium and water-avid state. However, recent data challenge the benefits of these restrictions. The ESC HF guidelines now advise limiting salt intake to no more than 5 g/day and considering fluid restriction of 1.5–2 L/day only in selected patients.

This clinical consensus statement aims to provide updated, evidence-based guidance on fluid and sodium intake for patients with acute and chronic HF. The authors emphasise that a more lenient approach may not be detrimental, while stringent restrictions could potentially be harmful in certain conditions.

<https://tinyurl.com/5yf9sczz>

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2. The Pharmaceutical Benefits Scheme (PBS). PBS website. <https://www.pbs.gov.au>. Last accessed March 2024.

AstraZeneca Pty. Ltd. Macquarie Park, NSW 2113. AU-18666. March 2024. For PBS and Product Information refer to primary advertisement on page 3.

The tricuspid valve: A review of pathology, imaging, and current treatment options

The tricuspid valve is a complex anatomical structure often underappreciated, yet it plays a crucial role in cardiac function. The American Heart Association (AHA) has published a scientific statement on the tricuspid valve, reviewing the pathology, imaging, and current treatment options. Tricuspid valve disease, particularly tricuspid regurgitation (TR), is associated with significant morbidity and mortality.

TR can be classified as primary (due to structural abnormalities) or secondary (functional, caused by right ventricular (RV) or atrial dilation). Imaging modalities like transthoracic echocardiography, transesophageal echocardiography, cardiac CT, and cardiac MRI are essential for accurately visualising tricuspid valve anatomy and pathology to guide treatment. Echocardiography is particularly important, as it can identify the mechanism and severity of TR and assess RV size and function.

Traditionally, treatment options for TR have been limited to medical therapy or surgery, but there has been growing interest and success in transcatheter tricuspid valve therapies in recent years. Treatment choice depends on the underlying cause and mechanism of TR, as well as the patient's clinical status and comorbidities.

Understanding the complex interplay between the RV myocardium and TR is crucial for clinical assessment and management. RV dilation and dysfunction can contribute to tricuspid annular dilatation and incomplete leaflet coaptation, perpetuating the cycle of TR. Timely identification and monitoring of RV changes are essential for implementing appropriate therapeutic strategies.

<https://tinyurl.com/a647upya>

Chronic right-sided heart failure and tricuspid regurgitation

The HF Association and the European Association of Percutaneous Cardiovascular Interventions of the ESC have published a clinical consensus statement on TR in right-sided HF (RHF). The statement summarises current knowledge about the epidemiology, pathophysiology, and treatment of TR in RHF and provides practical suggestions for patient identification and management.

RHF and TR are common conditions strongly associated with poor quality of life and increased risk of HF, hospitalisation, and death. The prevalence of RHF varies widely, with studies reporting a range of 19–77% in heart patients with HF, depending on the definition used. Regardless of the definition, RV dysfunction is independently associated with increased morbidity and mortality. The impact of RHF on survival is most severe when there is a combination of reduced tricuspid annular plane systolic excursion, NYHA class IV symptoms, peripheral oedema, and the need for diuretic therapy.

Moderate or severe TR affects 3–6% of the general population but is much higher in patients with left-sided valve disease and HF, ranging from 10–23%. TR is associated with increased mortality and HF hospitalisation, and this prognostic impact increases with TR severity. TR can lead to a vicious cycle of RV volume overload and further RV impairment, contributing to RHF progression.

Right atrial remodelling, often associated with atrial functional TR and mild or absent RV dysfunction, can also contribute to RHF in patients with long-standing atrial fibrillation or HF with preserved ejection fraction.

Multiple causes of TR and RHF exist, including left ventricular failure, left-sided valvular heart disease, primary RV dysfunction, pulmonary arterial hypertension, and lung disorders. Permanent atrial fibrillation and right-sided leads can also contribute to TR and RHF. Primary TR, although rare in adult patients, can also cause RHF.

Patients with chronic RHF and TR often present late when signs and symptoms are advanced, and treatment options are limited. Early identification is crucial, as optimal management requires understanding the different mechanisms and causes. Transthoracic echocardiography is the first-line diagnostic tool, but additional imaging modalities, such as transesophageal echocardiography, cardiac magnetic resonance, and cardiac computed tomography, may be needed to confirm the diagnosis and identify the underlying cause. Right heart catheterisation is key in assessing pulmonary hypertension and distinguishing pre- from post-capillary phenotypes. Treatment strategies aim to address the predominant cause of RHF and TR, with diuretics being the mainstay of medical therapy. Transcatheter tricuspid valve interventions are emerging as potential treatment options for selected high-risk patients, but further research is needed to understand their impact on prognosis clearly.

A multidisciplinary approach involving various specialists is essential for the comprehensive evaluation and management of patients with RHF and TR, from early identification to lifetime follow-up.

<https://tinyurl.com/yxcmjr5j>

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HFpEF
LVEF >40%

REFERENCES: 1. FORXIGA[®] Approved Product Information. 2. The Pharmaceutical Benefits Scheme (PBS). PBS website. <https://www.pbs.gov.au>. Last accessed March 2024. AstraZeneca Pty. Ltd. Macquarie Park, NSW 2113. AU-18666. March 2024.



Intravenous iron therapy in patients with heart failure and iron deficiency

Iron deficiency is a common comorbidity in patients with HF, affecting up to 50% of ambulatory patients. Iron is crucial in homeostatic processes, including energy production and haemoglobin synthesis. Iron deficiency in patients with HF is linked to higher cardiovascular and all-cause mortality, repeated HF decompensation, and decreased exercise tolerance.

Intravenous (IV) iron therapy has emerged as a promising treatment approach for patients with HF with concomitant iron deficiency. A recent review outlines this treatment's benefits, safety, and guidelines.

Several randomised clinical trials have demonstrated that IV iron therapy, particularly with ferric carboxymaltose, can improve quality of life and exercise capacity and reduce HF hospitalisations in these patients. The FAIR-HF, CONFIRM-HF, and AFFIRM-AHF trials have all shown significant benefits of IV iron therapy in patients with HF with iron deficiency.

However, concerns remain about the potential long-term cardiotoxic effects of IV iron therapy, including the risk of iron overload. Unlike oral iron, IV iron can result in the accumulation of non-transferrin-bound iron, which can lead to oxidative stress and endothelial damage. The balance between iron replacement and preventing iron overload is critical in these patients.

The 2022 ACC/AHA guidelines recommend IV iron therapy as a Class 2a recommendation for eligible patients with HF with iron deficiency to improve functional status and quality of life. The 2023 Focused Update of the 2021 ESC Guidelines also strongly recommends IV iron supplementation in patients with HF with reduced or moderately reduced ejection fraction and iron deficiency.

While IV iron therapy has shown promise, further research is needed, particularly in patients with preserved ejection fraction and acute HF, to fully elucidate the safety and efficacy of this treatment approach in diverse HF populations. Careful consideration of IV iron therapy's potential risks and benefits is essential to ensure the optimal management of iron deficiency in patients with HF.

<https://tinyurl.com/3bpa7c2n>

Diagnosing and managing cardiac sarcoidosis

Cardiac sarcoidosis (CS) is an infiltrative cardiomyopathy caused by granulomatous inflammation of the myocardium. It can present with high-grade conduction disease, ventricular arrhythmias, and right or left ventricular dysfunction. The prevalence of CS has increased over the past decades, likely due to growing awareness and diagnostic advances. Accurate diagnosis is challenging due to diverse and nonspecific presentations. The AHA recently published a scientific statement on diagnosing and managing CS.

The pathophysiology of sarcoidosis involves a dysregulated T-cell immune response, leading to the formation of non-necrotising granulomas. Genetic susceptibility, mainly related to human leukocyte antigen class II alleles, plays a role. Around half of patients with CS initially present without clinically evident extracardiac involvement, underscoring the need for thorough organ assessment.

Electrocardiography and echocardiography have limited sensitivity but can provide clues to the presence of CS. Cardiac magnetic resonance (CMR) imaging and fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) are the fundamental imaging modalities for diagnosing CS. CMR can detect late gadolinium enhancement (LGE) as a marker of myocardial involvement, with specific LGE patterns associated with a higher risk of arrhythmic events. FDG-PET can identify areas of active inflammation. Combining CMR and FDG-PET can provide complementary information.

Treatment should be initiated in individuals with clinical manifestations and active inflammation, with corticosteroids as first-line therapy. The lack of randomised trials has led to treatment decisions based on cohort studies and consensus opinions, resulting in substantial variation across centres. The AHA scientific statement aims to provide a framework for diagnosing and managing CS to guide clinical practice and facilitate management conformity.

<https://tinyurl.com/3cw7496n>

Earn CPD

Nursing and Midwifery Board of Australia (NMBA) Journal reading and watching videos (including Research Reviews¹) may be considered a self-directed activity set out in the [NMBA Registration Standard: Continuing Professional Development](#). One hour of active learning will equal one hour of CPD. Details at [NMBA CPD page](#).

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ARR=absolute risk reduction; CI=confidence interval; CV=cardiovascular; HF=heart failure; HFpEF=heart failure with preserved ejection fraction; HFrEF=heart failure with reduced ejection fraction; HR=hazard ratio; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; RRR=relative risk reduction; †In DAPA-HF worsening HF was defined as either an unplanned hospitalisation or an urgent visit resulting in intravenous therapy for HF; in DELIVER worsening HF was defined as either an unplanned hHF or an urgent visit for HF;^{2,3} HFrEF defined as NYHA class II-IV HF and ejection fraction of $\leq 40\%$; ² HFpEF defined as NYHA class II-IV HF and ejection fraction of $>40\%$.³

REFERENCES: 1. FORXIGA® Approved Product Information. 2. The Pharmaceutical Benefits Scheme (PBS). PBS website. <https://www.pbs.gov.au>. Last accessed March 2024. 3. McMurray JJV *et al.* *N Engl J Med.* 2019;381(21):1995–2008. 4. Solomon SD *et al.* *N Engl J Med.* 2022;387(12):1089–1098.

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Patient-centred adult cardiovascular care

The AHA has published a scientific statement on patient-centred adult cardiovascular care. This collaborative approach involves tailoring management decisions to the patient's beliefs, preferences, and values. It aims to establish a partnership between the healthcare team and the patient/family in care planning and decision-making. This contrasts with a disease-centred approach that may not address what matters most to many patients.

Shared decision-making is a critical component of patient-centred care. It involves clinicians providing clear information to patients, engaging in collaborative discussions to understand patient values and preferences, and arriving at a shared decision that aligns with the patient's goals. Shared decision-making has increased patient knowledge, self-efficacy, and use of healthcare resources in cardiovascular disease. A collaborative care approach with an interprofessional team can help provide comprehensive, personalised care tailored to the patient's needs. This mainly benefits patients with advanced disease, complex comorbidities, or challenging psychosocial contexts. Medication management should also be patient-oriented, considering factors like polypharmacy, adherence, and pharmacogenomics.

Importantly, patient-centred care must address disparities in cardiovascular outcomes. Underrepresented racial/ethnic groups and socioeconomically disadvantaged populations are disproportionately affected by cardiovascular disease. Clinicians should undergo training to mitigate the impact of unconscious bias and discrimination and leverage community partnerships to provide equitable, culturally competent care.

<https://tinyurl.com/fsv7bfnp>

Overcoming clinical inertia with SGLT2 inhibitors

A recent publication discusses the challenges in implementing SGLT-2 inhibitors, a new class of medications now recommended as the "fourth pillar" of guideline-directed medical therapy (GDMT) for HF management.

The authors identify three key drivers of clinical inertia that have led to the underutilisation of SGLT-2 inhibitors in patients with HF: 1) lack of education, training, and practice organisation, 2) use of "soft" reasons to avoid intensification of therapy, and 3) overestimation of care provided.

Although hospitalists are broadly trained in HF management, they lack specific knowledge about the benefits of inpatient SGLT-2 inhibitor initiation. Guidelines now unambiguously recommend SGLT-2 inhibitors as part of "quadruple therapy" alongside other GDMT, with evidence showing significant reductions in HF hospitalisations and mortality.

"Soft" reasons contributing to clinical inertia include concerns about side effects, cost, and the unclear role of hospitalists versus specialists in prescribing SGLT-2 inhibitors. The authors argue that the benefits of these medications outweigh the risks, costs are often manageable, and hospitalists are well-positioned to initiate SGLT-2 inhibitor therapy.

Finally, physicians may overestimate the care they provide, failing to intensify therapy despite clear indications. Overcoming clinical inertia is important to ensure patients receive the full benefits of SGLT-2 inhibitors, which can prevent hundreds of thousands of hospitalisations and extend life expectancy.

Overall, the authors urge hospitalists to update their practices and advocate for system-level changes to accelerate the adoption of SGLT-2 inhibitors as part of quadruple therapy for patients with HF.

<https://tinyurl.com/m6a9k3z5>

Earn CPD

Royal Australasian College of Physicians (RACP) MyCPD participants can claim the time spent reading and evaluating research reviews as CPD in the online [MyCPD program](#). Please contact MyCPD@racp.edu.au for any assistance.

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.

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Regulatory News

Chronic heart failure treatment

Vericiguat (Verquvo[®]; 2.5 mg tablet; 5 mg tablet; 10 mg tablet) has had an amendment to remove the grandfather restriction. Authority applications for initial treatment can be made either in real-time using the Online PBS Authorities system or by telephone. Prescriptions for continuing treatment are Authority Required (STREAMLINED)

<https://tinyurl.com/34zdepvt>

Newly diagnosed systemic light chain amyloidosis

Daratumumab (Darzalex SC[®]; 1.8 g/15 mL injection, 15 mL vial) has had an amendment to remove the grandfather restriction. Authority applications for initial treatment can be made either in real time using the Online PBS Authorities system or in writing. Authority applications for continuing treatment can be made either in real time using the Online PBS Authorities system or by telephone.

<https://tinyurl.com/34zdepvt>

Changes to the prescription process from 1 July 2024

The Department of Health and Aged Care has reviewed and remade several key pharmaceutical benefits instruments, including the National Health (Listings of Pharmaceutical Benefits) Instrument 2012, the National Health (Prescriber bag supplies) Determination 2012, and the National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011. The National Health (Pharmaceutical Benefits) Regulations 2017 have also been amended. These legislative changes will take effect from April 1, 2024.

The key changes are that Services Australia will no longer require the original prescription to assess PBS Authority Required applications, and they will not record the Authority Approval Number on the prescription or forward approved prescriptions to the patient. During the transition period from April 1 to June 30, 2024, prescribers can continue to submit the original prescription or a copy of the proposed prescription. From July 1, 2024, Services Australia will only accept a legible copy of the original PBS Authority prescription, and they will retain a copy for processing while returning the original to the prescriber.

Prescribers should be aware that Services Australia is updating PBS Authority prescription pads to remove the 'Tick for return to patient' checkbox, and they should not send the original PBS Authority prescription to Services Australia after July 1, 2024. Prescribers can submit written PBS Authorities through the Health Professional Online Services (HPOS) Form Upload function or request and obtain approvals in real-time using the Online PBS Authorities system.

<https://tinyurl.com/mryj5xx4>

News in Brief

Medicines Repurposing Program established

The Medicines Repurposing Program aims to identify new therapeutic uses for existing medicines in Australia, improving patient access. Stakeholders, including clinicians, can suggest potential new therapeutic uses for existing medicines, which must be approved by the TGA and considered for listing on the PBS by PBAC. The program is part of Strategic Agreements 2022–2027. Further, the 2020 National Strategic Action Plan for Rare Diseases lists repurposing medicines as an action item.

<https://tinyurl.com/2hkxxu53>

ACHD Workforce Global Survey

Have your say in a global survey on factors influencing the decision to pursue ACHD as a career. The primary objective is to gather insights on what motivates cardiologists and trainees to pursue a career in ACHD and identify factors that may discourage them. This questionnaire will request demographic and training factors and can be completed in 5–7 minutes.

<https://tinyurl.com/8u7mmt79>

COVID-19 Resources for Cardiologists

CSANZ <https://tinyurl.com/y3xp2729>

ACC <https://tinyurl.com/y68aud3a>

ESC <https://tinyurl.com/wn3fst5>

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

[Dapagliflozin across the range of ejection fraction in heart failure](#)

[Vericiguat in heart failure and reduced ejection fraction](#)

[Cardiology Research Review](#) with Associate Professor John Amerena

[Heart Failure Research Review](#) with Professor Andrew Coats, and Dr Mark Nolan

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