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EDITORIAL

Time to Rethink our Approach to Guidelines? International Cascade Guidelines for Heart Failure

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The primary reason for clinical guidelines is to encourage best practice to improve health outcomes. While many guidelines provide a comprehensive summary of the evidence, there remain a number of limitations including their currency, generalisability and subsequent uptake into clinical practice. The last National Heart Foundation of Australia (NHFA) and Cardiac Society of Australia and New Zealand (CSANZ) heart failure (HF) guidelines were published 7 years ago [1], such that most clinicians in Australia and New Zealand now refer to more contemporary guidelines from Europe, North America or Asia or local consensus statements [2–5]. However, even those guidelines may become out-of-date within hours of their launch and their applicability to the broader global community has been questioned [6]. A recent survey of 2,622 clinicians from 138 countries identified that the greatest obstacle to implementing HF guidelines identified by clinicians from low- to middle-incomes countries was that guidelines were from high-income countries, whereas the most frequent obstacle identified by clinicians from high-income countries was that guidelines were too text heavy [6].

In this issue of *Heart, Lung and Circulation*, the iCARDIO Alliance (International Cardio Alliance to improve Disease Outcomes) HF 2025 guidelines provide concise, practical recommendations for the prevention, diagnosis and management of HF [7]. The iCARDIO Alliance represents an international collaboration that aims to gather leading cardiovascular societies, including CSANZ, to address some of the limitations of previous guidelines [8]. A writing task force comprising authors from all inhabited continents was established with over half the panel coming from outside Europe and North America to increase their applicability to the broader global community. A consensus approach considered prior HF guideline recommendations and new evidence published after those guidelines were developed, with recommendations graded as "strongly recommend", "recommend", "suggest" or "do not do". Additional context-specific recommendations tailored to individual patient needs were provided where resource limitations were relevant. A peer review team comprising worldwide experts then reviewed the document followed by a final phase of open public review [7].

Prior to proceeding to the recommendations, it should be noted that the iCARDIO Alliance HF guidelines aligned with the 2018 NHFA/ CSANZ HF guidelines by categorising HF with a left ventricular ejection fraction (LVEF) below 50% as HF with reduced ejection fraction (HFrEF) [1]. In 2018, we also elected to move away from the European Society of Cardiology mid-range category (LVEF 40%–49%) [9], because there was no clear defining syndrome recognised for this category (as opposed to having either a reduced or preserved LVEF), that the reproducibility of tests to measure LVEF made it difficult to accurately identify the mid-range group and it was unclear how a mid-range category would inform clinical

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management given that these patients benefited similarly from HFrEF pharmacological therapies [1].

Based on recent studies, HF prevention recommendations in the iCARDIO Alliance guidelines include recommending evidence-based sodium-glucose cotransporter-2 inhibitors (SGLT2I) in patients with type 2 diabetes mellitus (T2DM) or chronic kidney disease (CKD), glucagon-like peptide-1 receptor agonists (GLP-1 RA) in patients with T2DM and the non-steroidal mineralocorticoid receptor antagonist (MRA), finerenone, in patients with both CKD and T2DM [7]. If resources are severely limited, other SGLT2Is and MRAs may be used. Relevant to our local context, appropriate antibiotics are recommended in patients with Group A beta haemolytic streptococcal infection for the primary and secondary prevention of rheumatic fever and rheumatic heart disease [7].

The recommendations for the diagnosis and workup of HF are largely unchanged compared with recent guidelines, with ancillary imaging investigations including cardiac magnetic resonance imaging, bone scintigraphy and positron emission tomography recommended in patients with suspected infiltrative or inflammatory cardiomyopathies. The evolving role of point-of-care ultrasound and pulmonary arterial pressure measurement with CardioMems to monitor congestion is also acknowledged [7].

Consistent with recent guidelines, four pillars of HFrEF management, namely renin angiotensin system inhibitors, HF-specific beta blockers, MRA and SGLT2I are strongly recommended to decrease mortality and morbidity, with preference of an angiotensin receptor neprilysin inhibitor (ARNI) over an angiotensin converting enzyme inhibitor (ACEI) [7]. However, if resources are severely limited, an ACEI or angiotensin receptor blocker may be used instead of ARNI. There is increased focus on medication titration and recognition that potassium binders may facilitate this process [7]. The soluble guanylate cyclase stimulator, vericiguat, is suggested to decrease HF hospitalisation and cardiovascular death in patients with HFrEF experiencing recent worsening HF despite these measures, especially if the N-terminal pro–B-type natriuretic peptide is below 5,000 pg/mL [7]. Intravenous iron supplementation (ferric carboxymaltose or ferric derisomaltose) is strongly recommended to improve symptoms and exercise capacity in patients with HFrEF who are iron deficient, and based on a recent meta-analysis that included six randomised, controlled trials [10], is also recommended to decrease HF hospitalisation and cardiovascular death [7]. Alternative non-dextran containing formulations may be used if resources are limited. These guidelines also acknowledge that a simplified biochemical definition of iron deficiency based on a transferrin saturation below 20% can be used [7].

The pharmacological recommendations for the management of HF with a preserved ejection fraction (HFpEF) are most notable, given the evidence is rapidly evolving [11–16]. The non-steroidal MRA, finerenone, is now recommended as a second pillar of care to decrease HF hospitalisation in HFpEF in addition to an evidenced-based SGLT2I (the latter being strongly recommended in patients with HF regardless of the LVEF) [7]. However, if finerenone is not available (including if resources are severely limited), spironolactone is suggested. ARNI is recommended in patients with HFpEF with the LVEF in the lower end of the spectrum, especially in women. GLP-1 RA-based therapies (tirzepatide or semaglutide) are strongly recommended in patients with obesity and HFpEF to decrease weight and improve symptoms and quality of life, and are also suggested to decrease HF hospitalisation [7].

Recommendations for implantable cardioverter defibrillators and cardiac resynchronisation therapy (CRT) are similar to previous guidelines. However, it is likely that a favourable recommendation likely to generate further discussion is that for cardiac contractility modulation using the Optimizer Smart system to improve symptoms and exercise capacity in patients with HFrEF (LVEF 25%–45%) despite guideline-directed medical therapy, who are not suitable for CRT. Updated recommendations are also provided for transcatheter valvular interventions, including transcatheter aortic valve implantation and mitral and tricuspid valve edge-to-edge repair [7].

Finally, subspecialised recommendations are provided for a range of conditions including transthyretin stabilisers and synthesis inhibitors for transthyretin cardiac amyloidosis, cardiac myosin inhibitors for refractory symptomatic obstructive hypertrophic cardiomyopathy and GLP-1 RA-based therapies in moderate to severe obstructive sleep apnoea associated with obesity [7].

These guidelines represent an important step towards addressing some of the limitations of current guidelines, including increasing their applicability to the broader global community. However, it remains to be seen whether this increases the uptake of best practice with the ultimate goal being to improve health outcomes in patients with HF.

Disclosure

The authors are the Australian co-authors of the iCARDIO Alliance Global Implementation Guidelines on Heart Failure 2025.

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