Heart Failure Research Review™

Making Education Easy

Issue 68 - 2022

In this issue:

Abbreviations used in this issue:

ACE = angiotensin converting enzyme; **AF** = atrial fibrillation; **ARB** = angiotensin receptor blocker; **ARNI** = angiotensin receptor neprilysin inhibition; **BP** = blood pressure; **CRT** = cardiac resynchronisation therapy; **CV** = cardiovascular; **EF** = ejection fraction; **GFR** = glomerular filtration rate; **HF** = heart failure; **HFPEF/HFREF** = HF with preserved/reduced EF; **ICD** = implantable cardioverter defibrillator; **KCCQ** = Kansas City Cardiomyopathy Questionnaire; **LV/RV** = left/right ventricular; **LVAD** = LV assist device; **NT-proBNP** = N-terminal prohormone of brain natriuretic peptide; **NYHA** = New York Heart Association; **QOL** = quality of life; **RAAS** = renin-angiotensin-aldosterone system; **RCT** = randomised controlled trial; **SGLT** = sodium-glucose cotransporter.

Welcome to issue 68 of Heart Failure Research Review.

This issue begins with research reporting on a simple one-page triage survey for identifying patients potentially eligible for referral to an advanced HF centre. The tolerability of sacubitril/valsartan in patients with advanced HF has been assessed using data from the 3- to 7-day run-in period of the LIFE trial, as tolerance to an RAAS antagonist was not required before starting sacubitril/valsartan in this trial. Other selected research reports that in patients without a history of HF who undergo either cardiac or noncardiac surgery, postoperative AF is associated with subsequent hospitalisation for HF. SGLT-2 inhibitor trials conclude this issue, with studies on the effects of starting empagliflozin early for acute decompensated HF on diuresis and kidney function (EMPAG-HF), and the short-term effects of dapagliflozin for HFREF on maximal functional capacity at 1 and 3 months (DAPA-VO_2).

We hope you enjoy this update in HF research. We look forward to your comments and suggestions.

Kind Regards,

Professor Andrew Coats
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A survey-based triage tool to identify patients potentially eligible for referral to an advanced heart failure centre

Authors: Murphy L et al.

Summary: With the aim of identifying patients potentially eligible for referral for assessment for advanced surgical HF therapies, these researchers developed a survey of 13 potential clinical markers of advanced HF, modified from the Heart Failure Association of the European Society of Cardiology's 'I NEED HELP' tool. The survey was distributed to 26 secondary and tertiary HF clinic services for completion over a 3-month period for consecutive patients aged <65 years with an EF <40% and HF duration >3 months; the survey was completed by 21 clinics that managed 4950 all-comer patients over the 3-month period, of whom 7.5% met the inclusion criteria and were surveyed. Around two-thirds of these patients (66%) had ≥1 potential marker for advanced HF (i.e. ~5% of the total all-comer population). Of the patients with potential markers detected, 27% had two or more, 20% had three and 16% had four or more, with the most frequently noted markers being ≥1 hospitalisation for HF or unscheduled clinic review (56%), RAAS inhibitor intolerance due to hypotension or renal dysfunction (29%) and β-blocker intolerance due to hypotension (27%). NYHA class III or IV symptoms were recorded for nearly a quarter of the patients. The number of actual referrals to the advanced HF clinic was also audited over a 9-month period, during which the number of patients actually referred to the advanced HF clinic during the same time period was <5% of the potentially eligible cohort.

Comment: This is an interesting report on the proportion of the HF population that may be suitable for referral for an advanced HF service. In a near universal national survey, specialist HF clinics in Ireland were asked to recruit consecutive outpatients with HF based on simple cutoff criteria to then look at whether they satisfied the published criteria for advanced HF of the Heart Failure Association (modified 'I NEED HELP' tool). Over a 3-month period, all HF patients aged <65 years with LVEF <40% and >3 months HF were assessed. Of the 7.5% of HF clinic attendees who satisfied the initial criteria, 66% had ≥1 potential marker for advanced HF (5% of the total all-comer HF population). During the period of this audit, the number of patients actually referred to the advanced HF clinic during the same time period was <5% (compared with 67%) of this potentially eligible cohort, suggesting a significant deficit of advanced HF services, should all potentially suitable patients be referred for such assessment.

Reference: ESC Heart Fail; Published online June 27, 2022
Abstract

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CHF patients aged ≥ 70 years deserve an age-proven β-blocker[1,2]

NEBILET reduced the risk of all-cause mortality or cardiovascular hospitalisation in a broad range of CHF patients aged ≥ 70 years*[1,2]

*vs placebo P = 0.039; patients ≥ 70 years regardless of age, gender or left ventricular ejection fraction

NEBILET: Age proven in CHF patients aged ≥ 70 years[1,2]

CHF = Chronic Heart Failure

PBS Information: Restricted benefit. Moderate to severe heart failure. Refer to PBS Schedule for full restricted benefit information.

Please review full Product Information before prescribing. The Product Information can be accessed at www.menarini.com.au/pi

NEBILET (nebivolol hydrochloride) tablets 1.25mg, 5mg, 10mg. Indication(s): Essential hypertension. Stable chronic heart failure (CHF) as an adjunct to standard therapies in patients 70 years or older. **Dose and Method of Administration:** Once daily dosing, can be given with or without meals, consistent approach is recommended. Indication 1 - Hypertension: 5 mg daily. Renal insufficiency: recommended starting dose is 2.5 mg daily, can be increased to 5 mg if needed. Patients > 65 years: recommended starting dose is 2.5 mg daily, can be increased to 5 mg if needed. Patients > 75 years: caution must be exercised and these patients should be monitored closely. Indication 2 - CHF: The initial up titration should be done gradually at 1-2 weekly intervals based on patient tolerability, starting at 1.25 mg once daily, increased to 2.5 mg, then to 5 mg and then to 10 mg once daily. Initiation of therapy and every dose increase should be done under close medical supervision for at least 2 hours. No dose adjustment is required in patients with mild to moderate renal insufficiency. Use in patients with severe renal insufficiency (serum creatinine ≥ 250 micromol/L) is not recommended. **Contraindications:** Hypersensitivity to the active or any of the excipients; liver insufficiency or liver function impairment; acute heart failure; cardiogenic shock or episodes of heart failure decompensation requiring IV inotropic therapy; sick sinus syndrome, including sino-atrial block; second and third degree heart block (without a pacemaker); history of bronchospasm (e.g. including COPD) and/or asthma; untreated phaeochromocytoma; metabolic acidosis; bradycardia (HR < 60 bpm prior to starting therapy); hypotension (systolic BP < 100 mmHg); severe peripheral circulatory disturbances. **Precautions:** Avoid abrupt cessation unless clearly indicated – reduce dosage gradually over 1-2 weeks. If it must be withdrawn abruptly, close observation is required. Anaesthesia; untreated congestive heart failure, unless stabilised; bradycardia; peripheral circulatory disorders (e.g. Raynaud's disease, intermittent claudication); first degree heart block; Prinzmetal's or variant angina; lipid and carbohydrate metabolism – does not affect glucose levels in diabetic patients, but may mask symptoms of hypoglycaemia; hyperthyroidism; COPD; asthma; phaeochromocytoma; various skin rashes; conjunctival xerosis; oculomucocutaneous syndrome; psoriasis; increased sensitivity to allergens and severity of anaphylactic reactions; galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption; hepatic insufficiency or impaired liver functions; severe renal insufficiency; children and adolescents; pregnancy (Cat C); lactation; driving vehicles or operating machines. See approved PI. **Interactions:** Combination not recommended: Class I antiarrhythmics; calcium channel antagonists (verapamil/diltiazem); centrally-acting antihypertensives; other beta-blockers (incl. eye drops). Combination to be used with caution: Class III antiarrhythmics; anaesthetics (volatile); insulin and other oral diabetic medicines; calcium antagonists (dihydropyridine type); catecholamine depleting agents; baclofen; amifostine. For other combinations requiring careful consideration, see approved PI. **Adverse effects:** Headache, dizziness, tiredness, fatigue, paraesthesia, constipation, nausea, diarrhoea, cardiac failure aggravated, bradycardia, hypotension, hypertension, atrial fibrillation, angina pectoris, dyspnoea, oedema, slowed AV conduction/AV-block, bronchospasm. Post-marketing reports of hypersensitivity, angioneurotic oedema, abnormal hepatic function, acute pulmonary oedema, acute renal failure, myocardial infarction, Raynaud's phenomenon, thrombocytopenia. See approved PI. [mPI Version 8.0]

References: 1. NEBILET® Approved Product Information, 13 November 2020.
2. Flather MD *et al. Eur Heart J* 2005; 26: 215–25.

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Empagliflozin improves outcomes in patients with heart failure and preserved ejection fraction irrespective of age

Authors: Böhm M et al., on behalf of the EMPEROR-Preserved Trial Committees and Investigators

Summary: This analysis of data from the EMPEROR-Preserved trial explored how age affected the treatment effect of the trial's investigational agent, empagliflozin; the 5988 trial participants were stratified by age at baseline as <65 years (n=1199), 65–74 years (n=2214), 75–79 years (n=1276) or ≥80 years (n=1299). For the trial's placebo group, the incidences of the primary outcome (CV-related death or HF hospitalisation) and CV-related death increased with age (respective p values for trend, 0.02 and 0.003). The primary outcome and the outcomes of first HF hospitalisation and first or recurrent HF hospitalisation were reduced in the empagliflozin arm for all age groups, with effects being similar at ages ≥75 years and >80 years (respective p values for interaction, 0.22 and 0.51). Empagliflozin recipients also experienced an improvement in KCCQ Clinical Summary Score at week 52 and attenuation in the decline of estimated GFR, with no interaction by age. Age group also had no significant impact on clinically relevant differences in adverse events between the empagliflozin and placebo groups.

Comment: This is yet another subgroup analysis of the EMPEROR-Preserved trial. This is the first positive trial in HFPEF, so it is also useful to see whether the results applied in all patients in the trial or whether there were subsets of patients with less benefit. This is particularly important when you have a condition like HFPEF where there is some uncertainty about the diagnosis in certain patients, particularly in the elderly with multiple comorbidities. Age is often a factor in the under-prescription of guideline-directed medical therapy, so if there is uncertainty about applicability of the benefits of empagliflozin in the EMPEROR-Preserved trial, it would be important to see whether there was any evidence that age was an important factor. The results of this very detailed analysis was that advancing age predicted an increased rate of the primary outcome and CV mortality, but that empagliflozin reduced the primary and secondary outcomes as well as improving KCCQ Clinical Summary Score (QOL) at week 52 and attenuating the decline of estimated GFR, irrespective of advancing age. In addition there were no clinically relevant differences in adverse events between empagliflozin and placebo across age.

Reference: J Am Coll Cardiol 2022;80:1–18
Abstract

Tolerability of sacubitril/valsartan in patients with advanced heart failure

Authors: Vader JM et al., on behalf of the LIFE Investigators

Summary: This analysis of the LIFE trial's 3- to 7-day run-in period of sacubitril/valsartan 24mg/26mg twice a day evaluated the tolerability of this treatment in the trial's participants, which consisted of 445 patients with chronic advanced HFREF. Intolerance to sacubitril/valsartan was seen in 18% of the trial participants, with the main reasons being systolic BP <90mm Hg (59%), hypotension or dizziness with systolic BP >90mm Hg (19%) and creatinine level >2.0 mg/dL (12%). A multivariate analysis revealed that intolerance to sacubitril/valsartan was predicted by lower mean arterial pressure, lower serum chloride level, presence of an ICD and/or CRT device, moderate or greater mitral regurgitation, ACE inhibitor or ARB nonuse at screening visit, and insulin use at screening. The likelihood of sacubitril/valsartan intolerance was 48.9% for participants with ≥4 predictors.

Comment: Sacubitril/valsartan has been an important advance in the management of HFREF patients. The trial databank for this treatment has however been limited to only one major RCT, PARADIGM-HF, which only recruited patients who had already shown that they tolerated high-dose ACE inhibitors. The LIFE trial looked at advanced HF patients with low EF and recent NYHA class IV symptoms, including patients who had not been shown to tolerate high-dose ACE inhibitor in the past. In this analysis, 18% of recruited patients were intolerant of open-label low-dose sacubitril/valsartan (24mg/26mg twice a day), due to low systolic BP (<90mm Hg), hypotension/dizziness and/or renal dysfunction (creatinine level >2.0 mg/dL). Factors such as lower mean arterial pressure, lower serum chloride level, presence of an ICD and/or CRT device, moderate or greater mitral regurgitation, nonuse of ACE inhibitor or ARB and the use of insulin all predicted intolerance, and in the presence of four such factors, nearly one half of patients were intolerant of sacubitril/valsartan initiation, showing that care is needed if planning sacubitril/valsartan initiation in similar patients.

Reference: JACC Heart Fail 2022;10:449–56
Abstract

Angiotensin receptor neprilysin inhibition and associated outcomes by race and ethnicity in patients with heart failure with reduced ejection fraction

Authors: Chapman B et al.

Summary: Data from the US-based prospective, observational CHAMP-HF registry were analysed to examine changes in health status and clinical outcomes following initiation of treatment with ARNIs according to race/ethnicity. For the analyses, 758 patients who had initiated ARNI treatment were propensity score-matched to 758 who had not, with stratification into Hispanic, non-Hispanic Black, non-Hispanic White and other non-Hispanic groups. The race and ethnicity groups were similar for changes in mean KCCQ score after ARNI initiation (3.5, 2.0, 5.5 and 3.2 points for non-Hispanic White, non-Hispanic Black, other non-Hispanic and Hispanic individuals, respectively), with no significant interaction between race or ethnicity and ARNI initiation (p=0.21). Similarly, no significant interaction was seen between race or ethnicity and ARNI initiation for the outcomes of hospitalisation for HF (p=0.82) or all-cause mortality (p=0.92).

Comment: One of the major drug classes recommended for the treatment of HFREF is the ARNI sacubitril/valsartan, but this agent has only been evaluated in one large scale RCT (PARADIGM-HF). As a result, the range of patients assessed with sacubitril/valsartan is limited. These authors use the large detailed US HFREF registry (CHAMP-HF) to look at patients initiating sacubitril/valsartan, to determine tolerability and health effects of such initiation and to see whether different races and ethnicities were associated with different responses to sacubitril/valsartan, using a propensity-matched analysis. Seven hundred and fifty eight patients in each of two groups (ARNI and no ARNI initiation) were compared. Changes in KCCQ QOL score after ARNI initiation were similar among all race and ethnicity groups, as well as no statistically significant interactions between race and ethnicity and ARNI initiation on HF hospitalisation, at least giving support for the applicability of the PARADIGM-HF trial results to different races in a US context.

Reference: J Am Heart Assoc 2022;11:e022889
Abstract

Post-operative atrial fibrillation and risk of heart failure hospitalization

Authors: Goyal P et al.

Summary: The association of postoperative AF with incident HF hospitalisation in adults with no HF history undergoing cardiac (n=76,536) or noncardiac (n=2,929,854) surgery was explored in this retrospective cohort study from the US. Incident postoperative AF occurred in 18.8% and 0.8% of patients from the cardiac and noncardiac surgery groups, respectively. In both the cardiac and noncardiac surgery groups, postoperative AF was associated with incident HF hospitalisation (respective adjusted hazard ratios 1.33 [95% CI 1.25–1.41] and 2.02 [1.94–2.10]), with the associations persisting in sensitivity analyses that excluded HF within 1 year of surgery (1.15 [1.01–1.31] and 1.49 [1.38–1.61]).

Comment: It is not known if the common complication of postoperative AF predicts future HF hospitalisation, even though statistically it has been shown there are increased risks of stroke and mortality. In this retrospective cohort study from the USA after adjusting for socioeconomic factors and comorbidities, postoperative AF was seen to be associated with a 33% increased risk of HF hospitalisation, significant even after 1 year. The authors suggest postoperative AF may be a marker for subclinical HF and an elevated risk for HF, suggesting perhaps a need for more careful evaluation subsequent to the episode of postoperative AF.

Reference: Eur Heart J 2022;ehac285
Abstract

Hemodynamic effects of cyclic guanosine monophosphate-dependent signaling through β3 adrenoceptor stimulation in patients with advanced heart failure

Authors: Bundgaard H et al.

Summary: Twenty-two patients with HFREF (NYHA functional class III–IV, LVEF <35% and increased NT-proBNP level) were randomised to receive oral mirabegron 300mg or placebo each day for 1 week added to recommended HF therapy. There were no significant between-group differences for invasive haemodynamic measurements during rest and submaximal exercise at 3 hours, but at 1 week mirabegron recipients had a significantly larger increase in cardiac index compared with placebo recipients (mean difference, 0.41 L/min per body surface area [p=0.039]) and a significantly greater decrease in pulmonary vascular resistance (–1.6 [p=0.02]) compared with placebo recipients. There were no significant between-group differences seen during exercise, or for change in heart rate, systemic vascular resistance, BP or renal function. Mirabegron demonstrated good tolerability.

Comment: Despite there being four foundational drug treatments recommended for the treatment of HFREF, we are always looking for new treatment options for advanced HF. What we have is limited by toxicity, and we are still waiting for a safe and effective positive inotropic agent that can be used more widely. We have had great success with adrenergic receptor modulation, and hence the previously poorly understood β3-receptor is an interesting target. This work from an Australian Danish group who have been studying this for some time is of interest, for although it is an early haemodynamic only study, it does suggest that there may be some potential clinical benefit of the cardiac β3-receptor stimulation in advanced HF patients. In this 1-week RCT in 22 NYHA class III–IV HFREF patients, mirabegron increased cardiac index and reduced pulmonary vascular resistance at rest with no differences in heart rate, BP or renal function, suggesting a possible future role in patients with worsening or terminal HF, but with a clear need for further larger trials.

Reference: Circ Heart Fail; Published online June 27, 2022
Abstract

Right heart failure following left ventricular device implantation: natural history, risk factors, and outcomes

Authors: Kapelios CJ et al.

Summary: These researchers reported on the natural history, risk factors and outcomes of right HF for 5537 patients entered in the STS INTERMACS database who had undergone continuous-flow LVAD implantation. The prevalence of right HF over 1 month postimplantation was 24%, with persistence of right HF in 5.3% of these patients at 12 months. *De novo* right HF first identified at 3 and 6 months occurred in 5.1% and 4.8% of the patients, respectively, with persistence out to 12 months in 17% and 25% of these patients, respectively. Factors significantly associated with incident right HF at 3 months were a 5 mg/dL increase in blood urea nitrogen level before LVAD implantation (odds ratios 1.03–1.09 [p<0.0001]), prior tricuspid valve repair/replacement (2.01–10.09 [p<0.001]), severely depressed RV systolic function (1.17–2.20 [p=0.004]) and centrifugal versus axial LVAD (1.15–1.78 [p=0.001]). Two-year survival was lower for patients with persistent right HF at 3 months than for those with *de novo* right HF or right HF that had resolved by 3 months (57% vs. 75% and 78%, respectively [p<0.001]).

Comment: The long-term management of severe advanced HFREF is restricted to transplantation or mechanical circulatory support. Despite years of effort, we still do not understand why some patients tolerate very poor haemodynamic function and others do not. One aspect that is difficult to assess is the role of RV dysfunction, and in particular, how this is best managed in the setting of advanced HF. This retrospective report from the STS INTERMACS registry of LVAD recipients looked at the role of short- and long-term RV function in determining long-term outcomes. Hearteningly, transient RV dysfunction at 1 and 3 months post-LVAD insertion did not seem to be a long-term problem, provided the RV function subsequently improved. Longer-term late-onset (>6 months) persistent RV dysfunction, however, was a significant marker of very poor outcomes. We clearly need better treatments for the right ventricle as we manage our advanced HFREF patients, and this study suggests we should evaluate RV function at 1, 3 and 6 months post-LVAD insertion for useful prognostic insights.

Reference: Circ Heart Fail 2022;15:e008706
Abstract

Vericiguat and health-related quality of life in patients with heart failure with reduced ejection fraction

Authors: Butler J et al., on behalf of the VICTORIA Study Group

Summary: This analysis of VICTORIA trial data evaluated vericiguat versus placebo on health status outcomes according to KCCQ score in 5050 patients with HFREF; 4664, 4741 and 4470 participants had median KCCQ clinical summary score (median 65.6), total symptom score (68.8) and overall symptom score (59.9) at baseline, respectively, with 94%, 88% and 82% having 4-, 16- and 32-week data. By week 16, both trial arms showed improvements in clinical summary score by a median of 6.3 points, with no significant difference in improvement in total or overall symptom score between the two groups; the 4- and 32-week trends were similar. Compared with placebo, vericiguat reduced the risk of CV-related death or hospitalisation for HF similarly across tertiles of the baseline clinical summary, total symptom and overall symptom scores (respective p values for interaction, 0.13, 0.21 and 0.65).

Comment: Our long-term aims in treating HFREF include reducing mortality and the risk of emergency HF hospitalisation, but also importantly improving QOL in our patients. Recent recommended therapies have been asked to also prove that they improve patient reported outcomes assessing QOL. The most commonly accepted measurement now is the KCCQ score, and recent drug classes, in particular the SGLT-2 inhibitors, have been shown to improve this parameter, particularly in the setting of acute HF. Thus this analysis of the Victoria trial of the soluble guanylate cyclase stimulator vericiguat is of interest. Although in this trial vericiguat reduced the risk of CV death or HF hospitalisation across the range of baseline KCCQ scores, it did not significantly improve KCCQ scores compared with placebo, which is disappointing as this is an unmet need for our severe HFREF patients.

Reference: Circ Heart Fail 2022;15:e009337
Abstract

Effects of early empagliflozin initiation on diuresis and kidney function in patients with acute decompensated heart failure (EMPAG-HF)

Authors: Schulze PC et al.

Summary: Sixty patients were randomised within 12 hours of hospitalisation for acute decompensated HF to receive empagliflozin 25 mg/day or placebo added to standard decongestive treatments (including loop diuretics) in this trial. Compared with placebo, the addition of empagliflozin was associated with: i) a 25% increase in median cumulative urine output over 5 days (primary endpoint; 10.8 vs. 8.7LmL [p=0.003]); ii) increased diuretic efficiency (p=0.041) without a significant impact on estimated GFR, total urinary protein level or urinary α1-microglobulin level; and iii) a greater decrease in NT-proBNP level at 5 days (–1861 vs. –727.2 pg/mL [p<0.001]). Safety events did not differ significantly between the two study arms.

Comment: The SGLT-2 inhibitor class of drugs has been a major treatment advance in HFREF. They started life as a treatment for type 2 diabetes for their ability to reduce blood glucose levels via inducing increase glucose excretion in the urine. This also produced an increase in sodium and water output. However, the demonstration of major clinical benefits in both HFREF and more recently in HFPEF have been felt unlikely to be entirely due to these effects on renal glucose sodium and water handling, but rather these effects may be of additional clinical benefit in patients with congestive HF, adding an extra diuretic element that comes with protection of renal function. In this EMPAG-HF trial, a single-centre RCT, 60 acutely decompensated HF patients were randomly assigned to empagliflozin 25mg daily or placebo on top of routine care. The primary endpoint of cumulative urine output over 5 days showed a 25% increase (p=0.003) without affecting markers of renal function (estimated GFR, 51±19 vs. 54±17 mL/min/1.73m^2 [p=0.599]) or renal injury, along with no differences in the incidence of safety events between groups. Thus the increasing drive to introduce SGLT-2 inhibitors early in an HF hospitalisation may come with clinical diuretic benefits. It should be noted that this study strangely chose to use 25mg rather than the HFREF approved dose of 10mg, meaning one cannot be certain the same benefits would be seen with 10mg.

Reference: Circulation; Published online June 29, 2022
Abstract

Short-term effects of dapagliflozin on maximal functional capacity in heart failure with reduced ejection fraction (DAPA-VO_2)

Authors: Palau P et al., the DAPA-VO2 Investigators

Summary: Stable patients with HFREF were randomised to receive dapagliflozin (n=45) or placebo (n=45) in this trial with a primary outcome of change in peak VO_2 at 1 month and 3 months. Dapagliflozin treatment was associated with significant increases in peak VO_2 at both 1 and 3 months by 1.09 and 1.06 mL/kg/min (respective p values, 0.021 and p=0.032), but there were no significant differences at either timepoint for the secondary endpoints of 6-minute walk distance, QOL and echocardiographic parameters.

Comment: The SGLT-2 inhibitors dapagliflozin and empagliflozin are recommended for the treatment of HFREF due to proven reductions in the composite endpoint of CV mortality or HF hospitalisation. Recent studies have also shown improvements in QOL as assessed by the KCCQ symptom score. What hasn't been so clear, however is whether this class of drug could increase exercise capacity in HFREF patients. The most accurate assessment of maximal exercise capacity is the cardiopulmonary exercise test assessing peak VO_2. In this DAPA-VO_2 trial in 90 stable HFREF patients, dapagliflozin significantly increased peak VO_2 (1 month, +1.09 mL/kg/min; and 3 months, +1.06 mL/kg/min) compared with placebo, showing an early and moderately sustained increase in objective exercise capacity in HFREF patients, adding to the benefits proven with this exciting new drug class in the treatment of HFREF. A 1 mL/kg/min increase in moderate-to-severe HF would be of useful clinical benefit.

Reference: Eur J Heart Fail; Published online May 23, 2022
Abstract

Heart Failure Research Review™

Independent commentary by Professor Andrew Coats

Andrew was born and schooled in Melbourne and studied medicine at Oxford and Cambridge. He has more than 110,000 citations, and an H-index of 141. He served as Editor-in-Chief of the International Journal of Cardiology from 1999 to 2016. Andrew published the first randomised trial of exercise training for CHF. Andrew has been Chairman or Committee member of multiple major clinical trials. He has served as Head of Cardiology at Imperial College and Royal Brompton Hospital, London, as Dean of Medicine and Deputy Vice-President at the University of Sydney, and as Joint Academic Vice-President of the University of Warwick, UK, and Monash University, Australia. He is presently President of the Heart Failure Association of the ESC.