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# December 2023 at a glance: Focus on medical therapy in chronic and acute heart failure

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## Consensus statement and reviews

The ESC Council on Stroke, the Heart Failure Association and the ESC Working Group on Thrombosis have published a consensus statement describing the interplay between heart failure (HF) and stroke, focusing on prevention, pathophysiology and patient's management.[1]

Qiliqiangxin is a commercial formulation of 11 different plant ingredients. In the QUEST trial, qiliqiangxin reduced the risk of cardiovascular (CV) death or HF hospitalization in patients with a background HF therapy. Packer reviewed multiple molecular pathways that may explain the benefits of qiliqiangxin highlighting similarities and differences with current treatments for HF, including sodium–glucose cotransporter 2 inhibitors (SGLT2i).[2,3]

Sudden cardiac death (SCD) remains an important cause of mortality in cardiomyopathies.[4] Polovina *et al.*[5] reviewed the incidence, risk factors and management of life-threatening arrhythmias and SCD.

## Chronic heart failure: Medical therapy

Hyperkalaemia and kidney dysfunction are among the most common reasons for guideline-directed medical therapy (GDMT) under-prescription and discontinuation.[6–9] A study including 33 942 patients with HF and reduced ejection fraction (HFrEF) from the Swedish Heart Failure Registry investigated the real-world use and safety of mineralocorticoid receptor antagonists (MRAs) across the entire spectrum of kidney function, measured by the estimated glomerular filtration rate (eGFR). MRAs were prescribed in 32%, 45%, 54%, 54% of patients with an eGFR <30, 30–44, 45–59 or ≥60 ml/min/1.73 $m^2$, respectively. MRA use was never associated with a higher risk of renal events (i.e. composite of dialysis/renal death/hospitalization for renal failure or hyperkalaemia), all-cause death as well as all-cause hospitalization across all the eGFR spectrum including also severe chronic kidney disease.[10]

COVID-19 affects outcomes and the conduct of clinical trials in patients with HF.[11–13] The DELIVER trial was conducted before and during the COVID-19 pandemic. Bhatt *et al.*[14] described the impact of COVID-19 in DELIVER participants. Out of 6263 patients, 9.4% developed COVID-19 and 52% of them required prolonged hospitalization or death. Treatment benefits of dapagliflozin persisted when censoring at COVID-19 diagnosis and pandemic onset. Patients surviving COVID-19 had a high early residual risk.

Both intravenous (IV) iron and SGLT2i have been associated with an increase in haemoglobin and haematocrit levels and outcome.[15–17] However, the effect of IV iron among patients using SGLT2i has not yet been studied. In a retrospective, single-centre study including HFrEF patients with iron deficiency treated with IV iron, those on concomitant treatment with SGLT2i experienced a greater increase in haemoglobin and haematocrit, compared to matched non-users consistently with stimulation of erythrocytosis by SGLT2i.[18,19]

Using pooled individual patient data from four large trials in patients with HF and mildly reduced and preserved ejection fraction (HFmrEF/HFpEF), Matsumoto *et al.*[20] analysed the association between calcium channel blocker (CCB) use and outcomes. Among 16 954 patients included, 34.6% used a CCB, mostly dihydropyridines. Treatment with CCBs was associated with similar risks of death and HF hospitalization and with a lower risk of pump failure death as compared to those not treated with CCBs, suggesting that these drugs may be safely used in patients with HFmrEF and HFpEF.

## Acute heart failure: Medical therapy

Acute HF is still associated with poor prognosis and efforts are needed to improve its prognosis.[21,22] A pre-defined sex-specific analysis of the GALACTIC (Goal directed afterload reduction acute congestive cardiac decompensation study) trial showed that a strategy of early intensive and sustained vasodilatation with rapid up-titration of renin–angiotensin–aldosterone system (RAAS) inhibitors versus usual care was less successful in women versus men both in the overall cohort and in patients with HFrEF.[23] In a previous analysis no significant treatment-by-sex interactions were found in the STRONG-HF trial.[24]

Implementation of GDMT affects kidney function.[8] An analysis of STRONG-HF described the association between changes in renal function and efficacy of rapid up-titration of GDMT according to the high-intensity care (HIC) strategy. The HIC group had less HF readmissions or death regardless of baseline eGFR at 180 days. An early decrease in eGFR at 1 week was associated with

lower average optimal doses of GDMT and smaller reductions in N-terminal pro-B-type natriuretic peptide during follow-up.[25]

## Percutaneous treatment of tricuspid regurgitation

Right-sided HF and tricuspid regurgitation (TR) are common and strongly associated with poor quality of life and prognosis.[26–28] Russo *et al.*[29] assessed characteristics and outcomes of patients with atrial versus ventricular secondary TR (STR) undergoing tricuspid transcatheter edge-to-edge repair (T-TEER) from the TriValve registry. Overall, 298 patients were included in the study, of whom 22% presented atrial STR and 78% ventricular STR. T-TEER effectively reduced TR in both groups. At 12-month follow-up, survival was higher in the atrial STR versus ventricular STR cohort.

## Exercise training

The effects of exercise training in HF are still discussed.[30] The Ex-VAD trial will assess the effects of a supervised exercise training programme on peak oxygen consumption and quality of life in patients with left ventricular assist device.[31] A Cochrane systematic review and meta-analysis including 60 trials (8728 participants) did not show a significant impact of exercise-based cardiac rehabilitation on all-cause deaths with, however, a reduction in all-cause hospitalization and an improvement of quality of life.[32]

## Quality of care and outcomes

Lower socio-economic status has been associated with worse prognosis.[33] Bobrowski *et al.*[34] examined the association between neighbourhood material deprivation, a metric estimating inability to attain basic material needs, with outcomes and processes of care among incident HF patients. Patients residing in the most deprived neighbourhoods had worse outcomes and reduced access to care than those less deprived. Significant interaction between age and deprivation quintile for outcomes were observed.

Kouranos *et al.*[35] described baseline characteristics, prognosis and predictors of outcome of 319 consecutive patients with cardiac sarcoidosis (CS). During a median follow-up of 2.2 years (range: 1 month–11 years), 8% of patients died. Patients with cardiac involvement as first manifestation of CS had a higher risk of morbidity and mortality. Natriuretic peptide levels, left ventricular ejection fraction and maximum standardized uptake value of $^{18}$F-flourodeoxyglucose positron emission tomography were independent predictors of outcome.

Machine-learning procedures have been successfully used to predict prognosis.[36] The InterTAK-ML is a machine-learning model developed to predict in-hospital mortality in 3482 patients with takotsubo syndrome. Considering the 10 most important variables, patients were clustered into six groups, and each group was associated with a specific risk of in-hospital death.[37]

The rationale and design of the ESC Heart Failure III Registry is published.[38]

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