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Management of Heart Failure in the Hospital: A Clinical Approach

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ABSTRACT

Despite significant improvements in pharmacology and non-pharmacology therapy, heart failure (HF) continues to be a substantial and increasing problem that involves major disability, hospital admissions, and considerable economic burdens. The combination of several comorbidities and overall frailty hinders clinical care. In recent times, notable advancements have been achieved in the management of HF. This study aims to review the latest available evidence, consider the indications outlined in worldwide recommendations, and expert opinions regarding the most effective treatment for individuals with HF. Our review concludes that heart failure is still a serious issue due to its high recurrence rate and poor prognosis. This can be attributed in part to low treatment adherence, poor diet, and early hospitalization. Therapeutic delay during down-titration is common and has been associated with a worse prognosis.

INTRODUCTION

Heart failure (HF) is a major cause of disease and economic burden worldwide, affecting 60 million people globally and 1-2% of patient admissions in healthcare facilities.[1–3] Even with tremendous breakthroughs in the diagnosis and management of HF, it remains a common cause to mortality rates. This is due to the high prevalence of HF and the generally frail patient population, in the clinical setting, which causes patients to need more complex therapeutic strategies.[4]

Multiple guidelines support early management and intervention of heart failure soon after diagnosis.[5,6] Uptitrating medication doses and reaching target therapeutic dose for each of the different class of HF drugs to achieve goal directed medical therapy (GDMT) has been demonstrated to significantly decrease overall death rates by up to 73% when compared to the

absence of treatment in individuals diagnosed with HF.[5]

This literature review aims to consolidate published data and provide a view of hospital-based HF management options such as using a multidisciplinary approach, pharmacological therapies, and relevant technologies. This review is meant as a guide for clinicians to use current approaches to management that focus on lowering morbidity and mortality related to heart failure.

LITERATURE REVIEW

Definition of Heart Failure

Multiple standards exist that provide definitions for heart failure. In general, heart failure (HF) is a pathological condition that presents with the presence of signs and symptoms that develop resulting from anatomical and/or physiological abnormalities of the heart. The diagnosis is supported with the presence of high natriuretic peptide (NP) or sign of systemic or pulmonary congestion. The categorization of HF is decided by the left ventricle ejection fraction (LVEF) observed during normal echocardiogram. The classifications of heart failure are as follows: heart failure with reduced ejection fraction (HFrEF), characterized by an ejection fraction (EF) of 40% or less; heart failure with mildly reduced ejection fraction (HFmrEF), characterized by an EF ranging from 41% to 49%; heart failure with preserved ejection fraction (HFpEF), characterized by an EF of 50% or greater; and heart failure with improved ejection fraction (HFimpEF), characterized by a previous EF of 40% or less, an increase in EF of at least 10%, and a current EF exceeding 40%.[2,7,8]

Inpatient Management of Heart Failure

Multidisciplinary Approach

The current recommendation is to utilize multidisciplinary strategies in order to effectively coordinate the management of HF across different care pathways, with the aim of lowering the probability of re-hospitalization and mortality.[9] Specialized nurses in the field of HF undertake the coordination of healthcare services, encompassing the gathering of patient data through both in-person and virtual interactions, as well as facilitating communication between healthcare professionals and specialists situated in various nations.[4] In France, there exists a national collaboration protocol that promotes the engagement of cardiologists in collaborative efforts with specialized HF nurses. The primary objective of this collaboration is to effectively coordinate therapy, facilitate unplanned nurse consultations, and efficiently manage heart failure telemonitor notifications.[10] This helps provide early therapy and close monitoring of heart failure

patients, stabilize the patient's condition immediately, slow the progress of heart failure, and reduce mortality and morbidity. A registry research conducted in Sweden demonstrated that patients diagnosed with heart failure who were referred to nurse-operated heart failure clinics exhibited improved survival rates.[11]

By leveraging collaborative practice agreements, pharmacists can effectively perform medication reconciliations, provide patient education, and assess potential drug-related concerns.[4] Pharmacists have an important role as the initial point of contact when patients return home. Although the number of pharmacists is increasing, their role is sadly underutilized.[12] it is recommended that in managing patient with HF, practitioners collaborated with other experts, such as pharmacists, psychologist, including pharmacists, nutritionists, mental health professionals, etc. However, the limited availability of resources in certain nations, such as Indonesia, makes implementation quite challenging.[13]

Optimizing Medical Therapy

Neurohormonal Antagonists

Neurohormonal antagonists, such as angiotensin receptor blockers (ARB), beta-blockers (BBs), angiotensin-converting enzyme (ACE) inhibitors, and mineralocorticoid receptor antagonists (MRAs) are essential in treating patients with HFeRF due to their ability to enhance the clinical outcome of the condition.[3] The PARADIGMHF research demonstrated that sacubitril/valsartan showed superiority over enalapril in terms of lowering mortality and hospitalization.[14] The TRANSITION study examined the feasibility of initiating angiotensin receptor-neprilysin inhibitor (ARNI) treatment for stable HFrEF patients following an acute HF event. The study found that patients who were newly diagnosed with HF experienced greater benefits from ARNI treatment compared to those with a previous HF diagnosis. Specifically, the patients demonstrated a more rapid reduction in the N-terminal prohormone of brain natriuretic peptide (NTproBNP) levels. The study also demonstrates lower high-sensitivity troponin T and re-hospitalization[15],

According to the ESC-EURObservational Research Program (EORP)-HFA Heart Failure Long-Term Registry, there were 84 percent of outpatients considered to be suitable candidates for sacubitril/valsartan medication. However, the percentage of patients who fulfilled the criteria outlined in the PARADIGM-HF trial and ESC guidelines ranged from 12 to 28 percent.[16] The reasons for this prescription shortage should be explored to ensure GDMT. Factors such as advanced age, the presence of hypotension, and a decline in renal function can contribute to the inadequate utilization of GDMT. The gradual titration of ARNI has been found to be linked with

enhanced efficacy of treatment among those with low systolic blood pressure. Additional investigation is required to assess the potential of novel potassium-lowering medications in optimizing therapeutic interventions.[3]

Sodium–glucose co-transporter 2 inhibitors (SGLT-2)

Notable advancements can be seen in the field of antidiabetic medications and their impact on cardiovascular risk. Additionally, novel therapeutic approaches for heart failure, apart from the traditional neurohormonal pathways, have been established.[3]

Sodium-glucose cotransporter 2 (SGLT2) inhibitors consistently show it's ability for minimizing the rate of hospitalization due to HF and mortality resulting from cardiovascular disease (CVD) among individuals with diabetes, irrespective of their baseline cardiovascular disease status and prior history of heart failure.[3] The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) trial was the first provided evidence of the significant advantages associated with SGLT-2 inhibitors. It revealed a notable decrease in the likelihood of experiencing adverse outcomes related to cardiovascular death or a worsening of HF in HFrEF patients regardless of whether they had diabetes or not (HR 0.74; 95% CI 0.65-0.85). The initial characteristics of participants in the DAPA-HF study were comparable to those observed in current registries and clinical investigations focusing on HFrEF.[17] The Reduced trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR) trial enrolled individuals with significant left ventricular systolic dysfunction, elevated natriuretic peptides, and decreased estimated glomerular filtration rate (e-GFR). The trial showed a decrease in the overall risk of mortality and hospitalization for HF in comparison to a placebo. In subgroup analyses (diabetes vs non-diabetes; ARNI treatment vs no ARNI treatment), the positive benefits remained consistent.[18]

The precise mechanisms responsible for the observed beneficial effects of SGLT2 inhibitors are not yet fully understood. Empagliflozin is believed to exert pleiotropic effects on cardiomyocytes, in addition to glycosuric and natriuretic effects. This therapy has beneficial effects on adenosine triphosphate synthesis, myocardial metabolism, diastolic function, and cardiac remodeling.[3,19]

Potassium Lowering Agents

The DIAMOND trial involved a sample size of 1642 patients who had HFrEF and hyperkalemia resulting from the use of renin-angiotensin-aldosterone system inhibitors (RAASi) from either the current or previous generation. The trial findings indicated that the administration of potassium-lowering agents resulted in a notable decrease in serum potassium

levels during the follow-up period. Additionally, patients who received these agents experienced fewer instances of hyperkalemia, were more likely to use high-dose mineralocorticoid receptor antagonists concurrently, and demonstrated an overall higher utilization of RAASi compared to those who received a placebo.[2,20]

Soluble guanylate cyclase stimulators

Vericiguat, a soluble guanylate cyclase activator, has demonstrated a reduction in the probability of cardiovascular mortality or hospitalization due to heart failure among individuals with HFrEF. The benefits were comparable in those with and without atrial fibrillation and across multiple ranges of eGFR. The administration of vericiguat shown a correlation with decreased urine albumin (UA) and high-sensitivity C-reactive protein (hs-CRP).. [2,21]

Cardiac Myosin Activator

The Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in HF (GALACTIC-HF) trial provided evidence on the effectiveness and safety of omecamtiv mecarbil, a selective cardiac myosin activator, in individuals diagnosed with chronic systolic heart failure and SBP ≤100 mmHg.[22] The results of the METEORIC-HF trial, which lasted of 20 weeks, indicate that the administration of omecamtiv mecarbil did not result in any significant improvements in the functional ability of HFrEF patients.[23] Therefore, this drug was recommended to improve the patient's condition. Danicamtiv, an adjunctive selective myosin activator, has demonstrated the potential to enhance contractility in the left ventricle and atrium in animal models during a Phase 2a clinical trial.[2]

Tafamidis

Transthyretin amyloid cardiomyopathy should be investigated in older patients with hypertrophic cardiomyopathy. The present research focuses on a unique and relatively new genetic disorder characterized by the buildup of amyloid fibrils within the myocardium, resulting in the development of HF.[4] Recent evidence suggests that tafamidis slows disease progression and improves survival. In a phase III placebo-controlled trial comprising 441 patients, it was observed that at the 30-month mark, the tafamidis group exhibited significantly lower rates of all-cause mortality and cardiovascular-related hospitalization compared to the placebo group ($P < 0.0001$). Tafamidis has been observed to decrease hospitalizations and mortality rates while enhancing the quality of life (QoL) in individuals with HF caused by transthyretin amyloid cardiomyopathy.[24]

Intervention Therapies

Cardiac Resynchronization Therapy

In appropriately selected HF patients, cardiac resynchronization therapy (CRT) demonstrated efficacy in improving cardiac function and reduce symptoms, leading to a reduction in both morbidity and mortality. This therapy may be the most realistic treatment that provides therapeutic improvement for HF patient with New York Heart Association (NYHA) Class IV. However, not all of eligible individuals referred for CRT.[2]

Heart Failure Association (HFA), European Heart Rhythm Association (EHRA), and European Association of Cardiovascular Imaging (EACVI), address the issue of underutilization of CRT, enhance the patient selection for CRT, and provide suitable post-implant care pathways.[25]

Implantation Cardioverter Defibrilator

The task of identifying individuals who may derive potential benefits from the utilization of an implanted cardioverter defibrillator (ICD) can be a difficult one. Individuals who have experienced a myocardial infarction and have an LVEF >35%, together with comorbidities such as diabetes and/or renal failure, have a notable risk of sudden cardiac death (SCD). However, the probability of experiencing a non-SCD event is even greater. This suggests that there may not be adequate reasons for extending the use of an ICD in these particular individuals.[3] A comprehensive analysis was conducted on four primary prevention studies involving patients with HFrEF to compare the impact of ICD placement between diabetes and non-diabetic individuals. The findings revealed that diabetic patients derived greater benefits from ICD implantation. The utilization of ICDs was found to be linked with a decreased likelihood of mortality in individuals without diabetes (HR 0.56; 95% CI 0.46-0.67), however no such association was observed in patients with diabetes.[26]

Cardiac Contraction Modulation

The implementation of cardiac contractility modulation (CCM) has been shown to enhance functional capacity and decrease hospitalizations related to CV and HF.[2] The full meta-analysis of patient data from all available randomized studies demonstrates that CCM yields statistically significant and clinically significant enhancements in functional capacity and QoL linked to heart failure. A European prospective registry of 503 individuals was utilized to examine the enduring consequences of CCM. CCM has been shown to enhance various aspects of

patient well-being, including QoL, functional status, and LVEF. Furthermore, there was a notable reduction in readmission for HF in comparison to the pre-treatment period.[27]

Percutaneous intervention for mitral and tricuspid regurgitation

The use of transcatheter mitral valve treatment has become an increasing popularity as a viable therapeutic approach for patients suffering from heart failure and severe secondary mitral regurgitation. Two randomized controlled studies were conducted to assess the prognostic impact of percutaneous edge-to-edge mitral valve replacement with MitraClip in patients with heart failure. MITRAFR did not demonstrate any significant decrease in hospitalizations due to HF or fatality rates. In contrast, COAPT shown a notable reduction in hospitalizations related to HF and mortality rates during a span of two years.[28] Observational trials have provided evidence to support the safety and effectiveness of the device in alleviating symptoms and enhancing the clinical condition of patients diagnosed with advanced heart failure, particularly those presenting with low EF and pulmonary hypertension.[3]

Orban et al. observed noteworthy enhancements NYHA class categorization, 6-minute walk test distance (6-MWT), and QoL among of 50 patients who underwent percutaneous edge-to-edge tricuspid valve surgery.[29] a study conducted by Schlotter et al. also show the outcomes of transcatheter tricuspid valve replacement in a cohort of 159 individuals diagnosed with severe functional tricuspid regurgitation. The patients were categorized into four distinct clinical scenarios according to their etiology: individuals receiving chronic hemodialysis, individuals exhibiting significant mitral regurgitation, individuals experiencing severe pulmonary hypertension, and individuals with a documented history of atrial fibrillation (AF).[30] The endpoint was seen to have the highest incidence among those diagnosed with pulmonary hypertension. Combined outcome of death, hospitalization for heart failure, or reintervention was observed in a greater proportion among patients who underwent hemodialysis, with the highest fatality rate recorded at 33.3%.[3]

Atrial fibrillation ablation

Ablation of paroxysmal or persistent AF is only recommended when one antiarrhythmic treatment fails or as an alternate primary treatment for paroxysmal AF alone. The amount of evidence supporting the use of ablation as a therapeutic intervention for both paroxysmal and chronic AF is expanding.[4] The CASTLE-AF trial comprised a cohort of 363 individuals diagnosed with systolic HF and AF.AF has been found to be correlated with a reduction in the overall number of deaths, hospitalizations resulting from worsening HF, and cardiovascular-related

mortality.[31] Furthermore, the CABANA prospective randomized study conducted a comparative analysis between catheter ablation and antiarrhythmic medication in a cohort of 2204 individuals presenting with symptomatic AF. The study findings indicate that catheter ablation did not yield a statistically significant reduction in the primary composite end goals, which encompassed death, severe stroke, serious hemorrhage, or cardiac arrest. However, these results were influenced by the low occurrence rate of predicted events and a substantial crossover rate (27.5%) observed in the medical group.[32] Furthermore, the procedures for AF ablation demonstrated significant advancements throughout the duration of the study.

Mechanical Circulatory Support

According to a retrospective study, patients who were awaiting transplantation of heart and got left ventricular assist devices (LVADs) demonstrated superior outcomes compared to those who received temporary biventricular assist devices or extracorporeal membrane oxygenation.[33] The implantation of a LVAD has the potential to enhance the restoration of LV function, particularly when utilized in conjunction with the administration of neurohormonal antagonists. According to the findings of the Postgraduate Course in Heart Failure (PCHF) VAD registry, patients with LVAD who were additionally implanted with a cardiac electronic device incorporating a defibrillator component had a significantly higher likelihood of survival (HR 0.64; 95% CI 0.46-0.91; P = 0.012).[34] Physical activities can provide supplementary advantages for those who utilize LVADs.[3]

However, more than half of patients with low EF and classified as NYHA Class III-IV who met criteria and eligible for heart transplantation or LVAD declined the offer to use LVAD. LVAF is plagued with problems such as infection, along with bleeding and thromboembolic events. Thus, LVAD is still in development and will be evaluated continuously.[3,35]

Outpatient Management of Heart Failure Patients

Diagnostic Consultation

According to the guidelines established by the ESC in 2016, it is recommended to implement a multi-disciplinary strategy in the care of individuals diagnosed with HFeRF in order to enhance medication adherence.[7] The existing lines of care in the field of Health and Social Services (HAS) propose consultations for diagnosis, and the French health care system's health agency has recently initiated a trial-specific treatment line. There continues to be a lack of sufficient patient understanding regarding HF and despite the strong recommendation for HF education to enhance survival rates, its integration into clinical practice remains challenging. Hence, conducting a consultation aimed at informing the patient's diagnosis presents a valuable

occasion to offer personalized self-care strategies using a language that is appropriate and comprehensible to the patient.[4]

Discharge checklist, in-hospital nurse consultation

It is highly advised to implement evidence-based treatment strategies aimed at enhancing outcomes and reducing the likelihood of re-hospitalization following hospitalization for HF. One such strategy involves utilizing a comprehensive checklist that encompasses many components, including providing clear discharge instructions with proper dose titration, offering patient education, implementing diligent monitoring, and ensuring close follow-up. Although discharge checklists have been shown to enhance post-hospital therapy and patient engagement, leading to a reduction in readmission rates and improved utilization of heart failure medications and dosage adjustments, their implementation remains limited. A study conducted in France examined the impact of checklist sheets on the titration of heart failure medications and their association with hospitalization rates. The findings of this study indicated that despite improved titration of heart failure drugs, there was no significant influence observed on the rates of hospitalization. Additional initiatives encompass the provision of online patient education, facilitation of post-discharge planning, and dissemination of useful checklists.[4]

Management of HF Patients at Home

Titration of therapies

The prescribing rate of neuro-humoral antagonists increased by 80-90%.[7] But a significant number of patients fail to achieve the recommended therapeutic doses for the primary categories of medications. Despite the presence of empirical evidence consistently linking strong adherence to initial therapy with improved prognosis, and recognizing hospitalization as a valuable chance to optimize treatment through re-titration, the current state of management remains insufficient.[4]

Limited health care network, patient's characteristic, and health are obstacles in titrating treatment.[4] The implementation of a new patient tracking system within the French universal health insurance scheme (CNAM) has been recently observed. This system is overseen by the national board of cardiology and focuses on monitoring five essential quality indicators. These indicators include the number and duration of hospitalizations within a year, the time elapsed between discharge and the first medical contact, the provision of cardiac rehabilitation, mortality rates, and the frequency of consultations. National insurers also provide support to regional interprofessional communities in order to facilitate the coordination of initiatives aimed at

enhancing the capacity of community healthcare organizations, networks, and the connection between hospitals and the community. This support is intended to encourage improved access to healthcare services. The introduction of the new master's degree program in nursing will provide nurses with the opportunity to develop specialized skills in the management and care of patients with heart failure in both hospital and community settings.[36]

Natriuretic Peptide guided therapy: biomarker for diagnosis and/or prognostic evaluation

The BNP and ICON studies are widely acknowledged as dependable approaches for evaluating concentrations of NP in instances of acute dyspnea. ESC guidelines encourage for the utilization of in the assessment and categorization of individuals who are suspected of experiencing either acute or chronic heart failure.[7] A recent investigation was conducted to evaluate the diagnostic efficacy of NT-proBNP and age-specific threshold values in the emergency department, in light of potential alterations in the characteristics of individuals with heart failure over the course of time. The findings of this study demonstrated a substantial negative predictive value of 98.0%. However, the positive predictive value exhibited a range of 53.6% to 62.0%. Nurse practitioners (NPs) may experience a decrease in effectiveness when providing care to elderly patients who are above 80 years of age.[37]

Soluble ST2 and galectin-3 have also been investigated with the aim of suggesting replacements or adjuncts for NP evaluation. Potential discrepancies between HF patients and controls for diagnosis may arise due to considerable overlap, as reported in studies.[4]

Natriuretic peptides for follow-up evaluation

While ESC guidelines do not support the regular utilization of BNP and NT-proBNP for monitoring HF, these biomarkers can still be considered suitable for normal clinical assessment.[7] The utilization of this economic methodology has promise in enhancing the identification of chronic heart failure, particularly in individuals thought to be at risk. A variance deviation of 30% may be deemed clinically small, although it has the potential to serve as an indicator of worry.[4,38]

Within the context of guided therapy, it is advised to step up medical intervention when the levels of natriuretic peptides above pre-established thresholds. More specifically, when the BNP levels reach 250 picograms per milliliter and the NT-proBNP levels reach 1,000 picograms per milliliter.[39] Despite the lack of evidence supporting its superiority, a comprehensive meta analysis has demonstrated that HF is associated with a decrease in hospitalizations (19%) in the NT group. This effect was found to be influenced by the interaction between age and HF type.

Additionally, a noteworthy increase in all-cause mortality was observed among patients more than 75 years with HFrEF when compared to those with HFpEF.[4]

Possible interactions of BNP and sacubitril/valsartan therapy

The mechanism of action of sacubitril/valsartan leads to an elevation in BNP concentrations, while not causing a rise in NTproBNP levels. This phenomenon has the potential to result in a paradoxical rise in BNP levels despite clinical improvement, while NT-proBNP levels drop. Variations in BNP levels exhibit differences depending on the specific assessment method used. The observed enhancement is often modest, with a mean increase of 35% and reaching 100% in the majority of patients. However, this improvement is not sustained beyond a period of three months. Of greater significance, BNP retains its ability to identify clinically severe deterioration.[4,40]

Comorbid

In a thorough study of HF trials, Khan et al. discovered that a mere 51% of studies focusing on HFrEF and 27% of studies focusing on HFpEF reported baseline comorbidities. The presence of both cardiac and non-cardiac comorbidities can have an impact on the provision of care and the outcomes for persons diagnosed with heart failure. These comorbidities may include conditions such as ischemic cardiomyopathy, atrial fibrillation, hypertension, hyperlipidemia, diabetes, chronic renal disease, anemia, and susceptibility.[41] The FRAGILE-HF study is an ongoing research project that seeks to investigate the prevalence, co-occurrence, and prognostic consequences of physical and social vulnerability, as well as cognitive dysfunction, in individuals admitted to hospitals due to HF. This study is being conducted at multiple centers simultaneously. There exists a multitude of susceptibility features that are correlated with heightened mortality and hospitalization rates among patients with HF.[42] Moreover, up to 30% of individuals with HF experience depression, while an even larger percentage display symptoms indicative of depressive states.[2,43]

Anemia and iron deficiency

Anemia and iron deficiency (ID) frequently occur in individuals diagnosed with heart failure (HF) and are correlated with a worse prognosis. The efficacy of ferric carboxymaltose (FCM) in enhancing QoL and improving outcomes among patients with HF and ID has been demonstrated.[2] However, based on statistical data obtained from the Swedish Heart Failure Registry, it is evident that hardly a quarter of patients undergo evaluation for ID, with only one in

five patients receiving FCM when it is considered appropriate.[44] Sierpinski et al. conducted a study to evaluate the levels of bone marrow iron reserves in a cohort of 30 patients diagnosed with ischemic HF and have LVEF of 45%. Additionally, a control group of 10 healthy individuals was included in the study. In addition to the presence of concurrent anemia, a significant proportion of individuals diagnosed with ischemic HF and a LVEF of 45% exhibited decreased levels of iron stored in the bone marrow. The presence of elevated levels of soluble transferrin receptor in the serum, which indicates a depletion of iron stores in the bone marrow, has been identified as the most precise biomarker among those examined in peripheral blood. This biomarker exhibits a good predictive capability for increased mortality in this specific subset of patients. The presence of iron deficiency has been observed to have a significant effect on the prognosis of patients, while its impact on exercise capacity in individuals with HFpEF appears to be rather limited.[45] When compared to a placebo, secondary analyses by DAPA-HF and EMPEROR-Reduced studies revealed that the use of SGLT2 inhibitors resulted in elevated levels of hemoglobin and hematocrit, as well as reduced rates of anemia. These effects are believed to be primarily attributed to the anti-inflammatory effects of SGLT2 inhibitors.[46]

The Effectiveness of Intravenous Iron Treatment vs Standard Care in Patients with Heart Failure and Iron Deficiency (IRONMAN) study was a prospective research done in 70 hospitals in the UK. It was a multicenter study that enrolled 1,137 persons who had HF, LVEF 45%, and iron deficiency (only 14% of participants had been hospitalized). The trial used an open-label design but employed blinded endpoints. This study examined the impact of iron supplementation on individuals diagnosed with iron deficiency. In conjunction with conventional HF therapy, patients were randomly assigned to either receive iron derisomaltose or no iron. The administration of additional iron is permissible following the reoccurrence of iron deficiency. During a median follow-up period of 2.7 years, the incidence rates of HF hospitalization and cardiovascular death were seen to be 22.4 and 27.5 per 100 patient-years in the iron derisomaltose and usual care groups, respectively [RR 0.82; 95% CI 0.66-1.02; P = 0.070].[47] The sensitivity analysis for COVID-19, as pre-determined by AFFIRM-AHF, demonstrated statistical significance. The drop in the primary outcome can be attributed to a notable reduction in hospitalizations related to heart failure, but there was also a considerable improvement in the QoL.[48] The safety of iron therapy has been confirmed, since it has been found to have lower cardiac side effects or other side effects of ferric derisomaltose. In contrast to the AFFIRM-AHF study, the present data were obtained through a more extended duration of follow-up and mostly involved outpatients. Moreover, there was no notable correlation found between the etiology of heart failure..[2]

Pulmonary Hypertension

Pulmonary hypertension (PH) is frequently observed in individuals suffering from HF, predominantly manifesting as post-capillary PH. Also, certain individuals exhibit the ability to generate pre-capillary components, resulting in the development of a concomitant pre- and post-capillary PH. The primary predictors of poor prognosis in individuals with HF, particularly those with HFpEF, are confirmed to be right ventricular (RV) dysfunction and PH. The presence of diffuse RV fibrosis is characterized in cases of HFpEF and PH.[2]

Worsening renal function

The treatment recommendations for worsening renal function (WRF) are outlined in the 2016 ESC guidelines and the recently published ESC position statement on renal function in heart failure.[7] The primary causes of WRF include congestion, hypotension, and significant depletion caused by diuretic use, with a heightened susceptibility observed in the geriatric population. The evaluation of renal function in patients with HFrEF poses challenges, however, the CKD-EPI equation has emerged as a reliable method for quantifying glomerular filtration rate (GFR). Renin-angiotensin-aldosterone system (RAAS) inhibitors exhibit a higher efficacy in persons with renal impairment but they are commonly subject to inadequate prescription and dosage. In the context of treating HFrEF using RAAS inhibitors, it is generally considered acceptable to see an elevation in creatinine levels of up to 50% compared to reference values, a reduction in GFR of up to 25 mL/min/1.73m2, or an increase in serum potassium levels of up to 5.5 mm/L during an interval of 15 to 30 days following the intervention.[4]

The inhibitory impact of RAAS has been substantiated by meta-analyses, which have demonstrated a decrease in overall mortality and enhanced prognosis compared to placebo. However, it is important to note that the RAAS inhibitor-treated group had a higher occurrence of renal adverse events. The assess, adapt, and monitor (A2M) method is utilized by physicians to aid in the care of patients who present with heart failure with HFrEF, WRF, and/or hyperkalemia.[4]

A consultation with a nephrologist is warranted when the serum creatinine level exceeds 100%, eGFR falls below 20 mL/min/1.73m2, and hyperkalemia surpasses 5.5 mmol/L. It is recommended to maintain the dosage of mineralocorticoid receptor antagonists, RAAS inhibitors, and beta-blockers, while reducing loop diuretics (specifically furosemide) to the least effective dose.[4]

CONCLUSION

Given its high rate of recurrence and unfavorable prognosis, heart failure remains a major problem. This is partly due to early hospitalization and poor diet as well as low adherence to treatment. The occurrence of therapeutic delay during down-titration occurs frequently and has been linked to a poorer prognosis. The objective of this guideline is to offer valuable suggestions for patients and clinicians in order to enhance patient prognosis and quality of life.

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