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Case Report and Literature Review

A comprehensive approach to managing heart failure with eeduced ejection fraction: A case study

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INTRODUCTION

Heart failure is a multifaceted clinical syndrome characterized by symptoms such as dyspnea or exertional limitation, resulting from impaired ventricular filling or ejection of blood, or a combination thereof. It is associated with considerable morbidity and mortality, with 1-year mortality rates of 7.2% and 1-year hospitalization rates of 31.9% in patients with chronic heart failure, which escalate to 17.4% and 43.9% in patients hospitalized for acute heart failure. Traditionally, heart failure has been classified based on the left ventricular ejection fraction (LVEF) into three categories: heart failure with preserved ejection fraction (LVEF ≥ 50%), heart failure with midrange ejection fraction (LVEF 41%-49%), and heart failure with reduced ejection fraction (HFrEF, where LVEF is ≤ 40%). The management of patients with HFrEF is constantly evolving with advancements in pharmacological and device-based therapies.[1]

HFrEF is often accompanied by pathological remodeling and dilation of the left ventricle, which can result in unfavorable outcomes. Reversing cardiac remodeling has been established as a treatment goal and standard of care for over two decades. Patients with HFrEF often experience recurrent hospitalizations and may require advanced therapies. Guideline-directed medical therapy has been shown to improve survival rates in these patients, with the primary target of treatment being the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS). In HFrEF, reduced effective stroke volume typically leads to activation of the sympathetic nervous system and RAAS. Activation of these systems results in vasoconstriction and fluid retention, contributing to adverse remodeling in heart failure.[2]

The four pillars of heart failure management, namely Angiotensin-Converting Enzyme inhibitors (ACE inhibitors)/ Angiotensin Receptor Blockers (ARB)/Angiotensin Receptor Neprilysin Inhibitors (ARNI), mineralocorticoid receptor antagonist (MRA), antagonism of the sympathetic system with selected beta-blockers, and sodium-glucose cotransporter 2 inhibitors (SGLT2i), play vital roles in improving outcomes in HFrEF patients. ACE inhibitors (ACEi) are recommended as first-line treatment, reducing mortality and worsening of symptoms. ARBs or ARNI should be considered as second-line agents if ACEi is not tolerated. MRAs reduce mortality by blocking aldosterone effects. Beta-blockers are used to antagonize the sympathetic system and lower heart rates, resulting in improved outcomes. SGLT2i, originally used for diabetes management, has also shown significant benefits in HFrEF, reducing the relative risk of cardiovascular events. These pillars, when used in combination, can greatly improve the prognosis of HFrEF patients.[2]

In this case report, we describe a 70-year-old woman with a history of hypertension who presented with shortness of breath, orthopnea, and leg swelling. Physical examination revealed signs of heart failure, and further evaluation showed that the patient had reduced ejection fraction (EF) of 40%, left ventricular hypertrophy, and grade III diastolic dysfunction. Despite being on amlodipine and lisinopril for 2 years, the patient's symptoms persisted, and she was referred to her family physician for further management. After a comprehensive evaluation, the patient was initiated on a four-pillar therapy regimen consisting of an ARNI, beta-blocker, MRA, and SGLT2i. With this therapy, the patient's symptoms improved, and she had no further hospitalizations. This case highlights the importance of using a combination of these four pillars in managing HFrEF patients to achieve optimal outcomes.

CASE PRESENTATION

A 70-year-old woman with a history of hypertension for which she has been taking amlodipine and lisinopril for the past 2 years was referred to her family physician by the emergency department for follow-up of shortness of breath, orthopnea, and swelling of her legs that she had experienced for two months. She denied any chest pain, palpitations, or syncope. She reported experiencing increasing shortness of breath on exertion, orthopnea, and swelling of her legs for the past 2 months, which prompted her visit to the emergency department.

On physical examination, the patient appeared uncomfortable and dyspneic at rest. She was afebrile and had a respiratory rate of 22 breaths/min. Her blood pressure was 160/92 mm Hg, and her pulse rate was 106 beats/min. Oxygen saturation was 92% on room air. The patient was alert and oriented, and there were no signs of mental status changes. Cardiac examination revealed regular rhythm, normal heart sounds with no murmurs, and no pericardial rubs or gallops.

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There were bibasilar crackles on lung auscultation, and the patient had bilateral pedal pitting edema up to the ankles. Abdominal examination revealed no hepatosplenomegaly, and there was no evidence of ascites. The patient had no signs of jugular venous distention or peripheral cyanosis.

In the emergency department, test results for electrolyte levels (Sr. Na++ 145 mmol/L; Sr. K+5.2 mEq/L; Sr. Bicarbonate 29 mmol/L) and Sr. Creatinine 1.3 mg/dL were within normal limits. An electrocardiogram showed sinus rhythm with LAD and left ventricular hypertrophy. An echocardiogram revealed an ejection fraction of 40%, concentric left ventricular hypertrophy with no substantial valvular abnormalities, and grade III diastolic dysfunction. Based on her medical history, physical examination, and diagnostic tests, the clinical presentation was consistent with a diagnosis of heart failure with reduced ejection fraction.

MANAGEMENT

The management of this case would involve a multidisciplinary approach to address the patient's symptoms and underlying conditions. She was started on sacubitril/valsartan to replace lisinopril and carvedilol to reduce heart rate. Furosemide was also prescribed to manage fluid overload. The patient was counseled on lifestyle modifications, including sodium and fluid restriction, weight management, and regular exercise. However, despite these interventions, the patient continued to experience dyspnea and swelling of the legs, indicating a need for further intervention. In light of recent evidence, the patient's treatment regimen was modified to include an SGLT2i, dapagliflozin 10 mg OD, due to its demonstrated efficacy in reducing cardiovascular events in patients with HFrEF. Dapagliflozin is a once-daily oral medication that works by inhibiting SGLT2, a transporter responsible for reabsorbing glucose in the kidneys. By blocking this transporter, dapagliflozin increases glucose excretion in the urine and leads to decreased blood glucose levels. In addition to pharmacological therapy, lifestyle modifications play a crucial role in managing heart failure. The patient was again advised to limit sodium intake to less than 2g per day, and fluid intake to less than 2L per day. Furthermore, light to moderate exercise for at least 30 minutes per day was encouraged, as tolerated.

To further reduce heart rate and improve cardiac function, metoprolol, a beta-blocker commonly used in the management of heart failure, was added to the patient's medication regimen. Metoprolol succinate extended-release tablets were started at 25mg once daily and titrated up to a target dose of 200mg once daily over several weeks. Spironolactone, a mineralocorticoid receptor antagonist (MRA), was also added to further improve symptoms and reduce the risk of adverse cardiovascular events. The patient was started on spironolactone 25mg once daily and titrated up to a target dose of 50mg once daily over several weeks. Regular follow-up visits and monitoring of clinical symptoms, blood pressure, renal function and electrolyte levels were scheduled to optimize therapy and prevent adverse outcomes.

OUTCOME

Follow-up of this case was conducted at 1, 3 and 6 months after the initiation of the treatment regimen. The patient reported significant improvement in her symptoms of dyspnea and swelling of the legs at 1 month. She reported a decrease in the frequency and severity of episodes of shortness of breath and was able to engage in more physical activity without experiencing symptoms. Her weight decreased by 2 kg at 3 months, and her blood pressure and heart rate remained stable. Physical examination revealed a reduction in jugular venous distension and peripheral edema, indicating an improvement in cardiac function. Furthermore, there was a reduction in left atrial volume and left ventricular end-systolic volume, indicating a reduction in left ventricular remodeling.

The multidisciplinary approach to the management of this case, which included pharmacological therapy and lifestyle modifications, resulted in a significant improvement in the patient's symptoms and cardiac function. Sacubitril/valsartan and furosemide were effective in managing fluid overload, while metoprolol and spironolactone further improved cardiac function and reduced the risk of adverse cardiovascular events. The addition of dapagliflozin, an SGLT2 inhibitor, was associated with significant improvement in symptoms, weight loss, and cardiac function.

DISCUSSION

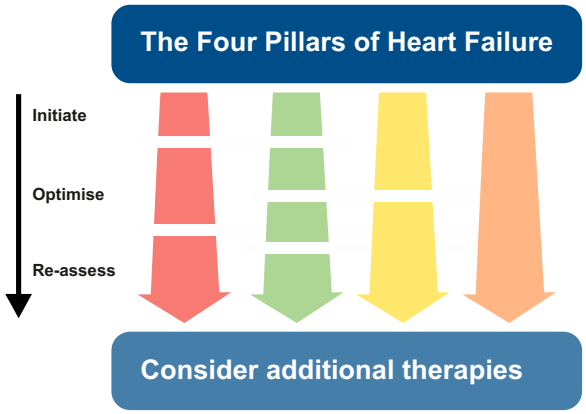
HFrEF is a serious condition associated with high mortality and hospitalization rates. Despite the availability of effective pharmacotherapy, there are gaps in the utilization of guideline-directed medical therapy, including ACEIs, ARBs, beta-blockers, and MRAs. However, in recent years, two new classes of medications, ARNIs and SGLT2i, have shown promising results in reducing hospitalizations and mortality rates in HFrEF patients. Despite their benefits and inclusion in major guidelines, these newer medications remain underutilized.

The majority of the pivotal cardiovascular outcome trials that established class I recommendations for managing HFrEF pharmacotherapy were conducted two to three decades ago. These studies showed that ACEIs, ARB, beta-blockers, MRAs, and vasodilators are effective treatments for reducing hospitalizations and mortality rates in HFrEF patients. Despite the existence of guidelines for managing heart failure with reduced ejection fraction, there are significant gaps in the use of recommended medications, as evidenced by a US-based outpatient registry known as the CHAMP-HF registry. Many eligible patients are not receiving guideline-directed medical therapy, including ACEI/ARB, beta-blockers, and MRAs, and most patients who do receive these medications are not taking them at target doses. However, in recent years, two new classes of pharmacotherapy have been developed to prevent and treat heart failure and its associated complications. One of these classes is the ARNI, which has been shown to reduce hospitalizations for worsening heart failure, improve quality of life, and attenuate decline of estimated glomerular filtration rate (eGFR). The PARADIGM-HF trial demonstrated that sacubitril/valsartan, an ARNI, reduced cardiovascular mortality by 20% and hospitalization for heart failure by 18% compared

to enalapril in patients with chronic HFrEF. These findings were further supported by the PIONEER-HF trial, which showed that sacubitril/valsartan resulted in a greater reduction in NT-proBNP (a biomarker for heart failure) by 46.7% and heart failure hospitalization by 43% compared to enalapril in patients stabilized from an acute heart failure episode. Despite the benefits of ARNI treatment and its inclusion in major guidelines, it remains underutilized, with many eligible patients not receiving this therapy.

The second new class of pharmacotherapy is the SGLT2i, which were originally developed and approved for the treatment of hyperglycemia in type 2 diabetes mellitus but their cardiovascular benefits, including heart failure protection, were serendipitously discovered in response to guidance from the Food and Drug Administration (FDA) in 2008 requiring all new glucose-lowering therapies to prove cardiovascular safety before market approval. The efficacy of SGLT2i in addition to standard therapies for people with HFrEF has been confirmed with consistent and near-identical 25% risk reduction of the primary endpoint of cardiovascular death or hospitalization for heart failure from both dapagliflozin and empagliflozin. The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) trial demonstrated the benefits of

Figure 1 - Initiation and optimisation of the Four Pillars of Heart Failure. All agents are initiated in parallel. This is followed by up-titration in one, two or three steps, as required. Additional therapies are then considered as a final step.



ARNI, angiotensin receptor-neprilysin inhibitors; BB, beta-blocker; MRA, mineralocorticoid receptor antagonists;SGLT2i, sodium-glucose co-transporter 2inhibitors.

dapagliflozin, in reducing the risk of cardiovascular death or worsening heart failure in patients with a left ventricular ejection fraction (LVEF) ≤40%. Adding dapagliflozin to a regimen that includes a RAS inhibitor (including in combination with a neprilysin inhibitor), a beta-blocker, and an MRA resulted in improved outcomes. Importantly, the treatment effect of dapagliflozin was consistent across the range of LVEF ≤40%, as reported in a pooled, individual patient data meta-analysis of the DAPA-HF and DELIVER trials. The benefits of dapagliflozin were also seen in patients with an LVEF >40%, including those with a prior LVEF <40% who showed improvement in LVEF but ongoing symptoms of heart failure, as demonstrated in the DELIVER trial. Therefore, dapagliflozin at a dose of 10 mg once daily is recommended as the fourth foundational therapy for patients with symptomatic heart failure and reduced ejection fraction (HFrEF) according to current guidelines.

CONCLUSION

This case presented here involved a 70-year-old woman with a history of hypertension who presented with symptoms of HFrEF and left ventricular hypertrophy with grade III diastolic dysfunction, despite being on amlodipine and lisinopril for two years. In order to improve the patient's symptoms, a four-pillar therapy regimen consisting of angiotensin receptor-neprilysin inhibitors (ARNIs), beta-blockers, mineralocorticoid receptor antagonists(MRAs), and SGLT2i was initiated. The patient responded positively to this therapy and had no further hospitalizations. This case highlights the significance of a comprehensive disease management approach in achieving optimal outcomes in patients with heart failure.[2,4-5]

The treatment of HFrEF is complex and requires a comprehensive approach that includes lifestyle modifications and pharmacological interventions. Evidence-based medications such as, angiotensin receptor-neprilysin (ARNIs) inhibitors, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and SGLT2i have been shown to improve outcomes in HFrEf patients, reducing the risk of hospitalization and mortality. Therefore, it is critical for healthcare professionals to adhere to clinical guidelines and initiate all recommended medications promptly. Titration of medication doses to appropriate levels and ensuring patient compliance with the medication regimen is also important for optimal outcomes. Failure to start evidence-based medications can result in poorer outcomes, leading to an increased burden on healthcare systems. Thus, a comprehensive approach to heart failure management with adherence to evidence-based guidelines is essential for improving patient outcomes and reducing the burden of heart failure.

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