PRINCIPLES OF HEART FAILURE TREATMENT

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Abstract

Introduction: Heart Failure is a complex syndrome that arises as a severe complication of various cardiac disorders. It is characterized by high mortality rates, akin to those seen in malignant diseases. It is categorized based on cardiac function into two main types: Heart Failure with preserved ejection fraction and Heart Failure with reduced ejection fraction. The latter is further subdivided into mild and severe reductions in function. Common clinical manifestations include dyspnea, peripheral edema, and fatigue. The etiology of Heart Failure may include ischemic, valvular, and myocarditis-related origins, among others influenced by factors such as post-tachycardia, pharmaceutical interactions, alcohol use, etc. The functional classification remains a crucial aspect of understanding and managing the disease.

Objectives: Given the severity of Heart Failure, it is imperative to manage the underlying causes effectively to prevent its onset. Lifestyle modifications and addressing modifiable risk factors are vital in thwarting the progression of this syndrome. In established cases, optimizing treatment strategies is essential to enhance survival rates and improve quality of life.

Materials and Methods: This paper draws on recent studies that explore innovative therapeutic approaches for heart failure, reflecting a significant body of ongoing research aimed at improving patient outcomes.

Conclusion: Effective management of Heart Failure involves recognizing and mitigating the risk factors that contribute to its development. Accurate diagnosis and appropriate treatment of cardiac pathologies are crucial. Furthermore, adopting newer treatment modalities is essential for the effective management of Heart Failure cases, aiming to prolong life and enhance its quality.

Keywords: syndrome, function, heart failure.

PARIMET E MJEKIMIT TË INSUFICIENCËS KARDIAKE

Abstrakt

Hyrje: Insuficienca kardiake është një patologji komplekse që vjen si ndërlikim i rëndë i sëmundjeve të ndryshme kardiake. Karakterizohet nga një shkallë e lartë vdekshmërie njëlloj si e patologjive malinje. Ajo klasifikohet mbështetur ne funksionin kardiak në dy lloje: Në Insuficiencën kardiake me fraksion ejeksioni të ruajtur dhe në Insuficiencën kardiake me fraksion ejeksioni të reduktuar. Ky i fundit nën-ndahet në variantin me reduktim të lehtë të fraksionit të ejeksionit dhe në variantin me reduktim sever të fraksionit të ejeksionit. Manifestimet klinike më të zakonshme përfshijnë dispnenë, edemat periferike dhe lodhjen. Etiologjia e Insuficiencës kardiake kongjestive mund të jetë me origjinë iskemike, valvular dhe nga miokarditi, dhe ndër të tjera mund të ndikohet nga faktorë si p.sh. post-takikardia, ndërveprimet medikamentoze, përdorimi i alkoolit etj. Klasifikimi funksional mbetet pika kyçe e kuptimit dhe trajtimit të kësaj patologjie.

Objektivat: Duke patur parasysh gravitetin e Insuficiencës kardiake, është e detyrueshme të trajtohen shkaqet që do të sillnin shpërthimin e klinikës së kësaj patologjie. Modifikimi i stilit të jetesës dhe ndikimi në faktoret e riskut të ndryshueshëm janë vitale për të penguar evolucionin e kësaj patologjie. Në rastet e stabilizuara optimizimi i strategjive terapeutike rrit mbijetesën dhe cilësinë e jetës së këtyre pacientëve.
Materialet dhe metodat: Ky punim prezanton një përmbledhje të studimeve të fundit që eksplorojnë përqasjet e reja dhe novative terapeutike të trajtimit të Insuficiencës kardiake kongjestive duke reflektuar studimet që po kryhen për të përmirësuar cilësinë e jetës së pacientëve.
Konkluzione: Trajtimi efikas i Insuficiences kardiake përfshin njohjen dhe eliminimin e faktorëve që do të kontribuonin në zhvillimin e saj. Diagnoza e kujdesshme dhe trajtimi i duhur i patologjive kardiake eshte thelbësor. Gjithashtu, adaptimi i modaliteteve të reja terapeutike është esencial për manaxhimin efikas të Insuficiencës kardiake kongjestive, duke synuar në zgjatjen e jetës dhe në përmirësimin e cilësisë së saj.

Fjalët kyç: sindromë, funksion, Insuficienca kardiake kongjestive

Introduction

Heart failure is a complex syndrome that is accompanied by the inability of the cardiac muscle to deliver sufficient blood flow to the body's vascularization. The American College of Cardiology Foundation (ACCF) / as well as the Heart Association (AHA) guidelines define Cardiac Insufficiency (CI) as a complex clinical syndrome, the result of structural and/or functional impairment of ventricular filling and ejection, which leads to the cardinal clinical symptoms of dyspnea and fatigue as well as signs of HF (respectively oedema and rales, etc.) (1). HF is a growing problem worldwide. The overall prevalence of HF in the adult population in developed countries is 2% (2). The prevalence follows an exponential pattern, increasing with age, and affects 6–10% of people aged > 65 (2). The etiology is numerous: ischemic, valvular, idiopathic, alcoholic, medicinal (antitumoral), metabolic, toxic, etc. HF is divided into two large groups: HF with preserved EF and HF with reduced EF. Clinical signs are: difficulty in breathing, general weakness, decreased diuresis, peripheral oedema, abdominal discomfort (from liquid), arrhythmia, etc.

Pathogenesis

HF is a progressive disorder that begins after an event or injury to the heart muscle that results in a functional loss of cardiac myocytes, or otherwise, impairs the ability of the myocardium to generate force, thereby making it impossible for the heart to contract normaly. This event may have a sudden onset, as in the case of an MI; it may have a gradual or insidious onset, as in the case of hemodynamic pressure or volume overload. Regardless of the nature of the event, the feature that is common to each of these events is that they all in some way produce a decrease in pumping capacity. Although the exact reasons why patients with left ventricular (LV) dysfunction may remain asymptomatic are not known, one possible explanation is that a variety of compensatory mechanisms are activated in the presence of an injured heart and/or LV dysfunction allowing patients to maintain and modulate LV function for a period of several months to several years (1). Compensatory mechanisms that have been described so far include: (a) activation of the renin-angiotensin-aldosterone system (RAAS) and the adrenergic nervous

system, which are responsible, respectively, for maintaining cardiac output through increased salt and water retention and (b) increased myocardial contractility. In addition, a family of antagonistic vasodilator molecules are activated, including atrial and brain natriuretic peptides (ANP and BNP), bradykinin, prostaglandins (PGE2 and PGI2), and nitric oxide (NO), which compensate for excessive peripheral vascular vasoconstriction. These compensatory mechanisms can modulate LV function within a physiological range. Thus, patients may remain asymptomatic or minimally symptomatic for years; however, at some point patients become markedly symptomatic. Although the exact mechanisms responsible for this transition are not known, the transition to symptomatic HF is associated with increased activation of the neurohormonal, adrenergic, and cytokine systems leading to a series of adaptive changes within the myocardium referred to as LV remodelling. Although diastolic dysfunction (see below) was thought to be the only mechanism responsible for the development of HF with a preserved EF, community-based studies suggest that additional extracardiac mechanisms may be important, such as increased vascular stiffness and impaired renal function, etc. The principles of HF treatment are based on these mechanisms. Which are divided into two groups: drug therapy and self-care (2). Drug Therapy: The last 50 years have witnessed great advances in the management of HFrEF. The treatment of symptomatic heart failure evolved from a diuretic and hemodynamic (digoxin, inotropic therapy) model of therapy to the era of disease-modifying therapy with neurohormonal antagonism. In this regard, RAAS inhibitors and beta-blockers form the cornerstone of pharmacotherapy that lead to the improvement of cardiac structure and function, with a reduction in symptoms, a reduction in hospitalizations and a decrease in mortality from Heart Failure and its clinical manifestations. Meta-analyses suggest a 23% reduction in mortality and a 35% reduction in the combined endpoint of mortality and hospitalizations for HF in patients treated with Angiotensin-converting enzyme inhibitor (ACE-I). Patients treated with beta-blockers provide a further 35% reduction in mortality on top of the benefit provided by ACE-I alone. Increased experience with both agents in a wide range of patients with HFrEF has demonstrated the safety of ACEIs in the treatment of patients with mild renal insufficiency and the tolerability of beta-blockers in patients with moderately controlled diabetes, asthma, and obstructive pulmonary disease. The benefits of ACE-I and beta-blockers extend to advanced disease symptoms (NYHA Class IIIb–IV). However, a significant number of patients with advanced heart failure may not be able to achieve optimal doses of neurohormonal inhibitors and require careful reduction of dose exposure to maintain clinical stability. Based on the investigations, the use of beta-blockers in HFrEF should ideally be limited to carvedilol, nebivolol, bisoprolol and metoprolol succinate – tested and proven agents that improve survival in clinical trials (3).

Beta blockers: The group of beta blockers is used in to counteract the harmful effects of catecholamines produced by activation of the sympathetic nervous system, reducing the heart's need for oxygen as well as exhibiting antiarrhythmic effects. This group has been seen in various studies that increases the life expectancy of patients (15). Depending on the type and aggressiveness of the arrhythmias, more powerful antiarrhythmics such as Amiodarone can be used. From the group of beta-blockers used in HF with reduced EF are Carvedilol, Bisoprolol, Metoprolol and Nebivolol.

Ivabradine slows the heart rate without a negative inotropic effect. Ivabradine is FDA-indicated to reduce the risk of hospitalization, exacerbation in patients with chronic, symptomatic heart failure with a left ventricular ejection fraction ≤35%, who are in sinus rhythm with resting heart rate ≥70 beats per minute, and or are in maximum tolerable doses of beta-blockers or have a

contraindication for the use of beta-blockers. Ivabradine reduced hospitalizations and death related to cardiovascular disease and HF (18).

ACEI: The ACEI group is very important in the treatment of HF. It works by inhibiting the renin-angiotensin system, through inhibition of the converting enzyme. In this way, the conversion of angiotensin to angiotensin II is inhibited and by further inhibiting the harmful effects of the activation of this system, which are the retention of water and salt in the body, the increase in arterial pressure, the further increase of the sympathetic system, hypertrophy, proliferation, etc (4).

Angiotensin receptor blockers ARBs: The ARBs group acts on the same system as ACE, i.e., the renin-angiotensin-aldosterone system, but the link of their action is at the level of angiotensin II receptors, so they are more specific than ACE in the action of theirs. Here we can mention valsartan, losartan, olmesartan, ibersartan, telmisartan etc (4).

ARNI (sacubitril/valsartan): This drug was approved by the FDA in 2015 for the treatment of HF and consists of sacubitril, which is a niprelysin inhibitor, and valsartan, which belongs to the group of ARBs. Niprelysin is an enzyme that participates in the degradation of natriuretic peptides. By inhibiting niprelysin, sacubitril increases the level of natriuretic peptides that in HF have a positive effect by promoting diuresis and natriuresis. Here is added the positive effect of valsartan as an inhibitor of angiotensin receptors, counteracting the harmful effects of the activation of the angiotensin renin system. Both medications act on HF by potentiating each other's action (8).

Regarding the three groups mentioned above: ACEI, ARBs and ARNI, one of them is used in the treatment of HF. All three or two groups cannot be used together (4).

Aldosterone antagonists: from the name itself, their curative action appears by counteracting the harmful effects of aldosterone (8). Aldosterone antagonism is associated with a reduction in mortality in all stages of NYHA class II to IV symptomatic HFrEF. Elevated aldosterone levels in HFrEF promote sodium retention, electrolyte imbalance, endothelial dysfunction, and may directly contribute to myocardial fibrosis. The selective agent eplerenone (tested in NYHA class II heart failure and after myocardial infarction) and the nonselective antagonist spironolactone (tested in NYHA class III and IV heart failure) reduce mortality and hospitalizations, with significant reductions in sudden death cardiac (9).

A new and very promising group in the treatment of HF is the group of Sodium-glucose Cotransporter-2 (SGLT2) inhibitors. This group acts by inhibiting the renal reabsorption of glucose and promoting diuresis. A positive effect on the myocardium from toxic effects and on cardiac remodelling has also been seen (1, 3).
Loop diuretics: these drugs act on the kidneys by promoting natriuresis and diuresis. The group of these medications has an effect on the clinical improvement of symptoms. Here we mention: Furosemide, Torasemide, etc. Neurohormonal activation results in salt and water retention.
Clinical trial data confirming efficacy are limited and no data suggest that these agents improve survival. Thus, diuretic agents should ideally be used in tailored programs to avoid overexposure. Indeed, diuretics are essential early on to achieve volume control before neurohormonal therapy is well tolerated or titrated (8, 9).

Digitalis (Digoxin) is used in HF that is usually associated with AF to decrease the heart rate and for the positive chronotropic effect. The latter is preferred in HF NYHA IV and significantly reduced cardiac function, even when the patient is with SR. Digitalis exert a mild inotropic effect, soften the baroreceptor activity of the carotid sinus and are sympatho-inhibitory. These effects decrease serum norepinephrine levels, plasma renin levels, and possibly aldosterone levels. Trials showed a reduction in hospitalizations for HF in the treatment group (patients with heart failure and sinus rhythm), but no reduction in mortality. It should be noted that low doses of digoxin are sufficient to achieve a potentially beneficial result, and higher doses violate the index of therapeutic safety. In general, the use of digoxin is now reduced as therapy for patients who remain profoundly symptomatic despite optimal neurohormonal blockade and adequate volume control (1, 2, 4, 6).

A combination of hydralazine with nitrates can be used as additional therapy. Vericiguat is a new drug in the treatment of HF, experience with which is still small (14). ICD/Cordaron are used to prevent life-threatening ventricular arrhythmias, which in these subjects are frequent and constitute the main cause of death (6). In addition to drug therapy, based on the patient's clinical condition, supportive treatment, as well as oxygen therapy, is of particular importance in the advanced stages of HF. In individuals with advanced stages, which is characterized by refractoriness to conventional therapy and with an increased burden of symptoms, frequent hospitalizations, poor quality of life and high risk of death, surgical options remain open. Cardiac Transplant, Circulation Assisted Left Ventricular Assist Systems (LVAS) (7).

It is very important to take good care of yourself.

- A healthy diet, balanced diet can help to improve symptoms and overall health. A balanced diet should include lots of fruit and vegetables, controlled amount of protein, low levels of fat, salt, and sugar. Regular physical activity can also help improve your symptoms and overall health. These patients need physical activity adjusted according to the NYHA scale, education, emotional support (13).
- Stop smoking can improve your overall health and reduce your risk of many other health problems.
- Limit alcohol consumption: In patients with HF, drinking a glass of wine may be allowed, but it is advised not to exceed the recommended limits of more than 14 units of alcohol per week. If HF is directly related to alcohol consumption, you may be advised to stop altogether (12).
- Vaccination in patients with HF is a condition that makes you more vulnerable to infections. Community-acquired respiratory infections are a common cause of hospital readmission in these patients and are associated with an increased risk of in-hospital mortality. Recent studies have shown that vaccination against common respiratory tract infections can reduce hospitalization in patients with HF. For example, in the PARADIGM-HF study, influenza vaccination was associated with a 19% reduction in all-cause mortality (in participants with HFrEF). Likewise, a community-based study of more than 140,000 Heart Failure patients also reported a 19% reduction in hospital readmissions in elderly patients who were vaccinated. It is now widely recommended that patients with Heart Failure be vaccinated annually against influenza, unless contraindicated. In addition, pneumococcal vaccination is also recommended for high-risk patients, including those with diabetes and/or CKD (10).
- Regular rechecking and monitoring. Patients with HF should monitor their condition at least every 6 months.

Conclusion

Heart failure (HF) remains a significant clinical and public health issue due to its complex pathophysiology and high prevalence, especially among the elderly. It emerges primarily from the progressive loss of cardiac myocyte function and subsequent myocardial remodeling processes. Modern therapeutic strategies have significantly evolved from basic symptom management to complex disease-modifying approaches, particularly through neurohormonal antagonism, which substantially improves patient outcomes. These advancements underscore the necessity for continuous medication optimization and the potential integration of new pharmacological agents like ARNI and SGLT2 inhibitors, which show promise in further reducing HF-related morbidity and mortality. Additionally, the role of lifestyle modifications and routine monitoring cannot be overstated, as these are crucial for managing HF symptoms and improving overall patient quality of life. As we continue to witness innovations in heart failure management, the integration of emerging drugs and tailored therapies offers a hopeful outlook for reducing the global burden of this challenging disease.

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