A Comprehensive Review of Epidemiology, Pathophysiology and Treatment of Acute Decompensated Heart Failure

Abstract

Acute decompensated heart failure is a heterogeneous clinical syndrome that usually leads to hospitalization due to a combination of interconnected renal dysfunction, cardiac dysfunction, and vascular compliance. Hospitalizations due to acute decompensated heart failure are associated with excess morbidity and mortality, with nearly half of patients readmitted within 6 months and short-term cardiovascular mortality. Importantly, the overall long-term outcome is still poor, combining rates of cardiovascular death, hospitalization for heart failure, myocardial infarction, stroke, or sudden death up to 12 months after hospitalization. Management of these patients remains a challenge, with an emphasis on end-organ perfusion (coronary and renal), primarily volume control and reduction of vascular resistance.

Keywords: Acute heart failure, decompensated heart failure, funny current inhibitor, diuretics, pitting edema.

Introduction & Background

Acute decompensated heart failure is a syndrome characterized by dyspnea, worsening fatigue, and edema that results from deteriorating heart function and usually leads to hospital admission or unscheduled medical intervention [1]. The primary principle of management of these patients is to discover and tackle known precipitants of decompensation [2]. Identification and management of medication nonadherence and use of prescribed medicines such as nonsteroidal anti-inflammatory drugs, cold and flu preparations with cardiac stimulants, and herbal preparations, including herbal forms of ephedrine, licorice, and ginseng, are required. Overt or covert pulmonary thromboembolism and active infection should be sought, identified, and treated when clinical clues suggest such direction [3]. Possibly, arrhythmias should be corrected by controlling the heart rate or restoring sinus rhythm in patients with poorly tolerated rapid atrial fibrillation and by correcting current ischemia with coronary revascularization or correcting offenders such as current bleeding in demand-related ischemia [4]. A parallel step in treatment involves the stabilization of hemodynamics in those with instability. Routine use of pulmonary artery catheters is not approved and should be limited to those who do not respond well to diuretics or who experience signs and symptoms suggestive of hypotension or low cardiac output when the therapeutic goal is unclear [5]. Analysis of hospital records revealed many parameters associated with serious outcomes. Systolic blood pressure is less than 115 mmHg. Art., blood urea nitrogen greater than 43 mg/dL (multiply by 0.357 to convert to mmol/L), greater than 2.75 mg/dL (multiply by 88.4 to convert to µmol/L), elevated troponin I [6]

Definition

Acute decompensated heart failure is the new onset or recurrence of clinical features of heart failure which require immediate treatment and most times results in hospitalization. A certain number of other terms have been used in the literature including: acute decompensation of chronic heart failure (ADCHF), acute heart failure syndromes (AHFS), and acute heart failure (AHF). Terms used in the literature indicates that acute decompensation heart failure is not a single diagnosis, rather it is a group of similar syndromes caused by different primary underlying diseases of the cardiovascular system that may be made worse by a variety of cardiac and non-cardiac conditions [1,2]. In patients suffering from ADHF, there is a crucial heterogeneity in the underlying pathophysiology, precipitants, time course, clinical presentation and underlying cause of heart disease. However, pulmonary congestion due to increased left atrial pressure in association with dyspnea, with or without clinical evidence of low cardiac output is a consistent finding in patients with this syndrome [7]. Most of the patients hospitalized for acute decompensated heart failure had a prior diagnosis of heart failure, some had newly onset heart failure, and the remaining few had progressive or refractory heart failure. Cardiac comorbidities, including cardiomyopathy, coronary artery disease, high blood pressure, and valvular heart disease, are often present. Non-cardiovascular conditions, including anemia, renal dysfunction, lung disease, diabetes, thyroid disease, substance abuse, obesity, sleep apnea, and infection, are frequently present and may contribute to decompensated heart failure [8].

Epidemiology

The number of hospitalized patients for heart failure tripled from 1979 to 2004, increasing from 1,274,000 in 1974 to 3,860,000 in 2004. Heart failure was the main diagnosis in 30-35% of these hospitalizations. Age-adjusted hospitalization rates also increased during this period. More than 80% of these hospitalizations were for patients 65 years of age or older and were paid for by Medicare or Medicaid [9]. In recent years, hospitalizations for acute decompensated heart failure are still declining. In accordance with the analysis of the hospitalized patients national claims history files from the centers for medicare &medicaid services (CMS) which identified all fee-for-service medicare beneficiaries who were hospitalized for heart failure from 1998 to 2008, the heart failure hospitalization rates adjustted for the age, gender and race declined from 2845 per 100,000 individual-years in 1998 to 2007 per 100,000 individual-years in 2008 (a decrease of 29.5%; $p < 0.001$). Black men had the smallest rate of age-adjusted decline for all race-gender categories. Importantly, risk-adjusted 1-year mortality after hospitalization reduced from 31.7 % in 1999 to 29.6 % in 2008 (a decline of 6.6 %; $p < 0.001$) [10]. Various multicenter observational registries in the united states and europe have significantly improved our understanding of the management patterns, demographics, clinical characteristics, comorbidities, and results of patients admitted with acute decompensated heart failure Prior to these registries, our understanding of acute decompensated heart failure came mainly from studies of younger patients with moderate to severe systolic dysfunction that were enrolled in single-center or multicenter randomized

controlled clinical trials conducted mainly at academic heart failure centers. The observational registries were organized to enroll a more representative sample of patients with acute decompensated heart failure that involved all patients admitted with heart failure at geographically diverse academic and non-academic medical centers. Ascertainment methods were used by the organized program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF) to identify 48,612 patients hospitalized at 259 centers in the united states for new or worsening heart failure as the primary cause of admission or who developed significant heart failure symptoms during hospitalization for a different diagnosis. Using a web-based registry, detailed data were collected including medical history, demographics, signs and symptoms, medications, laboratories, diagnostic testing procedures, discharge status, outcomes and adherence to performance indicators. A pre-specified subgroup that was ≥ 10 % of the total number of patients was followed for 60-90 days after discharge for the collection of outcomes data [11]. The acute decompensated heart failure national data registry (ADHERE) database was a prospective observational registry that was created to provide a large national database to describe clinical characteristics, management and outcomes of inpatients with heart failure at 286 hospitals in the united states. Thirty-one percent of the participating organizations were academic hospitals. From 2002 to 2004, data were collected from 159,168 hospitalizations starting with the point of initial care and ending with the patient's discharge or in-hospital death [12-14]. The euroheart failure survey I (EHFS I) was a retrospective registry in which demises or discharges from 117 hospitals (50% university hospitals) from 25 european countries were examined to discover patients with known or suspected heart failure. Clinical characteristics, evaluation, demographics, treatment and outcomes were assessed [15-17].

Pathophysiology

Acute decompensated heart failure is a syndrome caused by a broad range of cardiovascular diseases [18-25]. The underlying pathophysiology is heterogeneous and it lies on the nature, time course and severity of the underlying cardiovascular disease and the presence and severity of non-cardiovascular precipitating factors. The heterogeneity of patients with acute decompensated heart failure makes it difficult to develop a single pathophysiologic model [26]. Despite this heterogeneity, there are some important themes in patients with acute decompensated heart failure that guide the approach to patient management. In heart failure, there is a reduction in cardiac output which results in activation of baroreceptors in the central circulation in response to vascular under-filling. This causes activation of the sympathetic nervous system leading to an increase in sympathetic outflow to the kidney and systemic vasoconstriction [26]. Reduced renal blood flow and sympathetic stimulation of the kidney cause release of renin from the juxtaglomerular apparatus which, in turn, leads to conversion of angiotensinogen to angiotensin I which is changed to angiotensin II by angiotensin converting enzyme (ACE) and other tissue proteases [25, 26]. Angiotensin II is a vasoconstrictor that causes systemic vasoconstriction, renal arterial efferent >afferent vasoconstriction, activation of the sympathetic nervous system, release of aldosterone, stimulation of sodium retention in the proximal tubule of the kidney, release of arginine vasopressin, and stimulation of thirst centers in the brain. Sodium and water reabsorption is increased by aldosterone in the distal tubule and collecting duct contributing to

extracellular fluid expansion and systemic congestion. Aldosterone also elevates sodium and water absorption in the colon. Hepatic congestion in the setting of elevated right atrial pressure reduces aldosterone metabolism causing increased aldosterone levels [27]. Patients do not have aldosterone escapein heart failure so that, unlike patients with isolated hyperaldosteronism, the distal tubule goes on to reabsorb sodium in response to increased aldosterone levels. Stimulation of increased angiotensin II levels and central baroreceptors stimulate the non-osmotic production of arginine vasopressin from the posterior pituitary gland. This causes an increased free water reabsorption in the collecting ducts which makes volume overload worse and it leads to the development of hyponatremia [25]. There is retention of sodium and water in heart failure, which is mediated by activation of the sympathetic nervous system, decreased systemic and renal perfusion, and activation of the renin angiotensin aldosterone system (RAAS). In some patients, salt and water retention cannot be reversed by pharmacologic blockade of the RAAS and sympathetic nervous system suggesting that neurohormonal activation is not the only mechanism accountable for salt and water retention [25-27]. An Increase in sodium and water consumption are mediated by a rise in thirst caused by stimulation of central thirst centers mediated by activation of baroreceptors in the central circulation and excessive production of angiotensin II. Systemic congestion is a result of an increase in total body salt and water mediated by a reduction in sodium and water excretion and an increase in intake. Activation of the sympathetic nervous system and RAAS lead to systemic vasoconstriction and a rise in systemic vascular resistance (SVR). Increases in SVR cause a reduction in stroke volume and cardiac output in patients with systolic dysfunction and an increase in functional mitral regurgitation in patients with ventricular dilation [12]. A lot of patients with acute decompensated heart failure present with the primary symptom of dyspnea either at rest or with activity. This is certain for people with new-onset or chronic heart failure and also for patients with and without systolic dysfunction. Many patients have signs on physical exams of pulmonary and systemic venous congestion [12,14]. Breathlessness in patients with acute decompensated heart failure is caused by an increase in left atrial and pulmonary capillary pressure. The fluid movement from the pulmonary capillary space to the pulmonary interstitium is ascertained by a balance between hydrostatic and oncotic pressures in the pulmonary capillary and the pulmonary interstitial space. The main factor that results in fluid to move out of the capillary is a difference between the increased hydrostatic pressure within the pulmonary capillary and the lower hydrostatic pressure in the surrounding interstitium [14]. This action of fluid is opposed by the difference between the colloid osmotic pressure (which is primarily provided by the concentration of albumin) in the capillary space and the interstitium, which decreases the transudation of fluid out of the tiny blood vessel. In normal physiology, lymphatic washout of albumin that goes into the interstitium causes an increase in the osmotic gradient between the interstitium and pulmonary capillary which reduces transudation of fluid [12]. In normal physiology, fluid continues to move from the capillary space into the interstitium and is then eliminated by the lymphatic system. When hydrostatic pressure in the pulmonary capillary significantly goes up, transudation of fluid into the interstitium increases with potential for spillover into the alveolar space [28] There are various protective mechanisms that prevent the development of pulmonary edema. First, the alveolar-capillary unit consists of a thin side and a thick side. The thin side consists of capillaries that closely oppose the alveolar air spaces. The epithelium of the alveolar and capillary endothelium is thinned, and the basal plate of the alveolar epithelium and capillary endothelium is combined, resulting in low salt and water permeability [28]. The thick section of

the alveolar-capillary unit contains an interstitial matrix with a gel-like protein component that separates the alveolar epithelium from the capillary endothelium. As the capillary hydrostatic pressure increases, edema first forms in the interstitial area away from the gas exchange area. Second, when fluid enters the interstitial space, hydrostatic pressure increases and tumor pressure decreases, preventing further movement into the interstitial space [29]. Third, the fluid formed in the interstitium moves along the negative pressure gradient to the interlobular septum, bronchial cavities and hilum. Edema also accumulates in the chest cavity. The lymphatic vessels, interlobular septum, and pleura of the bronchial vascular membrane contribute to wastewater clearance [30]. Pulmonary lymphatics are greatly recruitable and, over time, are able to increase clearance of lung water by more than tenfold. Fourth, active sodium ion transport across the alveolar-capillary barrier by type II alveolar epithelial cells lining the alveoli is responsible for clearance of alveolar edema. Sodium ion enters the alveolar epithelial cells through apical amiloride sensitive sodium ion channels and other sodium ion channels and, by a process that consumes energy, is pumped out of the cell by the sodium ion, K+-ATPase located in the basolateral membrane [28-30]. In patients with HFrEF and HFpEF, the left ventricular filling pressure required to support a given amount of left ventricular work is elevated. As left ventricular end-diastolic pressure (LVEDP) increases, so do left atrial and pulmonary capillary pressures as pulmonary capillary pressure goes up, there is an increase in the transmural filtration of fluid into the pulmonary interstitium. There is a stage at which the capacity of the lymphatic system to eliminate fluid from the interstitium is surpassed and fluid starts to accumulate in the alveoli [30]. The cumulation of extravascular fluid in the pulmonary interstitium and alveoli is associated with clinical symptoms of paroxysmal dyspnea, impaired gas exchange, orthopnea, and dyspnea [21]. The functions of lungs and symptoms are influenced by water content of the lungs. The underlying pathophysiology of dyspnea in acute decompensated heart failure is multifactorial and complex with contributions from: decreased lung volume; airflow obstruction from reflex bronchoconstriction; geometric reduction in airway size from reduced lung volumes, intraluminal edema and mucosal swelling; reduced lung compliance; reduced alveolar-capillary membrane conductance with acute and chronic decreases in DLCO; impaired gas exchange due to alveolar swelling; arterial hypoxemia; raised work of breathing; respiratory muscle weakness in the critically ill patient; activation of chest wall sensors, an increase in the elastic work of breathing caused by cardiac enlargement and vascular engorgement with chest wall expansion past the usual or physiologic position; and stimulation of nerve endings in response to vascular distention and interstitial swelling [28]. A traditional understanding of why patients suffering from chronic heart failure develop acute decompensated heart failure indicates that patients with chronic heart failure commonly have a gradual rise in total body salt and water reflected by gradual weight gain and the gradual development of clinical features of pulmonary and systemic venous congestion [23]. While this paradigm happens in some of the patients with chronic heart failure, it may not be applicable to a huge number of patients with acute decompensated heart failure. A nested case-control study of patients referred to a home monitoring system by managed care organizations matched 134 case patients with heart failure hospitalization with 134 control patients without heart failure hospitalization [29]. Case patients experienced gradual weight gain starting about 30 days before admission to hospital. Within 7 days of hospitalization, weight patterns between case and control patients started to diverge more substantially with greater weight gain strongly associated with a greater odds ratio for hospital admission for (>2-5 lbs HR 2.77; >5-10 lbs HR 4.46; >10 lbs HR 5.65). However, only 46% of patients

hospitalized for acute decompensated heart failure gained more than 2 pounds in weight, indicating that weight gain was not a reason for hospitalization in about half of patients.

Classification of ADHF

Heart failure is the last and most common cause of many cardiovascular diseases. Underlying causes of cardiovascular dysfunction in patients with ADHF, timing of symptoms, comorbidities and triggers, and underlying pathophysiology. Several attempts have been made to classify acute decompensated heart failure based on onset, underlying heart disease, major hemodynamic abnormalities, and clinical profile. The International Working Group on Acute Heart Failure [8] emphasized the onset of heart failure. However, the American College of Cardiology/American Heart Association (ACC/AHA) classification stages for ADHF:

1. Exacerbation of chronic heart failure: LVEF is reduced or preserved. ACC/AHA stage C heart failure. 70% of all hospitalization.

2. New heart failure: This is usually the result of acute coronary syndrome. as well as a sudden increase in blood pressure in patients with left ventricular dysfunction or acute myocarditis. People with ACC/AHA stage A (with risk factors but no structural heart disease) or B stage (pre-existing heart disease but no clinical signs of heart failure). 25% of all hospitalization.

3. Progressive heart failure: severe left ventricular systolic dysfunction (LVAD, heart transplant, hospice) associated with persistent worsening of heart failure, resistant to traditional heart failure treatment and requiring special treatment. ACC/AHA stage D 5% of all registrations.

The 2009 ACCF/AHA guidelines for the diagnosis and management of heart failure in adults [12] reported three clinical profiles of patients with acute decompensated heart failure, focusing on the clinical manifestations of systemic perfusion and congestion.

1. Hypervolemic patients with pulmonary and systemic congestion, often resulting from an acute increase in chronic hypertension.

2. Extremely low heart rate in patients with renal failure, hypotension and shock syndrome.

3. Patients with clinical signs of fluid overload and shock.

The 2008 European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic heart failure listed six clinical scenarios for patients with acute decompensated heart failure [17]. EHFS II used modifications of ESC contours to classify patients included in the registry [18]:

1. Exacerbation or decompensation of chronic heart failure: a history of known progressive exacerbation of chronic heart failure. Clinical signs and symptoms of exacerbation of heart failure with signs of systemic and pulmonary venous congestion [16]. The patient may have a reduced or preserved ejection fraction. (65% of EHFS II patients).

2. Pulmonary Edema: Patients with diffuse pulmonary convergence, severe respiratory failure, hypoxia (without supplemental oxygen), oxygen saturation alveolar edema on chest X-ray. (16% of EHFS II patients) [18].

3. Hypertensive heart failure: Hypertensive patients show clinical symptoms of heart failure. There is evidence of increased heart rate and increased sympathetic tone with signs of vasoconstriction. The patient may have maintained systolic function. Often these patients present with symptoms of pulmonary congestion without signs of systemic congestion [16]. Response to heart failure treatment is generally rapid and in-hospital mortality is low (1.5% in EHFS II). (11% of EHFS II patients).

4. Cardiogenic shock: Patients with end-stage hypoperfusion after heart failure with adequate or elevated left ventricular end-diastolic blood pressure [18]. These patients usually have low urinary output, low systolic blood pressure, and low cardiac index (Most patients have severe pulmonary congestion, and mortality in this population is high. (4% of EHFS II patients).

5. For isolated right heart failure: There is clear evidence of increased jugular venous pressure, systemic venous congestion, and decreased cardiac output without signs of pulmonary congestion [17].

6. Acute coronary syndrome due to heart failure: (This is not included in any other EHFS II classification) Heart failure with clinical signs and laboratory evidence of acute coronary syndrome. About 13.6% of patients with acute coronary syndrome have clinical signs of heart failure [17,18]. In EHFS II, acute coronary syndrome was a precipitating factor in 42% of patients with new-onset or heart failure and 23% of patients with pre-existing heart failure.

Causes of acute decompensated HF

Decompensation of preexisting chronic HF from a precipitating factor (e.g., natural progression of underlying disease, dietary indiscretion [excessive fluid or salt intake], medication nonadherence, infection, new myocardial ischemia, metabolic stress [e.g., anemia, hyperthyroidism], medication use [e.g., nonsteroidal antiinflammatory medications that lead to sodium retention]) [30]. Hypertensive crisis (e.g., hypertensive emergency). Myocardial infarction or ischemia, especially if a papillary muscle is involved, leading to severe mitral regurgitation; a massive anterior myocardial infarction occurs; or a right ventricular infarct results in a low cardiac output state [28]. Acute tachycardia. Acute endocarditis leading to severe reflux. Acute dilated cardiomyopathy (eg myocarditis, cocaine, toxins). cardiac tamponades [29]. Advanced HF (eg Paget's disease, thyrotoxicosis, beriberi, sepsis).

Clinical Symptoms

The main signs of heart failure are shortness of breath and fatigue. Generally, fatigue has been attributed to the low cardiac output in heart failure, it is likely that the skeletal-muscle abnormalities and other noncardiac comorbidities (e.g., anemia) also contribute to this symptom [21]. In the early

stages of heart failure, shortness of breath is observed only during exertion; however, as the disease advances, shortness of breath occurs with less strenuous activity, and it eventually may occur even at rest. The origin of shortness of breath in heart failure is likely multifactorial [8, 21]. The prime mechanism is pulmonary congestion with accumulation of interstitial or intra-alveolar fluid, which activates juxtacapillary J receptors, which in turn stimulate the rapid, shallow breathing characteristic of cardiac dyspnea. Additional factors contributing to dyspnea during exercise include increased airway resistance, decreased lung compliance, respiratory muscle and/or diaphragm fatigue, and anemia [1]. Shortness of breath may become less frequent when tricuspid regurgitation and right ventricular failure begin. Orthopnea: This is shortness of breath that occurs when lying down. Traditionally, this is a later symptom of heart failure rather than dyspnea on exercise [3]. This occurs when the internal circulation and fluid in the lower extremities are redistributed from the supine position to the central circulation, which increases the capillary pressure in the lungs. Nocturnal cough is a regular manifestation of this process and a frequently neglected symptom of heart failure. Orthopnea normally is relieved by sleeping with additional pillows or sitting upright. Although orthopnea is a very specific symptom of heart failure, it may happen in patients with ascites or abdominal obesity, and patients suffering from pulmonary disease whose lung mechanics favor an upright posture [1-3]. Cheyne-stokes respiration: refers to the periodic respiration or cyclic respiration, cheyne-stokes respiration occurs in about 40% of patients with advanced heart failure and normally is in association with low cardiac output [27]. It is caused by an increase in the sensitivity of the respiratory center to arterial PCO2 and a lengthy circulatory time. There is an apnea phase in which arterial PO2 decreases and arterial PCO2 increases [14]. These changes in arterial blood gases (AH) stimulate the respiratory center, leading to hypocapnia and hyperventilation and recurrent apnea [27]. Acute pulmonary edema: An additional symptom that may be present in patients with heart failure is gastrointestinal symptoms [14]. Anorexia, nausea and early satiety, abdominal pain and bloating are common symptoms and may be associated with intestinal edema and/or liver congestion. Congestion of the liver and stretching of the capsule can cause pain in the right hypochondrium [27]. Cerebral manifestations such as disorientation, confusion, and sleep and mood disturbances may be seen in patients with severe heart failure, especially elderly patients with cerebral arteriosclerosis and low cerebral perfusion. Nocturia is common in heart failure and may contribute to insomnia [24].

Physical examination

A thorough physical examination is often warranted in the assessment of patients with heart failure, in order to ascertain the cause of heart failure, also to evaluate the severity of the syndrome [30]. The general appearance and vital signs in mild and moderately severe heart failure, the patient appears in no distress at rest except for feeling uncomfortable when in a prone position for more than a few minutes. In more severe heart failure, the patient must sit upright, may have labored respiration, and may be unable to complete a sentence because of dyspnea [25]. Systolic blood pressure can be normal or elevated in the early stages of heart failure, but usually decreases in advanced heart failure due to severe left ventricular dysfunction. Pulse pressure may decrease, indicating a decrease in stroke volume. Sinus tachycardia is a nonspecific symptom due to high adrenergic activity [23]. Peripheral

vasoconstriction is also due to excessive adrenaline activity, which causes the peripheral extremities to cool and cyanosis of the bottom of the lips and nails. Jugular vein: The jugular vein assessment provides an estimate of right atrial pressure. Jugular venous pressure (JVP) is best measured in a supine position with the patient tilted at a 45° angle. JVP estimates the height of the venous column above each sternum in centimeters and then quantifies it in centimeters several weeks by adding 5 cm abdominal jugular reflux. Giant v waves indicate the presence of tricuspid regurgitation [28]. Lung examination: phlegm or wheezing due to leakage of intravascular fluid into the alveoli [27]. In people with pulmonary edema, rales may be heard widely over both lung fields and may be followed by expiratory wheezing (cardiac asthma). When present in people without concomitant lung disorder, rales are specific for heart failure. Importantly, rales are occasionally not seen in patients with chronic heart failure, even when left ventricular filling pressures are increased, because of elevated lymphatic drainage of alveolar fluid. Pleural effusions result from the increase of pleural capillary pressure and the resulting transudation of fluid into the pleural cavities [27-29]. Cardiac examination: examination of the heart, although important, generally does not provide helpful information about the severity of heart failure [30]. In the presence of cardiac hypertrophy, the point of maximum stimulation is displaced down the 5th intercostal space and lateral to the midclavicular space, and the shock is felt above the two intercostal spaces. Severe left ventricular hypertrophy leads to persistent PIM. In some patients, a third heart sound at the apex is auscultated and felt [20]. People with dilated right ventricles may have persistent, prolonged left exoskeleton impulses that propagate throughout systole. S3 is usually heard in volume overload patients with tachypnea and tachycardia and often indicates severe hemodynamic impairment. The fourth heart sound is not a specific indicator of heart failure, but is commonly seen in patients with diastolic dysfunction. Mitral and tricuspid valve murmurs are often seen in patients with advanced heart failure [23]. Abdomen and extremities: Hepatomegaly is an important finding in patients with heart failure. In this case, the enlarged liver is often painful and may pulsate during systole in the presence of tricuspid regurgitation [28]. Ascites, a late sign, is caused by increased pressure in the veins of the liver and veins draining the peritoneum. Jaundice, is also a late finding in heart failure, results from impairment of hepatic function secondary to hepatic congestion and hepatocellular hypoxemia and is associated with elevations of both direct and indirect bilirubin [23]. Peripheral edema is a prime manifestation of heart failure, but it is nonspecific and usually is absent in patients who have been treated satisfactorily with diuretics [21]. Peripheral edema is generally symmetric and dependent on heart failure and occurs mainly in the ankles and the pretibial region in ambulatory patients. In bedridden people, edema may be found in the scrotum and sacral area. Prolonged edema may be associated with indurated and pigmented skin [23]. Cardiac cachexia: Significant weight loss and cachexia can occur in severe chronic heart failure. The mechanisms of cachexia are not fully understood, but they are likely multifactorial. The presence of cachexia indicates an adverse overall prognosis [22, 23].

Diagnosis

Diagnosis of heart failure is relatively straightforward when a patient has the typical signs and symptoms of heart failure. However, the clinical signs of heart failure are neither specific nor sensitive. Key to

making the diagnosis is the presence of a high suspicion index, especially for high-risk patients [1,2,8]. When these patients present with signs or symptoms of heart failure, additional laboratory investigations should be performed. Routine laboratory testing: patients with new-onset heart failure and those with acute decompensated heart failure and chronic heart failure should have a complete blood count (CBC), a hepatic panel, a panel of electrolytes, serum creatinine, blood urea nitrogen, and a urinalysis [25]. Selected patients should have evaluation for diabetes mellitus, dyslipidemia, and thyroid abnormalities. Electrocardiogram (ECG): a routine twelve-lead ECG is recommended [25]. The major importance of the electrocardiogram is to evaluate cardiac rhythm and determine the presence of left ventricular hypertrophy or a prior MI as well as to determine QRS width to ascertain if the patient may benefit from resynchronization therapy. A normal electrocardiogram virtually does not include left ventricular systolic dysfunction [24]. Chest x-ray: a chest x-ray provides useful evidence about heart size and shape, also the state of the pulmonary vasculature, and may recognize non-cardiac causes of the patient's symptoms [22]. Although patients with acute heart failure have evidence of pulmonary hypertension, and interstitial edema, the majority of patients with chronic heart failure do not. The absence of these findings in patients with chronic heart failure reflects the increased capacity of the lymphatics to eliminate interstitial fluid [15]. Assessment of left ventricular function: noninvasive cardiac imaging is crucial for the assessment, diagnosis, and management of heart failure. Two-dimensional (2-D) echocardiogram/doppler is the most useful test, it provides a semiquantitative assessment of left ventricular size and function as well as the presence or absence of valvular and/or regional wall motion abnormalities [21]. The presence of left atrial dilation and left ventricular hypertrophy, together with abnormalities of left ventricular diastolic filling provided by pulse-wave and tissue doppler, is helpful for the evaluation of heart failure with a preserved ejection fraction. The 2-D echocardiogram/doppler is also useful in assessing right ventricular size and pulmonary pressures, which are critical in the assessment and management of cor pulmonale [15]. Magnetic resonance imaging also provides a complete analysis of cardiac anatomy and function and is now the gold standard for assessing left ventricular mass and volumes. MRI also is emerging as an invaluable and accurate imaging modality for assessing patients with heart failure, both in terms of evaluating left ventricular structure and for determining the cause of heart failure [22]. Biomarkers: circulating levels of natriuretic peptides are helpful and prime adjunctive tools in the diagnosis of patients with heart failure [6]. Both B-type natriuretic peptide and N-terminal pro-BNP, which are released from the failing heart, are relatively sensitive markers for the presence of heart failure with depressed ejection fraction; they are also increased in heart failure patients with a preserved ejection fraction, albeit to a lesser degree [21]. In ambulatory patients with shortness of breath, the measurement of BNP or NT-proBNP is helpful to support clinical decision-making concerning the diagnosis of heart failure, particularly in the setting of clinical uncertainty. Additionally, the measurement of BNP or NT-proBNP is helpful for establishing prognosis or disease severity in chronic heart failure and can be helpful to achieve optimal dosing of medical therapy in select clinically euvolemic patients [20]. Nevertheless, it is important to identify that natriuretic peptide levels increase with age and renal impairment, are more increased in women, and can be increased in right heart failure from any cause

BNP levels may be elevated in patients taking the angiotensin receptor inhibitor neprilysin [5,30]. In obese patients, the level may be erroneously reduced. Other biomarkers such as soluble ST-2 and

galectin-3 are novel biomarkers that can be used to determine the prognosis of patients with heart failure. Exercise tests: Treadmill or cycling tests are generally not recommended for patients with heart failure, but both are useful in evaluating the need for heart transplantation in patients with advanced heart failure [30]. Peak oxygen consumption (vo2) of less than 14 ml/kg per minute is associated with a relatively poor prognosis. Patients with a vo2 less than14 mL/kg per min have been shown, in general, to have better survival when transplanted than when treated medically [22].

Medical management

The main objectives of treatment for heart failure (HF) are to improve prognosis, reduce the burden of symptoms, and ultimately decrease morbidity and mortality. Additionally, it also includes: reducing the length of hospital stay and frequency of readmission, prevent end-organ damage, and to adequately manage co-morbid conditions that may worsen the outcome [30]. The 2010 HFSA (heart failure society of america) guidelines, the updated 2013 ACA/AHA (american college of cardiology/american heart association) guidelines, and the 2008 ESC (european society of cardiology) guidelines, all provide different levels of evidence for the management of HF patients. This reports management of HF cases will be under two categories; In-hospital and out-patient care [19, 29, 30]. In-hospital management: it is so recommended to admit the patient to the telemetry bed or the intensive care unit (ICU) and provide care based on the - oxygen levels (PaO2 less than 60% or SaO2 less than 90%), and noninvasive positive pressure ventilation (NIPPV) given in cases with respiratory distress to support ventilation. Several pharmacological agents can be administered depending on presenting signs/symptoms and on the contributing factors: Diuretics: loop diuretics, thiazides, and potassium-sparing diuretics for years have been the mainstay for managing HF cases. Loop diuretics inhibit NA-K-2CL cotransporter on the luminal membrane of the ascending limb of the loop of henle to reduce renal reabsorption of sodium chloride. Examples are furosemide, torsemide, bumetanide, and ethacrynic acid as an option in cases of sulfa allergy [22, 27]. Diuretics reduce volume overload in HF patients. Angiotensin-converting enzyme inhibitors (ACEIs)/or angiotensin receptor blockers (ARBs)/angiotensin-neprilysin receptor. Blockers: this category works by suppressing the renin-angiotensin-aldosterone system (RAAS) and is considered the gold standard to modulate RAAS in HF patients for more than two decades [24]. ACEIs block the conversion of angiotensin one to angiotensin two. However, it potentiates bradykinin accumulation which promotes both positive and negative effects. ARBs are the alternatives to ACEIs in patients that cannot tolerate ACEIs. ARBs specifically block the angiotensin ii receptors and do not decrease the breakdown of bradykinin online ACEIs [25]. A newer therapy class, the angiotensin receptor neprilysin inhibitor (ARNI), was brought about by adding a neprilysin inhibitor to angiotensin receptor inhibition [26]. Being an endopeptidase, neprilysin breaks down various endogenous vasoactive peptides [27]. These effects lead to appreciable hypotensive outcomes and are massively beneficial in comparison with ACEIs or ARBs. The ARNI is fast replacing ACEI/ARB as the gold standard RAAS blocker due to its clinical advantages for HF cases [27, 5]. Beta blockers (BBs): by inhibiting the actions of the sympathetic nervous system, BBs have shown improved outcomes for HF management. Subsequently, BBs decrease ischemia of the myocardium and possesses antiarrhythmic effects which help to maintain energy levels required for myocyte function by enabling glucose instead of fatty acid metabolism. As well, beta blockers inhibit

renin secretion [28]. Mineralocorticoid receptor anatagonists (MRAs): this class of drugs prevent the binding of aldosterone to the mineralocorticoid receptors, mostly found in the vascular smooth muscle cells and in the myocardium. Furthermore, they demonstrate antifibrotic effects by suppressing the production of matrix metalloproteinases and other factors that contribute to myocardial remodelling [22, 24, 26, 28]. Sodium-glucose cotransporter - 2 (SGLT-2) inhibitors: recently proven to be efficacious in treating Hf, especially HF with reduced ejection fraction (HFrEF). It increases renal glucose excretion by blocking SGLT-2, promoting osmotic diuresis and natriuresis [23]. Although it was originally manufactured as an anti-diabetic agent, it has clinical benefits for HFrEF in both diabetic and non-diabetic patients [24]. Ivabradine: patients benefit from the use of this drug as a result of its inhibition of the inward rectifying potassium channel (funny currents inhibitor), which slows depolarization during diastole eventually reducing the heart rate [25]. Thromboembolism risk is reduced by anticoagulants if needed. Vasodilators: such as hydralazine and nitrates combined are substantially considered to improve patient symptoms. Hydralazine is a direct arteriolar vasodilating agent whereas nitrates primarily mediate venodilation, lowering ventricular preload [26]. Oral soluble guanylate cyclase stimulators: example - vericiguat. Lately, found to enhance positive end results among HF patients at high risk. Its main mechanism of action involves boosting endogenous nitric oxide by directly binding to and stimulating the soluble guanylate cyclase [27]. Positive oral inotropes: restores perfusion and decreases congestion in HFrEF patients so as to increase cardiac output. It includes digoxin and omecamtiv mecarbil. The latter is a new drug, acting as an activator of cardiac myosin beneficially improving the left ventricular function [28, 29]. In summary, the proper medical management should follow the steps below: reduce preload (preferably with loop diuretics). Administer oxygen if hypoxemia is present. Reduce afterload with ACEI if systolic blood pressure measures more than 100mmHg. Intravenous agents are recommended if hypertensive crisis is present (i.e., sodium nitroprusside). Increase inotropy if there are evidences of hypoperfusion (i.e., milrinone, dobutamine), but beware of increase in ventricular arrhythmias with inotropic agents. Digoxin reduces hospitalizations and improves clinical symptoms, but does not lower mortality rate. Consider adding digoxin when patients have symptoms despite adequate therapy with ACEI, β-blockers, and AA. NB: β-blockers are successfully used later when heart failure is compensated and stroke volume improves. They can worsen decompensated heart failure by their inotropic effects. Mineralocorticoid antagonist e.g,. spironolactone, which helps reduce morbidity and mortality. Funny current inhibitor e.g,. ivabradine which significantly increases survival rate by 120% and prolongs average survival time by 20%. Angiotensin receptor-neprilysin inhibitor, e.g,. sacubitril/valsartan. Certain agents from the above listed have been demonstrated to significantly lower morbidity and mortality, hospitalizations, and prevent cardiac remodelling. They are; beta blockers, ACEIs/ARBs, MRA, and ARNI(sacubitril/valsartan) [22-26]. SGLT-2 inhibitors also highly improve quality of life when incorporated into current standard drugs [24, 26, 28]. Out-patient management: [29, 30] counsel should be tailored to meet the patients specific needs, patient education, promote self-care, strategies to enhance patient medication adherence, observing signs and symptoms of fluid overload, regular follow-up, access to healthcare services and assistance as required.

Implantable devices and surgical procedures to treat heart failure:

Cardiac resynchronization therapy (CRT) is done to help the heart beat with the right rhythm. It uses a pacemaker to restore the original timing pattern of the heartbeat [23]. Left ventricular assist device: this device is used for patients who have reached the last stage of heart failure. It is a battery-operated, mechanical pump, which is surgically fixed in the chest. It helps the main pumping chamber of the heart (left ventricle) to pump blood to the rest of the body [23, 25]. HeartMate 3: this is a centrifugal, continuous flow pump that is placed in the thorax and is engineered to be a more hemocompatible LVAS. The device is created with a fully magnetically levitated motor, offers wider blood flow paths, and even exhibits a fixed intrinsic pulse (by the motor ramping its speed up and down at 2 s intervals) [25]. Total artificial heart: it is not every patient that is a candidate for a LVAS, especially those with severe right-sided heart failure or conditions that do not permit placement of an LVAS (massive anterior myocardial infarction, restrictive cardiomyopathy, complex congenital heart disease). In similar patients, either a biventricular assist device approach or a total artificial heart pump can be considered [30]. The syncardia total artificial heart is a pulsatile, implantable pump that comprises two polyurethane ventricles with pneumatically driven diaphragms, and four tilting disc valves. This requires excision of the native ventricles and hence cannot be employed as a myocardial recovery strategy. There are a lot of specific clinical issues that are peculiar to the total artificial heart management [24]. This machine operates on a steep physiological curve and has little adaptability to tolerate either systemic blood pressure changes or large shifts in blood volume. Heart valve surgery: diseased heart valves can be treated with both traditional heart valve surgery and balloon valvuloplasty [30]. Coronary artery bypass grafting surgery: this is considered in heart failure caused by coronary artery disease [27]. Heart transplantation: some patients have severe, progressive heart failure that cant be helped by drugs or dietary and lifestyle changes. In similar cases, a heart transplant may be the only beneficial treatment option. The damaged heart is changed with a healthy heart from a donor who has been declared brain dead [23]. However, it takes some time to find a donor whose heart matches the tissues of the recipient.

Conclusions

Acute decompensated heart failure is a regular cause of hospitalization and has a tall risk of rehospitalization and mortality. From the diagnosis and risk stratification of the acute decompensated heart failure, determination of the clinical hemodynamic profile is essential to guide therapy including pharmacological and non-pharmacological measures, and, in refractory cases, VAD and cardiac transplantation.

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