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Heart failure in the elderly

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Abstract

The aging of the population is, currently, a major phenomenon, drawing the attention of a number of investigators. The significant increase of life expectancies over the past few decades, in addition to social and economic consequences, has lead to a major change in the morbidity and mortality profile of elders. Heart failure (HF) is a condition in which the heart can not pump enough blood to meet the body's needs. HF is predominantly a disorder of the elderly with rates increasing exponentially. The prevalence of HF approximately doubles with each decade of life. As people live longer, the occurrence of HF rises, as well as other conditions that complicate its treatment. Impaired heart function implies a reduced duration of survival. Fortunately, many factors that can prevent HF and improve outcome are known and can be applied at any stage. This review emphasizes the importance of factors inherent in aging itself, focusing on heart disease, particularly as a disease of aging, can help critically refine management of this acute and chronic disease, as well as foster preventive strategies to reduce the incidence of this common malady.

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1 Heart failure

Heart failure (HF) is a complex clinical syndrome resulting from the inability of the heart to adequately supply the metabolic demands of tissues, or do so only with elevated filling pressures. HF can result from disturbance of contractility, with reduced ejection fraction of the left ventricle (systolic HF) or by alterations in the filling and/or ventricular relaxation, with a preserved ejection fraction (diastolic HF or HF with preserved systolic function).

HF is a disease of high prevalence and incidence throughout the world. About 400,000 new cases are diagnosed in the United States every year. Data from the Framinghan study demonstrate that the incidence of HF increases progressively in both genders according to age.[1] This prevalence is about 3.3% in population ≤ 45 years, 10.5% in individuals ≥ 65 years, and around 20.0% in population ≥ 75 years[2,3] making HF is the leading cause of hospitalization in the geriatric population.

The most common causes of HF in the elderly are coronary atherosclerotic disease and arterial hypertension, which often coexist. Other common causes in developing countries are: arrhythmias, endocrinopathies, infiltrative, idiopathic and dilated cardiomyopathy, infection and alcohol.[4] Age is also an isolated risk factor for the development of HF after acute myocardial infarction.

Clinically, HF is manifested by physical exercise intolerance, fluid retention, edema and visceral congestion, which often leads to hospitalization, poor quality of life and reduced life expectancy. In recent decades, HF has become increasingly prevalent phenomenon closely linked to the aging population, with growing awareness in clinical geriatrics.

2 Clinical diagnosis

The careful analysis of signs and symptoms is crucial for establishing the diagnosis; however, in the elderly, it is

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difficult to interpret, due to the concomitance of other diseases and by the atypical way they are externalized.[5] The evaluation should be initiated by a well-conducted anamnesis followed by a thorough physical examination and appropriate laboratory tests.

The manifestations of HF can be variable, depending on the time course of the syndrome and the possibility of activation of compensatory mechanisms, ranging from light asymptomatic ventricular dysfunction to acute left ventricular failure.

In elderly patients, the complaint of fatigue is quite common and should not be considered a symptom of aging itself. It is a rather complex symptom related to low cardiac output, peripheral hypo-perfusion and skeletal muscle deconditioning, which may lead to misdiagnosis.[6]

The exertional dyspnea, orthopnea, lower extremity edema and reduced exercise tolerance are the cardinal symptoms of HF, in both the young and the elderly, but it can be difficult to interpret, especially in the elderly, in the obese and in women.[2]

Dyspnea is the primary symptom of HF, with a progressive and varied intensity according to the condition of cardiac performance.

The initial presentation is exertional dyspnea. In the elderly, it may be associated with increasingly sedentary lives. Dyspnea progresses to orthopnea, paroxymal nocturnal dyspnea, dyspnea at rest and, without any intervention, leads to acute pulmonary edema. Dyspnea is the clinical expression of pulmonary venocapilar hypertension, but fatigue and tiredness are related to lower perfusion and vasoconstriction of skeletal muscle.

In contrast, atypical symptoms, such as confusion, memory deficit, sleepiness, episodes of delirium, irritability, syncopal states, fatigue, anorexia, and reduced level of activity, gradually become common manifestations of HF in the elderly, especially after age 80. In the geriatric population, gastrointestinal symptoms, such as nausea, vomiting, constipation or diarrhea, occur more often and when associated with anorexia will lead to cachexia. Once the diagnosis has been established, it is recommended to scale the severity of HF through the symptoms (Table 1).

Table 1. Heart failure functional classification (New York Heart Association).

Class I – No difficulty with usual physical activities, with no manifestation of dyspnea, fatigue or palpitations.
Class II–Slight limitation for usual physical activities. Patient asymptomatic at rest; in physical activity, expression of fatigue, dyspnea and palpitations.
Class III–Significant limitation of physical activities, although comfortable at rest. Symptoms of dyspnea, fatigue and palpitations on exertion.
Class IV–Symptoms present even at rest, and discomfort with any physical activity.

The diagnosis of HF in the elderly may be difficult due to the presence of co-morbidities, with increasing prevalence of atypical symptoms and signs. Usually, the physical examination shows clinical signs that vary with the extent and severity of the disease. In the early stages, the patient may experience relatively good clinical status, while chronically ill patients may be malnourished or cachexia.[7,8] Edema due to increased hydrostatic pressure and sodium retention is often found in the elderly, requiring special attention. However, it is often underrated as a sign of HF, for it may be due to the clinical picture of malnutrition with hypo-proteinemia, venous circulatory disorder or renal origin. Peripheral edema is preceded by hepatomegaly, which may progress to anasarca, with ascites and pleural effusion. Pleural effusion, when unilateral, is generally prevalent in the right hemi-thorax.

Fine rales at the lung bases in elderly lose fidelity, not an uncommon complication, considering that in this age group the lack of physical activity or periods of prolonged bed rest lead to the appearance of rales in the bases.

The great variability in the detection and interpretation of signs and symptoms by the examiners, however, are associated with low sensitivity and specificity in clinical diagnosis of HF in the elderly, leading some authors to develop criteria in order to improve the diagnostic accuracy.[9,10] The Framingham researchers listed criteria classified into major and minor from the signs and symptoms of HF, which were used in this study. The presence of two major signs (main criteria) or one major and two minor signs (secondary criteria) would be needed for the diagnosis of HF (Table 2).

The HF may be caused by either systolic or diastolic dysfunction, or the combination of both.[11] The differential diagnosis of these clinical entities, with the determination of the predominance of one over the other, is essential for successful treatment. In 50% of the patients, particularly those at 70 years old or more, the HF is caused by alterations in the diastolic function. When HF is caused by isolated diastolic dysfunction, congestive symptoms result from pulmonary venous hypertension, with normal systolic function and without

Table 2. Clinical criteria for the diagnosis of heart failure.[1]

Major criteria	Minor criteria
Paroxynal nocturnal dyspnea	Ankle edema
Jugular venous distention	Coughing at night
Hepato jugular reflection	Hepatomegaly
Rales	Pleural effusion
Acute pulmonary edema	Vital capacity less than or equal to the one third of the predicted maximum
Cardiomegaly	Tachycardia 120 beats/minutes
Third heart sound (gallop)	
≥ 4.5 kg weight loss in 5 days in response to the treatment of Heart failure.	

the occurrence of increased cardiac area.[12] The mortality rate in these cases is comparable to that of systolic HF, with approximately 50% survival rate at five years. The diagnosis of HF should, in any situation, seek to identify the underlying cause, a fundamental condition for the specific and individualized therapy.

3 Etiology and precipitating factors

Arterial hypertension and coronary artery disease account for 70% to 80% of cases of HF in the elderly.[13,14] The main root causes of HF are displayed in Table 3.

Table 3. Common causes of heart failure.

Coronary artery disease: acute and chronic
Hypertensive heart disease
Valvular heart disease
Cardiomyopathy
Ischemic
Non-ischemic: alcohol; chemotherapy; inflammatory myocarditis; idiopathic dilated cardiomyopathy
Hypertrophic
Obstructive
Unobstructive
Restrictive
Pericardial disease
Triggering factors
Chronic anemia; thiamine deficiency; hyperthyroidism; arteriovenous fistula; fever; medications; diet high in salt and water; endocrine diseases; chronic obstructive pulmonary disease; non adherence to therapy; arrhythmias; renal failure; pulmonary embolism.
Diastolic dysfunction related to age

4 Complementary investigations

Complementary examinations aid in the diagnosis of HF, and contribute to the identification of the causative or precipitating factors. The electrocardiogram, although not specific, is usually abnormal, showing a negative predictive value of about 90%.[15] It can display rhythm disturbances, bundle branch blocks, cardiac chamber overload as well as signs of myocardial ischemia. According to the II Cardiogeriatrics Guidelines (2010), (grade of recommendation I, level of evidence.[9,16]

Chest radiography (CR) should be part of the initial investigation of HF. A careful evaluation is required for the elderly. Some symptoms of HF may be confused with chronic obstructive pulmonary disease (COPD) and respiratory infections. The finding of cardiomegaly favors the diagnosis of HF, especially if associated with pulmonary congestion and pulmonary hypertension with reversal of the vascular pattern, presence of Kerley lines and pleural effusions. In the elderly, chest deformities, a feature of the aging process, make difficult the interpretation of the cardiac area. CR is the most common diagnostic method in clinical practice (grade of recommendation I and level of evidence C).[15]

Doppler echocardiography should also be performed routinely. It is indispensable for the accurate diagnosis of HF because it provides data to the anatomical and functional assessment. It is crucial for the diagnosis of heart diseases through its capacity to quantify valvular lesions, pressure gradients, diameter of cardiac cavities, wall thickness, myocardial contractility, ventricular ejection fraction and ventricular complaisance and relaxation.

Ejection fraction below 45% corroborates the diagnosis of ventricular dysfunction. On the other hand, ejection fraction ≥ 45%, with signs and/or symptoms of HF and echocardiographic abnormalities consistent with alterations in left ventricular filling characterize left ventricular dysfunction with preserved ejection fraction (Grade of recommendation I and level of evidence B).[9,15]

The exercise test (ET) has limited value for diagnosis of HF.[15] A maximum normal test in patients, without treatment, rules out the diagnosis. On the other hand, in patients on drug therapy, the analysis of parameters obtained in the ET may have limitations due to resulting pharmacological effects. However, ET is useful in assessing the functional capacity and patient´s response to the treatment.[15]

The 6-minute-walk test is a good choice for the functional evaluation of patients with HF. It is better tolerated than the ET, inexpensive, and can provide important information, both prognostic and therapeutic assessment, in rehabilitation programs. The distances below 300 meters are of poor prognosis, while the ones at 450 meters are correlated with lower rates of mortality and hospitalization. The radionuclide ventriculography is performed to assess ventricular ejection fraction with higher accuracy compared to echocardiography. Its disadvantages are the high cost, time to perform it and exposure to radiation (grade of recommendation level of evidence A).[9]

The β-type natriuretic peptide (BNP) is a hormone produced mainly by ventricular cardiomyocytes, whose secretion is associated with the stretching of myocardial fibers. Quantitative analysis of plasma concentrations of BNP are useful to confirm the diagnosis, provide an estimate prognosis and guide treatment in patients with HF. Elevated plasma concentrations of BNP have 97% sensitivity and a specificity of 84% for the diagnosis of HF due to systolic dysfunction, with a negative predictive value around 98%. The low specificity limits its diagnostic value in the diastolic dysfunction.[17]

However, such concentrations can establish the differential diagnosis between diastolic HF dyspnea and non-cardiac disease assessments in emergency conditions (grade of reco-

mmendation I level of evidence A).[9] It is particularly indicated when given access to echocardiography is limited.

Laboratory tests are performed in order to identify associated diseases and to evaluate blood glucose, electrolyte disturbances and renal function. Other tests should be performed with specific clinical indications, such as evaluation of thyroid, respiratory and liver function.

5 Treatment

The treatment of HF is scheduled in Table 4.

Table 4. Treatment of heart failure.[15,17]

Determine the etiology and remove the cause
Eliminate or correct precipitant factors
Non-pharmacological measures
Pharmacological measures
Diuretics
Angiotensin converting enzyme (ACE) inhibitors
Digitalis
Non digitalis inotropic agents
Vasodilator
Beta-adrenergic blockers
Antiarrhythmics
Anticoagulants
Pacemakers–implantable defibrillater
Assisted circulation
Surgical procedures
Cardiac transplant

5.1 Non-pharmacological measures

Non-pharmacologic measures include appropriate diet, cessation of smoking, increased physical activity, and immunization.[9,15,17] The measures also include dietary sodium restriction, alcohol and net weight reduction in obese patients and nutritional care in patients with cachexia, an important predictor of longer life expectancy.[2] Elderly patients with HF should be immunized against influenza and pneumococcus, although there is no documented evidence of effectiveness. Patients should stay home uncompensated.[15,17] The stable, functional class II-III, should perform physical activity through well planned physical conditioning programs resulting in an increased tolerance to stress. Prolonged bed rest, wherever possible, should be contraindicated. In addition, the use of certain medications should be avoided, including anti-inflammatory steroids, tricyclic antidepressants, corticosteroids, lithium, class I antiarrhythmic agents, among others.[15]

5.2 Pharmacotherapy

The treatment of HF in the elderly is similar to that of younger cohorts, having to respect some peculiarities of this age group. The normal doses of drugs are, in general, less well tolerated and it is necessary to be careful with the maximum doses recommended in clinical studies. Co-morbidities should be considered, as well as poly-pharmacy, common in the elderly who are most likely prone to iatrogenic and drug interactions.

5.2.1 Diuretics

These medications act more quickly in controlling symptoms of HF when fluid retention is present in the form of edema and pulmonary congestion. Their use results in rapid control of dyspnea and improves physical exercise tolerance.[9,15,17] Loop diuretics are initially used (grade of recommendation I, level of evidence C). Thiazide diuretics should be added when there is refractoriness to loop diuretics. Thiazides, however, lose their efficacy in patients with moderate renal impairment (creatinine clearance $\leq$ 30 mL/minutes).

Among the potassium sparing diuretics, spironolactone was associated with a 27% reduction in total mortality. It should be considered in patients in functional class III-IV and should be accompanied by strict control of potassium and creatinine. In the elderly, it is recommended to avoid the association with ACE inhibitors, angiotensin receptor blockers (ARBs) and aldosterone inhibitors.[18]

The elderly are more prone to adverse reactions, therefore the treatment should be started with low doses. The main diuretics and their dosages are listed in Table 5.

Table 5. Oral diuretics.

	Initial dose (mg)		Maximum dose daily (mg)		Side effects
Loop diuretic					
Furosemide	20–40		250–500		Hypocalemia, hypomagnesemia, hyponatremia
Bumetamide	0.5–1.0		5–10		Hyperuricemia, intolerance glucose, Basic acid disturbance
Thiazide					
Hydrochlorothiazide	25		100		Hypocalemia; hypomagnesemia, hyponatremia
Indapamine	2.5		2.5		Basic acid disturbance
Potassium sparing	+ ACEi	– ACEi	+ ACEi	– ACEi	
Amiloride	2.5	5	20	40	Hypercalemia, rush
Triamterene	25	50	100	200	Hypercalemia
Espironolactone	12.5–25	50	50	100–200	Hypercalemia, gynecomastia

ACEi: Angiotensin Converting Enzyme inhibitors.

5.2.2 Digitalis

Some studies show that digitalis related compounds are effective in controlling symptoms and improving physical exercise tolerance in patients with HF. Digoxin is a first line drug for treating atrial fibrillation associated with HF (grade of recommendation IIa, level of evidence A).[19]

The elderly are less responsive to the effects of digitalis and experience higher toxic effects due to lower muscle mass, associating itself with the highest myocardial concen tration for the same dose. The serum concentration of digoxin is effective from 0.5 ng/mL to 0.9 ng/mL, whereas higher concentrations are associated with increased toxicity. Its side effects can be exacerbated by the concomitant use of other cardioactive drugs. The daily dose in the elderly should not exceed 0.125 mg and the plasma concentration should not exceed 1 ng/mL.[20]

5.2.3 ACE inhibitors

Several studies have shown that ACE inhibitors reduce total mortality determined by HF and the combined events compared to placebo.[15] Despite scientific evidence of improvement of symptoms, reduction of disease progression and reducing mortality and hospitalization for HF, there are limited studies for patients older than 75 years old.[15]

ACE inhibitors should be given to all patients with HF and systolic left ventricular dysfunction after myocardial infarction, unless there is contraindication (grade of recommendation is I and level of evidence A).[9] But in patients with diastolic dysfunction the value of ACE inhibitors, per se, has not been established.

ACE inhibitors are contraindicated when serum potassium is above 5.5 mEq/L in the presence of bilateral renal artery stenosis, symptomatic hypotension, renal failure and previous history of angioedema with their use.

Low doses should be started in the elderly with gradual increases until the recommended doses in clinical trials have been reached. However, more often in the elderly irritating dry cough, hypotension, renal failure and reduction or loss of taste occur, leading to loss of appetite.[21]

The main drugs are listed in Table 6.

5.2.4 ARBs

ARBs are more appropriate when there is intolerance to ACE inhibitors or in association to these drugs for a limited time. ACE inhibitors remain the agents of choice in the treatment of HF.

The main studies that evaluated the benefit of ARBs in the treatment of HF are VAL-HeFT[22] and CHARM,[23] which included elderly and showed significant results in reducing mortality. ARBs are mainly indicated in patients with chronic HF and systolic ventricular dysfunction who have intolerance to ACE inhibitors.

Table 6. Angiotensin converting enzyme inhibitors.

Drug	Initial dose	Drug target dose
Captopril	6.25 mg, tid	50 mg, tid
Enalapril	2.5 mg, bid	10 mg, bid
Lisinopril	2.5–5.0 mg/d	20 mg/d
Ramipril	2.5 mg/d	10 mg/d
Perindopril	2 mg/d	8 mg/d

5.2.5 Beta-blockers

Clinical studies[24–26] clearly show the benefits of treatment with beta blockers. The SENIORS,[27] a placebo-controlled trial using nebivolol and involving 2128 subjects aged 70 years or more, showed a risk reduction of 14% for the end point (death and hospital admissions for any cardiac reason).[26]

The combination of a beta-blocker and conventional therapy with diuretics, ACE inhibitors and digitalis leads to an improvement of symptoms, functional class and left ventricular function (grade of recommendation I, level of evidence A). The dosage of beta-blockers used in HF are shown in Table 7.

When the target doses are not tolerated, lower doses should be maintained. Beta blockers are contraindicated in the presence of bradycardia, advance atrioventricular block (AVB), hypotension with blood pressure below 90 mmHg, bronchospastic disease and in decompensated HF.

Side effects are more common in the elderly, mainly asthenia, fatigue, sleep disturbance, peripheral vascular disorder, bradycardia and AVB.

Table 7. Doses of beta blockers used in heart failure.

	Initial dose (mg)	Target dose (mg)
Carvedilol	3.125, bid	25, bid
Sustained-release Metopropolol (succinate)	12.5, qd	200, qd
Bisoprolol	1.25, qd	10, qd

5.2.6 Direct vasodilators

The combination of isosorbide dinitrate and hydralazine for the treatment of HF is recommended for patients on digitalis, diuretics and beta-blockers, that cannot tolerate ACE inhibitors or ARBs, or in presence of renal failure, hyperkalemia (K > 5.5 meq/L) or worsening of glomerular filtration rate with serum creatinine > 2.5 mg/dL (grade of recommendation IIa, level of evidence B).[9]

5.2.7 Anticoagulants

Anticoagulants are indicated in patients with atrial fibrillation, a history of thromboembolic events and left ventricular aneurysm. The use of subcutaneous unfractionated heparin is indicated for patients with decompensated HF and bedridden for the prevention of pulmonary thromboembolism.[9,15]

6 Resynchronizers

Ventricular resynchronization is indicated in patients with advanced HF in functional class III or IV, ejection fraction less than or equal to 35% and a QRS complex equal to or greater than 0.12 seconds, associated with optimal pharmacological therapy (grade of recommendation I, level of evidence A).[9,28]

Resynchronization is not indicated in patients whose functional condition and life expectancy are limited by non-cardiac causes (grade of recommendation III, level C).[9]

7 Diastolic heart failure (DHF)

DHF or HF with preserved systolic function has a high prevalence (about 50%), involving specially the elderly, women hypertensive, and diabetics patients. Its diagnosis is based on symptoms and signs of HF in patients with normal ejection fraction in the echocardiogram.[11] The inclusion of the BNP measurement can increase the diagnostic accuracy.[28]

In contrast with the treatment of systolic heart failure, only few clinical trials are available to guide the management of patients with DHF. It is important, however, to follow some general principles: (1) Control of the heart frequency and arterial blood pressure, (2) Reduction of the volume overload and (3) Relief of myocardial ischemia. Drug therapy involves mainly the use of diuretics. However, excessive volume depletion and arterial hypotension should be carefully avoided in older patients, because they are more sensitive to preload reduction. Calcium channel blockers,[29] beta-blockers, ACE inhibitors or ARBs[30] and espironolactone are useful to relief of symptoms and reduce morbidity and mortality. The use of digitalis is not well established, except in the presence of atrial fibrillation with high ventricular response.

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