Heart Failure: Basic issues of a growing epidemic

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ABSTRACT
Heart failure is a great public health problem in the world, either by its increasing prevalence, or the cost for a proper treatment. Heart Failure is a complex problem resulting from a structural or functional disorder that impairs the ventricular filling and ejection of blood ability. It is also characterized by the presence of cardinal symptoms such as dyspnea, fatigue and fluid retention. The main causes of heart failure are ischemic heart disease, hypertensive heart disease, dilated cardiomyopathy and valvular heart disease. In the initial stages, cardiac function at rest may be regular but it does not properly increase with exercise; in advanced stages it becomes abnormal even at rest.

Key words: Heart failure, Dilated cardiomyopathy, Hypertension, Valvular heart disease, Dyspnea

DEFINITION
Heart failure (HF) is defined as the pathophysiological and clinical condition in which the heart is unable to provide blood according to the peripheral metabolic requirements. The hallmark of this disease is a progres-
sive maladaptive cardiac remodeling; it starts from an episode that causes a decrease in the pump capacity of the heart and thus compromises the ability of the ventricles to satisfactorily fill and pump blood. Similarly, it is considered the common final end of many of the most prevalent diseases, such as: hypertension, coronary disease, valvular heart disease, diabetes mellitus, among others.

The cardinal signs of HF are dyspnea and fatigue, which may limit the ability to perform physical exertion (exercise intolerance), and may end in processes that lead to pulmonary and systemic congestion, and increased peripheral vascular resistance. The progressive functional limitations it imposes will cause a shock on the productive capacity of those affected. The setting is a myocardial disorder which may be diffuse or segmental that usually starts without symptoms or disability.

The prognosis of cardiac dysfunction has been compared to the most common cancers, and has revealed higher mortality than breast and ovarian cancer in women, surpassed only by lung cancer. Its epidemiological behavior is far from being correlated with the medical advances in recent decades; it is estimated that 2% of the population (about 5.8 million people) in the United States have HF; it is estimated that in Spain the prevalence reaches 6% in the population over 40 years; but also they confirm that the aging population will increase the incidence of this disease in the coming years, and demonstrate that HF has a linear relationship with age. Although many advances in treatment have saved, or at least prolonged many people's lives, a significant number of patients die or have severe disability due to irreversible cardiomyopathy.

ETIOLOGY

The 3 main causes of HF are: hypertensive heart disease, ischemic heart disease associated with a previous infarction and dilated cardiomyopathy. Other causes include: arrhythmias, valvular heart disease, infections, diseases infiltration, alcoholism, endocrine disorders and genetic diseases.

Right and left sided HF is considered an anatomical and topographical term, where systemic venous congestion predominates in the first, while pulmonary in the second. Its evolution compromises both cavities function, so in advanced stages there is a so called global HF, as systemic and pulmonary venous systems retrogradely become congested, leading to the syndrome symptoms and signs.

HF can be classified in different ways. Systolic dysfunction refers to a clinical syndrome characterized by symptoms and signs of HF in the context of a structural heart disease, which causes a decrease in the left ventricle contractile function. Diastolic dysfunction refers to any alteration of the left ventricle relaxation due to dysfunction at cellular level, or any alteration in the passive properties as a result of ventricular fibrosis, infiltration, or interaction with the right ventricle by pericardial constriction.

According to its functional state, in order to know to what extent HF affects the patient's physical activity, the New York Heart Association (NYHA) defined four classes depending on the symptoms and physical activity. Class I: Normal exercise tolerance; Class II: symptoms with ordinary exertion; Class III: symptoms with only mild exertion and Class IV: symptoms at rest. This classification from The American College of Cardiology/American Heart Association (ACC/AHA) based on the structural damage is useful in defining HF stages. ACC/AHA guidelines propose a new classification scheme with 4 categories (A, B, C, D), which aims to reinforce the preventive recommendations during A and B stages, for they do not correspond to HF, but are previous stages which may not lead to it.

PHYSIOPATHOLOGY

Myocyte alterations cause HF, from the pathophysiological point of view, they lose their normal contraction ability due to biochemical changes, as it happens in idiopathic cardiomyopathies or due to alteration of the physiological mechanisms that reduce oxygen delivery to the myocardium, which alters cell function, just like coronary disease. This case and others, such as right ventricular infarction by extension of an inferior-posterior of the left, volume overload, as in the case of interventricular communication and, less frequently, by interatrial communication and pulmonary hypertension, are the 4 main causes of right HF (RHF), which together with all these impairments cause an alteration in preload, afterload and difficulty in left ventricle emptying during systole, which initially causes increased cardiac contractility finally ending in clau-
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Table 1. Acute and chronic HF classification.

<table>
<thead>
<tr>
<th>Acute HF (SEC)</th>
<th>Chronic HF (ACC/AHA)</th>
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<tbody>
<tr>
<td>Decompensated acute HF</td>
<td>Stage A. No structural damage or functional impairment.</td>
</tr>
<tr>
<td>Hypertensive acute HF</td>
<td>Stage B. Structural alteration strongly related to HF development</td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>Stage C. Symptomatic HF associated with cardiac structural damage</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>Stage D. HF with symptoms at rest despite maximal treatment; advanced cardiac structural alteration.</td>
</tr>
<tr>
<td>High output HF</td>
<td></td>
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<tr>
<td>Acute right HF</td>
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ACC/AHA, American College of Cardiology/American Heart Association; HF, heart failure; SEC, Spanish Society of Cardiology, by its acronym in Spanish.

dication, and leads to ventricular dilation and decreased cardiac output, all of which is manifested in patients with signs of hypovolemia, dyspnea, fatigue, shortness of breath, sweating, abnormal pressure, edema and decreased miccion (Figure 1).

Such alterations cause a myocardial injury that leads to ventricular remodeling, term by which is meant “the genomic expression resulting in molecular, cellular and interstitial changes clinically manifested as changes in size, shape and heart function, after injury.”

This remodeling is accompanied by left ventricle shape alterations, which becomes more spherical, rather than elliptical, for a bigger growth in the transverse axis. It may occur after a myocardial infarction, pressure overload (aortic stenosis, hypertension) or volume (valvular regurgitation), inflammatory myocardial disease (myocarditis), or dilated idiopathic cardiomyopathy (Figure 2).

It is also important to note that in the presence of ventricular dysfunction, the heart tries to maintain its function, so it uses three basic mechanisms: increased preload (Frank-Starling law), ventricular
hypertrophy, and increased sympathetic system activity and neurohumoral activation; since structural changes are primarily modulated by hemodynamic, mechanical and humoral factors. Neurohormones increase produces tachycardia with increased inotropic state (catecholamines), vasoconstriction and sodium and water retention (angiotensin and aldosterone). Catecholamines induce direct myocardial damage while angiotensin and aldosterone rise loading conditions, generating the determining vicious cycle of disease progression (Figure 3).

**PREVALENCE**

More than 20 million people suffer from HF worldwide and despite treatments progress in this disease, most patients with advanced forms die one year after diagnosis.

HF epidemiological data available in the United States and Europe indicate that this is the most common cause of cardiovascular death and hospital admittance in people over 65 years.

Prevalence in the United States is estimated at 4 to 5 million patients a year, almost 500,000 new cases are diagnosed annually, and about 10 million people in countries represented by the European Society of Cardiology have HF.

European data indicate that the prevalence of symptomatic patients is 0.4-2.0%, but this percentage increases rapidly with age. There is a group of patients, about 30% of the general population, who has ventricular dysfunction and remains asymptomatic at first, such HF latent condition was called subclinical HF.

It is known that about half of patients have died 4 years after diagnosis, but when having a severe clinical situation, their mortality is greater than 50% within the first year, so their condition is considered as very lethal, hence it is higher than that compared to some neoplasias.

Cardiac dysfunction is the reason for 12 to 15 million doctor visits and 6.5 million hospital stays besides representing 2-3% of hospital admissions.

Latin American countries are facing a coronary heart disease epidemic that has led to a significant increase in cardiac dysfunction incidence.

HF is the third cause of cardiovascular death in Spain, behind ischemic heart disease and cerebrovascular disease. Controlling risk factors such as hypertension and ischemic heart disease, responsible for 75% of HF, is the only means to control the predictable increase of this disease in the future.

**DIAGNOSIS**

HF symptoms are wide and variable, having both, less accurate and more specific signs and symptoms. In order to diagnose this problem the HF working group of the European Society of Cardiology proposed the presence of 3 mandatory and simultaneous criteria:

1. HF Symptoms (at rest/on exertion) dyspnea, edema, fatigue.
2. Evidence of systolic or diastolic cardiac dysfunc-
3. HF improvement after treatment.

Framingham’s clinical criteria, presented in 1971 are the most accepted for diagnosis (Table 2). According to Atamanuk and Bortman, Michael R. Bristow proposed to group HF causes according to their physiological and anatomical situation: a) coronary, b) myocardial, c) arrhythmic, d) valvular...
Supplementary tests

Echocardiography

Allows to differentiate 4 physiopathological mechanisms groups: systolic and diastolic dysfunction, valvular and pericardial abnormalities. Echocardiography should be used in all patients with suspected HF, as it can provide valuable information on the degree of left ventricular dilatation and deterioration of its contractile function.

Chest X-ray

Chest radiography is useful as the first complementary method to use when there is clinical suspicion of HF in a patient with dyspnea and will allow ruling out its pulmonary origin. Characteristic findings are: increased cardiothoracic index > 0.50; pulmonary vascular cephalization; the appearance of Kerley B lines and the presence of pleural effusion.

A systematic analysis from published papers on the value of chest radiography for HF diagnosis allows to state that blood flow distribution and cardiomegaly are the best predictors of increased preload and decreased left ventricular ejection fraction.

Electrocardiogram

Electrocardiographic abnormalities commonly found in HF include: the presence of necrotic or ischemic changes, rhythm disorders, hypertrophy of cardiac cavities and overloading patterns.

Cardiac magnetic resonance imaging (MRI)

Cardiac MRI is a versatile image technique that allows evaluating volumes, mass, global and regional function of both ventricles with greater accuracy and reproducibility.

Laboratory

Laboratory testing permits to determine complete blood count, electrolytes (sodium, potassium, magnesium), urea nitrogen and creatinine, cardiac enzymes (troponin, D-dimer, creatine kinase-MB fraction), arterial blood gas, B-type natriuretic peptide levels and thyroid function tests, all of which allows confirming or ruling out underlying, precipitating or adjuvant diseases.

TREATMENT

Pharmacotherapy

HF treatment has been classically aimed to reduce central venous pressure with diuretics, reduce after-
load with peripheral vasodilators and increase cardiac contractility with inotropic agents. Unfortunately, clinical studies with these drugs have yielded disappointing results as little has been achieved with regard to the prolonged survival of these patients.

It has been reported that beta adrenergic blockers improve systolic function and reverse remodeling after 3-4 months of use, which is explained by the control they produce on exacerbated sympathetic stimulation in chronic HF. Their effects are associated with an increase in ejection fraction, a decrease in hospital admissions and survival and sudden death incidence.

All patients with heart failure due to left ventricular systolic dysfunction should receive angiotensin-converting enzyme inhibitors (ACEI), unless proven intolerance or contraindication to the use of these medications. (Table 3). The use of ACEI and angiotensin II receptor antagonists has improved the survival of patients with HF. It has been found that these types of drugs reduce afterload and left ventricular hypertrophy as well.

Diuretic therapy, especially thiazide and loop, maintain their dominant place, they allow controlling volume overload and characteristic symptoms of congestion. Spironolactone and other aldosterone receptor inhibitors under study prevent salt retention, urinary potassium loss, and the newest, reduce cardiac fibrosis.

Digitalis, besides their classic positive inotropic effect, increases the release of the baroreceptors afferents which is accompanied by a decreased sympathetic activity over the heart. Amiodarone, rather than prolonging repolarization, has additional effects regarding sodium inflow currents and the sympathetic-lytic properties. This drug has shown to have beneficial effects on mortality and has reduced the number of deaths from arrhythmias in patients with compromised left ventricular function.

The pharmacological treatment of HF has basically been palliative and less aimed to affected molecular mechanisms. Research is also done with apoptosis preventing drugs that sensitizes calcium myofilaments and block V2 receptors for the anti-diuretic hormone ADH.

Non-pharmacological treatment

Non-pharmacological therapeutic measures constitute a cornerstone in HF treatment. The two essential aspects are patient self-care and adherence to treatment; health education provides the basic tool to obtain them in both cases. Self-care should include the following aspects: a) actions to maintain physical stability, b) avoid behaviors that may worsen the disease, and c) promote early awareness and identification of deterioration or decompensation symptoms or signs. These measures, coupled with a low calorie diet and fluid restriction are very useful; however, the need to restrict liquid consumption is more controversial. Although highly recommended, some only prescribe it when the patient is hyponatremic, but there are no controlled studies evaluating this aspect; 800 to 1000 ml per day fluid restrictions are recommended for hospitalized patients with severe HF, and any electrolyte or renal

<table>
<thead>
<tr>
<th>Stage A</th>
<th>Stage B</th>
<th>Stage C and D</th>
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<tbody>
<tr>
<td>Primary prevention</td>
<td>Secondary prevention</td>
<td>Tertiary prevention</td>
</tr>
<tr>
<td>- Treat HT, diabetes and dyslipidemia.</td>
<td>- Stage A measures</td>
<td>- Stage A measures</td>
</tr>
<tr>
<td>- Treat thyroid diseases.</td>
<td>- ACEI</td>
<td>- ACEI + beta blockers</td>
</tr>
<tr>
<td>- Giving up harmful habits (tobacco, alcohol, other drugs)</td>
<td>- Beta blockers</td>
<td>- Salt restriction</td>
</tr>
<tr>
<td>- Regular physical exercise.</td>
<td></td>
<td>- Diuretics if fluid retention</td>
</tr>
<tr>
<td>- Heart rate control in tachyarrhythmias</td>
<td></td>
<td>- Persistence of symptoms: ARA II, hydralazine and nitrates, digital.</td>
</tr>
<tr>
<td>- Use of ACEI in selected patients.</td>
<td></td>
<td>- CRT- ICD in selected patients.</td>
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</tbody>
</table>

ACEI, angiotensin converting enzyme inhibitors; CRT, cardiac resynchronization therapy; HT, hypertension; ICD, implantable cardioverter-defibrillator.

Table 3. HF treatment strategies.
function imbalance is strictly controlled. In the outpatient, restrictions are between 1200 and 1500 ml per day, to a further release fluid intake when the patient has reached his "dry" weight; thereafter fluid and diuretics intake control is done depending on daily weight, so if the patient increases between 1.5 and 2 kilograms in 24 hours, that would mean there is liquid retention; in these cases the patient has been previously instructed to restart fluid restriction and add diuretics again. In addition to daily weight control, a plan of controlled physical exercise, smoking and alcoholism cessation and the use of a low sodium diet is also necessary. Restricting sodium intake has been considered a key component in HF treatment, even in the presence of a suitable diuretic therapy. Recommendations on sodium intake restriction are 3 grams of salt a day, and less than 2 grams for patients with severe HF refractory to treatment.

Cardiac Rehabilitation

Cardiac rehabilitation programs consist of an initial learning phase from 2 to 6 months, and a subsequent of exercise, usually unsupervised for the rest of life. Physical training, a key part though not exclusive of cardiac rehabilitation programs, increases physical capacity, reduces myocardial ischemia, helps control effort angina, improves endothelial function by local increase of the secondary nitric oxide to the effect of shear, has anti-inflammatory action, prevents arrhythmias, improves ventricular and vascular compliance, diabetes, hypertension, and meets many other benefits at the level of different organisms systems (Figure 4). These and many other effects positively influence life quality and prognosis of patients with HF.

Cardiac resynchronization therapy

It is based on a three chamber pacemaker implantation, with or without defibrillator, in order to set an optimum atrioventricular interval for each patient that allows ventricular resynchronization through programmed stimulation. According to clinical practice guidelines on cardiac pacing and cardiac resynchronization therapy (CRT) of the European Society of Cardiology, it is considered class I indi-

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**Figure 4.** Beneficial effects of physical training. ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; DM, diabetes mellitus; EF, ejection fraction; HDL, high density lipoprotein; HF, heart failure; HR, heart rate; HT Hypertension, LDL, low-density lipoprotein; MPA, main pulmonary artery; NO, nitric oxide; LV, left ventricle.
cation with level of evidence A for CRT for chronic HF patients and left ventricle ejection fraction ≤ 35% still in outpatient NYHA II, III or IV despite adequate medical treatment, when presenting left bundle branch block and QRS> 150 ms. For these same patients but with QRS between 120 and 150 ms, the indication is class I level of evidence B.

It is important to note that CRT improves systolic function without increasing myocardial oxygen consumption, unlike some other inotropic drugs that do increase it proportionally to contractile performance increase. CRT aims to improve survival and reduce the number of congestive HF patients hospitalizations by acting on atrioventricular, inter- and intraventricular dyssynchronies. Some of the most important CRT effects are mentioned in Figure 5.

**Circulatory assist devices**

These are devices designed to replace the function of one or both ventricles in different clinical situations, from patients having irreversible biventricular dysfunction at risk of imminent death and candidates for heart transplantation, to those with unprotected left coronary artery angioplasty with low ejection fraction. They are capable of generating circulatory flow to partially or totally replace heart function and can provide hemodynamic support to the left, right, or both ventricles. There are several types depending on their characteristics which can be classified into:

1. **According duration**
   - Temporary
   - Permanent
2. **According to the effective time of use**
   - Short term: <7 days
   - Medium term: 7-30 days
   - Long term: > 30 days
3. **According to the assisted chamber**
   - Left
   - Right
   - Biventricular
4. **According to ventricular assistance type**
   - Partial
   - Total
5. **According to the type of generated flow**
   - Continuous
   - Pulsating
6. **According to the device location**
   - Paracorporeal
   - Intracorporeal
7. **According to treatment strategy**
   - Prophylactic: Temporary use to prevent any complications that have a high probability to occur in the absence of a ventricular assist device.
   - Bridge to transplant: It is used to maintain the patient's hemodynamic who would otherwise die or worsen while waiting for transplantation.
   - Bridge to recovery: Keep patient's hemodynamic, the time his heart needs for recovering after surgery.
   - Bridge to decision: Ventricular assistance device is used in order to stabilize the patient to define the most appropriate therapeutic strategy; but it may be the solution while studies are properly completed.
   - Bridge to bridge: The types of assistance or intention-to-treat are modified over time.
   - Final therapy: When there is no possibility of transplantation.

**Surgical treatment**

Depending on the cause, patients with severely com-
promised ventricular function may benefit from different surgical approaches, such as valve surgery, pacemaker implantation and defibrillators, reconstruction of the left ventricle, coronary artery bypass graft surgery and heart transplantation, among others. Coronary bypass is very beneficial in those with evidence of ischemia; however, many studies have shown how long-term survival is decreased compared with patients with normal ventricular function.

Accumulating evidence on this bypass benefits compared with medical treatment has caused that since 1999 the ACC/AHA clinical practice guidelines established that abnormal left ventricular function combined with multivessel disease is an anatomical indication for surgical treatment.

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