

Advances in the Management of Heart Failure (II)

Heart Failure: Etiology and Approach to Diagnosis

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In spite of its high prevalence and the huge burden it imposes on health care systems, heart failure is a clinical syndrome that has not yet been defined satisfactorily. In actual practice, diagnosis requires the presence of typical signs and symptoms along with data from complementary tests that indicate definite cardiac dysfunction. In this article we review current concepts of the disease, stages of development, common underlying causes, and the value of different diagnostic tests. Among these tests, measurement of B-type natriuretic peptide has proved useful for population screening and the differential diagnosis of heart failure. This indicator seems to be the ideal link between the large population of patients in whom heart failure is suspected and the subgroup for whom cardiac ultrasound, the most informative test in this disease, is warranted.

Key words: *Heart failure. Etiology. Diagnosis.*

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Etiología y evaluación diagnóstica en la insuficiencia cardíaca

A pesar de su elevada prevalencia y de la enorme carga que supone sobre los sistemas de salud, la insuficiencia cardíaca es un síndrome clínico para el que no existe aún una definición satisfactoria. En la práctica, su diagnóstico requiere la presencia concomitante de síntomas y signos típicos, junto con datos derivados de exploraciones complementarias que muestren algún tipo de disfunción cardíaca. En la presente revisión se repasan los conceptos actuales sobre la enfermedad, sus etapas evolutivas, las causas más frecuentes y el valor de las distintas exploraciones para su diagnóstico. Entre estas últimas destaca la reciente incorporación de la determinación de péptido natriurético tipo B por su utilidad en el cribado de poblaciones y en el diagnóstico diferencial con otras entidades clínicas. Su papel parece servir de conexión entre la gran población en la que existe sospecha clínica de insuficiencia cardíaca y el subgrupo en el que se justifica la realización del ecocardiograma, la prueba que más información aporta en esta situación.

Palabras clave: *Insuficiencia cardíaca. Etiología. Diagnóstico.*

INTRODUCTION

As presented in the first chapter in the series "Update: Advances in the Management of Heart Failure I,"¹ heart failure (HF) is a major health problem in western societies due to its high

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prevalence, morbidity and mortality, comparable to severe neoplasia. Given its chronic character, with frequent acute events often requiring hospitalization, HF consumes a huge amount of human, technical and economic resources. Thus, it is extremely important that professionals involved in the evaluation and treatment of these patients deal with the disease efficiently. The aim of this chapter is to provide, in practical terms, a systematic and rational approach to diagnosing this syndrome.

The various consensus documents—clinical guidelines—created by experts in the treatment of HF, published in 2001 by the European Society of Cardiology² and the American Heart Association/American College of Cardiology,³ are an invaluable aid in this field and are required reading for the interested reader.

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ABBREVIATIONS

BNP: B-type natriuretic peptide.
 ECG: electrocardiogram.
 HF: heart failure.
 AHT: arterial hypertension.
 LV: left ventricle.

DEFINITION, STAGES AND ETIOLOGY OF HEART FAILURE

Definition and Types of Heart Failure

Although recognizing typical cases of HF is straightforward in clinical practice, no concise definition of this event exists which satisfactorily embraces all its facets.^{2,4} During the 20th century, as our knowledge of the disease increased, our concept of it has changed; thus, until the 1950s, HF was understood as a situation where the kidney was unable to eliminate water retention caused by cardiac dysfunction (the cardiorenal model). In the 1960s, with the development of cardiac catheterization, the focus shifted toward alterations in pressure, flow and gradients in the different cardiac and vascular chambers (the hemodynamic model). In the mid-80s, the discovery of the neurological and hormonal systems activated in HF demonstrated their important systemic involvement (neurohormonal model) and allowed for substantial advances in its treatment. The present period is characterized by research into molecular mechanisms targeting different locations, genetic and transcriptional, as well as the expression of receptors, cytokines and other mediators of cellular interaction. All this has given rise to a molecular model of HF, which not only contributes to a new concept of the disease but also entails advances in its treatment and, possibly, prevention in subjects at risk. It is important to note that each of these models does not replace the previous one, but includes and fine-tunes it.

In practical terms, we can define HF as a pathophysiological state where some kind of heart dysfunction gives rise to its inability to pump blood in the amount needed to fulfill the organism's metabolic demands.² This definition continues to be barely acceptable in clinical practice, and therefore we need the aid of some descriptive terms to better delimit the concept.^{2,5} Some of these are described next.

Anterograde and Retrograde Heart Failure

Initially, HF was considered a retrograde event cha-

racterized by the inability of the ventricles to drain, with a consequent increase in pressures in the atria and the venous territory draining towards the affected ventricle. The transudation of fluids from the capillary territory to the interstitium is the final step that provokes the edema which causes the symptoms, both in the pulmonary and the systemic territories. Later, HF was conceived as a fundamentally anterograde phenomenon, where the main problem was the inability of the heart to maintain adequate perfusion to: the various organs, such as the kidneys, leading to water and sodium retention; the musculo-skeletal tissue, causing fatigue; and the brain, causing reductions in the level of consciousness.

In fact, both aspects of HF occur simultaneously in clinical practice.⁶ However, given that the compensatory mechanisms are mainly directed at maintaining tissue perfusion rather than at eliminating the edema, the signs and symptoms of anterograde HF are less clear (especially in chronic forms) and its diagnosis is often missed.

Acute and Chronic HF

The rapid onset of heart failure determines its manifestations: when an individual abruptly suffers an anatomical or functional injury to the heart without there being enough time for compensatory mechanisms to appear, severe symptoms of congestion (mainly acute pulmonary edema) or hypoperfusion (cardiogenic shock) usually appear, without global fluid retention, increases in weight and cardiomegaly, characteristic of chronic HF, taking place.

The most common type of HF is the chronic form, with occasional acute decompensations. This is the type of HF referred to in this work, unless specified otherwise.

Left and Right Heart Failure

This refers to a situation in which the clinical manifestation is due mainly to congestion of the pulmonary venous (left HF) or systemic (right HF) territory. In the first case, the dominant symptoms are progressive dyspnea, orthopnea, cough while lying down and paroxysmal nocturnal dyspnea, whereas in right HF jugular venous distension, hepatomegaly, ascites and edemas predominate.

Systolic and Diastolic Heart Failure

Systolic dysfunction of the left ventricle (LV), indicated by dilatation of the cavity and a low ejection fraction, is the most classic manifestation of heart failure. Most such patients are middle and older-aged men with ischemic heart disease. However, the presence of typical symptoms of HF with preserved

TABLE 1. Symptomatic Classification for Heart Failure Following the New York Heart Association

Class I	No limitation: ordinary activity does not cause fatigue, dyspnea, or inappropriate palpitations
Class II	Slight limitation of physical activity: asymptomatic at rest, but ordinary physical activity causes fatigue, dyspnea, or palpitations
Class III	Marked limitation of activity: asymptomatic at rest, but any degree of effort whatsoever causes symptoms
Class IV	Unable to engage in any type of activity without problems; heart failure symptoms present even at rest and increase with any degree of physical effort

LV systolic function is as frequent as the latter situation: the study of these patients (in general, individuals of advanced age, with a high proportion of women and a frequent background of arterial hypertension) shows alterations in LV filling, usually with myocardial hypertrophy without cavity without dilatation. Given the current relevance of this form of HF,^{7,8} we dedicate a full chapter to it.

THE STAGES OF HEART FAILURE

The New York Heart Association’s (NYHA) classification provides a useful gauge of the severity of the symptoms of HF patients (Table 1). In fact, the NYHA’s functional class has become so widespread that it has become synonymous with the severity of the underlying symptoms, and is used in workplace and legal medicine to estimate the level of handicap and prognosis of the patients. However, for various reasons this approach ignores serious conceptual problems: *a)* the classification involves a high degree of subjectivity, both on the part of the patient as well as the doctor; *b)* the functional class of a specific HF patient can fluctuate over short periods, especially when decompensatory situations exist, which is why it is advisable to avoid using this scale during unstable periods, and *c)* the functional class of the NYHA presents little correlation with the level of ventricular dysfunction⁹ and with the prognosis of patients.¹⁰

Given the preceding, and a better understanding of the developmental process leading to HF, various authors on both sides of the Atlantic^{3,11} advocate the use of a classification more in line with present concepts which include the preclinical stages of HF development, in which the identification of patients enables effective preventive interventions. The clinical guidelines of the American Heart Association/American College of Cardiology of 2001³ propose a staging of HF, presented in Table 2, that outlines the sequence of HF events in a simple and practical manner. Stage A identifies patients at risk of

TABLE 2. Stages in the Evolution of Heart Failure, Following the Clinical Practice Guidelines of the American College of Cardiology/American Heart Association

Stage	Description	Examples
A	Patients at a high risk of developing HF because of the presence of conditions that are strongly associated with the development of HF. They present no structural or functional abnormalities of the pericardium, myocardium or cardiac valves and have never shown signs or symptoms of HF	Systemic hypertension. Coronary artery disease. Diabetes mellitus. History of cardiotoxic drug therapy or alcohol abuse. Family history of rheumatic fever. Family history of cardiomyopathy
B	Patients who have developed structural heart disease that is strongly associated with the development of HF but who have never shown signs of symptoms of HF	Left ventricular hypertrophy or fibrosis, Left ventricular dilatation or hypocontractility. Asymptomatic valvular heart disease. Previous myocardial infarction
C	Patients who have current or previous symptoms of HF associated with underlying structural heart disease	Dyspnea or fatigue due to left ventricular systolic dysfunction. Asymptomatic patients undergoing treatment for prior symptoms of HF
D	Patients with advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy and who require specialized interventions	Patients frequently hospitalized for HF and who cannot be safely discharged from the hospital. Patients in the hospital waiting for heart transplantation. Patients at home receiving continuous intravenous support for symptom relief or with a mechanical circulatory assist device. Patients undergoing palliative care for the management of HF

developing HF, but who still lack structural cardiac abnormalities; stage B includes patients with structural disorders of the heart, generally due to progressive left ventricular remodeling, who have not yet presented clinical evidence of HF; Stage C indicates the presence of structural abnormalities with previous or current evidence of HF, and stage D refers to patients with severe forms of HF resistant to normal treatment, who require measures such as continuous infusion of inotropes, ventricular assist devices, heart transplants, etc. Unlike the NYHA classification, this indeed reflects the expected progression of patients over the course of the disease and is useful for taking a specific

TABLE 3. Resume of the Main Etiological Factors in Heart Failure With the Most Common Examples Found in Clinical Practice*

Cause		Examples
Predisposing causes		
Etiological		Coronary artery disease, congenital heart disease
Probably etiological		AHT, diabetes, history of rheumatic fever
Non-etiological		Age, masculine sex, obesity, tobacco use
Determining causes		
Cardiomyopathy	Primary	Cardiomyopathy dilated, hypertrophic, and restrictive cardiomyopathy
	Secondary	Ischemic, infectious, toxic, and metabolic cardiomyopathy
Ventricular overload	Pressure	AHT, aortic/pulmonary stenosis, pulmonary hypertension
	Volume	Valve insufficiency, shunts
Altered ventricular filling		Ventricular hypertrophy, mitral/tricuspid stenosis, tumors, cardiac tamponade, constrictive pericarditis
Arrhythmias		Bradycardia, tachycardia, tachycardiomyopathy
Precipitant causes		
Cardiac		Arrhythmias, ischemic cardiomyopathy, negative inotropic drugs: calcium antagonists, beta-blockers, antiarrhythmics, others
Extracardiac		Infections, non-completion of treatment, pulmonary embolism, anemia, drugs (NSAIDs), surgery, effort, toxic substances

*AHT indicates arterial hypertension; NSAIDs, non-steroid anti-inflammatory drugs.

therapeutic approach in each phase, aimed at slowing down or stopping the advance of HF. Nevertheless, the aim of this new stratification system is not to replace, but to complement the information provided by the NYHA classification, thus making it advisable to use both methods in the evaluation of each suspected HF patient.

Etiology of Heart Failure

The diseases that can lead to HF are very different and their detection is of great importance, as this can modify the diagnostic, therapeutic and preventive approach, as well as determine prognosis.¹² Thus, a nonspecific diagnosis of “heart failure” in patient reports is unacceptable; the type of structural cardiac abnormality and the risk factors that caused it must be included as well as the factors triggering the acute decompensation when relevant.

In practical terms, and in line with the main textbooks,^{13,14} we will refer to three types of causes of HF: predisposing, determining and precipitating. The main causes are presented in Table 3.

Predisposing causes, also known as risk factors, are indicators associated with a greater probability of HF and can be identified in the population without heart disease or symptoms of HF. In turn, these are divided into etiological, probably etiological, and non-etiological causes.

Predisposing etiological causes include structural alterations, congenital or acquired, where there is a disorder of the peripheral vessels, coronary

circulation, pericardium, myocardium, endocardium or cardiac valves that produces alterations in the normal physiology of the heart. The main one is coronary artery disease which is responsible for more than 50% of HF cases in the United States,¹⁵ mainly in males. Within coronary artery disease, previous myocardial infarction is the single main factor, carrying an HF risk 10 times higher than in the normal population during the first year after the infarction and up to 20 times in the following years. Dilated cardiomyopathy and congenital cardiac abnormalities are other less prevalent predisposing etiologies of HF in the population.

The predisposing, probably etiological, causes are associated with a greater incidence of HF, without a demonstrated causal relation, although it is likely that they have an “indirect” influence on the progressive deterioration of ventricular function. The main one is arterial hypertension (AHT), which is especially prevalent in women and black individuals with HF. According to the Framingham study, HF risk is double in the population with mild AHT and four-fold when arterial pressure goes above 160/95 mm Hg. Elevated systolic arterial pressure involves an increased risk of development of HF which is double that of elevated diastolic arterial pressure. Left ventricular hypertrophy, mainly caused by AHT, is also a risk factor for the development of HF (involving a relative risk 17 times greater than in the normal population).¹⁶⁻¹⁸ Diabetes mellitus and a history of rheumatic fever are also predisposing causes, probably etiological. Diabetes is a risk factor for coronary artery disease

frequently coexisting with AHT or dyslipidemia, which are also coronary risk factors. The risk of HF in diabetic women is 5 times higher than in non-diabetic women, and higher than in diabetic men.

Non-etiological predisposing causes have no direct cause-and-effect relationship with HF. They have been identified by multivariate analyses carried out on large populations and should be understood as risk indicators only.¹⁹ These include advanced age, male sex, obesity, cardiomegaly, reduced vital capacity, cigarette smoking, proteinuria and anomalies in baseline electrocardiogram (such as left bundle branch block and alterations in ventricular repolarization). From the age of 40 onwards, each additional decade doubles the risk of suffering HF; approximately 8% of those older than 85 years present HF.²⁰ A progressive increase in weight increases the risk of developing HF in both sexes; obesity increases cardiac workload and favors the appearance of AHT, diabetes mellitus and dyslipidemia. Tobacco use is a first-order risk factor for the development of coronary artery disease which, as mentioned previously, is the main cause of HF.

The determining causes of HF are those that alter the regulating mechanisms of the ventricular function, hemodynamic load conditions and heart rate. These can be classified into primary or secondary myocardial alterations, hemodynamic overload, ventricular filling defects, ventricular dysynergy and alterations in heart rate.

There are three patterns of primary myocardial alteration that can cause HF: idiopathic dilated cardiomyopathy, hypertrophic cardiomyopathy and restrictive cardiomyopathy.

Idiopathic dilated cardiomyopathy affects both sexes. This is characterized by predominant LV systolic dysfunction, although there may be dilatation of the four cardiac chambers. When appropriate clinical testing is done (frequently via coronary angiography) no known etiology is detected, and endomyocardial biopsy shows myocardium as normal or it presents nonspecific alterations. As its name indicates, the underlying pathogenic mechanisms are unknown. However, when the etiology is investigated with specialized techniques the existence of family and genetic factors are found in up to 20% of cases, and in others there is a history of viral myocarditis or autoimmune processes.

Hypertrophic cardiomyopathy is a disease with a clear genetic origin in many cases (mutations in genes that encode proteins of the sarcomere), characterized by hypertrophy of the LV without apparent cause. In half the cases, there is autosomal dominant inheritance and it is the most frequent cause of sudden death in young adults, particularly athletes. Restrictive cardiomyopathy is characterized by an alteration in

cardiac compliance, with rapid early diastolic filling. This is the least common of the three types of cardiomyopathy and normally has a poor prognosis.

The secondary myocardial alteration that more frequently causes HF is coronary artery disease which occurs via several mechanisms: chronic myocardial infarction, chronic ischemia, ventricular aneurysm and mitral valve dysfunction. Other less frequent cardiomyopathies are those with an infectious origin (viral myocarditis, Chagas' disease, toxoplasmosis, mycosis, mycobacteriosis, diphtheria, rickets), toxic cardiomyopathies (from toxic substances, such as alcohol, and, less frequently, cocaine, lead, cobalt, and mercury, or from drugs such as adriamycin, cyclophosphamide, chloroquine, zidovudine, didanosine, etc), metabolic cardiomyopathies (associated with diabetes mellitus, hyperthyroidism, hypothyroidism, pheochromocytoma, Cushing's disease, hypocalcemia, hypophosphatemia), cardiomyopathies of genetic origin (such as glycogenosis), cardiomyopathies associated with neuromuscular diseases (such as Duchenne's or Becker's dystrophies, Friedreich's ataxia, and Steinert's myotonic dystrophy), cardiomyopathies associated with nutrient deficits (thiamine, selenium, carnitine) and the cardiomyopathies of inflammatory origin (associated with collagen diseases, hypersensitivity myocarditis, and sarcoidosis).

The determining causes characterized by hemodynamic overload can be due to a pressure or volume overload. In AHT and aortic stenosis, there is an increase in afterload that causes a pressure overload in LV, finally leading to the appearance of HF. In the right cavities, pulmonary artery hypertension and pulmonary stenosis lead to the same consequences. A special case of pulmonary hypertension is observed in patients with chronic obstructive pulmonary disease, that gives rise to the so-called *cor pulmonale*, manifesting as right HF. With regards to volume overload, HF can be caused by hypervolemia, mitral and aortic insufficiency, interventricular communication and persistent arterial duct (in the left cavities), as well as tricuspid insufficiency or interatrial communication (in the right cavities).

HF can also be caused by situations in which a ventricular filling defect exists, such as alterations in compliance associated with ventricular hypertrophy, ventricular outflow tract obstruction, hypovolemia, cardiac obstruction, pericardial constriction, and intracardiac masses. Similarly, ventricular aneurysms can cause HF, since part of the expelled blood volume during systole distends them, without forming part of the effective systolic volume.

On the other hand, alterations in heart rate (tachycardias, bradycardias, loss of AV synchrony) can also appear alongside HF. Tachycardiomyopathy is a type of dilated cardiomyopathy that develops in

patients with prolonged tachycardia and is reversible if this tachycardia disappears.

The precipitating causes of HF^{13,14} are those factors that cause a decompensation in a stable situation in patients with or without previous diagnosis of HF, but with an underlying structural cardiac abnormality. These are divided into cardiac and extracardiac causes. Cardiac causes are arrhythmias, the appearance of a new muscle damage (the most frequent is acute myocardial infarction) and inotropic drugs (calcium antagonists, beta-blockers, antiarrhythmics, tricyclic antidepressants, adriamycin). Extracardiac causes are infections (mainly respiratory ones), drugs that cause sodium retention (especially NSAIDs, which are in very wide use), abandoning treatment or diet, pulmonary embolism, physical or psychological stress, anemia or intercurrent disease, surgery, and toxic habits, such as tobacco use and alcoholism.

According to the study by Opasich et al,²¹ the most frequent causes in an Italian series of 324 HF decompensations were arrhythmias (24%), along with infections (23%), followed by non-adherence to myocardial treatment (15%), ischemia (14%), and iatrogenic factors (10%).

DIAGNOSIS OF HEART FAILURE

Diagnosis of Heart Failure: From Theory to Practice

In contrast to what might be thought regarding such a frequent disease, HF is difficult to diagnose. Obviously, few problems exist in the recognition of moderate or severe forms, where patients present a profusion of typical signs and symptoms with echocardiography showing severe LV systolic dysfunction. However, the situation is more complex when evaluating patients with mild or subtle forms of this syndrome which is not accompanied by LV contractile dysfunction, especially in women and elderly or obese patients or those with comorbidities. Thus, according to the work of Remes et al,²² approximately half of the HF diagnoses in primary care were erroneous; on the other hand, one recent publication states that 43% of the clinical diagnoses of HF in patients who were admitted to the emergency ward with dyspnea were "uncertain or doubtful."²³

The first attempts to systematize the diagnosis of HF arose from the Framingham¹⁶ study and were based on the concomitant presence of a series of criteria (two main ones or one main and two minor) selected from a list (Table 4). Due to the imprecision and practical limitations of this system, other scales arose, such as the NHANES or Boston criteria, used in epidemiological works, but not in clinical practice. The European Society of Cardiology guidelines² offer an excellent contribution which is very simple and

practical, and provide the diagnostic criteria that appear in Table 5, based on the presence of signs indicating HF along with objective data on cardiac dysfunction, which in most cases are obtained from the echocardiogram. There is an intentional ambiguity on the part of the authors when defining the typical symptoms of HF and LV dysfunction, which allows for the non-exclusion of a diagnosis of HF in individuals with borderline findings.

Diagnostic Approach to Patients With Heart Failure

Clinical history and physical examination are the cornerstones of diagnosing HF. Usually, the confirmation or exclusion of HF is determined by various complementary examinations that also provide valuable prognostic information.

Clinical history must include cardiovascular risk factors, toxic habits and noncardiac diseases that might contribute to HF. Special care must be taken to find out precisely what the patient's symptoms are. Dyspnea on exertion is the most frequent, although very unspecific; more advanced forms, such as orthopnea and paroxysmal nocturnal dyspnea, have higher specificity, but these are much less prevalent in HF. Fatigue is another very common symptom, but is even less specific than dyspnea, and can be a manifestation of almost any disease. A history of ankle edema is also very frequent, but can be due to other causes; in fact, it is the prime cause of false diagnoses

TABLE 4. Framingham Criteria for the Diagnosis of Heart Failure⁶

Major criteria	
	Paroxysmal nocturnal dyspnea, or orthopnea
	Jugular venous distension
	Rales
	Cardiomegaly
	Acute pulmonary edema
	Third heart sound gallop
	Central venous pressure >16 mm Hg
	Circulation time >25 s
	Hepatojugular reflux
Minor criteria	
	Ankle edema
	Night cough
	Exertion dyspnea
	Hepatomegaly
	Pleural effusion
	One-third reduction in vital capacity in relation to the maximum
	Tachycardia (>120 beats/min)
	Weight loss >4.5 kg in 5 days in response to treatment (this can also be a main criterion)

Two main criteria or one main and two minor are required. Other possible causes should be discarded from the minor criteria.

TABLE 5. Definition of Heart Failure Following the Guidelines of the European Society of Cardiology for the Diagnosis and Treatment of Chronic Heart Failure²

Essential criteria
1. Symptoms or signs typical of heart failure (at rest or during exercise)
2. Objective evidence of cardiac dysfunction (at rest).
Confirmation (where the diagnosis is in doubt following the previous criteria)
3. Good clinical response to HF treatment

Criteria 1 and 2 should be met in all cases.

of HF in elderly women, who most usually present venous insufficiency. In previously diagnosed patients or those who are admitted due to acute symptoms, it is important to investigate all possible precipitating factors including those described previously, diet and concomitant treatment.

The signs yielded by physical examination in these patients, like symptoms, belong to two groups: first, there are those, such as tachycardia, pulmonary rales and pitting edema, that are very frequent in patients with HF, but also in other diseases, which is why they are not very specific. There are also relatively specific signs but which are only present in the most serious forms of HF, such as displacement of the apical beat, jugular venous distension and gallop rhythm. The identification of the latter two is of special interest, because they involve a worse prognosis.²⁴

Table 6 presents the sensitivity, specificity and predictive value of each of the symptoms, signs and clinical background in the diagnosis of HF, according to the excellent study of Davie et al.²⁵ In general terms, the symptoms as well as the classic signs of HF can have high sensitivity (dyspnea) or specificity (orthopnea, paroxysmal nocturnal dyspnea), but not both simultaneously.⁴ It is also known that the degree of interobserver agreement is low regarding the presence or absence of clinical signs/symptoms of HF, increasing the difficulties still further.²⁶ For this reason, in practice, we need the objective information provided by additional examinations. The following are among those that must be carried out:

1. Systematic analysis. In the HF patient these include:

- Hemogram to detect anemia as a precipitating factor.
- Renal function and serum electrolytes; these can be altered as much by HF treatment (diuretics) as by renal hypoperfusion in severe cases. This is a sign of poor prognosis.
- Transaminases, bilirubin and parameters of coagulation (alterations in ischemia or hepatic

TABLE 6. Diagnostic Value of Various Clinical Features in Systolic Heart Failure*

	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Exertion dyspnea	100	17	18	100
Orthopnea	22	74	14	83
Paroxysmal nocturnal dyspnea	39	80	27	87
History of myocardial infarction	59	86	44	92
History of edemas	49	47	15	83
Jugular venous distension	17	98	64	86
Rales	29	77	19	85
Gallop	24	99	77	87
Edema upon examination	20	86	21	85

*NPV indicates negative predictive value; PPV, positive predictive value. Taken from Davie AP et al.²⁵

congestion).

- Glycemia and cholesterol to screen for cardiovascular risk factors.
- Thyroid hormones, because hyperthyroidism and hypothyroidism can both cause HF.
- Elementary urine analysis to eliminate/exclude proteinuria, glucosuria, or nephropathies.
- In special situations, the evaluation of the plasmatic values of certain pharmaceuticals (such as digoxin, if there is suspicion of toxicity or underdosing) is justified as well as arterial blood gases in patients with acute edema of the lung.

2. The electrocardiogram (ECG) offers important diagnostic and prognostic information. A normal ECG virtually excludes LV systolic dysfunction, with a sensitivity of 94% and a negative predictive value of 98%; on the other hand, a pathological ECG is not a good predictor of a low ejection fraction, having a specificity of 61% and a positive predictive value of 35%.^{4,27}

Thus, a normal ECG reading should lead us to consider an alternative diagnosis. The ECG allows us to detect alterations in heart rate (tachycardia is associated with a worse prognosis), rhythm (atrial fibrillation) and conduction (patients with left bundle branch block have worse systolic function and worse prognosis) as well as hypertrophy, Q waves (that support the ischemic origin of HF) and alterations in repolarization (by overload, electrolytic disorders, pharmacological effects or ischemia).

3. Chest x-ray might be normal or, more often, show cardiomegaly, as well as signs of pulmonary congestion (venous capillary hypertension, interstitial, peribronchial, perivascular and alveolar edema, dilatation of vascular elements) or pleural effusion. It is important to bear in mind that the presence and intensity of radiological findings depend on the duration and severity of HF.²⁸ Thus, the absence of cardiomegaly with complex left HF signs indicates an

acute process, whereas signs of pulmonary congestion might be absent in chronic patients, while having typical symptoms such as dyspnea and orthopnea. Repeated chest x-rays are very useful to track the evolving picture.

4. The echocardiogram is, without doubt, the most informative examination in HF and is the most used technique,²⁹ as it allows us to:

- Confirm the diagnosis of cardiac abnormality, and quantify alterations in LV systolic and diastolic function, myocardial hypertrophy, etc.

- Determine the etiology of HF in many cases, allowing the diagnosis of valvular heart disease, diseases of the pericardium, typical patterns of myocardial disorders (dilated, restrictive or hypertrophic cardiomyopathies, or segment contraction dysfunction, indicating an ischemic origin), congenital malformations, etc.

- Obtain important prognostic information: several parameters of LV systolic dysfunction are associated with worse evolution, such as reduction in ejection fraction and shortening as well as increase in end-systolic and end-diastolic diameters. The presence of significant mitral insufficiency, secondary to dilation of the mitral ring, has a similar meaning. In addition, severe diastolic dysfunction with restricted physiology, shown by an E wave with brief high-speed filling with a very short deceleration time, involves high diastolic pressures and a less favorable prognosis.³⁰ In the presence of LV systolic dysfunction, patients with hypocontractility of the right ventricle present worse evolution, which is why it is normal practice to determine parameters such as tricuspid annular plane systolic excursion (TAPSE).³¹

- It provides other information with therapeutic implications: the presence of thrombi, defects which can be surgically corrected, pulmonary hypertension, etc.

Since such examination is innocuous, comfortable and easily repeatable for monitoring the process, it is difficult to disagree with the systematic use of echocardiograms in each patient with suspicion of HF. However, this would involve a huge overload on the health system, because the test requires sophisticated and expensive technology, as well as an expert operator, while being very time-consuming. In addition, only 25% of patients sent for echocardiogram with a clinical diagnosis of HF in primary care eventually present LV systolic dysfunction.³² This means that, in practice, the echocardiogram is underused in HF, particularly in elderly people.³³

Thus, it would be very desirable to have available an HF indicator to screen the population with suspicion of HF. Ideally, it should be fast, inexpensive

and offer high negative predictive power, such that it could reliably eliminate the large sub-group of patients with low to medium clinical suspicion of HF in whom the echocardiogram does not show any relevant disease. Several of these requirements are met in the determination of B type natriuretic peptide (BNP). B type natriuretic peptide, as well as the inactive part of its precursor molecule, the proBNP N-terminal, can be determined quickly and reliably “at the patient’s bedside.” Most importantly, both show good sensitivity and excellent negative predictive value (between 90% and 100%), both in general population, with a low prevalence of HF,³⁴ and in a cohort with a high probability of HF, such as patients who are admitted to the emergency ward with dyspnea.³⁵ Other qualities that make the determination of BNP still more attractive include: its capacity to detect asymptomatic forms of both systolic and diastolic LV dysfunction, its utility regarding prognosis and the appearance of events, and as a guide to the treatment of HF, etc.³⁶⁻³⁸

The advent of these peptides is beginning to change the sequence of diagnosing HF: they will probably be used between the initial clinical evaluation and the echocardiogram, which would be reserved for patients with elevated values.⁴ This is an area of enormous interest and relevance, and so it will be dealt with as a monograph in a later article in this series.

Other useful complementary examinations for certain patients with HF are: isotopic ventriculography, which allows precise evaluation of left and right ventricular function, but offers less anatomical information than echocardiograms. This is especially indicated in patients with a poor acoustic window that interferes with reliable echocardiograms. Indications for left heart catheterization with coronary angiography for HF is well-established in the North American Guidelines to Clinical Practice published in 2001.³ These are presented in Table 7. In general, their use is restricted to cases of HF with suspicion of coronary artery disease (not necessarily with typical angina) in which a diagnosis of coronary heart disease can be followed by coronary revascularization. Angiographic ventriculography allows the visualization of aortic and mitral alterations in global and segmental contractility, as well as valvular heart disease. Hemodynamic control by means of right catheterization is carried out in patients with chronic HF refractory to conventional treatment and allows an evaluation of prognosis. Normally, cardiac output and index, pulmonary capillary pressure and pressure in the pulmonary artery, right ventricle and right auricle are determined, as well as pulmonary vascular resistance. Endomyocardial biopsy is only occasionally needed, which, when carried out systematically, offers etiologic information in less

TABLE 7. Indications for Coronary Angiography in Patients With HF³

Class I (there is evidence or general agreement that the procedure is useful)
 Patients with angina who are candidates for revascularization (level of evidence: B)

Class IIa (the weight of opinion is that the procedure is useful)
 Patients with chest pain with neither previous evaluation of coronary anatomy nor contraindications to revascularization (level of evidence: C)
 Patients with known or suspected coronary artery disease, without angina, who are candidates for revascularization (level of evidence: C)

Class III (there is evidence or general agreement that the procedure is not useful or could be harmful)
 Repeat angiography or noninvasive testing for ischemia if coronary artery disease has previously been excluded as the cause of left ventricular dysfunction (level of evidence: C)

Levels of evidence: level B indicates that evidence derives from a single randomized trial or nonrandomized studies; C indicates that consensus opinion is the main source of recommendation.

than 15% of cases. High suspicion of disorders that have no other means of diagnosis (e.g. myocarditis, endocardial fibrosis, some cases of amyloidosis, sarcoidosis or hemochromatosis) justifies its use.

Other useful diagnostic tests for HF aimed at an objective evaluation of functional capacity include ergospirometry. This allows the measurement of the peak consumption of oxygen, is a good prognostic predictor of HF and can help to differentiate dyspnea of pneumological origin. Another is the 6-min walk test, which determines effort capacity in submaximal conditions. The Holter monitor test (outpatient 24-48 hour electrocardiographic record) and electrophysiological study are used to evaluate the incidence of arrhythmias and their correlation with symptoms in patients with clinical suspicion of HF.

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