CorSalud 2016 Jan-Mar;8(1):58-70

CorSalud

Cuban Society of Cardiology

Review Article

Cardiocentro Ernesto Che Guevara Santa Clara Cuba

Heart Failure: Basic issues of a growing epidemic

Javier E. Pereira-Rodríguez, MD✉; Gina Rincón-González, BS; and Damaris R. Niño-Serrato, BS

Grupo RehabilitarCI – Colciencias. Cúcuta, Colombia.

Este artículo también está disponible en español

ARTICLE INFORMATION

Received: October 1, 2015
Modified: November 17, 2015
Accepted: December 22, 2015

Competing interests
The authors declare no competing interests

Acronyms
ACC: American College of Cardiology
ACE: angiotensin-converting enzyme
AHA: American Heart Association
CRT: cardiac resynchronization therapy
HF: heart failure
NYHA: New York Heart Association

On-Line Versions:
Spanish - English

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

Insuficiencia cardíaca: Aspectos básicos de una epidemia en aumento

RESUMEN
La insuficiencia cardíaca representa un gran problema de salud pública en el mundo, ya sea por su creciente prevalencia, como por el costo que implica el tratamiento adecuado de los pacientes que la padecen. Esta afectación es un complejo problema que se origina de un desorden estructural o funcional y deteriora la capacidad de llenado o expulsión ventricular de la sangre. Se caracteriza a su vez, por la presencia de síntomas cardinales, como la disnea, fatiga y retención de líquido. Las principales causas de la insuficiencia cardíaca son la enfermedad isquémica, la cardiopatía hipertensiva, las cardiomiopatías dilatadas y las valvulopatias. En las etapas iniciales, la función cardíaca puede ser normal en reposo, pero no aumenta adecuadamente con el ejercicio; en estadios avanzados se vuelve anormal también en reposo. En esta revisión se resumen los aspectos básicos principales de este síndrome.
Palabras clave: Insuficiencia cardíaca, Miocardiopatía dilatada, Hipertensión, Enfermedades valvulares, Disnea

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[1]. The hallmark of this disease is a progres-

✉ *JE Pereira-Rodríguez*
Avenida 8E #4-105 Quinta Oriental.
Cúcuta, CP 540001, Colombia.
E-mail address: jepr87@hotmail.com

sive maladaptive cardiac remodeling[2]; it starts from an episode that causes a decrease in the pump capacity of the heart[3] and thus compromises the ability of the ventricles to satisfactorily fill and pump blood[4]. 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[5].

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[6-8]. The progressive functional limitations it imposes will cause a shock on the productive capacity of those affected[9]. The setting is a myocardial disorder which may be diffuse or segmental that usually starts without symptoms or disability[10].

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[11].

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[12]; it is estimated that in Spain the prevalence reaches 6% in the population over 40 years[13]; 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[14]. 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[15].

ETIOLOGY

The 3 main causes of HF are: hypertensive heart disease, ischemic heart disease associated with a previous infarction and dilated cardiomyopathy[16]. Other causes include: arrhythmias, valvular heart disease, infections, diseases infiltration, alcoholism, endocrine disorders and genetic diseases[17].

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[18]. 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[19].

HF can be classified in different ways[20]: 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[21]. 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[22].

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[23]. Class I: Normal exercise tolerance; Class II: symptoms with ordinary exertion; Class III: symptoms with only mild exertion and Class IV: symptoms at rest[24]. This classification from The American College of Cardiology/American Heart Association (ACC/AHA) based on the structural damage is useful in defining HF stages[16]. ACC/AHA[16] 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 (Table 1)[25].

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[18]. 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)[26], 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-

Table 1. Acute and chronic HF classification.

Acute HF (SEC)	Chronic HF (ACC/AHA)
Decompensated acute HF	**Stage A.** No structural damage or functional impairment.
Hypertensive acute HF	**Stage B.** Structural alteration strongly related to HF development
Acute pulmonary edema	**Stage C.** Symptomatic HF associated with cardiac structural damage
Cardiogenic shock	**Stage D.** HF with symptoms at rest despite maximal treatment; advanced cardiac structural alteration.
High output HF	
Acute right HF	

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[27] 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[28] (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"[29].

This remodeling is accompanied by left ventricle shape alterations, which becomes more spherical, rather than elliptical, for a bigger growth in the transverse axis[30]. It may occur after a myocardial infarction, pressure overload (aortic stenosis, hypertension) or volume (valvular regurgitation), inflammatory myocardial disease (myocarditis), or dilated idiopathic cardiomyopathy[29,31] (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

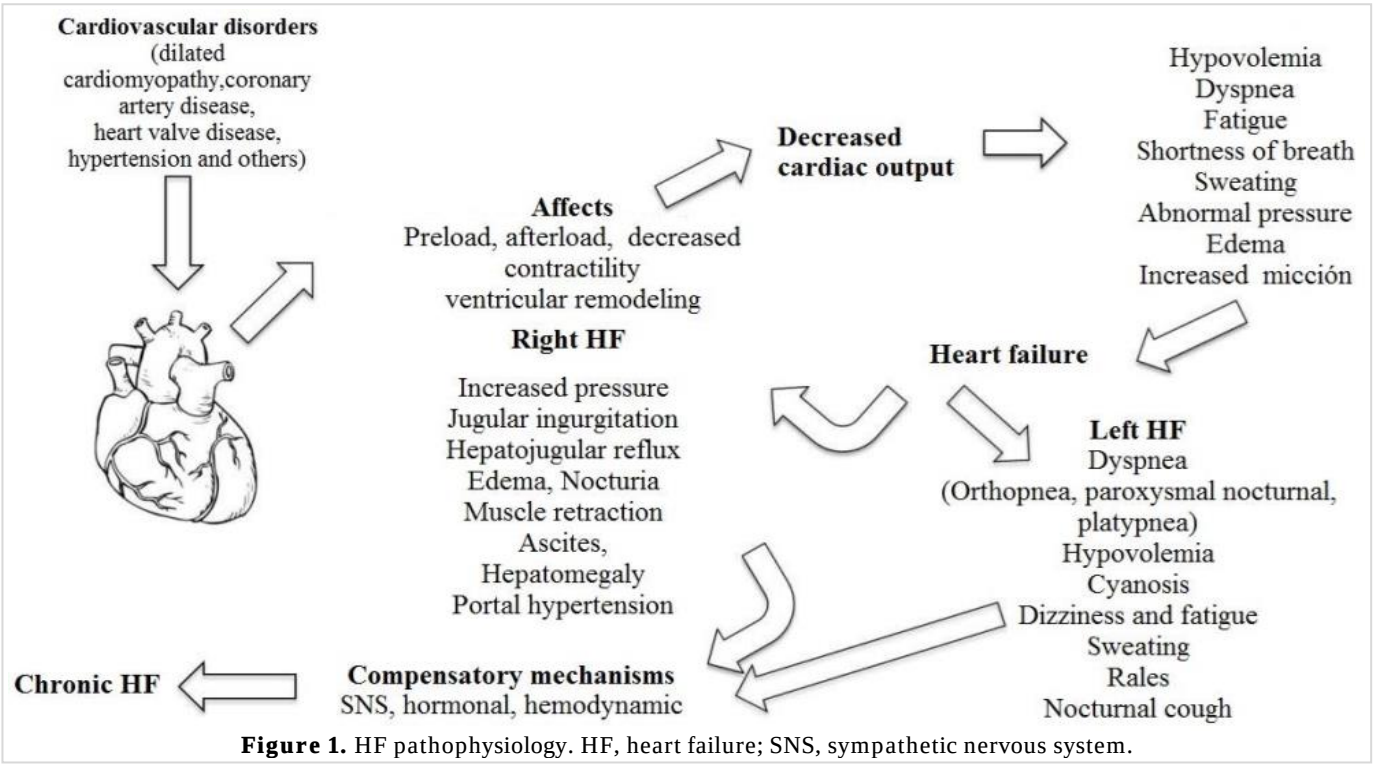

Figure 1. HF pathophysiology. HF, heart failure; SNS, sympathetic nervous system.

hypertrophy, and increased sympathetic system activity and neurohumoral activation; since structural changes are primarily modulated by hemodynamic, mechanical and humoral factors[32]. 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 progresssion[5] (Figure 3).

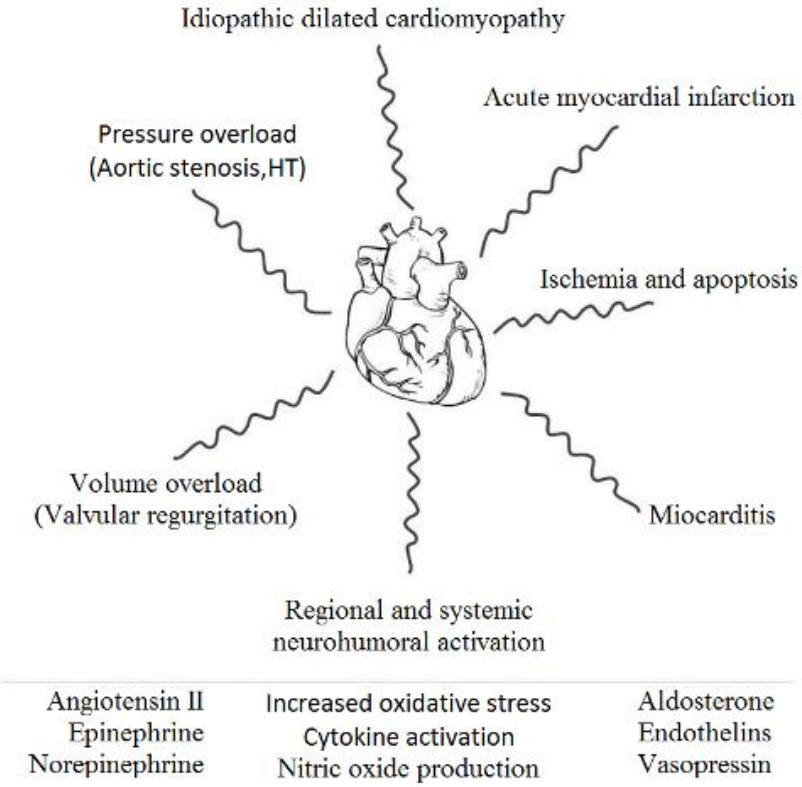

Figure 2. Factors influencing ventricular remodeling. HT, Hypertension.

PREVALENCE

More than 20 million people suffer from HF worldwide[11,33] and despite treatments progress in this disease, most patients with advanced forms die one year after diagnosis[34].

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[17].

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[35].

European data indicate that the prevalence of symptomatic patients is 0.4-2.0%, but this percentage increases rapidly with age[36]. There is a group of patients, about 30% of the general population, who has ventricular dysfunction and remains asymptomatic[37] at first, such HF latent condition was called subclinical HF[38].

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[39], so their condition is considered as very lethal, hence it is higher than that compared to some neoplasias[40].

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[41]. Latin American countries are facing a coronary heart disease epidemic that has led to a significant increase in cardiac dysfunction incidence[42].

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[43].

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[44,45]:

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

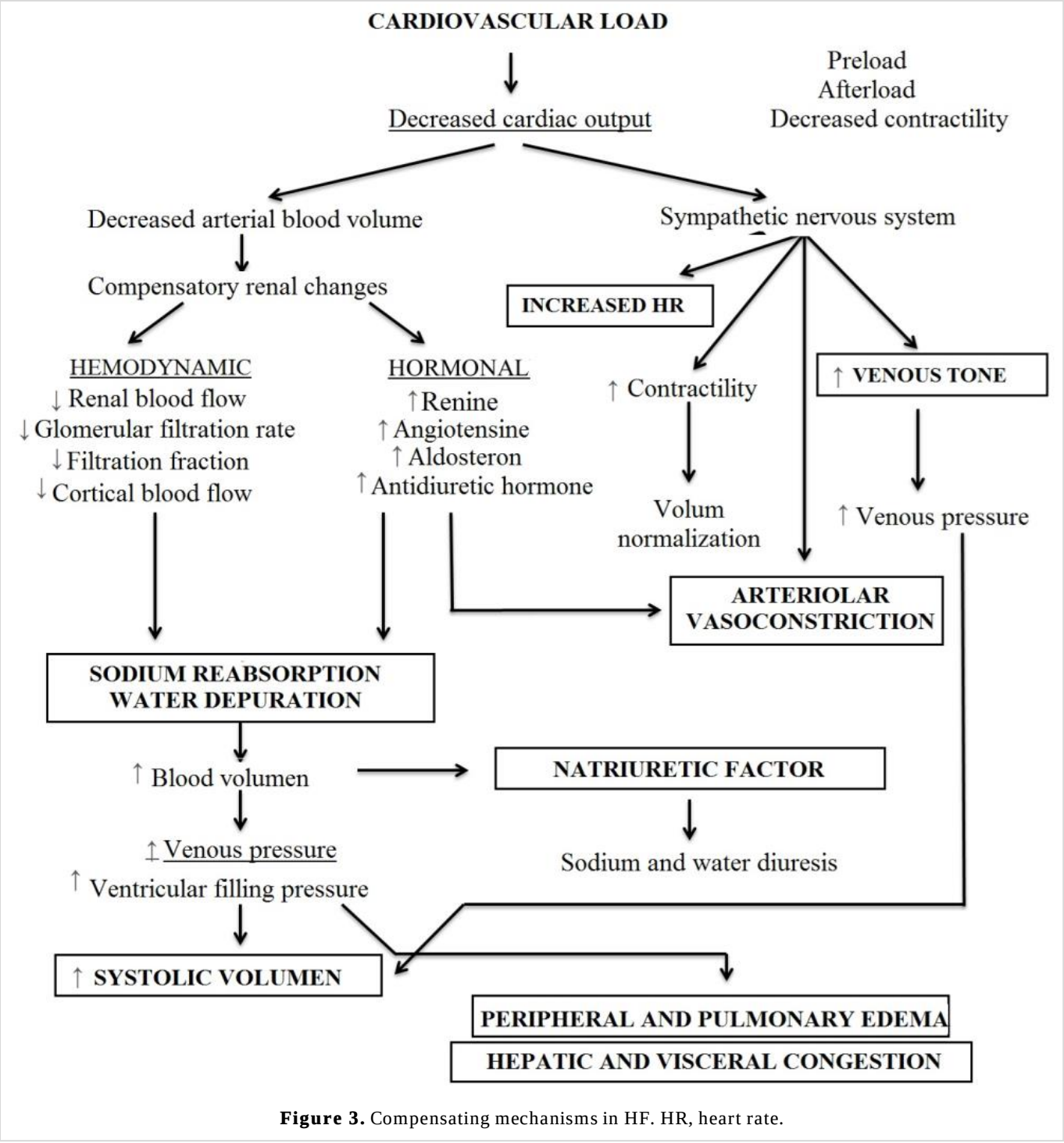

Figure 3. Compensating mechanisms in HF. HR, heart rate.

tion at rest, preferably by echocardiography, which would be essential in doubtful cases.

3. HF improvement after treatment.

Framingham's clinical criteria, presented in 1971 are the most accepted for diagnosis (Table 2)[45]. According to Atamañuk and Bortman[46], Michael R. Bristow proposed to group HF causes according to their physiological and anatomical situation: a) coronary, b) myocardial, c) arrhythmic, d) valvular

Table 2. Framingham clinical criteria.

Major	Minor	Major or minor
Paroxysmal nocturnal dyspnea	Bilateral ankle edema	Thinning ≥4,5 kg after 5 days treatment
Neck vein distension	Nocturnal cough	
Rales	Dyspnea on ordinary exertion	
Radiographic cardiomegaly	Hepatomegaly	
Acute pulmonary edema	Pleural effusion	
S_3 gallop	A decrease in vital capacity 1/3	
Increased central venous pressure > 16 cmH_2O	Tachycardia	
Hepatojugular reflux		

e) pericardial.

Supplementary tests

Echocardiography

Allows to differentiate 4 physiopathological mechanisms groups[44]: 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[6].

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[47]. Characteristic findings are: increased cardiothoracic index > 0.50; pulmonary vascular cephalization; the appearance of Kerley B lines and the presence of pleural effusion[6].

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[48].

Electrocardiogram

Electrocardiographic abnormalities commonly found in HF include: the presence of necrotic or ischemic changes, rhythm disorders, hypertrophy of cardiac cavities and overloading patterns[44].

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[49].

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[41,44].

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[50]. Unfortunately, clinical studies with these drugs have yielded disappointing results as little has been achieved with regard to the prolonged survival of these patients[33].

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[51]. Their effects are associated with an increase in ejection fraction, a decrease in hospital admissions and survival and sudden death incidence[52].

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[15] (Table 3). The use of ACEI and angiotensin II receptor antagonists has improved the survival of patients with HF[50]. It has been found that these types of drugs reduce afterload and left ventricular hypertrophy as well[53].

Diuretic therapy, especially thiazide and loop, maintain their dominant place, they allow controlling volume overload and characteristic symptoms of congestion[52]. Spironolactone and other aldosterone receptor inhibitors under study prevent salt retention, urinary potassium loss, and the newest, reduce cardiac fibrosis[53].

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[54]. 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[41].

The pharmacological treatment of HF has basically been palliative and less aimed to affected molecular mechanisms[55]. Research is also done with apoptosis preventing drugs that sensitize calcium myofilaments and block V^2 receptors for the antidiuretic hormone ADH[56].

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 3. HF treatment strategies.

Stage A Primary prevention	Stage B Secondary prevention	Stage C and D Tertiary prevention
- Treat HT, diabetes and dyslipidemia. - Treat thyroid diseases. - Giving up harmful habits (tobacco, alcohol, other drugs) - Regular physical exercise. - Heart rate control in tachyarrhythmias - Use of ACEI in selected patients.	- Stage A measures - ACEI - Beta blockers	- Stage A measures - ACEI + beta blockers - Salt restriction - Diuretics if fluid retention - Persistence of symptoms: ARA II, hydralazine and nitrates, digital. - CRT- ICD in selected patients. - Transplantation - ICD - Continuous infusion of inotropic - Care in special centers

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

function imbalance is strictly controlled. In the outpatient, restrictions are between 1.200 and 1.500 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[41]. 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[57].

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[41].

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[58,59] (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[60]. According to clinical practice guidelines on cardiac pacing and cardiac resynchronization therapy (CRT) of the European Society of Cardiology[61], it is considered class I indi-

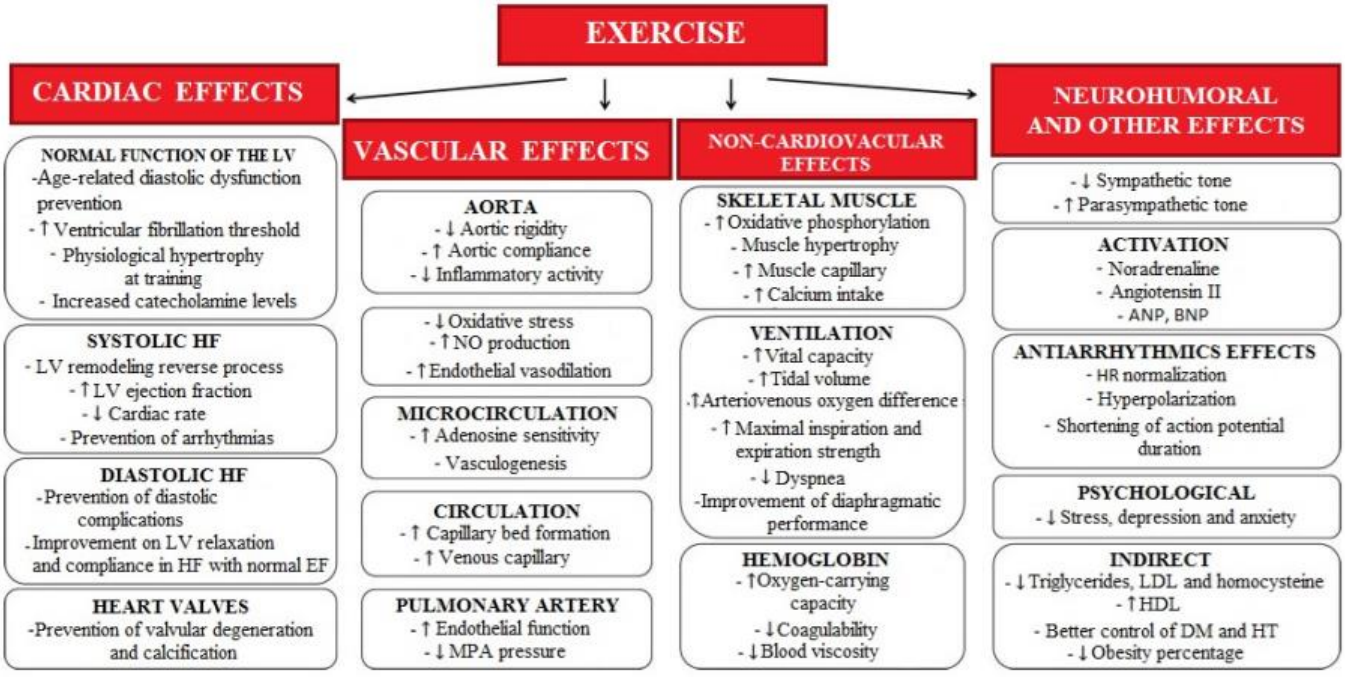

Figure 4. Beneficial effects of physical training. ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; DM, diabetes mellitus; EF, ejection fraction; HDL, high density lipoprotein; HF, heart failure; HR, heart rate; HT Hypertension, LDL, low-density lipoprotein; MPA, main pulmonary artery; 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[41]. CRT aims to improve survival and reduce the number of congestive HF patients hospitalizations by acting on atrioventricular, inter- and intraventricular dyssynchronies[62]. Some of the most important CRT effects are mentioned in Figure 5.

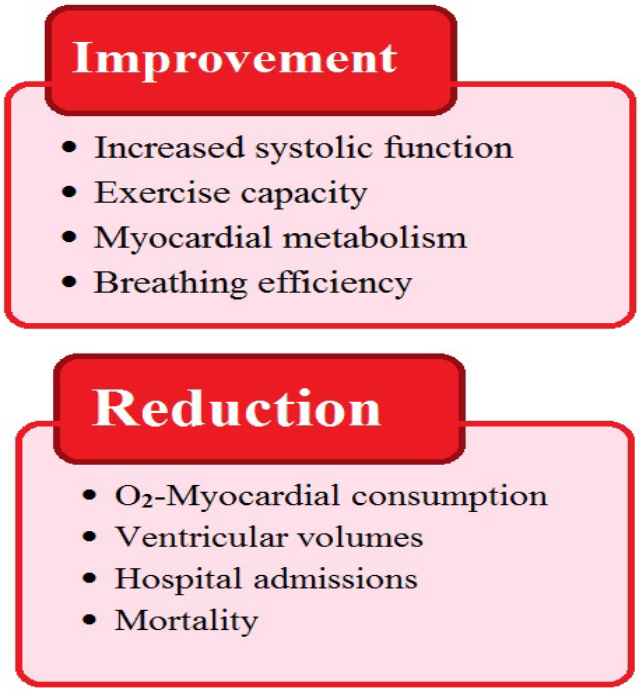

Figure 5. CRT effects.

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[63]. There are several types depending on their characteristics[64] which can be classified into:

a) According duration
   - Temporary
   - Permanent
b) According to the effective time of use
   - Short term: <7 days
   - Medium term: 7-30 days
   - Long term: > 30 days
c) According to the assisted chamber
   - Left
   - Right
   - Biventricular
d) According to ventricular assistance type
   - Partial
   - Total
e) According to the type of generated flow
   - Continuous
   - Pulsating
f) According to the device location
   - Paracorporeal
   - Intracorporeal
g) 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[65]; however, many studies have shown how long-term survival is decreased compared with patients with normal ventricular function[66].

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[16,61,67].

REFERENCES

1. Jalil J, de Petris V. Insuficiencia cardíaca I: Mecanismos [Internet]. Santiago de Chile: Escuela de Medicina - Pontificia Universidad Católica de Chile; 2012 [citado 11 Nov 2015]. Disponible en: http://medicina.uc.cl/docman/1432/cat-view/10/pagina-3
2. Terzic A, Pérez-Terzic C. Terapia celular para la insuficiencia cardíaca. Rev Esp Cardiol. 2010;63: 1117-9.
3. Francis GS, Tang WH. Pathophysiology of congestive heart failure. Rev Cardiovasc Med. 2003; 4(Supl. 2):S14-20.
4. Batista Júnior ML, Delascio Lopes R, Leite Seelaender MC, Lopes AC. Efecto antiinflamatorio del entrenamiento físico en la insuficiencia cardiaca: Rol del TNF-α y de la IL-10. Arq Bras Cardiol. 2009;93:692-700.
5. Cagide A. Evolución del tratamiento de la insuficiencia cardíaca. Insuf Card. 2015;10:49-55.
6. Sociedade Brasileira de Cardiologia. Revisão das II Diretrizes da Sociedade Brasileira de Cardiologia para o diagnóstico e tratamento da insuficiência cardíaca. Arq Bras Cardiol. 2002;79(Supl. 4):1-30.
7. Larsen AI, Lindal S, Aukrust P, Toft I, Aarsland T, Dickstein K. Effect of exercise training on skeletal muscle fibre characteristics in men with chronic heart failure. Correlation between skeletal muscle alterations, cytokines and exercise capacity. Int J Cardiol. 2002;83:25-32.
8. Veiga Guimarães G, Vaz da Silva MS, Moraes d'Avila V, Ayub Ferreira SM, Pereira Silva C, Alcides Bocchi E. Peak VO_2 and VE/VCO_2 slope in betablockers era in patients with heart failure: a Brazilian experience. Arq Bras Cardiol. 2008;91: 39-48.
9. De la Serna F. Epidemiología de la IC. En: Insuficiencia cardíaca crónica [Internet]. 3ra. ed. Argentina: FAC; 2010 [citado 5 Nov 2015]. Disponible en: http://www.fac.org.ar/edicion/inscac/cap01_2010.pdf
10. LeJemtel TH, Sonnenblick EH. Heart failure: Adaptative and maladaptative processes. Introduction. Circulation. 1993;87(Supl. VII):VII-1-VII-4.
11. Stewart S. Prognosis of patients with heart failure compared with common types of cancer. Heart Fail Monit. 2003;3:87-94.
12. Writing Group Members, Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, *et al*. Heart disease and stroke statistics - 2010 update: A report from the American Heart Association. Circulation. 2010;121:e46-215.
13. Sánchez E, Rodríguez C, Ortega T, Díaz-Molina B, García-Cueto C. Papel de la diálisis peritoneal en el tratamiento de la insuficiencia cardíaca. Insuf Card. 2010;5:105-12.
14. Conthe P. La insuficiencia cardíaca en el siglo XXI. Med Clin (Barc). 2001;2(Supl. 3):1-2.
15. Cowie MR, Mosterd A, Wood DA, Deckers JW, Poole-Wilson PA, Sutton GC, *et al*. The epidemiology of heart failure. Eur Heart J. 1997;18:208-25.
16. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, *et al*. ACC/AHA 2005 Guideline update for the diagnosis and management of chronic heart failure in the adult: A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the evaluation and management of heart failure): Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society. Circulation. 2005;112:154-235.
17. Swynghedauw B. Phenotypic plasticity of adult myocardium: molecular mechanisms. J Exp Biol. 2006;209:2320-7.
18. Navarrete Hurtado S. Clasificación y diagnóstico de la insuficiencia cardíaca. En: Charria García DJ, Guerra León PA, Manzur Jattin F, Llamas Jiménez A, Rodríguez Guerrero NI, Sandoval Reyes NF, *et al*. Texto de Cardiología. Colombia: Socie-

dad Colombiana de Cardiología y Cirugía Cardiovascular; 2007. p. 704-11.
19. Chávez RI. Cardiología. México DF: Médica Panamericana; 1993.
20. Rodríguez JA, Aldamiz-Echevarría B, Pereira S, Caeiro J. Insuficiencia cardíaca. Guías Clínicas [Internet]. 2005 [citado 3 Ago 2015];5. Disponible en: http://www.clinicamedica1.fcm.unc.edu.ar/trabajos/archivos/Insuficiencia%20Cardiaca.pdf
21. Jiménez-Navarro MF, García-Pinilla JM, Montiel Trujillo Á, de Teresa Galván E. Tratamiento médico de la insuficiencia cardiaca por disfunción sistólica. Rev Esp Cardiol. 2006;6(Supl. F):46-52.
22. Muñoz Martínez L. Utilidad del ecocardiograma en la valoración del paciente con insuficiencia cardíaca diastólica. Rev Urug Cardiol. 2005;20:102-15.
23. Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, *et al*. Guías de práctica clínica sobre el diagnóstico y tratamiento de la insuficiencia cardíaca crónica. Versión resumida (actualización 2005). Rev Esp Cardiol. 2005;58:1062-92.
24. Koch F. La insuficiencia cardíaca en el adulto. Rev Fac Med Tucuman [Internet]. 2006 [citado 19 Jul 2015];7:27-33. Disponible en: http://www.fm.unt.edu.ar/Servicios/publicaciones/revistafacultad/vol_7_n_1_2006/pag27-33.pdf
25. Muñiz García J, Crespo Leiro MG, Castro Beiras A. Insuficiencia cardíaca en España. Epidemiología e importancia del grado de adecuación a las guías de práctica clínica. Rev Esp Cardiol. 2006; 6(Supl. F):2-8.
26. Sandoval Zárate J. Insuficiencia ventricular derecha en la hipertensión arterial pulmonar. Consideraciones fisiopatológicas. Arch Cardiol Mex. 2001;71(Supl. 1):164-7.
27. Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol. 2001;38:2101-13.
28. Sokolow M. Cardiología Clínica. México: El Manual Moderno; 1992.
29. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling - Concepts and clinical implications: A consensus paper from an international forum on cardiac remodeling. J Am Coll Cardiol. 2000;35:569-82.
30. Mitchell GF, Lamas GA, Vaughan DE, Pfeffer MA. Left ventricular remodeling in the year after first anterior myocardial infarction: A quantitative analysis of contractile segment lengths and ventricular shape. J Am Coll Cardiol. 1992;19:1136-44.
31. Chatterjee K. Remodeling in systolic heart failure: therapeutic implications. Indian Heart J. 2003;56: 99-109.
32. Brum PC, Rolim NP, Bacurau AV, Medeiros A. Neurohumoral activation in heart failure: the role of adrenergic receptors. An Acad Bras Cienc. 2006;78:485-503.
33. Farr MA, Basson CT. Sparking the failing heart. N Engl J Med. 2004;351:185-7.
34. Remme WJ, Swedberg K; Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J. 2001;22:1527-60.
35. Mosterd A, Hoes AW, de Bruyne MC, Deckers JW, Linker DT, Hofman A, *et al*. Prevalence of heart failure and left ventricular dysfunction in the general population; The Rotterdam Study. Eur Heart J. 1999;20:447-55.
36. Doval HC, Tajer CD. Evidencias en Cardiología: De los ensayos clínicos a las conductas terapéuticas. 2da. ed. Buenos Aires: GEDIC; 2001.
37. Petit GM. Suficiencia e insuficiencia cardíacas, fisiología, fisiopatología y tratamiento. Barcelona: Salvat Editores SA; 1984.
38. Cleland JG, Gemmell I, Khand A, Boddy A. Is the prognosis of heart failure improving? Eur J Heart Fail. 1999;1:229-41.
39. Stewart S, MacIntyre K, Hole DJ, Capewell S, McMurray JJ. More "malignant" than cancer? Five-years survival following a first admission for heart failure. Eur J Heart Fail. 2001;3:315-22.
40. Grigioni F, Carinci V, Favero L, Bacchi Reggiani L, Magnani G, Potena L, *et al*. Hospitalization for congestive heart failure: is still a cardiology business? Eur J Heart Fail. 2002;4:99-104.
41. Vélez Peláez S, Navarrete Hurtado S, Gómez López EA, Bermúdez Echeverry JJ, Gómez Echeverri CA, Restrepo Jaramillo CA, *et al*. Insuficiencia cardíaca. En: En: Charria García DJ, Guerra León PA, Manzur Jattin F, Llamas Jiménez A, Rodríguez Guerrero NI, Sandoval Reyes NF, *et al*. Texto de Cardiología. Colombia: Sociedad Colombiana de Cardiología y Cirugía Cardiovascular;2007. p. 694-785.
42. Rodríguez-Artalejo F, Banegas Banegas JR, Gua-

llar-Castillón P. Epidemiología de la insuficiencia cardíaca. Rev Esp Cardiol. 2004;57:163-70.
43. Agustí A, Danés I, Rodríguez D, Casas J. Novedades en el tratamiento de la insuficiencia cardíaca. Aten Primaria. 2006;38:107-15.
44. Vilches Moraga A, Rodríguez Pascual C. Insuficiencia cardíaca congestiva. En: Tratado de geriatría para residentes. Madrid: SEGG; 2007. p. 313-23.
45. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med. 1971; 285:1441-6.
46. Atamañuk N, Bortman G. Diagnóstico etiológico y funcional de la insuficiencia cardíaca. Grados de insuficiencia cardíaca. Insuf Card. 2009;4:59-65.
47. Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davis JL, *et al*. ACC/AHA/ASE 2003 Guideline update for the clinical application of echocardiography: Summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). Circulation. 2003;108; 1146-62.
48. Badgett RG, Mulrow CD, Otto PM, Ramírez G. How well can the chest radiograph diagnose left ventricular dysfunction? J Gen Intern Med. 1996; 11:625-34.
49. Richardson A, Bayliss J, Scriven AJ, Parameshwar J, Poole-Wilson PA, Sutton GC. Double-blind comparison of captopril alone against furosemide plus amiloride in mild heart failure. Lancet. 1987; 2:709-11.
50. Ulate-Montero G, Ulate-Campos A. Actualización en los mecanismos fisiopatológicos de la insuficiencia cardiaca. Acta Méd Costarric [Internet]. 2008 [citado 5 Ago 2015];50:5-12. Disponible en: http://www.scielo.sa.cr/pdf/amc/v50n1/3698.pdf
51. Goldberg LR, Jessup M. Stage B heart failure: Management of asymptomatic left ventricular systolic dysfunction. Circulation. 2006;113:2851-60.
52. Bristow MR. β-Adrenergic receptor blockade in chronic heart failure. Circulation. 2000;101:558-69.
53. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. N Engl J Med. 1999;341: 577-85.
54. Cody RJ. Diuretic therapy. En: Poole-Wilson P, Colucci WS, Massie BM, Chatterjee K, Coats AJ, editors. Heart Failure. New York: Churchil Livingstone; 1997. p. 635-48.
55. Dávila DF, Núñez TJ, Odreman R, Mazzei de Dávila CA. Mechanisms of neurohormonal activation in chronic congestive heart failure: pathophysiology and therapeutic implications. Int J Cardiol. 2005;101:343-6.
56. Minamisawa S, Sato Y, Cho MC. Calcium cycling proteins in heart failure, cardiomyopathy and arrhythmias. Exp Mol Med. 2004;36:193-203.
57. González Juanatey JR, Varela Román A, Gómez Otero I, Grigorian Shamagian L, Otero Barreiro MC, Otero Fernández D. Manual de diagnóstico y tratamiento de insuficiencia cardíaca crónica [Internet]. Santiago de Compostela: Complexo Hospitalario Universitario de Santiago; 2011 [citado 2 Nov 2015]. Disponible en: http://www.sergas.es/gal/publicaciones/docs/atespecializada/pdf-2057-ga.pdf
58. Gielen S, Schuler G, Adams V. Cardiovascular effects of exercise training: molecular mechanisms. Circulation. 2010;122:1221-38.
59. Maroto-Montero JM, de Pablo Zarzosa C. Rehabilitación Cardiovascular. Madrid: Panamericana; 2011.
60. Guevara E, Sánchez Lucero D, Casas JM, Galizio N, González JL, Favaloro LM, *et al*. Terapia de resincronización cardíaca. Rev Cubana Cardiol Cir Cardiovasc [Internet]. 2010 [citado 13 Sept 2015]; 16:224-40. Disponible en: http://www.revcardiologia.sld.cu/index.php/revcardiologia/article/view/169/110
61. Gómez Bueno M, Segovia Cubero J, Alonso-Pulpón L. Asistencia mecánica circulatoria y trasplante cardíaco. Indicaciones y situación en España. Rev Esp Cardiol. 2006;6(Supl. F):82-94.
62. Consenso de Recuperación Cardiovascular SAC 2012 (Versión resumida). Rev Argent Cardiol. 2014;82:425-45.
63. Jessup M, Núñez-Gil I. Insuficiencia cardíaca y asistencias ventriculares: nuevas respuestas para antiguas preguntas. Rev Esp Cardiol. 2008;61:1231-5.
64. Gheorghiade M, Teerlink JR, Mebazaa A. Pharmacology of new agents for acute heart failure syndromes. Am J Cardiol. 2005;96(6 Supl.):68-73.
65. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol. 2002;39:1151-8.
66. Caicedo Ayerbe VM, Sandoval Reyes NF, Santos Calderón H, Orjuela Lobo H. Tratamiento quirúr-

gico de la insuficiencia cardíaca. En: Charria García DJ, Guerra León PA, Manzur Jattin F, Llamas Jiménez A, Rodríguez Guerrero NI, Sandoval Reyes NF, *et al*. Texto de Cardiología. Colombia: Sociedad Colombiana de Cardiología y Cirugía Cardiovascular;2007. p. 764-7.

67. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, *et al*. Guía de práctica clínica de la ESC 2013 sobre estimulación cardiaca y terapia de resincronización cardiaca. Rev Esp Cardiol. 2014;67:58.e1-e60.