I LATIN AMERICAN GUIDELINES FOR THE ASSESSMENT AND MANAGEMENT OF DECOMPENSATED HEART FAILURE

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Introduction

Reasons for I Latin American Guidelines on Decompensated Heart Failure (DHF)

Heart failure (HF) is an endemic syndrome all over the world, which can occur as a chronically stable or decompensated disease. According to the I Latin American Guidelines on Decompensated Heart Failure, DHF can be acute (of recent onset), decompensated (with instabilization of a chronic condition), or refractory and persistent. DHF is the leading cause of hospitalizations in developed countries. In Brazil, it is the third general cause of hospitalization and the first cardiovascular cause, with high mortality rate.

Since the patients generally present a decompensated form of HF before the progressive HF (which is a main cause of deaths), the great challenge in the treatment of DHF is the prevention of death and the improvement of life quality. For this treatment, the cardiologist must use the best available evidence. Nevertheless, as it can be easily noticed in these Guidelines, the available evidence is in most cases classified as grades C or D, and they are insufficient as a basis for better decisions. Thus, in view of limited evidence, the opinions of expert cardiologists in this area play a fundamental role in helping the doctors who treat patients with DHF. Likewise, the participation of cardiologists from all Latin American countries is a unique opportunity to include the expertise of specialists from different geographic locations, with cultural and social standards that are not always similar, which allows for the application of the I Guidelines to the whole region.

Consequently, the availability of this I Latin American Guidelines on Decompensated Heart Failure, a result of the joint work of most Latin American societies and a critical review of the assessment and treatment of DHF, will assist those who face the challenge of management and treatment of this serious and frequent syndrome.

Participants and project of the I Latin American Guidelines of Decompensated Heart Failure

The Heart Failure Studies Group [Grupo de Estudos de Insuficiência Cardíaca (GEIC)], through the Brazilian Society of Cardiology, required that the members of Latin American Societies be specialists in heart failure, either in research or assistance. Some names were suggested, but the final decision was made by each Society. Following a program that included the essential items in DHF, a preliminary text was prepared by GEIC members and distributed to each participant to check for changes. A definitive meeting was held in which, initially, each participant was part of a group that elaborated a chapter or section. Each resulting text was discussed in a joint meeting including all the participants, and was voted respecting their individual privacy. Consequently, a combination of a “consensus opinion” and votes originated the official document presented here. We believe that this design allowed for Guidelines with the most independent conclusions. Few Societies which could not send their representatives in time for the final meeting have also reviewed the document later and agreed with it.

Dr. Edimar Alcides Bocchi

Classification of the Recommendation Grades and Evidence Levels

Recommendation Grades:

Class I: Evidence and/or general agreement that the procedure is beneficial and effective.

Class II: Conflicting and/or diverging evidence about the usefulness and efficacy of the procedure or treatment.

IIa. Evidence and opinions favor the use of the procedure or treatment

IIb. Evidence and opinions do not appropriately support the use or efficacy of the procedure or treatment.

Class III. Evidence and/or agreement that the procedure or treatment is not beneficial, and it could be harmful.

Evidence Levels:

A: Data obtained from various randomized assays or from meta-analysis of randomized clinical assays.

B: Data obtained from a single randomized clinical assay, or from various non-randomized studies.

C: Data obtained from studies including a series of cases.

D: Data obtained from consensual opinions of experts on the subject.

I. Epidemiological Importance of DHF

Heart failure (HF) is a disease of high prevalence and incidence throughout the world. About 400,000 new cases are diagnosed in the United States every year[1]. Data from the Framinghan study demonstrate that the incidence of DHF increases progressively in both genders according to age, reaching yearly more than 10 new cases in 1,000 individuals in the 70's and about 25 new cases in 1,000 individuals in the 80's[2]. The interaction between age and onset of DHF was also demonstrated in prevalence studies performed in various European countries[3]. DHF is the most frequent isolated cause of hospitalization in the elderly population, a phenomenon that has been progressively increasing. Hospital discharges with a final diagnosis of HF, for example, were up from 377,000 in 1979 to 999,000 in 2000, an absolute increase of 164%.

In Brazil, hospital admissions due to HF represent approximately 4% of all hospitalizations and 31% of hospitalizations due to cardiovascular problems in 2002[2]. Table 1 shows the admission data related to HF in public hospitals in Brazil in the last 3 years.

A. Morbidity and mortality

After the first hospitalization due to DHF, the rate of readmissions in emergency rooms and hospitals is particularly high, and it may represent the unavoidable progression of the syndrome and/or, possibly, an early hospital discharge. Approximately 60% of North-American patients above 70 years of age are readmitted within 90 days[5]. An international comparison involving two hospital records of patients hospitalized because of HF in Brazil and in the U.S. demonstrate readmission rates within 90 days of 36% and 51%, respectively[6].

Various international studies attempted to identify the factors associated with readmission after hospitalization due to HF[7]. Although the results are not consensual, the clinical characteristics predicting the most frequent types of hospital readmissions are shown in Table 2.

However, in approximately 30-40% of the cases, it is not possible to identify the cause of the clinical decompensation or the factor predisposing to hospitalization[8]. Brazilian data suggest important differences in etiology, in the factors responsible for decompensation, in the treatments and prognosis of patients with HF in different regions in Brazil[9,10].

In the U.S., the overall mortality rate due to HF in 2000 was 18.7 per 10,0000 inhabitants, and there was a total of 262,300 deaths. Based on follow-up data in 44 years, the mortality rate in 1 year is close to 20% and it is estimated that, after diagnosis, less than 15% of the patients will be alive in 8-12 years. In Brazil, in-hospital mortality due to HF in SUS hospitals (Brazilian Public Health System) varied between 5.6%-6,0% in the last 3 years (Table 1). International data show a great variation among different types of institutions in the rates of in-hospital deaths (between 8.5% and 23.1%)[11], which is possibly due to substantial differences in the clinical characteristics and treatments in each population studied. Some data also demonstrate a time trend in the reduction of in-hospital mortality[12].

B. Costs and cost-effectiveness

Most therapeutical interventions in HF (digoxin, use of hydralazine/nitrate, of inhibitors of the angiotensine-converting enzyme and beta-blockers) have shown favorable cost-effectiveness ratios within internationally accepted parameters[13]. In the SOLVD study, for example, treatment with enalapril has saved U$ 717 per treated patient and it cost only U$115 per life-year saved and adjusted to the life quality (QALY - Quality-Adjusted Life Years) [14]. An initial economic analysis of the LIDO study suggests that the use of levosimendan in patients with HF hospitalized with signs of low cardiac output implies a relatively low additional cost per life-year saved when compared with the use of dobutamine[15].

Multidisciplinary interventional strategies are efficient in reducing readmissions 90 days after hospital discharge, in addition to significantly lowering the costs when compared with the conventional treatment[16]. Multidisciplinary approaches involving the follow-up of patients with HF in day hospitals also seem to be cost-effective[17]. At last, few studies have assessed the cost-effectiveness ratio of ventricular assist devices or heart transplants. A study published over 15 years ago suggested the heart transplant cost of U$ 44,300.00 per life-year saved[14].

II. Definition of Decompensated Heart Failure (DHF)

Decompensated Heart Failure (DHF) is defined as a clinical syndrome in which a structural or functional heart abnormality leads to the incapacity of the heart to eject and/or accommodate the blood within physiologic pressure values, thus causing functional limitation and requiring immediate therapeutic intervention. This condition can be acute or it can be an exacerbation of chronic conditions, being classified as such in order to facilitate its terminology and to integrate the therapeutic objectives that are specific for each type of clinical presentation[18].

Table 1 - Heart Failure* in Brazilian Public Hospitals of the Brazilian Unified Health System

	Year 2000	Year 2001	Year 2002
Number of Hospitalizations (N)	393.559	381.446	368.783
Deaths (N)	25.911	25.101	25.639
Mortality Rate (%)	6.58	6.58	6.95
Hospital Stay (Days)	5.8	5.8	5.8
Total expenses (R$)	200.8 million	198.4 million	195.8 million

• ICD I50.0 for patients >15 years old

Table 2 - Independent predictors of rehospitalizations due to HF in different clinical trial

Clinical History	Old age
	Males
	Blacks
	Clinical comorbidities
	Frequent previous hospitalizations
	Long lasting symptoms
	Ischemic etiology
	Functional Classes III-IV
Physical Exam	Increased heart rate
	Low systolic arterial pressure
Complementary exams	Chronic atrial fibrillation
	Left bundle branch block
	Impairment of cardiac function
Treatment / Adherence	Inadequate treatment
	Nonadherence to the proposed treatment
	Social isolation

A. Acute Heart Failure (without a previous diagnosis) - corresponds to the clinical situation in which a certain aggression triggers the development of the clinical syndrome of heart failure in patients with no previous signs and symptoms of heart failure. Clinical conditions that exemplify this condition include acute myocardial infarction (with or without mechanical complications) and acute myocarditis. These represent the minority of hospitalization cases due to DHF.

B. Chronic Decompensated Heart Failure (acute exacerbation of a chronic condition) - corresponds to the clinical situation in which there is acute or gradual exacerbation of signs and symptoms of heart failure in patients at rest with a previous diagnosis of heart failure who require additional and immediate therapy. The vast majority of patients present signs and symptoms of congestion, which can be more or less clinically evident, but whose severeness is relevant enough to limit their physical activities in an incapacitating way. This clinical presentation represents, by far, the most important cause of hospitalization due to DHF.

C. Refractory Chronic Heart Failure (chronic low output or/ and various degrees of congestion) - corresponds to the clinical situation in which patients with a previously known diagnosis of heart failure present low output and/or systemic congestion and/ or persistent functional limitation refractory to the best possible clinical treatment.

D. Acute pulmonary edema - corresponds to the clinical situation in which there is a sudden increase in the pulmonary capillary pressure leading to an increase of fluid in the interstitial and alveolar pulmonary spaces which causes sudden and intense dyspnea at rest. Opposed to what is observed in the exacerbations of chronic heart failure, this situation usually occurs in patients with a preserved or slightly reduced systolic function. It occurs more often with elderly or patients with hypertension or diabetes.

E. Diastolic dysfunction or Heart Failure with preservation of Ejection Fraction - corresponds to the clinical situation in which there are signs and symptoms of heart failure due to a disturbance in the ventricular filling due to a marked reduction of ventricular distensibility and ejection fraction preserved at rest. It includes patients with hypertensive or hypertrophic cardiomyopathy with ventricles generally not dilated. The data available indicate that approximately 40% of the heart failure cases show this ventricular function pattern[19].

The clear difficulty to define and classify the clinical presentations of decompensated heart failure partially hampers the standardization of the limited therapeutic tools available, contributing to the poor results related to its management and the high rates of morbidity and mortality. The combination of difficult classification or terminology with the heterogeneity of the involved populations as well as the controversies about the therapeutic purposes to be reached (relief of symptoms and/or improvement of survival rate) also contribute to the difficulty in managing these patients[5,20].

III - Etiology and Pathophysiology of DHF

A. DHF due to systolic ventricular dysfunction

The most common cause of DHF in the clinical practice is the reduction of myocardial contractility, frequently associated with ischemic cardiomyopathy, idiopathic dilated cardiomyopathy, hypertensive cardiopathy or chagasic cardiopathy. Other causes of DHF are those in which the heart is subjected to hemodynamic overload (volume or pressure overload), disturbances of heart rate or conditions that might interfere with the ventricular filling. In most forms of DHF, the inadequate tissue perfusion is a consequence of the reduced cardiac output (CO). DHF can also be characterized as a multisystemic syndrome which includes abnormalities of the heart, skeletal muscle, renal and metabolic functions associated with the increased stimulation of the sympathetic nervous system and a complex pattern of neurohumoral and inflammatory changes[14].

The pathophysiology of DHF starts with a primary myocardial damage that produces ventricular dysfunction. This ventricular dysfunction triggers adaptive mechanisms associated with the neurohumoral stimulation and generates changes in the shape and mechanical efficiency of the heart (ventricular remodeling) and peripheral circulatory changes, as well as secondary damages due to the increased oxidative stress, inflammation and cellular death (apoptosis). The syndrome of DHF can evolve from a compensated and asymptomatic stage up to more advanced forms that cause DHF. Different determinants contribute to the performance of heart function, and some or many are involved in the development of heart failure decompensation, according to the main damage mechanism and time evolution.

The hemodynamic disturbances initially triggered in the DHF are associated with systemic neurohumoral changes (renin-angiotensin-aldosterone system, sympathetic system, vasomotor peptides such as endothelin-1 and nitric oxide) with repercussions at the cardiac tissue level in which the action of these factors leads to the apoptosis of myocytes and changes in the heart structure (extracellular matrix), characterizing the ventricular remodeling. In addition to this, there is recognized inflammatory activity associated with the progression of HF, in which the cytokines play important roles[21]. The vasodepressant proinflammatory cytokines (TNF-alpha, interleukin-6 and interleukin-1 beta) seem to be the most important ones in this process[22]. On the other hand, protective elements (vasodilators and diuretics) such as the natriuretic peptides, bradykinin and some prostacyclins are increased in the HF[23,24]. In cases of decompensation of HF there is evidence of greater activation of some of these systems, as for example, the levels of catecholamines and cytokines increase significantly.

B. DHF due to Ventricular Diastolic Dysfunction

Cases of heart failure with preservation of the ejection fraction are in this category. In spite of an important gap in studies involving this type of clinical presentation, the epidemiological data suggest that approximately 40% of cases of heart failure are included in this category. Two types of disturbances share the most important pathophysiological mechanisms in diastolic dysfunction: changes in the ventricular relaxation or compliance, although these phenomena might also occur jointly.

1. Diastolic Ventricular Dysfunction predominantly secondary to impaired relaxation - Diastolic dysfunction due to a reduction of the diastolic relaxation phase occurs in the presence of ventricular asynchrony, increased afterload, delay in the termination of contraction (disturbance in the recapture of calcium into the sarcoplasmic reticulum) and ischemia, since this is an active process that requires consumption of ATP. This type of alteration is predominant in such cases as hypertrophic cardiomyopathy, ventricular hypertrophy as a consequence of aortic stenosis, and hypertensive cardiopathy and myocardial ischemia.

2. Diastolic Ventricular Dysfunction predominantly secondary to reduced compliance - Three basic mechanisms contribute to reduce the ventricular compliance and alter the diastolic properties of the ventricules: 1) increase in the filling pressures (volume overload – aortic or mitral insufficiency); 2) increase of myocardial stiffness (infiltrative processes – amyloidosis, endomyocardial fibrosis, or myocardial ischemia); 3) extrinsic compression of the ventricle (pericardial tamponade, constrictive pericarditis).

Finally, in the context of dilated cardiomiopathy, there is a component of diastolic dysfunction even with an advanced systolic involvement. This is a restrictive pattern with low compliance found i association with large increases of ventricular volumes[25].

C. Acute Cardiogenic Pulmonary Edema

In this condition, a sudden increase of the filling pressures due to a reduction of the ventricular compliance or marked hypervolemia leads to the increase of capillary hydrostatic pressure and causes pulmonary edema[26]. Nevertheless, in cases of chronic HF, adaptive mechanisms might be in operation for a longer period and this might allow the chronic accommodation to the increased volumes, preventing acute pulmonary edema. Therefore, cardiomegaly may not be present in the acute pulmonary edema, and there might be a predominance of diastolic involvement with preservation or slight involvement of the ejection fraction. Examples of this type of condition include acute myocardial infarction and hypertensive crisis.

IV. Clinical and Laboratory Assessment of DHF

A. Primary Assessment of patients with DHF

In the initial clinical approach to the patient with a suspected case of DHF it is necessary that the doctor knows the clinical forms and the natural history of DHF. During the evolution course of the patient with chronic DHF we can observe three characteristic clinical patterns: 1 - chronic phase, during which the patient's symptoms are stable or slowly progressive; 2 - phase of rapid impairment due to acute decompensation or exacerbation, which can occur several times during the natural history of the disease, and frequently requires hospitalization; 3 - terminal or refractory phase, which responds poorly to the drug treatment and causes a markedly low quality of life[27].

1. Identification of patients with DHF

The patient with decompensated heart failure generally presents dyspnea and/or signs and symptoms of peripheral hypoperfusion and/or congestion of different importances[28,29].

The initial assessment must determine if it is acute heart failure secondary to a recent myocardial damage or if it is chronic decompensated heart failure. This differentiation is important, as it determines a different diagnostic and therapeutic management and implies different prognoses.

Tables 3 and 4 describe the main differential characteristics present in patients with acute HF versus decompensated chronic HF and systolic HF versus diastolic HF[30, 31].

2. Identification of causes and precipitating factors of DHF

The identification of the etiology of DHF is relevant as it can be potentially reversible, mainly in patients with acute HF. The prognosis can also be worse in some etiologies such as chagasic cardiomyopathy. For example: acute coronary syndromes, myocarditis, acute valvular dysfunction, hypertensive emergencies, bradyarrhythmias, tachyarrhythmias and cardiac tamponade.

In patients with decompensated chronic HF, in addition to the hypertensive, ischemic and valvular etiologies, other cardiomyopathies are also present such as chagasic, idiopatic, hypertrophic, restrictive and alcoholic. In this group, the search for the decompensation factors is essential in the clinical assessment because they can be identified and corrected in most patients, thus preventing new hospitalizations[32] (Table 5).

3. Assessment of volume and peripheral perfusion

The definition of the clinical/hemodynamic profile of the patient is systematization used to approach the patients with HF and may be important in the initial treatment, mainly without invasive monitoring procedures available. The patients can be divided into 4 subgroups, depending on the presence of congestion/edema and the quality of peripheral perfusion[29]: a) pulmonary congestion without signs of hypoperfusion (warm and moist skin); b) pulmonary congestion and signs of hypoperfusion (moist and cold skin); c) hypoperfusion without pulmonary congestion (dry and cold skin); d) absence of pulmonary congestion and hypoperfusion (dry and warm skin). The first 3 subgroups are of decompensated patients and the last one is composed of compensated patients. The assessment of the hemodynamic profile in these subgroups can be more accurately established, when indicated, by means of invasive hemodynamic monitoring.

B. Secondary assessment of patients with DHF

Soon after the initial assessment, the patient undergoes a secondary assessment in order to identify cardiac and laboratory structural changes which may have an impact in the treatment management.

Table 3 - Differential Characteristics of Acute DHF versus Chronic DHF

Characteristics	Acute HF	Decompensated Chronic HF
Dyspnea	Sudden onset	Exacerbated
Jugular venous pressure	Normal/Elevated	Elevated
Pulmonary rales	Frequent	Frequent
Peripheral edema	Rare	Frequent
Weight gain	Absent or Mild	Frequent
Cardiomegaly	Uncommon	Frequent
ECG	Normal/Acute abnormalities	Chronic abnormalities
Reversible lesion	Common	Occasional
BNP	Increased	Increased
Ejection fraction	Normal, increased or reduced	Frequently reduced
Hospital mortality	Depending on the cause	5-10%

Table 4 - Differential Characteristics of Systolic DHF versus diastolic DHF

Characteristics	Diastolic HF	Systolic HF
Age	Predominantly in the elderly	Any age, mainly 50-70 years
Gender	Predominantly in women	Predominantly in men
Gallop rhythm	S4	S3
LV Ejection Fraction	>. 45%	= 45%
LV Diameter	Usually normal or LV hypertrophy	Usually dilated
ECG - LVH	Common	Uncommon
ECG - LBBB, Grade III	Uncommon	Common
ECG - Old myocardial infarction	Uncommon	Common
ECG - Atrial ibrillation	Paroxysmal/Persistent	Persistent
Thoracic Teleradiography	Congestion with or without Cardiomegaly	Congestion and cardiomegaly
Preexistent conditions		
Arterial Hypertension	+++	++
Diabetes Mellitus	+++	++
Previous Myocardial Infarction	+	+++
Obesity	+++	+
Chronic Pulmonary Disease	++	0
Chronic Dialysis	++	0
In-Hospital Mortality	3-5%	5-10%
Rehospitalizations	50% in one year	50% in one year
Presentation Forms		
Acute HF	Hypertensive Acute Edema, occasionally Acute Myocardial Infarction	Myocardial Acute Infarction, Valvulopathies and Myocarditis
Decompensated Chronic HF	Hypertensive Acute Edema	Congestive Syndromes

0. absent, + little frequent, ++ frequent, +++ very frequent. LVH = Left Ventricular Hypertrophy; LBBB = Left Bundle Branch Block

1. Laboratory assessment and identification of structural abnormalities

Basic laboratory tests[33,34] such as hemogram, blood glucose, urea, creatinine, electrolytes and urine analysis are simple methods which help in the assessment of the severity of DHF and the presence of comorbidities that may have triggered the decompensation. Serial measurement of markers of myocardial necrosis, in addition to liver enzymes, TSH (in the absence of a defined etiology for HF and in cases where associated thyroid disease is suspected), serology for cardiotropic viruses, TTPa and INR are indicated in selected cases.

Thoracic teleradiography is a method that aids the identification of cardiomegaly, pulmonary congestion and in the presence of associated diseases, such as pneumonia or aortic dissection, which can be triggering factors or differential diagnosis of DHF[35].

The electrocardiogram is useful to identify ischemic cardiopathy, which is one of the main etiologies of DHF, as well as in the assessment of associated arrhythmias, atrioventricular conduction disorders and/or bundle branch blocks and cavity overloads. A normal ECG is uncommon in chronic HF[36].

Doppler ecocardiogram is one of the main non-invasive methods in the diagnosis of DHF since it can define the presence of systolic dysfunction, diastolic dysfunction or both, left and/or right ventricular involvement, associated orovalvular lesions, changes of segmental contractility, in addition to cavity dimension and thickness[37]. More recently, tissue Doppler imaging has been used to assess the diastolic function.

Nuclear cardiology, with myocardial perfusion scintigraphy with thalium or technetium (assessment of ischemia, necrosis and myocardial viability), radioisotopic ventriculography (to assess the left and right systolic and diastolic ventricular functions, as an alternative to echocardiography) and the use of gallium 67 (study of inflammatory activity, as in myocarditis) are helpful techniques in DHF[38].

Magnetic Resonance Imaging (MRI) has likewise been used as an auxiliary method in the anatomical and functional assessment in DHF both in its systolic and diastolic forms.

Among the invasive methods we should emphasize coronary arteriography, which is useful to define the coronary anatomy (ischemic etiology) for a better definition of the therapeutical strategy. The endomyocardial biopsy is important in suspect cases of myocarditis. Hemodynamic monitoring with a Swan-Ganz catheter is indicated in the pharmacologic management of DHF,

defining intracavitary pressures which will indicate the best therapeutic strategy to be used[39].

The degrees of recommendations and levels of evidence of the use of the initial complementary tests are shown in Table 6. More recently, and as a complement to the clinical assessment, the B-type natriuretic peptide (BNP) by means of a rapid measurement method (*point of care*) has been used as an important method in the differential diagnosis of dyspnea in the emergency room, in the diagnosis and in the prognostic assessment of HF as well as in the therapy follow-up. BNP is elevated both in cases of systolic and diastolic ventricular dysfunctions, with higher levels in the former one[40,41] (Table 7). More recently, pro-BNP has been studied in this context and, although it seems to be equivalent to BNP, there are still no definite data establishing its real role[42].

2. Assessment of the evolution pattern and treatment response

The initial care takes place at the Emergency Unit or at the Heart Failure Unit and the priority should be the acute syndromic treatment, by means of basic and advanced life support measures. The purpose is to maintain an adequate tissue perfusion, a reduction of congestion/edema, and a hemodynamic and respiratory status to prevent the impairment of the already existing conditions, and the occurrence of secondary lesions due to ischemia/hypoxia such as renal failure or ischemia of the Central Nervous System (CNS). Depending on the clinical status, the patient must be hospitalized (Table 8).

Table 5 - Precipitating Factors of DHF

Excessive salt and water intake
Nonadherence to treatment and/or no access to medication
Excessive physical activity
Acute atrial fibrillation or other tachyarrhythmias
Bradyarrhythmias
Systemic Arterial Hypertension
Pulmonary Thromboembolism
Myocardial Ischemia
Fever, infections
Increased room temperature
Anemia, Nutritional deficits, AV fistula, Thyroid dysfunction, Decompensated Diabetes
Excessive alcohol consumption
Renal Failure
Pregnancy
Depression
Substance Abuse (Cocaine, Crack, Ecstasy, among others)
Social Factors (Abandonment, Social Isolation)
Physician related factors
Inadequate prescription or insufficient doses (Different from those recommended in the Guidelines)
Lack of training in the management of patients with HF
Lack of adequate orientation to the patient regarding his/her diet and physical activity
Undetected volume overload (Lack of daily weight control)
Intravenous fluid overload during hospitalization
Drug-related factors
Digitalis Intoxication
Drugs that cause water retention or inhibit prostaglandins: NSAID, steroids, estrogens, androgens, chlorpropamide, minoxidil
Negative inotropic drugs: Group I antiarrhythmic agents, Calcium antagonists (except Amlodipine), Tricyclic Antidepressants
Drugs that are toxic to the myocardium: Cytostatic drugs such as Adriamicine > 400 mg/m^2
Self-medication, Alternative Treatments

NSAID = Nonsteroidal Anti-inflammatory Drugs

Following this stage and, often simultaneously with the described above, there is a stage of reassessment and follow-up of the therapeutic response. In this phase, hospitalization is indicated in one of the different units able to provide support to these patients – intermediary unit, intensive care unit, ward/private room, observational unit for HF, until the patient is discharged from the hospital.

Patients with decompensated chronic HF without using any medication or presenting hypertensive acute edema with normal systolic function respond promptly to oxygen therapy and to simple pharmacological therapy with intravenous diuretics and vasodilators. Consequently, it is possible to forecast for this group a low complexity, low cost and a favorable evolution. Patients with acute HF due to cardiogenic shock from myocardial infarction, valve disease or myocarditis and those with refractory HF require a complex management, associated with high costs and specialized approaches, supported by an infrastructure that assures intensive care with inotropic and/or vasodilator agents, invasive hemodynamic monitoring, assisted circulation devices, hemofiltration/dialysis, ventilatory support, heart surgery and a complete specialized team with high technology, in addition to a lengthy hospitalization.

Adherence to clinical, hemodynamic and respiratory parameters must be adequate to the patophysiological model of DHF. In any context, the follow-up and assessment of the vital parameters must be performed with the help of non-invasive monitors with a large capacity for records/memory and preferably with the possibility of detecting ventricular arrhythmias, atrial fibrillation and deviations from the standard ST-T segment. The following data must be monitored: daily weight, blood pressure, heart rate and rhythm, respiratory frequency and pattern, pulse oximetry, assessment of the subjective degree of respiratory discomfort, consciousness level and urinary output, by means of which the renal perfusion is indirectly assessed.

The objectives of drug therapy are to achieve, whenever possible, the end of orthopnea, normal jugular venous pressure, re-

Table 6 - Degrees of Recommendations and Levels of Evidence for the use of the initial complementary tests

Complementary Tests	Recommendation Degree	Level of Evidence
1. Basic Laboratory Tests, Hemogram, glycemia, electrolytes, urea, creatinine, hepatic enzymes, TSH and urine test. Markers of myocardial necrosis in suspected cases of acute coronary syndrome	I	C
2. Thoracic Teleradiography	I	C
3. 12-lead Electrocardiogram	I	C
4. Bidimensional Transthoracic Doppler Echocardiography	I	C

Table 7 - Degrees of Recommendations and Levels of Evidence for the use of BNP in DHF

Condition	Degree of Recommendation	Level of Evidence
Differential Diagnosis	IIa	B
Therapeutic Follow-up	IIa	B
Prognostic Evaluation	IIa	C

BNP = Type B Natriuretic Peptide

duction of peripheral and pulmonary edemas (absence of rales and pleural effusion), systolic pressure >80 mmHg and pulse pressure of at least 25%, stable renal function and ability to walk without dizziness or dyspnea.

Frequent monitoring of the renal function is important because 25% of the patients with DHF have their renal functions impaired during hospitalization. High levels of urea and creatinine, as well as hyponatremia, are associated with worse intra or out-hospital survival. Cardiorenal syndrome in DHF is a factor refractory to treatment and maintenance of pulmonary and systemic congestion. It can sometimes determine the discontinuation of the treatment with ACE-I or antagonists of AT1 receptors and of spironolactone, in case the creatinine levels are maintained above 3 mg%[43,44]. Some patients may present impairment of the renal function due to hypovolemia as a consequence of excessive use of diuretics.

New noninvasive techniques such as bioimpedance, implantable monitors and measurement of BNP are being tested to assess the importance of monitoring the effects of the therapeutics adopted and its impact on the morbidity-mortality of DHF.

Recent evidence points to the prognostic importance of measuring troponins, whose increased values are related to higher rates of in-hospital mortality[45]. Troponins are useful to detect a myocardial infarction not diagnosed two weeks before, because their levels remain high even when other markers are normal again.

Patients with HF and preserved systolic function require a different approach related to the control of hypertension, myocardial ischemia, and heart rate, particularly when atrial fibrillation is present. The reduction of the ventricular filling pressures is necessary for the improvement of the symptoms; however, the excessive use of diuretics and vasodilators can cause arterial hypotension, syncope, fatigue and a negative repercussion in renal function.

Once the criteria for compensation and clinical stability are reached, the patient may be discharged from the hospital. Table 9 lists the criteria adopted for hospital discharge of patients with DHF. In terms of hospital discharge, the improvement of the functional class has traditionally been used, and the patient must preferably be in functional class I or II of NYHA during the use of oral medication, and stable weight and arterial blood pressure and creatinine and urea levels as well as the absence of frequent or progressive angina, symptomatic ventricular arrhythmias and/or firing of the implantable cardioverter-defibrillator (ICD). Some very serious patients do not reach these classes and they may be discharged even in functional class III provided they can be free of intravenous medication. Recently, the use of BNP levels has been suggested as a criterion for hospital discharge. Values of BNP <430 pg/ml at the time of hospital discharge have shown to be a good predictive value that is negative for readmission.

At the time of hospital discharge, the patient shall preferably be referred to an HF clinic, since this strategy reduces the rates of hospital readmissions.

3. Prognostic Assessment (Table 10)

In DHF, the prognosis will depend on the severity of the baseline disease[46]. While in the acute ischemic syndromes these parameters are well defined (Killip-Kimball classification, Forrester classification, clinical, electrocardiographic and laboratory data, left ventricular function and presence of ventricular arrhythmias, etc.), they are not yet defined in other etiologies. In decompensated chronic heart failure there are numberless prognostic factors described, emphasizing clinical, hemodynamic, neurohumoral and inflammatory markers.

V. General Treatment

A. General Measures (Table 11)

1. Physical Activity: Patients with DHF must be encouraged to practice neither routine physical activities nor complete rest;

Table 8 - Criteria for Hospitalization

Criteria for Immediate Hospitalization
Pulmonary edema or respiratory discomfort in the sitting position
Arterial oxygen saturation < 90%
Heart rate >120 bpm in the absence of chronic atrial fibrillation
Systolic arterial pressure ≥ 75mmHg
Mental abnormality attributed to hypoperfusion
Decompensation in the presence of acute coronary syndromes
Acute DHF
Criteria for emergency hospitalization
Serious hepatic distension, large volume ascites or anasarca
Decompensation in the presence of acutely decompensated noncardiac conditions, such as pulmonary disease or renal dysfunction
Rapid and progressive onset of heart failure symptoms
Consider hospitalization
Rapid decrease in serum sodium below 130 mEq/L
Rapid increase in creatinine, above 2.5 mg/dl
Persistent symptoms at rest, in spile of optimized oral treatment
Comorbidity with expected impairment of HF

Bpm = Beats Per Minute

Table 9 - Criteria for Hospital Discharge

Criteria for Hospital Discharge
Improvement of the Functional Class (NYHA) with treatment and maintenance of this Functional Class in the presence of oral medication
30% reduction in BNP associated with resolution of signs/symptoms of DHF (if available)
Controlled baseline disease
Correction of precipitating factor
Absence of the Factor which caused hospitalization
Absence of significant malperfusion
Absence of congestion in physical exam

BNP = Brain Natriuretic Peptide

Table 10 - Determinants of poor prognosis in Decompensated Chronic HF

Elderly (>65 Years Old)
Hyponatremia (Sodium <130mEq/L)
Progressive elevation of creatinine
Anemia (Hemoglobin <11g/dL)
Signs of peripheral hypoperfusion
Cachexia
Complete LBBB
Atrial Fibrillation
Restrictive Pattern on Doppler
Persistent BNP increase in spite of treatment
Persistent Congestion
Persistent S3
Sustained Ventricular Tachycardia or Ventricular Fibrillation

LBBB = Left Bundle Branch Block

the physical activity must be customized according to the patient's diagnosis and clinical status. During the episodes of acute decompensation, the patients must remain at rest according to their limitations.

2. Oxygen: Initially, the routine use of supplementary oxygen therapy is recommended with the purpose of maintaining an adequate O_2 saturation (≥ 90%). In the setting of pulmonary congestion, CPAP is recommended, as it is a non-invasive and effective measure to reach the desired O_2 saturation.

3. Water and salt restriction: In patients in a congestive status, the liquid intake must be restricted according to the body surface, attempting to reach an initially negative water balance until a normovolemic status is attained. The amount of the maximum restriction can be up to 600-700 ml/m^2 body surface/day. The maximum sodium ingestion can be 2-3 g/day and this can be modified according to serum sodium and tolerance to a low sodium diet.

4. Nutrition: The patient must have a protein-calorie intake that meets his/her needs and that is adequate to his comorbidities. The routine use of superalimentation or dietary supplements is not indicated.

B. General Pharmacological Treatment

1. Diuretics (Table 12)

Intravenous diuretics are indicated to all patients with pulmonary and/or systemic congestion, whose severity results in hospitalization, since the reduced intestinal perfusion, reduced intestinal motility and edema of the intestinal loops all reduce the oral absorption of the drug. This defect is reversible after control of the edema with intravenous therapy and it further allows the use of oral administration[47].

Treatment must be performed with loop diuretics and the dose must be individualized, in order to reduce the patient's congestive status and at the same time carefully avoiding hypovolemia. Diuretics, especially those of the loop type, can alter the hydroelectrolytic status, which must be monitored. After the congestive status is resolved, the maintenance treatment by oral administration is initiated, in order to prevent the recurrence of liquid accumulation[48-51].

Some patients develop resistance to diuretics, which is characterized by absence of an adequate response to the usual doses of the drug. The treatment of diuretic resistance starts with the increase of the serum level and, consequently, of the rate of urinary excretion of the drug, and increasing the dose of the diuretic up to its maximum effective dose, and/or addition of a diuretic with a different site of action. High doses must be administered slowly in 30-60 minutes in order to reduce the risk of ototoxicity. The initial bolus administered intravenously to a patient with chronic use of diuretics must be 50% of the previous total oral dose. Afterwards, a continuous infusion of furosemide can be started in a dose of 20 mg/h. If diuresis is not maintained, a second bolus is administered and followed by an infusion of 40 mg/h. The risk of further increasing the infusion must be weighed against the other options such as hemofiltration or ultrafiltration procedures. In such cases, the continuous infusion, when compared with the intermittent bolus administration, has been shown to be as effective and potentially safer in terms of adverse effects[52]. For furosemide, the maximum effective intravenous daily dose is 80-120 mg. If concomitant renal failure is present, the dose can be 160-240 mg and in the presence of serious acute renal failure the dose can be up to 500 mg.

2. Aldosterone Antagonists (Table 12)

Spironolactone must be used in association with the standard treatment of DHF, with a recommended mean dose of 25 mg per day; the serum levels of potassium and creatinine must also be monitored. With serum levels of potassium between 5.0 and 5.5 mEq/L the dose should be reduced, as well as other medications that might cause hyperkalemia. Potassium levels above 5.5 mEq/L require suspension of the drug[53,54]. This drug is not recommended for patients with serum creatinine above 2.5mg/dL.

Eplerenone is an antagonist of aldosterone which has shown to be effective in the treatment of patients with post-infarction

Table 11 - General Measures

Indication	Class	Grade
Physical activity individualized according to patient's diagnosis and clinical condition. Bed Rest during acute decompensation	I	C
Routine use of supplementary oxygen therapy with the purpose of maintaining an adequate O_2 saturation (=90%)	I	C
CPAP or BIPAP for patients with pulmonary congestion who did not respond to initial measures or acute pulmonary edema	I	B
Water restriction up to 600-700 ml/m^2 body surface/day trying to achieve an initially negative water balance until a normovolemic status is reached	I	C
Maximum sodium ingestion 2-3g/day; it can be modified according to serum sodium.	I	C
Protein-calorie intake to meet the patient's needs and adequate to his/her comorbidities	I	C
Use of routine dietary supplements	III	C

Table 12 - Diuretics and aldosterone antagonists

Indication	Class	Grade
Intravenous diuretics to all patients with pulmonary and/or systemic congestion	I	C
Continuous infusion of loop diuretics to patients resistant to diuretics	IIa	C
Association of loop diuretics and thiazides in patients resistant to diuretics	I	C
Spironolactone in patients with preserved renal function (Creatinine <2.5)	I	B
Eplerenone in patients with DHF after acute myocardial infarction	I	B
Eplerenone in patients with non-ischemic dilated cardiomyopathy who do not tolerate spironolactone due to gynecomastia	IIb	D

heart failure[55]. Although it has not been studied yet in cases of DHF, this drug could be used in patients who develop gynecomastia due to spironolactone.

3. Intravenous Peripheral Vasodilators (Tables 13 and 14)

Patients with DHF frequently need pharmacological support with vasoactive drugs in an attempt to improve their heart performance, reduce the filling pressures and systemic and pulmonary vascular resistance, facilitate diuresis and promote clinical stability. Vasodilator drugs for intravenous use in heart failure available in Latin America are sodium nitroprusside, nitroglycerin and prostacyclin. Nesiritide is still not marketed in this region. These drugs are preferably used in situations of high ventricular filling pressures, significant increases of pulmonary and systemic vascular resistance, in addition to acute volume overload secondary to regurgitant valvular lesions (mitral and aortic insufficiency)[56]. They can increase the cardiac output and diuresis as a consequence of the vasodilator effect. To use them isolatedly it is necessary that the systemic arterial pressure is adequate and ideally ≥ 85 mm Hg.

a) Nitroglycerin: It is a direct vasodilator that acts by means of the increase of intracellular GMPc. In low doses, it has a predominantly venodilator effect and its arterial vasodilator effect is observed with higher doses. It is helpful in the treatment of heart failure, both by reducing pulmonary congestion and also by increasing coronary blood flow. Like other nitrates, it can produce reflex tachycardia, headache and hypotension. Its continuous use is not recommended due to pharmacological tolerance. In emergency situations, it is very practical because of its immediate action onset and end, allowing for more precise dose adjustments according to the patient's hemodynamic status. The initial dose is 0,5µ g/Kg/min, and it can be increased every 5 minutes until the control of the symptoms and the limitating side effects is attained.[57]

Its use is particularly helpful in cases of myocardial ischemia without hypotension. Nitroglycerin use is not recommended for patients with right ventricular dysfunction.

b) Sodium Nitroprusside: It is a powerful arterial and venous vasodilator, extremely important to manage heart failure in the presence of arterial hypertension and/or major regurgitation (mitral or aortic) by reducing the afterload that it promotes. It improves the left ventricular performance, and it also has a pulmonary artery vasodilator effect which reduces the right ventricular afterload. As it is rapidly metabolized into cyanide, which is further transformed by the liver into thiocyanate, it must be used with caution in patients with renal and/or liver dysfunctions. Its extended use may require the monitoring of the serum levels of thiocyanate (toxic level >10 ng/mL). The initial dose is 0.2µ g/Kg/minute, titrated every 5 minutes until hemodynamic improvement. Since it requires continuous monitoring of the arterial pressure, its use is almost always restricted to the emergency room or to the ICU.

4. Inotropic Agents

Inotropic therapy in patients with low cardiac output may be necessary to improve the tissue perfusion[58,59]. Its hemodynamic action and indication with levels of evidence are described in Tables 15 and 16.

The inotropic agents are divided into 3 categories: beta-adrenergic agonists, phosphodiesterase III-inhibitors and calcium sensitizers.

a) Agents that stimulate beta-adrenergic receptors (dopamine, dobutamine, norepinephrine, isoproterenol, epinephrine). Beta-adrenergic agonists stimulate the beta receptor in the heart to increase the levels of the second messenger cyclic AMP (cAMP), thus generating the signal for increasing the intracellular calcium and producing a positive inotropic effect. Dopamine and norepinephrine must be used if serious hypotension is present. Dobutamine is indicated in cases of low cardiac output and tissue hypoperfusion, and it can be associated with dopamine or norepinephrine. There are various adverse effects related to the increased intracellular influx of calcium produced by the beta-adrenergic stimulation: increased energy consumption, myocardial ischemia, cardiac arrhythmias, activation of intracellular proteases, endonucleases and phospholipases, which are part of the process of cellular death and necrosis[60,61]. Additionally, drugs that increase the levels of cAMP lead to a decreased sensitivity to calcium by means of phosphorylation of troponin-I. These actions can result in adverse clinical effects[62-65].

b) Phosphodiesterase Inhibitors: Phosphodiesterase inhibitors act by inhibiting the degradation of cAMP, thus increasing the availability and concentration of calcium in the cells, as well as inotropism[66]. They also have a peripheral vasodilator effect by means of their action on the cGMP and the production of nitric

Table 13 - Hemodynamic Effects of Vasodilator Agents

Agent	CO	PCP	SAP	HR	Arrhythmia	Onset of action	Duration of effect	Diuresis
Nitroglycerin	-	↓↓↓	↓↓	-	No	Rapid	Short duration	(Indirect)
Sodium Nitroprusside	-	↓↓↓	↓↓↓	-	No	Rapid	Short duration	(Indirect)

CO = Cardiac Output; PCP = Pulmonary Capillary Pressure; SAP = Systemic Arterial Pressure; HR = Heart Rate; indirect = indirect

Table 14 - Indication of Intravenous Vasodilators in DHF

Indication	Class	Grade
Nitroglycerin - Treatment of DHF associated with coronary insufficiency in patients without hypotension	I	B
Nitroprusside - Treatment of DHF associated with emergency hypertension in patients with continuous monitoring of systemic arterial pressure	I	B
Nitroprusside in patients using invasive hemodynamic monitoring and increased peripheral vascular resistance associated or not with inotropic agents	I	B

Table 15 - Hemodynamic Effects of Inotropic and Vasopressor Agents

Drug	CO	PCP	AP	HR	Arrhythmia	Onset of Action	Duration of Effect	Diuresis
Dopamine	0	0	0	0	0			
< 3µ G/Kg/Min	+	0	+	+	++	Rapid	Short	++
3-7µ G/Kg/Min	++	0	++	++	+++			+/-
7-15µ G/Kg/Min								0
Dobutamine	+++	-	-	+	++	Rapid	Short	0
Milrinone	++	-	-	+	++	Rapid	Short	0
Levosimendan	+++	---	-	0	0	Rapid	Prolonged	++
Epinephrine	++	0/+	+++	+++	++++	Rapid	Short	0
Norepinephrine	++	0/+	+++	++	+++	Rapid	Short	0
Isoproterenol	+++	0/+	0/-	+++	+++	Rapid	Short	0

CO = Cardiac Output; PCP = Pulmonary Capillary Pressure; AP = Systemic Arterial Pressure; HR = Heart Rate; 0 = No Direct Action, although it can have an indirect influence; Short = Loss of Rapid Action After Interruption of Infusion

Table 16 - Indications of Inotropic Agents

Clinical Indication	Dobutamine	Milrinone	Levosimendan
Treatment for a short period of decompensated patients with Low Cardiac Output Syndrome, unresponsive to usual treatment, without hypotension	IIa/C	IIb/C	IIa/B
Treatment for a short period of decompensated patients with Low Cardiac Output Syndrome and serious hypotension (≤80 mmHg)	IIa/B	IIb/B	IIb/D
Treatment for a short period of patients with DHF, with insufficient response to initial intravenous optimization therapy (impairment of renal function, persistent dyspnea and/or edema)	IIa/C	IIb/C	IIa/B (UP TO)
Intermittent infusion with the purpose of improving the symptoms in patients with refractory disease, compromised life quality, frequent rehospitalizations or persistent Functional Class IV, without indication of heart transplant	III/B	III/B	III/D

oxide. They can be used with or without a loading dose, with a higher occurrence of hypotension with this dosage. Inodilator agents must be used with caution in patients with serious hypotension. Recent studies have demonstrated that the use of milrinone in patients with DHF, but without low cardiac output, increases the incidence of atrial fibrillation and hypotension[66].

With the increasing number of patients with DHF using beta-blockers, the therapy with phosphodiesterase inhibitors can be more attractive, as it does not compete with beta-adrenergic receptors. However, data for such recommendation are still insufficient in this specific situation[67].

c) Calcium Sensitizers: These drugs compose a new therapeutic class for the treatment of DHF, represented by pimobendan and levosimendan; only the latter is available in Latin America. This agent performs its inotropic action by increasing the sensitivity of troponina-C to calcium already available in the cytoplasm with neither any additional calcium overload nor increased oxygen consumption[68,69]. Levosimendan increases myocardial contractility and hemodynamics in a level comparable with the one observed with beta-agonists and phosphodiesterase inhibitors and it has a vasodilating action resulting from the activation of ATP-dependent potassium channels[70-72]. In randomized clinical trials, it was associated with lower mortality both in short and long-term follow-ups[73,74]. In the presence of a beta-blocker, the hemodynamic effects of levosimendan are potentialized when compared with dobutamine.

5. Digitalis (Table 17)

No major study has been performed about the effect of digitalis on DHF. In patients with atrial fibrillation (AF) and high ventricular response, the use of this agent reduces HR and can contribute to clinical improvement.

6. Angiotensin-Converting Enzyme Inhibitors (ACE-I) (Tables 17 and 18)

Angiotensin-converting enzyme inhibitors (ACE-I) reduce the pulmonary capillary pressure, leading to a decrease in the preload and systemic arterial pressure, thus reducing the afterload[75]. In the short run, these effects are desirable and can accelerate the compensation and improvement process of the symptoms.

Studies in patients with CHF functional classes III and IV demonstrate that ACE-I have a strong impact in the life quality and long-term survival[76,77], which allows us to conclude that these drugs must not be suspended in the decompensated phase, except in cases of hyperkalemia, marked impairment of renal function or major and refractory hypotension.

The initial dose must be low (especially if the patient needs to be hospitalized, if there is hypotension or if impairment of renal function is present [creatinine = 2.5 mg%]) and it must be gradually titrated until the ideal dose is reached. If the patient is already using the drug and its administration has been interrupted, the drug should be re-introduced in the same way. The ideal dose is the same as for patients with chronic CHF (Table 17). In patients using intravenous inotropic agents and vasodilators, it is recommended that the ACE-I be introduced before the withdrawal of those drugs.

7. Angiotensin-II Receptor Antagonists (Table 17)

This drug class has not been tested in the treatment of DHF. Due to its long-term benefits on mortality, the maintenance of the same dose previously used is recommended, except if hyperkalemia, marked impairment of renal function, and major and refractory hypotension are present. The indication is for patients who do not tolerate ACE-I.

8. Heparins (Table 17)

Low molecular weight heparins or unfractionated heparins should be used in immobilized patients in order to prevent deep vein thrombosis and pulmonary embolism, with the following subcutaneous doses: unfractionated heparin (5,000 IU twice a day), nadroparine (0.3 mL once a day), enoxaparin (40 mg once a day) and dalteparin (200 IU/kg once a day).

9. Beta-blockers (Table 17)

In patients with chronic use of beta-blockers it is advisable not to suspend the drug even for those who need inotropic drugs, except in cases of marked hypotension, bradyarrhythmia or other serious side effects. The risk of rebound effect is undesirable, especially in cases of myocardial ischemia. Additionally, there is new evidence that patients who use beta-blockers benefit its maintenance[78], with a potential benefit of these drugs in preventing in-hospital sudden death.

In class IV CHF patients (NYHA), even in those treated with intravenous inotropic agents up to 2 days before, the careful introduction and titration of the beta-blocker dose can be well tolerated[79,80].

Table 17 - Indication of Digitalis, ACE-I, ARA-II, Heparin, β-blocker, Hydralazine + Nitrate and Amiodarone for DHF

	Class	Grade
Digitalis		
Systolic dysfunction and atrial fibrillation with rapid ventricular response	I	B
Systolic dysfunction in sinus rhythm	IIa	C
ACE-I		
Systolic dysfunction	I	B
AARA-II		
Systolic dysfunction with intolerance to ACE-I	I	D
Heparin		
Heparins in prophylactic doses	I	D
βeta-blockers		
Maintenance	IIa	C
Introduction with signs of congestion	III	D
Hydralazine + nitrate		
Intolerance to ACE-I or ARA-II	IIa	D
Renal failure (Cr > 2.5)	I	D
Amiodarone		
HR > 90 bpm especially in non ischemic cardiomyopathy	IIa	B
Atrial fibrillation, to control ventricular rate	IIa	C
Frequent symptomatic and/or complex ventricular arrhythmia	IIa	D
Others:		
Vasopeptidase Inhibitors (INEP, endothelin antagonists, prostacyclin, etanercept)	III	B

ACE-I = angiotensin-converting enzyme inhibitors; ARA-II = angiotensin-II receptor antagonists; cr = creatinine (mg/dl); HR = heart rate

Table 18 - Initial dose and maximum target dose of angiotensin-I converting enzyme inhibitors

Drug	Initial Dose	Target Dose
Captopril	6.25 mg b.i.d.	50 mg t.i.d.
Enalapril	2.5 mg b.i.d.	10 mg b.i.d.
Ramipril	1.25 mg b.i.d.	5 mg b.i.d.
Lisinopril	2.5 mg o.d.	10 mg o.d.
Trandolapril	1 mg o.d.	2 mg o.d.
Benazepril	2.5 mg o.d.	10 mg o.d.
Fosinopril	5 mg o.d.	20 mg o.d.
Perindopril	2 mg o.d.	8 mg o.d.

C. Drugs for selected patients (Table 17)

1. Hydralazine and nitrates

There are no studies with this association in which class IV or decompensated patients have been specifically included. Nevertheless, the possibility of a similar effect between enalapril and the association of dinitrate and hydralazine is an attractive one, especially in the patient with an ischemic etiology. The use of this association is justified because it has been demonstrated that hydralazine prevents the development of tolerance to nitrates. However, the dosing regimen of this association is more complex[81], and there is no evidence of benefits when such drugs are used isolatedly[82-86].

2. Amiodarone

The oral use of low doses of this drug is well tolerated; however, the intravenous use of higher doses requires closer observation, especially in DHF due to the risk of hypotension. Amiodarone is indicated in DHF for the control of ventricular response in patients with AF, chemical cardioversion of AF and treatment of frequent and/or complex ventricular arrhythmias[87,88].

A reduction in hospitalization time was noticed, mainly in functional class IV, which showed an improvement[89,90]. In patients with HR >90 bpm the use of amiodarone may be beneficial[90], probably because of the antiadrenergic effect. More recently, small case series have demonstrated the benefits of amiodarone in patients with heart failure who did not tolerate beta-blockers[91].

D. Drugs or procedures under investigation (Table 17)

1. Nesiritide

Recently approved in the U.S.A., it is a recombinant human B-type natriuretic peptide with natriuretic effect, partly due to the inhibition of aldosterone and vasodilation. Nevertheless, it is still unavailable in Latin America. The studies have shown a greater reduction in pulmonary capillary pressure when compared to nitroglycerin[92-95], with no increase of baseline heart rate and with no proarrhythmic effect[94]. A non-blind study suggested that nesiritide can reduce costs and mortality when compared with dobutamine[96].

A recent metanalysis raised doubts about the drug safety in relation to its effects on short-term mortality[97], but more delineated studies are necessary to assess the mortality, even though the studies suggest that nesiritide is helpful in dealing with DHF patients.

2. Vasopressin Antagonists

These drugs block V1, V2 or both receptors. Several drugs are being tested and they are showing their usefulness to control patients in advanced stages of the disease, when vasopressin is especially high. Vasopressin antagonists are indicated in patients with edema, low serum sodium, a condition in which the conventional treatment has shown little efficacy[98-100].

3. Cytokine Antagonists

The attempt to counteract the tumor necrosis factor alfa with the use of etanercept and other cytokine antagonists did not yield effective results[101,102]. It has been suggested that pentoxifylline

and thalidomide can be useful to treat HF. Preliminary studies have demonstrated that pentoxifylline and thalidomide reverse ventricular remodeling, and one mechanism of this action is mediated by reducing the levels of tumor necrosis factor alfa[103,104].

4. Growth Hormone (GH)

There is evidence of resistance to GH action in HF. Preliminary results of the administration of GH in cachectic patients seem to determine some clinical improvement and optimization of the treatment[105]; however, randomized studies are necessary to assess its real effect[106,107]. It must be used with caution in patients at risk for cancer or with arrhythmias.

5. Use of bone marrow progenitor cells

Heart regeneration by means of progenitor cells obtained from the bone marrow through aspiration or from the peripheral blood after mobilization, or simply with mobilization, has been investigated in patients with refractory heart failure caused by chagasic, ischemic and dilated cardiomyopathy. The cells obtained can be injected by intracoronary, transendocardic or transepicardic routes, by the coronary venous sinus or during surgery. Preliminary results of non-controlled studies have demonstrated some benefits in DHF[108-111].

E. Drugs of nonconfirmed efficacy (Table 17)

1. Vasopeptidase Inhibitors (INEP)

Ecodatril, candoxatril and omapatrilate are drugs which block the enzyme responsible for degradation of the natriuretic peptides and, theoretically, could offer similar benefits to those with the administration of neseritide in DHF. There are no studies about DHF with these drugs and, in compensated CHF there are no evidences of possible benefits yet[112].

2. Endothelin Antagonists

Although endotheling antagonists such as bosentan, sitaxsentan, darusentan, tezosentan and enrasentan have a beneficial hemodynamic effect, their use in humans has not shown any benefits[92,113].

3. Prostacyclin

The results with the use of prostacyclin (epoprostenol) for the treatment of HF have shown an impairment of the survival and the study was cut short[112,114].

VI. Assessment and treatment of special populations

A. Patients with confirmed or suspected Coronary Heart Disease (CHD) (Table 19 and 20)

The definition of DHF etiology results in significant prognostic and therapeutical implications with an emphasis on ischemia. It has been demonstrated that the etiology of heart failure can be considered a major determinant of long-term survival. Thus, patients with an ischemic etiology in general present worse prognoses when compared with non-ischemic patients[1,2,3,114-116]. It is not known if the relationship between etiology and evolution can be applied in the context of the decompensated disease; however, unpublished data from the study called OPTIME CHF[4,66] suggest that patients with ischemic cardiomyopathy have a worse short-term prognosis when compared with patients with another etiology.

It is also believed that CHD accounts for two thirds of the patients with heart failure due to left ventricular systolic dysfunction[5,17]. Thus, it seems to be useful to define the presence, the anatomical characteristics and the functional significance of CHD in selected cases that present such syndrome. Considering that, for most patients with acute ventricular failure, ischemia is the major cause of reduced myocardial contractile reserve and that, in many patients this process represents the hibernation or stunning (potentially reversible conditions) just as the treatment of ischemia, the rapid control of the ischemic event must be the treatment target.

The initial clinical and laboratory evaluation of ischemia in patients with decompensated heart failure includes the access of the functional and hydric status, early biochemical and hematological tests, in addition to the electrocardiogram and thoracic teleradiography.

Early echocardiographic assessment is important to appraise the regional ventricular function and to identify any mechanical complication, such as serious valve damage, or septum or free wall tears, as the causes of the acute dysfunction. The presence of one of these complications requires immediate surgical repair after clinical stabilization.

Patients with CHD and ischemia – It is well established that the coronary artery bypass graft improves the evolution of patients with heart failure and ischemia. Since the revascularization is recommended in individuals with ischemic thoracic pain, in spite of the degree of ischemia or viability, a small role could be attributed to non-invasive tests in these patients. Coronary angiography should be directly performed in patients with angina and ventricular dysfunction.

Patients with CHD without ischemia – It is unclear if myocardial revascularization can improve the symptoms and survival in patients with heart failure who do not have myocardial ischemia. However, revascularization is recommended in patients with significant stenosis of the left coronary branch and in those with large non-infarcted but low perfusion areas presenting a hypocontractile myocardium in noninvasive tests.

Patients with undefined thoracic pain – Over one third of the patients with non-ischemic cardiomyopathy complain of thoracic pain. Coronary angiography is generally recommended since revascularization has a positive effect in ischemic pain. Nevertheless, noninvasive tests are common before coronary angiography in this population since heterogeneous nuclear images and abnormal ventricular motility patterns are frequent in cases of non-ischemic cardiomyopathy.

Repetitive invasive and noninvasive tests are not indicated for patients in which CHD was excluded as a cause of left ventricular dysfunction.

In the case of DHF, myocardial ischemia may play an important role as a decompensating agent. Patients with demonstrated ischemia require appropriate anti-ischemic therapy including aspirin, heparin, glycoprotein IIb/IIIa inhibitors, as well as strategies of

Table 19 - Assessment of patients with suspected or confirmed Coronary Heart Disease		
	Recommendation	Level of Evidence
Ability to perform regular activities	I	C
Volemia	I	C
Initial Hematologic and Biochemical Evaluation	I	C
Initial ECG and Thorax Radiography	I	C
Initial Echocardiogram and Radioisotopic Ventriculography to assess left ventricular function	I	C
Coronary Angiography in patients with known coronary disease and possible candidates to myocardial revascularization	IIa	C
Coronary Angiography in patients with ischemia not previously investigated and without contraindications to revascularization	I	C
Coronary Angiography in patients with suspected or confirmed coronary disease, without ischemia	IIa	C
Noninvasive Imaging Exams to detect ischemia and viability in patients with known coronary disease after stabilization	IIa	C

Table 20 - Procedures or Therapeutic in Patients with Ischemic DHF		
	Recommendation	Level of Evidence
Reperfusion in acute myocardial infarction with ST elevation	I	B
Optimized clinical therapy and percutaneous coronary intervention in acute myocardial infarction/unstable angina with no segment elevation	I	B
Nitrates and aspirin in patients with DHF and angina	I	B
β -blockers in patients with DHF (after stabilization)	IIa	C
Calcium Channel Antagonists (amlodipine) in patients with DHF (when β-blocker is contraindicated)	IIb	C
Intraortic balloon	I	B
Myocardial revascularization in patients with coronary disease and ischemia	I	A
Myocardial revascularization in patients with coronary disease and asymptomatic ischemia	IIa	B

myocardial revascularization concurrently with the management of decompensation. New therapies are bein studied[117,118] for the management of DHF in the setting of myocardial ischemia.

Patients with ST segment elevation myocardial infarction must undergo prompt primary percutaneous coronary intervention. Another option if percutaneous intervention is not available, is the thrombolytic therapy. In cases of non-ST segment elevation myocardial infarction, maximum anti-ischemic therapy must be initiated, followed by risk stratification and percutaneous coronary intervention, if possible. The placement of an intra-aortic balloon as a method of immediate reduction of the ischemic phenomenon and as a device to improve the cardiovascular performance is highly effective in the treatment of heart failure secondary to refractory myocardial ischemia.

It is recommended that, after initial stabilization, the patients who evolve with heart failure during an ischemic event be submitted to immediate coronary angiography, followed by complete revascularization due to the serious combination of both syndromes. For patients with DHF who do not show signs of ischemia, an early test to assess both viability and ischemia is recommended (either scintigraphy or stress echo test with dobutamine), considering the possibility of angiography.

After stabilization, drug therapy must be introduced in low doses and titrated up to maximum doses in order to avoid hypotension and vasodilation. Angiotensin-converting enzyme inhibitors (ACE-I) are currently the only class of agents with established benefits in this setting[119, 120]. These agents can be substituted by angiotensin receptor antagonists if side effects occur. Beta-blockers, which are extremely beneficial in the long-term treatment of HF, should be administered to patients with DHF only when the clinical condition is fully compensated. Calcium channel blockers, which also present negative inotropic effects, must be avoided.

B. Cardiogenic Shock after Acute Myocardial Infarction (Table 21 and 22)

1. Diagnosis

Cardiogenic shock is characterized by serious arterial hypotension (systolic pressure <90 mmHg or 30% below baseline levels) for a minimum period of 30 minutes, showing signs of tissue hypoperfusion and organic dysfunction (tachycardia, paleness, cold extremities, mental confusion, oliguria and metabolic acidosis), of cardiac etiology (acute myocardial infarction, cardiomyopathy, valvular heart disease, arrhythmias). In this setting, there are evidences of volume overload or, if not, the shock is not reverted by volume restoration[121].

In spite of developments in the treatment of acute myocardial infarction, this complication is still responsible for about 60% of the mortality in hospitalized patients[122]. Shock mechanisms include left ventricular insufficiency (78% of cases), acute mitral insufficiency (7%), interventricular septum rupture (4%), isolated right ventricular insufficiency (2.8%) and myocardial rupture (2.7%).

2. Clinical and Laboratory Evaluation

Laboratory evaluation allows the appraisal of the shock repercussion in various organs, as well as the identification of comorbidities. The hemogram is important to evaluate anemia, polycythemia and infections. Renal dysfunctions (such as prerenal failure and acute tubular necrosis) and disorders of the hydro-electrolytic balance have an influence on the levels of urea, creatinine, sodium, potassium and urinary sediment. Blood glucose levels can change either by diabetes or by the patient's critical condition. Coagulogram can reflect liver dysfunction in addition to being necessary before the performance of some invasive procedures. The increase in the levels of arterial or central venous lactate is due to tissue

Table 21 - Laboratory evaluation and monitoring in patient with Cardiogenic Shock

	Recommendation	Level of Evidence
Hemogram, sodium, potassium, urea, creatinine, glycemia, coagulogram, urinary sediment, lactate, arterial and central venous gasometry	I	D
Markers of myocardial necrosis in suspected cases of Acute Coronary Syndrome or myocarditis	I	D
Electrocardiogram, thorax radiography, transthoracic echocardiogram	I	D
Transesophageal echocardiogram in suspected cases of mechanical complications not defined by the transthoracic echocardiogram	I	D
Hepatic enzymes, calcium, phosphorus, magnesium, T3, TSH, total proteins and protein fractions	IIa	D
Invasive Arterial Monitoring		
Serious Arterial Hypotension (SAP <80mmHg) and/or cardiogenic shock	I	C
Use of vasopressor agents	I	C
Use of sodium nitroprusside and/or other potent vasodilator agents	IIa	C
Pulmonary artery catheterization		
Cardiogenic Shock	I	C
Suspected mechanical complications from the infarction (rupture of papillary muscle, interventricular septum, or tamponade)	IIa	C
Arterial hypotension nonresponsive to volume, without pulmonary congestion (e.g.: right ventricle acute infarction)	IIa	C

Table 22 - Treatment of patient with Cardiogenic Shock secondary to AMI

	Recommendation	Level of Evidence
Volume infusion, if hypovolemia signs are present	I	C
Control of cardiac arrhythmia and correction of electrolytic abnormalities	I	D
Inotropic and/or Vasopressor Agents	IIa	B
Intraortic balloon	IIa	C
Other devices for ventricular assistance	IIb	C
Thrombolysis	IIa	C
Percutaneous coronary angioplasty	I	A
Surgical myocardial revascularization	IIb	C
Surgical correction of mechanical complications	I	C

hypoperfusion and anaerobic metabolism, and its serial evaluation has evolutionary value. Gasometry (both arterial and venous) is important in initial assessment and in the follow-up. Metabolic acidosis, generally of lactic type, reduces oxygen affinity to hemoglobin, further decreases myocardial function and favors the occurrence of arrhythmias. Oxygen and carbon dioxide partial pressures reflect the patient's respiratory status, and are helpful to indicate ventilatory support. Oxygen saturation in mixed venous blood reflects its extraction by the tissues. Dosing of liver enzymes, total proteins and protein fractions, calcium, phosphorus and magnesium can also be useful. Dosing of myocardial necrosis markers (CKMB, troponins T and I, myoglobin) is indicated in suspected cases of acute coronary syndrome or myocarditis. Electrocardiogram helps in the etiologic diagnosis of cardiogenic shock. Thorax X-rays are used in the assessment of cardiothoracic index, as well as pulmonary abnormalities due to congestion, infection or thromboembolism. Transthoracic echocardiogram is a fundamental test in the assessment of cardiogenic shock due to acute myocardial infarction and it allows for the diagnosis of abnormalities in segmental and global contractility (hypokinesias, akinesias, dyskinesias), mechanical complications (mitral insufficiency, rupture of the interventricular septum or the free wall, pulmonary thromboembolism). Transesophageal echocardiography is indicated in cases of unfavorable acoustic window and when a mechanical complication is suspected.

3. Monitoring

Monitoring of the patient with cardiogenic shock is essential for the evolutionary assessment of the disease and the treatment. Fundamental and routinely monitored variables include: heart rhythm and rate, arterial blood pressure (noninvasive), respiratory rate, pulse oximetry, temperature and urinary output.

Arterial blood pressure should be measured by invasive means (arterial catheterization) in the following situations: serious arterial hypotension (systolic pressure < 80 mmHg) and/or cardiogenic shock, use of vasopressor agents (class I), use of sodium nitroprusside or other potent vasodilators (class IIa).

Pulmonary artery catheterization is useful to assess the hemodynamic status and to guide the treatment of the patient with cardiogenic shock more precisely than with the clinical exam[123-126]. Its indications in the acute myocardial infarction are[127] cardiogenic shock, suspected mechanical complications due to the infarction such as rupture of the papillary muscle, rupture of interventricular septum or pericardial tamponade, nonresponsive arterial hypertension, administration of volume in the absence of pulmonary congestion, such as in the right ventricular infarction.

Limitations to the pulmonary artery catheterization include the interobserver interpretation variability in the analysis of the tracings[128] with consequent treatment inadequacy, as well as the occurrence of potentially fatal complications.[129]

4. Treatment

4.1. Ventilatory Support - The purposes of ventilatory support in cardiogenic shock following acute myocardial infarction are to assure the patency of airways, provide adequate oxygenation and reduce respiratory work. The first step is to provide oxygen by means of a catheter or Venturi mask in increasing concentrations,

with the objective of maintaining percutaneous saturation above 90%. The noninvasive mechanical ventilation (CPAP or BiPAP) is the next step because, in addition to improving the oxygenation, it reduces the pulmonary shunt and it has beneficial hemodynamic effects (reduction in preload and afterload, increase in cardiac output). These ventilatory aspects may reduce the need of invasive mechanical ventilation[130]. The invasive mechanical ventilation must be performed when the noninvasive mechanical ventilation fails or in cases of serious hemodynamic instability, complex arrhythmias, current myocardial ischemia, reduction in the consciousness level and need for sedation.

4.2. Pharmacological Support - It is essential to assess the volemic status and to promptly correct the existing hypovolemia by means of crystalloids, colloids or hypertonic solution. Electrolyte abnormalities must be corrected; cardiac arrhythmias require special attention because they can precipitate or worsen the shock. Acute atrial fibrillation associated with ischemia or hemodynamic repercussion should be treated with electric cardioversion, while less critical conditions may be treated with drugs that have no significant negative inotropic effect (digitalis, amiodarone). Sustained ventricular tachycardia (VT) or ventricular fibrillation must be treated with electric cardioversion (start with 100J if monomorphic VT and 200J if polymorphic VT or VF; if necessary, apply a second shock between 200 and 300J, and if necessary, a third shock of 360J is applied), followed by the maintenance drug (lidocaine, amiodarone). With reference to the positive inotropic drugs, vasopressors and vasodilators, the recommendations are the same as those previously discussed. Platelet antiaggregating agents must be routinely administered to patients with cardiogenic shock due to acute myocardial infarction (aspirin, or in case of allergy or intolerance, clopidogrel or ticlopidine).

4.3. Myocardial Reperfusion Therapy - In spite of the reduced efficacy, thrombolysis can be considered for patients with cardiogenic shock due to acute myocardial infarction, if angioplasty or surgery is unavailable, respecting its indications and contraindications and, if possible, associated with vasoactive drugs and intra-aortic ballon. Data from the literature demonstrate that the mortality with isolated use of thrombolytic agents was 63% compared with 47% when used in association with intra-aortic ballon[131]. Percutaneous coronary angioplasty also demonstrated a reduction of mortality when compared with clinical treatment[132]. Although this procedure is indicated, at first, for the treatment of the artery related to the event, the patients with multiarterial involvement who present cardiogenic shock may benefit from the approach to all proximal lesions.

4.4. Surgical Treatment - Myocardial revascularization surgery is indicated when the coronary anatomy is not favorable to the percutaneous intervention, in patients with multiarterial involvement initially treated with emergency angioplasty or in cases of mechanical complications of acute myocardial infarction. There is evidence suggesting that early myocardial revascularization (within 6 hours), either by angioplasty or surgical revascularization, can reduce mortality in 6 months[133,134].

4.5. Mechanical Support - The intra-aortic balloon, by means of the mechanism of counterpulsation, reduces the left ventricule afterload, improves coronary perfusion during diastole, increases cardiac output up to 30%[133], reduces mortality by 32% when used isolatedly and by 39% when associated with measures for restoration of myocardial perfusion[134]. Ventricular assist devices used temporarily can replace the organ function, and the most currently used ones are Roller, BioPump, Sarns, BVS 5000, Thoratec, HeartMate, Novacor, and LionHeart.

C. Acute or Decompensated Chronic Heart Failure in Patients who underwent Cardiac and Noncardiac Surgeries (Table 23)

1. Noncardiac Surgeries

Cardiovascular complications are the most common cause of death in patients who undergo surgical procedures[135,136], in whom DHF and recent acute myocardial infarction are the two most important predictors of perioperative risk[137,138].

DHF can occur during the perioperative period in two situations: patients with DHF who require emergency surgical procedures, and patients with chronic and stable HF who develop decompensation during or after the surgery. Perioperative mortality in heart failure is related to the functional class[139] and with the presence of pulmonary congestion[140], especially when a third heart sound occurs[2]. The adverse events during the perioperative period are related to the condition of the patient at the time of surgery, more than to the intensity of cardiopathy[2].

The best recommendation to patients with acute or decompensated chronic HF who are candidates to surgery is to postpone the procedure until the decompensation is resolved[141]. Only emergency surgeries must be performed in patients with DHF. For those patients whose surgery cannot be postponed, the perioperative evaluation must be fast, simple and effective, and it must be focused on vital signs, evaluation of the volemic and hemodynamic status, and the analysis of simple tests such as electrocardiogram and thoracic radiography. Only essential interventions should be recommended before the emergency surgical procedure; the more detailed analyses should be performed in the postoperative period.

Laboratory Evaluation: It is recommended that patients with DHF during or after noncardiac surgeries be evaluated for the levels of urea and creatinine, sodium and potassium abnormalities, levels of hemoglobin and hematocrit, CKMB and troponin when acute coronary syndrome is suspected.

Electrocardiogram: There are no studies that have evaluated the 12-lead electrocardiogram in the preoperative assessment of patients with DHF. In asymptomatic patients, the finding o “q” waves was correlated with adverse events, in addition to being related to the left ventricular ejection fraction[142,143]. The electrocardiogram is recommended because it is a simple, fast, and low cost exam. Special attention must be paid to the occurrence of ischemia, blocks, ventricular and supraventricular arrhythmias without a control of the ventricular response.

Echocardiogram: Studies demonstrate a correlation between perioperative events and the finding of left ventricular ejection fraction < 35%. Nevertheless, there is no information that indicates the benefit of the routine exam of perioperative echocardiogram in patients with HF already documented.

The transthoracic echocardiogram is recommended in patients without a previously known echocardiogram, when a mechanical cause is suspected as the precipitating or contributory factor in HF

Table 23 - Recommendations in patients with DHF in view of the need of cardiac and non cardiac surgery

Situation	Recommendation	Level of Evidence
Prescription of β-blockers to patients with DHF who will undergo emergency cardiac and noncardiac surgeries	III	D
Use of inotropic agents in patients with DHF who underwent cardiac or noncardiac surgeries	IIa	D
Echocardiogram in patients who present cardiac decompensation starting in the perioperative period	I	D
Perioperative monitoring with CAP in patients with DHF who will undergo cardiac and noncardiac surgery	IIa	D
Routine use of IAB in cardiac or noncardiac surgeries	IIb	D
Use of IAB in noncardiac surgeries in patients with refractory tissue hypoperfusion	IIa	B
Use of IAB in cardiac surgeries in patients with refractory tissue hypoperfusion	I	B

CAP (Catheter Access Port) = Pressure monitoring with Swan-Ganz catheter; IAB = Intraortic Balloon

(following acute myocardial infarction, cardiac tamponade, valvular insufficiency, pulmonary embolism), or in HF decompensation following noncardiac surgeries. The echocardiogram can be useful to detect new areas of low contractility and valvular dysfunctions, and it is a comparative method of the left ventricular function, diagnostic in the cardiac tamponade and evaluator of the right ventricular function in suspected cases of pulmonary embolism.

Few studies have assessed the usefulness of transoperative transesophageal echocardiography in noncardiac surgeries in patients with decompensated HF. Some studies suggest that this procedure might be able to detect the presence of ischemia[144]. There is no evidence to recommend the use of transesophageal echocardiography in noncardiac surgeries.

Invasive Hemodynamic Monitoring: Monitoring with pulmonary artery catheter (PAC) intends to obtain optimal adjustments in perfusion and tissue oxygenation, and it has been proposed for patients in different clinical settings with conflicting results[145-148]. The use of PAC was related to the high frequency of complications and high costs[128], and its interpretation has high variability among physicians[149].

Different prospective studies have evaluated the efficacy of invasive monitoring of the pulmonary artery in high risk surgical patients[150-152]. There were no differences among the patients who received therapy guided by parameters offered by the pulmonary artery catheter and the patients with a clinical follow-up. A recent metanalysis studied trauma patients with high surgical risk who underwent elective surgery and presented septic shock, and it suggested some improvement in the mortality rate for patients who had hemodynamic optimization[153].

However, there are no prospective studies about the value of PAC in patients with DHF who underwent noncardiac surgeries. Considering the seriousness of these patients and until more precise information is available, it is recommended that their perioperative care be carried out in an intensive care unit with hemodynamic and tissue oxygenation adjustments guided by invasive hemodynamic monitoring.

Perioperative Management: Beta-blockers reduce mortality in patients with risk for ischemic heart disease when administered during the preoperative period[154,155]. The use of carvedilol has recently been described during the preoperative period in patients with class III and IV heart failure (NYHA) who underwent heart surgery[156]. No studies have evaluated the introduction of beta-blockers in patients with heart failure who underwent noncardiac surgeries. Beta-blockers must be introduced prior to elective surgeries in patients with DHF and maintained during all the perioperative period, especially in individuals with ischemic cardiomyopathy. Nevertheless, there is no data to justify the recommendation to start this medication in patients who were not previously using it and who have DHF before undergoing emergency surgeries.

The patients must also be maintained as close as possible to an euvolemic status since pulmonary congestion is associated with more frequent events. Pulmonary congestion is more commonly caused by excessive administration of fluids during surgery and, it generally occurs 24-48 hours after the surgery, when the patient is weaned from mechanical ventilation with positive pressure and there is mobilization of accumulated fluids in the extravascular space. The use of diuretics, however, must be cautious since the depletion of the intravascular volume may precipitate the occurrence of hypotension during anesthesia.

Intravenous inotropic agents are recommended in the presence of tissue hypoperfusion (oliguria, acidosis, increased lactate, reduced consciousness level or hypotension). Inotropic agents have been related with increased mortality in patients with heart failure, and therefore should not be used as a prophylactic treatment in the preoperative period.

The use of a contrapulsation intra-aortic balloon (IAB) has been suggested in patients following acute myocardial infarction undergoing emergency surgery[157,158]. Nevertheless, there are no randomized studies that have evaluated its use in patients with DHF undergoing emergency surgery. The use of IAB should be considered only in individuals who maintain hypotension or tissue hypoperfusion, in spite of the use of inotropic agents.

2. Cardiac Surgeries

Ventricular dysfunction, both left and right, is a risk factor for patients undergoing cardiac surgeries. Like noncardiac surgeries, the cardiac surgeries must be postponed in patients with DHF. In cases of emergency surgery, it is important to seek the best possible compensation still in the preoperative period.

A recent retrospective study with 1,586 patients suggested a beneficial effect of beta-blockers in patients with normal ventricular function undergoing myocardial revascularization surgeries[159]. Another recent study suggested the administration of beta-blockers prior to cardiac surgeries in order to reduce the perioperative risk in patients with ventricular dysfunction due to ischemic or valvular cardiomyopathy. Beta-blockers must be introduced before elective surgeries in patients with DHF already stabilized and must be maintained during all the perioperative period, especially in patients

with ischemic cardiomyopathy. Nevertheless, there is no data that recommends starting these medications in patients who were not previously receiving them and who have DHF prior to an emergency surgery.

Patients with DHF who will undergo heart surgery must be monitored with a pulmonary artery catheter[160,161]. Some authors have suggested the routine use of transesophageal echocardiography in heart surgery[162]; nevertheless, there is no data recommending the routine use of intraoperative transesophageal echocardiography in patients with HF.

The use of inotropic agents is indicated in patients with hypotension or signs of tissue hypoperfusion. Different studies compared the effects of inotropic agents in patients who underwent heart surgeries[163,164], but there is no evidence that corroborates with specific recommendations for any of them. The use of phosphodiesterase inhibitors as well as nitroglycerin has been suggested for patients with pulmonary hypertension due to their pulmonary vasodilator effect. If hypotension is present, vasopressor drugs such as norepinephrine, epinephrine and/or dopamine should be used.

In patients with serious heart failure and signs of tissue hypoperfusion, in spite of the use of intravenous inotropic agents, mechanical circulatory support must be considered as a support therapy until myocardial recovery (e. g., in myocardial depression associated with extracorporeal circulation) or until heart transplantation. IAB has been recommended for patients with obstruction of left coronary branch[165] in mitral insufficiency in a condition of postoperative low output[166]. In patients whose signs of left ventricular dysfunction and tissue hypoperfusion are intense since the beginning, or in where the IAB failed to restore tissue perfusion, the implant of artificial ventricular support must be considered[167,168].

D. Stunned and Hibernating Myocardium (Table 24)

1. Definition

In ischemic cardiomyopathy, the abnormalities of the myocardial contractility are due to both tissue fibrosis and viable cells dysfunction in variable combinations. The viable myocardium presents potentially reversible mechanical dysfunction and it can be classified as stunned and hibernating. While the hypocontractility of the stunned myocardium remains in spite of the reperfusion already attained, in the hibernating myocardium it represents an adaptation to the chronic low flow. Several studies have demonstrated the potential improvement of function by means of myocardial revascularization in patients with preoperative identification of viable segments[169-175]. Thus, in patients with ischemic HF, the assessment of myocardial viability is important to verify the partial or total reversibility of ventricular dysfunction with surgical treatment. It must be emphasized, however, that these studies were performed in stable patients. To this day, there are no data in the literature about the assessment of myocardial viability in patients with DHF. Viability tests must be performed after stabilization of the clinical status.

Table 24 - Evaluation Methods of myocardial viability and reversibility potential (indicated after clinical stabilization)

	Recommendation	Level of Evidence
Echodopplercardiography with dobutamine	I	B
Scintigraphy with Thalium-201	I	B
Positron Emission Tomography	I	B
Nuclear Magnetic Resonance	I	B

2. Methods of Myocardial Viability Evaluation

2.1. Stress Echocardiography with dobutamine[176,177]. The viable myocardium has its own preserved contractile reserve (responsiveness to inotropic agents). Dysfunctional segments - markedly hypokinetic, akinetic or dyskinetic - typically present a biphasic response to dobutamine, with improved contractility with low doses and impairment with dose increments. Sensitivity ranges between 75-80%, while specificity ranges between 80-85%. This method has a high positive (85%) and negative (93%) predictive value, but it requires a skilled evaluator and an adequate thoracic window.

2.2. Scintigraphy with ^{201}thalium[178,179]. While the initial uptake of this tracer depends primarily on perfusion, late uptake (>24 hours) is a result of the integrity of the cell membrane in the hibernating myocardium. The sensitivity is high (85-90%), but its relatively low specificity (65-70%) can overestimate the potential for regional recovery. The positive and negative predictive values are 33% and 94%, respectively.

2.3. Positron emission tomography (PET)[180,181]. The F-18 FDG tracer is a glucose analogue absorbed by metabolically active cells. The presence of viability is demonstrated when there is disparity between flow and metabolism. It also has a specificity lower (70-75%) than stress echocardiography with dobutamine. Considered a gold standard in the assessment of myocardial viability, this method is limited by its high cost and restricted availability.

2.4. Magnetic Resonance Imaging[182,183]. It can be associated with stress echocardiography with dobutamine to assess the contractile reserve. Sensitivity and specificity are 81% and 95%, respectively. It has a high spatial resolution, allowing for the discrimination between areas of transmural and non-transmural abnormalities.

The relationship between viability, increased contractility, improvements of the clinical condition and prognosis needs to be demonstrated in randomized prospective studies.

E. Diastolic Dysfunction (Table 25)

Approximately 50% of the patients with HF present with no or minimum involvement of the systolic function and they are, by exclusion, diagnosed as having diastolic HF[184-187]. Diastolic heart failure is the one related to the increases in the diastolic filling in part of or in the whole heart. Different conditions can lead to diastolic dysfunction. This current analysis focuses on the myocardial causes[188,189].

1. Diagnosis: In spite of the lack of clinical and electrocardiographic criteria, the presentation of HF in a patient with preserved systolic function probably represents diastolic failure. The inclusion of the B-type natriuretic peptide measurement can increase the diagnostic accuracy[190]. It is crucial to pay close attention to some general principles in the treatment of diastolic failure: reduction of volume overload, control of the arterial blood pressure and

Table 25 - Treatment of patients with DHF with Preserved Ejection Fraction

Situation	Recommendation	Level of Evidence
Calcium channel antagonist and beta-blocker to control heart rate	IIa	B
Calcium channel antagonist, beta-blocker, ACE-I, ARA-II and diuretics, when ventricular hypertrophy secondary to SAH is present	IIa	B
Digitalis to control heart rate	IIa	B
Diuretics to reduce congestive episodes	I	B
Calcium channel antagonist, beta-blocker, ACE-I, ARA-II and diuretics to control SAH	I	B

ACE-I = angiotensin-converting enzyme inhibitor; ARA-II = angiotensin-II receptor antagonist; SAH = Systemic Arterial Hypertension

relief of the myocardial ischemia. Drugs that block the renin-angiotensin-aldosterone system are particularly attractive based on pathophysiologic studies.

2. General Treatment: Drug therapy in general involves the use of diuretics and negative inotropic agents. Calcium channel blockers and beta-blockers have shown benefits to enhance physical capacity and, in small studies and subgroup analyses, to reduce mortality[188]. In the study conducted by the *Digoxin Investigators Group*[191], digoxin showed an impact on the reduction of hospitalization rates in patients with and without systolic dysfunction (it is believed the mechanism involved is the control of ventricular rate). For patients with atrial fibrillation, the restoration of sinus rhythm and organized atrial contraction may improve diastolic filling[192].

Clinical and experimental studies revealed that blockade of the renin-angiotensin-aldosterone system may improve the diastolic performance in view of the deleterious role of angiotensina II in the ventricular relaxation[14,193, 194]. Short-term treatment with losartan seems to be associated with an improvement in exercise tolerance, which might be due to afterload reduction[195]. In addition to that, inducers of hypertrophy regression seem to be beneficial in cases where the left ventricular hypertrophy (LVH) is the main element of diastolic dysfunction.

The study *Losartan Intervention for Endpoint Reduction in Arterial Hypertension* (LIFE)[23,196] demonstrated, in patients with hypertension associated with LVH (diagnosed with ECG), a reduction of the cardiovascular complications when compared with atenolol. It is possible that losartan has a beneficial action in the reduction of myocardial fibrosis and reduction of wall stiffness[24,197]. Currently, various multicentric, randomized, placebo-controlled studies are being conducted, aiming at assessing the role of the angiotensin conversion inhibitors, antagonists of angiotensin receptor and beta-blockers in patients with diastolic heart failure[25,188]. Candersartan may reduce hospitalization due to heart failure in patients with diastolic heart failure[198].

3. Treatment under investigation: Aldosterone seems to be important in the development of fibrosis, both in systolic HF remodeling and in the development of LVH. In the study *Randomized Aldactone (spironolactone) Evaluation Study for Congestive Heart Failure* (RALES)[199], directed to systolic dysfunction, placebo group patients with the highest serum values of collagen degradation markers had the poorest performance, but they were the ones who best responded to spironolactone. It is unknown whether this benefit could be observed in patients with diastolic dysfunction.

4. Comorbidities: Arterial hypertension is the largest risk factor for the development of CHF. Therefore, strict control of arterial blood pressure is essential in these patients. Occasionally, diastolic heart failure may require a complete investigation for coronary ischemia. Ischemic episodes can lead to diastolic dysfunction through changes in the ventricular relaxation, which can result in pulmonary congestion. Drug therapy and myocardial revascularization (percutaneous or surgical) reduce the symptoms and can prolong the survival of patients with CHD, who must be treated according to the current guidelines[200].

F. Acute Pulmonary Edema (Table 26)

Patients with acute pulmonary edema (APE) tend to be older, have higher blood pressure and preserved left ventricular ejection fraction[24,28,17,124]. APE episodes are frequently associated with ischemia (transmural or subendocardial) and/or poor dietary and/or blood pressure control. This group is generally poorly represented in clinical assays, which leads to a limited applicability of the information contained in them.

Improvement in oxygenation can usually be attained with the patient sitting, and with the administration of oxygen through high flow masks. It has been recently proposed that the use of noninvasive ventilation (NIV) with positive pressure can improve the oxygen exchange[201].

Two prospective, randomized studies were performed with this purpose. In the first one[202], NIV was compared with the use of high doses of nitrates. The study was interrupted early because of the excessive number of adverse events and reduced efficacy in the NIV arm. On the other hand, a better control of pulmonary edema has been demonstrated[203] with NIV, when compared with conservative treatment. Therefore, its use must be considered as an alternative strategy reserved for patients who did not respond to the conventional supply of oxygen and drug treatment.

Furosemide and morphine have long been considered as the

Table 26 - Treatment of patients with Acute Pulmonary Edema

	Recommendation	Level of Evidence
Noninvasive ventilation with positive pressure[#]	IIa	B
Nitrate with mean systemic arterial pressure >100 mmHg	I	B
Diuretic	I	B
Oxygen	I	C
Morphine	I	B

* for patients without response to standard treatment

standard treatment of APE. A recent study[204] randomized patients to receive low doses of nitrates and a *bolus* of 80 mg furosemide or 40 mg furosemide and high doses of nitrate administered in repeated intravenous (IV) *boluses* of 3 mg isosorbide dinitrate. The study showed that high doses of intravenous (IV) nitrate are clearly superior to furosemide in the treatment of APE.

Recent studies[124,205-207] showed that the most important predictor of immediate therapeutic success (measured as oxygen saturation >95% in 60 min) was the capacity to reduce arterial blood pressure by 15-30% in 15-30 min. This represents a decrease of systemic vascular resistance, which confirms the importance of rapid arterial dilation as a primary objective in the treatment of APE.

However, in patients with acute heart failure with reduced myocardial reserve, the inappropriate vasodilation may cause an important drop in arterial blood pressure, which can result in hemodynamic instability, ischemia, renal failure and shock. Therefore, it is essential to pay close attention to arterial blood pressure monitoring. Medication doses should be reduced if systolic pressure is lower than 90-100 mm Hg and they must be discontinued if there is a new drop in arterial blood pressure. In the first 24 hours, the vasodilator dose must be progressively reduced in order to prevent recurrent episodes of inappropriate vasoconstriction.

The drug selected for use to prevent new episodes of decompensation, after initial stabilization in patients hospitalized because of acute heart failure is not well defined yet. Nitrates have never been assessed in prospective, randomized studies. Two classes of vasodilators were recently developed for the treatment of acute heart failure; fast-acting endothelin antagonists are in phase II investigation. Larger studies are necessary to verify its exact role in acute heart failure. The second class of vasodilators is composed of natriuretic peptides. The first drug investigated in a clinical trial was niseritide[93]. The drug was effective to improve the subjective score of dyspnea, as well as to induce significant vasodilation, having been recently approved by the FDA for the treatment of acute HF. Another group of drugs used in the first days after the initial stabilization is composed of diuretics. Although with a proven benefit in clinical practice, its excessive use can be harmful[205,206]. A recent study compared low doses of dopamine with high doses of intravenous furosemide in patients with an episode of refractory decompensation[207]. The study was discontinued due to significant adverse events in the furosemide arm. Therefore, the dose of furosemide administered to patients with DHF must be titrated with the purpose of reducing the symptoms and congestion, without triggering adverse effects.

G. Peripartum Cardiomyopathy (Table 27)

Peripartum cardiomyopathy (PP-CMP) is a serious, rare disease, with a mortality rate around 18-56%, of unknown etiology, and its occurrence is related to the gestational-puerperal cycle[209,210]. It occurs in women without any previous cardiomyopathy, from the last quarter of gestation until 6 months after delivery. The incidence is estimated to be 1/1,435 to 1/15,000 deliveries, which would affect 1,000-1,300 women every year in the U.S.A. Risk factors include multiparity, twin pregnancy, advanced age, preeclampsia, gestational hypertension and black ethnicity. Its diagnosis requires the exclusion of other causes of cardiomyopathy and it is confirmed by echocardiogram showing signs of systolic ventricular dysfunction. Endomyocardial biopsy may be indicated if the patient is refractory to treatment, and it may show myocarditis.

H. Myocarditis (Table 28)

Myocarditis is defined as an inflammation in the cardiac muscle, frequently caused by an infectious agent which usually affects the myocytes, interstitium, vascular elements and the pericardium.

Myocardial aggression basically occurs through three mechanisms: 1) immune-mediated lesion, which is probably the main mechanism[211]; 2) direct action on the myocardium; 3) production of a myocardial toxin (e.g., diphtheria).

Diagnostic suspicion is raised in the presence of an acute HF, after an infection, or a short-term clinical condition. The clinical manifestation of a myocarditis varies from an oligoasymptomatic condition to deadly HF. Among the findings, one of the main characteristic ones is tachycardia disproportional to the elevation of temperature, almost always accompanied by a third heart sound, mitral regurgitation murmur and arrhythmias. The main agents associated with myocarditis are viruses (adenovirus, arbovirus, coxsackievirus, cytomegalovirus, echovirus, hepatitis virus, human immunodeficiency virus, influenza, poliomyelitis and *Mycoplasma pneumoniae);* rickettsial diseases (endemic typhus and Q fever); bacterial infections (*Streptococcus, Staphylococcus, Pneumococcus, Haemophilus* and diphteria); parasitic infections (cysticercosis, toxoplasmosis, schistosomiasis, trypanosomiasis) and fungal infections (aspergillosis, actinomycosis, blastomycosis and candidiasis).

Late consequences of myocarditis can be related to the activation of cellular and humoral autoimmunity. Therefore, some authors believe that immune suppression may be beneficial in selected cases. Immune suppression has an important role in the treatment of patients with cardiac dysfunction due to autoimmune diseases, such as scleroderma, lupus erythematosus, polymyositis or sarcoidosis. Intravenous use of immunoglobulin, however, did not demonstrate a beneficial effect in immunosuppression[212-214].

I. After heart transplant (Table 29, 30 and 31)

HF syndrome in the heart transplant postoperative period can be a consequence of several clinical conditions, and it can emerge both in the immediate postoperative period and during the late follow-up. It is important to consider the electrophysiologic and hemodynamic changes due to the cardiac denervation, as well as the effects of pulmonary hypertension of the receptor on the functional performance of the graft[215].

Left ventricular dysfunction in the immediate postoperative period with DHF is generally serious and can be related to:

1. poor myocardial preservation correlated with cardioplegic solution, cardiac contusions, use of high doses of catecholamines, ischemia time and use of inadequate preservation solutions, inappropriate care of donors or poor quality of donors;

2. bradyarrhythmias, whose main causes are acute cellular and humoral rejection, influence of the suture line, surgical manipulation close to the sinus node, graft ischemia, influence of drugs used in the preoperative period (beta-blockers and amiodarone).

Table 27 - Recommendations for Diagnosis and Therapy of DHF due to Peripartum Cardiomyopathy during pregnancy

Diagnosis	Class	Evidence
Transthoracic Echocardiogram	I	C
Routine Endomyocardial Biopsy	IIb	C
Endomyocardial Biopsy (in case of refractory HF)	IIa	C
Therapy		
Water and salt restriction	I	C
Water and salt restriction	I	C
ACE-I / ARA II (during pregnancy).	III	C
Hydralazine and nitrates	IIa	C
Digitalis	IIa	C
β-eta-blockers (after compensation)	IIa	B
Oral Anticoagulant (except post-partum, when indicated)	IIb	C
Immunosuppressants for active myocarditis, confirmed with biopsy, and clinically refractory (after two weeks of adequate treatment)	IIa	C
Heart Transplant (after delivery due to persistence of the clinical condition and following the indication criteria)	I	C

ACE-I = Angiotensin-converting enzyme inhibitor; ARA II = angiotensin-II receptor antagonist

Table 28 - Complementary Diagnosis and Treatment of Myocarditis with DHF

	Degrees of Recommendation	Level of Evidence
Investigation		
Creatine phosphokinases (CPK,CKMB) and troponins (T and I)	IIa	C
ECG: to detect changes in ST segment T wave, atrial and ventricular arrhythmias, atrioventricular and intraventricular conduction disturbances, and more rarely, pathological Q waves	IIa	C
Thoracic Teleradiography: cardiomegaly and signs of pulmonary venous congestion	IIa	C
Echocardiogram: systolic ventricular dysfunction, frequently regional	IIa	C
Myocardial Scintigraphy with Gallium - 97	IIa	C
Endomyocardial Biopsy in patients with refractory HF	IIa	C
Viral culture in myocardial fragments	IIb	C
Elevated titration of specific antibodies	IIb	C
Treatment		
Diuretics	I	C
ACE-I	I	A
Beta-blockers in the stabilized patient	I	A
Digitalis	IIb	C
Intravenous inotropic drugs	IIa	C
Circulatory support devices	IIa	C
Immunosuppression	IIb	B
Specific Immunoglobulin	IIb	B
Antiviral strategy	IIb	C
Support treatment during decompensation	I	A

ACE-I = Angiotensin-converting enzyme inhibitor

3. acute rejection, a frequent cause of left ventricular and/or biventricular dysfunction in the postoperative period of heart transplant, mainly when the humoral component is present. Humoral rejection is serious, has a high mortality rate and is characterized by vasculitis, edema, necrosis and capillary deposits of immune complexes and complements[216].

Right ventricular dysfunction accounts for about 50% of cardiac complications of the postoperative period and 19% of total early deaths. The main cause of inadaptation of the right ventricle is pulmonary hypertension and poor preservation of the graft[217,218]. Further on, HF can be caused by graft vascular disease, rejection and tricuspid insufficiency. Graft vascular disease is the main late complication after heart transplant. The occurrence of acute HF is a consequence of acute myocardial infarction, usually asymptomatic, since the patients are denerved.

J. Valve Diseases (Table 32)

The presence of HF means a more advanced natural history and it implies a possible surgical correction.

Pharmacological management of HF in valve diseases has the purpose of adjusting the hemodynamic condition by means of optimization of preload and afterload, in addition to actions on the myocardial contractility, heart rate and correction of occasional decompensation factors[219].

1. Mitral Stenosis (MS)

Symptoms of HF in MS are related to the reduction of valve area, increased heart rate and elevation of pulmonary pressure.

2. Mitral Insufficiency (MI)

Surgical correction[220] is determined by the presence of HF symptoms with normal ventricular function or in asymptomatic patients with some damage of ventricular function or in patients with acute symptomatic MI (mitral insufficiency). The treatment of mitral regurgitation is introduced for relief of the symptoms until the surgical treatment and to prevent complications.

Table 29 - Diagnosis and Treatment of Acute Humoral and Cellular Rejection [364-366]

	Degrees of Recommendation	Level of Evidence
Diagnosis		
Right ventricular endomyocardial biopsy	I	B
Scintigraphy with gallium-67	IIb	C
Echodopplercardiogram-Tissue Doppler	IIb	C
Magnetic resonance with gadolinium	IIb	C
Treatment of humoral rejection		
Plasmapheresis	I	B
Change from azathioprine to mycophenolate mofetil	IIa	C
Change from cyclosporine to tacrolimus	IIa	C
Ciclophosphamide	IIa	C
Monoclonal or polyclonal antithymocyte globulins	IIa	C
Methotrexate	IIb	C
Treatment of cellular rejection		
Hemodynamically stable patients: Methylprednisolone	I	B
Oral Pulsotherapy (for ambulatory)	IIa	C
Unstable patients and / or ventricular dysfunction: Methylprednisolone	I	B
Monoclonal or polyclonal antithymocyte globulins	IIa	B
Change from cyclosporine to tacrolimus	IIb	B
Change from azathioprine to mycophenolate mofetil	IIa	B
Refractory or persistent rejection: Methotrexate and Rapamicine	IIb	C

Table 30 - Diagnosis and Treatment of Graft Vascular Disease causing DHF [367-370]

	Degrees of Recommendation	Level of Evidence
Diagnosis		
ECG	I	C
Cineangiocoronariography	I	B
Intravascular ultra-sound	IIa	C
Stress echocardiogram with Dobutamine	IIa	B
Treatment		
Angioplasty in selected cases and with distal area favorable to the procedure	IIa	C
Myocardial Revascularization	IIb	C
Retransplant	IIb	C
Change from azathioprine to mycophenolate mofetil	IIa	C
Laser	IIb	D

Table 31 - Treatment of Left and Right Ventricular Dysfunctions [371-373]

	Degrees of Recommendation	Level of Evidence
Left Ventricular Dysfunction		
Dobutamine and milrinone: immediate postoperative period	I	C
Chronotropic deficit: isoproterenol	I	C
Chronotropic deficit: stimulation with epicardial electrode	I	C
Chronotropic deficit: epinephrine	IIa	C
Chronotropic deficit: theophylline	IIa	C
Intra-aortic balloon or artificial ventricle	IIa	C
Retransplant: hyper-acute rejection and refractory dysfunction	IIb	C
Right Ventricular Dysfunction		
Dobutamine and milrinone: immediate postoperative period	I	C
Inotropic Agents	I	C
Pulmonary Vasodilators: nitric oxide, prostacyclins, sodium nitroprusside and prostaglandins	I	B

3. Aortic Stenosis (AS)

The clinical treatment of HF in AS does not alter the natural history and the need of surgery. The basis for the treatment is the control of precipitating factors of HF while surgical correction is awaited.

4. Aortic Insufficiency (AI)

In acute aortic insufficiency, there is no time for ventricular adaptation and a sudden increase in left ventricular diastolic pressure occurs, followed by pulmonary edema and sometimes shock.

L. Decompensated Chagasic Cardiopathy (Table 33)

Chagasic cardiopathy can occur in its chronic phase as an HF syndrome with arrhythmias and thromboembolim[221]. Such presentations can occur isolatedly or in association; the concurrence of HF and arrhythmias is more frequent[2]. Although rare, chagasic cardiomyopathy in its acute phase can also occur more frequently as HF syndrome.

Chronic HF usually evolves, appearing around 20 years of age or over, after acute infection. Its most frequent presentation is a biventricular heart failure, with predominance of symptoms related

Table 32 - Treatment of DHF due to Mitral Stenosis, Mitral Insufficiency, Aortic Stenosis and Aortic Insufficiency [374-384]

	Degrees of Recommendation	Level of Evidence
Water and salt restriction; diuretics	I	C
Mitral Stenosis		
Control of heart rate (sinus tachycardia or atrial fibrillation) with normal ventricular function with beta-blockers and/or calcium channel blockers (diltiazem and verapamil)	I	B
Control of heart rate (sinus tachycardia or atrial fibrillation) with normal ventricular function with:		
Digitalis:	IIa	C
Amiodarone:	IIa	C
Control of heart rate (sinus tachycardia or atrial fibrillation) with abnormal ventricular function with beta-blockers and/or calcium channel blockers (diltiazem and verapamil)	IIb	B
Control of heart rate (sinus tachycardia or atrial fibrillation) with abnormal ventricular function with:		
Digitalis:	I	B
Amiodarone:	IIa	C
Reversal of acute atrial fibrillation: effective anticoagulation for 3 weeks and further reversal	I	B
Cardioversion after a negative transesophageal echocardiogram for the presence of atrial thrombus	IIa	B
Immediate cardioversion restricted to hemodynamic instability	I	C
Emergency surgical treatment or balloon valvoplasty in patients with hemodynamic instability and/or refractory pulmonary edema	I	B
In pregnant women with acute pulmonary edema (Surgical treatment or valvoplasty)	IIa	C
Mitral insufficiency		
Digitalis in left ventricular dysfunction or control of heart rate	I	B
ACE-I: to control HF until surgical correction	I	B
In acute mitral insufficiency (rupture of chordae tendinea, infection or acute myocardial infarction); additional measures: sodium nitroprusside and/or hydralazine associated or not with inotropic agents	I	C
In acute mitral insufficiency (rupture of chordae tendinea, infection or acute myocardial infarction); additional measures: Intra-aortic balloon	I	C
Mitral insufficiency due to ischemia: revascularization and valve correction when the reflux is moderate to intense	I	B
Aortic Stenosis		
Diuretics	I	C
Digitalis: in patients with reduced ejection fraction, if concurrent tachycardia is present	IIa	C
Betabloqueadores e/ou bloqueador de cálcio	III	C
Sodium nitroprusside: acute pulmonary edema	IIb	C
ACE-I: refractory HF when the surgical treatment is contraindicated, association of ventricular dysfunction and arterial hypertension	I	C
Surgical treatment	I	B
Balloon aortic valvuloplasty in hemodynamic instability and refractory acute edema, if immediate surgery is	IIb	C
not possible	IIb	C
Aortic insufficiency		
Digitalis and ACE-I	I	B
Intra-aortic balloon	III	C
Inotropic agents associated with sodium Nitroprusside	I	B
Nifedipine and hydralazine in asymptomatic patients to postpone the need of surgical treatment	IIb	B
Beta-blockers in patients with arterial hypertension and dissection, where it can be administered with caution	I	C

ACE-I = Angiotensin-converting enzyme inhibitor; MI = mitral insufficiency

to a larger compromise of the right ventricle. The diagnosis of chagasic cardiomyopathy is based on epidemiologic data, direct demonstration of antibodies against *Trypanosoma cruzi* antigens or serologic tests (indirect immunofluorescence test, indirect hemoagglutination, complement fixation and immunoenzymatic test). The diagnosis is suggested by the presence of total right bundle branch block and anterosuperior left bundle branch bock in the ECG, the presence of an apical left ventricular aneurysm in echocardiogram, with or without a thrombus, and posterobasal akinesia. Patients with HF due to chagasic cardiomyopathy usually have a worse prognosis than other etiologies, a high prevalence of myocarditis, and conduction system disturbances or bradyarrhythmias.

The treatment of DHF secondary to Chagas disease normally follows the same treatment for other etiologies. However, due to its particularities, it is possible that patients with DHF and Chagas disease do not have the same therapeutic response. To this date, there is no literary evidence regarding the efficacy and safety of the use of beta-blockers in chagasic cardiopathy. This disease occurs with a high prevalence of advanced atrioventricular blocks and bradyarrhythmias that can get worse with the use of beta-blockers. If its use is decided, after compensation or in persistent DHF, the management must be extra cautious. The use of benzonidazol in the reactivation of the disease or in the acute phase should be mentioned. Heart transplant for the treatment of heart failure seems to have better results than other etiologies[222].

M. HF in fetuses, infants and children (Tables 34 and 35)

The most frequent cause of HF in infants and children are the congenital cardiac defects, with an annual incidence of 0,1-0,2% of newborns[223]. The main causes of HF are[224]: (1) congenital defects (due to left to right blood deviation; obstructive lesions of the systemic flow, such as left heart hypoplasia, aortic arch interruption and aortic coarctation; extracardiac arteriovenous fistulae leading to enlargement of the right chambers; anomalous origin of left coronary artery; (2) cardiac tamponade; (3) ventricular dysfunction caused by acute myocarditis, acute presentation of congenital or acquired cardiomyopathies (inborn errors of metabolism, muscular dystrophies, infection, drugs, toxins, Kawasaki

Table 33 - Treatment of DHF due to Chagasic Cardiopathy

	Degrees of Recommendation	Level of Evidence
Benzonidazole: Acute Chagas disease or age <12 years, or post-transplant reactivation	I	C
Benzonidazole for chronic forms	IIb	C
Diuretics	I	C
Spironolactone	I	C
ACE-I	I	C
Digitalis	Ia	C
Beta-adrenergic receptor blockers*	IIa	C
Anticoagulation in AF, previous embolism or a floating cavity thrombus	Ia	C
Amiodarone: SVT	I	C
Amiodarone: NSVT and symptomatic extrasystoles	IIa	C
Heart Transplant	I	B

ACE-I = Angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; SVT = sustained ventricular tachycardia; NSVT= non-sustained ventricular tachycardia

Table 34 - Recommendations for Diagnosis of DHF in Fetus, Infant and Child

	Degrees of Recommendation	Level of Evidence
Electrocardiogram, Thoracic teleradiography, echocardiogram, Holter (in arrhythmias)	I	C
Coronariography in case of inconclusive echocardiogram in the diagnosis of anomalous coronary artery	I	C
In myocarditis: viral PCR of tracheal aspirate and serologic tests	I	C
In autoimmune diseases: anti-Ro, anti-La, tests for systemic Lupus erythematosus (antinuclear antibody, rheumatoid factor), screening for autoantibodies (antibody for βanti-myosin)	I	C
In mitochondrial diseases: carnitine, acyl-carnitine, lactate, glycemia, hemogram, urine to test for methylglutaconic acid, muscle biopsy	I	C
Fetus: serial echocardiograms to assess signs of fetal hydrops	I	C
Post heart transplant: acute cellular rejection: noninvasive methods, pulmonary hypertension (echocardiogram and hemodynamic parameters such as central venous pressure, pulmonary artery pressure, evidence of humoral rejection: endomyocardial biopsy)	I	C
Graft Vascular Disease: cineangiocoronariography	I	B
General: Endomyocardial biopsy	IIa	C
General: determination of BNP levels	IIa	C

disease), mitochondriopathies, nutritional and idiopathic deficiencies, rheumatic fever[225]; (4) arrhythmias; (5) heart failure in fetus; (6) myocardial dysfunction after correction of cardiac defects (in immediate postoperative period after extracorporeal circulation or during late phase); (7) after orthotopic heart transplantation (primary failure of the graft, pulmonary hypertension, cellular rejection, humoral rejection, posttransplant coronary heart disease) and (8) Eisenmenger syndrome.

The most common clinical manifestations of DHF in infants are tachypnea, tachycardia, and reduced food intake. Other signs include hepatomegalia and gallop rhythm during physical exam. The presence of intercostal retractions, sudoresis and paleness may indicate imminent circulatory collapse. Pulses and arterial blood pressure must be assessed in the four limbs. Cardiomegaly and pulmonary edema can be visualized in a thoracic teleradiography. Older children may exhibit tachycardia and tachypnea; however, the most typical manifestation is fatigue and exercise intolerance. Lack of appetite, slow growth and development impairment are also frequent in the clinical history. Venous distension and peripheral edema can also be seen. Adolescents present adult-like symptoms. The *New York Heart Association*[226] modified classification is used for children and the Ross scale is used for infants[227].

Table 34 illustrates the diagnostic evaluation[228].

Table 35 shows the main recommendations[229] for the treatment of congenital cardiac defects[230], cardiomyopathies[231], myocarditis[232], low output after correction of congenital defects[233], heart transplant[234], Eisenmenger syndrome, arrhythmias and fetal cardiopathies.

VII. Surgical Treatment and Mechanical Strategies in the treatment of DHF

DHF can result from complications originating from various cardiac conditions which can be surgically treated, or by invasive means with the use of catheters. The most frequent causes are acute coronary failure, bradyarrhythmias, tachyarrhythmias and acute decompensation of cardiac valvulopathies or advanced cardiomyopathies are the most frequent causes. Because of its high mortality, surgical therapy must always be considered as a complement to clinical therapy when the latter does not show a favorable response. However, any therapeutic intervention must be based on the immediate diagnosis to evaluate the type and severeness of the problem, as well as the factors involved in its prognosis. The surgical options for treatment include myocardial revascularization, correction of the mechanical complications of myocardial infarction, valve reconstruction or replacement, heart transplant, procedures in the pericardium, pacemaker or automatic defibrillator implantation, as well as the temporary use of mechanical devices for circulatory support.

A. Surgical Procedures (Tables 36, 37, 38)

DHF due to myocardial infarction or its complications frequently evolves with cardiogenic shock and pulmonary edema. In cases of uncomplicated acute myocardial infarction, clinical measures and/or percutaneous coronary revascularization are the first line procedures. The indication for myocardial revascularization surgery

Table 35 - Recommendations for treatment of DHF in Fetus, Infants and Children

	Degrees of Recommendation	Level of Evidence
Inotropics, vasodilators and diuretics	I	B
In newborns with obstructive lesions of the systemic flow: prostaglandin E1, mechanical ventilation with no supplementary oxygen	I	C
Structural congenital heart defects: correction of the defect	I	B
Fetus: digoxin, antiarrhythmic specific for tachyarrhythmias	I	B
Refractory ventricular dysfunction: heart transplant	I	B
After heart transplant due to primary failure: mechanical support	I	B
After heart transplant due to primary failure: retransplant	I	C
Acute rejection: pulse therapy, antithymocyte globulin	I	B
Humoral rejection: measures of acute rejection associated with plasmapheresis, cyclophosphamide or mycophenolate mofetil	I	B
Pulmonary Hypertension (nitric oxide)	I	C
Noninvase mechanical ventilation	IIb	C
Mechanical support for acute myocarditis, severe low output after heart surgery, a bridge to transplant in case of refractory cardiomyopathy and severe pulmonary hypertension	IIa	B
Immunotherapy (acute myocarditis)	IIb	C
Eisenmenger Syndrome and right HF: hemodilution	IIa	C
Retransplant: graft vascular disease	IIb	C
Oxygen therapy in newborns with suspected canal-related cardiopathy until the diagnosis is clarified	III	C
Eisenmenger Syndrome: systemic vasodilator	III	C

Table -36 - Indication of surgical treatment in acute myocardial infarction in patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Myocardial revascularization with evidence of extensive ischemia; when anatomy is unfavorable for angioplasty	I	B
Myocardial revascularization with evidence of extensive ischemia, after an unsuccessful scoronary angioplasty	I	A
Correction of interventricular communication	I	C
Correction of mitral valve insufficiency due to dysfunction or rupture of papillary muscle	I	C

Table 37 - Indication of surgical treatment in ischemic cardiopathy in patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Myocardial revascularization with evidence of ischemia and myocardial viability when coronary anatomy is favorable	I	B
Brection left ventricle aneurysms with extensive areas of contraction dyskinesi	I	B
Surgery for ventricular remodeling in patients with intensely dilated left ventricle and extensive areas of akinesia	IIb	C

Table 38 - Indication of Valve Correction or Replacement in Patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Acute aortic insufficiency due to aortic dissection	I	C
Acute aortic insufficiency due to infectious endocarditis in native valve	I	C
Intense mitral stenosis with a valve area ≤1.5 cm^2, if score is not favorable to balloon valvotomy or if this technique is unavailable	I	B
Intense mitral stenosis with a valve area ≤1.5 cm^2, in the presence of a left atrial thrombus	I	C
Mitral valve insufficiency caused by rupture of leaflet or subvalvar apparatus	I	C
Acute mitral insufficiency due to infectious endocarditis in native valve	I	C
Infectious endocarditis in valve prosthesis	I	C
Thrombosis in valve prosthesis	IIa	C

is reserved for patients who evolve with cardiogenic shock and evidence of ischemia, and for those who present unfavorable anatomy for percutaneous angioplasty. Likewise, other patients included are those who have undergone this procedure without success, as long as they have coronary arteries with a distal portion favorable to the surgical approach[235-237].

Surgical treatment is always considered in complications of the acute myocardial infarction evolving with hemodynamic instability, such as interventricular communication[238] and mitral insufficiency due to rupture or dysfunction of the papillary muscle[239]. Under these conditions, surgery must be performed urgently, and it is important to have the best possible stabilization during the preparation, including the support from an IAB (intraaortic balloon).

Ischemic cardiopathy can also be accompanied by clinical signs of chronic HF which may require surgical therapy during the decompensation phases, either associated with left ventricular aneurism or not.

Valvulopathies that evolve with signs of DHF are generally caused by large and acute lesions. These situations include acute aortic regurgitation (typically associated with aortic dissection),

mitral insufficiency caused by rupture of the leaflets or components of the subvalvular system, and valve insufficiencies caused by infectious endocarditis. Valvular stenosis can also be responsible for signs of cardiac decompensation in the final phases of chronic evolution of the problem. Valvulopathies can lead to cardiogenic shock and pulmonary edema generally due to changes in the circulatory mechanics, therefore surgical treatment must be indicated as long as there is no irreversible involvement of the ventricular function[240]. Ideally, in all these situations, the clinical condition must be stabilized before the surgical procedure, including the placement of an IAB when it is not contraindicated.

The main option of surgical treatment in patients with myocardial diseases evolving with DHF is the heart transplant (Table 39)[241]. Alternative procedures have been investigated, but nowadays only the correction of functional mitral insufficiency has also been indicated in the treatment of ischemic or idiopathic cardiomyopathies[242]. Heart transplantation can also be considered in patients with hemodynamic instability refractory to drug treatment during the postoperative period of cardiac surgery or after acute myocardial infarction, as long as there are no other surgical treatment alternatives. On the other hand, the need to wait for the organ occasionally leads to the use of mechanical circulatory assist devices as a bridge to transplant. Finally, the specific contraindications to transplant must always be considered when discussing its indication. Palliative procedures can be indicated in certain cases (Table 40).

B. Surgical Procedures for arrhythmias and conduction blocks

1. Catheter ablation for the treatment of cardiac tachyarrhythmias (Table 41)

In a specific group of patients with tachyarrhythmias, ventricular dysfunction can occur with the subsequent development of DHF, in the absence of another detectable cause. This reversible dysfunction, caused by chronic arrhythmias, is called tachycardiomyopathy. Any supraventricular tachyarrhythmia occurring for a long period, with increased heart rate and/or irregular heart rhythm, or an unrelenting ventricular tachycardia can lead to tachycardiomyopathy. In other patients, tachyarrhythmia can aggravate an already installed cardiomyopathy. In both cases, the tachyarrhythmia can be diagnosed and/or become symptomatic in the presence of DHF[243-245].

Catheter ablation by means of radiofrequency energy is indicated then, and it is employed with good results (90-99% success) in patients with accessory pathways, AV nodal reentrant tachycardia, atrial tachycardia and atrial flutter[246]. AF is present in 15-30% of patients with HF. Although the introduction of beta-blockers has eased the control of the ventricular response, in some refractory cases this control can be obtained through the ablation of the atrioventricular junction together with the insertion of a definitive pacemaker[247-249].

Unrelenting ventricular tachycardia can be a result of proarrhythmia and affect mainly those patients with structural cardiopathy, such as chagasic or ischemic etiology with serious involvement of the ventricular function. It can also be present in patients with advanced HF and candidates to heart transplant. On rare occasions, patients without baseline structural cardiopathy can show gradual impairment of ventricular function when chronically affected by idiopathic unrelenting ventricular tachycardia. Catheter ablation should be considered in these cases, with a success rate around 85%. Upon restoration of sinus rhythm, a gradual and progressive improvement in ventricular function is expected. The insertion of an implantable cardioverter defibrillator is contraindicated in unrelenting ventricular tachycardia.

2. Artificial Cardiac Stimulation (Tables 42 and 43)

Important bradyarrhythmias may eventually lead to DHF, and total AV block is the abnormality found in most of these patients. As long as it is not a consequence of reversible factors such as drugs, hydro-electrolytic and/or metabolic disturbances, the insertion of a definitive pacemaker is indicated. In cases of spontaneous recovery of AV conduction, such as following acute myocardial infarction, if there is any doubt regarding the level of the block and the risk of progression to total AV block, the electrophysiologic study is indicated.

Recent multicentric, prospective and randomized assays in patients with HF with predominance of FC III and increased QRS complex have demonstrated that the biventricular stimulation can improve the ventricular function and life quality.

Rehospitalizationas due to HF were also significantly reduced. However, about 20-30% of patients may not show any clinical improvement, which must be taken into consideration because of the cost of this treatment[250,251]. Some studies suggest that the benefit might be small in ischemic cardiomyopathy[252,253]. In all studies, patients were also included only after optimization of the clinical treatment for HF and with the same drug dosages for at least 30 days. Therefore, there are no specific studies about the use of this therapy in patients with DHF.

C. Mechanical Circulatory Support

Mechanical circulatory support means any temporary auxiliary measure to maintain circulatory conditions essential to the body. Mechanical devices for circulatory support have been employed to favor the myocardial recovery and as a bridge to a corrective

Table 39 - Indication of Heart Transplant in Patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Refractory HF, with previous optimization of drug therapy, with no surgical option to reduce mortality	I	B
After clinical compensation, in the presence of sustained ventricular tachycardia not conventionally treatable and an ejection fraction < 25% (radioisotopes)	I	C
After clinical compensation, in the presence of maximum oxygen consumption < 10 ml/Kg/min	I	B
After clinical compensation, in the presence of maximum oxygen consumption between 10-14 ml/Kg/min	IIa	B

surgical procedure or heart transplant. These devices include intraaortic balloon (IAB), continuous flow pumps, paracorporeal or implantable artificial ventricles, and the total artificial heart.

Intraaortic Balloon (IAB) (Table 44): IAB is able to increase the primary cardiac output by 10-30%, to reduce the peripheral vascular resistance (afterload) and globally improve the perfusion. Its use is well established in the literature[254-257], and it should be indicated for the treatment of cardiogenic shock of difficult reversion with pharmaceutical therapy. Specific contraindications to the use of IAB include only the aortic valve insufficiency and the involvements of the thoracic aorta. In diseases of the abdominal aorta and its branches, the insertion can be done through the subclavian artery or through the ascending aorta when the thorax is open.

Mechanical Circulatory Assist Devices (Table 45): Continuous flow pumps work by pumping the blood in a single direction, without the need of interposed valves. These pumps are inserted in parallel with left or right circulation through canules externalized in the thorax. Its use is restricted to an average of one week, in view of the continuous flow limitations and the little mobility provided to the patient.

Artificial ventricles are devices composed of one valve chamber with a diaphragm that moves and ejects the blood out of the pumping area and aspirates it back when returning to the initial position. Paracorporeal ventricles with pneumatic activation can be inserted in parallel with the left or right circulation by means of canules sutured on the cardiac structures and externalized in the abdominal area. In spite of being external, they provide a relative mobility to the patient, and they are able to maintain the circulation for several months. Implantable ventricles electromechanically activated are used only to assist the left circulation; they are sutured directly onto the cardiac structures and the only externalized part is the power cord. They can be used for over one year. The total artificial heart is implanted as a replacement to the patient's heart. There are several kinds of activation, and the most common is the pneumatic type.

The indication and selection of total circulatory assist devices are invariably influenced by their availability and the experience of the surgical team. The situations justifying the use of such devices are presented in Table 45[258-261].

Regarding the use of these devices, several factors are related to the poor postoperative prognosis and must be considered as contraindications: age >65 years, episode of pulmonary embolism in the previous month, prolonged oral intubation (> 48 hours), episode of cardiopulmonary resuscitation in the previous 24 hours; acute neurological sequela, acute or chronic renal failure with creatinine >2.5 mg/dl and/or urea >100 mg/dl, liver dysfunction with total bilirubins >3 mg/dl and active infectious condition.

VIII. Treating patients with special conditions and comorbidities

A. Pulmonary Thromboembolism (Tables 46 and 47)

Patients with HF have an increased risk of pulmonary thromboembolism (PTE), which constitutes a relatively frequent cause of decompensation. The predisposing conditions are: low cardiac output through dilated chambers, ventricular hypocontractility, abnormalities in the segmental kinetics, endocardial surface modified after myocardial infarction or inflammatory or infiltrative cardiomyopathies, hypercoagulability and the presence of AF[262,263].

Right ventricular dysfunction is present in 50% of cases and it constitutes a marker of poor prognosis, especially in patients with hemodynamic instability. Contrary to patients without previous HF, small emboli can cause large hemodynamic repercussion in the presence of HF. About 90% of patients in shock had a previous cardiopulmonary disease, while 56% of patients with previous

Table 40 - Indication of Alternative Surgical Treatment in Dilated Cardiomyopathy in Patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Annuloplasty or mitral valve replacement in patients with secondary valvar insufficiency of moderate or intense grade.	IIb	C

Table 41 - Indications of Catheter Ablation in Patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
ACatheter ablation in patients with probable tachycardiomyopathy due to supraventricular tachyarrhythmias or, occasionally, of ventricular origin*	I	C
Ablation of AF or the AV junction associated with placement of a definitive pacemaker, in patients with AF and increased ventricular response refractory to electric cardioversion and pharmacological treatment	I	B
Implantable cardioverter-defibrillator in patients with ventricular dysfunction and episodes of sustained VT not treated with catheter ablation (e.g., branch to branch reentry)	I	B

* Atrial flutter, atrial tachycardia, AV nodal reentrant tachycardia and tachycardia due to accessory pathways; AF = atrial fibrillation; AV= atrioventricular; VT = ventricular tachycardia

Table 42 - Indications for Implant of a Definitive Pacemaker in Patients with DHF

Condition	Degrees of Recommendation	Level of Evidence
Type II Second Degree AV Block or Third Degree AV Block independent of anatomic level as the presumable level of decompensation	I	C
Sinus node dysfunction (spontaneous or resulting from the use of drugs that cannot be interrupted) as a presumable cause of decompensation	I	C

Table 43 - Indications of Ventricular Resynchronization in Patients with DHF		
Condition	Degrees of Recommendation	Level of Evidence
Patients with HF refractory to optimized clinical treatment, with QRS >0.13; ejection fraction <35%* and functional class IV - NYHA*	IIb	D

*For improved symptomatology

Table 44 - Indication of Intra-aortic Balloon in Patients with DHF		
Condition	Degrees of Recommendation	Level of Evidence
In acute myocardial infarction, as a supportive measure for myocardial recovery or stabilization to perform any intervention	I	B
In mechanical complications of myocardial infarction, as a stabilization measure to perform surgical correction	I	C
In acute cardiomyopathies or in acute decompensation of dilated cardiomyopathies, as a supportive measure for myocardial recovery or stabilization to perform the heart transplant	I	C
Postoperative of heart surgery as a supportive measure to myocardial recovery	I	C
Hemodynamic instability in patients with large areas of myocardium under risk of ischemia, as a stabilization measure to perform any intervention	IIa	C

Table 45 - Indication of Mechanical Circulatory Support Devices, except Intra-aortic Balloon, in patients with DHF		
Condition	Degrees of Recommendation	Level of Evidence
In acute myocarditis or in acute decompensation of dilated cardiomyopathies, as a supportive measure for myocardial recovery or stabilization to perform heart transplant	IIa	B
In postoperative of heart surgery as a supportive measure for myocardial recovery in patients nonresponsive to intra-aortic balloon	IIa	C
In acute myocardial infarction as a stabilization measure to perform heart transplant	IIa	C
In acute myocardial infarction as a supportive measure for myocardial recovery in patients nonresponsive to intra-aortic balloon	IIb	D

cardiopulmonary disease were in shock, compared with 2% of patients without this condition[264]. Massive obstruction =50% is uncommon in this population which suggests that patients with previous cardiopulmonary disease affected by massive PTE frequently do not survive to be included in the clinical assays.

The exact incidence and prevalence of PTE related to HF is still controversial, and the data diverge among clinical studies and studies from autopsies[76,265-269]. In VHeF-T and SOLVD studies, the proportion of PTE was similar to systemic events (10-20%), but different from that of stroke (60-80%)[270].

The diagnosis of PTE in patients with HF must always be assessed by searching the presence of hemoptysis, thoracic pain or persistent cough. Risk factors associated with these events such as AF, previous embolic phenomenon or image diagnosis of an intracavitary thrombus must be valued. Standard signs and symptoms used to estimate the seriousness of the embolic event in patients with subjacent cardiopulmonary disease may not be reliable indicators. The presence of cardiogenic shock (systolic AP =90 mmHg) is associated with a 3-7 fold increase in mortality, with most deaths occurring during the first hour of onset. A fast integration of history and suggestive physical exam coupled with laboratory tests is necessary, and subsequently, the establishment of a diagnostic and therapeutic strategy in a short time. All patients must undergo a thoracic teleradiography to exclude other morbidities that may simulate PTE. Echodopplercardiography is a very useful exam since it can be performed at bedside, it is not invasive, and it allows for the differentiation of the cause of shock and recognition of the characteristics of PTE. A ventilation-perfusion pulmonary scintigraphy in critically ill patients may be difficult to be performed. Helical computerized tomography has been used to gradually replace the pulmonary angiography for confirmation of the diagnosis; it can substitute the transthoracic and transesophageal echocardiograms. Pulmonary angiography is considered the golden standard to confirm the diagnosis, despite being invasive, costly, requiring skilled professionals, and not always available. The levels of D-dimer are increased in an acute thromboembolic event, but they are not enough to confirm the diagnosis of PTE; however, a negative test can exclude the diagnosis (Table 46).

In the early phase of evaluation, the patients require aggressive stabilization and therapy[271,272] (Table 47). Hypoxemia (refractory) not reverted with high concentrations of oxygen requires mechanical ventilatory assistance; arterial hypotension that does not reverse with volume administration requires inotropic therapy. Thrombolytic therapy has been considered the choice option in patients with hemodynamic instability, with or without right ventricular dysfunction; embolectomy is reserved for those cases in which thrombolysis is contraindicated. Other potential indications of thrombolytic agents are right ventricular dysfunction, serious hypoxemia, respiratory insufficiency and massive ileofemoral thrombosis. Fractionated or unfractionated heparin is reserved for cases without hemodynamic instability.

B. Anemia (Table 48)

Although anemia (and its correction) is a well known comorbidity in several clinical conditions including myocardial ischemia, only recently its role in HF has been recognized as a prognostic

Table 46 - Recommendations for Management of Patients with DHF and Pulmonary Thromboembolism

	Degrees of Recommendation	Level of Evidence
Diagnosis:		
Hemodynamically Stable Patients		
D-Dimer	IIa	B
Ventilation-Perfusion Pulmonary Scintigraphy	I	B
Transthoracic Echocardiogram	I	B
Transesophageal Echocardiogram (when transthoracic is not elucidative)	IIb	B
Helical Tomography	I	B
Pulmonary Arteriography (if doubt persists after echocardiogram and scintigraphy)	I	C
Hemodynamically Unstable Patients		
D-Dimer	IIa	B
Ventilation-Perfusion Pulmonary Scintigraphy	III	B
Transthoracic Echocardiogram	I	B
Transesophageal Echocardiogram (when transthoracic is not elucidative)	IIb	B
Helical Tomography	IIa	B
Pulmonary Arteriography (for possible therapy)	I	C

Table 47 - Treatment of Pulmonary Thromboembolism

	Degrees of Recommendation	Level of Evidence
PTE with evidence of hemodynamic instability (SAP < 90mmHg) or signs of shock: initiate therapy with thrombolytic agents	I	A
PTE without evidence of hemodynamic instability (PaO_2 < 60mmHg, HR > 120 bpm, RR > 28 pm, Mean Pulmonary Pressure > 20mmHg, signs of right ventricular dysfunction on echocardiogram, positive troponin test, SAQRS > 90):: initiate therapy with thrombolytic agents	IIa	B
PTE with hemodynamic stability: initiate therapy with fractionated or unfractionated heparin	I	A
Vena Cava filter in recurrent events in the presence of adequate anticoagulation, contraindication to anticoagulation or presence of a large thrombus in LE, in spite of previous anticoagulation	I	C

SAP = systolic arterial pressure; PTE = pulmonary thromboembolism; HR = heart rate; RR = respiratory rate (inspirations per minute); LE = lower extremities

Table 48 - Recommendations for Treatment of Patients with DHF and Anemia

	Degrees of Recommendation	Level of Evidence
Venous erythropoietin/iron to correct anemia (Hb < 10g/dl) in patients with HF or CRF or coronary artery disease or age > 60 years, or slected patients	IIa	B
Blood transfusions in patients with anemia (Hb < 9g/dl), with ischemic cardiomyopathy and decompensated HF	I	C
Blood transfusions in patients with anemia (Hb < 7g/dl) and DHF	I	C

CRF = Chronic Renal Failure

factor independent of morbidity and mortality, but its pathophysiology is not well established yet. Several mechanisms determine its occurrence: (1) iron deficiency due to low ingestion, poor absorption or chronic loss, especially in ischemic cardiomyopathies with the use of platelet antiaggregation agents which lead to digestive losses due to bleeding; (2) associated comorbidities such as diabetes, arterial hypertension and chronic renal failure; (3) urinary losses of erythropoietin and transferrin; (4) use of ACE inhibitors[273]; (5) increased cytokine activity, causing bone marrow depression[274]; and (6) hemodilution.

Approximately 50% of patients with HF are anemic (Hb < 12 g/dl and/or Ht < 37%). Anemia prevalence and seriousness increase with functional class (FC) of HF (NYHA), with studies pointing to a percentage of anemic patients of 52.6% in FC III and 79.1% in FC IV[275,276], being more common among the elderly, women, hypertensive patients and in the presence of associated renal disease[277-279]. Anemia and chronic renal failure are independent prognostic factors for mortality in patients with HF and they are associated with impairment of the symptoms and reduction of functional capacity[280-282].

Serious and acute anemia is usually well tolerated in normal hearts at rest, but the presence of coronary heart disease impairs the myocardial ability to adapt to these conditions, since anemia can predispose the myocardium to ischemia, repetitive stunning, apoptosis and necrosis, contributing to the progression of ventricular dilation and HF[283,284].

Cardiorenal syndrome is a vicious circle that occurs in HF, caused by low flow, leading to renal failure and subsequent reduction in the production of erythropoietin, which causes anemia. Ventricular dysfunction and anemia lead to exacerbation of myocardial and peripheral hypoxia, increase in venous return, increase of cardiac work and left ventricular hypertrophy. Hypoxia still causes the activation of neurohormones and cytokines which, by themselves, exacerbate the anemia and aggravate the vicious circle. Anemia impairs the HF, which worsens the renal failure and reduces even more the production of erythropoietin.

Evidence is still scarce about blood transfusions for the treatment of DHF in anemic patients. Most Guidelines recommend blood transfusions for patients who are not critically ill only when hemoglobin levels are below 7-8 g/dl. However, high risk patients

who may benefit from blood transfusions should be individualized and screened, such as the elderly, coronary heart disease patients and patients with chronic renal failure (CRF) whose hemoglobin levels should be maintained around 10 g/dl[285,286]. Erythropoietin is a glycoprotein growth factor produced by the kidneys to adjust the production of red blood cells. It was originally successfully used in anemic patients with chronic renal failure (CRF) during dialysis or predialysis. In a retrospective study with 26 patients with serious HF and anemia (Hb < 12 g%) considered resistant to optimized clinical treatment, the use of subcutaneous erythropoietin and intravenous iron raised the levels of Hb from 10.16 ± 0.95 to 12.10 ± 1.21g/dl, after a period of 7.2 ± 5.5 months with subsequent improvement in heart function, ventricular ejection fraction from 27.7 ± 4.8 to 35.4 ± 7.6, and a reduction of hospital stays of 91.9%[287].

C. Chronic renal failure (Table 49, 50, and 51)

Cardiovascular diseases (CVD) are the ones that most contribute to morbidity and mortality in uremic patients. Mortality due to CVD is increased by 10-20 times; the prevalence of HF is 12-36 times higher in patients undergoing renal replacement therapy than in the general population, and it is responsible for up to 50% of deaths in the final stage of the disease. The etiology of HF in CRF is multifactorial: uremia, increased levels of calcium, phosphate, diabetes, systemic arterial hypertension (SAH) and coronary heart disease. The myocardial abnormalities observed include left ventricular hypertrophy (LVH), degenerative arterial lesions involving coronary arteries and, less frequently, calcified pericarditis and valve diseases[288]. Although this population is excluded from large studies on primary and secondary, even in the advanced stages of the disease, specific treatments for SAH, anemia, hyperparathyroidism and dyslipidemia have been beneficial[289,290].

Correction of anemia in HF and CRF: Some data indicate that the correction of anemia with Hb < 10g/dl with a consequent improvement of HF is frequently associated with slowness or stabilization of the progression of CRF[291], even in patients with diabetes[292], improving life quality and exercise capacity, with no impact on mortality[293].

Anemia is considered an independent risk factor for left ventricular dysfunction, risk of hospitalizations for HF, and recurrent decompensations and mortality in patients with CRF undergoing dialysis[294]. The following measures are important: (1) intensification of dialysis with ultrafiltration sessions if necessary in order to restore ideal volemia, improve urea levels and electrolyte disorders; (2) implement the treatment for associated SAH, an important predisposing factor for HF decompensation; (3) treatment of myocardial ischemia when present; (4) use of ACE inhibitors or angiotensin II inhibitor is indicated in patients undergoing dialysis regardless of the creatinine levels; (5) digitalis must be used with caution and the serum levels must be frequently monitored; (6) the use of ACE-I is contraindicated in patients with serum creatinine ≥ 2.5

Table 49 - Recommendations for Treatment of DHF in Patients with Substitutive Renal Therapy

	Degrees of Recommendation	Level of Evidence
Intensification of dialysis with ultrafiltration sessions if necessary	I	B
Treatment of associated arterial hypertension	I	B
Treatment of myocardial ischemia when present	I	B
ACE-I or angiotensin II inhibitor	I	B

ACE-I = angiotensin-converting enzyme inhibitor

Table 50 - Recommendations for Treatment of DHF in Patients without Substitutive Renal Therapy

	Degrees of Recommendation	Level of Evidence
Intensification of therapy with diuretics	I	C
Treatment of associated arterial hypertension	I	B
Treatment of myocardial ischemia (when present)	I	B
Ultrafiltration sessions, if necessary	IIa	B
Nitrate and hydralazine if creatinine ≥2.5 mg/dL and/or serum potassium ≥5.5 mEq/L	I	B
ACE-I or angiotensin-II inhibitor if creatinine ≤2.5 mg/dL and/or serum potassium ≤5.5 mEq/L	I	B

ACE-I = angiotensin-converting enzyme inhibitor

Table 51 - Recommendations for Treatment of Patients with DHF and Aggravated Renal Failure

	Degrees of Recommendation	Level of Evidence
Determine the ideal volemia	I	B
Closely monitor diuresis	I	C
Monitor the levels of urea, creatinine, sodium, potassium, and magnesium	I	C
Monitor the levels of drugs with renal elimination	I	C
Venous inotropic agents to improve renal perfusion	IIa	C
ACE-I or angiotensin-II inhibitor if creatinine ≤2.5 mg/dL and/or serum potassium ≤5.5 mEq/L	I	B
Nitrate and hydralazine if creatinine ≥2.5 mg/dL and/or serum potassium ≥5.5 mEq/L	I	B
Adjust the doses of diuretics and vasodilators to control water retention, alleviate congestion, reduce filling pressures and improve renal perfusion.	I	B
Initiate ultrafiltration or hemodialysis if serious renal failure (creatinine > 5 mg/ dL) or progressive renal failure is present	I	B

mg/dL and/or serum potassium ≥ 5.5 mEq/L who are not receiving dialysis, and it can be replaced by the association of hydralazine and nitrate.

D. Aggravated Renal Failure

Most patients with chronic HF of enough severity to result in hospitalization have renal function abnormalities. Renal dysfunction can be secondary to low renal perfusion, intrinsic renal disease or due to the drugs used in the treatment of HF, and it can be impaired during the acute decompensation of HF and its therapy. The cause of renal failure in the context of DHF seems to be associated with a complex cardiorenal interaction which is beyond the reduced cardiac output alone[295].

Associated diseases such as atherosclerosis, SAH, diabetes mellitus and amyloidosis can cause intrinsic renal disease. Several other factors can contribute to renal hypoperfusion: decreased cardiac output, decreased renal blood flow, increased pressure in renal veins caused by elevated right atrial pressure and tricuspid regurgitation[296,297]. The increase of vasoconstrictive substances in the circulation – norepinephrine, endothelin and angiotensina – is a contributing factor to renal dysfunction. Additionally, the altered release and/or sensitivity of endogenous vasodilators such as natriuretic peptides and nitric oxide can affect the renal function[298-230].

In addition to the hemodynamic changes, the therapy for HF can directly influence renal function. Renal function can be impaired by the treatment with diuretics or ACE-I, although these changes are usually transient and reversible. Persistent or progressive renal dysfunction is associated with deterioration of the baseline renal disease and a reserved prognosis. In spite of these potential adverse interactions, most patients with HF tolerate mild to moderate renal dysfunction without the need to suspend their medications. However, if serum creatinine is >3mg/dL, the presence of renal failure can limit the treatment efficacy and predispose to drug intoxication caused by the medications prescribed for HF treatment. Patients with creatinine levels >5mg/dL generally require dialysis or hemofiltration to control water retention, to reduce uremia/hyperkalemia risk, and to permit the use of medications necessary for the appropriate treatment of HF[301,302].

Renal changes may have an impact on HF therapy. Renal dysfunction can result in suspension of diuretics and ACE-I before the optimum treatment is reached, reducing the filling pressures to levels considered ideal, and with subsequent maintenance of the congestive symptoms. ACE-I are beneficial even in patients with moderately high levels of creatinine[303]. A common practice is to use the levels of urea and creatinine as indexes of global perfusion during progressive diuresis. Mild changes in urea and creatinine levels can be misinterpreted as a decreased cardiac output due to excessive diuresis, which may lead to a reduction in the therapy intensity in spite of elevated filling pressures. There is evidence that slight increases in urea and creatinine levels rarely indicate a reduction of cardiac output, but they usually reflect other cardiorenal factors. Patients receiving optimal therapy frequently have elevations of 10-20% in urea and creatinine[304]. To this date, there are no recommendations in the Guidelines regarding the baseline levels of creatinine, estimated creatinine glomerular filtration or limits of acceptable increases during the therapy. However, patients with renal failure defined as an increase ≥25% in creatinine levels and reaching levels ≥2.5mg/dL require careful management. There are few options available to relieve the congestive symptoms in patients who develop progressive renal dysfunction during HF therapy. Ultrafiltration or hemodialysis can be recommended to improve the patient's life quality and comfort.

E. Sleep apnea in Heart Failure (Tables 52 and 53)

Obstructive apnea and central apnea or Cheyne-Stokes respiration are common in HF and the pathophysiology in these two conditions is closely related. The conventional approach to assessment and management of HF needs to be modified in view of increasing evidences that the sleep related respiratory disorders increase the risk of complications and accelerate the progression of HF, being independent risk factors for mortality in HF[305].

1. Obstructive Sleep Apnea

During sleep, in the phase of absence of rapid eye movement (about 85% of total sleep time), a reduction of sympathetic activity, metabolic rates, heart rate, arterial blood pressure and cardiac output is noticed[306,307]. Obstructive sleep apnea is caused by the pharyngeal collapse during sleep, which occurs mainly in obese individuals who are sleepy during the day and with nasalized voice[308]. The recurrence of obstructive apnea during sleep causes periods of hypoxia and hypercapnia with an exaggerated elevation of the negative intrathoracic pressure (leading to an increase of afterload and reduction of preload and, consequently, reduction of cardiac output) with intense release of sympathetic activity, inhibition of vagal activity, elevation of inflammatory mediators, elevation of oxidative stress and subsequent elevation of arterial blood pressure and pulmonary artery pressure, as well as increase of heart rate[309-311]. These changes can predispose to arrhythmias, ischemia, apoptosis, adverse remodeling and progression of DHF.

For the definitive diagnosis of obstructive sleep apnea it is necessary to use the technique called polysomnography which has the inconvenience of being an expensive test and therefore not generally used in patients with HF. The general therapeutics in these patients include weight loss, abstinence of alcohol and sedatives which predispose to pharyngeal collapse during sleep and use of continuous positive airway pressure, either nasal or oral, whenever indicated. It is also necessary to treat systemic arterial hypertension and the plurimetabolic syndrome. There is no evidence that the drugs used in the treatment of DHF have any impact on the severeness of obstructive sleep apnea. No randomized assay about HF has analyzed the impact of sleep apnea on the cardiovascular endpoints. However, acute resolution of obstructive sleep apnea with the use of CPAP in patients with HF prevents the recurrence of hypoxia, can increase left ventricular ejection fraction, can reduce ventricular diameters, arterial blood pressure, nocturnal heart rate and sensitivity of arterial baroreflex.

2. Central Sleep Apnea or Cheyne-Stokes Respiration (CSR)

Cheyne-Stokes Respiration (CSR) is a pattern characterized by increasing ventilatory frequency followed by hypoventilation until apnea. It is found in patients with Central Nervous System dysfunction, in individuals climbing to high altitudes, patients with HF and it is associated with a poor prognosis. Although it has long been described, its physiopathogenic mechanism has only recently been better understood. There seems to be an inadaptation and slowness to detect blood signs related to the concentrations of PaO_2 and $PaCO_2$ in the pulmonary receptors and carotid bodies due to the low cardiac output present in HF[312].

Table 52 - Recommendations for the Management of Patients with DHF and Obstructive Sleep Apnea		
	Degrees of Recommendation	Level of Evidence
Weight loss, metabolic control and control of arterial pressure	I	B
Treatment of the baseline disease	I	B
Continuous Positive Airway Pressure (CPAP) or (BIPAP)	I	A
Polysomnography evaluation	I	B

Table 53 - Recommendations for the Management of Patients with DHF and Central Sleep Apnea		
	Degrees of Recommendation	Level of Evidence
Therapy with nasal supplementation of O_2 in Central Sleep Apnea	IIa	B
Therapy with continuous positive airway pressure in Central Sleep Apnea	IIa	B

The specific treatment for CSR has been consolidated in the last decade[313]. Nasal oxygen supplementation reduces the episodes of apnea, reduces urinary catecholamines, improves the respiratory capacity and functional class of HF[314]. However, no clinical assays have analyzed the impact on mortality. Considering that CSR is a manifestation of advanced HF, the first consideration would be to optimize the treatment of HF. An aggressive treatment with diuretics to lower the filling pressures, administration of ACE-I and beta-blockers can reduce the severeness of the sleep central apnea; however, metabolic alkalosis can result from the excessive use of diuretics and predispose to Cheyne-Stokes Respiration. If Cheyne-Stokes Respiration persists in spite of optimization of the DHF treatment, other interventions should be considered: (1) nocturnal oxygen therapy can eliminate apnea associated with hypoxia, relieve the pattern of Cheyne-Stokes Respiration, reduce the nocturnal levels of norepinephrine and improve V_{O2} max; (2) CPAP was tested in randomized clinical trials in patients with HF, confirming that it reduces both cardiac preload and afterload, reduces the sympathetic activity, improves the ejection fraction, mitral regurgitation and life quality.

F. Thyroid Dysfunction (Table 54)

1. Low T_3 Syndrome

Thyroid diseases are comorbidities that can be associated with the HF syndrome[315]. More than 80% of the biologically active hormone triiodothyronine (T_3) is derived from the peripheral conversion of the prohormone thyroxine (T_4), which is secreted by the thyroid gland. At least 30% of patients with HF have low concentrations of free circulating T_3 and elevations of the levels of reverse T_3 (rT_3), without a compensating increase of TSH concentration. These changes are proportional to the functional class of the HF, being correlated with the seriousness of the disease.[316] In HF there is a reduction of the peripheral conversion of T_4 into T_3 which results in the low T_3 syndrome or the sick euthyroid that is described in the DHF[317-320]. The functional integrity of this hormonal axis is not completely explained, although an attenuation of the response of TSH to TRH has been described. In patients with advanced HF, a low T_3/rT_3 ratio is associated with serious ventricular dysfunction and it is a predictor of a poor prognosis in the short term.

Initial attempts to improve the cardiac function with thyroid hormone administered to patients with serious HF have been promising[321,322]. These observations suggest that the reduction of T_3 levels in non-thyroid diseases adversely affects the cardiac function and patients benefit from the hormone replacement, similarly to what occurs in hypothyroidism. The inability of patients with non-thyroid diseases to convert T_4 into T_3, maybe due to an increase of interleukin-6 and a reduction in the activity of hepatic type I deiodinase suggests that the hormone replacement must be performed with T_3 in doses that can bring the serum levels to normal. Although small studies have suggested that the intravenous administration of T_3 is beneficial in patients with advanced HF, additional studies are necessary to establish the specific recommendations for the treatment.

2. Hyperthyroidism

Patients with hyperthyroidism can occasionally present stress dyspnea or signs and symptoms of HF. Patients with chronic and serious hyperthyroidism may occasionally present serious deficit of cardiac contractility, low cardiac output, signs and symptoms of HF, third heart sound and pulmonary congestion. This complex condition generally occurs due to persistent tachycardia or AF. The early detection and appropriate management of cardiac manifestations is crucially important in patients >50 years old since cardiac complications are the main cause of death after the treatment of hyperthyroidism. The initial treatment should include beta-adrenergic antagonists, such as propranolol or atenolol, to reduce the heart rate to normal levels. After that, the definitive therapy with Iodine-131 isolatedly or in combination with an antithyroid drug must be initiated.

3. Hypothyroidism

As opposed to hyperthyroidism, low concentrations of thyroid hormones are associated with decreases of cardiac output, heart rate, systolic volume, and myocardial contractility, as well as increases in the systemic vascular resistance. The cardiac manifestations include bradycardia, pericardial effusion and HF. However, HF is rare because the cardiac output is usually enough to supply the peripheral demands of oxygen. Thyroxin therapy reverses all the cardiovascular manifestations.

4. Amiodarone-induced Thyroid Disease

Chronic treatment with amiodarone (a drug commonly used in patients with HF to treat ventricular and supraventricular arrhythmias) is another factor responsible for thyroid dysfunction. Its high iodine content can cause thyroid dysfunction in patients with

Table 54- Recommendations for Treatment of Thyroid Dysfunction in DHF

	Degrees of Recommendation	Level of Evidence
Initial treatment of hyperthyroidism with beta-adrenergic blocking agents before initiating antithyroid drugs	I	C
Treatment of hypothyroidism with thyroxin	I	C
Administration of thyroid hormone in Low T3 Syndrome which occurs in serious HF	IIb	B
Hormonal replacement therapy must be performed with T3 (patients unable to convert T4 into T3) in Low T3 Syndrome	IIb	C
Amiodarone-induced hypothyroidism can be treated with thyroxin; amiodarone does not need to be suspended	IIa	C
Amiodarone-induced hyperthyroidism can be treated with antithyroid drugs; amiodarone does not need to be suspended	IIb	C

preexistent thyroid disease or destructive thyroiditis in patients with a previously normal thyroid gland. The combined incidence of hyperthyroidism or hypothyroidism in patients using amiodarone is around 14-18%. Chronic treatment with amiodarone in euthyroid patients with no evidence of a baseline thyroid disease results in increases of the T4 concentrations and normal T3.

Hyperthyroidism: Two types of hyperthyroidism can be induced:

1. Type I hyperthyroidism: each 200mg amiodarone tablet contains 70mg iodine, which is enough to induce hyperthyroidism in patients with nodular goiter or remittent Graves disease. This does not necessarily constitute an indication to discontinue amiodarone because many patients can be managed with concurrent antithyroid medication. However, this type of hyperthyroidism can be very difficult to treat.

2. Type II hyperthyroidism, which is caused by a thyroiditis due to the use of amiodarone without preexistent thyroid disease. Most cases present spontaneous resolution after suspension of amiodarone. The differential diagnosis between the two types can be difficult.

Hypothyroidism: Amiodarone can cause hypothyroidism in patients with preexistent Hashimoto's thyroiditis. However, the increase in serum levels of TSH before or during the treatment is not a contraindication to the use of amiodarone since the thyroid insufficiency can be adequately treated with thyroxin.

G. Cardiac Cachexia (Table 55)

Cachexia is an important complication associated with a bad prognosis, occurring in chronic diseases, such as HF, but its definition is controversial. Some authors define malnutrition as the body fat content <22% in women and <15% in men; others, more simplistically, define it as dry weight loss >7.5% in a 6-month period (excluding other clinical conditions that may lead to cachexia)[323-325]. Weight loss >15% can be classified as serious while weight loss between 7.5-15% is classified as initial or moderate. Since HF prevalence and survival have been increasing, cardiac cachexia affects these patients and cause more morbidity with mortality rates of 50% in a 18-month follow-up[326].

The main factors involved in the etiology of cardiac cachexia seem to be related to nutritional deficiency, intestinal malabsorption, metabolic dysfunction, right ventricular dysfunction, increased serum catecholamines, neurohumoral activation, immune mechanisms, increased catabolism and tumoral necrosis factor (TNF)[327-329]. Other cytokines such as interleukine-1 and -6, γ-interferon and growth factor beta also increase in the cachectic stage of patients with HF[330]. The main hypotheses for the elevation of TNF are the production of this factor in the myocardium and also the bacterial translation in the intestine with endotoxinemia[331].

The therapeutics for patients with cardiac cachexia has the purpose of increasing skeletal muscle tissue and, consequently, the improvement of physical capacity. ACE-I and beta-blockers, in addition to reducing mortality, also reduce weight loss in HF[332]. The patient must be advised to have an appropriate nutritional support. Cases of serious anorexia and subsequent marked malnutrition may require nasoenteral nutrition.

H. Terminal Heart Failure

1. Definition

Approximately 10% of patients with HF have the advanced form of the disease. The terminology of chronic HF in its advanced stages is not very accurate, and the terms "advanced, serious, refractory and terminal" are indiscriminately used as synonyms. The term terminal HF was created in the last decade and it reflects a bad prognosis. The introduction of new treatments in clinical practice requires a continuous assessment of the evidences and, if possible, with well defined criteria[333].

There is no simple definition for the complex syndrome of advanced HF[334]. As a matter of fact, the functional classification of HF (NYHA) commonly used to describe the clinical status of the patient is also imprecise. The functional class is a temporal evaluation of the patient but the clinical status may fluctuate so much that a single evaluation is not a safe basis for classification. By definition, a patient in Class IV is symptomatic at rest. However, after intensive treatment, this patient can migrate to Class III, but probably remains with advanced HF. A complex definition was developed, encompassing signs and symptoms, functional capacity, duration of symptoms, left ventricular ejection fraction (LVEF) and other criteria such as catecholamines and hyponatremia was developed. Patients who meet all these criteria have a strong negative impact on survival. However, even this classification system is not applicable to all patients. Some patients may have reversible ventricular dysfunction and others may experience a major improvement with optimized clinical treatment. Thus, a definition for this complex syndrome would include patients who, in spite of the optimized clinical treatment, remain mostly symptomatic with evidence of disease progression and high mortality rates within one year. Several clinical trials have shown that the survival of patients

Table 55 - Recommendations for Treatment of Cachexia in the Context of DHF

	Degrees of Recommendation	Level of Evidence
Oral nutritional support, including nasoenteral diet in cases of serious anorexia with severe malnutrition	IIa	C

who reach Class IV is dramatically reduced even with the treatment strategy modulating the neurohumoral system[76,112,335,336].

If a reversible condition is not present or if heart transplant is not a feasible option, by definition it becomes a terminal disease. Obviously, the treatment with ACE-I, beta-blockers and spironolactone can reduce morbidity and mortality even in this group of patients. However, even with optimized treatment, some patients with serious HF continue to present a deterioration of their clinical condition and evolve extremely symptomatic. Nowadays, there are few options available for this increasing number of patients with terminal HF who are refractory to clinical treatment[337,338]. Although the patients with the most serious form of the disease represent a smaller proportion, they account for a larger number of hospitalizations and, consequently, a great economic overload.

2. Palliative Measures and final stage evolution management (Table 56)

Palliative care is used in patients whose disease does not respond to curative treatment, and the objective is centered on their life quality and of their families.

The planning of medical care for the patient with terminal HF involves several problems because there is no defined model for this group. Traditionally, hospice care was offered to patients with terminal cancer and, only recently, these treatments have been extended to other chronic diseases including terminal HF. HF can be included in the hospice programs since the patients present marked dyspnea and may require frequent administration of intravenous diuretics and, in some cases, intravenous inotropic agents, anxiolytics and narcotics to relieve their suffering.

Traditionally, the indication for hospice care requires a forecast of death within 6 months, which is a difficult operational policy to be applied, mainly in patients with HF. An estimated survival prognosis of about 6 months, patient and family agreement on not accepting more aggressive treatment measures are criteria for inclusion in the program. These terminal care modalities exclude the treatments that cure the baseline disease or treat the underlying pathophysiology. As opposed to cancer, a predictive model for death in patients with HF can be very difficult and complex. Death can occur from other unexpected causes such as stroke, myocardial infarction, arrhythmias or infection. Other patients can survive more than 6 months. Many of them become increasingly refractory to the escalating doses of medications and they die due to hemodynamic deterioration. The inability to accurately predict life expectancy leads to an extended hope of survival and the patient undergoes the painful transition from seriously sick to extremely sick.

The largest trial performed regarding this issue was SUPPORT[339], in which patients with HF were analyzed along with their preferences, prognosis, treatments and outcomes. In this study, only 23% of patients with class IV heart failure refused resuscitation. More than 50% of patients demonstrated their wish for comfort and relief from their symptoms such as pain or dyspnea in the last days of their lives. More than 60% had serious dyspnea 3 days before dying. About 40% received at least 1-3 types of life support treatment – feeding tubes, mechanical ventilation and cardiopulmonary resuscitation. In spite of the patients' wished and preferences, many of them received aggressive treatment.

Palliative care can be offered by a multidisciplinary team, at home or in the hospital (with the hospice programs), including intravenous diuretics, in some cases intravenous inotropic agents (in some cases), morphine, oxygen supplement, with or without hospitalization. The World Health Organization added further objectives to palliative care[340]: (1) reaffirmation of life and consideration of death as a natural process; (2) no acceleration or postponement of death; (3) providing relief from pain and relief from other painful symptoms; (4) integrating the psychological and spiritual aspects of treatment; (5) providing support in helping patients to remain active until death; (6) helping the family cope with the patient´s pain and disease.

The main symptoms common to terminal patients can be managed at those places, at home or in hospitals.

Dyspnea: More than 50% of patients with terminal disease suffer from serious dyspnea. The treatment of this symptom includes treating the baseline disease. Opiates are very helpful; they relieve coughing, anxiety, pain, exhaustion and reduce the physical and psychological stress. Oxygen therapy can be useful even in cases without hypoxemia.

Nausea and vomiting: Peptic ulcer and constipation must be treated. Histamine blockers can exacerbate delirium; therefore, antacids are preferred. Metoclopramide is an excellent antiemetic, but it can also cause delirium, depression and extrapiramidal effects. Serotonin antagonists such as ondansetron have an excellent antiemetic action although they are very expensive. Phenotiazines can be efficient, but they also have extrapiramidal and anticholinergic effects.

Anorexia and cachexia: The loss of appetite is stressful for the patient and his/her family. It has a multifactorial origin, including the increased production of cytokines. The treatment intends to improve the baseline cause whenever possible. Appetite stimulants can be useful.

Table 56 - Recommendations for Palliative Care in Terminal DHF

	Degrees of Recommendation	Level of Evidence
Acknowledge the prognosis of terminal DHF and instruct patients and family members	I	C
Palliative treatment of terminal DHF	I	C
Indication of hospice care for patients with terminal DHF with expected 6-month survival	IIa	B
Improve the patient life quality	I	C
Alleviate concurrent symptoms	I	C
Alleviate physical and psychological stress	I	C
Instructions to patients and family members	I	C
Emotional and psychological support to patients and family members	I	C
Respect the patient's preferences	I	C
Implant a cardioverter-defibrillator in terminal patients with no chance of recovery	III	C

Anxiety and depression: Anxiety and depression frequently occur in terminal patients as a result of pain, dyspnea or other causes. Clinical depression is common and must be treated with anxiolytics and antidepressants whenever necessary.

Suffering: No discussion about palliative measures is complete without including the patient´s suffering. Suffering goes beyond physical pain and affects all the aspects of personal life. Suffering is felt by people and not by bodies, and it can be alleviated merely by the doctor´s presence showing that he is committed with the patient and has not abandoned him.

Many patients are not prepared to accept this course of treatment. On average, patients are admitted to hospices about a month before dying. In the SUPPORT study, 58% of patients died at the hospital, 27% at home and only 3% died in hospices. In general, patients prefer a treatment in which they have a higher chance of survival. Hospices are used in the last days of life, therefore other options should be available before this terminal stage. Some algorithms have recently been proposed for the complex management of refractory HF, which include treatment options at home and in hospices[341].

3. Home hospitalization (Table 57)

A program of home hospitalization can be transient or long-term. This type of service usually allows a physically disabled person to become more independent, providing multidisciplinary approaches to patients with chronic diseases. Several studies about home hospitalization for patients with HF show a reduction in hospitalizations, improvement in functional class and cost reductions. Considering the increasing number of elderly patients diagnosed with HF, and increased numbers of cases of chronic and advanced HF, this program seems to be very appropriate to treat patients with HF. These programs offer a variety of services such as intravenous inotropic therapy, intravenous diuretics, pulse oximetry, oxygen therapy, electrocardiographic monitoring and a multidisciplinary team. The treatment ranges from patient education and physical rehabilitation to intravenous medications[15,342-344].

IX. Follow-up programs and specialized treatment of DHF (Table 58)

A. Heart Failure Clinics

Among the general measures to be applied in patients with frequent episodes of decompensation or in advanced stages of the syndrome, we emphasize the patient´s closer follow-up in HF clinics or in facilities functioning as such[345-347]. Several studies demonstrate the superiority and cost-benefit of specialized centers for the treatment of HF[348]. Many of these are observational studies, using a before-after dynamics; the interventions vary from simple follow-up by phone to more sophisticated programs[349]. In the few existing randomized studies, the results are similar[350]. Therefore, when it is not performed in an HF clinic, the efficiency of the clinical treatment of patients with serious and advanced HF is limited by the underuse of medications, poor adherence to medicaton/diet and loss of a systematic monitoring of patients, etc. Nonadherence may be the most important limitation to treatment[351]. The use of an HF clinic increases the adherence to diet and medications with consequent improvement of functional class and exercise capacity[352,353].

The programs of an HF clinic basically consist of intensive educational programs of HF and monitoring of the follow-up (Tables 58 and 59). The programs of HF clinics can be classified according to their service structure, and it involves the type of treatment, human resources, multidisciplinary team, monitoring, education and facilities offered[354].

The objectives are patient education to assure adherence to the diet and medication, and early identification of symptoms, factors related to decompensation, or events that are treatable/preventable outside the hospital (Table 60). However, the optimal intervention is not defined yet, and it can be simple or complex, in addition to being influenced by the clinical practice and the population. The monitoring system can also be performed in several ways. Strategies for increasing consistent adherence to treatment are also developed, by acknowledging individual factors related to adherence.

The patient is advised to contact the team when certain signs and symptoms occur. The objective is early detection or prevention of factors related to cardiac decompensation, emphasizing arterial hypertension, cardiac arrhythmias/atrial fibrillation, myocardial ischemia/infarction, unrecognized valve disease, infection, alcohol consumption, inadequate fluid and salt intake, inadequate use of medications, low adherence to the treatment prescribed, social factors, such as social isolation, or lack of social support, behavioral factors, pulmonary/peripheral embolism, thyroid disease, anemia, systemic disease, hypovolemia, iatrogenic factor, excessive tachycardia or bradycardia, impairment of mitral insufficiency, pregnancy, digitalis intoxication, depression and comorbidities such as hepatopathy, etc.

The programs of HF clinics increase the use and doses of recommended medications[355,356]. HF is the most common cause of hospitalization in patients >65 years, who also have a high

Table 57- Recommendations for Home Hospitalization in Terminal DHF

	Degrees of Recommendation	Level of Evidence
Patients with DHF depending on intravenous medication and frequent hospitalizations	IIa	C
Patients with DHF and difficulty to walk; elderly patients	IIa	C

Table 58 - Specialized Programs for Heart Failure

Heart Failure Clinic
- Instructions to patient/family members
- Additional instructions to patient/family members
- Cardiologist specialized in the treatment of Heart Failure
- Multidisciplinary team
- Therapeutic Optimization

Monitoring of Follow-up in the Heart Failure Clinic
- Based on the evaluations at the clinic
- Remotely by phone
  - By phone, with a nurse supervised by a doctor
  - Communication with self-monitoring of weight/viral signs Supervised by nurses and doctors
- Home care
  - Care in the traditional home
  - Care in the multidisciplinary home

Association of Clinics and Monitoring Methods

Table 59 - Instructions to Patients with Heart Failure

- General Education
  - What is heart failure and its symptoms
  - Causes of heart failure and basic principles of pathophysiology
  - How to recognize signs and symptoms
  - How the symptoms appear and when to inform immediately
  - How to check body weight and monitor arterial blood pressure
  - Rationale for treatment
  - Importance of compliance to pharmacological and non-pharmacological prescriptions
  - Quit cigarette smoking/alcoholic beverages, if indicated/drugs, etc
- Instructions about Medications
  - Effects, doses and duration of administration
  - Side effects, signs of intoxication
  - Instructions about doses, self-manipulation of medications
  - Avoid nonsteroid anti-inflammatory drugs, Class I antiarrhythmic drugs, calcium antagonists, tricyclic antidepressants, corticosteroids, lithium, etc
- Instructions for Rest and Physical Exercise
  - Rest, Work, Daily physical activity, Sexual activity
  - Rehabilitation
- Vaccines, Trips
- Diets and Social Habits
  - Control of diet and salt, when necessary; avoid excessive fluids
- Reduce side effects of medications
- Simplify treatment
  - Reduce complexity; prescribe once a day, if possible
  - Treatment adequate to patient's activities
- Improve doctor-nurse-patient relationship
  - Spend more time with patient
  - Easy communication for the patient to understand
  - Involve the family for better compliance
  - Improve perception of the disease
  - Containers for pills
  - Regulate visits and evaluation
  - Eliminate unnecessary medications. Simplify the prescription
- Instructions to contact the Team
  - Weight gain >1.2kg in 2-3 days not responding to diuretics in use; slow progressive increase in weight > 300 g per day, uncertainty about diuretics, new edema in lower extremities or abdomen, impairment of dyspnea with light physical exercises, paroxysmal nocturnal dyspnea, orthopnea, impairment of coughing, persistent vomits or anorexia, dizziness unrelated to posture, syncope, blood-stained sputum, fever, persistent tachycardia, motor deficit/paralysis, persistent or very high fever, unexplained thoracic pain

Table 60 - Compliance with medication for Heart Failure

- Factors related to shorter time of continued use
  - New prescription of angiotensin-converting enzyme inhibitor
  - Renal failure
- Factors related to smaller dose
  - Number of administrations per day
- Factors Related to increased time of continued use
  - Male gender
  - More frequent visits
  - Digitalis
- Factors related to higher doses
  - Young age
- Reasons for non-compliance
  - Disease does not require further treatment
  - Cost of treatment
  - Access or long waiting time
  - Loss of cure
  - Number of medications and complex therapeutic regimen
  - What the patient thinks about his disease
  - Poor doctor-patient relationship
  - Side effects
  - Hostility
  - Marriage
  - Elderly (side effects) or age-related
  - Young age (interferes in lifestyle)
  - African-Brazilians
  - Depression
  - Limited social condition
  - Absence of symptoms
  - usência de sintomas

Table 61 - Recommendations to patients with DHF in a Heart Failure Clinic

	Degrees of Recommendation	Level of Evidence
Patients with DHF	I	B
Recurrent hospitalizations	I	B
Risk of hospitalization	I	B
Patients in a HT waiting list	I	B

HT = Heart Transplant

risk of early rehospitalization (29-47% in 3 to 6 months). A prospective study showed that 53% of early readmissions could possibly be prevented[357]. The management of HF patients in specialized centers or HF units can be associated with better clinical progress, lower hospitalization rates and better survival[349,358-360].

In a study involving a limited number of elderly patients to evaluate mortality there was a trend towards mortality reduction, with a 3-month survival rate of 91% in the treated group and 75% in the control group, respectively. A recent prospective, randomized study evaluating domiciliary interventions followed by telephone monitoring resulted in reduction of hospitalizations combined with mortality in addition to decreased number of hospitalizations[347]. A recent study with domiciliary interventions demonstrated in an average follow-up of 4.2 years that the effects are sustained in the long term, reducing mortality, unplanned hospital readmissions and consequent cost reductions[361]. A recent study with a limited number of patients demonstrated an increase in the left ventricular ejection fraction from 24% to 36% and a reduction in the diastolic diameter from 65mm to 59mm[362], as well as in the treatment cost[363]. Table 61 shows the recommendations for the Heart Failure clinic. V

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