Cirrhotic Cardiomyopathy

Jessica Bicca, Luiza Porto Jarske, Thamires Oliveira Silva, Ronaldo Gismondi, Luís Otávio Mocarzel, Pedro Gemal Lanzieri

Universidade Federal Fluminense – Faculdade de Medicina – Curso de Graduação em Medicina – Niterói, RJ - Brazil

Abstract

Cirrhotic cardiomyopathy (CCM) is a chronic cardiac dysfunction that affects cirrhotic patients without history of heart disease. It is an initially asymptomatic disease that appears in situations of increased metabolic demand due to lower cardiac capacity to increase inotropism. Diagnosis is based on disorders revealed by electrocardiography and echocardiography. There is no specific treatment for CCM. Similar symptomatic medications are established to treat heart failure. This review aims to describe the pathophysiological, clinical and diagnostic aspects of CCM, showing the clinical, laboratory, electrocardiographic and echocardiographic characteristics in assessing cardiac dysfunction in cirrhotic patients.

Keywords: Cardiomyopathies; Liver cirrhosis; Heart failure; Hepatic insufficiency

Introduction

Cirrhosis is a chronic disease that affects the liver. It is characterized by a modification to the structure of the parenchyma and distortion of the hepatic vascular architecture in response to chronic tissue injury. This structural modification is caused by sustained tissue fibrosis and regeneration lumps. Cirrhosis develops in two ways: firstly, the patient is asymptomatic. This is the compensated phase. As the disease progresses, and this evolution period varies according to the patient, cirrhosis is decompensated and this phase is characterized by systemic symptomatology. The main organs affected by chronic liver disease are: heart, lung, kidneys, adrenal glands, brain and immune system. Impairment to the systemic hemodynamic balance is the most important pathophysiological mechanism.

The main etiologies associated with liver cirrhosis include hepatitis B and C. The alcoholic etiology is also very common and its relevance compared with viral etiologies as a cause of liver cirrhosis varies according to the country studied. Other etiologies associated with liver cirrhosis are: Wilson’s disease, non-alcoholic steatohepatitis, autoimmune hepatitis and cryptogenic cirrhosis.

Men are more affected by digestive diseases than women (men/women ratio: 1.6) and liver cirrhosis is the prevalent disease. In Brazil, epidemiological data are scarce due to inefficient reporting. In the DATASUS database, in 2002, the rate of specific mortality from liver cirrhosis was 7.79 per 100,000 inhabitants. São Paulo (10.31:100,000 inhabitants) and Rio de Janeiro (8.80:100,000 inhabitants) are two states with the highest mortality rate; Pará (3.52 specific deaths from liver cirrhosis in 100,000 inhabitants) and Tocantins (3.64 in 100,000 inhabitants) are among the lowest specific mortality rates for liver cirrhosis. These data generate questions with regard to underreporting of cases, as, regarding chronic hepatitis B, the North of Brazil presented the highest prevalence of 630:100,000 inhabitants, while the Southeast presented the lowest prevalence of 291:100,000 inhabitants. The same problem is observed with respect to chronic hepatitis C, an etiology that is also most
The progression of fibrosis, a characteristic of liver cirrhosis, culminates in portal hypertension and portosystemic shunt, the main causes of hemodynamic balance disorders. Loss of liver function impairs the metabolism of vasoactive substances such as atrial natriuretic peptide, adrenaline, noradrenaline, renin, angiotensin II, substance P, ADH and aldosterone. Concomitantly, there is significant increase in the production of nitric oxide (NO), a potent vasodilator, and reduction in vasoconstrictor response due to counterregulation of beta-adrenergic receptors, impairment to the affinity of these receptors and signaling cascade, favoring arterial vasodilation. There is increased NO production by endothelial cells arising from portal hypertension, in order to promote adequate blood flow supply and consequent splanchnic vasodilation. Increased NO also stems from chronic inflammation caused by cirrhosis, as well as transient bacteremia with the increase of cytokines and endotoxin. The combination of these disorders decrease systemic vascular resistance and splanchic vasodilation, important factors for systemic impairment caused by cirrhosis.

Systemic vasodilation causes redistribution of circulation and central hypovolemia which, in turn, lead to activation of systemic compensatory mechanisms such as the renin-angiotensin-aldosterone system (RAAS) and increased release of vasopressin and sympathetic nervous system activity. These factors, altogether, cause hyperdynamic and vascular hyporeactivity state, which, associated with systemic endothelial dysfunction and autonomic dysfunction, results in cardiovascular damage.

Cardiac dysfunction related to cirrhosis is called cirrhotic cardiomyopathy (CCM). In the past, it was believed that cardiac disorders happened only in alcoholic cirrhosis due to direct toxicity of alcohol. Now, it is known that cardiac dysfunction is present in cirrhosis, regardless of its etiology.

This review aims to describe the pathophysiological, clinical and diagnostic aspects of CCM, showing the clinical, laboratory and electrocardiographic and echocardiographic characteristics in assessing cardiac dysfunction in cirrhotic patients.

**Cirrhotic cardiomyopathy**

CCM is characterized by chronic cardiac dysfunction in patients with liver cirrhosis in the absence of previous heart disease, with reduced cardiac contractile response to physiological or pharmacological stress, but with normal cardiac output (CO) at rest. The aspects related to cardiac dysfunction include systolic and diastolic dysfunction, electrophysiological disorders and chronotropic disorders.

**Pathophysiology**

Several mechanisms are involved in the pathogenesis of cirrhotic cardiomyopathy, especially increased cardiac output related to hyperdynamic state of circulation. In patients with liver cirrhosis, regardless of the etiology, there is increased vasodilator production and activity, such as NO, endocannabinoids and carbon monoxide, and decreased metabolism of other vasodilators due to liver failure and portosystemic shunt. All of these aspects contribute to reduced peripheral vascular resistance, hyperdynamic circulation and insufficient cardiac output for metabolic demand.

Furthermore, there is chronotropic and inotropic dysfunction, which is related to impairment of beta-adrenergic receptors. In cirrhotic patients, there is a reduced number of these receptors, disorders in calcium signaling and impairment to membrane permeability (increased phospholipid and cholesterol). These modifications contribute to myocardial contractility disorders at the expense of contractile force and heart rate. Prolonged exposure to noradrenaline and sympathetic overactivity cause direct damage to cardiomyocytes and also cause beta-adrenergic receptor disorders. This sympathetic hyperactivity occurs via baroreceptor due to decreased peripheral vascular resistance and reduced blood pressure.
**Splanchnic-circulatory disorders**

The development of portal hypertension in cirrhotic patients causes two systemic consequences in an attempt to compensate for this disorder. The first one is increased production of vasodilators to correct portal hypertension, which, associated with smaller degradation of vasodilator factors by the sick liver, results in splanchnic arterial vasodilation that affects the system. Decline in systemic vascular resistance, arterial hypotension and central hypovolemia are the main consequences.

Response to that vasodilation is the second consequence of the development of portal hypertension. There is reflex hyperactivation of the sympathetic nervous system, increasing cardiac output and leading to a condition known as hyperdynamic circulation. Initially, this system compensates vasodilation caused primarily in the splanchnic circulation. With the progression of cirrhosis, however, greater vasoconstrictor activity is necessary to maintain effective volume and blood pressure, thus leading to RAAS activation. This effect causes more severe systemic vasoconstriction and may contribute to complications of cirrhosis such as ascites and hepatorenal syndrome.

The hyperdynamic state and the rise of vasoconstrictor factors cause reduced vascular and cardiac response to noradrenaline and angiotensin II. Prolonged exposure to high levels of these factors leads to exhaustion of beta-adrenergic receptors and reduces G protein expression. These factors decrease the myocardial response expected. The heart of cirrhotic patients presents greater deposits of cholesterol, which helps modifying this process by changing the myocyte membrane structure, making it stiff. Ion channels also have their functioning modified, contributing to the hyporesponsive state of cardiomyocytes to beta-adrenergic stimulation, explaining the progression of cardiac dysfunction.

NO is a potent vasodilator and plays an important role in signaling to change the membrane of myocytes, as it generates inhibition of beta-adrenergic receptor mediators, such as the cGMP protein. In cirrhotic patients, there is a constant inflammatory state that is the basis for systemic abnormalities. These inflammatory cytokines, particularly TNF-α and IL-1, stimulate NO synthesis, systemically increasing their levels. NO, then, performs its vasodilator function and contributes to the reduction of myocyte response to catecholamines. Associated with this, there are studies showing that NO accumulates in the cardiac tissue, reaching high levels in the papillary muscle, which reverses the pattern of myocardial contractility, reducing contractile response.

Other components involved in the alteration of beta-adrenergic cardiac response are the endocannabinoids. Increase in cardiac endocannabinoids levels accompanies increased serum TNF-α. These endocannabinoids inhibit the beta-adrenergic receptors, with an action that is similar to NO in the inhibition of the myocardial contractile response.

In addition to the mechanisms mentioned, there is increased bacterial endotoxins — as portal hypertension favors intestinal bacterial translocation and increases systemic inflammatory reaction. This condition increases the circulating TNF-α, favoring the abnormalities mentioned. In addition, studies show that these bacterial endotoxins have direct interference in myocardial function, regardless of TNF-α levels.

The impaired cardiomyocyte membrane due to increased phospholipid deposits presents decreased calcium and potassium channel density, which leads to insufficient cardiac contraction and prolonged QT interval.

Cirrhotic patients presents many components that impair their circulatory state, leading to an imbalance between splanchnic vasodilation and sympathetic and RAAS vasoconstrictor compensation, allowing the vasodilatory state to prevail in the terminal phase of the disease. The final result is a reduced state of effective blood volume, low blood pressure and central hypovolemia with cardiac dysfunction of insufficient myocardial contractility to maintain homeostasis balance.

**Impaired electrical conduction**

In CCM, the main electrical impairments to the heart include electromechanical uncoupling, chronotropic incompetence and QT interval prolongation. The abnormalities seen on the electrocardiogram of cirrhotic patients, regardless of the etiology, are secondary to portal hypertension, autonomic dysfunction, hyperdynamic circulation and the presence of the pro-inflammatory factors affecting the patient’s myocardium.

- QT internal prolongation
  Ventricular repolarization is sensitive to minor modifications to the portal pressure, therefore, it is observed in patients with CCM on electrocardiogram.
(ECG). It is probably caused by slowing repolarization of cardiomyocytes due to abnormalities of potassium channels and reduction in the concentration of these channels in the plasma membrane, essential to the repolarization of the cardiac muscle cells and sympathetic hyperactivation, which inhibits activation of these channels. Dysfunctions in ion channels cause prolongation of the action potential of myocardial cells, resulting in longer ventricular systole and QT prolongation. Longer contraction time implies impaired relaxation, causing diastolic dysfunction.

- Electromechanical dyssynchrony
Electromechanical uncoupling is defined by dyssynchrony between electrical stimulus and systolic mechanical response of the heart, which seems to be related also to the dysfunction of potassium channels, and occurs more frequently in patients who presented QT prolongation. This dyssynchrony causes progressive loss of myocardial function, culminating in congestive heart failure. Patients undergoing treatment with vasopressin during bleeding of esophageal varices or receiving blood transfusion seem to be more affected by the anomaly.

- Chronotropic incompetence
In patients with chronotropic incompetence, sinus node is unable to respond to physiological or pharmacological stimuli. Cirrhotic patients present reduced systolic index, i.e., cardiac output/body mass ratio; they also present smaller responsive capacity to physical stimulation (exercise, medication infusion or postural modification), with inefficient increase of heart rate and left ventricular ejection fraction (EF). This heart rate is lower than the maximum frequency in patients without cardiac involvement.

**Systolic and diastolic dysfunction**
Cardiac dysfunction is consequent to structural and contractility impairments, and are associated with the severity of liver cirrhosis. They are often asymptomatic and may be present in patients with compensated cirrhosis. Even with the progression of liver disease, the patients often present symptoms only in situations of physiological and/or pharmacological stress. It is also worth noting that the reduction in systolic and diastolic functions may lead to heart failure with reduced left ventricular ejection fraction and is a determining factor for the development of hepatorenal syndrome, which worsens the prognosis.

Diastolic dysfunction usually precedes systolic dysfunction, which is observed in situations of increased CO demand associated with decreased myocardial contractility, as in situations of hemodynamic stress — infectious processes, exercise, use of certain drugs and surgeries. Exercise in cirrhotic patients, for example, increases left ventricular (LV) end-diastolic pressure without appropriate increase in LV ejection fraction, meaning that there is a deficit in ventricular contraction capacity, i.e., the heart in cirrhosis is under maximum working conditions due to hyperdynamic circulation, with no ventricular reserve for situations of stress. Some aspects observed on echocardiography are: increased LV diameter at end-diastole, decreased peak systolic velocity and systolic deformity rate.

Diastolic dysfunction is characterized by decreased premature passive (E) and late (A) ventricular relaxation capacity in the ventricular filling phase, with consequent increase in atrial pressure and isovolumetric relaxation time. This disorder occurs due to increased myocardial stiffness caused by hypertrophy, fibrosis and subendothelial edema, causing high atrial and left ventricular pressure filling. Histopathological findings of diastolic dysfunction reveal that besides cardiomyocyte and interstitial fibrosis hypertrophy, myocyte pigmentation and vacuolization are impaired. It is important to emphasize that, as diastolic dysfunction impair ventricular filling and consequent increase in atrial volume, it may precipitate atrial fibrillation.

The echographic findings that can be observed in diastolic dysfunction of CCM are: reduced premature early (E) and late (A) ventricular relaxation capacity and decreased E/A ratio with extension of the E wave deceleration time. Ascites is relevant in further impairing cardiac function as the diaphragm elevation associated with increased intrathoracic pressure decreases ventricular and right atrial compliance causing right ventricular diastolic dysfunction. Moreover, patients with ascites have higher reduction of the E/A ratio. Paracentesis was shown to be a method that improves diastolic cardiac function, because it improves ventricular filling by reducing preload and by reducing RAAS and adrenergic agents activity (adrenaline and noradrenaline). In contrast, transjugular intrahepatic portosystemic shunt (TIPS) worsens cardiac function as it increases the preload, causing cardiac depletion, which increases the risk of cardiac insufficiency, hence mortality.
Diagnosis

In 2005, at the World Congress of Gastroenterology in Montreal, a group of experts got together to determine the criteria that define CCM (Chart 1). These criteria are divided into systolic and diastolic dysfunction, and support criteria, but can be didactically divided into laboratory results, ECG results and imaging tests (echocardiography, magnetic resonance imaging and scintigraphy). As these structural disorders occur in asymptomatic patients, the clinical manifestations do not define the diagnosis, but are associated with CCM.

<table>
<thead>
<tr>
<th>Systolic dysfunction</th>
<th>Diastolic dysfunction</th>
<th>Selection criteria</th>
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<tr>
<td>EF&lt; 55%</td>
<td>E/A &lt;1.0</td>
<td>Efficient chronotropism</td>
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<tr>
<td>Reduced contraction in response to physiological or pharmacological stress</td>
<td>Deceleration time &gt;200 ms</td>
<td>Electromechanical uncoupling</td>
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<td>Isovolumetric relaxation time &gt;80 ms</td>
<td>QT interval prolongation</td>
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<td>Structural impairments</td>
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<td>LA dilation and LV hypertrophy</td>
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<td>High BNP or Troponin I</td>
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Source: Gassanov et al.9

EF – ejection fraction; E/A – ratio between passive ventricular filling time and active ventricular filling time; LA – left atrium; LV – left ventricle; BNP – B-type natriuretic peptide; CCM – cirrhotic cardiomyopathy

Clinical effects

The clinical effects of CCM appear in stress situations, a state that requires greater cardiac activity to maintain hemodynamic balance.3 There are no studies proving that cardiac dysfunction has a defined clinical picture to be addressed, or that it is a major or determining factor in any clinical condition. There are case reports of cirrhotic patients who probably presented CCM through hepatorenal syndrome and/or adrenal insufficiency. One of these patients was receiving medical attention at Hospital Universitário Antônio Pedro (HUAP). These patients treated for heart failure and presented improvement of their renal condition, which was refractory to hepatorenal syndrome treatment known in the literature.31

Many studies have stated that procedures such as liver transplantation and TIPS can cause sudden heart failure and pulmonary edema postoperatively if diastolic and systolic dysfunction is not detected before surgery.42,43 The QT interval prolongation on ECG is also a marker of poor prognostic and postprocedural clinical decompensation.44 In the case of TIPS, diversion of blood from the portal system to the systemic circulation requires improved myocardial performance, otherwise, cardiopulmonary complications may occur.43

The hepatorenal syndrome can be precipitated by the vasodilation state of the cirrhotic patient. Chronotropic incompetence of the heart and systolic dysfunction play a major role in its pathogenesis.42 When this occurs, the cardiac disorders cited as part of the pathogenesis also serve as aggravating factors for the complication developed, as the cardiac output maintained by the heart is insufficient to meet the hemodynamic needs presented in oxidative stress.45 The same occurs in severe sepsis, where the increase of inflammatory cytokines in a heart affected by cirrhosis worsens the baseline condition and leads the patient to circulatory failure.42 In cirrhotic patients, sepsis is usually caused by spontaneous bacterial peritonitis. This condition of metabolic stress due to infection generates a decrease in cardiac output due to the mechanisms mentioned, clinically manifested by blood pressure drop.3,42

Sudden death is a rare condition in cirrhotic patients, even when associated with QT interval prolongation. From a clinical perspective, the largest impact of these electrical disorders are arrhythmias.42 Increased QT influences mortality as it predisposes to serious arrhythmias. The use of some medications such as
macrolides, quinolones and domperidone promotes decompensation; the same is observed in situations of metabolic stress. There is a study that associates gastrointestinal bleeding — that leads to increased inflammatory cytokines and hyperactivation of the sympathetic nervous system — with greater QT prolongation and increased mortality rate in six weeks.

High aldosterone levels — either due to lower hepatic degradation or RAAS hyperactivation — may lead to cardiac hypertrophy, left ventricular diastolic dysfunction and left atrial hypertension, the clinical characteristics of which is arrhythmia of atrial origin. This hypertension is transmitted to pulmonary circulation, causing pulmonary hypertension, which evolves with hepatic venous congestion — further reducing aldosterone degradation rates, determining increase in blood levels and promoting clinical arrhythmias. Cirrhotic patients are also at increased risk for cancer due to impairments with systemic repercussions, constant inflammatory state and impaired hemodynamic function due to cardiomyopathy.

CCM causes heart incompetence to deal with situations that require increased cardiac output and predisposes to complications arising from the baseline condition of cirrhosis. In the final stages, diastolic and systolic dysfunction and chronotropism are so pronounced that they affect the system even without any stress conditions triggering them. They clinically appear as an aggravation of the complications of cirrhosis, when in place, or predisposing them when not in place.

**Laboratory findings**

Some serum markers can be high in CCM and, therefore, become part of the criteria for diagnostic support. Atrial natriuretic peptide, for example, is secreted in response to atrial stretch, reflecting volume overload, and it is present in patients with cirrhosis; its release culminates in reduced blood pressure and preload.

B-type natriuretic peptide (BNP) is secreted by the ventricles in response to volume or pressure overload, or myocardial ischemia, to compensate for the RAAS action through renal elimination of sodium and water. It also reduces heart hypertrophy and fibrosis — the greater the interventricular septum and ventricular wall thickness, the higher the serum BNP. The more severe the liver and heart diseases the higher its levels, which is associated with the degree of myocardial hypertrophy and diastolic dysfunction. BNP may be abnormal even in the CCM at an early stage. Therefore, it is an early marker of cardiac involvement.

Increase of cardiac troponin I is also observed, as it is a marker of myocardial lesion.

Adrenomedullin is another substance that can be high in cases of cirrhosis with or without clinical cardiac involvement (from asymptomatic patients to patients with left ventricular hypertrophy and/or heart failure). This hormone, produced in the cardiac tissue, regulates the vascular tone and natriuresis and influences inotropism through cyclic adenosine monophosphate (cAMP), which increases the production of NO. This vasodilator is released to reduce afterload and dilate the coronary vessels. A recently identified biomarker, galectin-3, has been associated with myocardial fibrosis and is high in cirrhotic patients. These disorders can be seen by examining the patient’s blood and help diagnosing and stratifying the severity of cardiac disease caused by cirrhosis.

**ECG – Electrocardiogram**

The disorders found in the ECG that help in diagnosis are initially QT prolongation, multiple extrasystoles and, in more advanced stages, bundle branch block, ST segment depression and electromechanical dissociation.

**Echocardiography**

It is a noninvasive method that is very useful in the diagnosis of CCM. It is believed that it serves as a cardiac disease screening tool for patients with liver cirrhosis. The main findings described in the literature are: increased end-diastolic left ventricular pressure, without appropriate LVEF increase; increased LV diameter at end-diastole; reduction of peak velocity and systolic deformity rate. Left atrial dilatation may also occur, showing chronic diastolic dysfunction.

Cardiac Doppler echocardiography in patients with CCM may show decrease and/or reversal of E/A ratio (<1) and prolonged E wave deceleration time and isovolumetric relaxation time. These findings are suggestive of ventricular relaxation delay and, therefore, diastolic impairment. Initial studies on global longitudinal strain (GLS) have shown that this parameter is effective for detecting systolic and diastolic dysfunction, being far superior in detecting systolic disorders at rest.
It has been recently determined that the most specific marker for detecting diastolic dysfunction is early diastolic mitral annulus velocity (e’) which can be identified by tissue Doppler echocardiography. Left ventricular diastolic dysfunction is characterized, in this case, by: septal e’ <8 cm/s; lateral e’ <10 cm/s; and left atrial enlargement (LA>= 34 mL/m²). LA evaluation can be done through 3D echocardiography and speckle tracking.10

Ejection fraction is a key measure to evaluate systolic function, but two-dimensional echography measures linear EF, whose calculation depends on geometric assumptions. Some methods are available to better calculate EF, such as the Simpson’s method, especially speckle tracking, which evaluates ventricular myocardium strain step by step in the radial, longitudinal and circumferential axis, being a very sensitive echocardiographic method in the evaluation of ventricular systolic function.20

Magnetic resonance (MRI)
It is known that cardiac MRI precisely defines the epicardial and endocardial borders, outdoing echocardiography in this respect, as it does not depend on the “acoustic window”. It is now considered the gold standard for determining the cardiac morphology.53 Using this method, it is possible to determine EF, the volume of the heart chambers (increased LV mass and LA and LV end diastolic volumes) and myocardial morphological disorders, including tissue impairments (areas of edema and fibrosis), identifying the lesion using contrasts, such as gadolinium.34 In patients with cirrhosis, cardiac MRI has revealed increased LV mass, increased LV volume at end-diastole and increased left atrial volume.9

Scintigraphy
Scintigraphy can reveal smaller EF increase in cirrhotic patients after physical exercise compared to patients without cirrhosis.55 Scintigraphy can provide very reliable data on left ventricular EF, which is a predictor of systolic function, when there is no reliable echocardiography data.30

Treatment
CCM has no specific treatment yet. Today, the treatment is the same one established for heart failure, regardless of its etiology, which includes water and sodium restriction, use of diuretics, RAAS and beta-blocker inhibitors.56 Studies with non-selective beta-blockers have shown reduced QT prolongation and improved electromechanical uncoupling, also promoting reduced portal pressure and prevention of bleeding of esophageal varices. Association of nitrate with beta-blockers has shown venous and coronary vasodilating effect, which reduces preload, one of the objectives in the treatment of LV diastolic dysfunction.9,57

The use of diuretics is beneficial in the case of fluid retention, but when used for long periods, they are associated with hepatorenal syndrome, electrolyte disorders and increased neurohormonal activation. Therefore, they must be used under supervision.9

Aldosterone antagonists and angiotensin-converting enzyme inhibitors (ACEI) reduce RAAS hyperactivity of cirrhotic patients and decrease LV wall thickness and dilatation, which leads to improved diastolic function.9 Attention should be paid to the vasodilator effect of ACEI due to the possibility of worsening hypotension in patients with cirrhosis. Regarding the aldosterone antagonists, potassium canrenoate reduces the venous hepatic pressure gradient, LV wall thickness and left end-diastolic volume in cirrhotic patients Child A.10,58 There are no studies with eplerone and spironolactone in CCM.28

Digitalis do not have a good effect in increasing cardiac contraction in cirrhotic patients. In a study of patients with alcoholic cirrhosis, the use of digitalis did not show any benefit in the improvement of left ventricular dysfunction.9,58 Therefore, they are not recommended for the treatment of CCM.

Adrenal dysfunction, also related to liver cirrhosis, when concomitant with CCM, aggravates the deficit of myocardial contraction. In such cases, there are studies showing that treatment with steroids can improve cardiac function under stress.57,60

Only liver transplantation was defined as an effective treatment of cirrhosis and CCM to demonstrate improvement in cardiac dysfunction. However, it has limitations due to the low availability of the organ for donation and the perioperative and postoperative risks of this procedure such as heart failure, myocardial infarction, arrhythmia and cardiac death. The benefits demonstrated by heart transplant are regression of ventricular wall thickness, diastolic dysfunction and improvement of systolic response and ability to perform physical exercises when under stress. These results were
observed after 6-12 months from transplantation.\textsuperscript{10,61} There is also a reduction in cardiac output and heart rate, decreased pulmonary artery pressure and increased blood pressure.

**Comments**

There is no evidence determining screening of the investigation of cirrhotic cardiomyopathy in asymptomatic patients. In addition to this, there is no pathognomonic clinical picture that signals cardiac involvement in these patients. Studies indicate that CCM signs and symptoms appear in situations of stress, when greater cardiac activity is required to maintain hemodynamic balance.

At HUAP, two patients met the criteria of hepatorenal syndrome and were treated unsuccessfully according to protocols established in the literature.\textsuperscript{41,62} In such cases, CCM is considered a determining factor of acute renal failure. Dobutamine with furosemide was administered and, in these two patients, there was regression of the hepatorenal syndrome with progressive improvement of renal function. One of these cases has been published and the second one is being drafted.\textsuperscript{41}

The cirrhotic patient’s heart works under maximum potential to maintain hemodynamic balance in hyperdynamic state. It is believed that the constant work demanded from the heart of these patient requires greater effort being made by the heart muscle. With the depletion of ventricular reserve, this function cannot be extended, causing the decompensation observed in the hepatorenal syndrome of cardiac origin. This occurs even in cases where no systolic dysfunction is observed on echocardiography, as observed in the HUAP patients mentioned above. Improvement of this condition using dobutamine is then explained, as it served as exogenous stimulus to the heart.

It is believed that CCM is well-known and understood, but further studies are required to understand its clinical manifestations and treatment. CCM addressed in the clinical suspicion of hepatorenal syndrome is supposed to be relevant.

**Potential Conflicts of Interest**

This study has no relevant conflicts of interest.

**Sources of Funding**

This study had no external funding sources.

**Academic Association**

This study is not associated with any graduate programs.

### References