DIAGNOSIS OF CIRRHOTIC CARDIOMYOPATHY

LORENA MĂRIEŞ[1], IOAN MANIŢIU[2]

[1]PhD candidate "Lucian Blaga"University of Sibiu, [2]"Lucian Blaga"University of Sibiu

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Abstract: *Though the hepatic impairment which associates to heart diseases is well known, terms like „cardiac cirrhosis" being established, not the same thing is happening to the heart impairment from the liver cirrhosis, the new clinical entity, the cirrhotic cardiomyopathy, being less known. It is because of this, as well as because of the lack of a diagnostic algorithm, that the cirrhotic cardiomyopathy is still insufficiently diagnosed. It can be diagnosed using a combination of clinical suspicion, electrocardiography, echocardiography and serum marker.*

Cuvinte cheie: *cardiomiopatie cirotică, ciroză hepatică, BNP, ecocardiografie*

Rezumat: *Dacă afectarea hepatică din insuficienţa cardiacă este bine cunoscută, termenii de „ciroză cardiacă" sau „ficat cardiac" fiind încetăţeniţi, nu acelaşi lucru se întâmplă cu afectarea cardiacă din ciroza hepatică, noua entitate clinică, denumită „cardiomiopatia cirotică", nefiind la fel de bine cunoscută. Din această cauză, precum şi a lipsei unui algoritm de evidenţiere, ea este încă mult subdiagnosticată. Cardiomiopatia cirotică poate fi diagnosticată folosind o combinaţie de suspiciune clinică, electrocardiogramă, ecocardiografie şi markeri serici.*

„Cirrhotic cardiomyopathy" is a recently recognized entity consisting in systolic incompetence in conditions of stress, diastolic dysfunction due to the modification of the diastolic relaxation and due to the electrophysiological modification in absence of any known cardiac disease.(1)

Clinically, the systolic incompetence is most obvious when patients are subject to stress, either physical, or pharmacological, or when the peripheral arterial vasodilatation requires an increased cardiac flow, as it happens in the case of bacterial infections.(1)

Also, during the treatment of hepatic cirrhosis, the patients may be subject to surgical interventions which represent stress factors for the heart. This is why the ability to diagnose this entity is important in the treatment of these patients, as well as in the selection process of those that may benefit from a liver transplant.

Cirrhotic cardiomyopathy may be diagnosed using a combination between electrocardiogram, two-dimensional echocardiography and serum markers, such as the natriuretic peptide B.(1) Also, due to concomitant pulmonary complications, due to its increased reliability and to the capacity to offer a complete cardio-pulmonary image, a thoracic X-ray may be added, even if it is made as a first intent.

Electrocardiogram in cirrhotic cardiomyopathy

Along the years, numerous rhythm disorders have been described in cirrhotic patients, including atrial fibrillation, atrial flutter, atrial and ventricular ectopics and ventricular arrhythmias. Three electrophysiological anomalies have been noticed in cirrhosis, regardless of its etiology: prolongation of QT interval, chronotropic incompetence and electromechanical delay.(2)

The prolongation of QT intervals is the result of the abnormal myocardial repolarization and it is occasionally associated with a high risk of peak distortion, ventricular tachyarrhythmia with lethal potential.

Numerous studies revealed and re-revealed in time this QT prolongation in cirrhotic patients, some also documenting a significant correlation between the severity of the hepatic disease (indicated by the Child-Pugh score) and the corrected QT interval.(2)

The mechanism leading to the prolongation of the QT interval in cirrhosis is not known. Numerous studies suggest that the chronic activation of the sympathetic nervous system (SNS) which occurs in cirrhosis plays an important part in the genesis of the prolongation of this interval. Other pathogenic mechanisms may also contribute to the prolongation of QT in cirrhosis. Its worsening was noticed after the insertion of TIPS in cirrhotic patients, and an improvement after the liver transplant, suggesting that a certain dysfunctional defect lies behind this prolongation. Nevertheless, recent discoveries that show that the prolongation of QT is correlated with the circulating concentrations of the natriuretic peptide B, suggest the sub-clinical cardiomyopathy that may be responsible for this prolongation.(3)

The cirrhotic patients show low cardiac responses to numerous physiological and pharmacological stimuli. The heart's incapacity to answer to these stimuli accordingly is called chronotropic incompetence. The significance of this phenomenon becomes obvious in situations when tachycardia is necessary, including the sympathetic answer of „run or fight", physical exercise or hemorrhage.(2)

Although the rest tachycardia is a characteristic of the hyper-dynamic circulation in cirrhosis, the maneuvers activating the sympathetic nervous system (SNS) or altering the sympathetic/vague balance in favor of SNS, such as the Valsalva maneuver, the isometric or isotonic exercise, do not cause the proper acceleration of the cardiac rhythm. Moreover, the circadian variability is perturbed in cirrhotic patients. It is not known whether and to what extent these chronotropic

[1]Corresponding author: Lorena Mărieş, Str. Dîrstelor, Nr. 15, Sibiu, România, E-mail: lorenamaries@yahoo.com, Tel: +40745387973
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anomalies have a clinical impact in the case of cirrhotic patients.(3)

The autonomous dysfunction is very frequent in patients with cirrhosis, and it is characterized by a relatively low parasympathetic activity and an increased sympathetic tonus. This dysfunction plays a pathogenic part in the development of cardiomyopathy and of central hipovolemia in the final stage liver disease. Another study compared the function of the autonomous nervous system in cirrhotic patients before and after the liver transplant. A rigorous and objective method was used, like the analysis of the variability of the cardiac frequency in 24 hours by ECG recording. It was discovered that, compared to the healthy subjects in the control batch, the patients suffering from cirrhosis have a reduced overall autonomous function, focusing on the parasympathetic component. This parasympathetic „defect" was obvious especially during the night, when the parasympathetic tonus prevails under normal circumstances.(4)

The third anomaly of the electrical conductance in cirrhosis is the electromechanical asynchrony of the systole, or the difference in time between the electrocardiographic evidence of the systole and its hemodynamic/physical evidence. This time difference between the electrical systole and the mechanical one was discovered to be significantly bigger in patients with a prolonged QT interval than in those with a normal QT interval. Finally, the time difference between the duration of electrical events (QT interval) and the duration of the mechanical systole, which, in normal subjects, is between 6-14ms, is much more dispersed in cirrhotic patients (between 120 and 158 ms), suggesting disconnection in coupling excitation with contraction in cirrhotic patients.(2)

The lack of coupling excitation with contraction occurs regardless of the etiology of cirrhosis and is more pronounced in patients with advanced cirrhosis than in patients with compensated cirrhosis.(3)

Echocardiography in cirrhotic cardiomyopathy

Apart from the electrical anomalies, in the cirrhotic cardiomyopathy are also met an increased contraction of the left ventricle at rest, and attenuation of the systolic contraction or of the diastolic relaxation when facing pharmacological, physiological or surgical stress.(2)

The increased cardiac flow is part of the hyper-dynamic circulation in cirrhosis and it is believed to be secondary both to the growth of the cardiac frequency, and to the ventricular beat volume. This growth of the cardiac flow may wrongly lead to the assumption that the cardiac function is intact or increased in cirrhotic patients, and that the arterial hypotension which occurs with them is only the expression of a marked peripheral vasodilatation. Nevertheless, in the last decades, numerous studies have shown that this assumption was incorrect.(2)

In other circumstances, this would lead to cardiac insufficiency, but, due to the low afterload reflected by the reduced systemic vascular resistance and by the increased arterial compliance, a left ventricular insufficiency may be latent in cirrhosis.(5)

Systolic dysfunction:

At rest, when the afterload is reduced, the cardiac pressures are almost normal and may thus mask a subjacent ventricular dysfunction. Thus, the cardiac insufficiency becomes manifest only in conditions of hemodynamic stress. Thus, after physical exercise, the end-diastolic pressure of the left ventricle grows, but the expected growth of the cardiac beat index and of the ejection fraction of the left ventricle is absent or subnormal.(5)

The most common method to quantify the function of the left ventricle is by estimating the ejection fraction measured by 2D conventional echocardiography. Nevertheless, this method describes the movements of fluids and not the dynamics of tissues, this is why it is not sufficiently sensitive to detect the myocardial dysfunction in details or in latent stage. New echocardiographic manners, such as the Doppler echocardiography of the soft tissues, allow the detection of the myocardial function in the long axis, and bring information on the myocardial function, which is impossible to obtain by 2D conventional echocardiography or by vascular Doppler.(6)

In a study performed on 44 patients suffering from cirrhosis, this type of Doppler emphasized, most frequently, a decrease of the systolic function at rest, which was present even though the ventricular ejection fraction was in normal spectrum. However, this situation remains undiscovered when patients are assessed by conventional echocardiographic methods.(6)

Diastolic dysfunction:

Using the Doppler echocardiography, the ventricular diastolic compliance and the corresponding diastolic function may be assessed by measuring the velocity of the blood flow in the left atrium towards the left ventricle during the first part of diastole (wave E) and the last part of diastole (wave A), afterwards calculating the E/A ratio. In other words, a low E/A ratio will be noticed in a rigid, non-complacent ventricle. Numerous studies have shown a low E/A ratio in cirrhotic patients. In many cases, the diastolic dysfunction precedes the systolic one, which tends to manifest only in conditions of stress.(2)

Recent studies concerning the diastolic ventricular filling in cirrhosis support the presence of the myocardial disease with diastolic dysfunction which, in patients suffering from ascites, improves after the paracentesis and aggravates after the insertion of transjugular intrahepatic portosystemic shunt. In these decompensated patients, the paracentesis seems to improve the diastolic function, but not the systolic one. Recently it has been proven that the liver transplant restores the cardiac functions, also eliminating the diastolic dysfunction.(5)

Dobutamine Stress echocardiography:

Leaning on the fact that it is well known that in the pathogenicity of the cirrhotic cardiomyopathy are involved defects of the signaling way β-adrenergic, numerous studies have tried to determine whether the cirrhotic patients manifest improper cardiac responses to the catecholamine stimulation, by means of Dobutamine stress echocardiography.(7)

Such a study included 71 patients suffering from cirrhosis. They were administrated Dobutamine intravenously, and echocardiographic recordings have been performed both at rest, and during the administration of Dobutamine. No significant differences of the echocardiographic indexes have been registered between the control group and the cirrhotic group, except for the markers of the diastolic dysfunction, such as the E/A ratio. Also, most patients showed chronotropic incompetence after the administration of Dobutamine.(8)

Due to the chronotropic incompetence and to the frequent use of β-blockers, between 26% and 56% of the studies using Dobutamine stress tests in cirrhotic patients, were not conclusive, because the target cardiac frequencies have not been reached. Certain studies have shown that these tests could be useful in assessing patients with advanced hepatic disease, but this technique is still under research.(9)

Natriuretic Peptide B (BNP)

BNP was initially discovered in the porcine brains (B=brain), but the largest concentrations of the peptide are in the heart. It is a peptide with 32-amino acids, synthesized in ventricles as response to the spreading of myocytes and/or

overpressure. It is released as an active hormone and as an inactive N-terminal fragment (NT-pro-BNP).(10)

Also, high concentrations of BNP in the plasma were noticed in the hypertrophic cardiomyopathy and diastolic dysfunction.(11)

Once released into the blood flow, BNP has numerous physiological actions, their net effect being to reduce the pre- and afterload. Specifically, BNP causes a low vascular tonus by relaxing the recti, causing the decrease of afterload. In addition, it induces the movement of fluids into the interstice, thus causing the decrease of preload.(12)

Numerous recent studies have shown that the patients with hepatic cirrhosis have increased plasmatic concentrations of BNP and NT-pro-BNP, representing in fact markers of early ventricular dysfunction. Henriksen et al. showed that these markers are correlated both with the gravity of the hepatic cirrhosis, and with that of cardiac dysfunction. BNP may thus have a prognosis value as regards the progress of cirrhosis. Also, NT-pro-BNP represents a useful marker to demonstrate the existence of a diastolic dysfunction of the left ventricle, determined by a chronic hepatic disease.(13)

A study carried out on 153 patients subject to a hepatic transplant determined their BNP levels immediately after the transplant and on days 1 and 7. The conclusion drawn was that a BNP level higher than 391 pg/ml immediately after the hepatic transplant seems to be a precocious marker of the cardiac dysfunction related to cirrhosis.(14)

Conclusions

The diagnosis of cirrhotic cardiomyopathy is still difficult to determine, due to the insufficient appraisal of this impairment, as well as due to the lack of a specific and certain diagnosis test. Nevertheless, there are multiple tests that may lead to a positive diagnosis, once there is a clinical suspicion.

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