

Observational Study

Cirrhotic cardiomyopathy: Isn't stress evaluation always required for the diagnosis?

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Abstract

AIM: To describe the proportion of patients with cirrhotic cardiomyopathy (CCM) evaluated by stress echocardiography and investigating its association with the severity of liver disease.

METHODS: A cross-sectional study was conducted. Cirrhotic patients without risk factors for cardiovascular disease were included. Data regarding etiology and severity of liver disease (Child-Pugh score and model for end-stage liver disease), presence of ascites and gastroesophageal varices, pro-brain natriuretic peptide (pro-BNP) and corrected QT (QTc) interval were collected. Dobutamine stress echocardiography (conventional and tissue Doppler imaging) was performed. CCM was considered present when diastolic and/or systolic dysfunction was diagnosed at rest or after pharmacological stress. Therapy interfering with cardiovascular system was suspended 24 h before the examination.

RESULTS: Twenty-six patients were analyzed, 17 (65.4%) Child-Pugh A, mean model for end-stage liver disease (MELD) score of 8.7. The global proportion of patients with CCM was 61.5%. At rest, only 2 (7.7%) patients had diastolic dysfunction and none of the patients had systolic dysfunction. Dobutamine stress echocardiography revealed the presence of diastolic dysfunction in more 6 (23.1%) patients and of systolic

dysfunction in 10 (38.5%) patients. QTc interval prolongation was observed in 68.8% of the patients and increased pro-BNP levels in 31.2% of them. There was no association between the presence of CCM and liver impairment assessed by Child-Pugh score or MELD ($P = 0.775$, $P = 0.532$, respectively). Patients with QTc interval prolongation had a significant higher rate of gastroesophageal varices comparing with those without QTc interval prolongation (95.0% *vs* 50.0%, $P = 0.028$).

CONCLUSION: CCM is a frequent complication of cirrhosis that is independent of liver impairment. Stress evaluation should always be performed, otherwise it will remain an underdiagnosed condition.

Key words: Dobutamine stress echocardiography; Cirrhotic cardiomyopathy; Cirrhosis; Corrected QT interval prolongation; Liver impairment

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Core tip: Our study demonstrates that cirrhotic cardiomyopathy (CCM) is a frequent condition that is independent of the severity of liver disease. Furthermore, it shows that CCM is currently underdiagnosed, even after a comprehensive evaluation at rest. Consequently, a stress test should always be considered in the diagnostic approach to CCM, as it is here. Moreover, an association between corrected QT (QTc) interval prolongation and the presence of gastroesophageal varices was revealed, irrespective of the diagnosis of CCM. As such, the clinical significance of QTc interval prolongation is emphasized and it can be regarded as a marker of severe liver disease.

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INTRODUCTION

The presence of cardiac dysfunction related to chronic liver disease was first hypothesized by Kowalski *et al*^[1] in 1953. Subsequent studies revealed that cirrhosis is associated with a hyperdynamic circulation (increased cardiac output and diminished systemic vascular resistance)^[2-6], which corresponds to a high-output heart failure under resting conditions^[7,8]. This clinical entity, formally named cirrhotic cardiomyopathy (CCM), is unrelated to the etiology of cirrhosis^[3-5,8-10] and is different from alcoholic disease^[9]. It has been defined as a cardiac dysfunction in patients with cirrhosis characterized by impaired contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other

known cardiac disease^[11]. Some decades ago, this cardiac dysfunction was attributed to the effects of alcohol toxicity on the heart; however, data from studies performed since 1980s showed that the dysfunction at rest and the blunted cardiac response to stress was associated with cirrhosis *per se* rather than being an adverse effect of alcohol, which justify the specific cardiac disease term - "CCM"^[3,8,12].

The pathophysiology of diastolic dysfunction is an increased stiffness of the myocardial wall, most likely because of a combination of mild myocardial hypertrophy, fibrosis and subendotelial edema^[3,9]. Systolic dysfunction relates to the inability of the heart to maintain an adequate arterial blood pressure and output^[5-7]. QT interval prolongation is the main electrophysiological abnormality in cirrhosis^[2-8,13,14]. Several mechanisms have been implicated in the impaired contractile function of the cardiomyocyte: Down-regulation of β -adrenergic receptors and impaired β -adrenergic signalling, altered cardiomyocyte plasma membrane biophysical characteristics, increased activity of the endocannabinoids, nitric oxide and cytokines systems, as well as abnormal myofilaments^[3-5,7-9]. Though almost always clinically silent at rest, due to diminished preload and afterload that occurs in liver cirrhosis, CCM has been described as a blunted ventricular contractile response usually unmasked by physiological, pharmacological and/or surgical stress^[3-9]. Consequently, overt congestive heart failure might result^[4,5,9]. CCM has been linked to sodium and water retention, ascites formation and hepatorenal syndrome development^[7,11,15-17], mainly following infections such as spontaneous bacterial peritonitis^[2,3,17-19]. The prevalence and natural history of CCM is not accurately known and studies that better describe it are still needed^[4,5,8]. It has also been proposed that this condition has prognosis significance^[5-7]. There is no specific treatment for CCM, the goal being the management of congestive heart failure^[2-5,7,8]. β -blockers therapy reduce the prolonged QT interval towards normal values^[20,21] but its impact on survival is not clear^[12,22]. Though liver transplantation may initially aggravate the CCM, it remains the ultimate therapy for cardiovascular complications of cirrhosis, being associated with normalization of cardiac function with improvements in cardiac hypertrophy, diastolic and systolic functions and QT interval, several months after transplantation^[5,7,23-25].

The aims of our study were: (1) to describe the proportion of patients with CCM evaluated by stress echocardiography in a population of cirrhotic patients, defining blunted ventricular contractile response and/or impaired diastolic relaxation as predictors of CCM; and (2) to investigate whether CCM is related to severity of liver disease.

MATERIALS AND METHODS

Study population

A cross-sectional study was conducted during 2011 and 2012. Cirrhotic outpatients followed at our department

were included. The diagnosis of cirrhosis was based on clinical, biochemical, echographic, endoscopic, and, when available, histological criteria. Exclusion criteria were: Age under 18, known or suspected risk factors for cardiovascular disease (diabetes, systemic hypertension, smoking and obesity defined as body mass index $> 30 \text{ kg/m}^2$), pulmonary major illness, severe anemia (Hb $< 7 \text{ g/dL}$), severe systemic disease, hyperthyroidism and hypothyroidism, pregnancy and baseline electrocardiographic or echocardiographic evidence of structural heart disease, such as bundle branch block, regional wall motion abnormalities or valvular heart disease. Inclusion criteria were as strict as dictated by the definition discussed at the 2005 World Congress of Gastroenterology in Montreal and presented thereafter, so the cardiac dysfunction can be attributed to the CCM *per se*; moreover, they are similar to that described in other reports^[26,27]. All the therapy interfering with cardiovascular system was suspended 24 h before the electrocardiographic and echocardiographic examinations not to alter the examinations' results. The study protocol was approved by the Ethics Committee of our hospital. Written informed consent was obtained from every patient included in the study.

Clinical and analytical data

Data regarding gender, age, etiology and severity of liver disease (Child-Pugh classification and model for end-stage liver disease (MELD), presence of ascites, gastroesophageal varices, history of overt encephalopathy, heart rate and systolic and diastolic blood pressure were retrospectively recorded. Compensated disease refers to Child-Pugh class A and decompensated disease includes Child-Pugh class B or C patients.

Laboratory parameters - hematological, biochemical [including pro-brain natriuretic peptide (pro-BNP)] and clotting profiles were measured in fasting venous blood samples.

Electrocardiographic examination

Patients were submitted to a 12-lead electrocardiogram and corrected QT interval (QTc interval), adjusted for heart rate, was calculated, according to Bazett's formula [$QTc = QT_{max}/(RR)^{1/2}$ interval]. A QTc interval $> 440 \text{ ms}$ was considered prolonged.

Echocardiographic examination

Transthoracic echocardiographic examination (standard 2D-echocardiographic imaging, pulsed Doppler interrogation of mitral inflow and tissue Doppler imaging (TDI) of the annular region of the left ventricle) using a General Electric™ Vivid 7, was performed by an experienced cardiologist in the echocardiography laboratory. Diastolic and systolic functions were evaluated at rest and after pharmacological stress with intravenous infusion of dobutamine. An initial dose of dobutamine at $5 \mu\text{g/kg}$ per minute was administered and increased to 10, 20, 30 and $40 \mu\text{g/kg}$ per minute every 3 min, in

order to achieve, at least, 85% of maximum heart rate predicted for age ($220 - \text{age}$). In case maximum heart rate was not reached, atropine (0.25 mg every minute up to maximum dose of 1 mg) was added to the $40 \mu\text{g/kg}$ per minute dobutamine infusion. After the examination, intravenous metoprolol (2.5 mg every 5 min up to a maximum dose of 10 mg) was administered until basal heart rate was achieved. Off-line analysis of echocardiographic images was performed by two investigators under blind conditions and agreement between the two observers was required.

Echocardiographic systolic left ventricular function parameters [left ventricular end-diastolic volume (LV EDV), LV end-systolic volume (LV ESV) and LV ejection fraction (LV EF) using Simpson's rule] were evaluated at rest and after a dobutamine inotropic dose perfusion ($20 \mu\text{g/kg}$ per minute), as recommended to assess LV contractile reserve (LV CR). LV systolic dysfunction was considered present at rest when LV EF was below 50%. A reduced left ventricular contractile reserve was defined as an increase in LV EF $< 10\%$ after dobutamine infusion.

To assess left ventricular diastolic function, peak early filling (E-wave) velocity, late diastolic atrial filling (A-wave) velocity and E-wave deceleration time (DT) were measured by pulsed Doppler examination and E/A ratio (early diastolic/atrial filling ratio) was calculated. Average early diastolic myocardial velocity (e'-septal and lateral sides of the mitral annulus average) was obtained by TDI. E/e' average ratio was calculated combining the parameter E from the pulsed wave Doppler and the parameter e' from the TDI. Left ventricular diastolic dysfunction at rest was diagnosed if septal e' velocity was $< 8 \text{ cm/s}$ and lateral e' velocity was $< 10 \text{ cm/s}$, according to the American Society of Echocardiography recommendations^[28] (patients whose e' velocities values were within normal limits for age were considered as not having diastolic dysfunction). Three categories of increasing severity of diastolic dysfunction were defined according to the following parameters: Grade I - E/e' average ratio ≤ 8 , E/A ratio < 0.8 and DT $> 200 \text{ ms}$; grade II - E/e' average ratio between 9 and 12, E/A between 0.8 and 1.5 and DT between 160 and 200 ms; and grade III - E/e' average ratio ≥ 13 , E/A ≥ 1.5 . E/e' average ratio at rest and after stress (using dobutamine maximum dose perfusion) has been applied in the diastolic stress test. If myocardial relaxation is normal, E and e' velocities increase proportionally, and the E/e' ratio remains unchanged or is reduced; in patients with impaired myocardial relaxation, the increase in e' with stress is much less than that of mitral E velocity and the E/e' ratio increases.

CCM

CCM was diagnosed when LV diastolic dysfunction and/or systolic dysfunction was present, irrespective of the presence of other supportive criteria [electrophysiological abnormalities as QTc interval prolongation or increased

Table 1 Baseline characteristics of cirrhotic patients

	<i>n</i> = 26 patients
Gender (male), <i>n</i> (%)	22 (84.6)
Age (yr)	54.6 ± 10.4
Cirrhosis etiology	
Alcoholic, <i>n</i> (%)	20 (77.0)
Viral, <i>n</i> (%)	3 (11.5)
Mixed, <i>n</i> (%)	3 (11.5)
Child-Pugh score (units)	6.2 ± 1.3
Child-Pugh class	
A, <i>n</i> (%)	17 (65.4)
B, <i>n</i> (%)	8 (30.8)
C, <i>n</i> (%)	1 (3.8)
MELD score (units)	8.7 ± 5.3
Medical therapy	
Propranolol, <i>n</i> (%)	15 (57.7)
Diuretics, <i>n</i> (%)	12 (46.1)
Ascites, <i>n</i> (%)	5 (19.2)
Mild/moderate (diuretic responsive) ascites, <i>n</i> (%)	3 (11.5)
Severe (diuretic refractory) ascites, <i>n</i> (%)	2 (7.7)
Gastroesophageal varices, <i>n</i> (%)	22 (84.6)
Decompensation by ascites, <i>n</i> (%)	12 (46.1)
Decompensation by variceal bleeding, <i>n</i> (%)	12 (46.2)
Decompensation by overt encephalopathy, <i>n</i> (%)	3 (11.5)
≥ 2 Decompensations by ascites, <i>n</i> (%)	5 (19.2)
≥ 2 Decompensations by variceal bleeding, <i>n</i> (%)	4 (15.4)
≥ 2 Decompensations by overt encephalopathy, <i>n</i> (%)	2 (7.7)
Heart rate (bpm)	67.8 ± 13.0
Systolic pressure (mmHg)	115.7 ± 11.6
Diastolic pressure (mmHg)	62.1 ± 21.6
Sodium (mEq/L)	140.6 ± 2.7
Creatinine (mg/dL)	0.9 ± 0.2
Albumin (g/dL)	3.6 ± 0.4

MELD: Model for end-stage liver disease.

cardiac biomarkers (pro-BNP)].

Statistical analysis

Statistical analysis was performed using SPSS 16.0 for Windows (SPSS INC. Chicago, IL, United States). Variables with normal distribution were expressed as mean ± SD and variables with non-normal distribution as median and range. Student's *t*-test, Fisher's Exact Test and Pearson's correlation were used when appropriate. *P* values < 0.05 were considered as significant. The statistical review of the study was performed by the author Mara Barbosa.

RESULTS

Clinical and analytical data

Seventy-three cirrhotic patients were evaluated and only 26 fulfilled the inclusion criteria. The main reasons for exclusion were: Diabetes mellitus (51%), hypertension (26%), ischemic cardiac disease (9%) and arrhythmia (6%). Regarding included patients, 22 (85%) were men, with mean age 55 ± 10 years. The etiology of cirrhosis was predominantly alcoholic (77%). The majority of patients (65%) were compensated (Child-Pugh class A). Mean MELD score was 8.7 ± 5.3. Five (19.2%) patients had ascites and the vast majority (84.6%) had gastroesophageal varices. Baseline characteristics of

patients are listed in Table 1. Non selective β-blockers (propranolol) were suspended in 15 patients and diuretics (furosemide and/or spironolactone) in 12 patients.

Pro-BNP levels were 110.8 ± 110.6 μg/mL and were elevated in 8 (30.8%) patients (normal levels < 125 μg/mL). Pro-BNP values were not significantly different between alcoholic and non-alcoholic patients (*P* = 0.757). Pro-BNP levels were similar in Child-Pugh class B/C and Child-Pugh class A patients (*P* = 0.651). There was no correlation between MELD score and pro-BNP values (*P* = 0.950). The presence of ascites, gastroesophageal varices and history of overt encephalopathy was not significantly associated with more elevated pro-BNP levels (*P* = 0.525; *P* = 0.615 and *P* = 0.186, respectively).

Electrocardiographic characteristics

QTc interval duration was 460 ± 23 ms. Prolongation of the QTc interval was found in 77% of the patients. The existence of a prolonged QTc interval or its duration was unrelated to the etiology of cirrhosis (alcoholic vs non-alcoholic) (*P* = 0.562 and *P* = 0.696, respectively). Regarding severity of disease, there was a significant correlation between QTc interval duration and MELD score (*P* = 0.453, *P* = 0.020) but not between QTc interval duration and Child-Pugh score (*P* = 0.322, *P* = 0.108); QTc interval prolongation was not more frequent in patients with decompensated (Child-Pugh class B/C) vs compensated cirrhotic patients (*P* = 0.380); however, patients with QTc interval prolongation tended to have higher MELD score (9.8 ± 3.7 vs 5.0 ± 8.2, *P* = 0.053). Patients with QTc interval prolongation had a statistically significant higher rate of gastroesophageal varices comparing with those without QTc interval prolongation (95.0% vs 50.0%, *P* = 0.028). However, the presence of QTc prolongation was not associated with the presence of ascites or history of overt encephalopathy (*P* = 0.678 and *P* = 0.438, respectively). Regarding QTc interval duration, there was no relation with ascites, gastroesophageal varices or history of encephalopathy. Although more elevated, pro-BNP levels were not significantly increased in patients with a prolonged QTc interval (*P* = 0.483). Furthermore, there was no correlation between pro-BNP levels and QTc interval duration (*P* = 0.125).

Echocardiographic characteristics

Echocardiographic examinations were performed as planned, maximum heart rate predicted for age was achieved in all patients and no adverse events were recorded.

Left ventricular systolic function: At rest, none of the patients had LV EF below 50% (69.1% ± 8.1%) and LV EDV and LV ESV were within normal limits (94.2 ± 29.7 mL and 28.4 ± 9.5 mL, respectively). A reduced LV CR was observed in 10 (38.5%) patients with LV EF mean increment of 0.4% ± 7.6% vs 20.7% ± 10.4% in the other 16 patients with normal LV CR. Comparing the two groups, at rest, LV EF and LV ESV were similar (73.0% ± 7.1% vs 66.7% ± 7.9%, *P* = 0.051 and 30.1 ± 12.3

Table 2 The characteristics of patients with and without cirrhotic cardiomyopathy

	CCM (<i>n</i> = 16)	Non-CCM (<i>n</i> = 10)	<i>P</i> value
Gender (male), <i>n</i> (%)	14 (87.5%)	8 (80.0%)	0.625
Age (yr)	52.8 ± 9.9	57.4 ± 11.2	0.284
Etiology (alcoholic/non-alcoholic), <i>n</i> (%)	14 (87.5)/2 (12.5)	9 (90.0)/1 (10.0)	0.677
Child-Pugh score (units)	6.3 ± 1.3	6.1 ± 1.2	0.775
Child-Pugh class (A/B + C), <i>n</i> (%)	9 (56.2)/7 (43.8)	8 (80.0)/2 (20.0)	0.399
MELD score (units)	8.1 ± 5.8	9.5 ± 4.6	0.532
Ascites, <i>n</i> (%)	4 (25.0)	1 (10.0)	0.617
Gastroesophageal varices, <i>n</i> (%)	14 (87.5)	8 (80.0)	0.625
History of overt encephalopathy, <i>n</i> (%)	1 (6.3)	2 (20.0)	0.538
Sodium (mEq/L)	140.7 ± 2.9	140.5 ± 2.3	0.865
Creatinine (mg/dL)	0.8 ± 0.2	0.9 ± 0.1	0.343
Albumin (g/dL)	3.6 ± 0.3	3.5 ± 0.4	0.446

CCM: Cirrhotic cardiomyopathy; MELD: Model for end-stage liver disease.

mL vs 27.3 ± 7.5 mL, *P* = 0.466, respectively), but LV EDV was significantly increased in the group of reduced LV CR (111.4 ± 32.8 mL vs 83.5 ± 22.4 mL, *P* = 0.016). After pharmacological stress, LV ESV mean reduction was significantly inferior in the group of reduced LV CR (6.1 ± 12.6 mL vs 44.0 ± 21.8 mL, *P* = 0.000) and LV EDV mean reduction was similar in the two groups (0.53 ± 11.6 mL vs 5.2 ± 18.5 mL, *P* = 0.481).

Left ventricular diastolic function: At rest, 2 patients were diagnosed with diastolic dysfunction (grade I). In 8 (30.8%) patients, the E/e' average ratio increased from 6.9 ± 2.0 to 9.1 ± 2.7; in the others, the E/e' reduced from 8.9 ± 1.9 to 6.8 ± 2.3.

CCM

Sixteen (61.5%) patients were diagnosed with CCM: 10 patients had systolic dysfunction, 8 patients had diastolic dysfunction and 2 presented with both cardiac systolic and diastolic dysfunction. Among those patients with CCM, QTc interval prolongation was observed in 11 (68.8%) patients and increased pro-BNP levels were measured in 5 (31.2%) patients. QTc prolongation and elevation of pro-BNP were simultaneously present in 5 (31.2%) cases and none of the alterations was observed in 5 (31.2%) patients. The characteristics of patients with and without CCM are listed in Table 2. Of note, the presence of CCM was unrelated to the etiology and severity of cirrhosis and presence of ascites, gastroesophageal varices and history of overt encephalopathy. Moreover, sodium, creatinine and albumin values were similar between patients with and without CCM.

DISCUSSION

In order to describe CCM prevalence, natural history and prognosis accurately, an effort to define diagnostic criteria has been made. However, universal consensus is still lacking and important points remain to be elucidated, such as: The minimum number of criteria required to make the diagnosis, the need to always

performing a stress test to unmask CCM and the most adequate stress test to use, as the disease is usually latent and revealed by stress. Moreover, recent studies have used tissue Doppler parameters to diagnose CCM^[28,29], as they are more sensitive and less dependent on loading conditions^[30,31], comparing with mitral inflow velocity variables. Consequently, there is a considerable heterogeneity in the results published in the literature.

Diastolic dysfunction relates to impaired myocardial relaxation^[28] and elevated left ventricular filling pressures is the main physiological consequence of it^[32]. During stress, left ventricular filling pressures change minimally in healthy subjects. However, if cardiac dysfunction is present, a rise in filling pressures is observed in order to maintain left ventricular filling and stroke volume^[28]. The E/e' ratio was shown to relate significantly to left ventricular filling pressures during stress^[33]. Diastolic dysfunction was present in only 2 cases at rest and in 8 after stress. In fact, stress dobutamine echocardiography could identify patients with diastolic dysfunction (average E/e' ratio increase) not recognized at rest. The observation of an impaired myocardial relaxation during stress provides a possible explanation for the frequent development of cardiovascular complications (such as pulmonary edema) after transjugular intrahepatic portosystemic shunt (TIPS) insertion and liver transplantation, as these interventions promote a sudden increase in the preload and, consequently, a rise in left ventricular filling pressures.

None of the patients was diagnosed with systolic dysfunction at rest, which is consistent with the data reported in the literature, when LV EF is used as diagnostic criteria. The pharmacological stimuli revealed the existence of a systolic dysfunction in a considerable number of patients (38.5%). Due to the hyperdynamic state, with central hypovolemia and diminished preload and afterload, it remains an underdiagnosed condition even after a careful echocardiographic evaluation at rest.

The proportion of patients with CCM in our population was 61.5%. A significant number of patients (68.8%) had concomitant QTc interval prolongation and a smaller fraction (31.2%) had increased levels of pro-BNP.

CCM was independent of the etiology of cirrhosis, as has already been described in previous studies^[3-5,8-10]. Controversy exists regarding the relation between the CCM and the severity of the disease. Some studies suggest that CCM can be more severe in decompensated liver disease while others report CCM is not directly related to disease severity^[7,26,29,33,34]. In our study, we did not find any relation between CCM and Child-Pugh classification or MELD. Furthermore, clinical markers of higher liver impairment (ascites, gastroesophageal varices and history of overt encephalopathy) did not predict the presence of CCM.

QTc interval prolongation was a very common finding in this population of cirrhotic patients. This result is in agreement with the data reported in the literature. It is already established that QTc interval prolongation is significantly related to the severity of the underlying liver disease^[13,35,36]. In our study, QTc interval duration was positively correlated with the degree of liver dysfunction assessed by MELD score, but not by Child-Pugh classification, probably because of small sample size. Interestingly, patients who were diagnosed with QTc interval prolongation had more commonly gastroesophageal varices, the last being an established surrogate of more severe liver disease and increased risk. However, this could not be demonstrated in patients with ascites. Recently, Trevisani *et al.*^[37] reported further QTc interval prolongation in the setting of acute gastrointestinal bleeding in cirrhotic patients. Although the clinical significance of QTc interval prolongation is not completely clarified^[2,4-7,13,22], it may increase the risk of cardiac events and be associated with a poorer survival^[13]. Therefore, close monitoring during stressful events is advised^[6].

In summary, our study demonstrated that CCM is a frequent condition that is independent of the severity of liver disease. Furthermore, it showed that CCM is currently underdiagnosed, even after a comprehensive evaluation at rest. Consequently, a stress test should always be considered in the diagnostic approach to CCM, as it is highlighted in the current study. Moreover, an association between QTc interval prolongation and the presence of gastroesophageal varices was revealed, irrespective of the diagnosis of CCM. As such, the clinical significance of QTc interval prolongation is emphasized and it can be regarded as a marker of severe liver disease. A limitation of our study is its small sample size.

Hepatologists should be aware of this silent entity and actively search for it because it is of major importance in the management of the cirrhotic patient as it contributes to the high cardiovascular morbidity and mortality related to TIPS insertion and liver transplantation. It remains of the utmost importance to better define CCM diagnostic criteria, to suggest specific stress test protocols and to update echocardiographic criteria for the diagnosis, probably including TDI parameters which have already been used in several studies besides ours, in order to achieve more reproducible results.

Also, the performance of strain evaluation by speckle tracking analysis, a new sophisticated echocardiographic technique, might be a promising method to diagnose CCM in patients with advanced liver disease as it can detect subtle systo-diastolic dysfunction before left ventricular ejection fraction becomes impaired^[12,29]. Data regarding the impact of CCM in the natural history of cirrhosis is also needed.

COMMENTS

Background

Cirrhotic cardiomyopathy (CCM) relates to a cardiac dysfunction in patients with cirrhosis characterized by impaired contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease. It is independent of the etiology of cirrhosis and is different from alcoholic disease. Although almost always clinically silent at rest, CCM is usually unmasked by physiological, pharmacological and/or surgical stress, such as transjugular intrahepatic portosystemic shunt or liver transplant. In this study, the authors aimed at describing the proportion of patients with CCM evaluated by stress echocardiography in a population of cirrhotic patients, and at investigating whether CCM is related to severity of liver disease.

Research frontiers

Very few prior reports address the question of diagnostic evaluation of CCM in cirrhotic patients using accurate criteria and stress testing. The results of the authors' study contribute to the diagnostic approach to CCM in these patients.

Innovations and breakthroughs

This study demonstrated that CCM is a frequent condition that is independent of the severity of liver disease. Also, it revealed that CCM is currently underdiagnosed at rest, even after a comprehensive electrocardiographic and echocardiographic evaluation. A substantial number of patients were diagnosed as having CCM only after the stress echocardiographic evaluation. Furthermore, an association between corrected QT (QTc) interval prolongation and the presence of gastroesophageal varices was revealed, irrespective of the presence of CCM. As such, QTc interval prolongation can be regarded as a surrogate of severe liver disease.

Applications

This study suggests that a stress test should always be considered in the diagnostic approach to CCM, otherwise it will remain an underdiagnosed entity.

Terminology

This study demonstrated that stress echocardiography was useful at revealing CCM. As such, it can identify patients at risk of cardiac decompensation and can be used as diagnostic tool of CCM in cirrhotic patients in clinical practice.

Peer-review

This is an interesting manuscript, and especially interesting for the general gastroenterologists, hepatologists, cardiologists and the internist.

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