CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

Correlation between cirrhosis severity and electrocardiographic and echocardiographic parameters in cirrhotic patients

Corrélation entre la sévérité de la cirrhose et les paramètres électro-échocardiographiques chez les patients atteints de cirrhose

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Summary

Background: Cirrhotic cardiomyopathy (CCM) is a clinical entity characterized by systolic and/or diastolic dysfunction and electrophysiological abnormalities occurring in cirrhotic patients in the absence of known underlying heart disease. The relationship between the severity of liver disease and the extent of cardiac involvement remains debated in the literature.

Objective: To assess the correlation between the severity of cirrhosis, evaluated using the Child-Pugh and MELD scores, and electrocardiographic and echocardiographic parameters in cirrhotic patients.

Methods: This cross-sectional analytical study included 76 cirrhotic patients without known cardiac disease, enrolled between September 2016 and May 2017. All participants underwent a standardized clinical examination, a 12 lead electrocardiogram with QT correction using the cirrhosis-specific "QTc cirrhosis" formula, and transthoracic echocardiography incorporating conventional measurements, tissue Doppler imaging, and global longitudinal strain (GLS) by 2D speckle tracking. The severity of cirrhosis was assessed using the Child-Pugh and MELD scores and associations between electro-echocardiographic parameters and these scores were evaluated using Spearman's correlation coefficient.

Results : The mean age was 54 ± 11.8 years (male-to-female ratio = 1.4). QTc prolongation was observed in 43.5% of patients, diastolic dysfunction in 51.3%, and systolic dysfunction in 5.3%. Cirrhotic cardiomyopathy was present in 53.9% of the cohort. Left atrial volume (LAV) showed a positive correlation with both Child-Pugh ($r = 0.351$; $p = 0.002$) and MELD scores ($r = 0.329$; $p = 0.004$). Similarly, the QT interval was positively correlated with Child-Pugh ($r = 0.292$; $p = 0.011$) and MELD scores ($r = 0.329$; $p = 0.004$). No other echocardiographic parameters demonstrated significant correlations with either severity score. On multivariate analysis, older age, female sex, and a Child-Pugh score ≥ 9 emerged as independent predictors of CCM.

Conclusion: Left atrial dilation and QT interval prolongation emerged as the electro-echocardiographic parameters most strongly associated with cirrhosis severity, whereas conventional indices of systolic and diastolic function remained largely independent of the extent of hepatic insufficiency. These findings support a strategy of targeted cardiac monitoring in patients with advanced cirrhosis.

Keywords

Cirrhotic cardiomyopathy; cirrhosis; Child-Pugh; MELD; QT interval; echocardiography

Résumé

Introduction : La cardiomyopathie cirrhotique est une entité clinique caractérisée par des anomalies de la fonction systolique, diastolique et/ou électrophysiologiques du cœur chez des patients atteints de cirrhose, en l'absence de cardiopathie sous-jacente connue. La relation entre la sévérité de l'atteinte hépatique et l'importance de l'atteinte cardiaque demeure controversée.

Objectif : Évaluer l'association entre la sévérité de la cirrhose, appréciée par les scores de Child-Pugh et de MELD, et les paramètres électrocardiographiques et échocardiographiques chez des patients cirrhotiques.

Méthodes : Il s'agissait d'une étude analytique transversale incluant 76 patients atteints de cirrhose, sans antécédent ni cardiopathie connue, recrutés entre septembre 2016 et mai 2017. Tous les patients ont bénéficié d'un examen clinique standardisé, d'un électrocardiogramme 12 dérivations avec correction de l'intervalle QT selon la formule spécifique à la cirrhose « QTc cirrhosis», ainsi que d'une échocardiographie transthoracique. L'évaluation échocardiographique comprenait les mesures conventionnelles, le Doppler tissulaire et l'analyse du strain longitudinal global (SLG) par speckle tracking bidimensionnel. La sévérité de la cirrhose a été déterminée à l'aide des scores de Child-Pugh et de MELD. Les corrélations entre les paramètres électrocardiographiques, échocardiographiques et les scores de sévérité ont été étudiées par le coefficient de corrélation de Spearman.

Résultats : L'âge moyen des patients était de 54 ± 11,8 ans, avec un sexe ratio H/F de 1,4. Un allongement du QTc a été observé chez 43,5% des patients, une dysfonction diastolique chez 51,3% et une dysfonction systolique chez seulement 5,3%. La prévalence de la cardiomyopathie cirrhotique était de 53,9%. Le volume de l'oreillette gauche était positivement corrélé aux scores de Child-Pugh ($r=0,351$; $p=0,002$) et de MELD ($r=0,329$; $p=0,004$). De même, l'intervalle QT présentait une corrélation positive avec le score de Child-Pugh ($r = 0,292$; $p=0,011$) et le score de MELD ($r=0,329$; $p=0,004$). Aucun autre paramètre échocardiographique n'était significativement corrélé aux scores de Child-Pugh ou de MELD. En analyse multivariée, l'âge avancé, le sexe féminin et un score de Child-Pugh ≥ 9 étaient identifiés comme des facteurs prédictifs indépendants de cardiomyopathie cirrhotique.

Conclusion : La dilatation de l'oreillette gauche et l'allongement de l'intervalle QT apparaissent comme les paramètres électrocardiographiques et échocardiographiques les plus étroitement associés à la sévérité de la cirrhose. À l'inverse, les indices conventionnels de fonction systolique et diastolique semblent globalement indépendants du degré d'insuffisance hépatocellulaire. Ces résultats soulignent l'importance d'une surveillance cardiovasculaire continue chez les patients ayant une cirrhose sévère.

Mots-clés

Cardiomyopathie cirrhotique, cirrhose, Child-Pugh; MELD, intervalle QT, échocardiographie.

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INTRODUCTION

Cirrhosis is characterized by systemic hemodynamic alterations, including a hyperdynamic circulatory state, reduced peripheral vascular resistance, and splanchnic vasodilation, that long obscured the presence of an intrinsic cardiac abnormality (1).

CCM is classically defined by the triad of latent systolic dysfunction, diastolic dysfunction, and electrophysiological abnormalities, most prominently prolongation of the corrected QT interval (QTc). Historically underrecognized in routine practice because it is masked by the resting hyperdynamic state, CCM typically becomes clinically apparent during physiological or pharmacological stress, such as infection, gastrointestinal bleeding, transjugular intrahepatic portosystemic shunt placement, or liver transplantation, when inadequate cardiac reserve is unmasked (1).

METHODS

Study design and population

This cross-sectional analytical study was conducted between September 2016 and May 2017 in the department of Hepato-Gastroenterology, in collaboration with the cardiology department, in Sahloul University Hospital. All patients with cirrhosis, whether hospitalized or followed as outpatients during the study period, were considered for inclusion. The diagnosis of cirrhosis was based on histopathological examination of a liver biopsy and/or on a combination of clinical, biological and endoscopic findings associating signs of hepatocellular insufficiency with signs of portal hypertension.

Patients were excluded if they had: a history of cardiovascular disease (arterial hypertension, coronary artery disease, moderate to severe valvular disease, cardiac arrhythmia, or heart failure); recent gastrointestinal bleeding (within the two months preceding inclusion); a body mass index > 30 kg/m^2; severe anaemia (haemoglobin < 7 g/dl); or chronic alcohol use exceeding 30 g/day.

Among 109 patients initially screened, 33 were excluded based on prespecified criteria: recent gastrointestinal bleeding (n = 7), severe anaemia (n = 6), arterial hypertension (n = 12), coronary artery disease (n = 3), arrhythmia (n = 3), moderate mitral regurgitation (n = 1), and chronic alcohol use (n = 1). Consequently, 76 patients were retained for final analysis.

Clinical and biological data collection

This For each patient, we collected sociodemographic data, comorbidities, current medications (particularly beta-blockers and diuretics), toxic habits, and hemodynamic parameters (heart rate, systolic, diastolic, and mean arterial pressure.

Laboratory work-up, performed within the three months preceding inclusion, included a complete blood count, prothrombin time and INR, a full liver panel (AST, ALT, GGT, alkaline phosphatase, total bilirubin), serum electrolytes, and an assessment of renal function using creatinine clearance (MDRD-6 formula adapted for cirrhotic patients).

The severity of liver disease was assessed using two standard prognostic scores: the Child-Pugh score, with advanced cirrhosis defined as a score ≥ 9, and the MELD score, calculated from serum bilirubin, creatinine, and INR.

Electrocardiographic evaluation

A standard 12 lead electrocardiogram (ECG) was performed in all patients. The QT interval, defined as the interval from the onset of ventricular depolarization to the end of repolarization, was measured and corrected for heart rate, given its inverse relationship with rate. Although several correction formulas are available (Bazett, Hodges, Framingham, Fridericia), this study employed the "QTc cirrhosis" formula (QTc = QT / [1 + 3.02 × (1/RR − 1)]^(1/3)), which demonstrates a near zero QT–RR independence coefficient and is therefore considered most appropriate for the cirrhotic population. QTc prolongation was defined according to the threshold specified in the consensus criteria adopted for this study.

Echocardiographic evaluation

All patients underwent transthoracic echocardiography (TTE), including:

- Conventional assessment of systolic function (left ventricular ejection fraction (LVEF)), fractional shortening, cardiac output, screening for left ventricular hypertrophy (LVH), and measurement of end diastolic and end systolic diameters and volumes (LVEDD, LVESD, EDV, ESV)
- Assessment of diastolic function patterns like septal and lateral e' velocities, E/e' ratio
- Measurement of global longitudinal strain (GLS) by two dimensional speckle tracking;
- Measurement of left atrial diameter and volume (LAD, LAV).

The diagnostic criteria for cirrhotic cardiomyopathy, proposed by the Cirrhotic Cardiomyopathy Consortium, define CCM as cardiac dysfunction in patients with cirrhosis in the absence of known structural heart disease, and rely on contemporary echocardiographic parameters aligned with ASE/EACVI heart failure guidelines. CCM is diagnosed when either systolic or advanced diastolic dysfunction is present.

Systolic dysfunction is defined by the presence of any one of the following echocardiographic criteria: a left ventricular ejection fraction (LVEF) ≤ 50%, or, in patients with preserved LVEF, an absolute global longitudinal strain (GLS) value < 18%. Advanced diastolic dysfunction is defined more stringently, requiring at least three of the following four parameters: septal e' velocity < 7 cm/s, E/e' ratio ≥ 15 (using medial/septal e'), left atrial volume index > 34 mL/m^2, and tricuspid regurgitation (TR) peak velocity > 2.8 m/s in the absence of primary or portopulmonary hypertension. Only advanced diastolic dysfunction (grade 2–3 pattern) qualifies for CCM diagnosis

QTc prolongation, chronotropic incompetence, and electromechanical uncoupling are recognized supportive features but are not part of the core diagnostic criteria. Other structural or ischemic cardiomyopathies, significant valvular disease, and portopulmonary hypertension must be excluded before attributing dysfunction to CCM.

Statistical analysis

Normally distributed quantitative variables were expressed as mean ± standard deviation, and non-normally distributed variables as median and interquartile range (IQR, 25th-75th percentile). The relationship between two quantitative variables was assessed using Spearman's correlation coefficient, given the non-Gaussian distribution of some variables. Means were compared using Student's t-test or the Mann-Whitney U test according to distribution, and percentages were compared using the Chi-square or Fisher's exact test. A backward stepwise logistic regression analysis was performed to identify independent predictors of CCM (entry threshold $p < 0.2$ on univariate analysis). Statistical significance was set at 5% for all tests.

The study was conducted with respect for patient integrity; informed oral consent was obtained from all participants.

RESULTS

General characteristics of the population

Among the 76 patients included, the mean age was 54 ± 11.8 years (range: 18–79), with a male predominance (45 men [59%] vs 31 women [41%]; male-to-female ratio 1.4). Comorbidities were present in 22 patients (29%), most commonly type 2 diabetes (9.2%). The most frequent presenting feature of cirrhosis was upper gastrointestinal bleeding (31.6%), followed by ascitic–edematous decompensation (27.6%). Regarding disease course, 47.4% had experienced at least one episode of gastrointestinal bleeding and 61.8% had a history of ascitic–edematous decompensation; at inclusion, 32.9% had ascites. Type 2 hepatorenal syndrome was observed in 5.3% of patients, and hepatocellular carcinoma in 13% of the cohort.

Prevalence of cirrhotic cardiomyopathy

41 patients had CCM, which mean a prevalence of 53.9%.

Severity of cirrhosis

Regarding cirrhosis severity, the majority of patients were classified as CHILD PUGH B (44.7%), while only 9 patients (11.8%) had CHILD PUGH C cirrhosis (Figure 1). A CHILD PUGH score ≥ 9 was observed in 23 patients (30.3%) (Figure2).

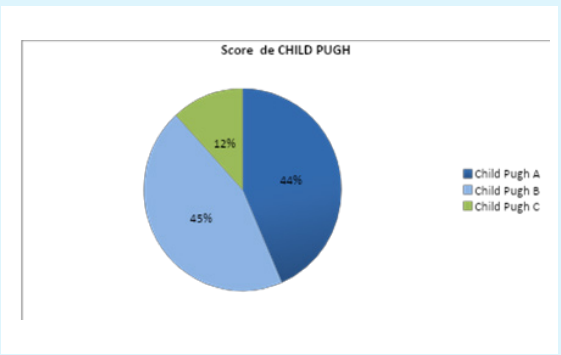

Figure 1. Distribution of cirrhotic patients according to CHILD PUGH score stages.

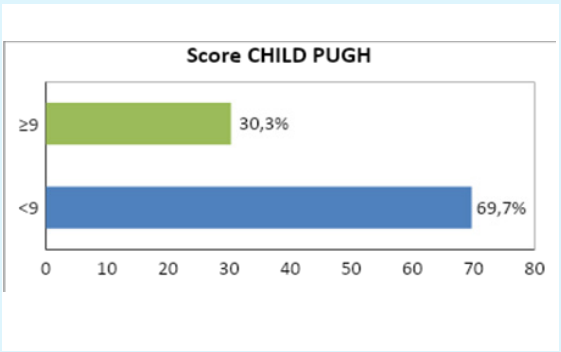

Figure 2. Distribution of cirrhotic patients according to CHILD PUGH score.

The median MELD score was 11, with an inter-quartile range of [10; 14], and the majority of patients (77.6%) had a MELD score ≤ 15 (Figure 3).

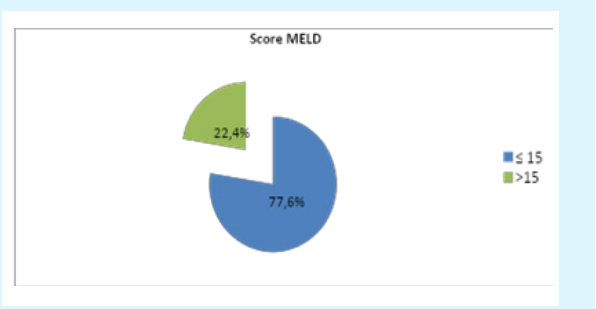

Figure 2. Distribution of cirrhotic patients according to MELD score

Electrocardiographic findings

The mean QTc interval was 434.5 ms (range: 380–494 ms), and QTc prolongation was observed in 33 patients, representing 43.5% of the study population.

Echocardiographic findings

Systolic function

Median LVEF was 67%. Systolic dysfunction was noted in 4 patients (5.3%) according to the conventional definition, whereas an abnormal GLS (> −18%), reflecting earlier impairment of longitudinal contractility, was found in 10 patients (13.2%).

Diastolic function

Analysis using tissue Doppler imaging and 2D strain, identified isolated SD in 6 patients (7.9%), isolated DD in 21 patients (27.6%), and combined SD-DD in 4 patients (5.3%).Furthermore, patients with cirrhotic cardiomyopathy had significantly lower septal and lateral e' velocities and a higher E/e' ratio compared with patients without cirrhotic cardiomyopathy; these differences were statistically significant ($p < 0.001$, $p < 0.001$, and $p = 0.01$, respectively). In contrast, there was no significant difference in global longitudinal strain (GLS) values between the two groups ($p = 0.11$) (Table 1).

Table 1. Comparison of echocardiographic Doppler tissue imaging and 2D strain parameters between patients with and without cirrhotic cardiomyopathy

Variable	No CCM	CCM	p value
GLS (%)	−21.2 ± 2.3	−20.5 ± 2.3	0.11
Septal e' (cm/s)	9.9 ± 2.3	6.7 ± 2.0	< 0.001
Lateral e' (cm/s)	14.1 ± 4.0	9.0 ± 2.5	< 0.001
E/e' ratio	7.3 ± 1.8	8.6 ± 2.7	0.01

Factors associated with the development of cirrhotic cardiomyopathy

On univariate analysis (Table 2), cirrhotic cardiomyopathy (CCM) was significantly more frequent in women than in men ($p = 0.04$) and in older patients (mean age 58 vs 51 years; $p = 0.01$). A Child-Pugh score ≥ 9 was significantly associated with CCM ($p = 0.002$), as was moderate to severe renal impairment (creatinine clearance < 60 mL/min; $p = 0.04$). In contrast, cirrhosis etiology, beta-blocker use, and a MELD score > 15 were not significantly associated with CCM ($p = 0.312$).

Table 2. Demographic and clinico-biological factors associated with cirrhotic cardiomyopathy in univariate analysis.

Variable	No CCM (n=35)	CCM (n=41)	OR (95% CI)
Age (years)	51 ± 11.7	58 ± 11	1.042 (1.001-1.084)
Female sex, n (%)	10 (32.2)	21 (67.7)	2.62 (1.01-6.824)
Creat. clearance < 60 ml/min, n (%)	32 (55.2)	26 (44.8)	6.154 (1.6-23.579)
Child-Pugh ≥ 9, n (%)	6 (26.1)	17 (73.9)	3.424 (1.167-10.046)
MELD > 15, n (%)	6 (35.3)	11 (64.7)	1.772 (0.579-5.421)

On multivariate analysis by backward stepwise logistic regression, three independent predictors of CCM were retained: age (adjusted OR 1.050; 95% CI 1.003-1.103; $p = 0.039$), female sex (adjusted OR 3.006; 95% CI 1.029-8.778; $p = 0.044$), and a Child-Pugh score ≥ 9 (adjusted OR 4.363; 95% CI 1.328-14.331; $p = 0.015$).

Correlation between the severity of cirrhosis and electro-echocardiographic parameters

Correlation analysis, summarized in Table 3, demonstrated that among all echocardiographic parameters evaluated, only left atrial volume (LAV) showed a positive and significant correlation with both the Child-Pugh score ($r = 0.351$; $p = 0.002$) and the MELD score ($r = 0.329$; $p = 0.004$). No other echocardiographic parameter, whether reflecting systolic function, diastolic function, or ventricular dimensions was significantly correlated with either severity score.

Table 3. Spearman correlation coefficients between echocardiographic parameters and the Child-Pugh and MELD scores

Parameter	Child-Pugh (r)	Child-Pugh (p)	MELD (r)	MELD (p)
LAV (left atrial volume)	0.351	0.002*	0.329	0.004*
LVEF	0.008	0.943	0.203	0.078
GLS	0.058	0.623	0.184	0.116
E/E'	0.033	0.770	0.060	0.960

LA: left atrium; LVEDD/LVESD: left ventricular end-diastolic/end-systolic diameter; LVEF: left ventricular ejection fraction; GLS: global longitudinal strain. (*p < 0.05)

Regarding the electrocardiographic parameter, the QTc interval was positively and significantly correlated with both severity scores: Child-Pugh (r = 0.292; p = 0.011) and MELD (r = 0.329; p = 0.004), as detailed in Table 4.

Table 4. Correlation between the QTc interval and the severity scores of cirrhosis. (*p < 0.05).

Parameter	Child-Pugh (r)	Child-Pugh (p)	MELD (r)	MELD (p)
QTc interval	0.292	0.011*	0.329	0.004*

Thus, in this cohort, the severity of cirrhosis appears specifically associated with two markers: left atrial dilation on echocardiography and QTc interval prolongation on electrocardiography (Figure 4 and 5).

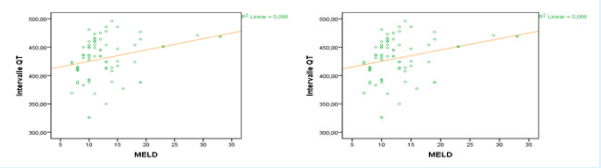

Figure 4. Correlation between MELD and Child-Pugh scores and QTc interval

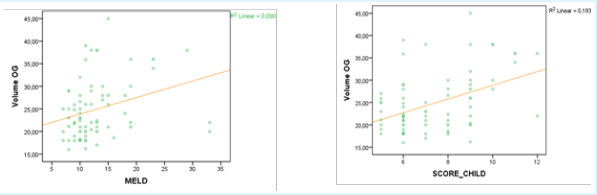

Figure 5. Correlation between MELD and Child-Pugh scores and left atrial volume

DISCUSSION

Pathophysiology of cirrhotic cardiomyopathy

Cirrhotic cardiomyopathy (CCM) is a distinct clinical syndrome defined as chronic cardiac dysfunction occurring in patients with established liver cirrhosis, in the absence of prior structural or ischemic heart disease. It is characterized by three cardinal features (1): a blunted systolic contractile response to physiologic, pathologic, or pharmacologic stress despite normal or elevated resting cardiac output (2); diastolic dysfunction with impaired ventricular relaxation and filling; and electrophysiological abnormalities, most consistently manifest as QTc interval prolongation (3). These abnormalities are independent of the underlying aetiology of cirrhosis and typically remain subclinical at rest, becoming apparent during high-demand states such as infection, gastrointestinal bleeding, transjugular intrahepatic portosystemic shunt (TIPS), or liver transplantation, when affected patients may develop disproportionate heart failure or hemodynamic instability.

Contemporary diagnostic frameworks integrate echocardiographic evidence of systolic impairment (reduced LVEF or abnormal global longitudinal strain), advanced diastolic dysfunction, and supportive biomarker and electrical findings to identify CCM in cirrhotic patients (2).

The relationship between liver disease severity and the extent of cardiac involvement in cirrhosis remains incompletely defined. While some studies report a significant association between advanced cirrhosis stage and cardiac abnormalities (3), others find no correlation, including for conventional echocardiographic parameters across severity groups. This heterogeneity likely reflects differences in diagnostic criteria, study populations, and echocardiographic endpoints, and may also indicate a non linear heart–liver interaction during disease progression. Pathophysiologically, multiple intertwined mechanisms have been implicated in cirrhosis related cardiac dysfunction: impaired β-adrenergic signalling due to receptor and G-protein uncoupling; myocardial overexpression of the nitric oxide pathway; accumulation of substances normally cleared by the liver (eg, bile acids and pro-inflammatory cytokines such as TNFα) that exert direct negative inotropic effects; and structural cardiomyocyte alterations, including hypertrophy, interstitial fibrosis, and subendocardial oedema. These processes converge on reduced contractile reserve and electrical remodelling that typically remain subclinical at rest owing to the compensatory hyperdynamic state, but may become manifest during hemodynamic stress (1).

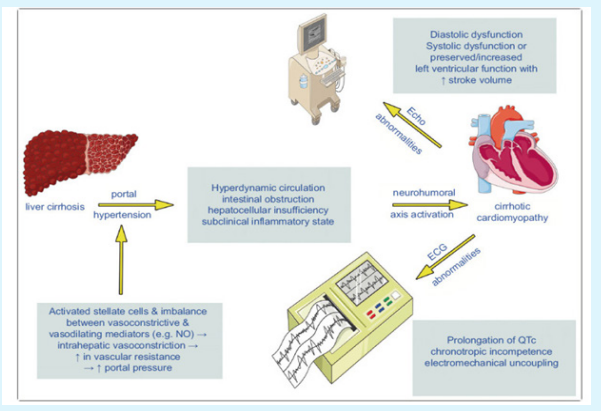

Figure 6. Pathophysiology of cirrhotic cardiomyopathy

Accordingly, this study examined, in a cohort of cirrhotic patients without known cardiac disease, the correlation between cirrhosis severity and a comprehensive set of electrocardiographic and echocardiographic parameters to identify markers most suitable for targeted cardiac monitoring in cirrhosis.

Systolic dysfunction

Resting systolic dysfunction, was uncommon in our series (5.3%), aligning with published reports (0–10%) (4). This low sensitivity of LVEF stems from its load dependence: cirrhosis-associated reduction in systemic vascular resistance tends to preserve or even elevate resting LVEF, thereby concealing true impairment of intrinsic contractility. Consequently, stress echocardiography and 2D myocardial deformation imaging have gained traction as more sensitive tools for detecting subclinical systolic dysfunction (5).

In our cohort, this was evidenced by a higher prevalence of systolic dysfunction when defined by global longitudinal strain (GLS) (13.2%) compared with LVEF alone (5.3%). Notably, GLS did not correlate significantly with either Child-Pugh ($r = 0.058$; $p = 0.623$) or MELD scores ($r = 0.184$; $p = 0.116$), indicating that longitudinal myocardial impairment, while more frequent than LVEF suggests, does not progress linearly with overall liver disease severity as captured by these composite prognostic indices (4,6).

Diastolic dysfunction

The prevalence of diastolic dysfunction in our series (51.3%) was likewise consistent with the literature, which reports rates ranging from 30 to 67% depending on the population and criteria used (5).

The E/E′ ratio showed no significant correlation with either Child-Pugh or MELD scores. Although this may appear paradoxical given the high prevalence of diastolic dysfunction in cirrhosis, it accords with several prior reports that similarly failed to demonstrate a linear relationship between DD severity and liver disease severity as quantified by these prognostic scores (5,7).

These observations support the concept that DD can emerge early in the course of cirrhosis and evolve largely independently of subsequent progression in hepatic dysfunction (8).

QT interval prolongation

QTc prolongation, identified in 43.5% of our patients using the "QTc cirrhosis" correction formula, lies within the broad prevalence range described in the literature (24–65% across series) and constitutes the most characteristic electrocardiographic abnormality of cirrhotic cardiomyopathy, together with chronotropic incompetence and electromechanical uncoupling (9). Pathophysiologically, this repolarization delay is thought to reflect electrical remodeling of the cirrhotic myocardium secondary to altered function of membrane potassium and calcium channels, themselves influenced by circulating factors retained in hepatocellular insufficiency, particularly bile acids (10). The positive and statistically significant correlations observed between the QT interval and both severity scores (Child–Pugh: $r = 0.292$, $p = 0.011$; MELD: $r = 0.329$, $p = 0.004$) further support the view that electrical involvement of the cirrhotic myocardium is not a fixed phenomenon but evolves in parallel with deterioration of hepatic function, unlike most echocardiographic parameters examined. These findings are consistent with a cumulative toxic mechanism, whereby progressive accumulation of substances normally cleared by the liver, such as bile acids and pro-inflammatory cytokines, drives an electrical remodeling that intensifies with increasing severity of hepatic insufficiency (11).

Left atrial dilation: a central marker

The most salient finding of our study is that left atrial volume was the sole echocardiographic parameter significantly associated with both cirrhosis severity scores (Child–Pugh: $r = 0.351$, $p = 0.002$; MELD: $r = 0.329$, $p = 0.004$), consistent with prior reports of similar correlation strength.

- Potential mechanisms include a progressive rise in preload due to volume expansion and sodium and water retention that intensify with hepatocellular dysfunction; atrial remodeling driven by chronic exposure to cirrhosis-related neurohormonal activation; and contributions from splanchnic vasodilation and altered venous return in advanced portal hypertension (12). By integrating cumulative hemodynamic burden over time more effectively than instantaneous Doppler measures, LAV may serve as a more robust and sensitive marker of the global cardiac load imposed by advancing liver disease. Clinically, these findings underscore the value of systematic LAV assessment, more reproducible and less load dependent than conventional transmitral Doppler indices—during echocardiographic follow-up of cirrhotic patients, especially those with deteriorating Child–Pugh or MELD scores (13).

Cirrhotic cardiomyopathy and severity of cirrhosis: a controversial relationship

The association between CCM and the severity of liver disease remains controversial, with heterogeneous and sometimes conflicting findings across studies (14,15,16).

In our cohort, a Child–Pugh score ≥ 9 was the strongest independent predictor of CCM (adjusted odds ratio 4.363), whereas no significant association was observed with MELD score. These results align with prior series reporting advanced Child–Pugh stage as an independent determinant of cardiac dysfunction, but contrast with other cohorts in which standard prognostic scores showed no relationship with echocardiographic parameters, which remained comparable across severity strata (8).

This apparent discrepancy between our binary analysis (significant association with Child–Pugh ≥ 9) and our continuous correlation analysis (absence of significant linear correlations for most echocardiographic indices with severity scores) highlights an important methodological consideration: the relationship between hepatic decompensation and cardiac involvement in cirrhosis may not be strictly linear. Instead, it may exhibit a threshold effect that emerges only beyond a critical degree of hepatocellular insufficiency. Such a nonlinear pattern would explain why only markers characterized by slow, cumulative kinetics namely left atrial volume and QT interval demonstrate statistically significant continuous correlations with disease severity, whereas more load dependent or instantaneous Doppler indices do not (13,17).

Clinical implications

These findings carry several clinical implications. First, they reinforce the value of systematic cardiac screening in all patients with cirrhosis combining a 12 lead ECG with QTc calculation and echocardiography that includes left atrial volume and global longitudinal strain, particularly in those with Child–Pugh score ≥ 9.

Secondly, the observed correlation between QT prolongation and cirrhosis severity should prompt heightened caution when prescribing QT prolonging agents (notably certain antibiotics such as quinolones and macrolides, and vasoactive drugs such as vasopressin analogues) in patients with advanced disease, who may be at increased risk for torsades de pointes.

Finally, given growing recognition of cirrhotic cardiomyopathy as a contributor to hepato-renal syndrome, via blunted contractile reserve and impaired cardiac output that limit renal perfusion during acute hemodynamic stress (eg, infection or bleeding), enhanced vigilance for this hepato-cardio-renal axis appears warranted in patients with both CCM and severe cirrhosis.

Research perspectives

Several research directions follow directly from these observations. Methodologically, prospective longitudinal studies with repeated echocardiographic reassessment as the Child-Pugh or MELD score progresses in the same patient would help confirm the dynamic, cumulative nature of the relationship observed between left atrial volume, QT interval, and hepatic severity, and clarify its timing relative to the onset of diastolic dysfunction. Incorporating circulating biomarkers (NT-proBNP, high-sensitivity troponin) and newer imaging techniques (left atrial strain, cardiac MRI with T1 mapping for quantification of diffuse myocardial fibrosis) could further improve understanding of cardiac remodeling in cirrhosis and refine risk stratification ahead of high hemodynamic-risk events such as transjugular intrahepatic portosystemic shunt placement or liver transplantation, during which a patient's cardiac reserve is severely tested. Finally, the independent prognostic value of LAV and QTc in terms of survival, risk of decompensation, or post-transplant complications, warrants testing in larger, longer-term cohorts.

CONCLUSION

In our cohort of 76 cirrhotic patients free of known cardiac disease, cirrhotic cardiomyopathy was common, with a prevalence of 53.9%. Among all electro-echocardiographic parameters examined, only left atrial volume and QTc interval showed statistically significant correlations with cirrhosis severity as quantified by Child-Pugh and MELD scores, whereas conventional indices of systolic and diastolic function remained largely independent of the degree of hepatic insufficiency. These observations suggest that left atrial dilation and QTc prolongation are preferential markers for cardiac monitoring in cirrhosis, particularly as liver disease advances, and support their systematic inclusion, given their ease of acquisition in routine practice, within cardiovascular risk stratification algorithms alongside standard hepatological assessment. Prospective, multicenter studies incorporating cardiac stress testing and longitudinal follow-up are warranted to validate the prognostic utility of these markers and to define their role in the comprehensive management of cirrhotic patients.

REFERENCES

1. Yumusak O, Doulberis M. Update on cirrhotic cardiomyopathy: from etiopathogenesis to treatment. Ann Gastroenterol. 2024 Jan-Feb;37(1):15-26.
2. Liu H, Naser JA, Lin G, Lee SS. Cardiomyopathy in cirrhosis: From pathophysiology to clinical care. JHEP Rep. 2023;6(1):100911.
3. Nazar A, Guevara M, Sitges M, Terra C, Solà E, Guigou C, et al. LEFT ventricular function assessed by echocardiography in cirrhosis: relationship to systemic hemodynamics and renal dysfunction. J Hepatol. 2013;58(1):51–57.
4. Sampaio F, Pimenta J, Bettencourt N, Fontes-Carvalho R, Silva AP, Valente J, et al. Systolic and diastolic dysfunction in cirrhosis: a tissue-Doppler and speckle tracking echocardiography study. Liver Int. 2013 Aug;33(7):1158-1165.

5. Sampaio F, Pimenta J. Left ventricular function assessment in cirrhosis: Current methods and future directions. World J Gastroenterol. 2016 Jan 7;22(1):112-125.
6. Rimbaş RC, Baldea SM, Guerra RDGA, Visoiu SI, Rimbaş M, Pop CS, et al. New Definition Criteria of Myocardial Dysfunction in Patients with Liver Cirrhosis: A Speckle Tracking and Tissue Doppler Imaging Study. Ultrasound Med Biol. Jan 2018;44(3):562-574.
7. Devi L, Malik P, Mallick J, Meher L. Study of Myocardial Dysfunction in Patients with Cirrhosis of Liver. J Adv Med Med Res. 10 jan 2017;24(8):1-7.
8. Falletta C, Filì D, Nugara C, Di Gesaro G, Minà C, Baravoglia CMH, et al. Diastolic dysfunction diagnosed by tissue Doppler imaging in cirrhotic patients: Prevalence and its possible relationship with clinical outcome. Eur J Intern Med. Dec 2015;26(10):830-834.
9. Bashir Bhatti A, Ali F, Akbar Satti S. Prolonged QTc Interval Is an Electrophysiological Hallmark of Cirrhotic Cardiomyopathy. Open J Intern Med. 2014;4(1):33-39.
10. Hansen S, Moller S, Bendtsen F, Jensen G, Henriksen JH. Diurnal variation and dispersion in QT interval in cirrhosis: Relation to haemodynamic changes. J Hepatol. 2007 May;46(5):818-825.
11. Kim SM, George B, Alcivar-Franco D, Campbell CL, Charnigo R, Delisle B, et al. QT prolongation is associated with increased mortality in end stage liver disease. Clin Cardiol. 2014 Dec;37(12):725-728.
12. Finucci G, Desideri A, Sacerdoti D, Bolognesi M, Merkel C, Angeli P, et al. Left ventricular diastolic function in liver cirrhosis. Scand J Gastroenterol. 1996 Mar;31(3):279-284.
13. Li X, Yu S, Li L, Han D, Dai S, Gao Y. Cirrhosis-related changes in left ventricular function and correlation with the model for end-stage liver disease score. Int J Clin Exp Med. 2014 Dec 15;7(12):5424-5432.
14. Carvalheiro F, Rodrigues C, Adrego T, et al. Diastolic Dysfunction in Liver Cirrhosis: Prognostic Predictor in Liver Transplantation? Transplant Proc. 2016;48(10):3301-3303.
15. Pozzi M, Redaelli E, Ratti L, Poli G, Guidi C, Milanese M, et al. Time-course of diastolic dysfunction in different stages of chronic HCV related liver diseases. Minerva Gastroenterol Dietol. juin 2005;51(2):179-86.
16. Karagiannakis DS, Vlachogiannakos J, Anastasiadis G, Vafiadis-Zouboulis I, Ladas SD. Diastolic cardiac dysfunction is a predictor of dismal prognosis in patients with liver cirrhosis. Hepatol Int. oct 2014;8(4):588-94.
17. Kazankov K, Holland-Fischer P, Andersen NH, Torp P, Sloth E, Aagaard NK, et al. Resting myocardial dysfunction in cirrhosis quantified by tissue Doppler imaging. Ultrasound Med Biol. 2011 Sep;37(9):1400-1408.