Original Research

Evaluation of Subclinical Left Ventricular Systolic Dysfunction Using Two-Dimensional Speckle-Tracking Echocardiography in Patients with Non-Alcoholic Cirrhosis

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Introduction: Cirrhosis is associated with certain abnormalities in left ventricular (LV) structure and function. Two-dimensional speckle-tracking echocardiography (2D-STE) enables a rapid and accurate analysis of regional LV systolic mechanics in the longitudinal, radial and circumferential directions. The aim of this study was to precisely assess the differences among the 3 directions in the early impairment of LV myocardial contraction in non-alcoholic cirrhotic patients with preserved LV pump function.

Method: A total of 75 subjects, including 38 cirrhotic patients and 37 healthy individuals, were enrolled. Using 2D-STE, the strain (S) and systolic strain rate (SR_S) values belonging to the radial (R), circumferential (C), and longitudinal (L) functions of the LV were measured.

Results: In the cirrhotic group, the L_S (20.57 ± 2.1 vs. 28.7 ± 43.1, p<0.001) and L_{SR-S} (1.1 ± 0.24 vs. 1.6 ± 0.3) values were found to be lower, whereas the C_S (24.82 ± 2.57 vs. 19.16 ± 4.58, p<0.001) and C_{SR-S} (1.41 ± 0.3 vs. 1.2 ± 0.4, p<0.004) values were found to be higher than in the healthy control group. The R_S and R_{SR-S} values did not differ among the groups. A relationship was observed between the MELD score, which shows the severity of the disease, and the C_S value (β: 0.211, p<0.01, 95%CI: 0.086-0.503).

Conclusion: LV myocardial contraction was impaired in the longitudinal direction. However, LV pump function was augmented by the circumferential shortening during the ventricular systole. Using the 2D-STE method for the regional evaluation of the LV, the LV damage can be detected in the subclinical phase in cirrhotic patients.

Cirrhosis is known to be associated with structural and functional cardiovascular abnormalities that are termed as cirrhotic cardiomyopathy (CCM).[1] Further investigations into the cardiovascular complications of cirrhosis have revealed the clinical aspects of CCM.[2] This is a condition comprising a constellation of cardiac abnormalities, which include hypertrophy of the myocardium, leading to a stiff ventricle and hence to diastolic dysfunction, and normal sys-tolic function at rest, with systolic incompetence under conditions of pharmacological or physical stress.[3] The pathogenetic mechanisms that underlie this syndrome include the impairment of beta-adrenergic receptor signalling, cardiomyocyte plasma membrane function, intracellular calcium kinetics, and humoral factors such as endogenous cannabinoids, nitric oxide and carbon monoxide. The inflammatory changes in the myocardial structure and the fibrosis that occur in patients with cir-

rhosis have been demonstrated by studies using cardiac MRI.[4,5] CCM-related heart failure is the third leading cause of death, following rejection and infection after transplants.[6,7] Therefore, it is important to evaluate the cardiovascular function in every patient with cirrhosis, especially if the patient is a candidate for any intervention that may affect haemodynamics.

The recently developed two-dimensional speckle-tracking echocardiography (2D-STE) method has enabled a simple and angle-independent evaluation of the LV deformation in the longitudinal, radial, and circumferential directions. Previous studies have indicated that 2D-STE is more sensitive than conventional echocardiography in detecting subclinical ventricular dysfunction in various clinical disorders.[8] Although the relationship between the presence and severity of cirrhosis and LV function has been investigated in various echocardiographic studies, no studies have investigated the regional function of the LV using 2D-STE in cirrhotic patients.

The aim of the present study was to investigate the regional function of the LV myocardium using 2D-STE in stable, non-alcoholic liver cirrhosis patients with preserved LV ejection fraction, and to assess the association between the presence and severity of the cirrhosis and the LV damage.

Methods

For the purposes of our study, we enrolled 38 clinically stable (i.e. had not been hospitalised or undergone any interventions due to cirrhosis or any related complications within the previous 6 months), non-alcoholic cirrhosis patients between the ages of 20 and 65, who were followed up at the Gastroenterology Department of the Akdeniz University School of Medicine between August 2011 and February 2012 and were referred to the echocardiography laboratory for the assessment of LV structure and function. The control group consisted of 37 healthy subjects of similar age and sex distribution, selected from individuals who had no history of cardiovascular disease and who underwent a routine physical examination with normal ECG and 2D-TTE findings. Detailed patient histories were taken from all the enrolled patients, and they all underwent physical examinations, electrocardiography (ECG), and two-dimensional transthoracic echocardiographic imaging (2D-TTE). Informed consent forms were signed by every individual enrolled and the study was approved by the local ethics committee of the Akdeniz University School of Medicine.

The exclusion criteria included coronary artery disease, severe or moderate heart valve disease, diabetes mellitus (fasting plasma glucose concentration ≥126 mg/dL, glycosylated haemoglobin >6.5%, or use of hypoglycaemic medication), hypertension (systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg, as an average of three separate blood pressure measurements taken at 10-minute intervals during the physical examination, or use of antihypertensive medication), New York Heart Association class III-IV heart failure, pericarditis or massive pericardial effusion, cardiac rhythm anomalies, low ejection fraction (EF<60%), suboptimal echocardiographic images (especially those with poor image quality for the 2D-STE analysis and with obscured endocardial borders on the images), body mass index (BMI) >35 kg/m^2, any metabolic or systemic diseases other than liver disease that might disrupt cardiac structure or function, smoking, and previous liver transplants that ended with rejection.

Blood pressure, heart rate and anthropometric measurements were recorded for all individuals before the echocardiography. BMI and body surface area were calculated from the anthropometric measurements. Biochemical parameters were obtained from the blood samples drawn after an 8-hour fasting period. Serum parameters were tested in the laboratory of the Akdeniz University Hospital.

The diagnosis of liver cirrhosis was based on the clinical examination, biochemical tests, and endoscopic findings in all patients. The cause of the cirrhosis was viral hepatitis in 60.5% (n=23), cryptogenic cirrhosis in 26.3% (n=10), and biliary cirrhosis in 13.1% (n=5) of the patients. According to the Child–Pugh classification, 23 patients were in class A, 12 patients were in class B and 3 were in class C. The clinical status was assessed based on the model for end-stage liver disease (MELD) score. The method for the MELD calculation has already been validated.[9] The MELD scores of the patients varied between 6 and 29, while the mean MELD score was calculated as 11.76 ± 4.92. Regarding prior medication, 18.4% (n=7) of patients were on treatment with spironolactone and 26.3% (n=10) were taking beta-blockers. Because of ethical considerations, these treatments were not suspended prior to the measurements.

Echocardiographic examination

Echocardiography was performed in the left lateral decubitus position using the GE-Vingmed Vivid 7

system (GE-Vingmed Ultrasound AS, Horten, Norway) ultrasound device and a 4S-RS (3.5 Mhz) probe. The examinations were carried out by two experienced cardiologists who were blinded to the groups into which the individuals were categorised. Images were obtained from the parasternal and apical positions using the 2D, M-Mode, and Doppler echocardiography techniques. All echocardiography examinations were performed according to the guidelines of the American Society of Echocardiography for the evaluation of LV structures, systolic and diastolic function, and the calculation of values dependent on the related functions.[10,11]

Tissue Doppler imaging (TDI) was performed from the apical four-chamber view using pulsed-wave Doppler with a 3 mm sample volume at the septal and lateral mitral annulus. All the annular velocities and time intervals of the tissue Doppler analysis were calculated as the average of values obtained from the two annular sites. The ratio between the mitral early diastolic flow velocity (E) and the average mitral annular early diastolic myocardial velocity (E') was calculated (E/E').[12] The averages of three consecutive end-expiratory cardiac cycles were measured for all the echocardiographic data.

2D-STE method

The offline analyses of the apical and parasternal short-axis 2D-STE views were performed with the help of the Echopac PC, version 8.0, GE Healthcare software package. Standard greyscale 2D images were obtained at a rate of 70-90 frames/s from the apical 4-, 2-, and 3-chamber and the parasternal short-axis views at the papillary muscle level. We measured the myocardial strain (S) and strain rate (SR), as previously described.[13,14] In each plane, 3 consecutive cardiac cycles were acquired at end-expiratory breath holding and digitally stored on a hard disk for offline analysis. The LV endocardial border of the end-systolic frame was traced manually. On the basis of this line, the computer automatically created a region of interest including the entire transmural wall and the software selected natural acoustic markers moving along the tissue. The automatic frame-by-frame tracking of these markers during the cardiac cycle yielded a measurement of the S and SR at any point of the myocardium. In the present study, the longitudinal strain (L_S), and longitudinal systolic strain rate (L_{SR-S}) were assessed for the 6 LV walls in the apical 4-, 2-,

and 3-chamber views. The averages of these values were used for the comparison of the cirrhotic patients with the controls. The circumferential and radial strain (C_S, R_S) and systolic strain rate (C_{SR-S}, R_{SR-S}) were assessed in the 6 LV walls on the parasternal LV short-axis view at the level of the papillary muscles and their mean values were used for the comparison.

Statistical analysis

The defining statistics were expressed as frequency, percentage, mean value, standard deviation, median, minimum and maximum values. When a normal distribution hypothesis was established in the analysis of the differences in certain measurements between the control and patient groups, Student's t-test was used, while the Mann–Whitney U-test was employed when this hypothesis could not be established. Spearman's correlation test was applied for the analysis of the relationship between the MELD score and the other echocardiographic variables. Among the variables with significant results in the correlation test, four items determined according to the magnitude of the value of the correlation coefficient and inter-relationship were included in the regression analysis. The analyses were performed with the help of the SPSS 18.0 software package. P-values <0.05 were accepted as statistically significant.

Inter- and intra-observer variability

After the initial measurement of the global longitudinal, radial, and circumferential strain in randomly selected cirrhotic patients, the intra-observer variability was determined by repeating the measurements by the same observer two weeks later. Inter-observer variability was determined by the measurement of these variables by a second observer using the same database. Bland–Altman analysis was used to assess the differences between the measurements.

Results

When the demographic and clinical data of the groups were compared, the systolic (p=0.036) and diastolic (p=0.033) blood pressures were observed to be lower in the cirrhosis group. When the biochemical values were evaluated, the international normalised ratio (p<0.001), aspartate transaminase

Table 1. Demographic, clinical and laboratory variables of groups. Data are presented as mean ± standard deviation or number (percentage).

	Controls	Cirrhosis	p
Age	45.4 ± 8.6	48.3 ± 12.4	0.239
Male (%)	20 (54.1%)	24 (63.2%)	0.423
BMI (kg/m^2)	26.6 ± 3.9	26.6 ± 3.5	0.955
Heart rate (/min)	74 ± 10	77 ± 10	0.117
SBP (mmHg)	119.1 ± 9.9	113.7 ± 8.8	0.036
DBP (mmHg)	73.5 ± 8.1	69.2 ± 6.2	0.033
Biochemical parameters:			
Creatinine (mg/dL)	0.77 ± 0.14	0.79 ± 0.32	0.479
BUN (mg/dL)	12.78 ± 3.85	13.42 ± 7.43	0.309
eGFR (mL/min/1.73m^2)	103.19 ± 13.98	103.95 ± 26.2	0.876
INR	0.96 ± 0.05	1.41 ± 0.36	<0.001
Total protein(mg/dL)	7.3 ± 0.37	6.87 ± 0.94	0.045
Albumin (mg/dL)	4.42 ± 0.41	3.76 ± 0.85	<0.001
AST (U/L)	21.22 ± 4.98	49.18 ± 33.83	<0.001
ALT (U/L)	21.65 ± 9.67	38.16 ± 34.18	0.006
GGT (U/L)	24.08 ± 13.77	49.05 ± 50.43	0.006
Total bilirubin (mg/dL)	0.46 ± 0.23	1.73 ± 1.67	<0.001
Direct bilirubin (mg/dL)	0.1 ± 0.06	0.71 ± 1.01	<0.001
MELD score	N/A	11.76 ± 4.92	

ALT – alanine transaminase; AST – aspartate transaminase; BMI – body mass index; BUN – blood urea nitrogen; DBP – diastolic blood pressure; eGFR – estimated glomerular filtration rate; GGT – gamma-glutamyl transferase; INR – international normalised ratio; MELD – model for end-stage liver disease; N/A – not applicable; SBP – systolic blood pressure.

(p<0.001), alanine transaminase (p=0.006), gamma-glutamyl transferase (p=0.006), total (p<0.001) and direct (p<0.001) bilirubin values were higher; while the total protein (p=0.045) and albumin (p<0.001) values were lower in the cirrhosis group. The demographic, clinical and biochemical data of the groups are presented in Table 1.

Conventional and tissue Doppler echocardiography results

In the cirrhosis group, the LV mass index (LVMI) (p<0.001), LV systolic (p=0.001) and diastolic (p<0.001) volumes, stroke volume (p<0.001), and cardiac output (p<0.001) were observed to be higher than in the control group. Among the Doppler parameters, the mitral valve late diastolic flow velocity (A) (p=0.001), mitral valve early diastolic flow (E) deceleration time (<0.001), isovolumic relaxation time (p<0.001), the ratio of the mitral valve early diastolic flow velocity to the mitral annulus early diastolic flow velocity (E/E') (p=0.042), and the left atrial volume index (LAVI) (p=0.003) were found to be higher in the cirrhosis group compared to the control group. In contrast, the E' value was lower in the cirrhosis group (p=0.026). Conventional and tissue Doppler echocardiographic results are presented in Table 2.

2D-STE findings

In the cirrhosis group, the C_S (p<0.001) and C_{SR-S} (p=0.004) values were higher, while the L_S (p<0.001) and L_{SR-S} (p<0.001) values were lower than in the control group. The R_S (p=0.465) and R_{SR-S} (p=0.574) did not differ between the groups. The 2D-STE findings of both groups are presented in Table 3.

In our study, the cirrhosis group was divided in two subgroups based on the median MELD score of 10.5, indicating the severity of the disease. The echocardiographic data of both groups were compared. In the MELD >10.5 group, the LVMI (p<0.001) and LAVI (p<0.001) values were found to be higher. When the 2D-STE values were compared, the L_S (p<0.001), and L_{SR-S} (p<0.001) values were observed to be lower in the MELD >10.5 group, while the C_S, and C_{SR-S} values were higher. The echocardiographic data of the groups according to the MELD score are presented in Tables 4 and 5.

The relationship between the MELD score and the echocardiographic parameters assessed in the study was evaluated through a correlation analysis. The LVMI, E/A, E/E', C_S, L_S, and the LAVI were observed to be associated with the MELD score. The regression analysis performed after the model had been formed with the related parameters confirmed the relationship between LVMI, C_S and LAVImax. The

Table 2. Conventional and TDI echocardiographic variables of healthy controls and patients with cirrhosis. Data are presented as mean ± standard deviation.

	Controls	Cirrhosis	p
LVDV (mL)	71.84 ± 15.55	97.39 ± 29.95	<0.001
LVSV (mL)	30.78 ± 6.52	36.92 ± 9.37	0.001
SV (mL)	41.05 ± 10.76	60.47 ± 21.72	<0.001
CO (L/min)	3.99 ± 0.68	5.66 ± 1.71	<0.001
LVEF (%)	66.16 ± 4.09	70.26 ± 4	0.033
LVMI (g/m^2)	126.47 ± 23.06	167.17 ± 52.56	<0.001
LAVI (mL/m^2)	22.08 ± 5.91	26.88 ± 7.5	0.007
Doppler parameters:			
E (m/s)	0.8 ± 0.17	0.84 ± 0.23	0.321
A (m/s)	0.69 ± 0.15	0.82 ± 0.15	0.001
E/A	1.21 ± 0.39	1.07 ± 0.37	0.156
E-DT (ms)	151.62 ± 31.1	203.97 ± 30.1	<0.001
IVRT (ms)	71.47 ± 11.76	82.75 ± 9.85	<0.001
S (m/s)	0.11 ± 0.02	0.11 ± 0.02	0.817
E' (m/s)	0.14 ± 0.09	0.11 ± 0.03	0.026
A' (m/s)	0.11 ± 0.02	0.12 ± 0.02	0.244
E/E'	6,42 ± 1.89	8.68 ± 2.27	0.042

A – mitral valve late diastolic velocity; A' – mitral annulus late diastolic velocity; CO – cardiac output; E – mitral valve early diastolic velocity; E' – mitral annulus early diastolic velocity; E-DT – E wave deceleration time; IVRT – isovolumic relaxation time; LAVI – left atrial volume index; LVDV – left ventricular diastolic volume ; LVEF – left ventricular ejection fraction; LVMI – left ventricular mass index; LVSV – left ventricular systolic volume ; S – mitral annulus systolic velocity; SV – stroke volume; TDI – tissue Doppler imaging.

Table 3. Two-dimensional speckle tracking echocardiography variables in healthy controls and patients with cirrhosis. Data are presented as mean ± standard deviation.

	Controls	Cirrhosis	p
Strain(%):			
Longitudinal	-28.74 ± 3.11	-20.57 ± 2.1	<0.001
Radial	52.67 ± 12.09	52 ± 14.5	0.465
Circumferential	-19.16 ± 4.58	-24.82 ± 2.57	<0.001
Systolic strain rate (1/s):			
Longitudinal	-1.6 ± 0.3	-1.1 ± 0.24	<0.001
Radial	2.08 ± 0.49	2.04 ± 0.55	0.574
Circumferential	-1.2 ± 0.4	-1.41 ± 0.3	0.004

results of the correlation and regression analyses are presented in Table 6.

Intra- and Inter-observer variability

Fifteen patients were randomly selected for the assessment of the intra- and inter-observer variability in the measurements of the strain parameters. Confidence intervals and mean differences for the inter-observer and intra-observer variability in the strain values are shown in Table 7.

Discussion

The present study demonstrates that there is a subclinical impairment in the longitudinal LV systol-ic function in cirrhotic patients with preserved LV pump function. During systole, the radial thickening is preserved, with an increase in the circumferential shortening and a decrease in the longitudinal shortening. This results in the maintenance of the LV ejection fraction.

In our study, the presence and severity of the cirrhosis were found to be associated with the LVMI. Previous reports have suggested that the tendency of the LVM to increase in cirrhotic patients may be attributable to the excessive mechanical overload due to the hyperkinetic circulation.[15] This interpretation is based on the assumption of a direct relationship between an increased haemodynamic load and LV enlargement—which, however, might be altered in these patients as a result of the activation of neurohormon-

Table 4. Comparison of LV conventional and TDI echocardiographic parameters in cirrhosis patients according to median MELD score. Data are presented as mean ± standard deviation.

	MELD<10.5	MELD>10.5	p
LVDV (mL)	94.68 ± 29.92	100.11 ± 30.55	0.483
LVSV (mL)	36.53 ± 9.3	37.32 ± 9.68	0.736
SV (mL)	58.16 ± 21.64	62.79 ± 22.13	0.474
CO (L/min)	4.53 ± 1.6	4.79 ± 1.85	0.690
LVEF (%)	70.37 ± 3.79	70.16 ± 4.31	0.848
LVMI (g/m^2)	126.04 ± 17.92	208.3 ± 42.526	<0.001
LAVI (mL/m^2)	21.46 ± 4.78	30.31 ± 5.52	<0.001
Doppler parameters:			
E (m/s)	0.78 ± 0.19	0.9 ± 0.24	0.095
A (m/s)	0.85 ± 0.18	0.79 ± 0.12	0.187
E/A	0.97 ± 0.38	1.17 ± 0.34	0.103
E-DT (ms)	210.16 ± 20.5	197.79 ± 36.74	0.208
IVRT (ms)	82.16 ± 8.57	83.34 ± 11.2	0.716
S (m/s)	0.11 ± 0.02	0.11 ± 0.02	0.970
E' (m/s)	0.11 ± 0.03	0.12 ± 0.04	0.965
A' (m/s)	0.12 ± 0.02	0.11 ± 0.02	0.078
E/E'	7.14 ± 1.81	8.21 ± 2.59	0.151

Abbreviations as in Tables 1 & 2.

Table 5. Comparison of left ventricular two-dimensional speckle tracking echocardiography parameters in cirrhotic patients according to median MELD score. Data are presented as mean ± standard deviation.

	MELD<10.5	MELD>10.5	p
Strain(%):			
Longitudinal	-21.7 ± 1.13	-19.44 ± 1.26	<0.001
Radial	51.69 ± 14.1	52.31 ± 15.27	0.782
Circumferential	-23.47 ± 2.43	-26.17 ± 1.93	<0.001
Systolic strain rate (1/s):			
Longitudinal	-1.19 ± 0.16	-0.93 ± 0.25	<0.001
Radial	2.05 ± 0.45	2.04 ± 0.64	0.966
Circumferential	-1.25 ± 0.22	-1.56 ± 0.3	0.001

MELD – model for end-stage liver disease.

Table 6. Echocardiographic parameters correlated with MELD score.

Correlation analysis:		R	p
Left ventricular mass index		0.942	<0.001
Ejection fraction		0.007	0.967
E-deceleration time		-0.207	0.213
Isovolumic relaxation time		0.034	0.841
S velocity		-0.064	0.701
E/E'		0.387	0.016
Left atrium volume index		0.924	<0.001
Radial strain		0.031	0.853
Circumferential strain		0.813	<0.001
Longitudinal strain		-0.555	<0.001
Regression analysis:	β	95% confidence interval	p
Left ventricular mass index	0.739	0.051–0.087	<0.001
Left atrium volume index	0.366	0.095–0.386	0.002
Longitudinal strain	0.01	-0.317–0.362	0.893
Circumferential strain	0.219	0.113–0.729	0.009

MELD – model for end-stage liver disease.

Table 7. Results of Bland–Altman analysis for intra- and inter-observer variabilities.

	Inter-observer		Intra-observer	
	Difference	95% CI	Difference	95% CI
Strain (%):				
Circumferential	-0.14	-0.41–0.13	-0.05	-0.23–0.13
Longitudinal	0.11	-0.51–0.72	-0.48	-0.91–0.05
Radial	0.09	-0.73–0.91	-0.38	-0.99–0.23

al and autocrine growth factors. Volume overload leading to the activation of neurohormones, including noradrenaline, angiotensin, and aldosterone, has been implicated in cardiac hypertrophy and fibrosis, resulting in structural remodelling through increased collagen accumulation in the interstitium.[16,17] The association of the increase in the LVMI with heart failure and cardiovascular complications, independently of the underlying pathologies, has already been demonstrated. The relationship observed between the MELD score and LVMI in our study also suggests that increased LVMI may be a sign of CCM.

In this study, we found significant abnormalities in LV diastolic function in the patients with cirrhosis, including a significant increase in the deceleration time of the E wave and isovolumic relaxation time, a decrease in the E' wave velocity with an increase in the E/E' ratio and the average mitral annulus velocity, and increased LAVI. Many patients with cirrhosis exhibit various degrees of diastolic dysfunction, which affects ventricular filling. Diastolic relaxation is impaired primarily because of the stiffening and/or hypertrophy of the LV, leading to decreased compliance and higher diastolic pressures compared to the controls. Diastolic dysfunction occurs before systolic dysfunction and may progress to systolic dysfunction.[18,19] In our study, when the cirrhosis group was divided into two subgroups according to the median MELD score of 10.5, it was observed that, among the diastolic function parameters, only the LAVI differed between the groups, being associated with the severity of the disease. LAVI is the morphological indicator of chronic LV diastolic dysfunction and it has been shown in various studies to be probably more valuable than the other parameters in evaluating the severity of the LV damage.[20,21] In our study, the relationship observed between the MELD score and LAVI suggests that the LAVI value may be used to assess the chronic LV damage in patients with cirrhosis. Diastolic dysfunction has recently been recognized as part of a condition known as cirrhotic cardiomyopathy. Some authorities contend that some degree of

diastolic dysfunction by simple echocardiography is not sufficient to differentiate true CCM patients from general cirrhotic patients.[22]

In our study, the resting LVEF was found to be higher in the cirrhosis group than in the control group. A number of animal and human studies on cirrhosis have shown that systolic function is apparently normal or even increased at rest; yet it becomes impaired after stress, exercise, or other forms of stimuli.[23] These have been considered to represent an underlying "pump dysfunction". Volume-derived measurements of LV function have important limitations in assessing myocardial contractile function, whereby a series of compensatory mechanisms, including an increase in LV end-diastolic volume and hypertrophy, can mask the underlying changes in myocardial force development.[24,25] Although myocardial dysfunction is observed in the early phases of cirrhosis, the LVEF may remain within normal limits because of the increase in the LV twist brought about by the increase in the LV preload and end-diastolic volume, and the decrease in the afterload.[26] LV hypertrophy may contribute to the detection of a normal EF despite impaired myocardial function, because of the cross-fibre shortening phenomenon.[27] For these reasons, when evaluating myocardial function using the 2D-STE method, the presence of CCM may be assessed during the subclinical stage in cirrhotic patients with preserved EF.

In general, longitudinal LV mechanics, which are predominantly governed by the subendocardial region, are the most vulnerable component of LV mechanics and are therefore most sensitive to the presence of myocardial disease. L_S and L_{SR} have been shown to be sensitive indicators of subclinical ventricular dysfunction and to correlate with myocardial fibrosis.[8] The contribution of the longitudinal contractile reserve to the global contractile reserve may be minor, because longitudinal shortening has relatively little impact on the LV ejection fraction or stroke volume, as described above.[28] Recent studies comparing the longitudinal and circumferential function have shown that the longitudinal function deterio-

rates early (i.e. before the onset of the clinical symptoms and the reduction in the global ventricular function) under pathological cardiac conditions. In contrast, the mid-myocardial and epicardial function may remain relatively unaffected during the subclinical stage, while circumferential strain and LV twist show exaggerated compensation to preserve the LV systolic performance. Furthermore, radial thickening is influenced by the complex 3-dimensional fibre rearrangement in the LV wall during systole.[29] In our study, the relationship observed between the MELD score and the C_S also supports the theory that circumferential function may influence the LVEF in patients with cirrhosis. Based on the results of the present study, LV systolic dysfunction may begin with a reduction in the longitudinal shortening during the subclinical stage, which is compensated for by an increase in the circumferential shortening in cirrhotic patients. Consequently, radial thickening may be preserved to some degree, maintaining the LVEF.

The MELD score was originally devised to evaluate the short-term outcome of patients who were to undergo surgery against the complications of cirrhosis, and it was shown to be superior to the Child–Pugh score as a predictor of survival in these patients. In our study, when the cirrhosis group was divided in two subgroups according to the MELD score, the longitudinal function in particular was observed to be reduced in the group with the higher MELD scores; this supports the results of similar studies investigating the association between the MELD score and myocardial damage.[30,31]

Limitations of the study

The present study had certain limitations. Although the efficiency of the 2D-STE method was validated in our study population, the limited number of patients may present a limitation to the validation of the efficiency of the method. Since the number of patients investigated in our study was small and the aim of the study was the evaluation of the relationship between cirrhosis and LV function, the influence of the metabolic changes observed in cirrhotic patients and the effects of the administered medications were not assessed. Since our study was designed to investigate the relationship between the presence and severity of cirrhosis and the LV damage using 2D-STE, the relationship with brain natriuretic peptide, which is the neurohormonal marker of LV dysfunction, was not evaluated. Although electrophysiological changes are

observed in cirrhotic patients as a result of the cardiac damage, since the aim of our study was to evaluate LV function, no electrocardiographic analysis was made. Since the number of patients receiving medications affecting the cardiac structure and functions was small, no analysis was made to evaluate the relation between these medications and the echocardiographic findings. Also, since our study excluded patients with alcoholic cirrhosis, our results do not refer to the whole of the cirrhotic patient group. Although a possible relationship between viral hepatitis — especially hepatitis C — and myocardial dysfunction has been mentioned, the cardiac assessment in our study did not involve the aetiology of cirrhosis.[32] This study was an observational study and did not include clinical follow up of the patients. Therefore, no evaluation was performed in terms of the relationship between the results and the patients' cardiovascular prognosis.

Conclusions

Cardiac disease is a common complication of cirrhosis that reduces survival rates, especially after surgical procedures. Many cardiovascular abnormalities occur in patients with cirrhosis and it is the role of the cardiologist to unmask these abnormalities in order to manage this group of patients appropriately. 2D-STE seems to be a useful and non-invasive method to detect cardiac dysfunction in cirrhotic patients where cardiac failure is not yet clinically evident. Therefore, besides the conventional echocardiographic methods, 2D-STE can also be used in cirrhotic patients to detect subclinical myocardial dysfunction in the early stages. A prospective study with a larger patient group is needed to confirm our findings and to evaluate the diagnostic value of 2D-STE in predicting cardiovascular events and CCM in cirrhotic patients.

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