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Assessment of Left Ventricular Diastolic Dysfunction in Cases with Liver Cirrhosis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Cirrhosis is a long-term inflammatory process of hepatic tissue condition that mainly affects people aged 50 to 60. This study aims to assess Left ventricular diastolic dysfunction (LVDD) in cases with cirrhotic liver by conventional, tissue Doppler and two-dimensional speckle tracking echocardiography to clarify the correlation between the severity of cirrhotic liver and LVDD.
Methods: A prospective case-control research involved 100 adult cases with confirmed HCV and HBV. Cases were divided into 4 equal group: Group A: Child A cases, group B: Child B cases, group C: Child C cases and group D (Controls): healthy non-hepatic subjects of the same age and sex who have normal blood pressure, nonsmoking participants with no further concomitant problems.
Results: Number of cases with LVDD had a statistical noticeable increase in Child A, B, and C ($p = 0.004$, <0.001, and <0.001 respectively. LAVi had a statistical noticeable increase in Child C / B ($p = 0.013$ and $p = 0.014$).

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Conclusion: Left atrial volume index (LAVi) had a statistical noticeable increase in Child C / B in comparison to the controls but E m, E l were statistical noticeable lower in Child C / B. /E had a statistical noticeable increase in Child C group, LVSRe had a statistical noticeable decrease in Child C group but it was insignificantly different across Child A / B/ C and controls and across Child B / C and controls.

Keywords: Left ventricular diastolic dysfunction; liver; cirrhosis; tissue doppler; 2D speckle tracking echocardiography.

1. INTRODUCTION

Cirrhosis is a chronic liver condition that mainly affects people aged 50 to 60 [1,2].

This important health issue is one of the leading causes of death in the globe and is linked to a wide spectrum of cardiovascular problems [3,4].

Cases with cirrhosis often have circulatory system dysfunction. Hyperdynamic circulation in individuals with cirrhosis of the liver results in structural and functional cardiac changes [5,6].

These modifications result in systolic and left ventricular diastolic dysfunctions (LVDD) and cardiomyopathy [7,8] due to myocardial remodelling and left ventricular enlargement.

Cirrhotic cardiomyopathy is characterised by reduced contractile reactivity to stress, LVDD, and electrophysiological abnormalities in the absence of overt heart illness [9,10].

Although this form of cirrhotic liver complication has been recorded since the 1960s, it has only lately been identified not just as a symptom of alcoholic cardiotoxicity, but also as a condition that may arise in cirrhosis of any cause [11].

Among cirrhotic cases, the most prevalent cardiac abnormality is left ventricular LVDD (LVDD) due to the development of myocardial fibrosis, hypertrophy, and subendothelial edoema [5, 6].

LVDD develops when the passive elasticity of the myocardium is diminished as a result of an increase in myocardial mass and modifications to the extracellular collagen [12].

2. METERIALS AND METHODS

This prospective case control study was conducted on 100 adults' cases with confirmed HCV and HBV referred for evaluation from Internal Medicine and Tropical Medicine Departments to Cardiology Department-Tanta University Hospital from March 2020 to February 2021.

Inclusion criteria were only cases with cirrhotic liver, which was identified based on clinical observation, laboratory and imaging tests, and severity of cirrhosis was determined using Child classification A/B/C.

Children (<18 years old), patients with chronic heart disease, such as valve pathology, coronary heart disease, arrhythmias, such as atrial fibrillation, and rare causes of liver insufficiency, such as toxic liver disease, septicemia were excluded.

Cases were divided into 4 equal group: Group A: Child A cases, group B: Child B cases, group C: Child C cases and group D (Controls): healthy non-hepatic subjects of the same age and sex group who are normotensive and non-smoker subjects with no other comorbid conditions.

All cases were subjected to full history taking, clinical examination, abdominal examination and ultrasonography, routine laboratory investigations (CBC, serum bilirubin, serum albumin and complete Urine analysis) and echocardiography (Conventional, tissue doppler and two-dimensional speckle tracking echocardiography).

2.1 Child Scoring

It classified cases into three groups: A - healthy liver function, B - moderately impaired hepatic function, and C - severe hepatic dysfunction.

Their initial scoring method categorizes individuals based on five clinical and laboratory criteria: serum bilirubin, serum albumin, ascites, neurological dysfunction, and clinical nutrition status [13]. Later, Pugh et al. updated the scoring method by replacing PT for clinical nutrition status. In addition, they implemented varying points for each criterion dependent on severity [14].

The seriousness of cirrhosis: Child A: between 5 and 6 points. 7 to 9 Child B points. Child C: ten to fifteen points.

Using standard echocardiography, LA was evaluated. To achieve a perpendicular measurement to the ventricle's long axis, the LV diameter and wall thickness were measured in the left parasternal long axis view at the level of the mitral valve (MV) tips. Ejection fraction (EF) and fractional shortening (FS) were computed using 2D guided M mode echocardiographic tracings in the parasternal long axis view using the Teichholz formula. Pulsed pulse Doppler was used to assess trans-mitral flow at the tips of the mitral leaflets in the apical four-chamber view. Periodic oscillation Doppler was used to record the tricuspid regurge systolic jet velocity in a four-chamber apical view. It was calculated the peak velocity of early (E) and late (A) atrial diastolic filling of the Doppler MV flow, the E/A ratio, and the E wave (DT).

2.2 TDI

In the apical four chamber view, pulsed wave TDI was utilised over the septal and lateral mitral annulus to get the following characteristics: Maximum diastolic velocity during the early filling phase at the septal and lateral mitral annulus (e') and average E/e' velocities.

2.3 Two-dimensional Speckle Tracking

Speckle tracking is an offline technique that is used to previously acquired 2D images. Strain and strain rate were measured using software on standard 2D grayscale images of the left ventricle (LV) from standard apical four-chamber and two-chamber views for longitudinal strain (LS) and standard parasternal short axis at the papillary muscle level for circumferential strain (CS) and radial strain (RS) (RS).

The longitudinal strain/strain rate (LS/LSR) was measured at basal, mid, and apical inferior septal and basal, mid, and apical antero-lateral wall segments from an apical four-chamber viewpoint. Basal, mid, and apical inferior wall and basal, mid, and apical anterior wall segments were examined for LS/LSR from an apical two-chamber perspective. The peak systolic (PS) global longitudinal strain/strain rate (GLS/GLSR) was obtained by computing the mean longitudinal strain/strain rate (LS/LSR) of the 12 LV segments of the 4-CH and 2-CH. The circumferential strain (CS) was measured along the midsegments of the antero-septal, anterior, antero-lateral, and infero-septal wall segments at the level of the papillary muscles. Peak systolic mid circumferential strain (MCS) was estimated by averaging the six LV segments in short axis view.

2.4 Statistical Analysis

Version 25 of the SPSS (Statistical Package for the Social Sciences) was used for statistical analysis (IBM Inc., Chicago, IL, USA). Using the Shapiro-Wilks normality test and histograms, the distribution of quantitative data was examined in order to identify the appropriate kind of statistical testing: parametric or nonparametric. The mean and standard deviation (SD) of parametric variables were used to compare the three groups using the F test, while the Tukey test was used to compare each pair of groups. Using the paired T test, two variables within the same group were compared. Non-parametric variables were reported as median and interquartile range (IQR) and examined using the Kruskal-Wallis test; the Mann–Whitney (U) test was then used to compare each pair of groups. Using the Wilcoxon test, two variables within the same group were compared. Categorical variables were reported in terms of frequency and percentage, and the Chi-square test was used to examine their statistical significance. A two-tailed P value of less than or equal to 0.05 was considered statistically significant.

3. RESULTS

Baseline characteristics (age, gender, and origin of cirrhosis) and systolic function parameters (LVEF, LS, CS, RS, and LVSRs) were insignificantly different among the studied groups Table 1.

Regarding the conventional echo parameters of diastolic function, E, E/A and DTE were insignificantly different among the studied groups. LAVi had a statistical noticeable increase in Child C / B (p =0.013 and p =0.014) but it was insignificantly different across Child A group / B/ C and controls and across Child B / C . E′m had a statistical noticeable decrease in Child C / B (p =0.005), but it was insignificantly different across Child A group / B/ C and controls and across Child B / C . E′l had a statistical noticeable decrease in Child C group (p =0.005), but it was insignificantly different across Child A group / B/ C and controls and across Child B / C and controls. E/E had a statistical noticeable

increase in Child C group (p =0.046), LVSRe had a statistical noticeable decrease in Child C group (p =0.026) but it was insignificantly different across Child A group / B/ C and controls and across Child B / C and controls.

Number of cases with LVDD had a statistical noticeable increase in Child A/ B/ C (p =0.004, <0.001, and <0.001 respectively. There was no statistical noticeable difference in LVDD (absence and grades) across Child A/B/C Table 3.

Table 1. Baseline characteristics and systolic function among the studied groups

		Child A	Child B	Child C	Control	p value
Age		38.64 ± 11.44	42.8 ± 11.74	36.24 ± 11.49	38.88 ± 13	0.281
Gender	**Male**	12 (48%)	16 (64%)	14 (56%)	13 (52%)	0.702
	Female	13 (52%)	9 (36%)	11 (44%)	12 (48%)	
Origin of cirrhosis	**HCB**	5 (20%)	8 (32%)	6 (24%)	-	0.611
	HCV	20 (80%)	17 (68%)	19 (76%)	-	
Systolic function						
LVEF (%)		67.7 ± 5.6	68.1 ± 5.8	66.0 ± 7.1	68.8 ± 6.7	0.449
LS (%)		-20.98 ± 2.74	-20.54 ± 3.72	-21.23 ± 3.49	-20.68 ± 2.7	0.870
CS (%)		-20.12 ± 4.73	-19.99 ± 5.81	-21.69 ± 4.93	-18.53 ± 3.71	0.159
RS (%)		56 ± 26	55 ± 27	57 ± 27	49 ± 18	0.641
LVSRs (cm/s)		-0.95 ± 0.24	-1.04 ± 0.22	-0.96 ± 0.21	-0.97 ± 0.27	0.478

HBV: Hepatitis B, HCV: Hepatitis C,LVEF: left ventricular ejection fraction, LS: left ventricular longitudinal strain, CS: circumferential strain, RS = radial strain, LVSRs: left ventricular longitudinal systolic strain rate

Table 2. Conventional echo and tissue doppler and speckle tracking echo parameters of diastolic function among the studied groups

	Child A	Child B	Child C	Control	p value
E (cm)	73.08 ± 22.47	73.44 ± 20.87	72.64 ± 23.18	77 ± 16.91	0.878
E/A	1.14 ± 0.53	1.15 ± 0.48	1.13 ± 0.49	1.21 ± 0.34	0.926
DTE (ms)	210.28 ± 57.02	213.36 ± 65.36	212.2 ± 71.63	195.08 ± 45.38	0.687
LAVi (mL/m^2)	39.32 ± 7.49	42.56 ± 12.62	42.68 ± 14.42	32.96 ± 7.96	0.007* P1 =0.727 P2 =0.704 P3 =0.181 P4 =1.000 P5=0.014* P6=0.013*
Tissue doppler and speckle tracking echo					
E´m (cm/s)	8.06 ± 2	7.33 ± 2.31	7.37 ± 1.82	9.33 ± 1.86	0.002* P1 =0.574 P2 =0.614 P3 =0.125 P4 =1.000 P5=0.005* P6=0.005*
E´l (cm/s)	10.99 ± 2.69	10.32 ± 2.85	9.56 ± 2.71	12.14 ± 2.39	0.008* P1 =0.813 P2 =0.236 P3 =0.429 P4 =0.743 P5 =0.083 P6 =0.005*
E/E′	7.54 ± 1.62	8.36 ± 2.15	9.06 ± 2.59	7.52 ± 1.71	0.026* P1 =0.497 P2 =0.051 P3 =1.00 P4 =0.631 P5 =0.472 P6=0.046*
LVSRe (cm/s)	1.22 ± 0.44	1.22 ± 0.41	1.03 ± 0.36	1.34 ± 0.31	0.043* P1 =1.000 P2 =0.280

Child A	Child B	Child C	Control	p value
				P3 =0.712 P4 =0.298 P5 =0.689 P6=0.026*

*E: Early diastolic filling wave, A: Late diastolic filling wave, DTE: E-wave deceleration time, LAVi = Left atrial volume indexed, E'm: medial mitral early diastolic tissue velocity, E'l: lateral mitral early diastolic tissue velocity, E: Early diastolic filling wave, E': mean mitral early diastolic velocity, LVSRe: Left ventricle early diastolic strain rate, *: statistically significant as P value ≤ 0.05. P1: significance between child A and child B, P2: significance between child A and child C, P3: significance between child A and controls, P4: significance between child B and child C, P5: significance between child B and controls, P6: significance between child C and controls*

Table 3. Diastolic dysfunction among the studied groups

		Child A	Child B	Child C	Controls	p value
Diastolic dysfunction	**No diastolic dysfunction**	17 (68%)	12 (48%)	7 (28%)	25 (100%)	P1:0.004* P2:<0.001*
	Presence of diastolic dysfunction	8 (32%)	13 (52%)	18 (72%)	0	P3:<0.001*
Diastolic dysfunction among the liver cirrhosis groups						
No diastolic dysfunction		17(68%)	12(48%)	7(28%)	0.094	
Grade I Diastolic dysfunction		7(28%)	7(28%)	9(36%)		
Grade II Diastolic dysfunction		1(4%)	5(20%)	7 (28%)		
Grade III Diastolic dysfunction		0	1(4%)	2(8%)		

**: statistically significant as P value ≤ 0.05. P1: Significance between child A and controls, P2: Significance between child B and controls, P3: Significance between child C and controls*

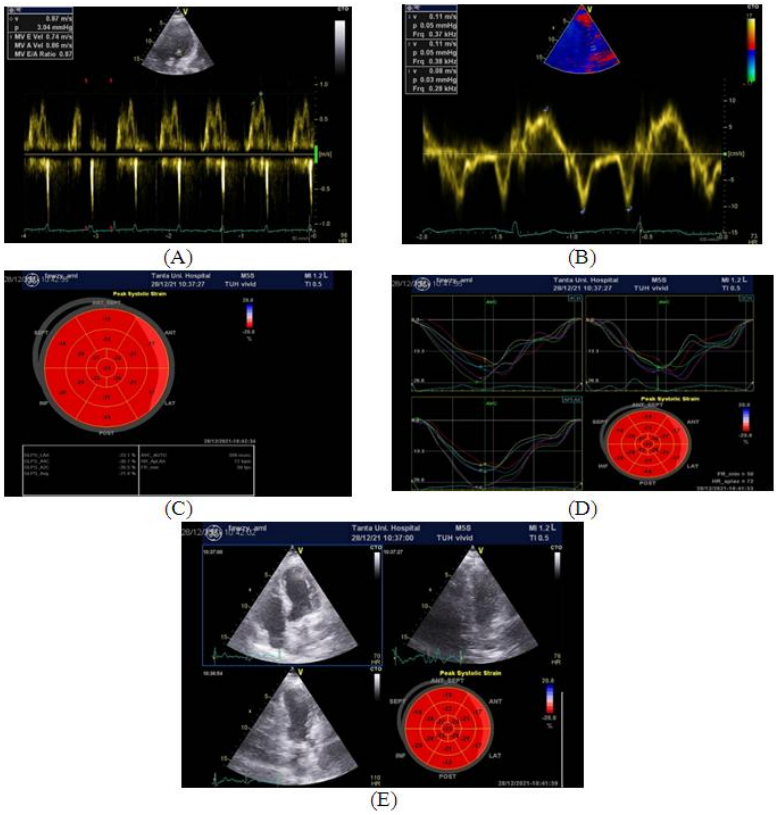

Fig. 1. (A) Conventional echocardiography (B) Tissue doppler (C), (D), (E) Speckle tracking echocardiography assessment of LV systolic function, Bull's eye view of global longitudinal strain (LS), as mean of four, two and three chamber views 6.7, LAVI 30 ml/m^2)

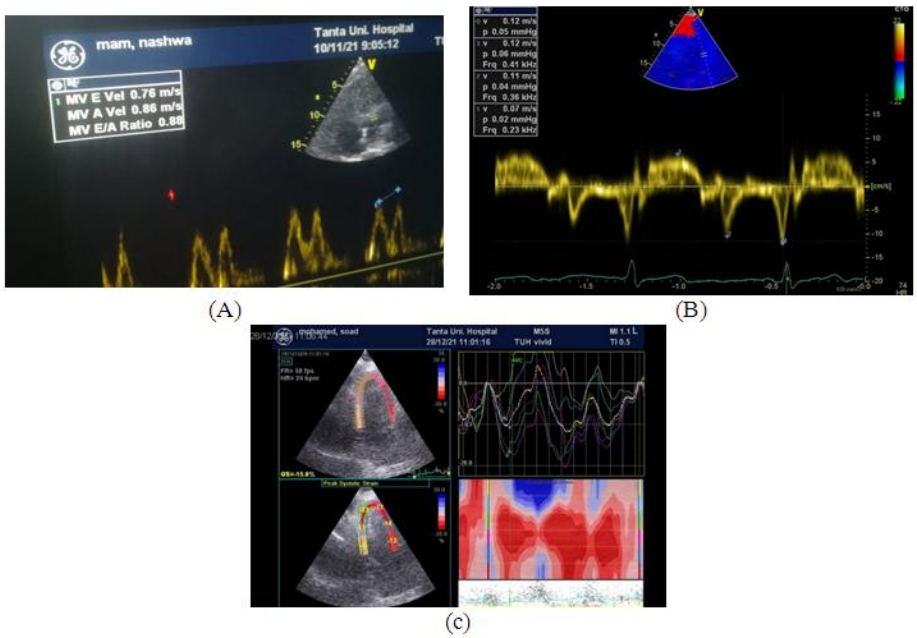

Fig. 2. (A) Conventional echocardiography (B) Tissue doppler (E 0.76 m/s, A 0.86 m/s, E/A ratio 0.88, E/ e' 6.9, LAVI 31 ml/m2, (C) Speckle tracking echocardiography assessment of LV systolic function. Global longitudinal strain (LS), as mean of two (GS= -15.6%)

40- years old female with past history of HCV and not diabetic or hypertensive (Child-Paugh A). Conventional echocardiography: Grade I diastolic dysfunction. STE finding: Normal systolic function Fig. 1.

54-years old female with past history of HBV and not diabetic or hypertensive (Child-Paugh B). Conventional and tissue doppler echocardiography: Grade I diastolic dysfunction. STE finding: Normal systolic function Fig. 2.

4. DISCUSSION

Cirrhotic liver is a major health problem that is associated with a wide range of cardiovascular abnormalities [15].

In our study, systolic function parameters as LVEF, LS, CS, RS, and LVSRs were insignificantly different among the studied groups.

Similarly, Cesari et al. [16] enrolled one hundred and thirteen cirrhotic cases underwent standard Doppler echocardiography and were in comparison to healthy individuals. Systolic/diastolic function, and the main hemodynamic parameters were assessed according to current guidelines. They found that all the systolic parameters as FS, EF, MWFS, septal S, septal strain, septal SRs assessed were similar between cases and controls. In contrast to systolic dysfunction, LVDD appears to be more prevalent, and some degree of LVDD is present in virtually every patient with cirrhosis [17].

We found in in the current study that the conventional echo parameters of diastolic function, E, E/A and DTE were insignificantly different among the studied groups. The current results agreed with Sampaio et al. [18], as they LAVi had a statistical noticeable increase in cirrhotic cases compared to controls (P<0.001).

In the present study, as regards tissue doppler and speckle tracking echo parameters of diastolic function; E′m had a statistical noticeable decrease in Child C / B (p =0.005), but it was insignificantly different across Child A / B/ C and controls and across Child B / C. E′l had a statistical noticeable decrease in Child C (p =0.005), but it was insignificantly different across Child A / B/ C and controls and across Child B / C and controls.

E/E had a statistical noticeable increase in Child C (p =0.046), LVSRe had a statistical noticeable decrease in Child C (p =0.026) but it was insignificantly different across Child A / B/ C and controls and across Child B / C and controls.

Further, Merli et al. [19] observed that E/E lateral ratio was higher statistical noticeable in cirrhotic cases compared to normal cases, yet insignificant difference was reported in E/E lateral ratio among Child A/B/C cases. This contradiction across both studies can be justified by larger sample size in their study compared to our study.

In the current study, the incidence of LVDD increased significantly in Child A, B, and C compared to controls ($p = 0.004$, < 0.001, and < 0.001 correspondingly). Moreover, there were no statistically significant differences in LVDD (absence and grades) between Child A, B, and C.

The present results correspond with Stundiene et al. [20] did a thorough literature review on the occurrence of LVDD in instances of cirrhosis of the liver. They were interested in the likelihood of a correlation between the severity of cirrhosis [as determined by Child classes and (MELD) scores] and LVDD [as defined by (ASE) guidelines (2009, 2016)], as well as the relative risk of dysfunction in cirrhotic cases. LVDD was identified in 44.6% of Child A cases, 62% of Child B cases, and 63.3% of Child C cases ($P = 0.028$). The proportion of patients with higher LVDD grades rises as cirrhosis severity increases ($P < 0.001$).

In cases with cirrhosis and graded according to Child-Paugh score, left atrial volume index (LAVi) had a statistical noticeable increase in Child C / B in comparison to the controls but E m, E l were significantly lower in Child C / B . E/E had a statistical noticeable increase in Child C, LVSRe had a statistical noticeable decrease in Child C but it was insignificantly different across Child A / B/ C and controls and across Child B / C and controls.

Limitations: The comparatively limited sample size was a statistical noticeable weakness of the study. The LV filling pressure was not invasively evaluated.

5. CONCLUSIONS

In cases with cirrhosis and graded according to Child-Paugh score, left atrial volume index (LAVi) had a statistical noticeable increase in Child C / B in comparison to the controls but E m, E l were statistical noticeable lower in Child C / B . E/E had a statistical noticeable increase in Child C, LVSRe had a statistical noticeable decrease in Child C but it was insignificantly different across Child A / B/ C and controls and across Child B / C and controls.

CONSENT AND ETHICAL APPROVAL

All participants provided their written, informed permission. The Ethics Committee of the Faculty of Medicine of Tanta University authorized the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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