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Original research article

Cardiac dysfunction in chronic liver disease: A tissue Doppler imaging study

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Abstract

Aim: The present aim of the study is to study cardiac dysfunction in chronic liver disease using 2D Echo cardiography and tissue Doppler Imaging.

Methodology: This was a hospital-based cross-sectional descriptive study conducted over 16 months (between March 2021 and June 2022) among patients seeking medical attention at Narayana Medical College & Hospital, Nellore.

Results: A total of 100 cirrhosis patients were recruited. The average age was 46.6±11.13 years (Range 23 to 80 years). 80% patients were males. Most of the male patients (30 patients) were in 41 to 50 years age group but most female patients (7 patients) were less than 40 years in age group. Alcohol was the most common etiology (69%). Abdominal distention due to ascites (59 patients) was the most common clinical presentation and eleven among them had spontaneous bacterial peritonitis. 53 patients were found to have some echocardiographic abnormalities at the time of assessment. All 53 patients had diastolic dysfunction. However, only 18 patients had an ejection fraction less than 55%, indicating significant LV dysfunction. 8% of patients had RV Systolic dysfunction, and 8% of patients had pulmonary arterial hypertension. Based on the complications developed by the patients, 53.19% of hepatic encephalopathy, 72.73% of SBP, 50% of cases with GI Bleeding and HRS had Echo changes. Likewise, 21.15% of cases with esophageal varices and 10% of cases with PHG & GAVE had Echo changes respectively.

Conclusion: The study concluded that to assess the cardiac dysfunction in chronic liver disease patients, it is preferable to do 2D Echo-Tissue Doppler Imaging rather than a conventional Colour Doppler study.

Keywords: 2D Echo-Tissue Doppler, Liver diseases, LV dysfunction, Ascites

Introduction

Chronic liver disease is a long term deterioration of liver functions, including bile excretion, detoxification of toxic metabolic products and production of albumin, clotting factors and other proteins. The final stage of chronic liver disease, cirrhosis, is marked by loss of hepatic architecture by extracellular matrix deposition, vascular reconfiguration, neo-angiogenesis, and nodule formation. Fibrosis and cirrhosis are primarily caused by the activation of stellate cells and fibroblasts and parenchymal regeneration is carried out by hepatic stem cells.

Cardiovascular (CV) dysfunction is an underappreciated side effect of CLD, especially with the worsening severity. It plays a significant role in decreased exercise tolerance and an inadequate response to various stresses, such as infections, which ultimately increases mortality in these patients.

Patients with cirrhosis are said to have cardiomyopathy, which is described as "chronic heart dysfunction characterized by altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac illness" [1, 3].

Systolic dysfunction, which often only appears during times of stress, usually follows diastolic failure in the majority of cirrhotic patients [4]. Tissue Doppler has emerged as the most sensitive technique for determining left ventricular diastolic function and filling dynamics due to its viability and relative preload independence when recording the early diastolic mitral annular velocity (E') in conjunction with the mitral inflow velocity (E).

While early diastolic trans-mitral velocity (E) increases progressively as LV filling pressure increases, the mitral annular E' velocity remains decreased at all stages of diastolic dysfunction [5].

Hence, the purpose of this cross-sectional tissue Doppler study is to study cardiac dysfunction in Chronic liver disease.

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Aim of the study

The present aim of the study is to study cardiac dysfunction in chronic liver disease using 2D Echo cardiography and tissue Doppler Imaging.

Objectives

- To find out the prevalence of cardiac changes in patients with chronic liver disease using echocardiography.
- To evaluate right and left ventricular systolic and diastolic functions in Chronic Liver Disease, using conventional echocardiography and tissue Doppler imaging.
- To correlate the clinical profile and echocardiographic changes in patients with chronic liver disease.

Materials and Methods

This was a hospital-based cross-sectional descriptive study conducted over 16 months (between March 2021 and June 2022) among patients seeking medical attention at Narayana medical college & hospital, Nellore. A total of 100 patients satisfying the inclusion and exclusion criteria were recruited after providing written informed consent. Diagnosis of cirrhosis of liver was made based on clinical history and examination, biochemical and serological evaluation, and ultra-sonographic imaging. Recruited persons were subjected to echocardiographic study to assess the cardiac status.

Inclusion criteria

- Age more than 18 years
- Cirrhosis of any cause

Exclusion criteria

- Patients who refused to participate in the study
- Patients with primary cardiac or pulmonary disease
- Diagnosed hypertensive patients
- Anaemia (Hb less than 7 gm %)
- Diabetes mellitus
- Pregnant & lactating mothers
- Acute or chronic kidney disease, which is not due to CLD
- Patients with hepatocellular carcinoma (extra-hepatic malignancy) or portal vein thrombosis.

Results

A total of 100 cirrhosis patients were recruited. The average age was 46.6±11.13 years (Range 23 to 80 years). 80% patients were males. Most of the male patients (30 patients) were in 41 to 50 years age group but most female patients (7 patients) were less than 40 years in age group. Alcohol was the most common etiology (69%). Abdominal distention due to ascites (59 patients) was the most common clinical presentation and eleven among them had spontaneous bacterial peritonitis. It was followed by altered sensorium due to hepatic encephalopathy (47 patients). Esophageal varices (52 pts) was the most common complication noted among these patients but only two presented with upper GI bleed. 37% of patients had no complications in the present study. 8% of patients were in Class-A, 35% of patients fell into Class-B, and 57% of patients in Class-C respectively. The mean CTPS score was 9.59 (±2.14), and the mean MELD score was 17.3 (±7.24). Table-1 gives the demographic features of the study subjects. Table-2 gives the various laboratory and echocardiographic findings of the patients.

Table 1: Baseline demographic features of patients

Age	
<40 years	29
41-50 years	36
51-60 years	24
>60 years	11
Gender	
Male	80
Female	20
Etiology	
Ethanol	69
HBV	12
HCV	6
Others	13
Clinical features	
Ascites	59
Splenomegaly	42
Jaundice	10

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Altered sensorium	47
Complications	
Encephalopathy	47
SBP	11
G I Bleed	2
HRS	2
Esophageal varices	52
PHG & GAVE	30
Nil	37
Child Pugh Class	
Class A	8
Class B	35
Class C	57

Table 2: Laboratory and echocardiographic findings

Variable(s)	Minimum	Maximum	Mean	Std. Deviation
Hb (g %)	7.2	15.3	9.9	1.7
Platelets (cells/µL)	20000	503000	119880	67832
WBC (cells/µL)	1300	40200	8418	6821
Neut (%)	22	91	67.4	12.62
Lymph (%)	1	44	20.4	9.78
PT (s)	12.8	62.3	24.3	8.52
INR	0.92	13.4	2.03	1.39
Urea (mg/dl)	12	144	35.44	26.83
Creatinine (mg/dl)	0.4	4.97	1.18	0.75
Na (meq/dl)	119	152	136.66	5.3
K (meq/dl)	2.2	5.3	4.66	4.1
Cl (meq/dl)	86	103	97	3.69
Total Bilirubin (mg/dl)	0.38	26	4.9	6.02
Direct Bilirubin (mg/dl)	0.16	25.8	3.36	5.08
SGOT (IU)	13	401	82.93	61.37
SGPT (IU)	12	356	40.62	40.6
Alkaline Phosphatase (IU)	126	1032	334.55	158.98
Total Protein (gm/dl)	2.1	6.49	3.15	0.59
Albumin (gm/dl)	2.1	6.49	3.15	0.59
Ejection fraction (%)	48	62	56.4	2.9
TAPSE (cms)	1.1	3	2.37	0.39
E (m/s)	35	87	61.03	11.03
A (m/s)	20	93	59.45	17.3
E/A	0.5	2.33	1.12	0.39
E’ (m/s)	5	15	7.54	1.82
A’ (m/s)	4	12	6.98	1.38
E/E’	4.14	12.5	8.47	1.99
Lateral Wall E' (cm/s)	6	15	10.08	2.43
MELD	7	45	17.3	7.24
CTPS	5	14	9.59	2.14

53 patients were found to have some echocardiographic abnormalities at the time of assessment. All 53 patients had diastolic dysfunction. However only 18 patients had an ejection fraction less than 55%, indicating significant LV dysfunction. 8% of patients had RV Systolic dysfunction, and 8% of patients had pulmonary arterial hypertension. More patients were found to have abnormalities using tissue doppler studies than with colour Doppler studies (53% vs 37%). (Table 3).

Table 3: Echocardiographic findings

2D echo Changes	
Yes	53
No	47
2D echo findings	
LV systolic dysfunction (EF<55%)	18
LV diastolic dysfunction (E/A < 1, E/E’ > 8, Lat. E’ < 10 cm/s)	53
RVSD (TAPSE < 1.5 cm)	8
PPAH	8
E/A < 1	37

Table 4: Conventional vs Tissue Doppler findings

Color Doppler	**Tissue Doppler**

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E/A (< 1)	E/E' (> 8)	Lateral wall E' (<10 cm/s)
37	53	53

Among the patients with echocardiographic abnormalities, 34% were below 40 years of age, 32.1% were between 41 to 50 years, 18.9% between 51 to 60 years, and 15.1% of patients were more than 60 years age. There was no association between the 2D Echo changes and age of the patient (P = 0.222). 79.2% of patients with echocardiographic abnormalities were males. There was no association between gender of patient and echocardiographic changes (0.841). No association was found between the etiology of liver disease and the presence of echocardiographic changes.

50% of Class A patients had Echo changes, 57.1% of Class B patients had Echo changes and 50.9% of Class C patients had Echo changes respectively. There was no association between the 2D Echo changes and severity of liver decompensation according to CTPS classification (P = 0.830). (Table 5) 53.19% of patients with hepatic encephalopathy, 50% of cases with Jaundice, 50% of cases with GI Bleeding and 49.15% of cases with ascites had 2D Echo changes. Based on the complications developed by the patients, 53.19% of hepatic encephalopathy, 72.73% of SBP, 50% of cases with GI Bleeding and HRS had Echo changes. Likewise 21.15% of cases with esophageal varices and 10% of cases with PHG & GAVE had Echo changes respectively. 46.65% of patients without any complications due to cirrhosis also had evidence of cardiac dysfunction by echocardiographic evaluation. (Figure 1)

Table 5: Association between 2D Echo changes and severity of cirrhosis

			2D Echo Changes		Total
			No	Yes	
CTPS Grade	Class-A	Count	4	4	8
		% within CTPS_Grade	50.0%	50.0%	100.0%
		% within 2D Echo Changes	8.5%	7.5%	8.0%
	Class-B	Count	15	20	35
		% within CTPS_Grade	42.9%	57.1%	100.0%
		% within 2D Echo Changes	31.9%	37.7%	35.0%
	Class-C	Count	28	29	57
		% within CTPS_Grade	49.1%	50.9%	100.0%
		% within 2D Echo Changes	59.6%	54.7%	57.0%
Total		Count	47	53	100
		% within CTPS_Grade	47.0%	53.0%	100.0%
		% within 2D Echo Changes	100.0%	100.0%	100.0%
Chi-square value = 0.373, P-value = 0.830					

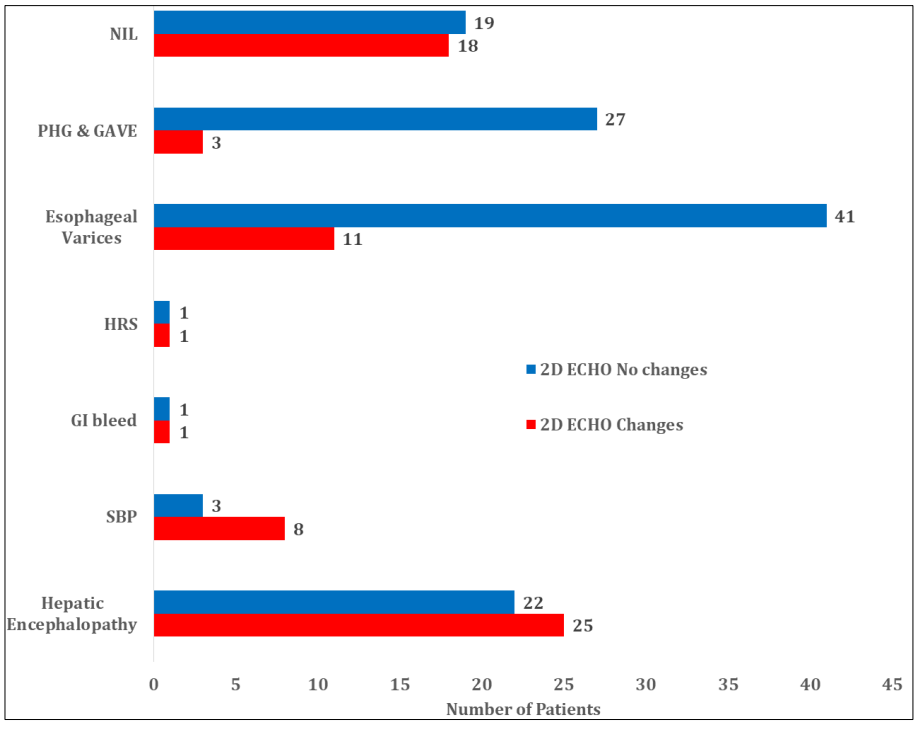

Fig 1: Echocardiographic changes among cirrhotic patients with complications

Discussion

It is long known that there exists a hyper-dynamic circulation in cirrhotic patients due to peripheral

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vasodilatation and increased cardiac output. It was even thought that cirrhotic patients were protected from heart failure unless affected by alcoholic cardiomyopathy. Subsequently it has been recognized that progressive splanchnic vasodilatation and inability of heart to maintain cardiac output are the reason for developing refractory ascites and hepatorenal syndrome [6].

Cardiac dysfunction characterized by impaired cardiac contractility to stress and abnormal diastolic function with electrophysiological abnormalities in cirrhotic patients with no known cardiac disease is known as cirrhotic cardiomyopathy. The diagnostic criteria proposed is as follows (a) systolic dysfunction: blunted increase in cardiac output on exercise, volume challenge or pharmacological stimuli or resting ejection fraction <55%, (b) diastolic dysfunction: the ratio of early to late (atrial) phases of ventricular filling or E/A ratio <1.0 (age-corrected), prolonged deceleration time (>200 ms), or prolonged isovolumetric relaxation time (>80 ms), (c) supportive criteria: electrophysiological abnormalities, abnormal chronotropic response, electromechanical uncoupling/dyssynchrony, prolonged QTc interval, enlarged left atrium, increased myocardial mass, increased brain natriuretic peptide (BNP) and pro-BNP, or increased troponin I [7]. Majority of CTPS class B & C patients manifest some evidence of cardiac dysfunction [8]. Diastolic dysfunction is present in most patients as demonstrated by cardiac MRI or echocardiography.

This study was done at a tertiary care hospital in rural Andhra Pradesh. A total of 100 patients were studied. Like in many other studies, the majority of patients with liver disease were in the productive age group of 40 to 50 years and males were affected more than females. This is consistent with the findings in studies from Manipal and Denmark where most patients were in 50 year age group and males predominated [9, 10]. This demographic pattern probably reflects the predominance of alcohol as the predominant etiology of liver disease in our country and the skewed prevalence of alcohol consumption among the males. Similar alcohol predominance as etiology of liver disease was found in other Indian and Iceland studies [9, 11]. Alcohol etiology was also associated with worse prognosis. Ascites was the most common clinical presentation as expected among cirrhotic patients. Esophageal varices that develop due to portal hypertension and opening up of porto-systemic collaterals was the next most common complication noted. A study from India reported 69% prevalence of esophageal varices [9]. Majority of patients had more advanced liver disease (CTP Class B and C). This is due to the selection bias inherent to tertiary care hospital. 53% of the study participants had some cardiac dysfunction as assessed by echocardiography. Diastolic dysfunction develops early and is more prevalent. The generalized vasodilation and reduced peripheral vascular resistance makes assessment of systolic dysfunction difficult. Hence a higher cutoff of ejection fraction less than 55% is taken to diagnose systolic dysfunction. Similar cutoffs are also followed in other conditions associated with peripheral vasodilation like aortic regurgitation and mitral incompetence. LV systolic dysfunction was found in 18% of the patients in our study. Punekar *et al* reported systolic dysfunction in 6% and diastolic dysfunction in 32% of cirrhotic patients. Apoorva Nirmal *et al* found systolic dysfunction in 6% and diastolic dysfunction in 28% of their patient group. Evaluation of cardiac function by echocardiogram using flow parameters and anatomic dimensions may not be adequate to detect early dysfunction. Use of more advanced techniques like tissue Doppler studies and speckle tracking techniques can detect cardiac dysfunction in a greater number of patients. This was seen in our study also where 37% of patients had abnormalities by flow parameters and 53% by tissue Doppler studies. Presence of ascites, pleural effusion and obesity can make the task of obtaining good quality images difficult in cirrhotic patients. Tissue Doppler echocardiography is also relatively easier to perform than speckle tracking techniques as it can be done without getting a very high quality imaging. Age and gender dependent changes in echocardiographic findings are common. But there was no such association found in our study. Alcohol by itself can affect heart by direct toxicity and thiamine deficiency and can be a confounding factor for the cardiac findings. In our study, there was no association between any of the identified etiologies. We believe that majority of patients in the idiopathic category were MAFLD related liver disease and cardiac involvement is common and the leading cause of death among these patients. Also poor nutrition is very prevalent among liver cirrhosis patients and can affect cardiac function. These factors can explain the lack of association of any particular etiologic agent with cardiac dysfunction in liver cirrhosis patients. It appears that physiologic changes induced by cirrhotic changes in liver happens equally irrespective of underlying cause. Apoorva Nirmal *et al* also reported no correlation between age, gender or alcohol etiology with cardiac findings in cirrhotic patients by logistics regression analysis. We did not find any difference in the prevalence of diastolic dysfunction based on severity of cirrhosis. This could be due to the fact that diastolic dysfunction develops early in the course of cirrhosis. It could also be due the fact that alcohol and MAFLD, the two leading causes of cirrhosis are also associated with development of diastolic dysfunction. Most of the studies have reported higher prevalence of diastolic dysfunction with advanced stages of liver cirrhosis. Punekar *et al* reported higher prevalence of cardiac dysfunction with worsening liver function. But there is an under representation of CTP class A patients in our study and CTP class C in Punekar's study [12]. Karagianakkis DS *et al* reported findings similar to our study [13]. However patients with spontaneous bacterial peritonitis had higher prevalence of echocardiographic abnormalities than those with other complications. SBP is more likely to develop in those with difficult to control ascites indicating a greater degree of cardiac functional impairment. Right ventricular systolic

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dysfunction as assessed by TAPSE was found only in 8% of patients. Other studies have also found that TAPSE remains within normal limits in majority of cirrhosis patients [4, 15].
The limitations of the current study are: a) small sample size. CTP Class A patients are under-represented. Some of the complications like HRS occurred in very few patients for any meaningful interpretation. b) It was a cross sectional study. Follow up study of this cohort might have given insight into significance of echocardiographic findings with respect to survival and development of complications.

Conclusion

It is important to evaluate the cardiovascular function in every patient with cirrhosis, especially if the patient is to undergo any intervention that may affect hemodynamics (TIPS and transplant). In order to assess the cardiac dysfunction in chronic liver disease patients, it is preferable to do 2D Echo-Tissue Doppler Imaging rather than a conventional Colour Doppler study. Mitigation of development, early detection and treatment of cirrhotic cardiomyopathy in chronic liver disease patients can prevent and minimize hospitalization in chronic liver disease-related complications, post-liver transplantation complications, and reduce the risk of morbidity and mortality.

Conflict of Interest: None

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