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Cardiology

STUDY OF MYOCARDIAL DYSFUNCTION IN PATIENTS OF CIRRHOSIS OF LIVER

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ABSTRACT **Objective:** Cirrhosis is a very common ailment in India mostly caused by alcoholism, viral hepatitis and malnutrition. The clinical picture of patients with cirrhosis is dominated by the classical complications such as ascites, bleeding from esophageal varices, portal hypertension and encephalopathy. Here, Cardiovascular abnormalities have been reported by several investigators.
Methods: It is a cross sectional and observational study done on 60 patients admitted to MKCG Medical College, Berhampur,. 2014 to Dec. 2015. The associations of circulatory and cardiovascular dysfunction in cirrhosis patients were analyzed. All the demographic and clinical history of study populations were analyzed with SPPSS software.
Results: Diastolic dysfunction is measured by E/A ratio was prevalent LVED diameter, IV septal thickness, left ventricular posterior wall thickness were proportional to severity of liver cirrhosis. Electro physiologically, 38.33% patients of cirrhotic liver patients had prolonged QTc interval. Here, as far as cardiac abnormality were considered, we found QTc prolongation more in severe degree of cirrhosis MELD score III (7 out of 10) 70%, than moderate (40%) MELD score II and mild (20%) MELD score I of cardiac QTc prolongation.
Conclusions; Diastolic dysfunction is a major criteria of cirrhotic cardiomyopathy which can be diagnosed by electro and echo cardiography

KEYWORDS : Cardiovascular, Cardiomyopathy, Cirrhosis, Diastolic dysfunction.

Introduction

Hyperdynamic syndrome is a well-known clinical condition found in patients with cirrhosis and portal hypertension [1-3]. It is characterized by increased heart rate and cardiac output, and reduced systemic vascular resistance and arterial blood pressure [4]. The leading cause of hyperdynamic circulation in cirrhotic patients is peripheral and splanchnic vasodilatation, due to an increased production/activity of vasodilator factors (such as nitric oxide [NO], carbon monoxide [CO], and endogenous cannabinoids) and decreased vascular reactivity to vasoconstrictors [4-6].

Although the presence of cardiomyopathy in cirrhotic patients has been described since 1960s, it had been erroneously attributed to alcoholic cardiotoxicity [1,7,8]. Only in the last 2 decades has it been shown that cardiac dysfunction is also present in nonalcoholic cirrhosis. The term "cirrhotic cardiomyopathy" was introduced to describe impaired contractile responsiveness to stress, diastolic dysfunction and electrophysiological abnormalities in the absence of known cardiac disease [9-12].

The circulatory dysfunction and the abnormal activation of systemic and renal neurohormonal regulation in advanced cirrhosis are the main determinant in the development of the hepatorenal syndrome (HRS). However some studies suggested that underlying cardiac dysfunction precedes the development of HRS [13-16]. Cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) insertion are at high risk of developing cardiovascular complications. This may be the consequence of diastolic dysfunction, common feature in this patient population [17,18]. Furthermore, the clinical consequences of cirrhosis-related cardiovascular dysfunction are evident during and after liver transplantation (LT) [19], and this may be manifestation of occult cirrhotic cardiomyopathy [20]. These data point out the importance of a careful cardiac assessment of cirrhotic patients, but also suggest the need for further studies to identify specific diagnostic protocols in this patient population.

This study discusses the circulatory and cardiovascular dysfunction in cirrhosis, examining the pathophysiologic and clinical implications in the light of the most recent published literature. Hepatopulmonary syndrome has been the topic of recent comprehensive reviews and will not be discussed here [21,22]. (2015)

Materials Methods

It is a cross sectional and observational study done on 60 patients admitted to MKCG Medical College, Berhampur,. 2014 to Dec. 2015 with following criteria: (a) Inclusion criteria: (i) Age group > 18 years, (ii) Patients with clinical features and laboratory tests suggestive of cirrhosis of liver (including ultrasonography). (b) Exclusion criteria: (i) Patients suspected of malignancy of liver (ii) Patients of IHD/Valvular heart disease, conduction defects, cardiac arrhythmias and congenital heart defects (iii) Known cases of diabetes and hypertension (iv) Hepatic encephalopathy (v) Patients having cQTC interval prolongation. Sample size was calculated at 95% confidence level assuming standard deviation of 5 in MELD score as observed in the study of Silvestre OM et al.[1] At the precision (absolute allowable error) of 1.3, minimum 60 patients of cirrhosis of liver were required as sample size. The study was approved by institutional scientific and ethics committee. The study was not funded by any government body or any company. There is no conflict of interest, if at all with any. USG of liver was done by GE Voluson promachine with probe frequency of 3.5 MHz and high frequency of 7-10 MHz for detection of cirrhosis and ascites with special reference to caudate lobe, portal vein and spleen.

12 lead ECG was done to calculate QT interval manually, and corrected QT (QTC) by using Bazett's formula as QTC = *RR Interval QT Interval* Prolonged QT interval was defined as value > 440 m sec (0.44 sec). 2D Echo were done by Philips HD (7 × E) with adult probe, and was used to assess cardiac anomaly with special reference to left atrial diameters left ventricle end diastolic volume, I.V.septal thickness, left ventricular posterior wall thickness and to assess E/A ratio where E stands for early maximum left ventricular filling velocity, and A for late diastolic left ventricle filling velocity; left ventricle systolic function was calculated using ejection fraction (EF %) and diastolic function was assessed by E/A and if ratio was < 1, it was taken as diastolic dysfunction. Lt. ventricular mass was calculated by ASE-cube formula: Lt. ventricle mass (in gms) = 0.8 {1.04 [([LVEDd +I VSd + PWs]3 - LVEDd3)]} + 0.6Here LVEDd stands for Left ventricle end diastolic diameter in mm. PWd = for posterior left ventricular wall thickness at end diastole (in mm) I VSd = for septal

wall thickness at end diastole (in mm) 1.04 = Sp gravity of the myocardium (g / cm3) Normal left ventricular mass in males is < 170 gm and in females it is < 160 gm Lt. ventricular mass index was calculated as Lt. ventricular mass for body surface area. Cirrhotic cardiomyopathy was declared by features found in those patients having:

(a) Diastolic heart failure sp. prolongation of QT interval (b) E/A ratio < 1 (corrected QTC - > 0.44 sec) (c) Increased wall thickness with LVEF > 50% and without structural lesions were labelled as cirrhotic cardiomyopathy. Patients grading for cirrhosis was done by MELD criteria (MELD stands for Model for End Stage Liver Disease) MELD = 3.78 [Ln Serum bilirubin (mg/dL)] + 11.2 [Ln INR] + 9.57 [Ln serum creatinine (mg/dL)] +6.43 MELD Scoring: Stage I MELD Score < 9 Stage II MELD Score 10-19 Stage III MELD Score > 20 Statistical analysis: Continuous variables were summarized as mean and standard deviation while nominal / categorical variables as proportions (%). ANOVA with post hoc Tukey HSD was used for analysis of continuous variables whereas Chi-square test was used for nominal/ categorical variables. pvalue < 0.05 was taken as significant. Medcalc 14.0.0 version software was used for all statistical calculation. Microsoft Word and Excel was used to generate graphs, tables and derivation.

Result

Total 60 patients were practice in this prospective study among the 52 (86.65%) were male and 8 (13.35) were females. Males are predominant to females (Table). In the age group it was that 41-50 year age patients are suffered more as compares to the other age group. (Table2). In clinically it was observed the aetology of 34 involves 46(76.67%) Hepatitis B12(20%) Hepatitis C, (1.07%) and idiopathic (1) 1.67 (Table 3). Whereas cites are 60 i.e. in all patients and encephalo paty at 20 patients (33.33%) and in 8 patients variceal bleeding (Table 4).

With QTC and ECG, it was revealed that 27 were prolonged and 33 were in normal from the 27 prolonged cases, 25 were male and rest 2 were female (Table 5) similarly in Ecocardiogrphic it was revealed that at an average 59.03% were ejection frustum and average deceleration time in see was 199.5 (Table 6). From this study 19 cases had diastolic dysfunction when are in 41 had in normal. 2 cases (40%) of class A, 6 cases 930%0 of call B, 19 cases (54%) of class C patients according to Child-Turcotte-Pugh classification were having prolonged QTc interval (Table 7). 16 cases were having mild degree of diastolic dysfunction out of which 12 cases were alcoholic and 4 cases were non-alcoholic. All the 3 cases that were having moderate degree of diastolic dysfunction. Systolic dysfunction was found in 6 alcoholic patients, 4 were having mild degree of systolic dysfunction and 2 cases were having moderate systolic dysfunction and 2 cases were having moderate systolic dysfunction. (Tbale 8). According to Child-Pugh score 5 cases (8.33%) belongs to stage A, 20 cases (33.33%) belongs to stage B and 35 cases (58.33%) belongs to stage C. 2 cases (40%) out of 5 cases of stage A cirrhotic patients, 2 cases (10%) out of 20 cases of stage B cases and 15 cases (42.85%) out of 35 cirrhotic patients of stage C were having diastolic dysfunction.

Discussion

Our study shows cirrhotic patients with or without ascites has both morphological and functional cardiac dysfunction. Cardiac dimension is enlarged in all the four chambers with increase in ejection fraction in cirrhotic patients with ascites. Type I and II Left ventricular diastolic dysfunction was present in seventy percent of cirrhotic patient with or without ascites. TDI with assessment of LAV, e′, E/e′ and DT can classify the LVDD. While the left ventricular systolic function was preserved in all the studied patients.

Diastolic dysfunction appears to be more prevalent in cirrhotic patients, indeed some authorities contend that some degree of diastolic dysfunction is present in virtually every patients with cirrhosis [17,18]. In most of the studies performed in the recent past, diagnosis of LVDD was based on E/A ratio <1 using 2-D Doppler echocardiography. Valeriano *et al* also found a similar lower mean E/A ratio in both left and right ventricle in ascitic subgroup than in non-ascitic subgroup [19]. Pozzi *et al* showed that removal of ascitic fluid by rapid total paracentesis reduced the A wave velocity and increased the E/A ratio to the values similar to those of cirrhotic patients without ascites, but still abnormal as compared to healthy controls [20].

However, E/A ratio have several limitations as it is strongly dependent on preload and often requires age correction [14,21]. Unlike transmitral valve Doppler flow, TDI directly measures the velocity of myocardial displacement as the LV expands in the diastole and therefore is independent of volume status and left atrial pressure. The ASE has included TDI parameters in the definition of LVDD. A recent study by Ruiz del Arbol *et al* showed LVDD in 37/80 (46.2%) with TDI in cirrhotic patients. They also found LVDD occurs simultaneously with other changes in cardiac structure and function and is associated with an impairment of effective arterial blood volume. LVDD was a sensitive marker of advanced cirrhosis, type 1 hepatorenal syndrome development, and mortality [22].

Our study shows left ventricular diastolic dysfunction is present in most of the cirrhotic patients which was detected by TDI in 70% of cases. This rate is somewhat more than the 50- 60% found in recent study conducted by both TDI and Doppler echocardiography [22,23]. Twenty three patients in the current study were already on β-blockers which could have added or aggravated the diastolic dysfunction. Another limitation of the current study was that Valsalva maneuver was not performed during mitral valve flow analysis by TDI, this might have over staged the diastolic dysfunctions in a few of the cases.

The mean peak systolic velocities in both the mitral and tricuspid annulus were comparable in all the three groups, whereas the ejection fraction which was significantly elevated in patients with decompensated cirrhosis as compared to health controls and compensated cirrhosis (P value 0.005). Various studies have shown stroke volume and contractile indices are typically normal or even increased at rest. However, under stressful stimuli such as exercise, renal failure, haemorrhage or drug infusions, cirrhotic patients may show an attenuated systolic function compared to healthy controls [24-26]. In our study systolic dysfunction was not seen, which probably reflects the exclusion criteria used in the current study; as patients with renal failure, tense or refractory ascites and terminal liver failure patient were excluded.

Lengeyl *et al* studied ninety six patients of various etiologies, and diastolic dysfunction was assessed by TDI and conventional echocardiography. They found that about 1/3rd of the patients could be classified into a diastolic dysfunction pattern only by using TDI [27]. In our study LVDD (Type I and II) was seen in eighty percent of cirrhotic patients with ascites as compared to sixty percent of cirrhotic patients without ascites (p value 0.09). Parameters regarding left ventricular systolic performance were within normal range. Further studies are required to assess the prognostic impact of left ventricular diastolic dysfunction in patients with cirrhosis and the cut off parameter to taper or abandon beta blocker. In conclusion, left ventricular diastolic dysfunction is commonly associated with advancement of hepatic dysfunction while systolic function is maintained till advanced hepatic failure. Peak early diastolic wave velocity, deceleration time and E/e′ ratio for diastolic dysfunction are accurately assessed by pulsed TDI.

Conclusions

60 cases of liver cirrhosis of either sex, age <65 years and any aetiology were included in our study to evaluate the myocardial dysfunction. Among them 46(76%) cases of alcoholic cirrhosis, 12(20%) cases of hepatitis B, 1 case of hepatitis C and 1 case of cryptogenic aetiology was found among all cases Prolonged QTc interval was present in 27(45%) cases and it was related to severity of liver cirrhosis. Systolic dysfunction was found in 6(10%) cases of liver cirrhosis and all them were alcoholic. Hence it could be due to direct effect of alcohol. Diastolic dysfunction was present in 19(31.66%) cases of cirrhosis of liver. There was no correlation of diastolic dysfunction with aetiology and severity of liver cirrhosis.

Table1: Gender wise distribution of cases

Gender	No. of cases	Percentage
Males	52	86.65
Females	8	13.35
Total	60	100.00

Table 2: Age wise distribution of cases

Age range in years	No. of cases	Percentage
21-30	1	1.67
31-40	11	18.33
41-50	23	38.33

51-60	21	35.00
61-64	4	6.67
Total	60	100.00

Table3: Aetiology of cirrhosis

Aetiology	No. of cases	Percentage
Alcoholic	46	76.67
Hepatitis B	12	20.00
Hepatitis C	1	1.67
Idiopathic	1	1.67
Total	60	100.00

Table4: Clinical parameters

Parameter	No. of cases	Percentage
Ascites	60	100.00
Encephalopathy	20	33.33
Variceal bleeding	8	13.30

Table5: Showing QTc interval in ECG

Corrected QT interval (sec)	No. of cases	Percentage	Mean	
			Male	Female
Prolonged	27	45	25 (0.57 ± 0.06)	2 (0.57±0.01)
Normal	33	55	27 (0.39±0.03)	6 (0.4±0.02)

Table 6: Echocardiographic finding of patients

Echocardiographic parameter	Mean ± SD
Ejection fraction in	59.03±4.76
E/A ratio	1.35±0.43
Deceleration time in msec	199.5±29.36

Table 7: Showing diastolic dysfunction

Diastolic dysfunction	No. of cases	Percentage
Present	19	31.66
Absent	41	68.34
Total	60	100.00

Table 8: Echocardiographic parameters (Myocardial dysfunction)

Aetiology	No. of cases with diastolic dysfunction			Systolic dysfunction		
	Mild (Grade I)	Moderate (Grade II)	Severe (Grade III)	Mild	Moderate	Severe
Alcoholic	12	3	0	4	2	0
Non-Alcoholic	4	0	0	0	0	0
Total	16	3	0	4	2	0

Table 9: Diastolic dysfunction according to severity of liver cirrhosis

Child Pugh score	No of cases	No of cases having diastolic dysfunction	Percentage
A	5(8.33%)	2	40
B	20(33.33%)	2	10
C	35(58.33%)	15	42
Total	60	19	

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