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ORIGINAL ARTICLE

THE EFFECTS OF VIRAL CIRRHOSIS ON CARDIAC VENTRICULAR FUNCTION

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Liver cirrhosis is a severe disease with complications and viruses take the first place in the etiology of cirrhosis. In this study, the effects of liver cirrhosis due to viral hepatitis cardiac ventricular functions were analyzed. Thirty patients (mean age 43.6±12, 20 male) with liver cirrhosis underwent echocardiographic studies and were compared with 30 healthy controls (mean age 37.3±2, 22 male). Right and left atrium and right ventricle dimensions, interventricular septum, right ventricle free wall thickness, pulmonary artery diameter and assumed mean pulmonary artery pressure measured with 2-dimensional echocardiography were significantly increased in the patient group. In Doppler echocardiographic studies, right ventricle diastolic functions were significantly impaired in the patient group. There were no significant differences in left ventricle systolic and diastolic functions between the groups. In conclusion, liver cirrhosis causes dilatation in right heart spaces and diastolic dysfunction.

Key words: Cirrhosis, cardiac function, echocardiography

INTRODUCTION

Liver cirrhosis which continues to be a major health problem in Turkey and especially in South Eastern Anatolia of Turkey is a clinical picture with severe complications. Hepatitis viruses hold a more important place than alcohol in cirrhosis etiology in Turkey, because it is an endemic region for hepatitis and alcohol consumption is relatively lower than Western countries.

Cirrhosis is a chronic liver disease characterized by diffuse fibrosis and regeneration nodules following hepatocellular necrosis in the liver. It is a disease with characteristic clinical findings and diagnosed with histopathology (1,2).

Cardiac failure causes functional disorders and damage in the liver. Studies have been carried out since 1950s on the association of hepatic cirrhosis with cardiovascular abnormalities.

Abelmann et al. (3) have claimed that cardiac function is impaired in cirrhosis and were the first to define hyper dynamic circulation provided by increased cardiac output and heart rate, decreased systemic vascular resistance in patients with alcoholic cirrhosis.

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Subsequent studies have claimed that nitric oxide and other endothelial dependent factors cause peripheral vasodilatation. Similar cardiac contractile function disorders found in non-alcoholic cirrhosis and in animal models under stress conditions have suggested that this is independent from alcohol intake and was named as cirrhotic cardiomyopathy (CMP) (4,5).

The aim of this study was to evaluate cardiac ventricular functions with echocardiography, in liver cirrhosis with viral origin.

MATERIAL AND METHODS

Patient selection

This study was carried out on 30 patients (mean age 43.6±12, 20 male) diagnosed to have liver cirrhosis with clinical, laboratory and ultrasonographic findings by hospitalization at Dicle University Faculty of Medicine Internal Medicine Clinic between December 2000 and December 2001.

HCV was found in the etiology of one patient. In the remaining 29 cases, HBsAg was positive and HBV-DNA was negative. In 4 cases, total anti-HDV was positive. 16 (47.7%) cases had ascites and 26 (86.7%) had pulmonary hypertension findings.

The patients were classified according to Child-Pugh staging. 5 (16.7%) were in Child A, 12 (40%) were in Child B and 13 (43.3%) were in Child C stage.

Table 1. General characteristics of patients

Age	43.6±12
Male/Female	22/8
Ascites	16
Encephalopathy	10
Portal Hypertension	26
Serology	
HBV	25
HBV+HDV	4
HCV	1
Child-Pugh score	
A	5
B	12
C	13
Albumin (g/dl)	2.8±0.1
Total Billirubin(mg/dl)	2.6±0.4
AST (U/L)	87±11
ALT(U/L)	72±11
Na (mmol/L)	135±1
K (mmol/L)	4.2±01
Urea (mg/dl)	35±4
Creatinine (mg/dl)	0.75±0.07

Thirty voluntary cases (mean age 37.3±2, 22 male) without portal hypertension and liver parenchymal disease findings in abdominal USG and without a history of alcohol abuse and with normal liver function tests were used as controls. Hepatitis B and C markers were negative in the contro group. Cirrhosis cases with non-viral etiology, ischemic heart disease, diabetes mellitus, hypertension, history of heart valvular disease and hyper or hypothyroidism were excluded from the study. All patients were informed about the study and their verbal consent was obtained. Complete blood count, biochemical and serologic data from laboratory findings and echocardiographic examinations were recorded.

Echocardiographic studies

Two-dimensional, pulsed Doppler, M-mode and color flow Doppler echocardiographic studies were made with Ving-Med ultrasonographic system (CFM-800) using 2.5 and 3.5-MHz transducers. Echocardiographic images were obtained from the parasternal and apical windows with the patient reclining on the left side. According to the recommendations of American Echocardiography Committee (15) examinations were performed using parasternal longitudinal axis and apical four-chamber windows. Mitral inflow velocity pattern was recorded by placing the pulsed wave Doppler sample volume between the mitral valvular endings. Left ventricle outflow pattern was recorded from the apical five space window by placing the pulsed wave Doppler sample volume just under the aortic valve.

In Doppler echocardiography accompanied by electrocardiogram, peak early filling velocity (E wave), peak atrial systolic velocity (A wave), early and late mitral diastolic flow ratio (E/A), ratio of E and A velocity time integrals, the time period between termination of aortic systolic flow and onset of early mitral diastolic flow as isovolumetric relaxation time (IVRT) and the time period between the peak level of early mitral diastolic flow and its termination as E deceleration time (EDT) were measured. With M-mode measurements, interventricular septum (IVS) and left ventricle posterior wall (LVPW) thicknesses separately at diastole and systole and left ventricle end-diastolic (LVED) and end systolic (LVES) diameters were determined.

In echocardiographic evaluation, right ventricle end-diastolic diameters (RVED), right ventricle end-systolic diameters (RVES), right atrium diameters(RAD), left atrium diameters(LAD), pulmonary arterial diameters and right ventricle free wall thicknesses were measured. Flow characteristics and rates of mitral, tricuspid, aortic and pulmonary valves were evaluated with Doppler studies. Pulmonary arterial pressure (PAP) was calculated on the tricuspid regurgitation flow. Doppler measurements were obtained at the apnea position.

Statistical analysis

Statistical analysis were made using the SPSS 10.0 computer program. Data were analyzed with student's t-test and chi-square test, and Spearman's rho test was used to determine the correlation between the data. A p value of <0.05 was considered as significant.

RESULTS

Mean pulse rate of the study group was 85 ±2, and that of the control group was 76±2, and the study group had significantly higher values ($p<0.05$). General characteristics of the patients were shown in Table 1.

Left ventricle posterior wall (LVPW) and IVS thicknesses, left atrium diameter were significantly higher in the patient group. Right atrium and pulmonary artery diameters and pulmonary artery pressures were again statistically increased in the patient group.

In Doppler studies, tricuspid flow E waves and deceleration times which reflect right ventricle diastolic functions were similar in both groups, whereas tricuspid flow A wave

Table 2. Echocardiographic results of patients and control group

	Patients	Control	p value
IVS(cm)	0.96±0.16	0.82±0.11	<0.05
LVDd(cm)	4.41±1	4.74±0.35	ns
LVPW(cm)	1.04±0.16	0.80±0.13	<0,05
LVDs(cm)	2.98±0.57	3.21±0.38	ns
LVEF(%)	70±8	68±5	ns
LA(cm)	3.61±0.42	3.24±0.28	<0.05
RA(cm)	3.47±0.49	3.12±0.28	<0.05
PAP(mmHg)	26±9	14±3	<0.05
TE(msn)	0.57±0.09	0.64±0.12	<0.05
TA(msn)	0.65±0.16	0.44±0.24	<0.05
TE/TA	0.92±0.24	1.43±0.24	<0.05
DT(tricuspit)	245±51	224±49	ns
RVDd(cm)	3.53±0.37	3.48±0.24	ns
RVDs(cm)	2.67±0.43	2.70±0.28	ns
ME(ms)	0.84±0.26	0,89±0.15	ns
MA(ms)	0.66±0.23	0,57±0,12	ns
ME/MA(ms)	1.31±0.42	1.58±0.38	ns
DT(mitral)	184±53	150±38	ns

LVPW: Left ventricle posterior wall, TE: peak early filling velocity of tricuspid flow, TA peak atrial systolic velocity of tricuspid flow, ME: peak early filling velocity of mitral flow, MA: peak atrial systolic velocity of mitral flow, IVRT: isovolumetric relaxation time, DT: deceleration time, IVS: interventricular septum, LVDd: left ventricle end-diastolic diameters, LVDs: left ventricle end-systolic diameters, RVDd: Right ventricle end-diastolic diameters, RVDs: left ventricle end-systolic diameters, PAP: Pulmonary artery systolic pressure, RAD: right atrium diameters, LAD: left atrium diameters.

was significantly high in the patient group. Right ventricular E/A wave ratio was 0.92 ±0.24 in the patient group and 1.43±0.24 in the control group, and the difference was statistically significant ($p<0.05$). Other 2-D, M-mode and Doppler parameters pertaining to both left ventricle and right ventricle were similar in both groups ($p>0.05$). Echocardiographic findings of both groups are shown in Table 2.

DISCUSSION

Pathoanatomic basis for cirrhotic CMP are histological changes expressed as patchy fibrosis, interstitial edema and increased heart weight due to cardiac hypertrophy. These changes affect myocardial wall stiffness and result in impaired left ventricular filling and diastolic dysfunction (7,8). The cause of increased cardiac wall thickness is not fully understood. But the role of renin angiotensin aldosterone system (RAAS) and adrenergic hyperactivity has been considered (7).

Systolic functions do not change in cirrhosis, but decrease in patients with ascites and improve following paracentesis. However, it does not reach the same level as normal people (7). These data are suggest that such changes are due to increase in preload.

The echocardiographic results obtained in this study show that the basic difference between cirrhotic patients and the control group is the dilation of right and left atria. This dilation can be perceived as an adaptation of cardiac hemodynamics to changes in peripheral circulation. However, similar changes could not be found in ventricular diameters. A probable reason for this could be the facilitation of left ventricle performance because of decreased peripheral vascular resistance. When it is taken into account that there is an abnormal cardiac response to physiologic and pharmacologic stress in cirrhotic CMP (8), we cannot rule out the decreased cardiac reserve in stress conditions because we evaluate all our patients in resting position.

Abnormalities in Doppler echocardiography ventricular filling pattern and changes in E/A ratio are considered to be markers of diastolic dysfunction in cirrhotic patients (9, 10).

Right ventricle diastolic dysfunction may be due to the decrease in cardiac preload, increase in the afterload or right ventricular relaxation or other abnormalities in compliance.

The appearance of diastolic dysfunction in cirrhotic patients may be due to the thickening of ventricular wall caused by cardiac hypertrophy and consequent impaired ventricular relaxation. Although there was a significant difference in IVS and posterior

wall thickness between the patient and control groups in our study, there was no marked ventricular hypertrophy. Our findings were in parallel with those of Valeriano et al. (11).

Another important finding that drew attention was the significantly higher pulmonary arterial pressure in the patient group. In fact, pulmonary vascular resistance was tended to decrease in cirrhotic patients (10,11). The mechanism of increased PAP is not fully understood, but previous studies suggested the increased levels of vasoactive substances in pulmonary circulation and the probable toxic effect of these substances on endothelial cells. Some authors have suggested that microthrombi can migrate to pulmonary vascular bed along porto-systemic shunts and can cause increase in vascular resistance (12). In a study on patients with alcoholic liver disease, Rector et al.(13) found increased right and left atrium diameters but normal ventricular diameters. Grose et al. (14) shown that cardiac end-systolic and end-diastolic volumes increase in cirrhosis and they attributed this to decreased cardiac contractility.

In conclusion, cirrhosis disrupts right ventricle diastolic functions together with dilatation of both atria, increases pulmonary artery pressure but does not affect left ventricle functions.

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