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Original Research Article

Tissue Doppler Study of Right and Left Ventricular Function in Nonalcoholic Fatty Liver Disease

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ABSTRACT

Introduction: Nonalcoholic fatty liver disease is characterized by focal or diffuse accumulation of fat in the liver parenchyma. The studies of cardiac performance among patients with nonalcoholic fatty liver disease are limited and controversial.

Objective: To assess right and left ventricular systolic and diastolic function in patients with nonalcoholic fatty liver disease with and without elevated liver enzymes using conventional echocardiography and tissue Doppler imaging.

Methods: This study involved 80 nonalcoholic fatty liver disease patients, 50 patients with normal ALT (group 1) and 30 patients with elevated ALT (group 2), in addition to 20 healthy volunteers serving as controls (group 3). All subjects were subjected to: clinical evaluation; routine laboratory evaluation; ECG; abdominal ultrasound; echocardiographic examination with tissue Doppler imaging.

Results: Mitral flow showed significant increase in deceleration time (DT) in both patient groups as compared to controls. Tricuspid flow showed significant decrease in early filling velocity (E) and early to late filling velocity (E/A) in both patient groups as compared to controls. Tissue Doppler at the mitral annulus showed a statistically significant increase in early filling velocity to early diastolic annular velocity by tissue Doppler (E/Ea), together with significant decreases in early diastolic annular velocity (Ea), early to late diastolic annular velocity (Ea/Aa) and peak systolic annular velocity (S) in both patient groups as compared to controls with a significant decrease in S velocity in group (2) compared to group (1). At the tricuspid annulus, there was a statistically significant increase in early filling velocity to early diastolic annular velocity by tissue Doppler (E/Ea), in the addition to significant decreases in early diastolic annular velocity (Ea), early to late diastolic annular velocity (Ea/Aa) and peak systolic annular velocity (S) in both patient groups as compared to controls, with significant decrease in S velocity in group (2) compared to group (1).

Conclusion: Nonalcoholic Fatty liver disease (especially if associated with elevated ALT and CRP levels) disrupts cardiac structure, systolic and diastolic function of both right and left ventricles, which can be early detected and quantified by pulsed tissue Doppler imaging.

Keywords: Nonalcoholic Fatty Liver Disease; Nonalcoholic Steatohepatitis; Echocardiography; Tissue Doppler Imaging; Alanine Aminotransferase.

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INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a clinico-pathological condition of emerging importance. It is now recognized as the most common cause of abnormal liver function tests. It is characterized by a wide spectrum of liver damage: simple steatosis may progress to advanced fibrosis and to cryptogenic cirrhosis through nonalcoholic steatohepatitis (NASH), and ultimately to hepatocellular carcinoma.[1]

The association of metabolic syndrome and NAFLD is so strong that NAFLD is considered as the hepatic manifestation of metabolic syndrome.[2,3] Steatosis is associated with an increased prevalence and incidence of cardiovascular disease (CVD).[4] The studies of cardiac function among NAFLD patients are limited and controversial.

It has been shown that nondiabetic, normotensive patients with NAFLD have echocardiographic features of left ventricular (LV) diastolic dysfunction.[5-7] Karaagac et al. found that LV diastolic dysfunction in NAFLD patients deteriorates with hepatosteatosis grade.[8] Şerban et al. concluded that in NAFLD patients, the assessment of diastolic dysfunction by tissue Doppler imaging detects early changes in myocardial stiffness and compliance,

which precede the late stages of myocardial dysfunction.[9] Few studies have been done to explore the involvement of right ventricular systolic and diastolic function in patients with NAFLD. Bekler et al. revealed significant right ventricular diastolic dysfunction in NAFLD patients.[10] Subjects with NAFLD have also an elevated risk of increased carotid intima media thickness[11], reduced endothelial function[12], increased coronary artery calcification and increased arterial stiffness.[13]

The pathogenesis of CVD in NAFLD might be through the over expression and systemic release of several inflammatory, hemostatic and oxidative-stress mediators.[14-16] Yoneda et al. reported that CRP was significantly elevated in cases of NASH and they suggested that CRP may be a clinical feature that distinguishes NASH from simple steatosis.[17] Foroughi et al. revealed that NAFLD grades were associated with CRP level.[18] Alanine aminotransferase (ALT) is shown to be positively associated with the increased risk of cardiovascular disease in patients with NAFLD.[19-20]

AIMS

We aimed to assess right and left ventricular systolic and diastolic function in patients with NAFLD with and without elevated liver enzymes by conventional echocardiography and tissue Doppler imaging.

PATIENTS AND METHODS

Patients: Inclusion criteria

The present study was conducted on 100 subjects from outpatients' services of Theodor Bilharz Research Institute Hospital, selected to represent 3 groups:

Group (1) included 50 patients with NAFLD and normal ALT.

Group (2) included 30 patients with NAFLD and elevated ALT.

Group (3) included 20 apparently healthy volunteers matched for age and sex to serve as control group. They have normal liver ultrasonography, normal liver function tests and negative hepatitis markers.

Hepatic steatosis was diagnosed by the presence of diffuse hyperechogenicity of liver compared to right kidney with vascular blurring and deep attenuation[21] together with negative hepatitis markers.

Exclusion criteria

- Heart Disease,
- Diabetes Mellitus,
- Hypertension (blood pressure >130/85 mmHg),
- Hyperlipidemia,
- Acute or chronic kidney disease,
- Malignancy,
- Alcohol Consumption,
- Liver Masses,
- Pregnancy,
- Anemia (hemoglobin less 10 gm%)
- Patients taking medications that have adverse effects on liver or cardiovascular system.

Methods

All subjects were subjected to:

- History taking and clinical examination.
- Blood sampling for blood picture, liver and renal function tests, serum electrolytes, lipid profile, CRP, HBS antigen and HCV antibody.
- Resting ECG.
- Abdominal ultrasound scanning which was performed by one member of the study team using a Toshiba Memo 30 scanner equipped with a 3.5 MHz linear transducer.

Echo-Doppler Study

All echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography.[22] These measurements were completed by three members of the study team and measurements were averaged.

M-mode, two dimensional echocardiography and Doppler ultrasound studies (pulsed, continuous wave, color flow and tissue Doppler imaging) were made using a high resolution (x11-15305) sonata plus ultrasound scanner equipped with a 2.5 MHz transducer. Left ventricular mass was calculated according to the equation of Devereux et al.:

LVM gm = 1.04 x {(LVED + IVST+ PWT) 3 – LVED3} × 0.8 + 0.6

LVED: Left ventricular end diastolic diameter,

IVST: Interventricular septum thickness, and

PWT: Left ventricular posterior wall thickness.[23]

Mitral E and A wave velocity (cm/s) was measured using pulsed wave Doppler in the apical four-chamber view with a 1- to 2-mm sample volume placed at the tips of the mitral valve leaflets during quiet respiration and E/A ratio was calculated.

Deceleration time (DT) (time in milliseconds from peak of E-wave to the decline of the velocity to baseline) was also measured. Isovolumic relaxation time (IVRT) was measured using continuous wave Doppler, which intersects both the left ventricular outflow and the mitral valve motion. Presenting the time interval (in milliseconds) from aortic valve closure (end of aortic valve velocity profile) to mitral valve opening (onset of mitral valve velocity profile). Tricuspid E and A wave velocity (cm/s) were also measured using pulsed wave Doppler in the apical four-chamber view with a 1- to 2-mm sample volume placed at the tips of the tricuspid valve leaflets during quiet respiration and E/A ratio was calculated. Deceleration time (milliseconds) was also measured.

Doppler Tissue Imaging

Pulsed wave Doppler tissue imaging velocities were obtained from the apical four-chamber view during quiet respiration by placing a sample volume in the lateral and septal mitral annulus. Cursor line was more aligned with examined wall (15–20º) to decrease incidence of angle error. The peak early diastolic mitral annular velocities (Ea, cm/s) and peak late diastolic mitral annular velocities (Aa, cm/s) were measured from the time-myocardial velocity wave forms of 2–3 consecutive cardiac cycles and the average was recorded. The lateral and septal E/Ea ratios (measure of LV filling pressure) were calculated. An average of the two velocities of the Ea and Aa were taken as mean velocities at mitral annulus (mean Ea and mean Aa). Furthermore, the average E/Ea and Ea/Aa were estimated. The mitral peak systolic annular velocity (Sa) was measured at the two annular sites and the average systolic velocity was calculated.

Pulsed wave Doppler tissue imaging velocities were additionally obtained from the apical four-chamber view by placing a sample volume in the lateral and septal tricuspid annuli. The average Ea, Aa, E/Ea, Ea/Aa, Sa were estimated.

Research Ethics

All patients were provided by informed consent, and the ethical committee of the hospital approved this study.

Statistical Analysis

Statistical analysis was performed using SPSS version 17. Data were expressed as the mean ± standard deviation (SD) for numerical variables. $P < 0.05$ was considered to be statistically significant and $P < 0.01$ was considered to be statistically highly significant

RESULTS

The demographic data of the patient groups (1 and 2) and control group (group 3) revealed mean ages 47.2±7.2, 46.3±7.8 and 45.8±8.5 years, respectively. In Group (1), 30 were males (60%) and 20 were females (40%). In Group (2), 20 were males (66.7%) and 10 were females (33.3%). In Group (3), 14 were males (70%) and 6 were females (30%). (Table1)

There were no significant differences in systolic and diastolic blood pressure and body mass index between the three groups. (Table 1)

Regarding abdominal ultrasonography, there was a significant increase in liver span in both patient groups compared to the control group with no significant difference in portal vein diameter between the three groups. (Table 1)

Table 1: Demographic data, blood pressure and abdominal ultrasound of the studied groups, patients (groups 1, 2) and control (group 3)

		Group 1	Group 2	Group 3	P1	P2	P3
Age (years)		47.2±7.2	46.3±7.8	45.8±8.5	0.49	0.83	0.6
Sex	**Male**	30(60%)	20(66.6%)	14(70%)	0.14	0.65	0.30
	Female	20(40%)	10(33.4%)	6(30%)			
Systolic blood pressure (mmHg)		124.2±7.2	122.7±6.8	120.6±7.3	0.06	0.3	0.36
Diastolic blood pressure (mmHg)		72.8±4.2	72.3±5.3	70.9±7.4	0.18	0.44	0.64
BMI (Kg/m2)		24.8±5.2	24.7±5.3	22.7±4.6	0.12	0.18	0.93
Liver span cm		16.29±0.85	16.3±1.2	14.65±0.46	0.000	0.000	0.94
Portal Vein mm		6.68±1.34	6.72±0.8	6.40±0.5	0.37	0.31	0.88

P1 value, between groups 1 and 3; P2 value, between groups 2 and 3; P3 value, between groups 1 and 2. P< 0.05=Significant, P<0.01= highly significant, BMI= Body Mass Index.

Table 2: Laboratory data of the studied groups, patients (groups 1, 2) and control (group 3)

	Group 1	Group2	Group 3	P1	P2	P3
Na mEq/L	139.25±5.58	140.23±5.6	141.71±1.99	0.06	0.263	0.449
K mEq/L	4±0.27	4.1±0.3	4.06±0.24	0.39	0.620	0.128
Creat mg/dL	1.21±0.28	1.1±0.18	1.07±0.29	0.06	0.653	0.058
BUN mg/dL	17.00±7.52	17.2±4.4	14.41±5.30	0.16	0.200	0.598
ALT U/L	15.04±20.07	45.6±18.7	13.94±2.08	0.808	0.000	0.000
AST U/L	16.42±19.01	47.8±17.4	14.82±4.07	0.711	0.000	0.000
Tbil mg/dL	0.93±0.42	0.97±0.4	0.76±0.24	0.09	0.063	0.687
Dbil mg/dL	0.42±0.24	0.44±0.2	0.32±0.21	0.11	0.068	0.703
Albumin g/dL	3.98±0.45	4.1±0.4	4.20±0.38	0.06	0.382	0.233
WBCs 10^9/L	6.44±2.48	6.6±2.5	5.72±0.57	0.20	0.099	0.781
Hb g/dL	12.83±1.14	12.6±1.08	13.06±1.12	0.45	0.153	0.376
Platelets 10^9/L	308.21±50.64	310.4±51.8	292.94±54.97	0.27	0.260	0.853
INR %	1.04±0.05	1.06±0.07	1.03±0.03	0.41	0.077	0.141
TG mg/dL	131.9±57.7	131.2±58	122.3±56.5	0.52	0.594	0.958
LDL mg/dL	117.6± 29.5	115.8±31.2	109.6±30.4	0.31	0.490	0.797
HDL mg/dL	46.2±21.6	44.8±17.2	48.8±16.8	0.63	0.420	0.764
CRP mg/L	5.4 ±1.6	7.8 ±2.5	4.2± 0.8	0.002	0.000	0.000

P1 value, between groups 1 and 3; P2 value, between groups 2 and 3; P3 value, between groups 1 and 2. P< 0.05=Significant, P<0.01= highly significant.

Na: serum sodium, K: serum potassium, BUN: blood urea nitrogen, Creat: creatinine, ALT: alanine aminotransferase, AST: aspartate aminotransferase, Tbil.: Total bilirubin, D bil.: Direct bilirubin, Alb: Albumin, WBCs: white blood corpuscles, Hb: hemoglobin, PLT: platelets, INR: international normalized ratio, TG: Triglycerides, LDL: low-density lipoprotein cholesterol, HD: high-density lipoprotein cholesterol, CRP: C reactive protein.

Table 3: M –mode Echocardiographic data of the studied groups, patients (groups 1, 2) and control (group 3)

	Group 1	Group2	Group 3	P1	P2	P3
IVST mm	10.3±1.4	11.4±1.4	9.3±1.3	0.008	0.000	0.001
LVPWT mm	10.3±1.3	11.3±1.3	9.2±1.3	0.002	0.000	0.001
LVM gm	197.01±55.11	236.2±48.34	155.55±41.61	0.003	0.000	0.002
LVEDD mm	49.5±5.3	52.8±5.8	48.0±4.7	0.27	0.000	0.01
LVESD mm	31.5±4.5	35.2±3.8	29.2±4.3	0.055	0.000	0.002
FS %	36.73±5.46	33.33±5.8	39.28±6.12	0.09	0.000	0.004
EF %	64.32±7.41	59.64±7.8	68.31±6.88	0.04	0.000	0.009
LA mm	39.8±4.5	43.7±4.7	35.6±4.2	0.000	0.000	0.113
AO mm	29.3±3.7	29.4±3	28.8±3.2	0.60	0.5	0.9
RVD mm	21.5±2.3	21.4±2.5	20.9±1.3	0.28	0.42	0.86

P1 value, between groups 1 and 3; P2 value, between groups 2 and 3; P3 value, between groups 1 and 2. P< 0.05= Significant, P<0.01= Highly significant.

IVST: interventricular septum thickness, LVPWT: Left ventricular posterior wall thickness, LVM: left ventricular mass. LVEDD: Left ventricular end diastolic dimension, LVESD: Left ventricular end systolic dimension, FS: Fractional shortening, EF: ejection fraction, left atrium diameter, Ao: aortic diameter, RVD: Right ventricular diameter.

Table 4: Diastolic function by echocardiography and tissue Doppler of the studied groups, patients (groups 1, 2) and control (group 3)

	Group1	Group2	Group3	P1	P2	P3
Mitral valve flow						
E (cm/s)	64.19±17.35	63.2±18.3	71.46±16.93	0.115	0.114	0.809
A (cm/s)	63.82±12.33	62.74±13.2	60.01±11.32	0.236	0.453	0.713
E/A	1.01±0.37	1.01±0.38	1.19±0.35	0.066	0.097	1.000
DT ms	188.55±43.22	189.2±43.6	163.61±36.19	0.026	0.035	0.948
IVRT ms	71.62±13.53	72.2±12.92	66.94±13.16	0.192	0.168	0.851
Mitral annulus						
Ea (cm/s)	8.76± 2.73	8.68±2.82	12.24±2.46	0.000	0.000	0.901
E/Ea	7.33±1.95	7.48±2.1	5.84±1.12	0.002	0.002	0.747
Ea/Aa	0.90±0.30	0.91±0.28	1.11±0.26	0.008	0.014	0.883
S (cm/s)	8.30±2.75	7.41±2.36	10.24±1.56	0.004	0.000	0.036
Tricuspid valve flow						
E (cm/s)	44.39±12.91	44.62±12.87	53.42±12.4	0.009	0.020	0.939
A (cm/s)	49.84±11.36	50.23±11.76	44.08±10.76	0.056	0.067	0.884
E/A	0.89±0.30	0.89±0.28	1.21±0.33	0.000	0.000	1.000
Tricuspid annulus						
Ea (cm/s)	7.35±2.13	7.23±2.24	10.93±1.98	0.000	0.000	0.816
E/Ea	6.04±2.12	6.13±2.31	4.89±1.98	0.04	0.036	0.582
Ea/Aa	0.83±0.22	0.81±0.24	1.09±0.36	0.000	0.000	0.705
S (cm/s)	10.76±2.96	9.8±1.87	12.3±1.69	0.03	0.000	0.002

P1 value, between groups 1 and 3; P2 value, between groups 2 and 3; P3 value, between groups 1 and 2. P< 0.05=Significant, P<0.01= highly significant. E: early filling velocity, A: late or atrial velocity, IVRT: Isovolumetric relaxation time, DT: deceleration time, E/Ea average: average early filling velocity to average early annular velocity by tissue Doppler, Ea/Aa average: average early annular velocity to average late annular velocity (atrial velocity) by tissue Doppler, S average: average peak systolic annular velocity by tissue Doppler.

Laboratory Data

The laboratory data showed significant increase of ALT, AST and CRP in group (2) compared to the group (1) and controls. There was also significant increase of CRP in group (1) compared to controls. (Table 2)

Echocardiographic Data

The M-mode echocardiographic data, showed significant increase in IVST, LVPWT, LVM, LVEDD, LVESD and LA diameter in addition to significant decrease in FS% and EF% in group (2) compared to group (1) and to controls. Also, we found significant

increase in IVST, LVPWT, LVM and LA diameter together with significant decrease in EF% in group (1) compared to controls. (Table 3)

Regarding diastolic function of the left ventricle (mitral flow) measured by conventional Doppler, we found insignificant increase in A wave velocity and IVRT with significant increase in DT, together with insignificant decrease in E wave velocity and E/A ratio in the patient groups as compared to control group. On the right side (tricuspid flow), there was an insignificant increase in A wave velocity, in addition to a significant decrease in E wave velocity and E/A ratio in both patient groups as compared to control group. (Table 4)

Pulsed wave tissue Doppler at the mitral annulus showed a statistically significant increase in average E/Ea ratio, together with significant decrease in the average Ea velocity, Ea/Aa and average systolic wave velocity (S) in both patient groups as compared to control group. Also, there was significant decrease in average systolic wave velocity (S) in group (2) compared to group (1). At the tricuspid annulus, there was a statistically significant increase in the average E/Ea, together with significant decrease in the average Ea velocity, Ea/Aa and average systolic wave velocity (S) in both patient groups as compared to control group. Also, we found significant decrease in average systolic wave velocity (S) in group (2) as compared to group (1). (Table 4)

DISCUSSION

The laboratory data in our study revealed that in addition to elevated liver enzymes (ALT and AST) in group (2), there was a significant increase in CRP as compared to group (1) and group (3). Ezzat and his colleagues have also found increased ALT and AST enzymes in patients having fatty liver disease especially those with steatohepatits.[24] Yoneda et al. suggested that CRP can differentiate NASH from simple steatosis and can also indicate the severity of hepatic fibrosis in cases of NASH.[25] Similar results were observed by Nigma et al., 2006[26]; Uchihara et al., 2006[27] and Oruc et al., 2009[28] who observed a statistically significant association between fatty liver grade and CRP level.

The M-mode echocardiographic data showed significant increase in IVST, LVPWT, LVM, LVEDD, LVESD and LA diameter in addition to significant decrease in FS% and EF% in group (2) compared to group (1) and (3). We also found significant increase in IVST, LVPWT, LVM and LA diameter in addition to significant decrease in EF% in patients with group (1) compared to group (3). These findings are similar to that of Goland et al., who found increased thickness of the interventricular septum, posterior wall and larger LVM in NAFLD group compared to normal controls.[5] Also Mantovani et al., on their study on NAFLD patients reported that NAFLD is associated with left ventricular hypertrophy independently of classical cardiovascular risk factors and other potential confounders.[29] Fotbolcu et al. found mild abnormalities in the LV structure, including increased LVM, LVM index and LV wall thickness in normotensive, non-diabetic patients with NAFLD.[6] The study of Bonapace et al., 2012 showed that patients with NAFLD, in the absence of other cardiovascular risk factors included in the metabolic syndrome, present alterations in left ventricular geometry.[7]

In agreement with our study Fotbolcu et al. have reported that patients with NAFLD have impaired LV systolic function even in the absence of morbid obesity, hypertension, or diabetes.[6] Trovato and his colleagues also found significantly greater LVM with slightly lower ejection fraction independently of BMI, dietary profile, physical activity in NAFLD patients.[30] Pacifico et al., agrees with our study in that patients with increased liver enzymes (which may be an indicator of steatohepatitis) had more pronounced decrease in systolic function.[31] The association between ALT level and cardiovascular disease has also been well documented.[19,20,32] NAFLD was associated with a higher prevalence of coronary heart disease in type 2 diabetes, and that plasma ALT levels may act as a marker of cardiovascular risk in these patients.[33] However, in the study of Domanski et al., no increased risk of cardiovascular disease was found among patients with NASH as compared with those with non-NASH fatty liver.[34]

Regarding diastolic function of the left ventricle (mitral flow) by conventional Doppler echo, we found significant increase in DT together with insignificant increase in IVRT and A wave velocity in the patient groups compared to control group. There was also insignificant decrease in E wave velocity and E/A ratio in the patient groups as compared to control group. The mitral inflow velocities (E and A waves) and time intervals (DT and IVRT) can be affected by alterations in LV end-systolic and or end diastolic volumes, LV diastolic pressures and LV elastic recoil.[26]

The current study is in agreement with that of Fotbolcu et al. in finding insignificant decrease in E wave velocity with insignificant increase in A wave velocity, in addition to significant increase in DT in NAFLD patients as compared to the controls.[6] Goland et al. concluded that patients with NAFLD had a significantly lower E wave velocity and E/A ratio.[5] On the other hand, Karaagac et al., found no significant differences in conventional echocardiography parameters, E, A, E/A, and DT between NAFLD group and the control group.[8]

In our study, pulsed wave tissue Doppler at the mitral annulus showed a statistically significant increase in average E/Ea ratio, together with significant decrease in the average Ea velocity, Ea/Aa and average systolic wave velocity (S) in both patient groups as compared to control group. Also, we found significant decrease in average systolic wave velocity (S) in group (2) compared to group (1). Ea wave velocity and E/Ea ratio have been recognized as having the best correlation with left ventricle relaxation and myocardial compliance indexes.[35] These findings are in agreement with that of Fotbolcu et al.[6] who also found increased E/Ea in addition to decreased Ea velocity, Ea/Aa and S velocity of the lateral mitral annulus in nondiabetic normotensive NAFLD patients.

Also, Goland et al. in 2006[5] and Karaagac et al.[8] in 2013 found decreased Ea velocity and Ea/Aa in patients with NAFLD that was correlated with hepatosteatosis grade. Our study agrees with the study of Bonapace et al., 2012 who concluded that patients with NAFLD, in the absence of other cardiovascular risk factors present early diastolic dysfunction.[7] Also, Pacifico et al., found that patients with NAFLD had features of LV diastolic dysfunction, including higher E/Ea ratio and lower Ea tissue velocity and that patients with definite-NASH had significantly lower Ea velocity and significantly higher E/Ea and Tei index (reflecting the combined systolic and diastolic LV function) than those without NASH. They concluded that patients with NAFLD exhibit features of early LV diastolic and systolic dysfunction, and these abnormalities are more severe in those with NASH.[31]

Several studies have been done to explore the cause of LV diastolic dysfunction in NAFLD. Granér et al., found that myocardial triglyceride, epicardial and pericardial fat increased with increasing amount of liver fat and visceral adipose tissue. They concluded that lipid deposition in cardiac myocytes is thought to promote the development of LV diastolic dysfunction.[36] Also, Perseghin et al., found higher intra and extra pericardial fat accumulation in NAFLD patients as compared to controls.[37]

Regarding diastolic function of the right ventricle, by conventional echocardiography we found significant reduction in E velocity and E/A of the tricuspid flow in patient groups as compared to control group. Pulsed wave tissue Doppler at the tricuspid annulus revealed significant decrease in Ea wave velocity, Ea/Aa and S wave velocity in addition to significant increase in E/Ea in patient groups as compared to control group. We also found significant decrease in average systolic wave velocity (S) in group (2) compared to group (1).

Few studies have explored the involvement of right ventricular systolic and diastolic function in patients with NAFLD. Bekler et al. in 2015[10] have investigated right ventricular function in NAFLD and in agreement with our findings; they found significant decrease in Ea wave velocity and Ea/Aa but with insignificant decrease of S wave velocity. In contrast to our findings, they revealed no significant differences between NAFLD group and control group as regarding E wave velocity and E/A by conventional echocardiography.

Sunbul et al., 2015 have evaluated RV function by two-dimensional (2D) speckle-tracking echocardiography (STE) in patients with NAFLD and they concluded that patients with NAFLD have impaired RV function that correlates with the severity of steato-hepatitis and that 2D STE can detect subclinical RV dysfunction despite normal conventional echocardiographic indices.[38]

Right ventricular dysfunction in patients with NAFLD may be secondary to impaired liver function and/or hepatomegaly which contribute to increased preload of right heart. Furthermore, increased liver size can anatomically disturb RV function. Therefore, increased preload due to high hepatic venous pressure can lead to RV dysfunction in NAFLD.[38] Xu in his study in 2004 found replacement of myocardium of right ventricle with fat in patients with fatty liver disease that may be the cause of right ventricular dysfunction and arrhythmia and even sudden death in these patients and he concluded that disturbances of lipid metabolism contribute to the development of both fatty liver and fatty replacement of right ventricle.[39]

CONCLUSION

Nonalcoholic fatty liver disease disrupts cardiac structure and function. It causes left ventricular hypertrophy with increased left ventricular mass, left atrium dilatation together with diastolic dysfunction and decreased systolic function of both the right and left ventricles that are more pronounced in patients with elevated ALT and CRP.

Although conventional Doppler echocardiography can be used to diagnose systolic and diastolic dysfunction of the right and left ventricles, tissue Doppler is more sensitive and can detect early systolic and diastolic dysfunction which may not detected by conventional Echo-Doppler.

Patients with NAFLD require aggressive cardiac risk factor modification in addition to close follow-up to prevent diastolic and systolic heart failure.

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ABBREVIATIONS

NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; CVD, cardiovascular disease; HCV, chronic hepatitis C virus; HBs, hepatitis B surface antigen; ALT, alanine aminotransferase; CRP, C-reactive protein; TDI, tissue Doppler imaging; LA, left atrium; LV, left ventricle; RV, right ventricle; IVST, interventricular septum thickness; LVPWT, left ventricular posterior wall thickness; LVM, left ventricular mass; CAD, coronary artery disease.

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