Cardiac Abnormalities in Nonalcoholic Fatty Liver Disease: Echocardiographic and Tissue Doppler Imaging Assessment

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Abstract

Background: Triglycerides cause liver fat buildup. Nonalcoholic Fatty Liver Disease (NAFLD) has a prevalence of 25.24%. Metabolic syndrome connects both NAFLD and heart disease. Imaging aids detection, understanding, and early intervention.

Objectives: To detect cardiovascular abnormalities in NAFLD patients, focusing on the effects of metabolic syndrome on Left ventricle (LV) geometry and function.

Patients and methods: This study is a cross-sectional study from March 2022 to March 2023 involving 100 NAFLD patients (20-60 yrs). Exclusion: age <20 or >60, severe liver disorders, alcoholic fatty liver, hepatitis B/C, active malignancy. Medical history, physical exam, lab (coagulation, liver enzymes, lipid profile, HbA1c, and CBC), radiological (echocardiogram, abdominal ultrasonography, and FibroScan).

Results: The majority had mild NAFLD grade (56%), 38% moderate, and 6% marked. Ejection Fraction positively linked to mild grade, negative to moderate. LSM negatively correlated with mild, positively with marked grades. Body Mass Index is positively related to severely fatty liver. AST, ALT uncorrelated; albumin correlated with grades. LDL positively correlated with mild, negatively with moderate, and marked grades. TG positively correlated with mild, negatively with marked grade; TC negatively with moderate, positively with marked grade. HbA1C negatively correlated with mild, positively with marked grade. Platelet count negatively connected with mild, positively with a moderate grade.

Conclusion: Cardiac motion abnormalities linked to higher fatty liver grades suggest a potential link between NAFLD and cardiac dysfunction . Positive correlations between ejection fraction and mild fatty liver grades suggest protective effects in early-stage NAFLD detection, while negative correlations suggest declining cardiac function with disease progression.

Keywords: Cardiac Abnormalities; Echocardiography; FibroSan; Tissue Doppler .

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Introduction

Triglyceride accumulation in hepatocytes causes hepatic steatosis in non-alcoholic fatty liver disease (NAFLD), a common condition. NAFLD prevalence is 25.24 percent globally, varying by region. NAFLD, formerly known for its hepatic symptoms, is now part of the metabolic syndrome and is linked to cardiovascular disease **(Devarbhavi et al., 2023).**

The possible influence of NAFLD cardiac anomalies on cardiovascular morbidity and death has drawn attention. Lifestyle changes, medication, and revascularization may treat ischemic heart disease that involves atherosclerosis or functional coronary circulation abnormalities. Some observational studies imply NAFLD patients have a higher risk of cardiovascular death, increasing heart health concerns **(Dong and Li, 2019; Niederseer et al., 2021).**

The association between NAFLD and cardiac problems may be more than just a correlation. Both illnesses share metabolic syndrome pathophysiological characteristics such as hypertension, insulin resistance, obesity, and dyslipidemia. These variables cause cardiac remodeling and dysfunction, especially in the left ventricular (LV) shape and function. Electrocardiography and tissue Doppler imaging (TDI) are essential for identifying cardiac problems **(Vachliotis et al., 2022; Chew et al., 2023).**

Echocardiography is a non-invasive, widely accessible imaging technology that reveals heart structure and function. TDI quantifies myocardial velocities and deformation, whereas echocardiography shows cardiac anomalies. Researchers and healthcare providers may better comprehend the complex relationship between NAFLD and cardiac alterations using sophisticated imaging. These approaches may also detect heart dysfunction early and uncover new cardiovascular disease risk factors **(Chun et al., 2019).**

This study aims to detect cardiovascular abnormalities in NAFLD patients, focusing on the effects of metabolic syndrome on LV geometry and function.

Patients and methods

This cross-sectional study was conducted at Qena University Hospital Internal Medicine Department from March 2022 to March 2023. The study involved 100 patients of both sexes, aged 20 to 60 years, with Nonalcoholic Fatty Liver Disease (NAFLD). Patient manifestations encompassed fatigue, abdominal discomfort, elevated liver enzyme levels (ALT and AST), insulin resistance, metabolic syndrome, hypertension, dyslipidemia, and cardiac dysfunction, including diastolic dysfunction and impaired relaxation. Exclusion criteria included patients under 20 years or over 60 years, individuals with severe liver disorders (cirrhosis), alcoholic fatty liver, active malignancy, or those testing positive for hepatitis B virus and hepatitis C virus were excluded.

Medical history and physical examination: All patients underwent detailed medical history and physical examination, including age, sex, family and past medical history, and coagulation disorder history. Physical examination involved arterial blood pressure measurement, body mass index (BMI) calculation, and abdominal and cardiac examination.

Laboratory investigations

Sampling: 6 mL blood was collected aseptically from each patient and divided into 3 tubes: 2 mL in an EDTA tube for complete blood count (CBC) and HbA1c, 2 mL in a Na citrate tube for Coagulation study, 2 mL in a plain tube for lipid profile and liver functions.

A) Coagulation study: Prothrombin time (PT), prothrombin concentration (PC), and

international normalized ratio (INR) were measured using an automated blood coagulation analyzer (CS-1600. Sysmex Corporation Dade Behring. CA analyzers Kobe, Japan).

B) Liver enzymes: Aspartate aminotransferase (AST), alanine transaminase (ALT), and albumin levels were measured Using Beckman Coulter AU 480-CA-USA.

C) Lipid profile: Serum total cholesterol, triglycerides, HDL cholesterol, serum phospholipids, LDL, VLDL, and HDL levels were measured. The total cholesterol/ HDL cholesterol ratio was calculated Using Beckman Coulter AU 480-CA-USA.

D) HbA1c: HbA1c test was performed using high-performance liquid chromatography (HPLC) using Bio-Rad D-10™.

E) Complete blood count: using cell dyne-Ruby cell counter (Abbott Diagnostics - Santa Clara-California-USA), included various parameters like red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cell count, platelet count, and differential leukocyte counts.

Radiological investigations

A) Echocardiogram: Echocardiography was performed using LOGIQ P7 Device (GE Healthcare, United States) to assess LV dimensions, ejection fraction, and motion abnormalities (**Fig.1,Fig.2**).

1. A wo-dimensional guided M-mode echocardiographic tracings to determine LV internal dimensions and wall thickness. These measurements were taken at mid-chordal, following the parasternal long-axis view. To assess ejection fraction using Teinchholz formula, **Arora et al (2010).** The, V mass (LVM) was calculated using formula outlined by **Devereux et al (1986).** All measurements adhered to the recommendations of the American Society of Echocardiography **(Gottdiener et al., 2004).**

2. The study assessed mitral inflow utilized pulse-wave Doppler recordings **(Simpson et al., 2007),** with the sample volume positioned at the mitral valve leaflet tips and recorded from the apical four-chamber perspective. Measuring early (E) and late (A) diastolic filling peak velocities, deceleration time (DT), and isovolumic relaxation time. The ratio of early-to-late diastolic mitral inflow velocity (E/A) was calculated. Additionally, Doppler recordings were used to measure the mitral valve shutting-to-opening time and the LV ejection time. The study used a color Doppler map and M-mode recordings to assess flow propagation velocity (Vp) from an echocardiographic window, focusing on early and late filling propagation velocities.

3. The study used tissue Doppler imaging (TDI) with pulse-wave Doppler filters to minimize background noise and allow clear tissue signals. Baseline settings and color velocity scale adjustments were made to introduce color aliasing. The apical 4-chamber view was used for diastolic velocity TDI. We positioned a 1.5-mm mitral annulus volume at the lateral corner and analyzed A0 and S0 for early, late, and systolic diastolic velocity **(Dallaire et al., 2015).**

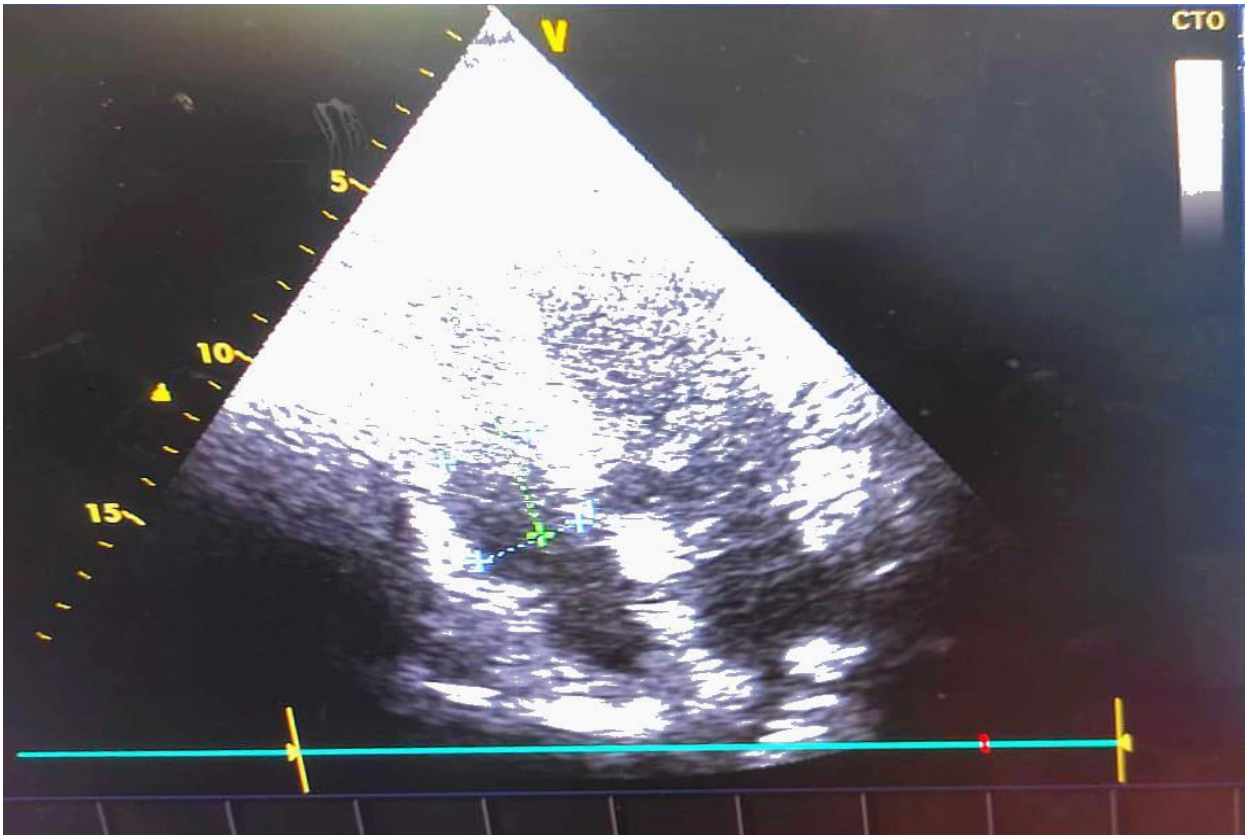

Fig.1. Echocardiography photo showing Normal cardiac function and dimension

Fig.2. Echocardiography photo showing preserved left ventricle systolic function

B) Abdominal ultrasonography: Abdominal ultrasonography was performed using **Vivid S5** (GE Healthcare, United States) to detect NAFLD based on specific criteria.

A high-resolution B-mode ultrasound system was used by experienced ultrasound specialists to measure the liver size in the midline and mid-clavicular lines, as well as its surface and echogenicity. Participants with two of the following three criteria could be diagnosed with fatty liver: (i) the liver near-field echo is diffusely enhanced, more so than the kidney; (ii) the liver-kidney contrast" was increased; (iii) the far-field liver echo was reduced and unclear. These criteria were utilized to identify the grade of NAFLD during the abdominal ultrasonography assessment. The evaluation was conducted to ensure accurate and reliable results regarding liver size, surface, and echogenicity, enabling the identification of individuals meeting the diagnostic criteria for NAFLD based on these ultrasound findings (**Goulart et al., 2015**).

C) fibroScan Examination: using the FibroScan 502 (Echosens, Paris, France) to measure liver stiffness (LSM) and Controlled Attenuation Parameter (CAP) scores (**Fig.3, Fig.4**).

The right liver lobe, in the intercostal space, was selected for measurement. Patients were positioned in a supine position with their right arm maximally abducted, and ultrasound time-motion The potential range of liver stiffness values obtained using TE imaging ranged from 2.5 to 75.0 kPa, with the liver stiffness value of healthy subjects approximately 5.5 kPa **(Myers et al., 2010).**

1. **M probe and XL probe:** The M probe was used for all patients initially to obtain both LSM and CAP values. If the M probe failed, the XL probe was used for obese patients (**Kwok et al., 2016).**
2. **LSM score:** The (LSM) score was obtained by taking the median of 10 measurements. The LSM score was considered reliable and included in the final analysis if 10 successful acquisitions were obtained (**Kwok et al., 2016).**
3. **CAP score:** The (CAP) score was obtained by taking the median value. CAP measurements were considered reliable and included in the final analysis if 10 successful acquisitions were obtained (**Kwok et al., 2016**).

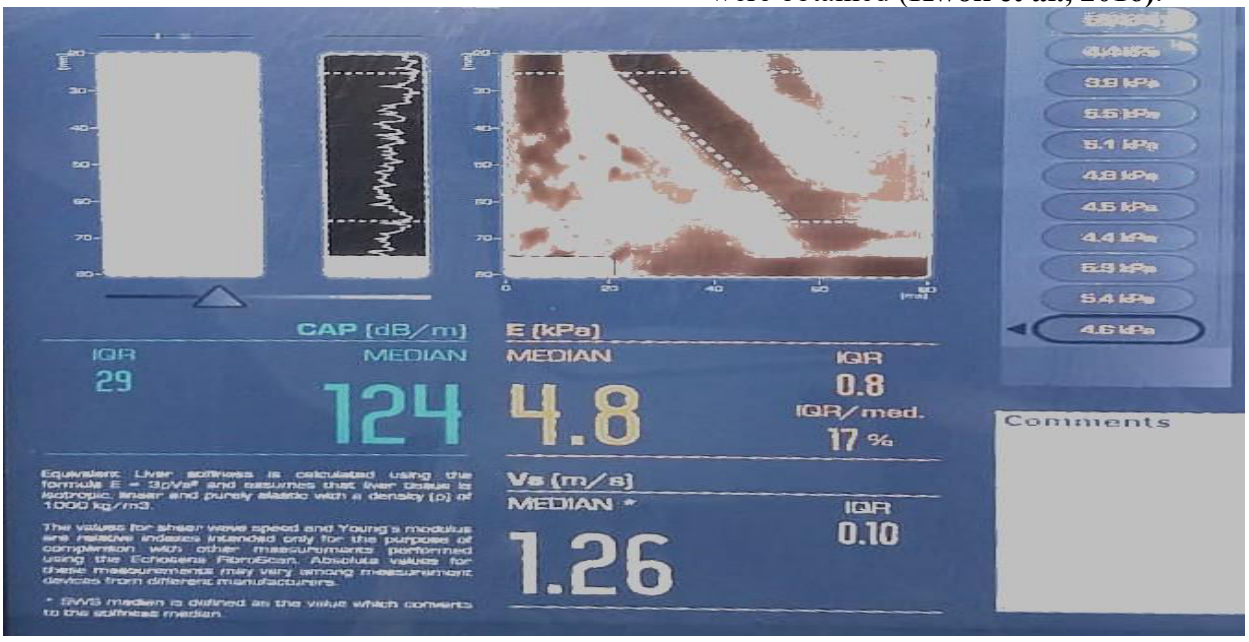

Fig.3. Patient with mild fatty liver in PAUS and fibro scan showing F1, S0

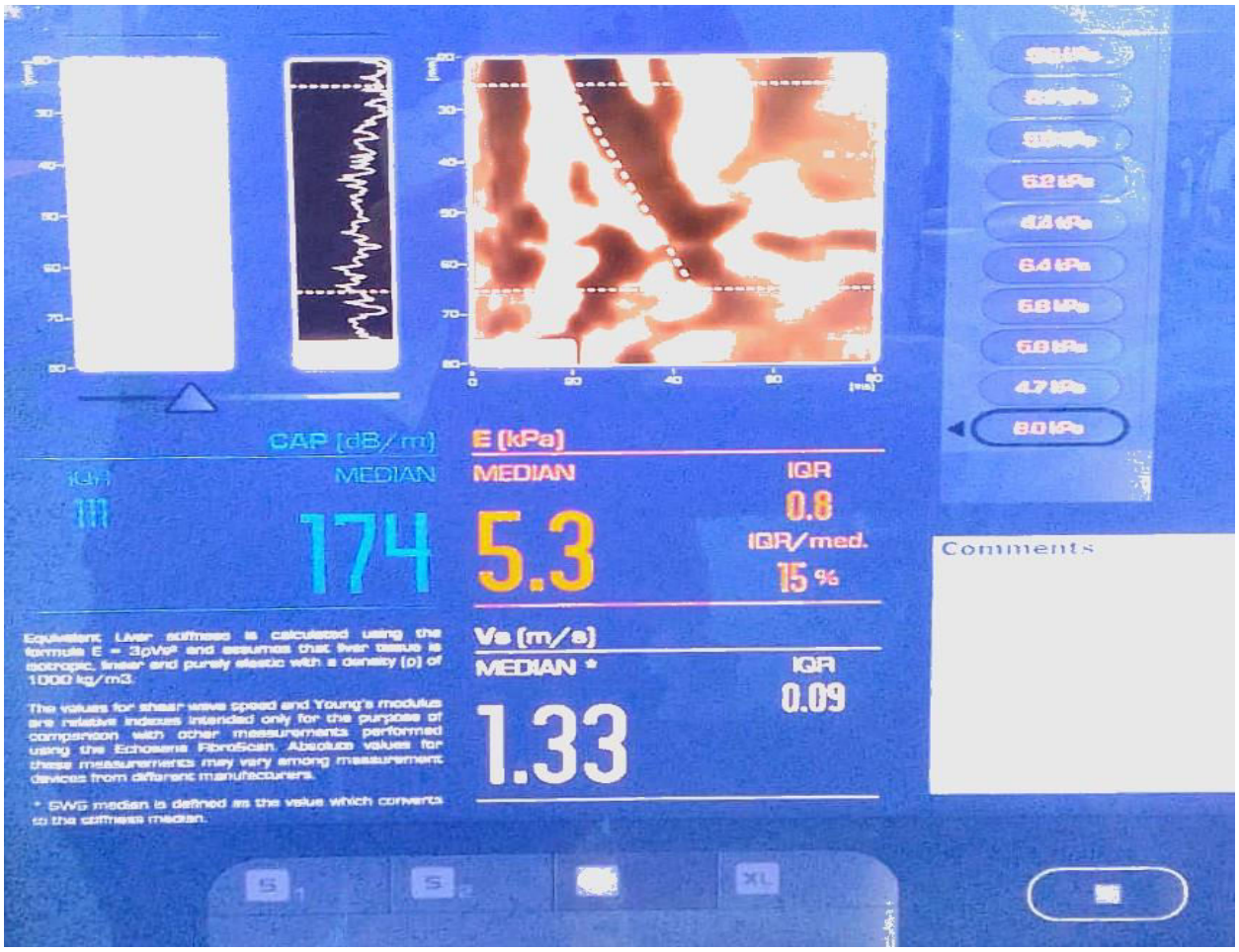

Fig.4. Patient with mild fatty liver in PAUS and fibro scan showing F1, S0

Ethical Considerations: The study was conducted under the ethical approval: SVU-MED-MED018-1-22-9-433

Statistical analysis

SPSS version 27 was used for data analysis. Quantitative data is represented as mean with SD and median with range. Qualitative data was represented as numbers and percentages. Kolmogorov-Smirnov test was used to ensure that the data were normal. ANOVA was used for comparison concerning continuous data and chi-square for categorical data. Pearson Correlation was used for calculating the degree of correlation between variables.

Results

Demographic data showed that the included 100 subjects aged 20 to 60 years, with an average age of 34.56 years (SD=9.19). 38% Of the participants were male while 62% were female. Among them, 44% had diabetes, and 43% had hypertension. The average BMI was 29.5 kg/m^2 (SD=4.89), with values ranging from 17.7 to 41.43 kg/m^2. In terms of fatty liver grades, the majority (56%) had a mild grade, 38% had a moderate grade, and 6% had a marked grade **(Table. 1).**

Table 1. Demographic data of all studies subjects

Parameters	**Value (N = 100)**
Age (Years)	
• **Mean ± SD**	34.56 ± 9.19

• **Median (Range)**	33 (20-60)
Sex (No(%))	
• **Male**	38 (38%)
• **Female**	62 (62%)
Co-Morbidities (No(%))	
• **Diabetes**	44 (44%)
• **Hypertension**	43 (43%)
BMI (Kg/m^2)	
• **Mean ± SD**	29.5 ± 4.89
• **Median (Range)**	29.54 (17.7-41.43)
Grade of NAFLD (No(%))	
• **Mild**	56 (56%)
• **Moderate**	38 (38%)
• **Marked**	6 (6%)

BMI: Body Mass Index

Lab investigation showed that AST level, 52.4 ± 36.21 IU/L; ALT level, 48.98 ± 39.23 IU/L; albumin level, 4.17 ± 0.65 g/dL; prothrombin concentration, 92.68 ± 8.16%; INR, 1.07 ± 0.09; LDL level, 96.93 ± 28.7 mg/dL; HDL level, 45.54 ± 15.09 mg/dL; TG level, 153.67 ± 53.35 mg/dL; TC level, 163.33 ± 28.42 mg/dL; Hb level, 12.23 ± 1.57 g/dL; WBCs, 8.31 ± 3 × 10^9/L; PLT count, 258.76 ± 85.93 × 10^9/L; HbA1C level, 6.22 ± 1.2%. **(Table. 2).**

Table 2. Lab investigations of all studies subjects

Parameters		**Value (N = 100)**
Liver Function Test		
AST (IU/L)	Mean ± SD	52.4 ± 36.21
	Median (Range)	39 (13-169)
ALT (IU/L)	Mean ± SD	48.98 ± 39.23
	Median (Range)	35 (10-188)
Albumin (g/dL)	Mean ± SD	4.17 ± 0.65
	Median (Range)	4.1 (2.8-5.8)
Coagulation Profile		
• **Prothrombin Concentration (%)**	Mean ± SD	92.68 ± 8.16
	Median (Range)	91.75 (74.3-114.5)
• **INR**	Mean ± SD	1.07 ± 0.09
	Median (Range)	1.04 (0.9-1.3)
Lipid Profile		
• **LDL (mg/dL)**	Mean ± SD	96.93 ± 28.7
	Median (Range)	88.5 (62-165.1)
• **HDL (mg/dL)**	Mean ± SD	45.54 ± 15.09
	Median (Range)	43.5 (23-95)
• **TG (mg/dL)**	Mean ± SD	153.67 ± 53.35
	Median (Range)	135 (60-284)
• **TC (mg/dL)**	Mean ± SD	163.33 ± 28.42

	Median (Range)	158 (95-225)
CBC		
• **HB (g/dl)**	Mean ± SD	12.23 ± 1.57
	Median (Range)	12.2 (10-15.2)
• **WBCS (*10^9/L)**	Mean ± SD	8.31 ± 3
	Median (Range)	8 (3.4-18.8)
• **PLT (*10^9/L)**	Mean ± SD	258.76 ± 85.93
	Median (Range)	236.5 (128-566)
HbA1C (%)	Mean ± SD	6.22 ± 1.2
	Median (Range)	5.9 (4.2-9.3)

AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, Albumin: A protein in the blood, Prothrombin Concentration, INR: International Normalized Ratio, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein, TG: Triglycerides, TC: Total Cholesterol, HB: Hemoglobin, WBCs: White Blood Cells, PLT: Platelets, HbA1C: Glycated Hemoglobin.

Fibroscan showed the (LSM) of 6.66 ± 1.25 kPa and a (CAP) of 294.47 ± 57.81 dB/m. Fibrosis grades range from F0 (58%, n=58) to F2 (18%, n=18), while steatosis grades vary from S0 (9%, n=9) to S3 (74%, n=74). Cardiac evaluations reveal (EF) of 61.6 ± 5.17%, 100% of subjects with motion abnormalities, and measurements for aortic root diameter (2.83 ± 0.51 cm), left atrium size (3.89 ± 0.08 cm), right ventricle size (3.19 ± 0.4 cm), interventricular septum thickness (0.87 ± 0.18 cm), LVEDD (4.58 ± 0.57 cm), LVEDD (3.16 ± 0.65 cm), and LV posterior wall thickness (0.86 ± 0.19 cm) **(Table.3).**

Table 3. Fibro-scan and cardiac evaluation data of included subjects

Parameters	**Value (N = 100)**
Fibro-scan	
LSM (kPa)	6.66 ± 1.25
CAP (dB/m)	294.47 ± 57.81
Fibrosis grade	
F0	58 (58%)
F1	24 (24%)
F2	18 (18%)
Steatosis Grade	
S0	9 (9%)
S1	7 (7%)
S2	10 (10%)
S3	74 (74%)
Cardiac Evaluations	
EF (%)	61.6 ± 5.17
Motion abnormalities	25 (100%)
Aortic Root Diameter (Cm)	2.83 ± 0.51
Left Atrium Size (Cm)	3.89 ± 0.08
Right Ventricle Size (Cm)	3.19 ± 0.4
IVSD (Cm)	0.87 ± 0.18
LVEDD (Cm)	4.58 ± 0.57

LVESD (Cm)	3.16 ± 0.65
LVPWD (Cm)	0.86 ± 0.19

LSM (Liver Stiffness Measurement), CAP (Controlled Attenuation Parameter), IVSD (Interventricular Septal Thickness in Diastole), LVEDD (Left Ventricular End-Diastolic Dimension), LVESD (Left Ventricular End-Systolic Dimension), LVPWD (Left Ventricular Posterior Wall Thickness in Diastole), EF (Ejection Fraction).

There is a significant increase in LSM (kPa) which was (5.85 ± 0.99 in mild, 7.54 ± 0.63 in moderate, and 8.53 ± 0.27 in marked NAFLD, $p < 0.0001$) and CAP (dB/m) (256.73 ± 47.93 in mild, 338.34 ± 21.88 in moderate, and 368.83 ± 11.72 in marked NAFLD, $p < 0.0001$). Fibrosis grades show a significant association with NAFLD severity, with marked NAFLD having the highest proportion of F2 fibrosis (100%). Steatosis grades also vary significantly among NAFLD grades, with severe steatosis (S3) being most prevalent in moderate and marked NAFLD cases (100%). However, the cardiac evaluation parameters, including (EF), motion abnormalities, and various cardiac dimensions, do not show significant differences among the different NAFLD grades. This data highlights the strong association between liver fibrosis and steatosis with NAFLD severity, while cardiac parameters appear relatively consistent across these NAFLD categories **(Table. 4).**

Table 4. Comparison between different NAFLD grades regarding Cardiac Evaluation and fibroscan

Variables	Mild NAFLD (N = 56)	Moderate NAFLD (N = 38)	Marked NAFLD (N = 6)	P. Value
Fibroscan				
• **LSM (kPa)**	5.85 ± 0.99	7.54 ± 0.63	8.53 ± 0.27	<0.0001*^{F}
• **CAP (dB/m)**	256.73 ± 47.93	338.34 ± 21.88	368.83 ± 11.72	<0.0001*^{F}
Fibrosis grade				
• **F0**	49 (87.5%)	9 (23.68%)	0 (0%)	<0.0001*^{X}
• **F1**	7 (12.5%)	17 (44.74%)	0 (0%)	0.00072*^{X}
• **F2**	0 (0%)	12 (31.58%)	6 (100%)	<0.0001*^{X}
Steatosis Grade				
• **S0**	9 (16.07%)	0 (0%)	0 (0%)	0.0211*^{X}
• **S1**	7 (12.5%)	0 (0%)	0 (0%)	0.0528^{X}
• **S2**	10 (17.86%)	0 (0%)	0 (0%)	0.01314*^{X}
• **S3**	30 (53.57%)	38 (100%)	6 (100%)	<0.0001*^{X}
Cardiac Evaluation				
• **EF (%)**	61.77 ± 4.73	61.58 ± 5.67	58.5 ± 3.42	0.3236^{F}
• **Motion abnormalities**	13 (23.21%)	10 (26.32%)	2 (33.33%)	0.86^{X}
• **Aortic Root Diameter (Cm)**	2.94 ± 0.52	2.69 ± 0.46	2.72 ± 0.56	0.0551^{F}
• **Left Atrium Size (Cm)**	3.89 ± 0.09	3.89 ± 0.07	3.88 ± 0.1	0.9604^{F}
• **Right Ventricle Size (Cm)**	3.17 ± 0.4	3.24 ± 0.41	3 ± 0.24	0.3525^{F}
• **IVSD (Cm)**	0.86 ± 0.18	0.89 ± 0.17	0.75 ± 0.21	0.1974^{F}
• **LVEDD (Cm)**	4.63 ± 0.57	4.55 ± 0.57	4.38 ± 0.58	0.5332^{F}

• **LVESD (Cm)**	3.15 ± 0.66	3.19 ± 0.6	3.05 ± 0.88	0.8761[F]
• **LVPWD (Cm)**	0.86 ± 0.18	0.87 ± 0.19	0.78 ± 0.18	.05387[F]

LSM (Liver Stiffness Measurement), CAP (Controlled Attenuation Parameter), IVSD (Interventricular Septal Thickness in Diastole), LVEDD (Left Ventricular End-Diastolic Dimension), LVESD (Left Ventricular End-Systolic Dimension), LVPWD (Left Ventricular Posterior Wall Thickness in Diastole), EF (Ejection Fraction). *:P<0.05 Statistically significant. F: ANOVA, X: Chi-Square

In all fatty liver grades, age did not correlate. Significant positive correlations were observed in patients with Mild, Moderate, and Marked NAFLD, showing the following associations: In Mild NAFLD, there were correlations with Albumin, EF, LDL, and TG levels. For Moderate NAFLD, correlations were found with motion abnormalities and PLT (platelet) count. Marked NAFLD exhibited significant positive correlations with LSM (liver stiffness measurement), motion abnormalities, prothrombin concentration, LDL, TC (total cholesterol), and HbA1C (glycated hemoglobin). **(Table.5).**

Table 5. Correlation between different grades of fatty liver with fibro scan, cardiac evaluations, and other parameters

Variables	Mild		Moderate		Marked	
	r	P. Value	r	P. Value	r	P. Value
Fibroscan						
• LSM	-.258**	0.00958	0.153662	0.12691	.225*	0.0244
• CAP	-.221*	0.02705	.218*	0.02948	0.016969	0.86692
Cardiac Evaluations						
Cardiac geometry						
• EF (%)	.272**	0.00625	-.231*	0.02053	-0.09492	0.34753
• Motion abnormalities	-.651**	<0.0001	.452**	<0.0001	.438**	<0.0001
• Aortic Root Diameter (Cm)	0.048	0.652	0.0362	0.659	-0.1014	0.09885
• Left Atrium Size (Cm)	-0.00201	0.98419	0.016929	0.86723	-0.03041	0.76394
• Right Ventricle Size (Cm)	-0.05156	0.61045	0.110641	0.27314	-0.11837	0.24082
• IVSD (Cm)	-0.02343	0.81699	0.105535	0.29602	-0.16672	0.09735
• LVEDD (Cm)	0.088172	0.38302	-0.04677	0.64404	-0.08871	0.38013
• LVESD (Cm)	-0.013	0.89785	0.034579	0.73269	-0.0435	0.66738
• LVPWD (Cm)	0.010486	0.91753	0.039988	0.69283	-0.10365	0.3048
Other parameters						
Age (years)	0.095167	0.34627	-0.0876	0.38614	-0.01988	0.84437
Liver function test						
• AST (IU/L)	0.003691	0.97093	0.045637	0.65209	-0.10099	0.31743
• ALT (IU/L)	-0.08361	0.40824	0.147174	0.14396	-0.12605	0.21143
• Albumin (g/dL)	.269**	0.00691	-.309**	0.00177	0.069893	0.48957
Coagulation Profile						
• Prothrombin Concentration (%)	-0.08027	0.42726	-0.04277	0.67264	.255*	0.01039
• INR	-0.06221	0.53863	0.1399	0.16506	-0.1559	0.1214
Lipid profile						
• LDL (mg/dL)	.260**	0.00894	-.520**	<0.0001	.518**	<0.0001

• HDL (mg/dL)	0.003704	0.97082	0.077521	0.44331	-0.16618	0.09844
• TG (mg/dL)	.302**	0.0023	-0.10847	0.28272	-.409**	0.00002
• TC (mg/dL)	0.119355	0.2369	-.265**	0.00774	.292**	0.00321
HbA1C (%)	-.266**	0.00752	-0.02034	0.84079	.597**	<0.0001
CBC						
• HB (g/dl)	-0.1032	0.30687	0.083179	0.41064	0.045709	0.65157
• WBCS (*10^9/L)	0.049928	0.62179	0.029396	0.77157	-0.16444	0.10208
• PLT (*10^9/L)	-.593**	<0.0001	.658**	<0.0001	-0.10419	0.30225

r: Pearson Correlation Coefficient, *:P<0.05 Statistically significant. LSM (Liver Stiffness Measurement), CAP (Controlled Attenuation Parameter), IVSD (Interventricular Septal Thickness in Diastole), LVEDD (Left Ventricular End-Diastolic Dimension), LVESD (Left Ventricular End-Systolic Dimension), LVPWD (Left Ventricular Posterior Wall Thickness in Diastole), EF (Ejection Fraction), AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, Albumin: A protein in the blood, Prothrombin Concentration, INR: International Normalized Ratio, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein, TG: Triglycerides, TC: Total Cholesterol, HB: Hemoglobin, WBCs: White Blood Cells, PLT: Platelets, HbA1C: Glycated Hemoglobin.

Discussion

NAFLD is hepatic steatosis without excess alcohol intake. NAFLD prevalence is up to 30% in developed and 10% in developing countries **(Smith et al., 2011).** Liver disease significantly contributes to mortality in heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) **(Ergatoudes et al., 2019).**

While some studies suggest increased cardiovascular mortality in NAFLD patients **(Zhou et al., 2012),** others do not confirm this association **(Kim et al., 2013).** NAFLD is part of the metabolic syndrome, and even in patients without hypertension, diabetes, or severe obesity, it can lead to early manifestations of LV diastolic dysfunction and mild LV geometry changes, with E0 on tissue Doppler being a relevant index **(Targher and Acaro, 2007).**

Both NAFLD and obesity independently increase cardiovascular disease (CVD) risk **(Ahmed et al., 2007, Adams et al., 2017, Polyzos et al., 2019, Ahmed A et al., 2015).**

Our study involved 100 young patients (mean age 34.56 years), with a higher proportion of women (62%) Common co-morbidities included diabetes (44%) and hypertension (43%). The average BMI was 29.5 kg/m2, 56% had mild fatty liver, 38% had moderate, and 6% had evident fatty liver.

In comparison to **(Trovato et al., 2016)** research**,** their participants had an average age of 50.52 years, and BMI of 27.4 ± 5.41. These differences in demographic statistics may be attributed to variations in random sample collection.

In our study, the average (LSM) was 6.66 kPa. The average (CAP) was 294.47 dB/m which indicated liver steatosis.

In a study conducted by **Tang et al. (2023),** a cohort of 2,047 young individuals were examined. Notably, their study reported a notably high prevalence of NAFLD, affecting 86% of their subjects. However, in contrast to our findings, the incidence of liver fibrosis was considerably lower, affecting only 2% of their population, indicating that the individuals in their study had relatively healthier livers in terms of fibrosis and stiffness.

In our study, lab tests showed normal liver function, liver synthetic capability, and stable coagulation. However, raised LDL and borderline high TG may alter NAFLD development and cardiovascular risk. CBC indicated normal blood values. There was a

correlation between average HbA1c level and NAFLD severity.

Awad et al. (2019) found that, NAFLD patients had substantially higher mean total blood cholesterol, TG, and LDL-C than controls. But, had considerably decreased HDL-C levels.

Compared to non-NAFLD patients, NAFLD patients exhibited higher levels of total cholesterol, LDL cholesterol, and HDL cholesterol, according to **(Sert et al., 2013; Romero et al., 2018; Awad et al., 2019).** The dyslipidemic profile is due to metabolic abnormality like insulin resistance or a severe NAFLD.

The proportion of patients with aberrant laboratory data, including dyslipidemia, increases semi-parallel with hepatic echogenicity in **Awad et al. (2019).**

This outcome matches **Duarte and Silva. (2011)** They discovered that steatosis was related to hypercholesterolemia and hypertriglyceridemia.

NAFLD patients often experience heart issues, with factors like LV hypertrophy, reduced e' tissue velocity, altered E/A and E/e' ratios, and diminished left ventricle longitudinal systolic function, which may suggest subclinical diastolic dysfunction. These cardiac changes in NAFLD appear unrelated to typical cardiovascular risk factors, making them valuable prognostic indicators for cardiovascular health. Identifying subclinical LV dysfunction through echocardiography can assist in recognizing NAFLD patients at risk of heart-related complications **(Dong and Li, 2019, Hassan et al., 2020).**

Our findings were similar to **Goland et al. (2006),** who found an increased LV mass index and greater diastolic dysfunction in non-diabetic NAFLD patients compared to matched controls. They also found a reduction in early diastolic relaxation (e') independently linked with NAFLD, supporting our research population motion abnormalities.

Fotbolcu et al. (2010) found LV systolic and diastolic dysfunction in normotensive and non-diabetic NAFLD patients. However, the study's limitations sample size, and lack of stress tests before participant inclusion must be considered.

According to **Fallo et al. (2009),** newly diagnosed untreated hypertension individuals with NAFLD had a greater frequency of diastolic dysfunction connected with hepatic steatosis. Our motion abnormalities suggest NAFLD-related heart dysfunction.

In an extensive NAFLD study, **VanWagner et al. (2015)** found reduced early diastolic relaxation (e') velocity as evidence of motion abnormality, elevated LV filling pressure, and worsened absolute GLS (global longitudinal strain), indicating subclinical myocardial remodeling and dysfunction. These findings complement our discovery of motion anomalies in certain subjects, indicating heart dysfunction or structural difficulties in NAFLD.

Even after controlling for variables, **Mantovani et al. (2015)** identified a link between NAFLD and mild to moderate LV diastolic dysfunction in type 2 diabetics. This supports our results of motion problems and heart concerns in certain subjects.

Bonapace et al. (2012) found an increased incidence of LV diastolic dysfunction in type 2 diabetics, including those with NAFLD, which matches our study motion abnormalities.

Cross-sectional studies in NAFLD patients revealed increased LV hypertrophy, concentric remodeling, and diastolic dysfunction **(Hallsworthet al., 2013; Petta et al., 2015). Li et al. (2021)** found similar findings suggesting a potential link between FLI and LV mass. Similar to **Trovato et al. (2016),** NAFLD patients had significantly higher LV mass and slightly lower ejection

fraction, particularly in males. Motion irregularities were observed in our investigation without substantial changes in the average ejection fraction. **Awad et al. (2019)** used (TDI) and found higher LV myocardial performance index values in NAFLD patients compared to controls, indicating NAFLD-related heart dysfunction. **Sert et al. (2013)** explored myocardial dysfunction in obese NAFLD and non-NAFLD groups, observing regional systolic and diastolic myocardial dysfunction in the interventricular septum and LV lateral wall. They also found compromised myocardial function in obese individuals with NAFLD, suggesting that obesity and NAFLD may impact myocardial function.

In **(Chinali et al., 2004)** study, lower mitral E/A ratio values with comparable DT were found in patients with the metabolic syndrome, but only increased blood pressure, even in the high normal range, was most strongly associated with changes in LV diastolic geometry and function**.** A previous study by **(Yang et al., 2021)** found significant differences in LV diastolic function between the nondiabetic, normotensive patients with NAFLD and the control group.

Our study found a correlation between cardiac motion abnormalities and greater fatty liver grades. Although **Awad et al., 2019)** used TDI to analyze LV myocardial performance index in NAFLD patients, **and Sert et al. (2013)** studied myocardial functional abnormalities in obese groups with and without NAFLD. All three studies using various methods, highlight the impact of NAFLD on heart health emphasize the need to monitor heart health in NAFLD patients.

Conclusion

Cardiac motion abnormalities linked to higher fatty liver grades suggest a potential link between NAFLD and cardiac dysfunction. Positive correlations between ejection fraction and mild fatty liver grades suggest protective effects in early-stage NAFLD detection, while negative correlations suggest declining cardiac function with disease progression. **List of abbreviation**

Abbreviation	Medical Term
NAFLD	Nonalcoholic Fatty Liver Disease
LV	Left Ventricle
EF	Ejection Fraction
LSM	Liver Stiffness Measurement
AST	Aspartate Aminotransferase
ALT	Alanine Transaminase
LDL	Low-Density Lipoprotein
TG	Triglycerides
TC	Total Cholesterol
HbA1c	Hemoglobin A1c/ Sugar Hemoglobin
CBC	Complete Blood Count
HPLC	High-Performance Liquid Chromatography
BMI	Body Mass Index
INR	International Normalized Ratio
CAP	Controlled Attenuation Parameter
CI	Confidence Interval

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