Frequency of Left Ventricle Dysfunction in non-Alcoholic Fatty Liver Disease (NAFLD) Patients Detected by Global Longitudinal Strain and Tissue Doppler Imaging in Babylon Province in Iraq

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Abstract

The aim of the study is an assessment of left ventricle systolic and diastolic function in patients with non-alcoholic fatty liver disease (NAFLD) by measuring global longitudinal strain, and tissue Doppler imaging TDI.

Method: A Case-control study enrolled 30 patients with non-alcoholic fatty liver disease (mean age 44.13 years) without a history of cardiac disease and 30 healthy controls (mean age 44.79 years). All participants had been undergone trans-thoracic echocardiography (TTE), tissue Doppler imaging (TDI) for assessment of mitral annular systolic velocity (S`), E/A ratio, and E/e', as well as left ventricle global longitudinal strain (GLS) using speckle tracking echocardiography (STE) technique.

Results: NAFLD patients had shown The E/e' ratio was significantly higher in the NAFLD group (9.86± 1.69 vs 6.85 ±1.23),(P = < 0.001) . The difference in the E/A ratio between the groups was significant (P = 0.04). GLS was also significantly lower negative in NAFLD patients in comparison with control (-18.85± 1.07 vs -23.05 % ± 1.19) but within normal values.

Conclusion: There is an increasing risk of subclinical LV dysfunction (systolic and diastolic)in NAFLD patientscan be early confirmed by DTI and GLS.

Keywords: *Left ventricle dysfunction, non-alcoholic fatty liver disease (NAFLD), global longitudinal strain, Doppler imaging, Babylon province.*

Introduction

One of the most chronic liver diseases worldwide is a non-alcoholic fatty liver disease (NAFLD) with hepatocytes infiltration by fatty deposit, its prevalence between 25% and 30 in the united states affecting all groups of age, suggestinga serious and growing problem[1][2]. NAFLD involves a wide spectrum of liver disease inflammation coexist following simple steatosis with different stages of fibrosis reach to hepatic cirrhosis and hepatocellular carcinoma HCC. Non-alcoholic steatohepatitis (NASH) is a subtype of disease progression indicating the extreme form of NAFLD. NAFLD is significantly associated with increased morbidly and mortalitydue to cardiovascular events[1]. The dysfunction of adipose tissue there is what is calledadipokine secretion that relates to overweight and obesity which leads to a wide spectrum of diseases mainly cardiovascular disease,although some adipokines have anti-inflammatory andgive protection against cardiovascular complications.[1]. Sub-clinical defects, CAD, LV, hypertrophy, HF, HHD, and arrhythmias are found in cardiovascular

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diseases. The discharge of mixture mediators including pro-inflammatory, procoagulant, and profibrogenic mediators is involved in the association of atherogenic dyslipidemia, systemic and Hepatic insulin resistance with obesity and hypertension[2][3][4]. In addition to the history of alcohol use (the appropriate limits of alcohol intake are 70g/week for females and 140 g/week for men), the over nutrition shows central obesity, primarily overweight persons make abdomen ultrasound with fatty changes, a diagnosis of NAFLD,and diagnosis for other liver diseases should be excluded. Although alcohol consumption in low amounts can be protected from complications, the estimated mortality is 1.6-fold. The lifestyle modification through a decrease weight of > 7% is less than 50%. The control of serum lipid is important to decrease the danger of cardiovascular diseases in NAFLD[5]. Although liver biopsy is the only effective way to distinguish NASH from NASH in NAFLD, a more new development in a noninvasive way is also possible. Even In the absence of obesity which is morbid, high blood pressure and hyperglycemia, NAFLD may cause impairment of LV function whether diastolic or systolic[6]. Speckle-tracking echocardiography (STE) isa new ultrasound technique that is a non-invasive by which we can do an evaluation,quantitively or objectively for the regional and global function of the myocardium[7][8].several studies show that the GLS was significantly reduced in NAFLD [9]. The exact mechanism of LV dysfunction is not well known yet, but the mean pathophysiological landmark is the resistance of insulin secretionwhich is mainly seen in non-alcoholic fatty liver disease (NAFLD), although the same process had been seen in patients of essential hypertension [10]. In control subjects without hepatic steatosis, NAFLD patients show atherosclerosis of high prevalence [11]

Method

A case-control study, done at Marjan city Teaching hospital, echocardiography unit,with the cooperation of the GIT disease unit and radiology unit for the period from 1st January to 1stMarch 2020. The case-control study included 30 outpatients individuals aged more than 18 years old with NAFLD, 16 females and 14 males. These individuals referred from ultrasound units in Merjan Medical city accidentally found to have fatty liver changes and all of them are non-alcoholic most of them have overweight and obesity with irritable bowel syndrome or renal colic without chronic diseases. Healthy control without previous history of cardiac diseasethose are 30 include 25 females and 5 males, These individuals referred from ultrasound units in Merjan Medical city accidentally found to have fatty liver changes All patients and control underwent conventional echocardiography. The examination was established by using a “Vivid E9 echo machine from GE Healthcare Company with an M5Sc probe with multiple frequencies. The patients had been done in the left lateral position, and views and measurements had been taken according to American guidelines of Echocardiography. A 2-Dimension-speckle tracking strain and TDI had been done to 30 control and 30 of the patients. This study was done in Echo Department in Marjan teaching Medical City. The following patients were not involved in this study:

1. Diabetes Mellitus
2. Hypertensive
3. BMI > 40
4. IHD
5. CMP
6. Other CLD (chronic liver diseases)
7. History of using hepatotoxic drugs

All participants underwent 2-dimensional transthoracic echocardiography, incorporating STE using a Vivid E9 system (GE, Norway). All measurements of 2-D echocardiography were worked and analyzed by the echocardiologist who was blinded to the patient group assignment, depending on the recommendations by the American Society of Echocardiography last one [12]. The same ultrasound machine was used to acquire all echocardiograms. The function of the diastole of LV was determined by using pulse wave (PW) and TDI. By using M-mode the systolic, the dimensions of end-diastole and septal thickness of the ventricle had been calculated. ejection fraction of the left ventricle (LVEF), end-diastole and end-systole volume (EDV, ESV) had been measured with the 4-chambers and 2-chambers apical views, and the modified Simpson’s biplane method had been used, which a method acquires the benefit of the enhancement in image inequality and in the ability to see the borders of endocardium clearly in end-systolic and end-diastolic views[13].Guidelines for use TDI to assess the diastolic function: by view of apex run pulse wave of TDI to get on annular velocities of the mitral valve, place the sample view at or 1 cm through the septal and lateral mitral leaflets, sweep the speed from 50 to 100 mm/s when expiration end, the

measure reveal the mean of three or more successive cycles, the measurements start with systolic, early (e'), and late (a') velocities of diastole, to assess entire LV diastolic function, the signals of tissue doppler obtain and calculate the lateral and septal sides of the annulus of the mitral valve and their mean, to outcome relaxation of LV on mitral E velocity, e' can be utilized for correction, and E/e' ratio (a marker of left atrial (LA) pressure)can be requested to predict the pressures of LV filling. The E/A ratio <1.5 along with both E/e' ratio <15 and e' velocity >8 cm/sec was considered as the normal diastolic function[14][15][9][11]. The E/é ratio is not a precise as an index of pressures filling in persons who are normal or patients with annular calcification that is heavy, disease of the mitral valve, and pericarditis that constrictive one[16]. By taking an apical 4 chamber view (4CV), PWD was put at the mitral valve tip and then the peak of E and A wave velocity was calculated in addition to measurements of E/A ratio. So the E/e' was measured automatically from the septaland lateral part of the annulus of the mitral valve. Then "Pulmonary capillary wedge pressure (PCWP)was measured by using this formula, PCWP= (E/e´ + 4).

LV Strain using Speckle Tracking Echocardiography (STE): The deformation analysis is an analytics issue of the shape and mechanics of the ventricles through the cardiac cycle. Deformation can be categorized by the strain of myocardium, rate of strain, and torsion, every one of them refers to a parameter difference in the change of shape during contractility and relaxation[17]. The Left ventricular GLS had been measured by the use of STE at the frame rate of 50 to 70 frames/s. It is recommended to begin with an apical three-chamber view (A3C) to choose the frame matching the aortic valve closure, the reference point corresponding to end-systole. In addition to this view, apical four chambers(A4C),and two-chamber view (A2C) which is necessary to complete the assessment. The GLS was automatically measured by the echo machine as an average of strain obtained from these three views. The normal value in a healthy person is around −20%, while it is abnormal if GLS more than -18 %. On 2-dimensional echocardiography, the GLS appeared the change of the myocardial length of the left ventricle (LV) propionates in-between end-diastole and end-systole. After optimization of the quality of the image, frame rate maximization, and minimization of foreshortening, the measurement of peak mid-wall GLS was taken in the standard of three views and AFI (automated function imaging) application had been averaged.[18] Analysis of statistics was carried out using SPSS version 23. variables category were obtained as frequencies and percentages. Continuous variables were presented as (Means ± SD). The student t-test was used to compare means between two groups. Chi-square test and Fisher-exact test were used to find the association between categorical variables. A p-value of ≤ 0.05 was considered significant.

Results

In this study, the results were expressed into 2 groups; Non-Alcoholic Fatty Liver disease (NAFLD) and normal control groups. 60 individuals were enrolled in the present study. The mean age of the participants was (44.6)and (47.2) years old in the case and control groups, respectively. Among the patients with NAFLD,(16) were male and (14) were female, with (5) male and (25) female in the control group. The E/e' ratio was significantly higher in the NAFLD group (9.86± 1.69 vs 6.85 ±1.23), P ≤ 0.001). The difference in the E/A ratio between the groups was significant (P = 0.04). GLS was significantly lower negative in NAFLD patients t in comparison with control (-18.85± 1.07 vs -23.05 % ± 1.19) but within normal values. LVEF was statistically insignificant between the groups. Regarding the lipid profile, the study failed to show a significant difference in Total cholesterol, S.TG, HDL, and LDL between NAFLD and the control group.

Table 1. The demographic characteristics of the participants and lipid profile.

Study variables	Control group n=30		NAFLD n= 30		P-value
	Mean	SD	Mean	SD	
Age (Years)	44.6	9.87	47.2	11.13	0.34
BMI (kg/m^2)	25.38	1.53	28.76	4.91	0.001
Smoking	0.16	0.37	0.07	0.25	0.27

*p value ≤ 0.05 significant

Table 2. Comparison of lipid profile in each group.

	Control Group n=30		NAFLD n= 30		
Study variables	No.	%	No.	%	P-value
TG (< 150 mg/dl)	18	60%	20	66.66 %	0.9
Total cholesterol (< 200 mg/dl)	19	63%	23	76.66%	0.82
HDL (>40 mg/dl female 50 mg/dl male)	17	56.66%	19	63.33	0.89
LDL (<130 mg/dl)	21	70%	24	80%	0.87

Table 3: Comparison of left ventricle systolic and diastolic function parameters between the control group and NAFLD.

Study variables	Control n=30		NAFLD n=30		P-value
	Mean	SD	Mean	SD	
LVEF (%)	65.26 %	2.39	64.93 %	1.96	0.56
SV (ml/beat)	64.56	3.38	64.40	3.25	0.85
CO (L/min)	4.44	0.40	4.42	0.52	0.86
GLS(%)	-23.05 %	1.19	-18.85%	1.07	< 0.001
S`(cm/s)	11.41	1.14	11.93	1.36	0.11
E/A	1.46	0.33	1.27	0.78	0.22
E/e’	6.85	1.23	9.86	1.69	< 0.001

*p value ≤ 0.05 significant

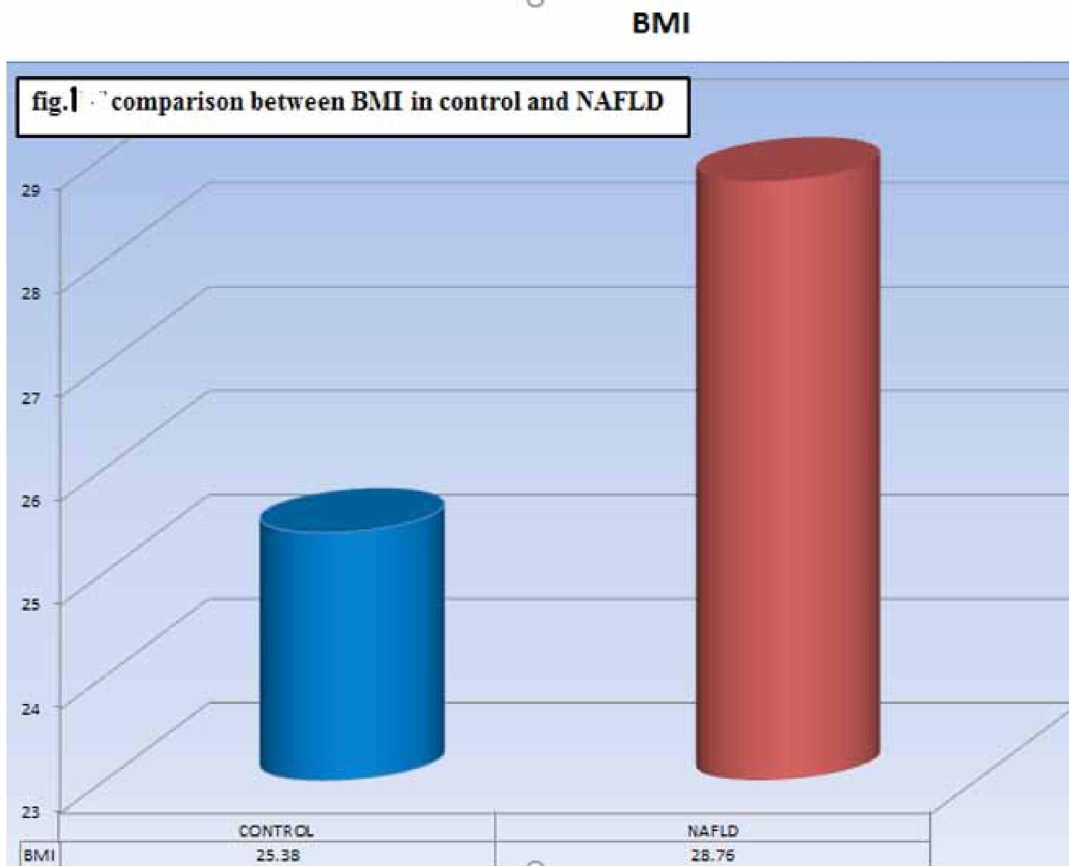

Figure 1: Comparison of BMI between NAFLD and Control group

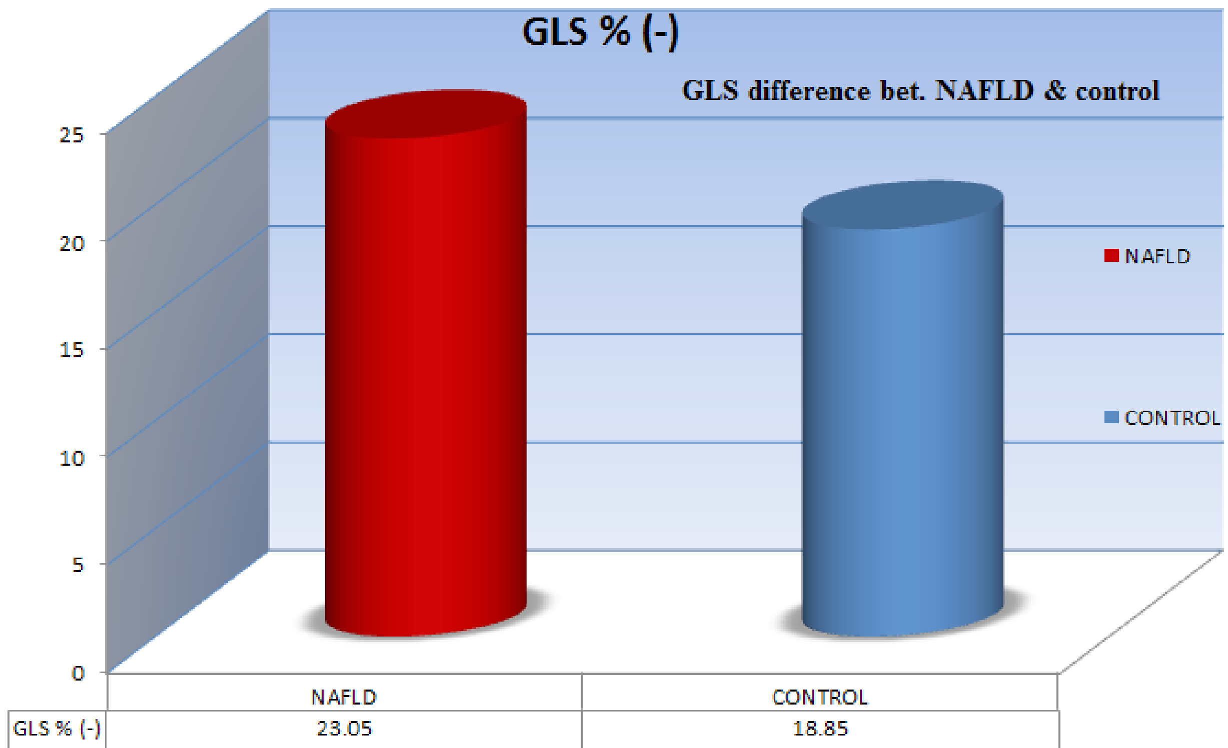

Figure 2. GLS difference between NAFLD and Control

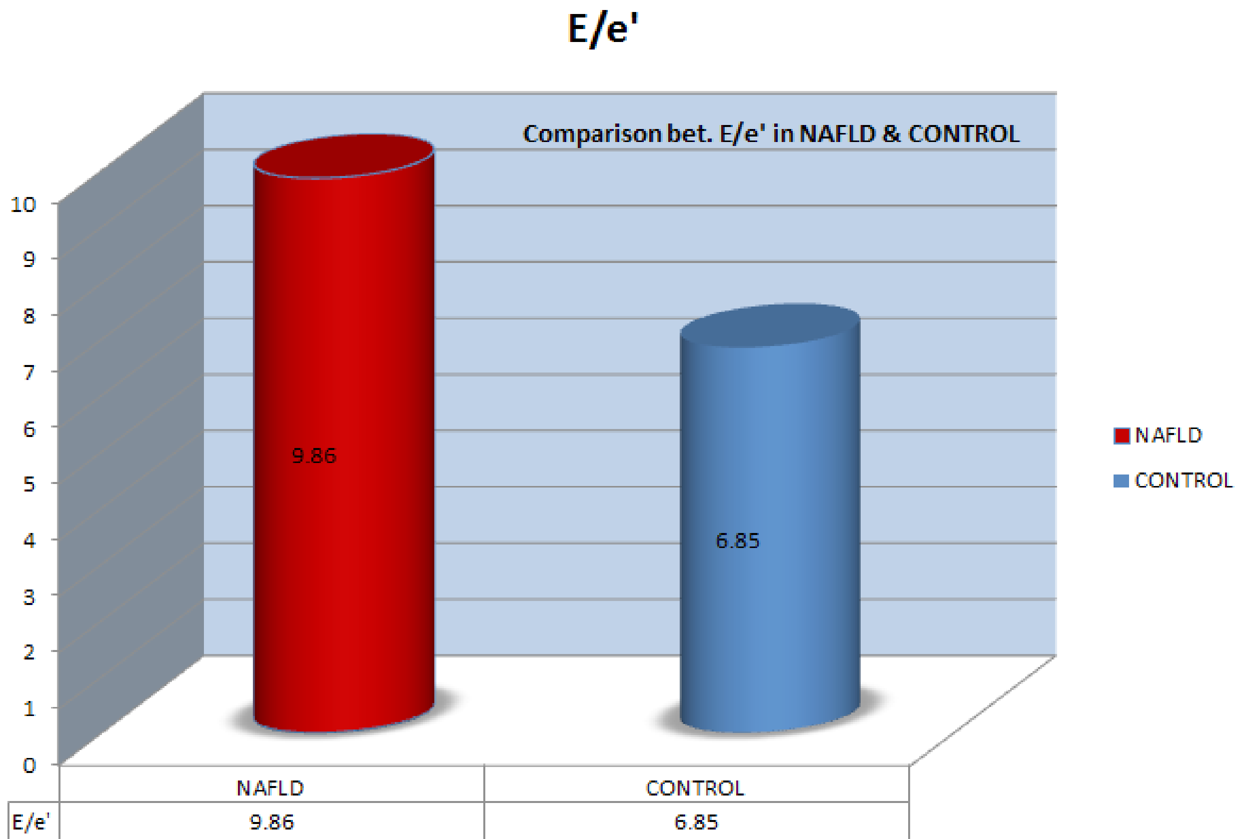

Figure 3. Comparison of E/e’ between NAFLD and Control

Discussion

In this study, there is a significant difference in GLS between NAFLD patients and the control, although there is no significant difference LVEF between both groups. and this compatible with the study done by Zamirian M, Samiee E, Moaref A, Abtahi F, Tahamtan M. 2018[8]. GLS, an indicator of systolic function, in patients with NAFLD evaluated with those without NAFLD was reduced; showing superior subclinical systolic dysfunction in NAFLD patients. This result is similar to those stated by Singh et al. and VanWagner et al. in a decreased value of GLS in adolescents and adults with NAFLD(14). The presence of LV diastolic dysfunction, including higher E/e' ratio, lower S', and e' tissue velocity in patients with NAFLD has been mentioned in previous studies using TDI, (6). However, the comparison of LVEF between the two groups did not reveal any significant difference, illustrating that the use of this conventional tool would result in missing the early stages of LV systolic dysfunction[19]. Regarding diastolic dysfunction, there is a lower E and E/A ratio in NAFLD patients, furthermore, the Vp and e'weresignificantly lowerand the last most independent parameter associate with NAFLD on multivariate analysis, that a study had been done by Goland et al at 2006[6].Aboutbody lipid deposition, in NAFLD, anepicardial fat thickness, the high one is correlated with the liver fibrosis severity, with a probable pathogenic role keepingthe ectopic fat depots with body organ damage as a whole, when compared with control but still, these changes are statistically not significant and this goes with the study done by Petta S et al at 2015[20]. In NAFLD patients, the rise in free fatty acids may lead to lipid deposition on the myocardium, with the sequelaeof the alterations in the left ventricle (LV) performance[20][21][22].

Conclusion

The 2 D Speckle tracking echocardiography by assessing GLS is a sensitive method and more valuable than the ordinary 2D echocardiography in the early detectionof subclinical LV involvement in NAFLD patients. The patients with NAFLD were provedthat have significantly lower e' velocity and higher E/e' ratio in comparison with the individual that age and sex-matched who do not have NAFLD; suggesting the adverse effects of NAFLD on diastolic indices.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: None

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