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# Comparison of Left Ventricular Function Between Patients with Non- Alcoholic Fatty Liver Disease and Healthy Individuals

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**ABSTRACT**

Non-alcoholic fatty liver disease, as an independent risk factor for development of cardiovascular events plays an increasingly prominent role worldwide.In this study, we evaluated systolic and diastolic functional parameters of left ventricles in NAFLD patients.30 normotensive, non-diabetic, non-obese NAFLD patients and 30 controls underwent laboratory examinations, liver ultrasound and finally a complete echocardiographic study including conventional, 4D and speckle tracking echocardiography. NAFLD patients had increased LAVI (30.47± 7.71 vs 25.1± 4.03, *p*=0.001) and DT (192.47±1 42.4 vs 163.13± 17.1, *p*=0.001) compared to the controls. E/A ratio was 1.12±0.24 in NAFLD patients and 1.27±0.18 in healthy individuals, *p*=0.01. LVEF% was 54.81±6.72 on 2DE and 55.83±8.03 on 4DE among patient group; and also 57.43±7.3 on 2DE, and 59.75±7.4 on 4DE among control group (*p*=0.79 and 0.59 respectively).GPSS was significantly lower in patient group in comparison with healthy individuals (18.96±2.31 vs 20.27±1.72, *p*=0.016), using speckle tracking technique.NAFLD patients have systolic and diastolic LV dysfunction even in the absence of hypertension, obesity and diabetes.

**Key words:** Non-alcoholic, NAFLD, Ventricular, Obesity and diabetes.

## INTRODUCTION

NAFLD affects approximately 30% of normal population[1-2]and this prevalence appears to be rising with obesity epidemic[3-4]. Nowadays, strong body of evidence shows that cardiovascular disease is leading cause of death in patients with NAFLD. Although a relationship between NAFLD and atherosclerosis risk factors has been established, NAFLD, per se, has a direct impact on developing atherosclerosis[5-9].

Until now, only few studies have been conducted on anatomical and functional disturbances of the heart in NAFLD patients[10-13].

In this study we investigated alterations in LV structures and function with newer techniques like speckle tracking and 4D echocardiography to determine systolic and diastolic functionin non-diabetic, normotensive, non-obese NAFLD patients.

## METHOD AND MATERIALS

The current study was carried out on 30 ultrasound-diagnosed NAFLD patients and 30 healthy controls with completely normal sonographic findings. Patients on antihypertensive medications and those who had BPe" 130/80 on three consecutive measurements at 5 minute intervals were excluded from the study. Patients

who meet the following criteria were also excluded from the study: NAFLD cases with BMI higher than 30, a history of or laboratory findings consistent with diabetes mellitus, known cases of coronary artery& valvular heart disease, patients with history of liver disease, persons with excess alcohol intake (>200 g weekly), patients under the age 19 and those aged 50 and over.

Hepatic ultrasonography was performed in all participants by a singleradiologist, who wasblinded to subjects' details. NAFLD was diagnosed based on ultrasonographic Hamagichi's criteria (scoree"2), and participants with a score of zero were included in the control group[14].

In both groups anthropometric data were measured and recorded. All study participant underwent phlebotomy after a 12-hour fast and blood samples were analyzed for FBS, Chol, TG, LDL, HDL, AST, ALT, ALP, HB and PLT.

A Comprehensive echocardiogram study, including conventional, 4D and speckle tracking echocardiography wasperformed in all study subjects by one operator, who was blinded for the clinical, laboratory and ultrasound results of the participants.

The following indexes were recorded from conventional 2D echocardiography: Ejection fraction (EF %), left ventricular internal systolic diameter (LVISD), left ventricular internal diastolic diameter (LVIDD), deceleration time (DT), E/A ratio and left atrial volume (LAV).Biplane area-length method was used to calculate LA volume. Left atrial volume index (*LAVI)* was calculated by dividing LA volume by body surface area. LV mass was calculated using the ASE formula and indexed to body surface area to obtain the LV mass index (LVMI). Left ventricular systolic function was assessed by measurement of global longitudinal peak systolic strain (GPSS) using two dimensional speckle tracking echocardiography.

**Ethical committee of Tabriz University of Medical Sciences approved this project**

All statistical analyses were performed by SPSS for Windows, version 16.0. All variables are presented as means ± SD and differences between two groups were evaluated with the *Student t test.*

**Table 1: Clinical and biochemical characteristics of the study population**

| Variables | NAFLD patients | Controls | *P* |
|---|---|---|---|
| Age(years) | 39.97±6.84 | 40.53±8.08 | 0.71 |
| Gender | | | |
| Male | 20(66.7%) | 16(53.3%) | 0.29 |
| Female | 10(33.3%) | 14(46.7%) | |
| Height [cm] | 170.93±54 | 172.03±10.57 | 0.87 |
| Weight [kg] | 79.90±10.5 | 74.4±7.08 | 0/02* |
| BMI [kg/m²] | 27.33±2.41 | 24.95±1.74 | <0.001 ð |
| WC [cm] | 101.57±8.32 | 95.9±6.24 | 0/004* |
| AST [U/L] | 33.74±16.01 | 26.5±7.27 | 0.02 ð |
| ALT [U/L] | 57.38±37.41 | 37.4±13.91 | 0.008 ð |
| ALP [U/L] | 181.23±37.55 | 170.87±44.25 | 0.33 |
| Hb [g/L] | 15.22±1.46 | 14.92±1.67 | 0.46 |
| PLT /microL | 267200±76794.57 | 258866±76176.17 | 0.670 |
| FBS [mg/dl] | 89.37±11.05 | 84.9±7.17 | 0.06 |
| TG [mg/dl] | 199.33±22.6 | 142.43±29.24 | 0.01 ð |
| Chol [mg/dl] | 191.47±40.32 | 186.13±34.03 | 0.58 |
| HDL [mg/dl] | 43.73±7.81 | 45.16±6.78 | 0.45 |

ð Statistically significant

A *P* value <0.05 was considered to be statistically significant.

## RESULTS

30 patients with NAFLD (mean age 39.97±6.84 years) and 30 controls (mean age 40.53±8.08years) were included in the study. The demographic, anthropometric and biochemical characteristics of participants are shown in Table.1.

Age, gender, height, ALP, Hb, PLT, Chol and HDL were similar between two groups, and the differences were not significant. Individuals with NAFLD hadsignificantly higher values for BMI (27.33±2.41 vs24.95±1.74, *p*<0.001) as well as WC (101.57±8.32 vs 95.9±6.24, *p*=0.004).Accordingly, compared with control subjects, those with NAFLD also had higher AST, ALT and TG values (*p*= 0.02, 0.008 and 0.01 respectively). Although the difference inFBS values was remarkable between two groups, it was not statistically meaningful.The only variable independently associated with NAFLD in multivariate analyses was BMI (CI=95%, *p*=0.001).The echocardiographic characteristics of participants are shown in Table.2.

Left atrial volume index (LAVI), Deceleration time (DT), and E/A ratio which all are representative parameters of diastolic function[15-16], were significantly different in two groups. NAFLD patients had increased LAVI (30.47± 7.71 vs 25.1± 4.03, *p*=0.001)and DT (192.47±1 42.4 vs 163.13± 17.1, *p*=0.001) compared to the controls. E/A ratio was 1.12±0.24 in NAFLD patients and 1.27±0.18 in healthy individuals, *p*=0.01.

Echocardiographic findings on LV geometry showed marked changes in NAFLD cases. Mean IVS was 0.99±0.15 in NAFLD group, and 0.89±0.13 in control group; LVPW was 0.94±0.18 and 0.85±0.12 respectively. No significant difference was observed for LVISD and LVIDD by conventional echocardiography.

Although LVESV and LVEDV measured by four-dimensional echocardiography[17-20], showed higher mean values among fatty liver patients, the difference was not remarkable (*p*=0.63 and 0.59). In the 4D study, LVM and LVMI showed significant increase in NAFLD patients (162.84±43.06 and 83.99±20.83 respectively).

LVEF% was 54.81±6.72 on 2DE and 55.83±8.03 on 4DE among patient group; and also 57.43±7.3 on 2DE, and 59.75±7.4 on 4DE among control group. LVEF% was lower in patient group

**Table 2: Echocardiographic characteristics of the study patients**

| Parameters | NAFLD patients | Controls | *P* |
|---|---|---|---|
| LAVI (ml/m²) | 30.47±7.71 | 25.1±4.03 | 0/001* |
| DT (s) | 192.47±42.4 | 163.13±17.01 | 0/001* |
| E/A Ratio | 1.12±0.24 | 1.27±0.18 | 0/01* |
| IVS (cm) | 0.99±0.15 | 0.89±0.13 | 0.01 ð |
| PW (cm) | 0.94±0.18 | 0.85±0.12 | 0.01 ð |
| LVIDD (cm) | 4.61±0.36 | 4.46±0.33 | 0.58 |
| LVISD (cm) | 3.18±0.33 | 3.08±0.3 | 0.68 |
| EF% by 2DE | 54.81±6.72 | 57.43±7.3 | 0.79 |
| EF% by 4DE | 55.83±8.03 | 59.75±5.4 | 0.59 |
| LVEDV (ml) | 88.96±19.1 | 82.57±14.34 | 0.63 |
| LVESV (ml) | 40.43±12.21 | 33.23±10.97 | 0.59 |
| LVM (g) | 162.84±43.06 | 118.9±32.98 | <0.001 ð |
| LVMI (g/cm²) | 83.99±20.83 | 65.23±11.28 | <0.001 ð |
| GPSS | -18.96±2.31 | -20.27±1.72 | 0.016 ð |

ð Statistically significant

by both 2DE and 4DE, but theEF% reduction was not statistically significant ($p$=0.79 and 0.59).

GPSS was significantly lower in patient group in comparison with healthy individuals (18.96±2.31 vs 20.27±1.72, $p$=0.016), using speckle tracking technique[21-23].

## DISCUSSION

This study revealed significant systolic and diastolic dysfunction, as well as marked structural changes of left ventricle in non-diabetic, non-obese, normotensive NAFLD patients.In our study the patient average age was 39.97±6.84 years. In order to exclude age bias on cardiac function, thepatients were selected within the age range 19 to 50. The mean age in Goland and Fotbolcu studies were 46.7±8 and 41.40±6.25 respectively[10, 13, 23].

Studies have shown that obesity per se contributes to cardiac systolic and diastolic dysfunction which seems to be mediated by several mechanisms[24, 25]; so in this study the obese adults (BMIe"30) were excluded. The mean BMI of patients in present study was 27.33±2.41 that was lower than that of 30.44±3.45 reported by Fotbolku et al. [1]p Although we tried to exclude obese participants, the mean BMI was still higher in patient group when compared to controls, which may have played a role in significant diastolic dysfunction seen in NAFLD patients(27.33±2.41 vs 24.95±1.74, $p$<0.001). Most of previous echocardiographic studies shared the same problem[10, 13].

LVPW and IVS found to be significantly higher in patients with NAFLD as compared with healthy controls. Same results observed in Goland and Fotbolku studies[10, 13].

According to our echocardiographic measurements, diastolic indices, such as LAVI, E/A, DT, all were significantly different between two groups, representing LV diastolic dysfunction in NAFLD group.Goland et al and Fotbolku et al, also reported LV diastolic dysfunction in NAFLD patients[10, 13].

In our study as well Goland study, EF% was lower among the patients with NAFLD, butthe analysis did neither reveal statistically significant results[13]. Conversely, EF% was insignificantly lower in healthy controls in Fotbolku study[10].

To date, only few studies have been conducted on structural and functional echocardiographic characteristicsin NAFLD patients. One advantage of our study was using newer and more accurate technologies, i.e. speckle tracking and 4D echocardiography, to assess cardiac function[17-22]. We demonstrated that although both conventional and 4D echocardiography showedinsignificant decrease inEF% of NAFLD patients, speckle tracking echocardiography showed a significant reduction in global peak systolic strain in patients group (-18.96±2.31 vs -20.27±1.72, $p$=0.016).The reduction in strain has been shown to denote LV systolic dysfunction. Thus, EF% fails to showearly subtle changes, and when decreased, it reflects irreversible heart damage.In this context we would need to conduct another study with larger sample size and minimizing the effects of confounding factors such as weight difference between case and control groups. Moreover, determination of optimal cut point for GPSS to screen subclinical ventricular dysfunction of NAFLD patients is necessary. Also the relation between severity of fatty liver and subsequent reduction of strain should be explored.

## CONCLUSION

NAFLD patients have systolic and diastolic LV dysfunction even in the absence of hypertension, obesity and diabetes; and speckle tracking echocardiographyis a new sensitive and non-invasive method provides useful information to detect early identification of cardiac dysfunction in asymptomatic NAFLD patients.

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