Predictive Value of Speckle Tracking Echocardiography to Detect Subclinical Cardiovascular Changes among Patients with Non-Alcoholic Fatty Liver Disease

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Background and study aim:
Considering the established correlation
between non-alcoholic fatty liver disease
(NAFLD) and cardiac abnormalities ,To
assess the relationship between fibroscanproven NAFLD and subclinical
cardiovascular changes utilizing speckletracking echocardiography (STE).

Patients and Methods: We recruited 50 patients from AL-Rajhy Hospital's Outpatient Clinic (internal medicine). Patients were diagnosed with NAFLD via abdominal ultrasound and confirmed by FibroScan. Demographic data, laboratory investigations, and anthropometric measurements were collected for all participants. Conventional echocardiography STE and were performed to assess cardiac function. CHA2DS2-VASc and ASCVD risk scores were calculated for all patients.

Results: A marked negative correlation coefficient was observed between both fibrosis and steatosis scores with STE parameters TAPSE and GLS (RV and LV). Also, it was found that both steatosis and fibrosis scores increased significantly with an increase in CHADSVASC and ASCVD scores.

Conclusion: NAFLD, even in asymptomatic adults, may serve as an independent subclinical cardiovascular dysfunction risk factor, regardless of traditional cardiovascular risk factors. STE emerges as a sensitive and critical tool for detecting early subclinical left ventricular (LV) dysfunction.

INTRODUCTION

Currently, NAFLD is presently the third most common liver transplantation indicator globally [1, 2]. Key risk factors for its development encompass obesity, dyslipidemia, type-2 diabetes mellitus (T2DM), and hypertension [3]. Fibroscan, a rapid and non-invasive tool, is frequently utilized to assess liver fibrosis and steatosis via measuring liver stiffness in cases with liver diseases [4].

NAFLD has also been linked to early subclinical abnormalities in cardiac function and structure, besides an elevated risk of LV hypertrophy and dysfunction, valvular heart disease, heart failure, arrhythmias, and coronary artery disease. There is a positive association between cardiomyopathy risk (primarily LV hypertrophy and dysfunction) and

NAFLD severity, resulting in arrhythmias and heart failure [5].

STE is a non-invasive ultrasound imaging modality employed in research to assess regional and global myocardial function. It enables the assessment of LV function in conjunction with other diastolic as well as systolic echocardiographic parameters [6]. Thus, we aimed this study to investigate STE's role in identifying subclinical cardiac alterations in NAFLD cases.

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PATIENTS AND METHODS

This observational study was performed at the outpatient clinics (Internal Medicine Department-Al-Rajhi Liver Hospital) between January 2023 and May 2025.

All patients >18 years old admitted for fatty liver assessment were included in the study.

Exclusion Criteria: Seropositivity for HIV, HCV, or HBV; autoimmune hepatitis; liver cirrhosis; being on steatosis-inducing drugs (such as amiodarone, methotrexate, high-dose estrogen, or corticosteroids within 6 months of inclusion); pre-existing malignancy, diabetes, or cardiac disease (arrhythmia heart failure, ischemic and valvular heart disease)

- All patients were subjected to the following:

A complete medical profile was obtained, including age, sex, smoking, and comorbidities. Waist circumference (WC) and BMI (kg/m2) were recorded, ECG was performed for all patients to exclude arrhythmia

Collection of blood samples: Serology, lipid profile, CBC, liver function, and autoimmune profile (HBsAg, HIV antibody, and HIV antibody(

CHA2DS2-VASc-HS

The CHA_2DS_2 -VASc score is a validated tool for predicting thromboembolic risk in atrial fibrillation patients. The acronym CHA_2DS_2 represents:

- Congestive heart failure
- Hypertension
- Age (\geq 75 years = 2 points; \geq 65 years = 1 point(
- Diabetes mellitus
- Stroke/transient ischemic attack (TIA) (2 points(

The VASc component incorporates:

- Vascular disease (peripheral arterial disease, prior myocardial infarction, aortic atheroma(
- Age (reiterated for \geq 75 years(
- Sex category (female sex (

Low risk equal 0 (male) or 1(female), moderate risk equal 1 (male), high risk equal 2 or greater [7.]

ASCVD (Atherosclerotic Cardiovascular Disease) risk score

The American College of Cardiology developed the ASCVD risk score. This calculation estimates the 10-year risk of experiencing a cardiovascular event, including strokes or heart attack. The risk estimate incorporates factors such as smoking status, age, diabetic status, medication use, race, blood pressure, cholesterol levels, and sex [8.[

NAFLD Ultrasound assessment and diagnosis

All patients received an abdominal ultrasound examination to assess two ultrasonographic parameters: steatosis grade and presence. Steatosis grading and ultrasound diagnosis were conducted in accordance with prior research [9]. The ultrasonographic assessment was conducted following an 8-hour fasting period, utilizing a real-time electronic 3.75 MHz convex-type scanner connected to a high-resolution ultrasound machine (Aplio; Toshiba Medical Systems Corporation-Tochigi-Japan .(

FibroScan assessment was conducted utilizing (Fibroscan® 502 Touch-Echosens-Paris-France). LSMs were performed following a 3-hour fasting period [10]. The cutoff value for limited fibrosis (≥F2) is 7.1 kPa, whereas that for cirrhosis (F4) is 12.5 kPa) [11 . [

Conventional transthoracic echocardiography (TTE(

Conventional TTE was performed utilizing the following systems:

- α 10 ultrasound system (SSD- α 10-Aloka Medical Systems-Tokyo-Japan) with a UST-52,105 probe (1.5–4.3 MHz.(

M-mode echocardiography from a parasternal long-axis view measuring left ventricular end systolic diameter (LVESD) and left ventricular end-diastolic diameter (LVEDD) and ejection fraction [12.[

Fractional area change (FAC) can also be assessed at the level of papillary muscles in a short axis view of the LV: FAC (%) (normal value 36–64%) [12.[

Speckle tracking echocardiography:

STE was performed utilizing a Philips epic 7 ultrasound machine to estimate GLS by averaging 18 segments from apical four-chamber (AP4), three-chamber (AP3), and two-chamber (AP2) views, with time-to-peak strain calculated for each segment.

GLS- LV : Global Longitudinal strain of the left ventricle , GLS- RV : Global Longitudinal strain of the Right ventricle were measured [13.]

Sample size and statistical analysis

The present study included 50 patients. Data coding, revision, collection, and tabulation were performed utilizing the SPSS software (Released 2015-NY: IBM Corp.Version 23.0-Armonk). Expression of quantitative data was in the form of M±SD and ranges, while qualitative variables were presented as frequencies (percentages.)

The comparison between groups concerning qualitative data was conducted utilizing the Chisquare test. The comparison of two independent groups with parametric distribution and quantitative data was conducted utilizing ANOVA and independent t-test. In addition, we assessed the association between study variables and liver stiffness using the Pearson correlation coefficient. The p-value is considered significant if it is less than 0.05.

RESULTS

Table (1) depicts the demographics of the studied patients. The subjects' mean age was 40.35 ± 10.23 between 25 and 57 years old. Most cases (60%) were females. The majority (80%) of patients came from rural areas, and only 7 (14%) patients were smokers.

The majority of patients, 30 (60%), exhibited an F1 fibrosis score, while 20 (40%) had F0 fibrosis. Controlled attenuation parameter (CAP) assessment revealed steatosis grades S0 in 23 (46%), S1 in 12 (24%), S2 in 10 (20%), and S3 in 5 (10%) patients. Ultrasonographic evaluation classified fatty liver severity as grade I in 20 (40%) (n = 20), grade II in 30% (n = 15), and grade III in 30% (n = 15) of patients (Table 2.(

Cardiovascular risk stratification (Table 3) demonstrated that 10% (n = 5), 60% (n = 30), and 30% (n = 15) of patients fell into high-, intermediate-, and low-risk ASCVD categories, respectively. Similarly, CHA₂DS₂-VASc scoring

identified 26% (n = 13) as low risk, 54% (n = 27) as moderate risk, and 20% (n = 10) as high risk.

Table 4 summarizes data from conventional echocardiography and STE among the study's patients. Fourteen (28%) patients had diastolic dysfunction, whereas 10 (20%) patients had valvular affection (Table 3.(

It was found that the grade of fatty liver increased significantly with an increase in the ASCVD score. All patients with low-risk scores had grade-I fatty liver, and all patients with high scores had grade-III fatty liver. A total of 10 (33.3%), 15 (50%), and 5 (16.7%) patients with intermediate-risk had grade-III, II, and I fatty livers, respectively (Table 5.(

It was found that the fatty liver grade increased significantly with the CHADSVASC score. The majority (77%) of patients with low-risk scores had grade-I fatty liver, and all patients with high scores had grade-III fatty liver. A total of 5 (18.6%), 12 (44.4%), and 10 (37%) patients with moderate risk had grade-III, II, and I fatty livers, respectively (Table 6.(

It was found that the fibrosis score increased significantly with the CHADSVASC score. The highest fibrosis was reported among patients with high-risk scores (11.11 \pm 2.78), and the lowest fibrosis score was noticed among patients with low-risk scores (4.22 \pm 1.33.(

Also, the degree of fibrosis was F0 among all low-risk score cases and F1 in all patients with high-risk scores. A total of 7 (25.9%) and 20 (74.1%) patients with moderate risk scores have F0 and F1 fibrosis degrees, respectively.

Also, the steatosis score increased significantly with increasing in the ASCVD score. The highest steatosis score was reported among high-risk score cases (266.17 \pm 29.10), and the lowest fibrosis score was noticed among low-risk score cases (219.11 \pm 21.45.(

The degree of steatosis increases substantially with the CHADSVASC risk score. Up to 30% of patients with a high score exhibited S3, whereas up to 84.6% of patients classified as low risk presented with S0 steatosis (Table 7.(

A significant negative correlation coefficient was observed between both fibrosis score and steatosis and speckle tracking echocardiographic parameters TAPSE and GLS (RV and LV). As

regards to atherosclerotic cardiovascular disease score revealed no significant correlation(Table 8)

Table (1): Baseline data of the studied patients

	N=50
Age (years)	40.35 ± 10.23
Range	25-57
Sex	
Male	20 (40%)
Female	30 (60%)
Residence	
Rural	40 (80%)
Urbane	10 (20%)
Obesity	
Normal N (%)	12 (24%)
Overweight N (%)	20 (40%)
Habits	
Smoking	7 (14%)
Measurements	
Waist circumference (cm)	88.09 ± 4.58
Body mass index (kg/m2)	28.09 ± 4.56

Data expressed as mean (SD), frequency (percentage).

Table (2): Assessment of LSM and CAP in studied patients

	Total (n= 50)
FibroScan assessment	
LSM (kp)	8.45 ± 2.22
F0	20 (40%)
F1	30 (60%)
CAP assessment	
Steatosis score (dm)	265.55 ± 33.79
S0	23 (46%)
S1	12 (24%)
S2	10 (20%)
S3	5(10%)
Grade of fatty liver by US	
Grade-I	20 (40%)
Grade-II	15 (30%)
Grade-III	15 (30%)

Data expressed as frequency (percentage). LSM: liver stiffness measurements; CAP: controlled attenuation parameter; US: ultrasound, S: steatosis, F: fibrosis

Table (3): Assessment of risk scores in studied patients

	Total (n= 50)
ASCVD score	
Low risk	15 (30%)
Intermediate risk	30 (60%)
High risk	5 (10%)
CHADSVASC score	
Low risk	13 (26%)
Moderate risk	27 (54%)
High risk	10 (20%)

ASCVD: Atherosclerotic cardiovascular disease

CHADSVASC : C (congestive heart failure) , H (Hypertension) , A (Age> 75 years) , D (Diabetes mellitus), S (Stroke , TIA , Systemic embolism) ,V (Vascular disease) , A (Age 65 -74 years) , S (Sex category)

Table (4): Echocardiography and speckle tracking echocardiography in patients

	Total (n= 50)
Convential echocardiography	
Ejection fraction (%)	56.78 ± 5.57
Diastolic dysfunction	14 (28%)
Valvular affection	10 (20%)
LVEDD (mm)	48.88 ± 8.78
LVESD (mm)	29.19 ± 3.10
FAC (%)	40.55 ± 3.97
TAPSE (mm)	22.18 ± 5.44
Speckle tracking	
GLS-RV (%)	21.11 ± 3.30
GLS-LV (%)	22.09 ± 2.86

Data expressed as frequency (percentage), mean (SD). FAC: fractional area change; TAPSE: tricuspid annular plane systolic excursion; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter

GLS-LV: Global Longitudinal strain of the left ventricle, GLS-RV: Global Longitudinal strain of the Right ventricle

Table (5): Degree of fatty liver based on ASCVD risk score

	Low (n= 15)	Intermediate (n= 30)	High (n= 5)	P value
Degree of fatty liver				< 0.001
Grade-I	15 (100%)	5 (16.7%)	0	
Grade-II	0	15 (50%)	0	
Grade-III	0	10 (33.7%)	5 (100%)	

Data was expressed as frequency (percentage). P value was significant if < 0.05

Table (6): Degree of fatty liver based on CHADSVASC risk score

	Low (n= 13)	Moderate (n= 27)	High (n= 10)	P value
Degree of fatty liver				< 0.001
Grade-I	10 (77%)	10 (37%)	0	
Grade-II	3 (23%)	12 (44.4%)	0	
Grade-III	0	5 (18.6%)	10 (100%)	

Data was expressed as frequency (percentage). P value was significant if < 0.05

Table (7): CHADSVASC Score according to the degree of steatosis and fibrosis:

	Low (n= 13)	Moderate (n= 27)	High (n= 10)	P value
Fibrosis scores	4.22 ± 1.33	7.89 ± 2.54	11.11 ± 2.78	< 0.001
Degree of fibrosis				
F0	13 (100%)	7 (25.9%)	0	< 0.001
F1	0	20 (74.1%)	10 (100%)	
Steatosis score	219.11 ± 21.45	249.09 ± 33.18	266.17 ± 29.10	0.001
Degree of steatosis				
S0	11 (84.6%)	10 (37%)	2 (20%)	
S 1	2 (15.4%)	7(23.3%)	3 (30%)	0.01
S2	0	8(29.6%)	2(20%)	***
S3	0	2(7.4%)	3(30%)	

Data was expressed as mean (SD), frequency (percentage). P value was significant if < 0.05

Table (8): Correlation of steatosis and fibrosis scores with other variables

	Fibrosis score	Steatosis score
TAPSE (mm)	-0.52 (0.01)	-0.49 (0.02)
GLS-RV (%)	-0.67 (0.001)	0.36 (0.01)
GLS-LV (%)	-0.45 (0.001)	0.28(0.04)
ASCVD risk score	0.67(<0.001)	0.60(<0.001)
CHADSVASC risk score	0.50(0.03)	0.28(0.04)

Data expressed as r value indicates strength of correlation and p value indicates significance of correlation. FAC: fractional area change; TAPSE: tricuspid annular plane systolic excursion; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter.

DISCUSSION

NAFLD is increasingly recognized for its association with early subclinical alterations in myocardial metabolism, cardiac structure, and function. **NAFLD** correlates with LV enlargement, impaired diastolic function. myocardial insulin resistance, abnormal cardiac energy metabolism. Nevertheless. the mechanistic pathways linking NAFLD to these cardiac abnormalities remain unclear [14.[

Numerous meta-analyses as well as systematic reviews have explored the relationship between NAFLD and cardiovascular event risk [15-17]. However, there is limited research addressing the correlation between STE, fibrosis degree, and cardiovascular risk scores (ASCVD CHADSVASC) in NAFLD patients.

This study enrolled 50 patients with NAFLD to elucidate the atherosclerotic cardiovascular risk correlated with the condition. The study also investigates the correlation between fibrosis degree and ventricular strain assessed by STE. The studied patients' mean age was 40.35 years, with females comprising up to 60% of the cohort

In concordance with our study, Karaoğlan and his colleagues [18] enrolled 61 NAFLD cases with a mean age of 44 years, and 40 (65.5%) were males, aligning with numerous prior findings [19,20,21]. Previous Egyptian studies also noticed male predominance of NAFLD [22,23,24]. NAFLD prevalence is more elevated in men compared to premenopausal women; however, this trend reverses post-menopause [25,26.]

A further finding in this study was derived from a US assessment. A total of 20 patients (40%) were classified with fatty liver grade-I, while 15 patients (30%) were categorized as grade-II and 15 patients (30%) as grade-III. Hsiao et al. conducted a study involving 600 patients diagnosed with NAFLD. In the US, a total of 499 patients (83.2%) were classified with grade-I fatty liver, 65 patients (10.8%) with grade-II, and 36 patients (6%) with grade-III fatty liver [27.]

Tissue Doppler echocardiography limitations in assessing myocardial function, primarily due to its dependence on the interrogation angle [28]. This underscores the necessity of developing an alternative imaging

technique, specifically STE, to assist clinicians in extending these limits alongside its clinical utility and reported accuracy in numerous pathologies [29.[

The present study revealed that fibrosis and steatosis scores negatively correlated with TAPSE and GLS (LV and RV) while exhibiting insignificant correlations with other echocardiographic parameters. Consistent with the aforementioned results, a prior study indicated that STE demonstrated a negative correlation between NAFLD cases and LV longitudinal systolic function despite the overall systolic ejection function not exhibiting a significant correlation (30). This observation is consistent with existing literature [31]. Singh et al. further corroborated these results, reporting substantially diminished early diastolic strain rates and LV global longitudinal systolic strain in obese individuals compared to lean controls, with further reductions in obese NAFLD individuals [32.[

GLS, a marker of systolic function, was notably lower in NAFLD patients than in non-NAFLD controls, indicating a greater subclinical systolic dysfunction degree in the NAFLD cohort. The comparison of LVEF between the two groups (NAFLD VS. Non-NAFLD) exhibited insignificant differences. This illustrates that reliance on this conventional tool may overlook the early stages of LV systolic dysfunction [33.[

The literature reveals a lack of studies assessing the ASCVD risk score in patients with NAFLD, and there is no research addressing the CHA2DS2-VASc score in this population. Our study revealed that patients with elevated ASCVD/CHA2DS2-VASc scores exhibited increased fibrosis and steatosis scores, as evaluated by fibroScan, along with an advanced fatty liver degree. Additionally, a greater degree of fibrosis and steatosis was observed in patients elevated cardiovascular risk (CHA2DS2-VASc/ASCVD score.(

Huang Y-C et al. illustrated that NAFLD cases exhibited significantly elevated ASCVD risk $(\geq 7.5\%; p < 0.001)$ in comparison to individuals without NAFLD. After controlling for cardiometabolic risk factors, the NAFLD grade among all participants and the NAFLD fibrosis score in NAFLD cases displayed a marked association with elevated ASCVD risk [34.[

Our study found a positive correlation between the CHA2DS2-VASc score and both fibrosis and steatosis scores. The majority of patients with F1 and S1 exhibited elevated CHA2DS2-VASc scores. This study represents the first examination of the CHA2DS2-VASc score in NAFLD individuals.

While this study is notable for being the first to address this issue in our locality and for determining the CHA2DS2-VASc score in NAFLD subjects, it also has several limitations. Initially, NAFLD was diagnosed in the absence of liver biopsy confirmation. A liver biopsy is considered the gold standard for diagnosing NAFLD; however, it is an invasive procedure that often causes distress and is unsuitable for asymptomatic patients. Abdominal ultrasonography demonstrated reliability and accuracy in detecting moderate to severe fatty liver.

CONCLUSION

NAFLD, even in asymptomatic adults, may serve as an independent subclinical cardiovascular dysfunction risk factor, regardless of traditional cardiovascular risk factors. STE emerges as a sensitive and critical tool for detecting early subclinical left ventricular (LV) dysfunction.

Ethical considerations: Prior to participating, all subjects provided written informed consent. The Faculty of Medicine's Ethical Committee granted the ethical approval (Assuit University-Egypt.(

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Contribution:

Lobna Abdel-Wahid , Reem Ezzat Mahdy and Sohair M.Kasem are responsible for idea of the manuscript.

Omar Mohamed Magdy and Ahmad Abdel fadeel Maghraby are responsible for data collection.

Lobna Abdel-Wahid , Reem Ezzat Mahdy , Sohair M.Kasem ,Omar Mohamed Magdy and

Ahmad Abdel fadeel Maghraby performed the statistical analysis and wrote the manuscript.

Echocardiography and speckle tracking echocardiography were performed to all patients by Salma Taha and Alaa Omar.

All authors revised the maniscrpt.

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Conflict of interest

None

HIGHLIGHTS

- Non-alcoholic fatty liver disease, diagnosed in asymptomatic adults may be a risk factor for remodeling the left ventricle over time, being associated with subclinical cardiovascular affection, regardless of the presence of other cardiovascular risk factors.
- This study showed that the new imaging technique, speckle tracking, represents both an important and sensitive tool in order to detect early subclinical dysfunction of the left ventricle, being appliable for patients diagnosed with non-alcoholic fatty liver disease. Also, we found that cardiovascular risk scores as determined by ASCVD risk score and CHADSVASC risk score were directly related to degree of fibrosis in patients with non-alcoholic fatty liver disease.

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