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Three-dimensional speckle tracking echocardiography for early detection of left ventricular dysfunction in children with non-alcoholic fatty liver diseases

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Abstract

Objectives: To detect early left ventricular dysfunction in children with non-alcoholic fatty liver disease using three-dimensional speckle tracking echocardiography. *Methods:* Forty obese children with non-alcoholic fatty liver disease were included as group I. Another 40 obese children without non-alcoholic fatty liver disease of matched age, sex, and weight were included as group II. Forty healthy controls of matched age and sex served as a control group. Anthropometric measurements, laboratory investigations, and echocardiographic examinations including three-dimensional speckle tracking echocardiography were measured for all included children. *Results:* Abnormal lipid profile was detected in children with non-alcoholic fatty liver disease. Troponin I levels were significantly higher in children with non-alcoholic fatty liver disease compared to obese children without non-alcoholic fatty liver disease and to healthy controls. Three-dimensional speckle tracking echocardiography examination revealed a significant reduction of left ventricular global longitudinal strain, circumferential strain, radial strain, and area strain in children with non-alcoholic fatty liver disease inspite of normal left ventricular fraction shortening measured by conventional echocardiography. All strains were negatively correlated with the grade of non-alcoholic fatty liver disease. *Conclusion:* Non-alcoholic fatty liver disease is associated with subclinical left ventricular dysfunction. Three-dimensional speckle tracking echocardiography can be helpful in identifying early left ventricular dysfunction in children with non-alcoholic fatty liver disease even in the presence of normal left ventricular ejection fraction.

Non-alcoholic fatty liver disease is considered nowadays the most common cause of chronic liver disease in all age groups including children due to the increased prevalence of obesity.[1] It is characterised by fatty infiltration of the liver in the absence of alcohol consumption and hence the name.[2] Non-alcoholic fatty liver disease has a wide spectrum ranging from simple steatosis to non-alcoholic steatohepatitis, which is characterised by inflammation and hepatic cellular injury that can lead to cirrhosis or hepatocellular carcinoma.[3]

Non-alcoholic fatty liver disease is associated with a higher risk of atherosclerosis, coronary heart disease, and subclinical left ventricular dysfunction as it is considered the hepatic manifestation of metabolic syndrome.[4–7] Several studies have investigated the association of non-alcoholic fatty liver disease with markers of subclinical cardiovascular disease, such as carotid artery intima-media thickness and troponin I levels, with controversial results.[8,9]

Recently, two-dimensional speckle tracking echocardiography has enabled the early detection of left ventricular dysfunction in patients with non-alcoholic fatty liver disease, even in the presence of a normal ejection fraction.[10] However, two-dimensional speckle tracking echocardiography is limited by foreshortened views, geometric modelling, and out of the plane motion of the speckles. To avoid these limitations, three-dimensional speckle tracking echocardiography was developed to provide rapid image acquisition with a shorter scan time independent of operator skills.[11] Several researchers have investigated the use of three-dimensional speckle tracking echocardiography to detect early myocardial dysfunction in adults with non-alcoholic fatty liver disease, but none have been performed in children.

This study aimed to detect early myocardial dysfunction using three-dimensional speckle tracking echocardiography in children with non-alcoholic fatty liver disease and to correlate different three-dimensional strains with variable echocardiographic and laboratory data.

Methods

This is a prospective observational case-controlled study that was performed on 40 obese children with ultrasound proven non-alcoholic fatty liver disease as group I. They were recruited from those attending the outpatient Endocrinology Clinic of the Paediatric Department at Tanta

University Hospital during the period from May 2017 to May 2019. Forty obese children, without non-alcoholic fatty liver disease, with matched age, sex and weight, were included in the study as group II. Forty healthy children with matched age and sex, but with normal weight, served as a control group. The study was approved by the Ethical Committee of our Faculty of Medicine. The patients were enrolled after obtaining informed consent from their parents.

Inclusion criteria: obese children and adolescents with ultrasound proven non-alcoholic fatty liver disease and elevated alanine aminotransferase level.

Exclusion criteria: children with other causes of fatty liver such as diabetes mellitus; children with syndromic obesity; children receiving drugs known to cause steatosis such as glucocorticoids; children with other chronic liver diseases such as viral hepatitis; children with congenital or acquired cardiac diseases; and children with any other systemic, metabolic, or genetic disease.

All included children had a full history taken and complete clinical examination. Anthropometric measurements were performed such as weight, height, waist circumference, and body mass index where body mass index equals the body weight in kilograms divided by height in square meters. Obesity was defined as body mass index ≥ 30 or body mass index $\geq$ 95th percentile for age and sex.

Laboratory investigations undertaken were:

- Liver enzymes: alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase.
- Lipid profile: total cholesterol, triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol.
- Fasting blood glucose level.
- Fasting serum insulin level: using human insulin enzyme immunoassay test kit according to manufacturer recommendations.
- Insulin resistance: was measured using the homeostasis model assessment method of insulin resistance, as estimated by the product of fasting serum glucose concentration (mmol/L) and fasting serum insulin concentration (μU/ml) divided by 22.5. Values ≥3 indicates insulin resistance.
- Serum cardiac Troponin I: using monoclonal antibody-based immunoassays specific for cardiac troponin I.

All patients were examined by abdominal ultrasound to detect the presence of liver fatty infiltration and to assess semi-quantitatively the degree of steatosis. A liver ultrasound was carried out using a convex 3.5–5.0 MHz probe. Sagittal hepatic sections that encompassed longitudinal images of the right liver lobe and the ipsilateral kidney were obtained. Hepatic ultrasound provides a good estimate of the degree or extent of hepatic steatosis present based on a series of ultrasound characteristics including hepatorenal echo contrast, liver echogenicity, visualisation of intrahepatic vessels, liver parenchyma, and the diaphragm.

Non-alcoholic fatty liver disease was graded by ultrasonography as: grade I if there is a slight diffuse increase in fine echoes in the hepatic parenchyma with normal visualisation of the diaphragm and intrahepatic vessel borders; grade II if there is a moderate diffuse increase in fine echoes with slightly impaired visualisation of the intrahepatic vessels and diaphragm; and grade III if there is an increase in fine echoes with poor or no visualisation of the intrahepatic vessel borders, diaphragm, and posterior portion of the right lobe of the liver.

Echocardiographic examinations were done for all included children using commercially available ultrasound transducer and equipment (Vivid 7 or Vivid 9, GE Healthcare, Horten, Norway) with a 3.5 MHz transducer, S7 and V3 matrix real-time three-dimensional probes. Digital loops were stored on the hard disc of the echocardiography machine and transferred to a workstation (Echo PAC PC, 113; GE, and Horten, Norway) for offline analysis.

Conventional two-dimensional echocardiography was used to measure both systolic and diastolic function of the left ventricle. Left ventricular systolic function was measured by left ventricular fraction shortening using M mode, while left ventricular diastolic function was measured by mitral inflow velocities using pulsed-wave Doppler in the apical four-chamber view. The ratio of trans-mitral early to late diastolic flow velocity (E/A ratio) was calculated.

Tissue Doppler imaging was used to measure the peak mitral annular systolic velocity, the peak early mitral annular diastolic velocity, and peak late mitral annular diastolic velocity. The ratios of mitral early to late annular diastolic velocity (E'/A' ratio) was calculated. The left ventricular myocardial performance index was also measured.

Three-dimensional speckle tracking echocardiography utilised a 3V-D matrix probe interfaced with a GE Vivid E7 or E9 ultrasound system. The three-dimensional left ventricular quantification function of Echo Pac was used to quantify the longitudinal, circumferential, radial, and area strain. Three-dimensional strain tracking is performed starting from a region of interest defined at the end-systole frame and is built up from an endocardial and an epicardial mesh. The endocardial mesh is based on the one used for the end-systolic volume measurement. The epicardial mesh is automatically generated from the epicardial mesh used in the left ventricular mass stage, by propagating it from end-diastole to end-systole. Three-dimensional strain analysis is integrated as the last step in the three-dimensional auto left ventricular quantification tools, which also includes volume and left ventricular mass measurements. The operator can correct the region of interest shape by placing attractor points to pull the nearby region of interest border towards where the user wishes it to go from the tracking results.

The primary outcome was to assess early myocardial dysfunction using three-dimensional speckle tracking echocardiography in children with non-alcoholic fatty liver disease. The secondary outcome was to correlate different three-dimensional myocardial strains with other echocardiographic, clinical, and laboratory data.

Statistical analysis

The collected data were statistically analysed using Statistical Package for the Social Sciences software version 13, SPSS Inc. Chicago, IL, USA. The quantitative data were expressed as means ± standard deviation, whereas categorical data were expressed as numbers and percentages. For categorical data, a comparison between the three groups was done using the Chi-square test (χ^2). Shapiro–Wilk test was used to assess the normality of the data. A comparison of the mean of the three groups was done using analysis of variance test for parametric data and the Kruskal–Wallis test for nonparametric data. Correlation between variables was evaluated using Pearson's correlation coefficient (r). Significance was adopted at $P < 0.05$.

The intra-observer reliability was measured by repeating the echocardiographic measurements by the same observer 1 week later. The interobserver reliability was measured by repeating the echocardiographic measurements by a second observer. Intraclass correlation coefficient was used to assess the inter- and intra-observer reliability.

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Table 1. Demographic, anthropometric measurements, and laboratory investigations in the studied groups

Variables	Group I	Group II	Control group	P value	P1	P2	P3
Age (years)	12 ± 2.7	11.1 ± 3	11.8 ± 3.2	NS			
Sex (male:female)	24:16	22:18	18:22	NS			
Height (cm)	142 ± 17.7	134.3 ± 17.6	135.5 ± 18.3	NS			
Weight (Kg)	69.9 ± 29.6	55.4 ± 21.1	36.9 ± 10.1	<0.001*	NS	<0.001*	0.011*
BMI	32.9 ± 7.2	30.1 ± 5.3	17 ± 1.9	<0.001*	NS	<0.001*	<0.001*
WC (cm)	93.2 ± 16.6	84.6 ± 17	47.3 ± 14.6	<0.001*	NS	<0.001*	<0.001*
Systolic BP (mmHg)	104.6 ± 15.7	100.3 ± 16.3	96.8 ± 11.4	NS			
Diastolic BP (mmHg)	70 ± 12.1	64.8 ± 11.5	61.5 ± 7.3	0.01*	NS	0.02*	NS
AST (U/L)	31 ± 23.3	22 ± 2.9	20 ± 11.5	NS			
ALT (U/L)	55.2 ± 13.4	28.4 ± 10.5	19 ± 7.8	<0.001*	<0.001*	<0.001*	NS
GGT (U/L)	25 ± 5.6	14 ± 4.7	11 ± 4	<0.001*	<0.001*	<0.001*	NS
Total cholesterol (mg/dl)	167.4 ± 34.1	141.6 ± 38.6	127.5 ± 31.6	<0.001*	0.03*	<0.001*	0.01*
TG (mg/dl)	166.7 ± 37.2	122.8 ± 52.8	109.9 ± 29.2	<0.001*	0.001*	<0.001*	NS
LDL (mg/dl)	122.4 ± 21.7	93.5 ± 27.8	78.6 ± 15.4	0.001*	0.02*	0.001*	0.04*
HDL (mg/dl)	40.3 ± 11.2	56.8 ± 13.3	70.9 ± 10.5	<0.001*	0.01*	0.001*	0.01*
Fasting blood sugar (mg/dl)	100.3 ± 13.3	89.1 ± 12.2	84.9 ± 12.6	0.02*	0.03*	0.01*	NS
Fasting serum insulin (mclu/ml)	15.4 ± 5.1	13.8 ± 5.2	6.9 ± 3	<0.001*	NS	<0.001*	<0.001*
HOMA-IR	5.6 ± 0.7	4.4 ± 0.8	1.5 ± 0.8	<0.001*	NS	<0.001*	<0.001*
Serum Troponin I (ng/ml)	0.12 ± 0.03	0.12 ± 0.04	0.04 ± 0.01	0.001*	NS	0.001*	0.001*
Grades of steatosis	- Grade I: 10 - Grade II:18 - Grade III:12						

P: P value of comparison between the three groups, P1: P value of group I versus group II, P2: P value of group I versus group III, P3: P value of group II versus group III.
*means significant, AST = aspartate aminotransferase; ATL = alanine aminotransferase; BMI = body mass index; BP = blood pressure; GGT = gamma-glutamyl transferase; HDL = high density lipoprotein; HOMA-IR = homeostatic model assessment of insulin resistance; LDL = low density lipoprotein; NS = non-significant; WC = waist circumference; TG = triglyceride.

Results

The demographic data of the three groups are presented in Table 1. Weight, body mass index, and waist circumference were significantly higher in group I and II compared to the control group. Furthermore, diastolic blood pressure as well as fasting serum insulin, homeostasis model assessment method of insulin resistance, and serum troponin I were significantly higher in obese children with or without non-alcoholic fatty liver disease compared to the control group ($P < 0.05$). Alanine aminotransferase, gamma-glutamyl transferase, total glycerides, total cholesterol, low-density lipoprotein, and fasting blood glucose were significantly higher in group I compared to group II and the control group. No significant difference was found between the three groups as regards age, sex, height, systolic blood pressure, or aspartate aminotransferase ($P > 0.05$). (Table 1)

Table 2 summarised the echocardiographic findings in the three groups. The three groups were comparable as regards left ventricular fractional shortening, ejection fraction, and mitral valve annulus velocity by both pulsed-wave Doppler and tissue Doppler imaging. Mitral E'/A' ratio as well as all three-dimensional cardiac strains were significantly lower in group I compared to group II and the control group, unlike the left ventricular myocardial performance index which was significantly higher in group I compared to group II and the control group. Left ventricular mass index was significantly higher in obese children with or without non-alcoholic fatty liver disease compared to the control group ($P < 0.05$).

Table 3 showed that mitral E/A ratio, as well as three-dimensional left ventricular ejection fraction, three-dimensional global longitudinal strain, three-dimensional global circumferential strain, three-dimensional global area strain, and three-dimensional global radial strain decreased with increasing grades of non-alcoholic fatty liver disease, where the highest values were in grade I and the lowest values were in grade III. In contrast, left ventricular myocardial performance index, left ventricular mass, and serum troponin I increased with increasing grades of non-alcoholic fatty liver disease, where the highest values were in grade III and the lowest values were in grade I.

Table 4 showed that all three-dimensional cardiac strains were significantly negatively correlated with grades of non-alcoholic fatty liver disease. The intra- and inter-observer reliability were excellent for different cardiac strains and the results are summarised in Table 5.

Discussion

The results of this study report the presence of subtle left ventricular dysfunction in children with non-alcoholic fatty liver disease that could be detected early by three-dimensional speckle tracking echocardiography. Regular follow up of these patients by three-dimensional speckle tracking echocardiography is therefore recommended.

In the present study, the mean values of alanine aminotransferase and gamma-glutamyl transferase were significantly higher

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Table 2. Echocardiographic data in the studied groups

Variables	Group I	Group II	Control group	P value	P1	P2	P3
Conventional echocardiography							
LV FS%	34.1 ± 5.2	35.4 ± 4.6	36 ± 4.2	NS			
LV EF%	59.6 ± 5.4	60.1 ± 4.3	62.2 ± 3.9	NS			
Mitral E/A ratio	1.2 ± 0.3	1.2 ± 0.2	1.3 ± 0.2	NS			
Tissue Doppler Imaging							
Mitral S' (cm/sec)	6.9 ± 0.8	6.6 ± 0.8	6.8 ± 0.6	NS			
Mitral E'/A' ratio	1.1 ± 0.2	1.4 ± 0.3	1.5 ± 0.2	0.01*	0.03*	0.01*	NS
LV MPI	0.57 ± 0.15	0.56 ± 0.12	0.37 ± 0.07	<0.001*	NS	<0.001*	<0.001*
3D-STE							
3D-LV EF%	61.8 ± 6	62.9 ± 6.9	63.6 ± 6.2	NS			
3D-GLS	−9.9 ± −3.9	−13.9 ± −5.7	−19.8 ± −4.3	<0.001*	<0.001*	<0.001*	<0.001*
3D-GCS	−10.0 ± −3.9	−14.4 ± −4.6	−20.6 ± −1.5	<0.001*	0.01*	<0.001*	0.001*
3D-GAS	−16.4 ± −5	−19.5 ± −8.2	−21.1 ± −3.4	0.008*	0.03*	0.001*	0.04*
3D-GRS	22.6 ± 7.1	30.2 ± 9.8	37.7 ± 5	<0.001*	0.001*	<0.001*	<0.001*
LV mass index (g/m^2)	112.2 ± 17	105.3 ± 16.1	89.8 ± 8.8	0.002*	NS	0.002*	0.001*

P: P value of comparison between the three groups, P1: P value of group I versus group II, P2: P value of group I versus group III, P3: P value of group II versus group III.
*means significant, 3D-LV EF = three-dimensional left ventricular ejection fraction; GAS = global area strain; GCS = global circumferential strain; GLS = global longitudinal strain; GRS = global radial strain; LV MPI = left ventricular myocardial performance; Mitral (S') = mitral annulus systolic velocity; NS = non-significant; STE = speckle tracking echocardiography.

Table 3. Echocardiographic parameters and troponin I levels among different grade of NAFLD

Variables	Grade I (N = 10)	Grade II (N = 18)	Grade III (N = 12)	P	P1	P2	P3
Mitral E/A	1.3 ± 0.3	1.1 ± 0.2	0.8 ± 0.1	0.001*	NS	<0.001*	0.01*
LV MPI	0.41 ± 0.11	0.53 ± 0.17	0.66 ± 0.11	0.001*	NS	<0.001*	0.04*
3D-LV EF%	64.9 ± 3	64.2 ± 3.4	57.6 ± 5.2	0.02*	NS	0.01*	0.01*
3D-GLS	−14.1 ± −2.2	−10.1 ± −2.4	−8.1 ± −3.7	<0.001*	0.002*	<0.001*	NS
3D-GCS	−13.6 ± −3.1	−9.6 ± −2.5	−6.4 ± −2.3	<0.001*	0.001	<0.001*	0.007*
3D-GAS	−21.3 ± −3.3	−17.4 ± −4.2	−12.3 ± −3.9	<0.001*	0.04*	<0.001*	0.004*
3D-GRS	29.7 ± 6.9	23.8 ± 6	15 ± 4.4	<0.001*	0.04*	<0.001*	0.001*
LV mass index	93.1 ± 13.1	98.7 ± 12	120 ± 16.5	<0.001*	NS	<0.001*	<0.001*
Troponin I	0.10 ± 0.02	0.11 ± 0.01	0.15 ± 0.02	<0.001*	NS	<0.001*	<0.001*

P: P value of comparison between the three groups, P1: P value of grade I versus grade II, P2: P value of grade I versus grade III, P3: P value of grade II versus grade III.
*means significant, 3D-LV EF = three-dimensional left ventricular ejection fraction; GAS = global area strain; GCS = global circumferential strain; GLS = global longitudinal strain; GRS = global radial strain; LV MPI = left ventricular myocardial performance; NS = non-significant; STE = speckle tracking echocardiography.

in obese patients with non-alcoholic fatty liver disease compared to obese patients without non-alcoholic fatty liver disease and healthy controls. This could be due to the presence of some degree of hepatic inflammatory reaction in children with non-alcoholic fatty liver disease with a subsequent increase of liver enzymes. This finding agrees with that reported by other investigators.[12] Interestingly, several studies revealed that elevated levels of serum gamma-glutamyl transferase are independently associated with an increased risk of heart failure and systolic dysfunction.[13–15]

Our results report an abnormally high lipid profile in children with non-alcoholic fatty liver disease compared to the control groups, similar to the results of other researchers.[16,17] An abnormally high lipid profile leads to myocardial lipid deposition and alteration of left ventricular performance and deformation.[18]

Our study showed that there was a significant increase of troponin I level in obese children with or without non-alcoholic fatty liver disease compared to the control group. This was in accordance with the results of Elsaidi et al[19] who revealed higher troponin I in obese patients compared to healthy controls denoting ongoing myocardial injury.

Left ventricular mass was significantly increased in obese children with non-alcoholic fatty liver disease compared to the control groups. The close relation between non-alcoholic fatty liver disease and left ventricular mass has been reported in several studies.[20–23] The mechanism underlying increased left ventricular mass in patients with non-alcoholic fatty liver disease could be related to the release of mediators from the inflamed liver such as endothelin-1, oxidative stress, and proinflammatory mediators, as well as the synergistic effect of obesity.[24] Higher left ventricular mass is

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Table 4. Correlation between three-dimensional different strains and other laboratory and echocardiographic data in the studied groups

	3D-GLS		3D-GCS		3D-GAS		3D-GRS	
Variables	r	P	r	P	r	P	r	P
Mitral (S')	0.047	NS	−0.032	NS	0.071	NS	0.060	NS
Mitral E'/A'	−0.116	NS	−0.094	NS	−0.001	NS	0.214	NS
LV MPI	0.188	NS	0.216	NS	−0.143	NS	−0.082	NS
LV EF	−0.105	NS	−0.134	NS	0.122	NS	0.240	NS
LV Mass index	0.014	NS	−0.017	NS	−0.162	NS	−0.001	NS
FBS	−0.168	NS	0.050	NS	0.195	NS	−0.059	NS
FSI	−0.096	NS	0.090	NS	0.161	NS	−0.161	NS
HOMA-IR	0.157	NS	0.134	NS	0.154	NS	−0.060	NS
Grades of NAFLD	−0.742	<0.001*	−0.108	0.04*	−0.502	<0.001*	−0.515	0.01*

*means significant, 3D-LV EF = three dimensional left ventricular ejection fraction; EF = ejection fraction; FBS = fasting blood sugar; FSI = fasting serum insulin; GAS = global area strain; GCS = global circumferential strain; GLS = global longitudinal strain; GRS = global radial strain; HOMA-IR = homeostatic model assessment of insulin resistance; LV MPI = left ventricular myocardial performance; Mitral (S') = mitral annulus systolic velocity; NAFLD = non-alcoholic fatty liver disease; NS = non-significant; STE = speckle tracking echocardiography.

Table 5. Intra- and inter-observer reliability for different cardiac strain

Parameters	Intra-observer reliability ICC (95% CI)	Inter-observer reliability ICC (95% CI)
3D-GLS	0.90 (087–0.97)	0.87 (0.83–0.97)
3D-GCS	0.91 (0.85–0.95)	0.90 (0.82–0.93)
3D-GRS	0.94 (0.88–0.97)	0.93 (0.88–0.96)
3D-GAS	0.93 (0.84–0.96)	0.86 (0.80–0.92)

CI = confidence interval; GAS = global area strain; GCS = global circumferential strain; GLS = global longitudinal strain; GRS = global radial strain; ICC = intraclass correlation coefficient.

associated with left ventricular diastolic dysfunction and lower E/A ratio inspite of the presence of normal ejection fraction.[6,9] This diastolic dysfunction was more with increasing grades of non-alcoholic fatty liver disease, similar to the results of Lee et al.[12] Several mechanisms are implicated in the pathophysiology of diastolic dysfunction in non-alcoholic fatty liver disease, such as increased epicardial fat thickness that has a paracrine effect on the myocardium and contributes to altered diastolic function.[25] Moreover, non-alcoholic fatty liver disease releases proinflammatory cytokines, adhesion molecules, and procoagulant factors that promote myocardial oxidative stress, fibrosis, and deposition of advanced glycation end-products with subsequent diastolic stiffness and dysfunction.[26]

However, left ventricular systolic function was normal by conventional echocardiography in obese children with non-alcoholic fatty liver disease but we have shown evidence of systolic dysfunction manifested by abnormal left ventricular three-dimensional strain. Recently, myocardial strain has been considered a sensitive measure of ventricular systolic function and can be used as an important predictor of both morbidity and mortality.[27–29] Three-dimensional myocardial strain is more sensitive than two-dimensional myocardial strain as it is angle independent, operator independent, avoids out-of-plane speckle loss, and foreshortening with shorter scan time.[11]

Our results revealed that left ventricular three-dimensional global longitudinal strain, global circumferential strain, global radial strain, and area strain were significantly lower in obese children with non-alcoholic fatty liver disease compared to obese children without non-alcoholic fatty liver disease and healthy controls. However, three-dimensional left ventricular ejection fraction was still normal. Our findings demonstrate that left ventricular systolic function is impaired long before the occurrence of any cardiac symptoms, as none of our patients had any cardiac complaints. Similarly, Karabay et al[29] reported that left ventricular global longitudinal strain and strain rate measured by two-dimensional speckle tracking echocardiography were significantly lower in patients with non-alcoholic fatty liver disease than controls. Additionally, the most affected strain was the global longitudinal strain. This could be due to the presence of longitudinal fibers in the sub-endocardium making it more sensitive to harmful factors such as ischemia.[30]

Few studies report a correlation between grades of non-alcoholic fatty liver disease and different myocardial strains. Interestingly, there was a strong negative correlation between different myocardial strains, namely three-dimensional global longitudinal strain, three-dimensional global area strain, and three-dimensional global radial strain, and grades of non-alcoholic fatty liver disease. This is in agreement with the results of Wang et al.[31] These findings demonstrate the negative impact of non-alcoholic fatty liver disease on cardiac systolic function.

Non-alcoholic fatty liver disease is one of the components of metabolic syndrome that has a negative impact on left ventricular systolic function.[32–34] Hepatic steatosis is associated with the deposition of advanced glycation end products, chronic inflammatory state, cardiac fibrosis, and insulin resistance that leads to the accumulation of free fatty acids and lipid metabolites in the myocardium (cardiac lipotoxicity) resulting in cardiac dysfunction.[12] This reinforces the importance of regular follow up of these patients by three-dimensional speckle tracking echocardiography for the early detection of cardiac dysfunction and subsequent appropriate management.

Conclusion

Non-alcoholic fatty liver disease is associated with subclinical left ventricular dysfunction. Three-dimensional speckle tracking echocardiography can be helpful in identifying early left ventricular dysfunction in children with non-alcoholic fatty liver disease, even in the presence of normal left ventricular ejection fraction.

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Conflict of interest. None.

Ethical standard statement. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees of Faculty of Medicine, Tanta University.

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