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# Speckle tracking echocardiography in Assessment of silent myocardial affection in MAFLD patients

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**Abstract**

Metabolic Associated Fatty Liver Diseases (MAFLD) is the most common liver disease which has a 25% incidence worldwide and a 31.6% prevalence in Egypt. It has been discovered that MAFLD raises the risk of cardiovascular disease. Using certain strains and specialized software, speckle-tracking echocardiography (STE) has gradually become more popular in clinical settings. Compared to traditional 2D echocardiography, STE is more sensitive and may identify slight changes in the subclinical myocardium. The aim of the work is to assess the subclinical effect of MAFLD on the myocardium. 482 subjects were included and assigned for history taking, physical examination and basic laboratory investigations. Steatosis was confirmed by transient Elastography and STE was used to detect silent myocardial affection. MAFLD group (49.2%) had significant higher E/é and left atrial diameter suggesting subclinical myocardial affection.

**Keywords:** MAFLD, non-MAFLD, BMI, HOMA-IR, hsCRP, Metabolic syndrome, TE, STE.

**Full length article** **Corresponding Author*, e-mail: dr.doaaesmat66@yahoo.com

## 1. Introduction

An alternative terminology to NAFLD was suggested in 2019 that reflects a better understanding of the disease, (MAFLD), which might be a better overall term because it represents a hepatic manifestation of systemic metabolic dysfunction [1]. MAFLD which affects around a quarter of the population worldwide with a significant health and financial burden and yet there is currently no approved therapy for it [2]. MAFLD prevalence is rising over time, mostly as a result of poor dietary habits, weight gain, and sedentary lifestyle [3]. Egypt is a Middle East that is populated to 100 million people, is regarded as one of the top ten countries with the greatest prevalence of obesity. In cross-sectional study in Egypt, results showed that 31.6% of the population had steatosis, of which 57.9% had S3 (severe) steatosis. People who are overweight or obese are more likely to develop steatosis than people who are lean. According to the study's findings, 1 in 20 Egyptians had moderate-to-advanced fibrosis and around 1 in 3 had steatosis [4]. Compared to other subjects, those with MAFLD had a noticeably greater incidence of CVD and more severe liver fibrosis. Applying the ASCVD risk score from the 2013 American College of Cardiology/American Heart Association (ACC/AHA) recommendations to assess the 10-year ASCVD risk, these findings were validated. A subject's risk of ASCVD was deemed high if their risk was greater than 10% [5]. Among patients with T2DM and greater BMI, it was found that hospitalization for heart failure (HF) and atrial fibrillation or flutter (AF/AFL) was more common [6]. Another study showed that bariatric surgery helped patients have Major Adverse Cardiovascular Events (MACE) [7]. Speckle-tracking echocardiography (STE) is an evolving technique to detect conditions such cardiomyopathy, valvular heart disease and ischemic heart disease. It detects LV myocardial strain using LV regional and global deformation as an indicator of elasticity and contractility in response to force [8]. Compared to standard echocardiographic measures that examine cardiac function based on blood volume in the cardiac chamber, such as ejection fraction (EF), STE provides significant value to traditional 2D echocardiography because it can assess heart function based on the direct measurement and quantification of myocardial deformation [9]. Thanks to this objective assessment of cardiac deformation, STE examination is substantially more sensitive and may identify slight changes in subclinical myocardium and valve dysfunction [8].

The STE Principle states that the technique is usually used to assess the amount of myocardial deformation, or strain, or the lengthening, shortening, and thickening of cardiac fibers. Strain may be computed by following the "speckles," or spots, in grayscale echocardiogram images that correspond to the back scatters of cardiac fibers using specialist software. The fractional length (L) variation between the systolic and diastolic phases is how strain is measured [8]. Depending on whether heart chambers are evaluated, the left atrium (LA), left ventricle (LV), right atrium (RA), or right ventricle (RV), as well as the orientation of the myocardial fibers, are the parameters for the STE strain analysis. Left Ventricular Strain: In clinical practice, global longitudinal strain, or GLS, is the most often utilized metric. LV GLS serves as a gauge for LV contraction and is indicative of the longitudinal axis myocardial fiber length change [10].

## 2. Subjects and methods

This study was a cross section study among health care workers of Beni-Suef University Hospital.

### *2.1. Inclusion criteria*

Adult subjects, both males and females who approved to be included in the study.

### *2.2. Exclusion criteria*

Subjects who were lost or missed the basic laboratory evaluation, fibro-scan or STE.

### *2.3. Methods*

All included participants were subjected to the following:

#### *2.3.1. Detailed history taking*

Detailed history taking of age, sex, smoking, drug intake, history of diabetes mellitus or hypertension, history of concomitant hepatic and cardiovascular disorders, history of the life style and regularity of physical activity. Physical activity was assessed by application of WHO definitions of physical activity status (minimum 150 minutes / week of moderate intensity aerobic physical activity according to World Health Organization guidelines in 2010 [11].

#### *2.3.2. Clinical Examination*

Vital signs and anthropometric measurements (including waist circumference and BMI). Subjects whom BMI below 25 kg/m$^2$ and fulfilling the diagnostic criteria for MAFLD were considered to be lean MAFLD [12].

#### *2.3.3. System examination*

Chest, cardiac and abdominal, examination with special emphasis on manifestations of hyperlipidemia (such as central abdominal obesity).

#### *2.3.4. Laboratory tests*

- Subjects were asked to be fasting for 8-10 hours before testing to ensure accurate results for lipid profile.
- CBC with differential count (Hemoglobin, total leukocytic count with differential, platelet count), lipid profile (total Cholesterol, TG, HDL-c, LDL-c), liver function test: ALT, AST, serum albumin, serum total bilirubin, INR, HCV antibodies and highly sensitive CRP (hsCRP) which is more sensitive to predict CVD and atherosclerosis risk than conventional CRP [13].

#### *2.3.5. After ASCVD 10-year risk score calculation*

After calculating the ASCVD 10-year risk score, people were initially classified according to their predicted risk: 5% to 7.5% represented borderline risk, 7.5-20% represented intermediate risk, and ≥20% represented severe risk in the 10-year ASCVD risk spectrum [14].

#### *2.3.6. Transient elastography study*

The degree of fibrosis and steatosis of the liver was evaluated using fibroscan. The fibroscan 502 (Echosens, Paris, France) was used to scan each patient. Medium probe (M probe) was used and XL probe was used with obese subjects. Results were considered credible only if they had 10 accurate shots and an interquartile range (IQR)/median liver stiffness ratio of 30%. The subjects were lying on their backs with their right arm lifted behind their heads as LSM and CAP were obtained from the same area of the liver parenchyma (between 25 and 65 mm in depth). The final CAP and LSM values are expressed in decibels per meter (dB/m) and kilopascals (Kpa), respectively. The CAP values for S0, S1, S2, and S3 were respectively <248dB/m (less than 10% steatosis), <268dB/m (10% to <33% steatosis (mild), <280dB/m (33% to <66% steatosis (moderate), and ≥280dB/m (more than 66% steatosis). Fibrosis staging (F0–F4) was determined using cut-off values for transient elastography associated with the Meta-analysis of Histological Data in Viral Hepatitis (METAVIR) scoring system. LSM <7.9kPa for F0–F1, 7.9 to <8.8kPa for F2, 8.8 to <11.7kPa for F3, and ≥11.7kPa for F4 [4].

#### *2.3.7. Speckle tracking echocardiography (STE)*

STE was done to detect sub clinical myocardial disorders. By assessing LV regional and global deformation in response to force as an indicator of contractility and elasticity, it estimates LV myocardial strain. In accordance with the guidelines provided by the American Society of Echocardiography, the chamber size, wall thickness, and ejection fraction were measured [15]. Using wall motion 2-dimensional tracking software, the STE pictures for myocardial strain and strain rate measurements were examined on a 16-segment basis for the LV mid wall layer. For offline analysis, three cardiac cycles were captured from each perspective. The change in segment length was used to determine strain, and the highest systolic value would be noted. Using speckle tracking software technology, a team of expert cardiologists at Beni-Suef University Hospital measured diastolic dysfunction, ejection fraction, global long strain (GLS), left atrial diameter, valvular function, and E/é, the ratio between mitral inflow velocity and mitral annular early diastolic velocity. The echocardiography study excluded twelve people; those who were very obese and had a poor heart view on examination, as well as those who had a moderate to severe valve lesion or dysfunction.

### *2.4. Statistical methods of analysis*

For statistical analysis, data were collected and calculated. SPSS version 25 (Statistical Package for Social Science) for Windows was used to analyze the data.

For parametric data, the quantitative variables were described as the mean and standard deviation (SD). Numbers (No.) and percentages (%) were used to describe the qualitative factors. Mann Whitney U test was used to compare between the subgroups regarding non-parametric scale variables while independent T test was used to compare between groups regarding normally distributed variables. The significance of the results was assessed in the form of P-value that was differentiated into: Non-significant when P-value > 0.05 and significant when P-value ≤ 0.05.

**3. Results and Discussion**

Our study was a cross-sectional analytical study on healthcare workers at Beni-Suef University hospitals to evaluate the silent myocardial disorders associated with MAFLD. In our study MAFLD prevalence was 49.2% among the included group. This result goes with the cohort study of Petta et al., (2018) who found the prevalence of the NAFLD was 48% of his study group [16]. Our study discovered that MAFLD group showed significantly higher smokers' prevalence (21.9%) than non-MAFLD group (11.1%) (p <0.001) and this result is explained by the fact that active smoking and BMI had a synergistic effect on the risk of prevalent MAFLD [17]. Our study showed significant differences between the two groups regarding physical activity. It was found that 50.2% of MAFLD group were physically inactive vs. 19.6% of non-MAFLD group were inactive. This could be explained by the fact that lack of physical activity and sedentary life are associated with more metabolic comorbidities and more MAFLD. Our results are similar but slightly higher than the results of Golabi et al., (2020), who also found that 46.3% of the NAFLD group were physically inactive [18].

Vilar-Gomez et al., (2020) also found that the NAFLD risk was lower in physically active versus inactive participants [19]. Our study showed a significant higher mean BMI in MAFLD group than non-MAFLD group of 34.70±7.07 kg/m$^2$ Vs. 27.75±4.21 kg/m$^2$ (p <0.001). This BMI mean is similar to the study of Hudert et al., (2018), when they found mean BMI of 34.7 ± 6.2 kg/m$^2$ in NAFLD patients of their study [20]. Our study showed that 61.2% of MAFLD group had comorbidities and 27.4% of them have T2DM. Younossi et al., (2016) found similar but slightly lower results that about 23% of patients with NAFLD of their study also have T2DM [21]. Glass et al., (2019) found high prevalence rates of comorbidities in MAFLD group (Obesity 60-90%, T2DM 70%, 53% metabolic syndrome, OSA 2-3 times than normal and CKD) [22]. Our study demonstrated that 40.1% of MAFLD subjects have HTN which is significantly higher than non-MAFLD group (6.9%) (p < 0.001). This goes with Ng, et al. study which documented that HTN is affecting up to 40% of individuals with NAFLD [23]. Nine patients of the MAFLD group (3.8%) had history of cardiac disorders vs. no subjects of the non-MAFLD group. This agrees with Margariti et al., (2012), who found that cardiac disorders of coronary artery disease were (4%) in NAFLD group [24]. Our study MAFLD group showed to have higher rates of TG, LDL-C, serum ALT and AST, with lower rates of HDL-C than non-MAFLD group with statistically significant differences (p < 0.05).

These results are similar to a study which found The NAFLD group had higher ALT, AST, TG, LDL-C, and lower HDL-C than the non- NAFLD group [25]. Our study showed that 159 (67.1%) patients of MAFLD group had dyslipidemia vs. 70 (28.6%) subjects of non-MAFLD group with statistically significant difference (p < 0.001). Martin et al., (2022) study showed similar rates of dyslipidemia in NAFLD patients (69%) when they analyzed 86 studies with patients with NAFLD from 22 countries [26]. Zhang and Lu in 2015 suggested that 20–80% of NAFLD patients may have dyslipidemia in comparison to the healthy controls (37.8 vs. 2.3 %) (P < 0.001 [27-28]. Our study showed that MAFLD group had a higher risk for CVD affection than non-MAFLD determined by hsCRP test mean level with significant differences between the two groups 1.58±3.23 in MAFLD and 0.57±0.51 in non-MAFLD group (p <0.001). This agrees with Kumar et al., (2020) study, that concluded that the levels of hs-CRP were significantly higher in patients with NAFLD when compared to the control group [29]. Our study mean CAP of all subjects was 243.03±64.49. This goes with Khan, et al., (2020) study, which showed the mean of FibroScan CAP was 245.82±50.89. 137 subjects (57.8%) of our MAFLD group were diagnosed to have severe steatosis (S3) by fibroscan [30]. This agrees with Tomah et al., (2021) study who found 57.9% of their NAFLD group also had S3 (severe) steatosis [4].

Our LSM results among the MAFLD group showed 3.0% of the group are F2 and 5.5% are F3, this agrees with Tomah, et al. who found 5% of subjects had transient elastography values equivalent to METAVIR F2-F3 fibrosis [4]. Fibroscan LSM results together with real time elastography concluded that fibrosis was significantly higher in MAFLD group more than non-MAFLD group (p < 0.001). This agrees with Abdu et al., (2020), who found that stages of fibrosis in NAFLD patients significantly higher than in the control group (P = 0.001) [31]. Our study revealed that ASCVD 10 years risk score was significantly higher in the MAFLD group than the non-MAFLD group (p < 0.001). This agrees with Jitrukthai et al., (2022) study, who found also that ASCVD in NAFLD group was significantly higher than non-NAFLD group (p = 0.003) [32]. When we conducted speckle tracking echocardiography on both groups it turned out that MAFLD group had significantly higher LV relaxation and filling pressures (E/e′ ratio), higher left atrial diameter and lower EF% than non-MAFLD group (p <0.001, p <0.001 and p < 0.008 respectively). This agrees with another study which concluded that NAFLD participants had relative wall thickness, LV mass and incident LV hypertrophy (p < 0.02). NAFLD participants had higher LV filling pressures (E/e′ ratio) and impaired LV relaxation, with lower LV ejection fraction (p < 0.01) [33].

**Table 1:** Classification of the included subjects.

| | | Frequency | Percent |
|---|---|---|---|
| **Non-MAFLD (245) 50.8%** | Normal | 62 | 12.90% |
| | Overweight | 128 | 26.60% |
| | Obese | 55 | 11.40% |
| **MAFLD (237) 49.2%** | Non lean-MAFLD | 210 | 43.50% |
| | Lean MAFLD | 27 | 5.60% |
| **Total (100%)** | | **482** | **100%** |

**Table 2:** Demographic, anthropometrics and comorbidities.

| Items | MAFLD (no=237) | Non MAFLD (no=245) | Total | P-value |
|---|---|---|---|---|
| **Age** (mean ±SD) | 45.60±8.78 | 39.51±9.29 | 42.50±9.54 | <0.001* |
| **Sex**<br>Males<br>Females | <br>126 (53.2%)<br>111 (46.8%) | <br>116(47.3%)<br>129(52.7%) | <br>242 (50.2%)<br>240 (49.8%) | 0.118 |
| **Smoking**<br>Non-smokers<br>Smokers | <br>185 (78.1%)<br>52 (21.9%) | <br>217 (88.9%)<br>27 (11.1%) | <br>402 (83.6%)<br>79 (16.4%) | <0.001* |
| **Physical activity**<br>Sufficient<br>Insufficient | <br>118 (49.8%)<br>119 (50.2%) | <br>197 (80.4%)<br>48 (19.6%) | <br>315 (65.4%)<br>167 (34.6%) | <0.001* |
| **BMI** (mean ±SD) | 34.70±7.07 | 27.75±4.21 | 31.17±6.75 | <0.001* |
| **Waist circumference** (mean ±SD) | 104.91±16.52 | 87.71±13.41 | 96.15±17.30 | <0.001* |
| **SBP** (mean ±SD) | 127.05±12.62 | 120.78±7.76 | 123.86±10.89 | <0.001* |
| **DBP** (mean ±SD) | 82.52±8.70 | 79.43±4.56 | 80.95±7.08 | <0.001* |
| **DM** | 65 (27.4%) | 6 (2.4%) | 71 (14.7%) | **<0.001*** |
| **HTN** | 95 (40.1%) | 17 (6.9%) | 112 (23.2%) | **<0.001*** |
| **HCV** | 16 (6.8%) | 18 (7.3%) | 34 (7.1%) | 0.470 |
| **Cardiac** | 9 (3.8%) | 0 (0.0%) | 9 (1.9%) | **0.002*** |

**Table 3:** Laboratory investigations of the included subjects.

| | | N | Mean± Std. Deviation | Sig. |
|---|---|---|---|---|
| **Hemoglobin (gm./dl)** | MAFLD | 237 | 12.53±1.57 | **.039*** |
| | non-MAFLD | 245 | 12.82±1.48 | |
| | Total | 482 | 12.67±1.53 | |
| **WBCsx10$^3$** | MAFLD | 237 | 6.92±2.28 | .336 |
| | non-MAFLD | 245 | 6.74±1.86 | |
| | Total | 482 | 6.83±2.08 | |
| **PLTx10$^3$** | MAFLD | 237 | 271.37±78.49 | .119 |
| | non-MAFLD | 245 | 282.14±72.79 | |
| | Total | 482 | 276.84±75.76 | |
| **Cholesterol (mg/dl)** | MAFLD | 237 | 192.73±38.90 | .000* |
| | non-MAFLD | 245 | 164.94±35.37 | |
| | Total | 482 | 178.60±39.63 | |
| **TG (mg/dl)** | MAFLD | 237 | 155.14±76.51 | .000* |
| | non-MAFLD | 245 | 111.65±47.18 | |
| | Total | 482 | 133.04±66.90 | |
| **HDL-C (mg/dl)** | MAFLD | 237 | 44.00±10.78 | .015* |
| | non-MAFLD | 245 | 46.06±7.63 | |
| | Total | 482 | 45.05±9.36 | |
| **LDL-C (mg/dl)** | MAFLD | 237 | 104.38±37.89 | .000* |
| | non-MAFLD | 245 | 84.79±26.90 | |
| | Total | 482 | 94.42±34.17 | |
| **hsCRP (mg/dl)** | MAFLD | 237 | 1.58±3.23 | .000* |
| | non-MAFLD | 245 | 0.57±0.51 | |
| | Total | 482 | 1.07±2.35 | |
| **ALT (U/L)** | MAFLD | 237 | 28.29±14.28 | .000* |
| | non-MAFLD | 245 | 21.78±10.30 | |
| | Total | 482 | 24.98±12.82 | |
| **AST (U/L)** | MAFLD | 237 | 30.79±14.36 | .000* |
| | non-MAFLD | 245 | 24.15±10.04 | |
| | Total | 482 | 27.41±12.78 | |

**WBCs**: White blood cells, **PLTs**: Platelets, **TG**: Triglycerides, **HDL**: High density lipoproteins, **LDL**: Low density lipoproteins, **hsCRP**: Highly sensitive C reactive protein, **ALT**: Alanine transaminase, **AST**: Aspartates transaminase.

**Table 4:** Transient elastography results.

| | | Diagnosis | | Total | P- value |
|---|---|---|---|---|---|
| | | **MAFLD (237)** | **non-MAFLD (245)** | | |
| **LSM** | F0/F1 | 209 | 236 | 445 | 0.002* |
| | | 88.2% | 96.3% | 92.3% | |
| | F2 | 7 | 0 | 7 | |
| | | 3.0% | 0.0% | 1.5% | |
| | F3 | 13 | 3 | 16 | |
| | | 5.5% | 1.2% | 3.3% | |
| | F4 | 8 | 6 | 14 | |
| | | 3.4% | 2.4% | 2.9% | |
| **CAP** | S0 | 0 | 219 | 219 | 0.001* |
| | | 0.0% | 89.3% | 45.4% | |
| | S1 | 17 | 15 | 32 | |
| | | 7.2% | 6.1% | 6.6% | |
| | S2 | 83 | 8 | 91 | |
| | | 35.0% | 3.2% | 18.8% | |
| | S3 | 137 | 3 | 140 | |
| | | 57.8% | 1.2% | 29.0% | |

**Table 5:** ASCVD score of the included subjects.

| | | **N.** | **Mean** | **SD** | | **p-value** |
|---|---|---|---|---|---|---|
| **ASCVD** | MAFLD | 237 | 6.4 | 9.1 | 0-<5% low risk<br>5%-<7.5% borderline risk<br>7.5%-<20% intermediate risk<br>≥20% high risk | **0.001*** |
| | Non- MAFLD | 245 | 2.4 | 4.1 | | |
| | Total | 482 | 4.4 | 7.3 | | |

**Table 6:** Speckle tracking echocardiography inputs of the included echocardiography groups.

| | | Number | Mean | SD | p-value |
|---|---|---|---|---|---|
| **E/é** | **MAFLD** | 226 | 7.13 | 2.17 | **0.001*** |
| | **non-MAFLD** | 244 | 6.55 | 1.42 | |
| | **Total** | 470 | 6.83 | 1.84 | |
| **Left Atrial diameter** | **MAFLD** | 226 | 3.24 | 0.34 | **0.001*** |
| | **non-MAFLD** | 244 | 3.16 | 0.16 | |
| | **Total** | 470 | 3.20 | 0.27 | |
| **GLS** | **MAFLD** | 226 | 18.75 | 1.83 | 0.381 |
| | **non-MAFLD** | 244 | 18.89 | 1.64 | |
| | **Total** | 470 | 18.83 | 1.73 | |
| **EF%** | **MAFLD** | 226 | 65.58 | 5.57 | **0.008*** |
| | **non-MAFLD** | 244 | 66.91 | 5.27 | |
| | **Total** | 470 | 66.27 | 5.45 | |

## 4. Conclusions:

Our work evaluated the silent myocardial affection of MAFLD patients among health care workers in Beni-Suef university hospitals through screening protocol. There were 482 subjects screened for MAFLD using fibroscan, with 49.2% of them were diagnosed as MAFLD. MAFLD group had significant higher comorbidities; such as HTN and cardiac disease than non-MAFLD group. MAFLD group had higher silent cardiac affection when assessed by speckle tracing echocardiography. They had significant lower EF, higher LV filling dysfunction and higher LA diameter than non-MAFLD group.

## References:


[1] M. Eslam, R. Alvani, G. Shiha. (2019). Obeticholic acid: towards first approval for NASH. The Lancet. 394 (10215): 2131-2133.

[2] M. Eslam, A. J. Sanyal, J. George, A. Sanyal, B. N. Tetri, C. Tiribelli, D. E. Kleiner, E. Brunt, E. Bugianesi, H. Y. Järvinen, H. Grønbæk, H. C. Pinto, J. George, J. Fan, L. Valenti, M. Abdelmalek, M. R. Gomez, M. Rinella, M. Arrese, M. Eslam, P. Bedossa, P. N. Newsome, Q. M. Anstee, R. Jalan, R. Bataller, R. Loomba, S. Sookoian, S. K. Sarin, S. Harrison, T. Kawaguchi, V. W. S. Wong, V. Ratziu, Y. Yilmaz, Z. Younossi. (2020). MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology. 158 (7): 1999-2014.

[3] J. Paul. (2020). Recent advances in non-invasive diagnosis and medical management of non-alcoholic fatty liver disease in adult. Egyptian Liver Journal. 10 (1): 1-18.

[4] S. Tomah, O. Hamdy, M. M. Hamdy, A. H. Hassan, N. Alkhouri, M. R. Al-Badri, H. Gardner, A. H. Eldib, E. A. Eid. (2021). Prevalence of and risk factors for non-alcoholic fatty liver disease (NAFLD) and fibrosis among young adults in Egypt. BMJ open gastroenterology. 8 (1): e000780.

[5] Y. Kim, E. Han, J. S. Lee, H. W. Lee, B. K. Kim, M. K. Kim, H. S. Kim, J. Y. Park, D. Y. Kim, S. H. Ahn, B. W. Lee, E. S. Kang, B. S. Cha, Y. H. Lee, S. U. Kim. (2022). Cardiovascular risk is elevated in lean subjects with nonalcoholic fatty liver disease. Gut and liver. 16 (2): 290.

[6] K. Oyama, I. Raz, A. Cahn, J. Kuder, S. A. Murphy, D. L. Bhatt, L. A. Leiter, D. K. McGuire, J. P. H. Wilding, K. S. Park, A. Goudev, R. Diaz, J. Špinar, I. A. M. G. Nilsson, O. Mosenzon, M. S. Sabatine, S. D. Wiviott. (2022). Obesity and effects of dapagliflozin on cardiovascular and renal outcomes in patients with type 2 diabetes mellitus in the DECLARE–TIMI 58 trial. European heart journal. 43 (31): 2958-2967.

[7] A. Sutanto, C. D. K. Wungu, H. Susilo, H. Sutanto. (2021). Reduction of major adverse cardiovascular events (MACE) after bariatric surgery in patients with obesity and cardiovascular diseases: a systematic review and meta-analysis. Nutrients. 13 (10): 3568.

[8] K. Sato, J. Chan, V. Appadurai, N. Obonyo, L. S. Hoe, J. Y. Suen, J. F. Fraser. (2022). Exploration of the utility of speckle-tracking echocardiography during mechanical ventilation and mechanical circulatory support. Critical Care Explorations. 4 (4).

[9] L. P. Badano, T. J. Kolias, D. Muraru, T. P. Abraham, G. Aurigemma, T. Edvardsen, J. D.

Hooge, E. Donal, A. G. Fraser, T. Marwick, L. Mertens, B. A. Popescu, P. P. Sengupta, P. Lancellotti, J. D. Thomas, J. U. Voigt, Industry representatives. (2018). Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. European Heart Journal-Cardiovascular Imaging. 19 (6): 591-600.

[10] C. Johnson, K. Kuyt, D. Oxborough, M. Stout. (2019). Practical tips and tricks in measuring strain, strain rate and twist for the left and right ventricles. Echo Research & Practice. 6 (3): R87-R98.

[11] Y. J. Yang. (2019). An overview of current physical activity recommendations in primary care. Korean journal of family medicine. 40 (3): 135.

[12] W. Wang, J. Ren, W. Zhou, J. Huang, G. Wu, F. Yang, S. Yuan, J. Fang, J. Liu, Y. Jin, H. Qi, Y. Miao, Y. Le, C. Ge, X. Qiu, J. Wang, P. Huang, Z. Liu, S. Wang. (2022). Lean non-alcoholic fatty liver disease (Lean-NAFLD) and the development of metabolic syndrome: A retrospective study. Scientific reports. 12 (1): 10977.

[13] A. Alkinain, K. E. A. Abdelsalam, A. F. Mannaa. (2022) Role of High Sensitivity C-Reactive Protein (HS-CRP) as a Predictive Marker for Coronary Heart Disease Compared to Troponin I Disease in Sudanese Patients in Khartoum State. Journal of MAR Pathology. 1 (1): 1-14.

[14] K. Arps, R. Blumenthal, S. Martin. (2018). New aspects of the risk assessment guidelines: practical highlights, scientific evidence and future goals. American College of Cardiology. 1-11.

[15] Q. Wang, W. Ma, J. Xia. (2018). Nonalcoholic fatty liver is associated with further left ventricular abnormalities in patients with type 2 diabetes mellitus: a 3-dimensional speckle-tracking study. Journal of Ultrasound in Medicine. 37 (8): 1899-1911.

[16] S. Xia, V. D. Marco, R. M. Pipitone, S. Pipitone, C. Buscemi, A. Craxì, S. Buscemi. (2018). Prevalence and severity of nonalcoholic fatty liver disease by transient elastography: genetic and metabolic risk factors in a general population. Liver international. 38 (11): 2060-2068.

[17] U. Nivukoski, M. Niemelä, A. Bloigu, R. Bloigu, M. Aalto, T. Laatikainen, O. Niemelä. (2020). Combined effects of lifestyle risk factors on fatty liver index. BMC gastroenterology. 20 (1): 1-10.

[18] P. Golabi, L. Gerber, J. M. Paik, R. Deshpande, L. de Avila, Z. M. Younossi. (2020). Contribution of sarcopenia and physical inactivity to mortality in people with non-alcoholic fatty liver disease. JHEP Reports. 2 (6): 100171.

[19] E. Vilar-Gomez, R. Vuppalanchi, S. Gawrieh, M. Ghabril, R. Saxena, O. W. Cummings, N. Chalasani. (2020). Vitamin E improves transplant-free survival and hepatic decompensation among patients with nonalcoholic steatohepatitis and advanced fibrosis. Hepatology. 71 (2): 495-509.

[20] C. A. Hudert, H. Tzschätzsch, J. Guo, B. Rudolph, H. Bläker, C. Loddenkemper, W. Luck, H. P. Müller, D. C. Baumgart, B. Hamm, J. Braun, H. G. Holzhütter, S. Wiegand, I. Sack. (2018). US time-harmonic elastography: detection of liver fibrosis in adolescents with extreme obesity with nonalcoholic fatty liver disease. Radiology. 288 (1): 99-106.

[21] Z. M. Younossi, A. B. Koenig, D. Abdelatif, Y. Fazel, L. Henry, M. Wymer. (2016). Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 64 (1): 73-84.

[22] L. M. Glass, C. M. Hunt, M. Fuchs, G. L. Su. (2019). Comorbidities and nonalcoholic fatty liver disease: the chicken, the egg, or both? Federal Practitioner. 36 (2): 64.

[23] C. H. Ng, Z. Y. Ng, N. W. Chew, K. E. Chan, J. Xiao, N. Sayed, W. H. Lim, D. J. H. Tan, R. W. K. Loke, P. W. L. Tay, J. N. Yong, G. Kong, D. Q. Huang, J. W. Wang, M. Chan, M. Dalakoti, N. Tamaki, M. Noureddin, M. S. Siddiqui, Arun, J. Sanyal, M. Muthiah. (2022). Hypertension is prevalent in non-alcoholic fatty liver disease and increases all-cause and cardiovascular mortality. Frontiers in Cardiovascular Medicine. 9: 942753.

[24] E. Margariti, M. Deutsch, S. Manolakopoulos, G. V. Papatheodoridis. (2012). Non-alcoholic fatty liver disease may develop in individuals with normal body mass index. Annals of gastroenterology. 25 (1): 45.

[25] L. Y. Qian, J. F. Tu, Y. H. Ding, J. Pang, X. D. Pang, H. Zou, D. S. Huang. (2016). Association of blood pressure level with nonalcoholic fatty liver disease in nonhypertensive population: normal is not the new normal. Medicine. 95 (29).

[26] A. Martin, S. Lang, T. Goeser, M. Demir, H. M. Steffen, P. Kasper. (2022). Management of dyslipidemia in patients with non-alcoholic fatty liver disease. Current Atherosclerosis Reports. 24 (7): 533-546.

[27] Q. Q. Zhang, L. G. Lu. (2015). Nonalcoholic fatty liver disease: dyslipidemia, risk for cardiovascular complications, and treatment strategy. Journal of clinical and translational hepatology. 3 (1): 78.

[28] M. Li, S. Zhang, Y. Zhang, J. Ye, X. Cao, J. Liu, Y. Sun, B. Zhong. (2015). Prevalence of insulin resistance in subjects with nonalcoholic fatty liver disease and its predictors in a Chinese population. Digestive diseases and sciences. 60: 2170-2176.

[29] R. Kumar, Y. C. Porwal, N. Dev, P. Kumar, S. Chakravarthy, A. Kumawat. (2020). Association of high-sensitivity C-reactive protein (hs-CRP) with non-alcoholic fatty liver disease (NAFLD) in Asian Indians: A cross-sectional study. Journal of Family Medicine and Primary Care. 9 (1): 390.

[30] A. M. Khan, H. Chaudhry, A. Ajibowo, A. Mahadevaiah, N. Mustafa, O. A. Kolawole, M. A. Ali. (2022). An Assessment of Atherosclerotic Cardiovascular Disease in Non-Alcoholic Fatty Liver Disease Patients with Type 2 Diabetes Mellitus. SSRN Electronic Journal.

[31] S. Abdu, B. Abdulaziz, E. E. Kharbotly, A. Nassief. (2020). Assessment of liver fibrosis in non-alcoholic fatty liver disease using real-time elastography. Benha Medical Journal. 37 (Special issue (Internal medicine and Hepatology)): 1-11.

[32] S. Jitrukthai, C. Kositamongkol, P. Boonchai, E. Mepramoon, P. Ariyakunaphan, P. Nimitpunya, W. Srivanichakorn, T. Chaisathaphol, C. Washirasaksiri, C. Auesomwang, T. Sitasuwan, R. Tinmanee, N. Sayabovorn, P. Charatcharoenwitthaya, P. Phisalprapa. (2022). Long-Term Outcomes Associated with NAFLD, ASCVD, and All-Cause Mortality of Patients with Metabolic Syndrome. Journal of Clinical Medicine. 11 (15): 4627.

[33] L. B. VanWagner, J. E. Wilcox, H. Ning, C. E. Lewis, J. J. Lewis, M. E. Rinella, S. J. Shah, J. A. C. Lima, D. M. L. Jones. (2020). Longitudinal association of non-alcoholic fatty liver disease with changes in myocardial structure and function: the CARDIA study. Journal of the American Heart Association. 9 (4): e014279.