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Nonalcoholic fatty liver disease (NAFLD) proven by transient elastography in patients with coronary heart disease

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Summary
Background/aim The relationship between nonalcoholic fatty liver disease (NAFLD) and coronary heart disease (CHD) is poorly understood. In the present study, we aimed to assess the frequency of NAFLD in CHD patients by using a new diagnostic tool: transient elastography (TE; Fibroscan®-CAP). Clarification of the present study may help to provide a new noninvasive tool for the assessment of NAFLD in this specific population of patients and may be of clinical importance in planning preventive strategies in high-risk patients.

Patients and methods A total of 75 patients with proven CHD were enrolled. Liver stiffness was used to assess liver fibrosis, and controlled attenuation parameter (CAP) was used to detect and quantify liver steatosis by using Fibroscan® (Echosens, Paris, France). By CAP being implemented on TE, both liver steatosis and fibrosis can be evaluated simultaneously.

Results Of the 75 patients, 45 (60%) had CAP >238 dBm^{-1} and, by definition, NAFLD. Among the patients with NAFLD, 24 (53.3%) had, in addition, liver stiffness >7 kPa. Analyzing the influence of the degree of liver steatosis (expressed by CAP values) on the degree of CHD (defined by single or multiple vessels involved), we found that patients with multiple vessels involved had higher CAP values ($p=0.002$). Furthermore, we noticed that significantly more patients with multiple vessels involved had liver stiffness >7 kPa ($p<0.0001$) indicating the more severe form of NAFLD in those patients.

Conclusion The main finding of our study is that TE provides the opportunity of noninvasive screening for NAFLD in CHD patients, as it is a quick, simple, reliable, and repeatable method and more cost-effective than liver biopsy.

Keywords Nonalcoholic fatty liver disease (NAFLD) · Transient elastography · Coronary heart disease

Nachweis einer nicht-alkoholischen Fettlebererkrankung (NAFLD) durch transiente Elastographie bei Patienten mit einer koronaren Herzerkrankung (CHD)

Zusammenfassung
Hintergrund/Ziel der Studie Der Zusammenhang zwischen der NAFLD und der CHD ist unklar. In der vorliegenden Studie wollten wir die Häufigkeit einer NAFLD bei Patienten mit einer CHD unter Verwendung eines neuen diagnostischen Gerätes (TE – Transiente Elastographie; Fibroscan®- CAP) erheben. Die Ergebnisse unserer Studie könnten helfen, ein neues nicht-invasives Gerät zur Erfassung einer NAFLD bei dieser besonderen Patientenpopulation einzusetzen. Der klinische Nutzen könnte in der darauf basierenden Planung einer präventiven Strategie bei Hochrisikopatienten liegen.

Patienten und Methodik Es wurden 75 Patienten mit nachgewiesener CHD in die Studie aufgenommen. Die

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Steifheit der Leber wurde zur Beurteilung einer möglichen Leberfibrose herangezogen. Der „Controlled Attenuation Parameter (CAP)" wurde mit Hilfe eines Fibroscan® (Echosens, Paris, Frankreich) erhoben und zur Erkennung und Quantifizierung einer möglichen Lebersteatose eingesetzt. Durch die Einbeziehung der CAP in die TE kann sowohl die Steatose als auch die Fibrose der Leber beurteilt werden.

Ergebnisse Von den 75 Patienten hatten 45 (=60 %) ein CAP >238 dBm^{-1} und damit per definitionem eine NAFLD. Von diesen Patienten mit NAFLD hatten 24 (=53,3 %) eine Lebersteife >7 kPa.

Die Analyse eines möglichen Zusammenhangs zwischen dem Grad der Lebersteatose (ausgedrückt in CAP Werten) mit dem Schweregrad der CHD (definiert durch die Anzahl der befallenen Gefäße) ergab, dass Patienten mit einer Mehrgefäßerkrankung höhere CAP Werte (p=0,002) aufwiesen. Auch eine Lebersteife >7 kPa wurde bei diesen Patienten mit Mehrgefäßbefall signifikant häufiger erhoben.

Schlussfolgerung Unsere Studie zeigt, dass die TE die Möglichkeit eines nicht-invasiven Screenings auf NAFLD bei CHD Patienten bietet. Die Methode ist ein rasches, einfaches, verlässliches und reproduzierbares Verfahren, - kosteneffizienter als eine Leberbiopsie.

Schlüsselwörter Nicht-akoholische fettleber (NAFLD) · Transiente Elastographie · Koronare Herzerkrankung

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in developed countries, encompassing a spectrum of conditions associated with lipid deposition in hepatocytes. It ranges from simple steatosis to nonalcoholic steatohepatitis (NASH), fatty liver with inflammation and hepatocellular injury with or without fibrosis, advanced fibrosis, and cirrhosis. Many authors have expressed their opinion that NAFLD represents a liver manifestation of metabolic syndrome (MS)—a disease commonly related to diabetes mellitus type 2, insulin resistance, central obesity, hyperlipidemia, and hypertension [1–3]. The importance of the liver in the regulation of metabolism has been recognized for more than a century and a half, but fatty liver has, for a long time, been considered a trivial finding. Therefore, the current importance of NAFLD and its link to the MS has encouraged an interest in its possible role in the development of atherosclerosis in recent years. [1–6]. Furthermore, recent studies have shown that NAFLD is not merely a marker of cardiovascular disease (CVD), but it may actually be actively involved in its pathogenesis [5, 7].

Many persons with NAFLD have no symptoms, and the condition is often discovered incidentally when laboratory examination shows elevated aminotransferase levels. Alkaline phosphatase (ALP) can be slightly elevated, while γ-glutamyl transferase (GGT) is frequently elevated and may be a marker of increased mortality in the general population. Liver biopsy is the gold standard to confirm a diagnosis of NAFLD, but it is an invasive procedure that can have serious complications and is prone to significant sampling error. Repetition of liver biopsy to monitor changes in steatosis is difficult. Moreover, today there are no clear recommendations whether liver biopsy is necessary to confirm the diagnosis of NAFLD [1, 4, 6]. Consequently, there are many noninvasive methods that are being intensively investigated as means of detecting hepatic steatosis and fibrosis. They are based on clinical signs and symptoms as well as laboratory tests and various imaging methods. Some of the biological scores such as AST-to-platelet ratio index (APRI) score, Forns index, Fib-4 score, and Hepatic Steatosis Index (HSI) are easily calculated and have shown themselves to be very useful in the assessment of liver fibrosis/steatosis [8–12]. Furthermore, in recent years, some noninvasive radiographic techniques have been intensively investigated in the assessment of hepatic steatosis, such as computed tomography and proton magnetic resonance spectroscopy. However, the use of these methods is limited by, in some cases, high cost, restricted availability, operator dependence, and poor sensitivity. Also, these methods cannot simultaneously asses liver fibrosis and steatosis. To overcome these limitations, a novel technology called transient elastography (TE) (Fibroscan®) has been developed a few years ago. It has shown promising results in the assessment of liver fibrosis. In addition, a novel noninvasive parameter, called the controlled attenuation parameter (CAP), has been developed to detect and quantify liver steatosis using the TE (Fibroscan®). CAP being implemented on TE, both steatosis and fibrosis can be evaluated simultaneously, enlarging the spectrum of noninvasive techniques for the management of chronic liver diseases. TE measures liver volume that is at least 100 times bigger than a biopsy sample. It is rapid, painless, easy to obtain, and more cost-effective than liver biopsy [13, 14].

In the present cross-sectional study, we aimed to assess the frequency of NAFLD in coronary heart disease (CHD) patients by using a new diagnostic tool: TE (Fibroscan®-CAP). Clarification of the present study may help to provide a new noninvasive tool for the assessment of NAFLD in this specific population of patients and may be of clinical importance in planning preventive strategies in high-risk patients.

Patients and methods

In this cross-sectional study, we included 82 patients who underwent coronary catheterization and had proven CHD. The exclusion criteria were serological evidence of chronic hepatitis B and/or C virus infection, alcohol abuse (>20 g of alcohol per day), presence of other autoimmune or cholestatic liver disease, history of drug treatment causing hepatic steatosis (e.g., corticosteroids, high-dose estrogen, methotrexate, or amiodarone within

6 months of enrollment), clinical and laboratory signs of impaired synthetic and/or metabolic liver function, and technical reasons (failed TE), mainly due to a body mass index (BMI) >30 kg/m². Also, patients with dilated cardiomyopathy diagnosed by echocardiogram with systolic dysfunction of one or both ventricles, ejection fraction lower than 55 %, ventricular dilatation, and left ventricular diastolic diameter larger than 57 mm were excluded from the study. Considering the aforementioned, 75 patients were enrolled in the study and 7 patients were excluded from this analysis (4 patients due to failed TE, 2 due to the use of hepatotoxic drugs, and 1 due to heart failure).

Comorbid illnesses include the presence of diabetes mellitus, dyslipidemia, and arterial hypertension, as well as obesity. These data were obtained by using a standard questionnaire. BMI was calculated as weight (kg) divided by height (m) squared. Overweight was defined as a BMI >25 kg/m², diabetes as fasting glucose level ≥ 7.1 mmol/L or drug treatment, and dyslipidemia as triglyceride levels ≥ 1.7 mmol/L or drug treatment and/or high-density lipoprotein level < 1 mmol/L in men and < 1.29 in women or drug treatment. Arterial hypertension was considered if the patients had a blood pressure ≥ 145/90 mmHg or used antihypertensive drugs.

Laboratory data included blood cell count, urea, creatinine, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), GGT and ALP, cholesterol, triglycerides, and serum iron values measured by standard clinical chemistry techniques. Glomerular filtration rate was calculated according to the Modification of Diet in Renal Disease formula.

The degree of CHD was defined with single or multiple vessels involved. The clinical and laboratory data were collected at the time of TE.

CAP was used to detect and quantify liver steatosis by using TE (Fibroscan®; Echosense, Paris, France). The cut-off value for defining liver steatosis was CAP ≥ 238 dBm^{-1}, and the cut-off value for defining the presence of fibrosis was liver stiffness >7 kPa [13]. Measurements were performed using the M probe (at 3.5 MHz) on the right lobe of the liver through intercostal spaces with the patient lying supine and placing the right arm behind the head to facilitate access to the right upper quadrant of the abdomen. The tip of the probe transducer was placed on the skin between the rib bones at the level of the right lobe of the liver where liver biopsy would be performed. This was done using only the M probe because the CAP algorithm is specific to this device. Ten successful measurements were performed on each patient, and only cases with ten successful acquisitions were taken into account for this study. Therefore, examinations with fewer than ten successful measurements were deemed failures. The success rate was calculated as the number of successful measurements divided by the total number of measurements. The ratio of the interquartile range (IQR) of liver stiffness to the median (IQR/M_{LSM}) was calculated as an indicator of variability. Furthermore, the final CAP value, which ranges from 100 to 400 decibels per meter (dBm^{-1}), is the median of individual measurements. The ratio of IQR in CAP values to the median (IQR/M_{CAP}) was used as an indicator of variability for the final CAP [13]. All scans were performed by the same investigator.

Conclusively, CAP being implemented on TE, both steatosis and fibrosis can be evaluated simultaneously. According to this evaluation, NAFLD was defined by the presence of steatosis with CAP values ≥ 238 dBm^{-1} regardless of the presence or absence of any stage of fibrosis. CAP values between 238 and 258 dBm^{-1} were categorized as steatosis grade 1 (S1), values between 259 and 292 dBm^{-1} as steatosis grade 2 (S2), and values >292 dBm^{-1} as steatosis grade 3 (S3) [13].

The APRI and FIB-4 scores were obtained to asses liver fibrosis, and were calculated based on the following formulas:

APRI = (AST level (measured)/AST level (upper normal) × 100)/Platelet count (10^9/L)

FIB-4 = age (years) × AST/platelet count × ALT

For the assessment of liver steatosis, HSI score was obtained according to the following formula:

HSI score = 8 × ALT/AST ratio + BMI + 2 (if diabetic) + 2 (if female) [8–12]

We compared the APRI and FIB-4, as well as the HSI score, with the presence and degree of fibrosis/steatosis detected by Fibroscan®.

Patients were informed of the purpose and method of the research, and the study was done in accordance with the Declaration of Helsinki. The study was approved by local ethical commission.

Statistical analysis

Statistical analysis of data was performed using descriptive statistics (mean and standard deviation). The Pearson or Spearman correlation coefficient was used to express correlations between variables. The importance of the difference between two independent groups was tested using *t*-test or analysis of variance. Univariate and multivariate analyses were assessed using the Cox regression analysis. Discrimination was tested using the receiver operating characteristic (ROC) curves and by comparing areas under the curve (AUCs). AUCs between 0.7 and 0.8 were classified as "acceptable" and between 0.8 and 0.9 as "excellent" discrimination. A p-value <0.05 was considered to be statistically significant. Statistical analysis was performed using MedCalc statistical software package, version 10 (MedCalc, Mariakerke, Belgium).

Results

The total cohort of 75 patients comprised 31 men and 44 women with proven CHD (average age: 64.6 ± 11.2 years). Table 1 shows the demographic characteristics of the 75 analyzed patients. Of the 75 patients, 45 (60 %) had CAP >238 dBm^{-1} and thus by definition NAFLD. There was no statistically significant difference between the two

Table 1 Demographic characteristics of analyzed patients

Characteristic	Total (n=75)	NAFLD (n=45)	Non-NAFLD (n=30)	p
Age (years)	64.6±11.2	64.8±9.5	64.2±13.5	NS
Sex, n (%)				
Male	31 (41.3%)	16 (35.6%)	15 (50%)	NS
Female	44 (58.7%)	29 (64.4%)	15 (50%)	NS
Hemoglobin (g/L; normal value: 138–175 g/L)	131.2±12.3	125.7±11.7	139.3±8	<0.0001
Iron (μmol/L; normal value: 11–32 μmol/L)	12.9±3.6	11.0±2.7	15.8±2.9	<0.0001
ALT (IU/L; normal value: 12–38 IU/L)	40.1±13.9	44.9±13.4	32.9±11.5	0.0001
AST (IU/L; normal value: 11–38 IU/L)	34.3±14.9	37.2±13.3	30.0±16.3	0.04
GGT (IU/L; normal value: 11–55 IU/L)	40.5±18.7	49.3±18.7	27.2±7.3	<0.0001
ALP (IU/L; normal value: 60–142 IU/L)	83.9±27.0	84.4±32.1	83.0±17.3	NS
Total cholesterol (mmol/L; normal value: <5 mmol/L)	5.2±0.9	5.7±0.7	4.4±0.6	<0.0001
Triglycerides (mmol/L; normal value: <1.7 mmol/L)	1.6±0.4	1.8±0.4	1.4±0.3	0.0001
eGFR (normal value: >60 mL/min per 1.73 m²)	67.7±6	67.7±6	69.1±5.6	NS
BMI (kg/m²)	27.5±3.2	29.0±3.2	25.3±1.6	<0.0001
Hypertension, n (%)	59 (78.7%)	40 (88.9%)	19 (63.3%)	0.018
Diabetes, n (%)	32 (42.7%)	24 (53.3%)	8 (26.7%)	0.04
Dyslipidemia, n (%)	49 (65.3%)	35 (77.8%)	14 (46.7%)	0.04
Smoking	45 (60%)	28 (62.2%)	17 (56.7%)	NS
Single vessel involved	37 (49.3%)	18 (40%)	19 (63.3%)	NS
Multiple vessels involved	38 (50.7%)	27 (60%)	11 (36.7%)	NS

NAFLD nonalcoholic fatty liver disease, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *GGT* γ-glutamyl transferase, *eGFR* estimated glomerular filtration rate, *BMI* body mass index, *NS* nonsignificant

groups related to age or gender. Analyzing the various biochemical and clinical parameters, we observed that hemoglobin and serum iron levels, ALT, AST, GGT, total cholesterol, and triglyceride levels, as well as BMI values, showed statistically significant difference between the two groups of patients. Examination of comorbid conditions revealed that there was statistically significant difference in relation to arterial hypertension, dyslipidemia, and diabetes mellitus between the two groups of patients, while there was no difference due to tobacco use (Table 1).

According to the literature, the grades of liver steatosis were defined by CAP values: 9 (20%) patients had grade 1, 12 (26.7%) had grade 2, and 24 (53.3%) had grade 3. Among the patients with NAFLD, 24 patients (53.3%) had, in addition, liver stiffness >7 kPa.

Table 2 Correlation of CAP values (liver steatosis) with the patients' laboratory and clinical data

Characteristic	Mean±SD	r	p
Age (years)	64.6±11.2	0.158	NS
Hemoglobin (g/L)	131.2±12.3	−0.348	0.002
Iron (μmol/L)	12.9±3.6	−0.678	<0.0001
ALT (IU/L)	40.1±13.9	0.524	<0.0001
AST (IU/L)	34.3±14.9	0.181	NS
GGT (IU/L)	40.5±18.7	0.621	<0.0001
ALP (IU/L)	83.9±27.0	0.042	NS
Total cholesterol (mmol/L)	5.2±0.9	0.672	<0.0001
Triglycerides (mmol/L)	1.6±0.4	0.602	<0.0001
BMI (kg/m²)	27.5±3.2	0.592	<0.0001

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *GGT* γ-glutamyl transferase, *ALP* alkaline phosphatase, *BMI* body mass index, *NS* nonsignificant, *SD* standard deviation

Table 3 Correlation of liver stiffness with the patients' laboratory and clinical data

Characteristic	Mean±SD	r	p
Age (years)	64.6±11.2	−0.130	NS
Hemoglobin (g/L)	131.2±12.3	0.010	NS
Iron (μmol/L)	12.9±3.6	−0.385	0.0006
ALT (IU/L)	40.1±13.9	0.345	0.002
AST (IU/L)	34.3±14.9	0.111	NS
GGT (IU/L)	40.5±18.7	0.245	0.03
ALP (IU/L)	83.9±27.0	0.040	NS
Total cholesterol (mmol/L)	5.2±0.9	0.340	0.002
Triglycerides (mmol/L)	1.6±0.4	0.224	0.053
BMI (kg/m²)	27.5±3.2	0.344	0.002

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *GGT* γ-glutamyl transferase, *ALP* alkaline phosphatase, *BMI* body mass index, *NS* nonsignificant, *SD* standard deviation

The severity of liver steatosis was positively correlated with the BMI values, total cholesterol, triglycerides, ALT, and GGT levels, while it was negatively correlated with hemoglobin and serum iron levels (Table 2).

Furthermore, the severity of liver fibrosis was positively correlated with GGT, ALT, total cholesterol, and triglycerides levels, as well as with BMI values, while it was negatively correlated with serum iron levels (Table 3).

In the next step, we were interested to explore whether the presence of liver steatosis/fibrosis defined by TE correlates with the three biological scores for the assessment of liver steatosis/fibrosis. After comparison of the AUCs of the ROCs (AUROC) of APRI, FIB-4, and HSI, we have observed that HSI correlated with the presence of steatosis (defined by CAP values; AUROC: 0.855, 95% confidence interval: 0.755–0.926), while FIB-4 (AUROC: 0.721, 95% confidence interval: 0.605–0.818) and APRI (AUROC: 0.716, 95% confidence interval: 0.600–0.814) scores correlated with the presence of fibrosis defined by TE.

Multivariate analysis demonstrated that BMI ($p=0.0001$), dyslipidemia ($p=0.04$), diabetes mellitus type 2 ($p=0.0001$), and arterial hypertension ($p=0.01$) were factors that contribute to NAFLD occurrence.

Analyzing the correlation between the degree of liver steatosis (expressed by CAP values) and the degree of CHD (defined by single or multiple vessels involved), we have found that patients with multiple vessels involved had higher CAP values ($p=0.002$). Furthermore, we have noticed that significantly more patients with multiple vessels involved had liver stiffness >7 kPa ($p<0.0001$), indicating the more severe form of NAFLD in those patients.

Discussion

To the best of our knowledge, this is the first study using TE (Fibroscan®-CAP) as a noninvasive approach for the detection of NAFLD in CHD patients. Our results demonstrate that CHD patients have a high prevalence of NAFLD (60%) defined by TE, compared with the prevalence of NAFLD in general population, which is between 10 and 25%. Because of the underlying metabolic disorders, NAFLD patients are expected to have higher risk of CHD. In our study, a great proportion of our patients had MS, and presumably this is the reason why so many patients had NAFLD. The results of our study are in accordance with the past observations that diabetes mellitus type 2, dyslipidemia, and obesity contribute to the development of NAFLD. In our multivariable model, BMI, diabetes mellitus, arterial hypertension, and dyslipidemia were the independent predictors of NAFLD occurrence. Previous studies showed that approximately 90% of patients with NAFLD have more than one component of the MS [1-6]. Many previous studies indicated that NAFLD is linked to increased risk of CVD, independently of underlying cardiometabolic risk factors. [3, 7, 15-23]. For example, an autopsy study of 742 children found that the prevalence of CHD is twofold higher in those with NAFLD [24]. The diagnosis of NAFLD in patients with MS is important because today it is believed that NAFLD is not merely a marker of CVD, but it may actually be actively involved in its pathogenesis, which is clearly shown in the study performed by Targher and colleagues [7]. In our study, we found positive correlation between degree of liver steatosis/fibrosis and severity of CHD, which might suggest that NAFLD could be directly involved in the etiopathogenesis of CHD. However, the cross-sectional format of our study does not allow conclusions whether the link between CHD and NAFLD is causal.

According to the literature, in all of previous investigations, NAFLD was detected by liver enzymes, liver ultrasonography, or liver biopsy. Nevertheless, it is noteworthy that the aminotransferase levels that are used as a marker of liver damage are normal in approximately half of all patients with NAFLD; therefore, normal values do not exclude NAFLD and liver fibrosis. In all our patients, the secondary causes of liver damage and possible causes of increased levels of liver enzymes, including heart failure, were excluded. Analyzing the correlation between liver enzymes and presence of NAFLD, we found that ALT and GGT levels were positively correlated with the presence of liver steatosis defined by CAP values acquired by TE. Also, these liver tests showed statistically positive correlation with liver fibrosis defined by TE, indicating the more severe form of disease in those patients. Consequently, as we anticipated, three biological scores that had shown usefulness in the assessment of liver steatosis/fibrosis in previous studies were significantly correlated with the liver steatosis/fibrosis defined by TE (Fibroscan®-CAP). So far, liver biopsy remained the gold standard in the diagnosis of NAFLD, but it is an invasive procedure that is prone to sampling error and cannot routinely be performed in patients with impaired coagulation, so definite conclusions about necessity of biopsy are yet to be made [1-6]. In our study, NAFLD was defined by TE and, to our knowledge, for the first time. According to our experience, we believe that TE could provide a new noninvasive tool for the assessment of NAFLD in a population of CHD patients as well as in everyday clinical practice.

As mentioned earlier in the text, NAFLD represents a liver manifestation of the MS and is an independent predictor of cardiovascular mortality. Insulin resistance is recognized as the pathophysiological hallmark of NAFLD. Today, it is believed that inflammation plays a key role in the initiation and progression of the atherosclerotic process, and according to many authors, atherosclerosis has been defined as "an inflammatory disease." In contrast, there is growing evidence suggesting that patients with NAFLD have increased production and release of various pro-inflammatory cytokines by hepatocytes and non-parenchymal cells, including Kupffer cells and hepatic stellate cells. The levels of these markers correlate with the severity of liver disease and insulin resistance. Therefore, enhanced oxidative stress, subchronic inflammation state that has been observed in NAFLD patients, and insulin resistance can consequently result in accelerated atherosclerosis and further cardiovascular damage progression [1-7]. In our study, hemoglobin and serum iron levels were negatively correlated with CAP values pointing to a potential role of subchronic inflammation. However, we did not investigate the role of other markers of inflammation in our patients, and we did not perform liver biopsy to diagnose a NASH, so we can only speculate about these observations, and further studies are needed.

Our study has some limitations. Firstly, the cross-sectional design of our study does not allow conclusions whether the link between CHD and NAFLD is causal. Secondly, we have a relatively small number of patients, so acquired data are insufficient for epidemiological analysis and we did not use liver biopsy to prove the diagnosis of NAFLD and compare histological features of liver biopsy samples with TE findings. In contrast, our results firmly suggest that NAFLD is highly prevalent in patients with CHD. The main finding of our study is that TE provides the opportunity of noninvasive screen-

ing for NAFLD in CHD patients because it is, contrary to liver biopsy and other imaging methods, a quick, simple, more cost-effective, reliable, and repeatable method. TE could provide a new noninvasive tool for the assessment of NAFLD in patients with MS. The results of noninvasive screening could consequently help to recognize high-risk patients for adverse cardiovascular events that should be aggressively treated to reduce their CVD morbidity and mortality. We sincerely hope that our research will encourage new prospective investigations on NAFLD in CHD patients as well as in those affected by MS.

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All the above authors are equally involved in the development of this article.

Conflict of interest
None declared.

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