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Original Article

Prevalence of ultrasound-diagnosed non-alcoholic fatty liver disease in a hospital cohort and its association with anthropometric, biochemical and sonographic characteristics

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Abstract: Non-alcoholic fatty liver disease (NAFLD) is considered as the most common liver disease in Western countries with still rising prevalence due to a lifestyle favoring the development of the metabolic syndrome. Aim: To investigate the prevalence of ultrasound-diagnosed NAFLD in patients with referral for sonographic examination of the abdomen, and to determine risk factors. Methods: After exclusion of patients with known liver disease or risk factors for secondary NAFLD, a total of 155 arbitrarily selected patients (mean age 53.6±17.4 years; 52.6% male) from the interdisciplinary ultrasound department of a German University Hospital were included in this prospective study. Each patient underwent a standardized ultrasound, anthropometric and biochemical examination. Results: The prevalence of ultrasound-diagnosed NAFLD was 40.0%. NAFLD-patients had significantly higher body mass index (BMI) and waist-to-hip ratio, higher rates of reported hypertension and diabetes mellitus, and lower HDL cholesterol serum levels. Furthermore, NAFLD-patients revealed significantly higher serum ALT levels (23.2±22.1 U/l vs. 15.0±8.2 U/l; p=0.001), lower AST/ALT ratio (1.76±0.79 vs. 2.11±0.94; p=0.019), and notably, decreased flow in the portal vein (22.9±6.3 cm/s vs. 26.7±10.5 cm/s; p=0.011). Multivariate analysis revealed BMI (odds ratio (OR): 14.05; 95% Confidence interval (CI): 3.3-59.8), AST/ALT ratio (OR: 0.39; CI: 0.18-0.82), and HDL-C (OR: 4.33; CI: 1.6-11.9) as independent risk factors. Conclusions: Ultrasound-diagnosed NAFLD is frequent in patients with referral for ultrasound examination of the abdomen, and our findings further support that NAFLD is the hepatic manifestation of the metabolic syndrome with obesity being the most important risk factor.

Keywords: Non-alcoholic fatty liver disease (NAFLD), ultrasound, diagnosis, prospective study, obesity, risk factor

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a condition defined by significant lipid accumulation (5-10%) in hepatic tissue in the absence of significant chronic alcohol consumption [1]. Most patients with NAFLD have increased liver fat content alone (simple steatosis), but others develop increasing hepatic inflammation known as nonalcoholic steatohepatitis (NASH), and up to 20% of patients reveal progressive hepatic fibrosis and may eventually develop cirrhosis or liver failure [1,2].

The association of NAFLD with obesity, type 2 diabetes, dyslipidemia and hypertension is well documented [2]. These conditions have insulin resistance as the common factor and cluster to form the metabolic syndrome (MS). With the rising rate of the MS, NAFLD emerges as the most common liver disease in various parts of the world [1,3,4].

Estimates from recent epidemiological studies indicate a prevalence rate of 10 to 30 percent in the Western adult population [3,5,6] similar to the one observed in Asian populations [7-10].

Most of these analyses have been performed as cross-sectional studies of the general population using ultrasound or magnet resonance spectroscopy to detect increased hepatic lipid content.

Regardless of the method used and the population screened, respectively, all studies clearly confirmed the association of NAFLD with (components of) the metabolic syndrome. Thus, today NAFLD is considered to be the hepatic manifestation of the metabolic syndrome [11,12].

One would expect that patients with an indication for ultrasound examination of the abdomen more often suffer from (components of) the metabolic syndrome compared to the general population. However, besides epidemiological studies, "brightness of the liver" as a surrogate marker for hepatic lipid accumulation or NAFLD, respectively, is often diagnosed by chance in patients undergoing sonographic examination of the abdomen, and with the exception of patients with (suspected) liver disease, the prevalence of this diagnosis is not well studied.

Thus, the aim of the present study was to perform a prospective and standardized study to investigate the prevalence of ultrasound-diagnosed NAFLD in the interdisciplinary ultrasound department of a University Hospital in Southern Germany and to correlate this finding with anthropometric, clinical, biochemical and sonographic characteristics.

Materials and methods

Subjects and exclusion criteria

506 randomly selected patients who were referred to the interdisciplinary ultrasound department of the University Hospital Regensburg in the year 2008 for sonographic examination of the abdomen were initially included in this study. The cohort included outdoor patients as well as hospitalized patients of all departments of the hospital. All participants signed a form of written consent, and the study was approved by the local Ethics Committee.

All patients participated in a face-to-face interview that was carried out by one of three interviewers (H.H., C.N., and C.B.) based on a standard questionnaire including a detailed history of 1) present and past medical conditions and medications, 2) alcohol, nicotine and drug consumption, 3) past blood transfusions, and 4) family history.

Patients with any of the following criteria were excluded from the study: 1. hepatobiliary diseases, 2. malignancies, 3. ascites, 4. medications known to cause hepatic steatosis (such as estrogens, corticosteroids, amiodarone, valproate; at present or within the last 2 years), 5. inflammatory bowel disease, 6. infection with the human immunodeficiency virus (HIV), 7. chronic drug or alcohol abuse (more than 20 g/day), 9. known (familial) hyperlipidemia, and 10. acute medical conditions with confounding effect on laboratory measurements.
Consequently, the remaining study population consisted of 155 patients.

Anthropometric measurements and clinical examination

All patients underwent measurements of height, body weight, waist and hip circumference. Waist and hip circumference were measured with flexible tape with the patients standing. Blood pressure and heart rate were measured in the sitting position after adequate resting time.

Biochemical analysis of serum parameters

All biochemical serum analysis were performed in the same laboratory, the certified Institute for Clinical Chemistry and Laboratory Medicine of the University Hospital Regensburg, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (γ-GT); triglycerides, very-low-density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and total cholesterol; albumin, total serum protein, bilirubine, choline esterase, alkaline phosphatase (ALP) and fasting glucose.

Ultrasound examination

In addition to the routine abdominal ultrasound examination based on the clinical indication, all patients underwent a standardized ultrasound examination by one of three investigators (H.H., C.N., and C.B.) using high-end ultrasound equipment (either Siemens Sonoline Elegra, Siemens ACUSON Sequoia 512 (Siemens, Erlangen, Ger-

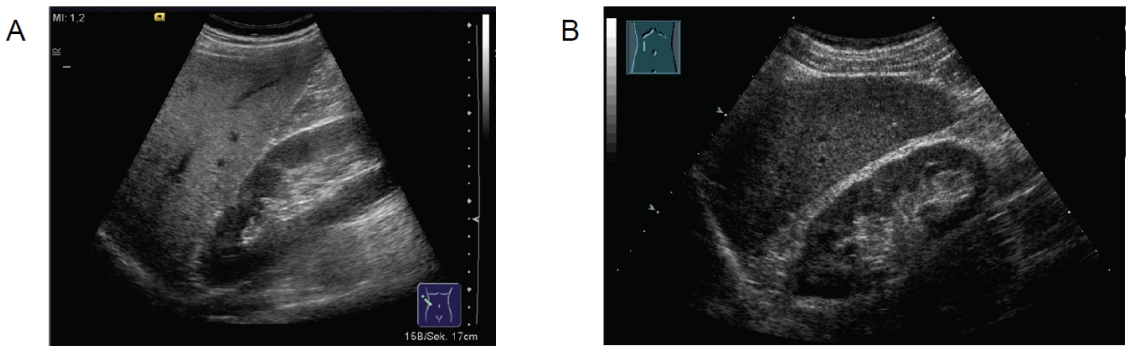

Figure 1. Ultrasound images of normal and steatotic livers. Ultrasound examination of liver parenchyma in longitudinal direction in the right midclavicular line using a 3-5 MHz transducer. **A**: steatosis hepatis with marked increase in hepatic echogenicity compared with the normal renal cortex. **B**: normal liver parenchyma with homogeneous echotexture compared with normal renal cortex.

many), GE Healthcare Logic 9 (GE Medical Systems, Wisconsin, USA) or Hitachi EUB-8500 (Hitachi Medical Corporation, Tokyo, Japan). First, examination of all visible liver parenchyma was performed with a 3-5 MHz transducer. Liver parenchyma was examined with sagittal as well as longitudinal guidance of the probe and completed by lateral and intercostals views. Use of Tissue Harmonic Imaging (THI) with both transducers was encouraged, but left to the examiners' decision. The examination of the liver was carried out in dorsal recumbence and in inspiration.

The presence of steatosis was recognized as a marked increase in hepatic echogenicity, poor penetration of the posterior segment of the right lobe of the liver, and poor or no visualization of the hepatic vessels and diaphragm. The liver was assessed to be normal if the texture was homogeneous, exhibited fine-level echoes, or was minimally hyperechoic or isoechoic compared with normal renal cortex, and if there was no posterior attenuation of the ultrasound beam. Representative examples of ultrasound examination of normal and steatotic livers are depicted in **Figure 1**.

Hepatomegaly was defined as a liver size above 155 mm measured as a subcostal diameter in the midclavicular line by using the 3-5 MHz probe.

With the use of portal duplex and color Doppler sonography, flow direction, flow velocity, vein diameter, and response to respiration of portal vein vessels were measured.

Additionally, fat thickness in the periumbilical and right subcostal regions was assessed using high frequency transducers (Sonoline Elegra: 7.5L40/5-9 MHz, ACUSON Sequoia 512: 15L8w -S 14 MHz, GE Healthcare Logic 9: 7L/3-7 MHz or 10L/4-10 MHz, Hitachi EUB-8500: EUP-L53/5-10 MHz).

Statistical analysis

For continuous variables results are expressed as means ± standard deviation. One-way analysis of variance (F test) was used to compare means. Correlations between categorical variables were assessed constructing contingency tables and applying the Chi-Square test. P values were corrected for multiple testing after the Bonferroni method. To identify independent predictors of NAFLD, the significance value of the Wald statistic in a multivariate logistic regression model was used. A p-value < 0.05 was considered significant. Statistical analysis was performed on a PC using SPSS 15.0 software.

Results

Characteristics of the study population

Baseline characteristics of the 155 subjects included in the study are summarized in **Table 1** according to whether they had ultrasound-diagnosed NAFLD (n=62) or did not reveal sonographic signs of hepatic lipid accumulation in abdominal ultrasound (n=93), respectively.

Average age did not differ significantly between patients with and without US-diagnosed NAFLD

Table 1. Baseline characteristics of the study population

Variables	All subjects (n=155)	ultrasound-diagnosed NAFLD no (n=93)	yes (n=62)	p*
age (years)	54.4 ± 17.7	52.2 ± 18.4	57.0 ± 16.4	0.098
male gender (%)	52.3%	47.3%	59.7%	0.089
alcohol consumption (g/day)	3.7 ± 6.7	3.6 ± 6.2	4.0 ± 7.3	0.727
smoking (%)	46.8%	45.7%	48.4%	0.739
pack years (n)	15.5 ± 23.6	11.7 ± 17.6	21.8 ± 30.4	**0.028**

NAFLD = non-alcoholic fatty liver disease
* by ANOVA or χ^2 test as appropriate
Bold-face figures indicate significant differences ($p<0.05$)

Table 2. Prevalence of features of the metabolic syndrome in patients with ultrasound-diagnosed NAFLD and control groups

	Ultrasound-diagnosed NAFLD		
	no (n=93)	yes (n=62)	p*
Body mass index (kg/m²)	24.8 ± 3.6	28.7 ± 5.9	**< 0.0001**
Waist circumference (mm)	869 ± 131	1022 ± 134	**< 0.0001**
Hip circumference (mm)	946 ± 110	1047 ± 140	**< 0.0001**
Waist to hip ratio	0.92 ± 0.10	0.98 ± 0.08	**0.0002**
Triglycerides (mg/dl)	124.4 ± 60.4	134.9 ± 55.2	0.287
Total cholesterol (mg/dl)	206.0 ± 49.0	197.7 ± 47.4	0.303
HDL cholesterol (mg/dl)	60.7 ± 19.4	47.1 ± 13.1	**< 0.0001**
LDL cholesterol (<150 mg/dl)	105.8 ± 37.9	109.8 ± 38.2	0.528
VLDL cholesterol	39.8 ± 18.4	41.0 ± 19.5	0.714
Reported diabetes mellitus type II (%)	11.0	23.3	**0.042**
Fasting glucose (mg/dl)	102.2 ± 31.3	107.9 ± 27.4	0.313
Reported hypertension (%)	31.2	46.8	**0.049**
Systolic blood pressure (mmHg)	130.5 ± 17.0	130.1 ± 16.3	0.901
Diastolic blood pressure (mmHg)	79.3 ± 11.2	76.7 ± 11.6	0.173

NAFLD = non-alcoholic fatty liver disease; HDL = high-density lipoprotein; LDL = low-density lipoprotein; VLDL = very-low-density lipoprotein
* by ANOVA or χ^2 test as appropriate
Bold-face figures indicate significant differences ($p<0.05$)

(57.0 ± 16.4 years vs. 52.2 ± 18.4 years, p=0.098). Prevalence of ultrasound-diagnosed NAFLD was higher in men (45.7 %) than in women (33.8 %, data not shown) but this difference did not reach statistical significance.
There were no significant differences with regard to the amount of alcohol consumption and the percentage of smokers. However, the number of pack years (py) for smokers in the NAFLD group was about twice as high as in the group of smoking control patients (21.8 py vs. 11.7 py, p=0.028).

Prevalence of features of the metabolic syndrome in patients with ultrasound-diagnosed NAFLD and control groups

The mean BMI of the whole study cohort (26.4 ± 5.0 kg/m²) indicated a tendency to be slightly overweight as it is also observed in the general German population [13]. Noteworthy, BMI as well as waist circumference, hip circumference and the waist to hip ratio were significantly higher in patients with ultrasound-diagnosed NAFLD **(Table 2)**. Furthermore, HDL-C levels were significantly lower in the NAFLD group (47.1 ± 13.1 mg/dl vs. 60.7 ± 19.4 mg/dl, p<0.0001), while serum levels of total cholesterol, LDL- and VLDL-cholesterol, and triglycerides did not significantly differ.

Remarkably, the rates of reported hypertension (46.8% vs. 31.2%, p=0.049) and diabetes melli-

Table 3. Liver related serum parameters of ultrasound-diagnosed NAFLD and control groups

	ultrasound-diagnosed NAFLD		
Variables	no (n=93)	yes (n=63)	p*
AST [U/l]	28.5 ± 14.0	31.6 ± 15.7	0.209
ALT [U/l]	15.0 ± 8.2	23.2 ± 22.1	**0.001**
AST/ALT ratio	2.11 ± 0.94	1.76 ± 0.79	**0.019**
γ-GT [U/l]	53.4 ± 72.6	76.4 ± 81.9	0.090
bilirubine [mg/dl]	0.58 ± 0.43	0.53 ± 0.42	0.434
ALP [U/l]	76.3 ± 36.6	77.0 ± 36.7	0.905
total serum protein [g/l]	74.8 ± 6.8	74.3 ± 8.5	0.710
albumin [g/l]	46.8 ± 6.4	45.4 ± 6.2	0.163
cholineesterase [U/l]	8564 ± 2100	9106 ± 2674	0.223

NAFLD = non-alcoholic fatty liver disease; AST = aspartate aminotransferase; ALT = alanine aminotransferase; γ-GT - gamma-glutamyl-transferase; ALP = alkaline phosphatase;
* by ANOVA or χ^2 test as appropriate;
Bold-face figures indicate significant differences (p<0.05).

tus type II (23.3% vs. 11.0%, p=0.042) were significantly higher in the NAFLD group than in the control group (as defined by history, review of medical files and/or use of hypertensive or anti-diabetic medication). In contrast, systolic and diastolic blood pressure, as well as fasting glucose levels did not differ significantly between both groups (**Table 2**).

Hepatic serum parameters of ultrasound-diagnosed NAFLD and control groups

Mean AST and γ-GT serum levels were slightly higher in the ultrasound-diagnosed NAFLD group as compared to patients without sonomorphological NAFLD signs but these differences did not reach statistical significance (**Table 3**). In contrast, serum ALT levels were significantly higher (23.2 ± 21.9 U/l vs. 15.0 ± 8.2 U/l; p=0.001), and the AST/ALT ratio was significantly lower (1.76 ± 0.79 vs. 2.11 ± 0.94, p=0.019) in the NAFLD group.

Constructing a ROC curve revealed that the best discriminating cut-off value of 19.8 U/l for ALT would yield sensitivity and specificity rates of 44 % and 80 %, respectively, for the identification of NAFLD (AUC=0.65, data not shown). The best discriminating cut-off value for the AST/ALT ratio of 1.43 would yield similar sensitivity and specificity rates (51% and 74 %, respectively; AUC=0.62; data not shown). Further, mean serum levels of total bilirubin, alkaline phosphatase, albumin, total protein and choline esterase were similar in both groups.

Sonographic characteristics of ultrasound-diagnosed NAFLD and control groups

In addition to the analysis of the "brightness" of the hepatic tissue as an indicator of hepatic lipid accumulation, ultrasound examination was applied to determine the size of the liver (e.g. length in the midclavicular line). Here, patients with ultrasound-diagnosed NAFLD revealed larger livers (145 ± 25 mm vs. 133 ± 26 mm, p=0.006) or a mild hepatomegaly, respectively (**Table 4**).

Furthermore, ultrasound was used to analyze the blood flow in the portal vein. Noteworthy, a significant decrease of the portal vein flow velocity was found in the NAFLD group in comparison to the control group without ultrasound signs of NAFLD (26.7 ± 10.5 cm/s vs. 22.9 ± 6.3 cm/s p=0.011; **Table 4**).

Moreover, the thickness of the subcutaneous fat tissue, e.g. the distance between skin surface and the muscular layer was determined in the right subcostal and the periumbilical region. At both anatomical regions the subcutaneous fat thickness was significantly higher in patients with ultrasound-diagnosed NAFLD (periumbilical: 21.4 ± 11.7 mm vs. 15.7 ± 9.2 mm, p=0.001; right subcostal: 7.8 ± 4.7 mm vs. 5.8 ± 3.3 mm, p=0.003; **Table 4**).

Table 4. Liver size, subcutaneous fat thickness and portal vein flow in ultrasound-diagnosed NAFLD and control groups

	Ultrasound-diagnosed NAFLD		
Variables	no (n=93)	yes (n=62)	p*
Liver length in the right midclavicular line (mm)	133 ± 26	145 ± 25	**0.006**
Portal vein flow (cm/s)	26.7 ± 10.5	22.9 ± 6.3	**0.011**
Right subcostal subcutaneous fat thickness (mm)	5.8 ± 3.3	7.8 ± 4.8	**0.003**
Periumbilical subcutaneous fat thickness (mm)	15.7 ± 9.2	21.4 ± 11.7	**0.001**

NAFLD = non-alcoholic fatty liver disease;
* by ANOVA;
Bold-face figures indicate significant differences ($p<0.05$).

Table 5. Multivariate analysis of risk factors for ultrasound-diagnosed NAFLD

Variable	Odds Ratio	95 % CI	p *
male gender	1.07	0.4-2.9	0.88
ALT (U/l)	1.02	0.98-1.06	0.27
AST/ALT ratio	0.39	0.18-0.82	**0.026**
HDL-C (mg/dl)	4.33	1.6-11.9	**0.004**
BMI > 25 and < 30 (kg/m^2)	3.21	1.2-8.4	**0.017**
BMI > 30 (kg/m^2)	14.05	3.3-59.8	**0.004**
reported hypertension	1.84	0.63-5.36	0.27
reported diabetes mellitus type II	2.96	0.66-13.4	0.16

NAFLD = non-alcoholic fatty liver disease
CI = confidence interval; ALT = alanine aminotransferase; AST = aspartate aminotransferase; HDL-C = high density lipoprotein cholesterol; BMI = body mass index
* Bold-face figures indicate significant p values (p wald χ^2 statistic <0.05).
A stepwise-backward regression after the maximum-likelihood method was applied. To assess the unique contribution of each variable in the context of other variables (adjusting for all other included variables) the significance value p of the χ^2 Wald statistic was used. The overall significance of the model was < 0.001, the percentage of correctly predicted cases 75.2 %.

Ultrasound-measured subcutaneous fat thickness significantly correlated with the BMI (periumbilical: Pearson's r (r) = 0.65, p <0.001; right subcostal: r = 0.53, p<0.001). Interestingly, diabetic patients revealed significantly higher subcutaneous fat thickness in the right subcostal region (0.84 ± 0.65 cm vs. 0.63 ± 0.32 cm, p=0.017) but not in the periumbilical region (2.00 ± 1.37 cm vs. 1.77 ± 0.98 cm, p=0.310) compared to patients without diabetes.

Multivariate analysis of risk factors for NAFLD

Logistic regression analysis revealed three factors independently related with ultrasound-diagnosed NAFLD: the BMI, AST/ALT ratio, and HDL-C (**Table 5**). The statistically significant association between ALT, reported hypertension, reported diabetes mellitus type II and NAFLD found in univariate analysis was not observed in the multivariate analysis.

Discussion

The aim of our study was to investigate the prevalence of ultrasound-diagnosed NAFLD in a clinical cohort (randomly selected referrals to the interdisciplinary ultrasound department of a University Hospital) that excluded individuals with possible causes for secondary hepatic steatosis. Furthermore, we examined the correlations between ultrasound-diagnosed primary NAFLD and anthropometric, clinical, biochemi-

cal and sonographic measurements.

The 40.0% prevalence of ultrasound-diagnosed NAFLD in our study population was higher than the prevalence observed in previous ultrasound-based cross sectional studies of the general population in Italy [3] (20 %) or Israel [6] (30.5%), as well as in Taiwan [7] (11.5 %), China [9,10] (15.3% and 17.2%), Sri Lanka [8] (32.6%) and Texas [5] (33% in whites, using magnetic resonance spectroscopy). Most likely, this difference can be explained or may have been expected, respectively, based on the higher prevalence of (components of) the metabolic syndrome in patients as compared to randomly selected individuals within the general population.

In line with this, reported rates of diabetes and hypertension as well as BMI and waist-hip-ratio as surrogates for obesity were significantly higher in the group of ultrasound-diagnosed NAFLD. On the contrary, the missing association of ultrasound-diagnosed NAFLD with measurement of systolic blood pressure and fasting glucose levels, respectively, is most likely explained by adequate medication. Similarly, HDL cholesterol was significantly decreased in NAFLD patients, while serum levels of total and LDL-cholesterol as well as triglycerides were similar as in control patients.

It is well recognized that the pattern of obesity plays a role in NAFLD development [14] and progression [15] with visceral obesity being the pathophysiologically critical condition. This effect is independent of hepatic steatosis and insulin resistance. Still, it is notable that in addition to BMI and waist circumference, ultrasound assessment of subcutaneous fat thickness revealed a significant correlation with ultrasound-diagnosed NAFLD. Since this measure is easy to obtain and gives quantitative values it may be added to future epidemiological NAFLD studies, ideally, in combination with analysis of visceral or perihepatic adipose tissue thickness [16-18].

Furthermore and in line with previous studies [19,20] we found decreased flow in the portal vein of NAFLD patients. The alteration in portal vein velocity suggests reduced vascular compliance in the liver, and further underscores, that hepatic steatosis is no bland condition but functionally affects the liver.

There is conflicting evidence on gender as a risk factor for NAFLD. While earlier studies indicated a higher NAFLD prevalence in women [21], studies both in Caucasian [5] and Asian populations [9] found male gender to be an independent NAFLD risk factor. In line with a large Italian study [3] we did not observe a significant difference with regard to the gender proportion in patients with ultrasound-diagnosed NAFLD and controls.

Furthermore, the percentage of smokers was similar in the NAFLD and control groups as observed in other studies [22,23]. However, the number of pack years (not examined by the previous studies) was significantly higher in NAFLD smokers (22.3 ± 30.2) than in no-NAFLD smokers (11.7 ± 17.6, $p = 0.028$) suggesting a possible, so far unknown link between excessive smoking and hepatic steatosis. Furthermore, it may be speculated that smoking is an independent risk factor for hepatic inflammation and fibrosis as observed in patients with chronic HCV [24,25] infection or primary billiary cirrhosis [26]. Hypoxia was identified as a potential underlying mechanism of progression of hepatic diseases [27], and in the light of a recent study, linking the oxygen-sensitive transcription factor hypoxia-inducible factor HIF-1 to hepatic lipid metabolism [28], hypoxia may also be involved in the observed association between nicotine and hepatic steatosis.

It is widely accepted that serum levels of transaminases are neither specific nor sensitive enough to screen for NAFLD [1,29,30], and this is confirmed in the present study. AST levels did not differ between ultrasound-diagnosed NAFLD and control patients, and even at the best discriminating point for ALT (19.8 U/l) the sensitivity (72 %) and specificity (60 %) to identify NAFLD were not satisfactory. One may speculate that these numbers are affected by comorbidities in a hospital cohort, however, population based studies reveal very similar figures [6]. Still and interestingly, the AST/ALT ratio was significantly lower in patients with ultrasound-diagnosed NAFLD, and multivariate analysis confirmed AST/ALT as an independent risk factor for hepatic steatosis also in our cohort of patients. Similarly, lower values for the AST/ALT ratio were found in NAFLD patients when compared to patients with alcoholic liver disease, and it has even been suggested that the AST/ALT ratio can be used to differentiate between

these conditions [31]. Another study demonstrated significance of the AST/ALT ratio even within the spectrum of NAFLD, as a lower AST/ALT ratio was associated with higher histopathological degree of hepatic steatosis in obese NAFLD subjects [32].

In summary, this study revealed a high prevalence of ultrasound-diagnosed NAFLD in patients with referral for sonographic examination of the abdomen, and further supports that NAFLD is the hepatic manifestation of the metabolic syndrome with obesity being the most important predictor of NAFLD. This is important, since the liver is not only a target of the metabolic syndrome but hepatic lipid metabolism and even subchronic inflammation, respectively, as observed in NAFLD promotes insulin resistance, the central pathophysiological mechanism of the metabolic syndrome [33,34]. Thus, identifying patients with NAFLD is not only important with regard to the risk of hepatic disease but also other conditions affected by the metabolic syndrome.

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