Nonalcoholic Fatty Liver Disease Is Associated With Carotid Atherosclerosis
A Case–Control Study

Angel Brea, Daniel Mosquera, Eva Martín, Ana Arizti, José L. Cordero, Emilio Ros

Objective—Nonalcoholic fatty liver disease (NAFLD) frequently coexists with obesity, diabetes, and dyslipidemia. We examined whether NAFLD was associated with atherosclerosis, as measured by ultrasound in the carotid arteries.

Methods and Results—Carotid atherosclerosis and cardiovascular risk factors were assessed in 40 patients with an ultrasound diagnosis of primary NAFLD and 40 matched population controls. The metabolic syndrome and all its individual traits, including elevated C-reactive protein, were significantly (P<0.005) more frequent in NAFLD patients than in control subjects. Patients with NAFLD showed more carotid atherosclerosis than controls, with mean intima-media thickness (IMT) of 0.70±0.20 mm and 0.54±0.13 mm (P<0.0001) and plaque prevalence of 50% and 25% (P=0.021), respectively. By multivariate analysis, older age (odds ratio [OR], 2.5 per 10 years; 95% CI, 1.4 to 4.4; P=0.002), the presence of NAFLD (OR, 8.4; 95% CI, 2.49 to 29.4; P=0.001), and elevated serum ferritin (OR, 3.1; 95% CI, 1.2 to 7.9; P=0.016) were independent predictors of an increased IMT.

Conclusions—Patients with NAFLD show a cluster of risk factors of the metabolic syndrome and advanced carotid atherosclerosis. NAFLD appears to be a feature of the metabolic syndrome, and its detection on abdominal ultrasound should alert to the existence of an increased cardiovascular risk. (Arterioscler Thromb Vasc Biol. 2005;25:1045-1050.)

Key words: atherosclerosis ■ metabolic syndrome ■ nonalcoholic fatty liver ■ cardiovascular risk factors ■ carotid ultrasound.

Nonalcoholic fatty liver disease (NAFLD) is a highly prevalent condition characterized by fatty infiltration of liver cells resembling that of alcohol-induced liver injury but occurring in patients who do not abuse alcohol.1–3 The spectrum of NAFLD ranges from fatty liver alone to steatohepatitis, which is histologically similar to alcoholic hepatitis and may progress to end-stage liver disease, a reason why this entity, long considered an incidental finding, has received increasing attention.4 NAFLD is strongly associated with obesity, type 2 diabetes, and dyslipidemia, and most patients have evidence of central adiposity and are insulin resistant.1–5 Thus, NAFLD shares many features of the metabolic syndrome (MetS), a highly atherogenic condition,6 and its presence could signify a substantial cardiovascular risk above and beyond that conferred by individual risk factors.

The potential cardiovascular risk associated with NAFLD has not been particularly investigated despite the evidence that mortality rates from coronary heart disease (CHD) equaled those attributable to cirrhosis in a large cohort of patients with biopsy-proven NAFLD followed for up to 18 years.7 In a case–control study, we investigated the association of NAFLD with carotid intima-media thickness (IMT) and plaque as surrogate measures of increased cardiovascular risk.8

Methods

Subjects Between November 2002 and March 2003, we screened all subjects referred for diagnostic abdominal ultrasound to the Radiology Service of Hospital San Millán-San Pedro, Logroño, for fatty liver. A "bright liver" (abnormally intense, high-level echoes arising from the hepatic parenchyma, with an amplitude similar to that of echoes arising from the diaphragm) in the absence of chronic liver disease or cancer was detected in 93 subjects, who were recruited into a protocol approved by the institutional review board. Sixty-six subjects accepted participation and gave signed informed consent. Participants were first given a complete clinical history, during which alcohol consumption was assessed as part of the interview, including the World Health Organization (WHO) Alcohol Use Disorders Identification Test8 and medication use. This was followed

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Since submission of this manuscript, the carotid ultrasound findings of a case–control study in men with and without NAFLD have been published8 and show a higher IMT in the former. The high frequency of MetS components in NAFLD was confirmed. The results support the atherogenic potential of NAFLD observed in our study.

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by blood sampling for liver function tests, including markers for viral, autoimmune, and metabolic liver diseases. Excluded were subjects abusing alcohol or having daily alcohol consumption >20 g (n=13), seropositive for hepatitis B or C viruses (n=12), or with serum transferrin saturation >45% (n=1), thus leaving 40 subjects with “primary” NAFLD. Sex- and age-matched control subjects, randomly chosen from local National Health Service card holders, were contacted by telephone and offered an abdominal ultrasound and participation in the study provided they did not abuse alcohol and that the liver was ultrasonographically normal. The radiologist was blinded to the identity and clinical and biochemical findings of the subjects. To find 40 controls, 61 persons were called (16 refused participation and 5 were excluded because a fatty liver was detected by ultrasound examination).

After signing informed consent, participants entered a study protocol consisting of clinical evaluation for cardiovascular risk factors: sampling of fasting blood for measurement of glucose, insulin, lipids, liver function tests, α-1 antitrypsin (AAT), and high-sensitivity C-reactive protein (CRP); an oral glucose tolerance test; and carotid ultrasound for determination of IMT and presence of plaque.

Clinical and Laboratory Measurements

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Obesity was defined as a BMI ≥ 30 kg/m². Waist circumference was measured after expiration at the midpoint between the lowest rib and the iliac crest. Hip circumference was obtained at the widest point between hip and buttock. Blood pressure was measured with a random-zero mercury sphygmomanometer. We used the mean of 2 measurements of systolic and diastolic blood pressure taken while subjects were sitting after a 5-minute rest.

Subjects fasted overnight before phlebotomy. Serum glucose, both fasting and 120 minutes after an oral glucose challenge (75 g in 200 mL water), was measured using a glucose dehydrogenase method. Serum insulin was determined by standard radioimmunoassay. Cholesterol and triglycerides were measured using enzymatic procedures. High-density lipoprotein (HDL) cholesterol was quantified after precipitation with manganese chloride. Low-density lipoprotein (LDL) cholesterol was calculated with the Friedewald equation. Apolipoprotein B (apoB) was determined by the use of turbidimetry. The index of insulin resistance was calculated using the fasting values of serum glucose and insulin according to the homeostasis model assessment (HOMA) method. The top quartile of control values was present in 16 (40%) NAFLD patients and 10 (25%) control subjects (P=0.003). Serum ferritin was also higher in NAFLD than in control subjects. Obesity was present in 24 (60%) patients with NAFLD and in 7 (17.5%) control subjects (P=0.001).

Table 1 shows that patients with NAFLD had higher fasting and 120-minute glucose and were more insulin resistant than control subjects. Metabolic testing uncovered 6 additional cases of diabetes among NAFLD patients. Two new cases of diabetes were also detected in the control group. Subjects with known and newly discovered diabetes had fair glycemic control, as judged by HbA1c levels (mean 7.4%; range 6.4% to 9.1%). Total cholesterol, LDL cholesterol, and apoB levels were similar, whereas HDL cholesterol was lower and triglycerides were higher in NAFLD than in controls. The levels of serum alanine aminotransferase (ALT) and γ-glutamyl transpeptidase (GGT) were nearly double in NAFLD. The AAT level was similar in the 2 groups, whereas CRP was higher in the NAFLD group than in control subjects. Regarding iron status, serum levels of total transferrin and ferritin were also higher in NAFLD than in controls.

Taking the upper quartiles of control values as normality limits, elevated serum CRP was present in 24 (60%) NAFLD patients and 10 (25%) control subjects (P=0.003), whereas a CRP >3.0 mg/L, the level above which cardiovascular risk is substantially increased, was detected in 17 (42.5%) and 2 (5%), respectively (P<0.001). In CRP level was strongly correlated with BMI (r=0.604), waist circumference (r=0.431), ln HOMA (r=0.604), and the serum ALT level (r=0.384). Other correlations of ln CRP were AAT (r=0.337; P=0.003) and systolic blood pressure (r=0.258; P=0.021). A serum ferritin above the upper quartile of control values was present in 16 (40%) NAFLD patients and 10 (25%) control subjects (P=0.23). In ferritin correlated strongly (P<0.001) with fasting glucose (r=0.358) and ALT (r=0.389); weaker but significant (P<0.05) correlations of ln ferritin were the serum GGT level (r=0.332), ln HOMA (r=0.280), waist circumference (r=0.221), and carotid IMT (r=0.254).

Criteria for MetS

Whether assessed by ATP III or WHO criteria, all the risk factors related to MetS (visceral adiposity, hypertension,
abnormal glucose metabolism, insulin resistance, hypertriglyceridemia, and low HDL cholesterol) were significantly (P<0.005) more prevalent in NAFLD patients than in control subjects, resulting in a 4-fold higher frequency of WHO-MetS (80% versus 20%, respectively) and a nearly 5-fold prevalence of ATP-MetS (72.5% versus 15%, respectively) in NAFLD. The prevalence of ATP-MetS and WHO-MetS in NAFLD was higher in women than in men (80% versus 70% and 85% versus 55%, respectively), whereas depending on the definition, control men had a 3- to 5-fold excess of MetS compared with control women (25% versus 5% by ATP criteria and 30% versus 10% by WHO criteria, respectively).

Findings of Carotid Ultrasound Studies

Compared with control subjects, patients with NAFLD also showed increased mean and maximum IMT and a 2-fold higher frequency of plaque (Table 2). The mean differences (95% CI) between NAFLD and controls were 0.16 mm (0.08 to 0.23 mm) for mean IMT and 0.17 mm (0.09 to 0.25 mm) for maximum IMT (P=0.0001 for both). Figure 1 shows that case–control differences in IMT and plaque frequency were more marked in women than in men. When subdividing the study population into

### Table 1. Clinical and Laboratory Data of Patients With NAFLD and Control Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=40)</th>
<th>Controls (n=40)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men/women</td>
<td>20/20</td>
<td>20/20†</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>53.2±12.6</td>
<td>51.6±10.9†</td>
<td>0.001</td>
</tr>
<tr>
<td>History of high blood pressure</td>
<td>20 (50)</td>
<td>6 (15)</td>
<td></td>
</tr>
<tr>
<td>History of diabetes</td>
<td>7 (17.5)</td>
<td>0‡</td>
<td>0.012</td>
</tr>
<tr>
<td>History of CHD</td>
<td>4 (10)</td>
<td>0‡</td>
<td>0.12</td>
</tr>
<tr>
<td>Current smoker</td>
<td>11 (27.5)</td>
<td>10 (25)</td>
<td>0.80</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.8±5.1</td>
<td>26.3±3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>104±13</td>
<td>91±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.93±0.07</td>
<td>0.89±0.07</td>
<td>0.015</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>141±16</td>
<td>124±16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>87±9</td>
<td>77±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>6.4±1.3</td>
<td>5.5±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>120-minute glucose, mmol/L</td>
<td>8.1±3.2</td>
<td>5.7±1.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>17.4±9.6</td>
<td>8.7±4.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin resistance (HOMA index)</td>
<td>4.12 (2.80–5.78)</td>
<td>1.63 (1.42–2.65)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>28 (70)</td>
<td>10 (25)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.9±1.1</td>
<td>5.8±1.0</td>
<td>0.65</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.8±0.9</td>
<td>3.9±0.9</td>
<td>0.55</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.1±0.3</td>
<td>1.3±0.3</td>
<td>0.013</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.6 (1.0–2.4)</td>
<td>0.9 (0.7–1.2)  §</td>
<td>0.005</td>
</tr>
<tr>
<td>ApoB, g/L</td>
<td>1.29±0.32</td>
<td>1.20±0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>ALT, μU/mL</td>
<td>43±23</td>
<td>22±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GGT, μU/mL</td>
<td>47±45</td>
<td>20±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AAT, g/L</td>
<td>1.71±0.28</td>
<td>1.62±0.31</td>
<td>0.24</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>1.85 (1.33–6.28)</td>
<td>1.10 (0.60–1.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum iron, ng/mL</td>
<td>83±36</td>
<td>78±29</td>
<td>0.53</td>
</tr>
<tr>
<td>Total transferrin, ng/mL</td>
<td>263±32</td>
<td>239±40</td>
<td>0.004</td>
</tr>
<tr>
<td>Transferrin saturation, percent</td>
<td>25.4±10.8</td>
<td>25.8±10.8</td>
<td>0.89</td>
</tr>
<tr>
<td>Ferritin, ng/mL</td>
<td>106 (68–163)</td>
<td>76 (39–121)</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Data are mean±SD or No. (percent) or median (interquartile range) for variables with skewed distribution. *Group comparisons by unpaired t test or chi-square test, with Fisher’s exact test (‡), and Whitney U test (§), when appropriate; †selection criteria not tested for statistical significance.

### Table 2. Carotid IMT and Plaque in Patients With NAFLD and Control Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=40)</th>
<th>Controls (n=40)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean IMT, mm</td>
<td>0.70±0.20</td>
<td>0.54±0.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Maximum IMT, mm</td>
<td>0.75±0.22</td>
<td>0.58±0.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean IMT above top quartile</td>
<td>27 (67.5)</td>
<td>10 (25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carotid plaque</td>
<td>20 (50)</td>
<td>10 (25)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Data as mean±SD or No. (percentage). *Group comparisons by unpaired t test or chi-square test.
subjects with and without MetS, by any definition, and with and without NAFLD, IMT progressed in the order: control without MetS < control with MetS < NAFLD without MetS < NAFLD with MetS (Figure 2).

**Figure 1.** Comparisons of mean carotid IMT (top) and plaque frequency (bottom) in patients with NAFLD and control subjects. Error bars represent SEM.

**Figure 2.** Sex- and age-adjusted mean carotid IMT in control (Ctrl) subjects and NAFLD patients with and without MetS by 2 definitions. Error bars represent 95% CIs.

**NAFLD and Carotid Atherosclerosis Predictors by Multivariate Analyses**

After adjustment for sex, age, the risk factors listed in Table 1 showing a significant bivariate relationship, the serum level of CRP and AAT categorized as abnormal when above the respective top quartiles, and the frequency of ATP-MetS or WHO-MetS components, independent associations of NAFLD by multivariate logistic regression were visceral obesity (OR, 4.65; 95% CI, 1.43 to 14.54; \( P = 0.010 \)) and MetS (OR, 8.67; 95% CI, 2.65 to 28.33; \( P = 0.0001 \)) when considering ATP-III criteria, and hyperlipidemia (OR, 4.50; 95% CI, 0.96 to 21.05; \( P = 0.056 \)) and MetS (OR, 5.91; 95% CI, 1.74 to 20.09; \( P = 0.004 \)) when using the WHO definition.

Logistic regression with similar adjustments, including the presence of NAFLD, and with abnormal IMT as dependent variable showed independent associations with older age (OR, 2.49 per 10 years; 95% CI, 1.41 to 4.39; \( P = 0.002 \)), the presence of NAFLD (OR, 8.38; 95% CI, 2.39 to 29.43; \( P = 0.001 \)), and serum ferritin above the top quartile of control values (OR, 3.14; 95% CI, 1.24 to 7.94; \( P = 0.016 \)). When considering plaque occurrence as the dependent variable, similar associations with age (\( P = 0.001 \)) and serum ferritin (\( P = 0.012 \)) were observed, but NAFLD was excluded from the equation and replaced by MetS, whether defined by ATP-III or WHO criteria (\( P = 0.001 \)). Exclusion of the 4 cases with previous CHD or the 7 patients with known diabetes did not appreciably change either the predictive variables or the ORs for abnormal IMT or plaque (data not shown).

**Discussion**

This case–control study assessed the frequency and magnitude of cardiovascular risk factors and measured carotid atherosclerosis in unselected patients with an ultrasound diagnosis of primary NAFLD. Confirming previous evidences, \(^1 \text{−}^5 \) patients with NAFLD showed a cluster of abnormalities related to MetS. A novel finding of this study is that patients with NAFLD had advanced carotid atherosclerosis. NAFLD was an independent predictor of an increased IMT, whereas MetS, present in 72.5% (ATP-III) or 80% (WHO) of NAFLD patients, was independently associated with carotid plaque. The findings support the view of NAFLD as a hepatic manifestation of MetS. \(^5,14,15 \) They also suggest that hepatic fat accumulation is atherogenic beyond its association with insulin resistance.

The diagnosis of NAFLD was based on the exclusion of known etiologic factors of liver disease and on ultrasound examination but was not confirmed by liver biopsy for ethical reasons. However, ultrasound examination is by far the commonest way of diagnosing NAFLD in clinical practice \(^16 \) and is very sensitive in the detection of significant hepatic steatosis in patients with biopsy-proven disease. \(^17 \) Indeed, Saadeh et al \(^17 \) reported that the presence of >33% fat on liver biopsy was optimal for radiological detection of steatosis; that is, moderate to severe fatty infiltration has to be present for the liver ultrasound pattern to become altered and suggest the diagnosis of NAFLD. Insulin resistance was not measured by the euglycemic clamp technique but by the simpler HOMA method. However, HOMA has been reported as a very reliable technique to assess insulin sensitivity. \(^10,18\)
MetS, whether defined by ATP-III\textsuperscript{11} or WHO criteria,\textsuperscript{12} was the strongest determinant of NAFLD in a multivariate model with adjustment for various confounders. This finding agrees with previous evidences of a strong association of NAFLD with individual features of MetS, such as obesity, type 2 diabetes, and dyslipidemia, or with the complete syndrome.\textsuperscript{1,5,14,15} As shown in recent reports from different populations,\textsuperscript{19–21} adults with MetS are at consistently increased risk for cardiovascular and all-cause mortality. Carotid plaque incidence, a measure of advanced atherosclerosis, was independently associated with MetS in our study. Likewise, an increased incidence and progression of carotid plaque in subjects with MetS has been reported recently from the prospective Bruneck Study.\textsuperscript{22} Thus, the close association of NAFLD with MetS might explain the high cardiovascular mortality observed in NAFLD.\textsuperscript{7}

In our study, carotid IMT was noticeably higher in NAFLD patients than in sex- and age-matched control subjects. Furthermore, by logistic regression with adjustment for various confounders, the presence of NAFLD was associated with an abnormal IMT independently of MetS and all its traits, regardless of definition. Moreover, sex- and age-adjusted IMT increased in the sequence: control without MetS<control with MetS<NAFLD without MetS<NAFLD with MetS (Figure 2). These findings suggest that NAFLD is atherogenic beyond its association with MetS. However, to prove this contention, larger numbers of subjects with and without NAFLD and with and without MetS need to be studied for carotid atherosclerosis or other cardiovascular risk markers.

As opposed to control subjects, women with NAFLD had carotid atherosclerosis to a similar or even higher extent than men with NAFLD (Figure 1). These observations agree with studies showing that several MetS traits\textsuperscript{23,24} or MetS by itself\textsuperscript{21} have a stronger effect on CHD risk among women than men.

A probable mechanistic explanation for the marked proatherogenic effect of NAFLD is the enhanced oxidative stress characteristic of this condition, which is believed to play a role in the progression from hepatic steatosis to steatohepatitis, fibrosis, and cirrhosis.\textsuperscript{1,4–25} Reactive oxygen species derived from steatosis-stimulated fatty acid oxidation, attendant hepatocyte injury and cytokine release, and the ensuing inflammatory milieu are likely to perpetuate the liver disease of NAFLD and add additional atherogenic stimuli to the already high oxidative/inflammatory status associated with MetS and epitomized by an elevated CRP serum level.\textsuperscript{26–28} CRP was higher in NAFLD patients than in control subjects in our study. As expected, the CRP level was strongly associated with adiposity measures and insulin resistance. However, CRP was also associated with ALT, the best serum marker of hepatic inflammation, and with AAT, a serine proteinase inhibitor and acute-phase reactant predominately synthesized in the liver.\textsuperscript{29} Together, these findings suggest that hepatic injury contributed to the inflammatory status in NAFLD.

Another potential mechanism by which NAFLD may increase cardiovascular risk beyond that imposed by MetS is abnormal lipoprotein metabolism. In NAFLD, hepatic apoB synthesis, a limiting step in very LDL (VLDL) formation, is reduced\textsuperscript{30} and postprandial apoB responses are flat and strikingly dissociated from triglyceride increases.\textsuperscript{31} Disturbances of VLDL assembly in NAFLD could be causal to the development of hepatic steatosis. Importantly, impaired VLDL secretion also results in a lower number of circulating particles that are large, triglyceride-rich, and highly atherogenic.\textsuperscript{32,33} Other conditions characterized by hepatic steatosis or impaired liver function, such as preeclampsia\textsuperscript{34} and fatty liver of pregnancy,\textsuperscript{35} also feature an accumulation of triglyceride-rich VLDL and remnants in the circulation. Our patients with NAFLD had elevated triglycerides, but the total serum apoB level was similar to control values (Table 1), suggesting the presence of triglyceride-rich lipoproteins. However, detailed lipoprotein compositional studies should be performed in NAFLD to prove this contention.

Ferritin serum levels were moderately increased in NAFLD patients compared with control subjects. The main function of ferritin is the storage and delivery of iron for cellular use, and the serum ferritin concentration reflects the level of total body iron stores. However, ferritin is also an acute-phase reactant that may increase in response to infection, inflammation, and other stimuli.\textsuperscript{36} Subjects with iron overload suggestive of hereditary hemochromatosis were excluded by study design. There are no evidences for a role of excess iron in the pathogenesis of NAFLD,\textsuperscript{3,5,15} presumably, a higher ferritin level in these patients could be linked to the existence of an inflammatory milieu associated with liver cell steatosis and necrosis. The finding in our study that the ferritin level was strongly correlated with markers of liver cell injury supports this theory.

Elevated ferritin was strongly and independently associated with an abnormal IMT and carotid plaque in our study. After much research and debate, the results to date do not support the theory that iron status is related to CHD.\textsuperscript{37,38} Although the observed association between ferritin and carotid atherosclerosis might add to the controversy, an alternate explanation for this finding involves the inflammatory state intimately linked to atherosclerosis: because ferritin genes are upregulated by inflammatory cytokines and are susceptible to induction in the course of plaque formation,\textsuperscript{39} the elevated serum ferritin level might just be reactive to the atherogenic process.

In summary, NAFLD is a strong risk factor for carotid atherosclerosis beyond its association with MetS. As illustrated by the frequency of previous CHD and uncovered diabetes in unselected patients with NAFLD, the clinical corollary to our findings is that the casual detection of a fatty liver on abdominal ultrasound examination should alert to the probable existence of multiple underlying cardiovascular risk factors warranting evaluation and treatment as much as the risk for advancing liver disease.

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References


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