Association between Nonalcoholic Fatty Liver Disease (NAFLD) and Coronary Artery Disease (CAD) in Patients with Angina Pectoris

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ABSTRACT

Background: Prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing in Iranian population. The aim of this study was the investigation of association between nonalcoholic fatty liver disease (NAFLD) and coronary artery disease (CAD) in patients with angina pectoris.

Methods: 82 patients with confirmed CAD by coronary angiography and 82 individuals with normal coronary angiography, as the control group, were selected. Hepatic ultrasound scanning was performed in all the subjects to determine the NAFLD. Data were analyzed by SPSS software and independent T-test and Chi-square tests.

Results: Findings gathered from the patients with angina pectoris showed that the prevalence of NAFLD in CAD patients was higher than the control group. Grade of fatty liver and the portal vein size in CAD patients were significantly more than the control group.

Conclusion: NAFLD is a risk factor of CAD in the angina pectoris patients. Increase in the prevalence of NAFLD can lead to the increase in cardiovascular diseases.

Keywords: Non-Alcoholic Fatty Liver Disease; Coronary Artery Disease; Angina Pectoris

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is one of the most common hepatic disorders [1]. Prevalence of this disorder is 10% - 30% in general population and its prevalence is increasing in both developing and developed countries [2-5]. NAFLD has been strongly associated with insulin resistance and metabolic syndrome; most of patients are overweight or obese, and they have glucose metabolism deficiencies, dyslipidemia, and hypertension which all are the risk factors of NAFLD [6-8].

Coronary artery disease (CAD) is the first cause of death in rich countries and the second cause of death in the medium and low income countries [9]. Risk factors of CAD include age, gender [10-14], diabetes mellitus [15-18], low physical activity, smoking, hyperlipidemia, metabolic syndrome, and diet [9]. Study that was conducted in Iranian population showed that 24% of adults in Isfahan city had these risk factors [19].

NAFLD has been thought to be a new risk factor for CAD. Other new risk factors are inflammatory markers and fibrinolytic and hemostatic dysfunctions. Recent studies revealed that NAFLD patients had an accelerated risk of increased carotid intima and media thickness [20,21], reduced endothelial function [22], increased coronary artery calcification [23,24], and increased arterial stiffness [20]. According to some studies, NAFLD and CAD have the similar risk factors including dyslipidemia, hypertension, physical inactivity, insulin resistance and inflammation, therefore, a possible relationship between NAFLD and CAD can be assumed and evaluated [8-25]. In addition, increase in liver enzymes has been identified as an independent risk factor for CAD and a large number of patients with CAD had abnormal liver function tests [26].

As regards, in Iran, the most common cause of increase in liver enzymes is NAFLD, and the increase in liver enzymes has been demonstrated as a risk factor for CAD. Aim of this study was investigation of the possible association between NAFLD and CAD in patients with angina pectoris.
2. Methods and Materials

2.1. Participants

This is a case-control study conducted on the patients with angina pectoris and the candidates for coronary angiography. Patients were chosen from those who referred to the Chamran and Khorsid hospitals in Isfahan city. Patients with the history of recent myocardial infarction or other general disorders, pregnant women and alcoholics were excluded. Coronary angiography was performed and the severity of CAD was assessed in those with the positive coronary angiography results. 82 patients with the confirmed CAD in coronary angiography and 82 individuals with matched age, sex, sugar and lipid profile, and weight and height as the control group with the normal coronary angiography results were selected with simple randomization for the present study. Sample size was calculated by this equation [27]:

\[ n = \left(\frac{z_{1-\alpha/2} + z_{1-\beta}}{d} \right)^2 \left[ P_1 (1 - P_1) + P_2 (1 - P_2) \right] \]

The relevant ethics committee of Isfahan University of Medical Sciences granted approval for this research (project number: 385,316). Informed consent form was completed by the subjects.

2.2. Conventional X-Ray Coronary Angiography

All participants were undergone standard clinical diagnostic x-ray angiography. Conventional x-ray coronary angiography was performed with an integrated digital cardiac catheter imaging system. All of the coronary angiographies were performed by one investigator. Then, the x-ray angiograms were investigated by the three cardiologists, and, the percentage of stenosis diameter, as the reference diameter, was determined, according to the SI Unit.

2.3. Hepatic Ultrasound Scanning

Hepatic ultrasound scanning was performed in all the subjects by one trained radiologist, who was unaware of all the clinical and laboratory characteristics of the patients, using a Toshiba Nemio 30 scanner (just vision model, Toshiba CO. Ltd., Tokyo, Japan) with a 3.5 MHz linear transducer. Participants were asked to lie in the supine and 60° left lateral positions during quiet inspiration. The presence or absence and the grading of fatty infiltration of the liver were recorded. Absence or grade 0 of fatty infiltration was defined when the echogenicity of liver moderately increased, with slightly impaired visualization of the diaphragm or intrahepatic vessels. Grade 3 (severe) of fatty infiltration was considered when the liver echogenicity markedly increased with the poor visualization of diaphragm, the intrahepatic vessels and the posterior portion of the right liver lobe [28].

2.4. Statistical Analysis

All data were analyzed by SPSS (version 16) software. Data are presented as the mean ± standard deviation (SD) or frequencies. Statistical analyses included the independent T-test (for continuous variables) and the Chi-square test (for categorical variables). p < 0.05 was considered statistically significant.

3. Results

This study was conducted on 82 CAD patients and 82 normal participants. Case and control groups were matched by age, sex, blood sugar and lipid profile, weight and height. There was 24 females (29.26%) and 58 males (70.73%) in each group (CAD patients and control group). Basic characteristics of participants in two groups are shown in Table 1.

Our results showed that the patients with CAD had significantly higher NAFLD compared to the control group (p = 0.001). In addition, the proportions of subjects with NAFLD in CAD patients group were significantly higher than control group in the two genders. 50 males and 20 females in CAD group had NAFLD (Table 2).

The mean severity of NAFLD in CAD group was significantly higher than the control group (1.24 vs 0.59). Frequencies of various grades of NAFLD in the CAD patients and control group are shown in Figure 1.

Table 1. Basic characteristics of participants.

<table>
<thead>
<tr>
<th></th>
<th>Normal group</th>
<th>CAD patients group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>44.2 ± 4.54</td>
<td>44.8 ± 4.20</td>
<td>0.83</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.8 ± 1.48</td>
<td>73.4 ± 2.30</td>
<td>0.63</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.8 ± 2.77</td>
<td>164.8 ± 4.08</td>
<td>0.66</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>115.8 ± 10.91</td>
<td>117.8 ± 11.47</td>
<td>0.78</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>211.6 ± 7.43</td>
<td>215.5 ± 7.04</td>
<td>0.45</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>160.2 ± 8.07</td>
<td>166.25 ± 6.29</td>
<td>0.26</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>44.8 ± 3.27</td>
<td>43.0 ± 2.58</td>
<td>0.40</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>108.0 ± 8.09</td>
<td>115.4 ± 1.67</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Mean ± standard deviation. CAD = coronary artery disease, FBS = fasting blood sugar, TC = total cholesterol, TG = triglyceride, HDL = high density lipoproteins, LDL = low density lipoproteins.
According to the findings, cardiovascular mortality rate is increasing in NAFLD patients [30]. Targher et al. [31] reported that NAFLD is a predictor of cardiovascular disease CVD in type II diabetes. Hamaguchi et al. [32] showed the relationship between NAFLD and CVD in healthy patients. Several mechanisms were suggested for the relationship between NAFLD and CAD. Oxidative stress increases in NAFLD and finally leads to the modification of low-density lipoproteins (LDL) and produces oxidized LDL that is a risk factor for atherosclerosis and CAD [33]. Studies showed that NAFLD is strongly associated with insulin resistance (IR) as well as reduced insulin sensitivity [34]. IR leads to the endothelial dysfunction and finally atherosclerosis [35]. Studies show that the levels of interleukin 6 (IL-6) and C-reactive protein (CRP) are increased in NAFLD, and NAFLD was considered as a chronic inflammatory condition. Inflammation mediates all the stages of atherosclerosis [9]. In addition, patients with NAFLD have reduced levels of adiponectin [36], and lower plasma adiponectin concentration is associated with early CAD onset and multiple atherosclerotic lesions in coronary arteries.

The limitation of our study is that NAFLD was diagnosed based on the ultrasonography appearance of liver. Gold standard for the diagnosis of NAFLD is liver biopsy but as this process is invasive and costly, we did not perform liver biopsy.

5. Conclusion

This study was conducted among the patients with angina pectoris showed that the NAFLD was more prevalent in CAD patients. Thus, NAFLD is a risk factor for the presence of CAD in patients with angina pectoris and clinicians must pay attention to this risk factor in health care.

REFERENCES


