

## Prevalence of non-alcoholic fatty liver disease in patients with coronary artery disease

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### Short Communication

#### Abstract

**BACKGROUND:** Several common metabolic risk factors contribute to development of both non-alcoholic fatty liver disease (NAFLD) and coronary artery disease (CAD). The aim was to determine prevalence of NAFLD in patients with CAD.

**METHODS:** This prospective study was carried out from December 2011 to June 2012. All patients with documented diagnosis of CAD with stenosis of one of the main coronary arteries or their branches were included in the study. Ultrasound examination of liver was performed in all patients to diagnose hepatic steatosis. Accordingly, the severity of steatosis was graded from 0 (absence of steatosis) to 3 (severe steatosis). Finally, prevalence of NAFLD was determined in the studied patients.

**RESULTS:** Among 170 patients with CAD included in the study, 63 and 17 had grade 1 and 2 hepatic steatosis in ultrasound examination, respectively, providing prevalence of 47% in studied population. There was no significant difference between patients with NAFLD and those without NAFLD regarding gender ( $P = 0.120$ ), presence of diabetes mellitus ( $P = 0.270$ ), hyperlipidemia ( $P = 0.210$ ) and hypertension ( $P = 0.870$ ). There was no association between involvement of left anterior descending artery and hepatic steatosis ( $P = 0.870$ ).

**CONCLUSION:** The present study indicated a high prevalence of NAFLD in patients with documented CAD.

**Keywords:** Non-Alcoholic Fatty Liver Disease, Coronary Artery Disease, Ultrasound

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#### Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by triglyceride deposition in the liver exceeding 5% of the total liver weight in the absence of a history of heavy alcohol intake and other etiologies of liver disease.<sup>1</sup> Based on a report from Tehran, capital of Iran, steatosis was found in 31.6% (283 out of 896) of liver samples obtained during autopsy, which was the most common silent liver disease in the study sample.<sup>2</sup> In a school-based study on 966 school-aged children in Iran, NAFLD was detected in 7.1% of children.<sup>3</sup> In addition, in a recent population-based study conducted on 819 individuals in Shiraz, Iran, the prevalence of NAFLD was reported 21.5%.<sup>4</sup>

NAFLD is closely associated with metabolic syndrome and insulin resistance<sup>5</sup> which some of them contribute to development of coronary artery disease (CAD).<sup>6</sup> Thus, it was hypothesized that

NAFLD correlates with CAD, which is one of the major causes of mortality worldwide.

Since CAD is usually symptomatic, finding significant relationship between CAD and NAFLD may indicate that patients who are diagnosed with CAD may benefit from screening for NAFLD to diagnose the disorder in early stages. Thus, the present study was designed and conducted to determine the prevalence of NAFLD in patients with CAD.

#### Materials and Methods

After approval of the Ethical Committee of Human Research of Lorestan University of Medical Sciences, Iran, this prospective study was conducted in Angiography Ward of Khorramabad Heart Center, Iran, from December 2011 to June 2012. All patients signed an informed consent before enrollment. Patients were selected among those

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underwent coronary artery angiography in Khorramabad Heart Center due to acute coronary syndrome, chest pain, or positive exercise test. Patients with or without any degree of stenosis in the coronary arteries or their branches in coronary angiography were included in the study, randomly. Patients with history of coronary artery bypass graft (CABG), excessive alcohol intake, any hepatic disorder, cor pulmonale, chronic renal disease, cancer, acute or chronic infections, positive serology for hepatitis B, C, human immunodeficiency virus (HIV) or syphilis, and heart failure were excluded from the study.

The Gensini scoring system was used to determine the severity of CAD.<sup>7</sup> In brief, the coronary artery tree was divided in 8 segments and in each segment the most severe stenosis scored based on the following classification: stenosis less than 25% was considered as score 0, 25%-49% scored 1, 50% to 74% scored 2, 75% to 99% scored 3, and 100% stenosis was considered as score 4. These score were then multiplied by a number indicating the importance of the lesion's location in the coronary artery tree. The number for the left main coronary artery was 5, for the proximal left anterior descending (LAD) or proximal left circumflex was 2.5, for the mid-part of the LAD was 1.5, and for the right coronary artery, distal LAD and mid-distal region of the left circumflex was 1.

Diagnosis of NAFLD was made based on the ultrasound findings. All ultrasound examinations were performed after 12 hours of fasting by one radiologist using the same device and criteria. Echogenicity of

liver was compared to the echogenicity of the left kidney and using the following grading system: grade 0, no fatty liver; grade 1, mild disease; grade 2, moderate disease; and grade 3, severe disease. The method described by Saverymuttu et al.<sup>8</sup> was used to assess hepatic steatosis. The method works based on the abnormally intense, high level echoes from the hepatic parenchyma, liver-kidney difference in echo amplitude and echo penetration into the deep portion of the liver and clarity of vascular pattern of the liver.

Sample size was calculated based on the study by Acikel et al.<sup>9</sup> By considering the 38% frequency of fatty liver disease in patients with CAD, we determined 135 patients required to achieve an accuracy of 0.05 with a type I error of 0.05. However, we included 170 individuals in the study period.

Statistical analysis was performed utilizing the MedCalc software version 12.2.1.0 (Mariakerke, Belgium) and SPSS software for Windows (version 17.0, SPSS, Inc., Chicago, IL, USA). Fisher's exact test and Student's independent t-test were used to analyze categorical and continues variables respectively. P-values less than 0.05 were considered to be statistically significant.

## Results

One hundred and seventy individuals including 93 females (54.7%) were enrolled in the study. Mean age of the patients was  $58.1 \pm 12.5$  years. Mean body mass index (BMI) of the studied patients was 26.4 ranging from 19.2 to 42.2 kg/m<sup>2</sup>. Table 1 demonstrates angiographic findings in studied patients.

**Table 1.** Angiographic findings of coronary artery in studied patients

Vessel stenosis	25%-49%	50%-74%	75%-99%	100%
Coronary artery	(Number)	(Number)	(Number)	(Number)
Proximal LAD	7	8	20	11
Mid-part LAD	11	15	24	3
Distal LAD	0	4	9	1
Diagonal arteries	2	8	21	3
Proximal left circumflex	3	7	8	3
Mid-part left circumflex	12	6	11	4
Distal left circumflex	2	3	3	0
Obtuse marginal	2	11	15	4
Proximal RCA	8	7	7	12
Mid-part RCA	12	10	8	5
Distal RCA	5	1	7	1
PDA	2	1	7	0
PLV	1	0	1	1

LAD: Left anterior descending; RCA: Right Coronary artery; PDA: Posterior descending artery; PLV: Posterior left ventricular branches

**Table 2.** Different study parameters in different degrees of non-alcoholic fatty liver disease

Characteristic	No NAFLD	Mild NAFLD (Grade 1)	Moderate NAFLD (Grade 2)	P
Gender				
Male	46 (59.7)	24 (32.1)	7 (9.1)	0.230
Female	43 (46.7)	39 (42.4)	10 (10.9)	
Age				
< 40 years	71 (55.9)	45 (35.4)	11 (8.7)	0.350
≥ 40 years	19 (44.2)	18 (41.9)	6 (14.0)	
Hypertension [n (%)]				
Yes	31 (51.7)	23 (38.3)	6 (10.0)	0.960
No	59 (53.6)	40 (36.4)	11 (10.0)	
Hyperlipidemia [n (%)]				
Yes	10 (41.7)	12 (50.0)	2 (8.3)	0.360
No	80 (54.8)	51 (34.9)	15 (10.3)	
BMI [n (%)]				
Normal	39 (63.9)	19 (31.1)	3 (4.9)	0.005*
Overweight	41 (50.6)	32 (39.6)	8 (9.9)	
Obesity	5 (21.7)	12 (52.2)	6 (26.1)	
CAD [n (%)]				
Yes	56 (50.9)	42 (38.2)	12 (10.9)	0.730
No	34 (56.7)	21 (35.0)	5 (8.3)	
Diabetes				
Yes	19 (44.2)	18 (41.9)	6 (14.0)	0.350
No	71 (55.9)	45 (35.4)	11 (8.7)	
Smoking				
Yes	27 (60.0)	15 (33.3)	3 (6.7)	0.470
No	63 (50.4)	48 (34.8)	14 (11.2)	

NAFLD: Non-alcoholic fatty liver disease; BMI: Body mass index; CAD: Coronary artery disease

\* P < 0.05 significant

Forty-three patients (25.2%) were diabetic, 60 (35.2%) suffered from hypertension and 24 individuals (14.1%) mentioned hyperlipidemia as co-existing medical conditions. History of smoking was found in 45 patients (26.5%).

Sixty-three and 17 cases had grade 1 and 2 steatosis (NAFLD) in ultrasound examination respectively, providing prevalence of 47% (80 patients) NAFLD in studied population. Mean BMI was significantly higher in patients with fatty liver disease compared to those without ( $27.3 \pm 4.4$  kg/m<sup>2</sup> versus  $25.6 \pm 3.4$  kg/m<sup>2</sup>, P = 0.005). There were no significant differences between patients with NAFLD and those without NAFLD regarding gender (P = 0.230), age (P = 0.350), presence of diabetes mellitus (P = 0.350), hyperlipidemia (P = 0.360), hypertension (P = 0.960) and smoking (P = 0.470) (Table 2). There was no significant association between NAFLD and CAD in none of the coronary artery branches (P = 0.730). There was

significant association only between NAFLD and BMI (P = 0.005). Multiple logistic regression model was used to remove confounding factors. Using this model, there was a significant association between NAFLD and CAD (odds ratio = 1.83; P < 0.001). The association between CAD and NAFLD changed to non-significant after adjustment for age, gender, hypertension, hyperlipidemia, BMI, diabetes and smoking (P = 0.430). There was only significant association between age and gender with CAD in regression analysis.

### Discussion

The association between CAD and NAFLD has been investigated widely. Kim et al. enrolled 4023 subjects without known liver disease or a history of ischemic heart disease in their study.<sup>10</sup> They found that coronary artery calcification was associated with NAFLD independent of traditional risk factors for CAD including body visceral adiposity. They suggested that

NAFLD should be considered as an independent risk factor of CAD. In the present study, we found fatty liver disease in 47% of patients with CAD which is inconsistent with the aforementioned studies supporting a close association between NAFLD and CAD. In agreement with our study, Assy et al. demonstrated that 67% and 52% of patients with NAFLD had calcified and non-calcified coronary plaque respectively which was significantly higher than controls<sup>11</sup> and supports high prevalence of NAFLD in CAD patients and vice versa.

It seems that development of coronary artery atherosclerosis in patients with NAFLD is independent of traditional risk factors for CAD, though concomitant presence of these risk factors and metabolic syndrome components potentiates pathogenesis of NAFLD. There are also evidences indicating that NAFLD can cause endothelial dysfunction, elevate biomarkers of inflammation and result in subclinical atherosclerosis in carotid artery.<sup>12,13</sup> In the present study, we found that NAFLD developed more frequently in patients with higher BMI as has been previously reported.<sup>1</sup>

In the present study, we used ultrasound for detection of NAFLD that should be considered as one of the limitations of our study. The study by Foster et al. demonstrated that ultrasound can only detect 60% of patients with fatty infiltration of the liver.<sup>14</sup> The false positive rate was very low in this technique; however, the range of changes in cirrhosis and liver steatosis were similar and experience of the operator was the only tool to distinguish these two conditions.<sup>14</sup> Using liver-kidney contrast technique which was utilized in this study have been shown to improve the detection of fatty liver changes. Yajima et al. indicated that combination of liver-kidney contrast with vascular blurring and deep attenuation can be used for semi-quantitative assessment of liver steatosis.<sup>15</sup> When fatty change is over 30% in the hepatic lobule, using both liver-kidney contrast and vascular blurring will provide sensitivity of 83%, specificity of 100%, and an accuracy of 96% for diagnosis of fatty liver disease.<sup>15</sup> Similarly some other authors suggested that ultrasound can be used with good results for diagnosis of hepatic steatosis.<sup>16</sup> In brief, it is possible that prevalence of fatty liver disease in our study has been underestimated due to limitations of ultrasound in diagnosis of NAFLD.

### Conclusion

Our findings indicated that NAFLD can be detected in high percentage of patients with documented

CAD (47%) and BMI is significantly associated with NAFLD. The present study along with previous reports may indicate the importance of screening for NAFLD in patient with CAD and vice versa.

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### Conflict of Interests

Authors have no conflict of interests.

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