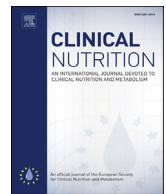




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## Original article

## Lifestyle predictors of obese and non-obese patients with nonalcoholic fatty liver disease: A cross-sectional study

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## SUMMARY

**Background & aims:** Most people with nonalcoholic fatty liver disease (NAFLD) are obese, and they usually eat more while being less physically active as compared to healthy individuals. However, little is known about the lifestyle patterns of non-obese or obese patients with NAFLD. The aim of this study was to investigate nutrition components and behavioral differences between non-obese and obese patients with NAFLD.

**Methods:** This is a cross-sectional study comprising of 209 patients. Nutritional components and physical activity status were compared in obese and non-obese subjects with NAFLD against healthy controls. Dietary intake was assessed using the 5-day food diary. Physical activity was measured using the protocol of Korea Health and Nutrition Examination Survey. Total and regional body composition analysis was conducted using anthropometry and tetrapolar multi-frequency bio-impedance. Visceral adipose tissue, total abdominal adipose tissue, abdominal subcutaneous adipose tissue as well as liver fat were measured using abdomen tomography.

**Results:** Non-obese subjects with NAFLD had higher levels of ALT, AST, GGT, triglyceride, fasting glucose; higher carbohydrate energy ratio; higher visceral fat area, subcutaneous area, body muscle mass, fat free mass and body fat compared to subjects without NAFLD. Subjects with obesity and NAFLD had higher ALT, AST, visceral fat, fasting glucose and HOMA-IR (homeostatic model assessment-insulin resistance), and less moderate-level physical activity compared to those with obesity who do not have NAFLD. Obese subjects with NAFLD also had higher blood pressure, visceral fat area, subcutaneous fat area, body fat, body fat percent and GGT compared to non-obese subjects with NAFLD. In multivariate analysis, carbohydrate energy ratio and physical activity less than moderate-level (<2 h/week) were predictors of NAFLD in non-obese subjects independent of the visceral fat, body muscle index, total energy intake, age and sex. Physical activity less than moderate-level was a predictor of NAFLD in obese subjects with NAFLD, independent of the HOMA-IR, visceral fat, total energy intake, fat energy percent, age and sex. **Conclusions:** Percentage of carbohydrate intake percent and physical activity, less than moderate-level were independent predictors of NAFLD in non-obese subjects. Meanwhile, physical activity, less than moderate-level, was an independent predictor in obese subjects.

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**Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DM, diabetes mellitus.

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## 1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is characterized by surplus fat accumulated in the liver, often associated with excessive energy intake. Mostly NAFLD patients are either obese or overweight and only a few have normal body weight [1]. Non-obese people with NAFLD account for 16–18% of the western population [2,3], and 15–22% of the eastern population [4,5]. However, little is known about the pathogenesis and clinical characteristics of NAFLD in non-obese patients. Globally, prevalence of NAFLD has been rising in the recent years along with its associated conditions, such as obesity, insulin resistance, metabolic syndrome and diabetes [6]. Previous studies reported that non-obese NAFLD patients are metabolically less healthy than obese NAFLD patients [7,8]. In a retrospective study of 29,994 subjects, the prevalence of factors for metabolic syndrome, such as hypertension and hyperlipidemia was higher in non-obese NAFLD than in obese NAFLD patients [9]. Another study suggested that metabolic disorders, such as insulin resistance and hyperlipidemia have a critical role in causing NAFLD, regardless of abdominal obesity [1,7]. Moreover, high fasting glucose was also an independent predictor for NAFLD [7]. In a cohort study in India, 54% of the patients with NAFLD had normal weight and waist circumference. Furthermore, another study found that even the NAFLD patients with body weight within normal range are highly likely to have insulin resistance and hypertriglyceridemia [1]. Eating and exercise habits are important factors for NAFLD and metabolic syndrome in both non-obese and obese patients with NAFLD; however, only a few studies investigated the difference between them [10,11]. To our knowledge, no study investigated the lifestyle patterns in non-obese subjects, which resulted in NAFLD beyond the central obesity and insulin resistance.

Weight reduction through lifestyle modification is the fundamental treatment for NAFLD [12–16]. Seven to 10% weight loss is the target of most lifestyle interventions in obese NAFLD patients, and 7% weight reduction results in improvements on the liver enzymes and/or histology [17]. However, an unresolved problem is how to recommend lifestyle changes related to diet and physical activities to NAFLD patients who are within normal range body weights. The intake of carbohydrates, vitamin C, vitamin K, folate, omega-3 fatty acids, nuts, seeds and vegetables are reported to be important NAFLD-related factors [9,18]. One study also showed that non-obese NAFLD patients had higher cholesterol and lower polyunsaturated fatty acid intake than the obese NAFLD patients; however, the sample sizes were small, with no comparison to a normal-control group [19].

Although NAFLD is associated with multiple factors including visceral fat, metabolic disorder, dietary habits and physical activities, only a few studies examined whether dietary habits and physical activity are related to NAFLD in people with normal body weight, beyond measuring visceral fat and abnormal metabolism indexes [11]. Therefore, the aim of the current study was to determine if nutrition components (macro and micro nutrients) and behaviors including physical activity are predictors beyond visceral obesity for NAFLD in obese and non-obese patients.

## 2. Methods

### 2.1. Study design and patient population

Subjects aged 20–69 years were recruited based on their obesity or NAFLD status from five different clinics. This cross sectional study was a subgroup analysis of a previous paper [18], comprising of 348 consecutively selected men and women who visit the outpatient clinics due to obesity or NAFLD. Baseline dietary and

physical activity information was evaluated by nutritionists. Among 348 participants, 139 were excluded due to inadequate data for physical activity ( $n = 27$ ), lack of abdominal CT scan ( $n = 87$ ), and inadequate data for laboratory finding ( $n = 25$ ). Finally, 209 subjects were recruited for the study and they underwent low dose abdominal computed tomography (CT) scan to measure visceral fat area as well as liver and spleen HU (Fig. 1). This study was conducted under the approval of the institutional review boards of the five participating hospitals (Sungkyunkwan University Hospital, Seoul, Korea, Soonchunhyang University Hospital, Cheonan, Korea, Hallym University Hospital, Chun Cheon, Korea, Eulji University Hospital, Seoul, Korea, Hanyang University Hospital, Seoul, Korea).

### 2.2. Inclusion criteria

To be included in the present study subjects had to be enrolled in the dietary education program and had an abdominal CT scan. Only newly diagnosed NAFLD patients were included. NAFLD was defined as the presence of fatty liver without significant alcohol consumption within the past two years. Fatty liver was assessed by abdominal CT scan and a significant alcohol intake was defined as  $>30$  g/day for men and  $>20$  g/day for women. Obesity was defined as BMI greater than or equal to  $25$  kg/m<sup>2</sup>. Our obesity registry adopted WHO definition of obesity in Asians. The WHO defines obesity as a BMI greater than or equal to  $30$  kg/m<sup>2</sup> in western population; however, BMI greater than or equal to  $25$  kg/m<sup>2</sup> is defined as obesity in the Asian population [20]. To be included in the present study, subjects had to have had their dietary behavior and physical activity assessed and recorded before they benefited from the dietary education program. All co-authors of the present study had access to the data and approved the final manuscript. A signed informed consent was obtained from all subjects.

### 2.3. Exclusion criteria

All subjects who were already diagnosed with NAFLD or were enrolled in a lifestyle modification program for diet and physical activities before the dietary education program were excluded. All subjects taking any medication that might cause fatty liver, including herbal medicines, steroids and amiodarone within last month were excluded. Hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (HCV Ab) tests were conducted with serological tests and patients with hepatitis B or C or autoimmune hepatitis were also excluded. In addition, subjects currently or previously enrolled in a nutrition education program for diabetes or blood pressure control were also excluded.

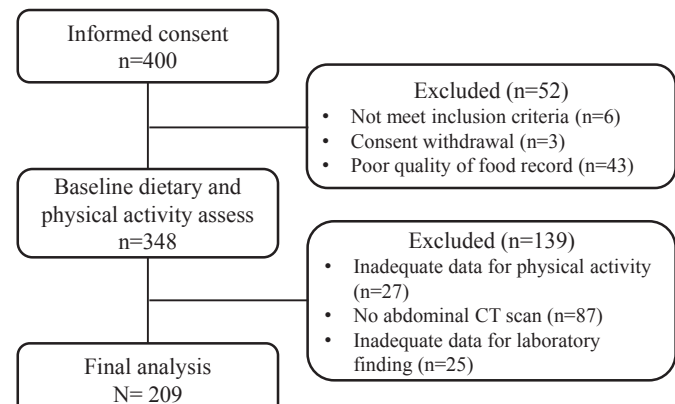


Fig. 1. Study patient population.

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