Effect of Nonalcoholic Fatty Liver Disease on the Development of Type 2 Diabetes in Nonobese, Nondiabetic Korean Men

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Background/Aims: We have a limited understanding of the effect of nonalcoholic fatty liver disease (NAFLD) on the development of type 2 diabetes. Methods: The study subjects included male who had received biennial medical check-ups between 2005 and 2009 and who had been diagnosed with fatty liver disease. The subjects with sustained NAFLD (FL, n=107) and sustained non-NAFLD (NFL, n=1,054) were followed to determine the development of type 2 diabetes. Results: In the FL group, there were more subjects with impaired fasting glucose (IFG), type 2 diabetes and high HOMA-IR than there were in the NFL group during the 5-year follow-up period (32.7 vs. 17.6%, 1.9 vs. 0.3%, 17.9 vs. 5.2% respectively, p<0.05). The FL group showed a higher risk than NFL group for abnormal glucose metabolism as determined using IFG (odds ratio [OR], 2.13; confidence interval [CI], 1.36 to 3.35), type 2 diabetes (OR, 7.63; 95% CI, 1.03 to 56.79) and high HOMA-IR (OR, 3.25; 95% CI, 1.79 to 5.91) and metabolic parameters such as body mass index (OR, 3.35; 95% CI, 1.87 to 6.02), triglyceride (OR, 3.05; 95% CI, 1.92 to 4.86) and fasting blood sugar (OR, 2.18; 95% CI, 1.39 to 3.41). Conclusions: Sustained NAFLD appears to be as sociated with an increased risk for the development of type 2 diabetes and deterioration of metabolic parameters in non-obese, non-diabetic Korean men. (Gut Liver 2012;6:368-373)

Key Words: Nonalcoholic fatty liver disease; Type 2 diabetes mellitus; Metabolic syndrome

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) includes a wide spectrum of liver damage ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), advanced fibrosis and hepatic cancer and is the most commonly encountered chronic liver disease. One study reported the prevalence of NAFLD in Korea as 18% among adults, and the prevalence is increasing due to high fat and high calorie diets, ageing of the population, lack of physical exercise, change in life style, and/or increased obesity. Recently, it was reported that quite a number of people who received health screening tests were found to have NAFLD.

NAFLD is considered to be a hepatic component of metabolic syndrome (MetS). It is associated with obesity, dyslipidemia, and type 2 diabetes, and increased level of serum fatty acid, and it also predicts the clustering of risk factors for cardiovascular disease.

More and more studies have reported that the presence of NAFLD plays a role as an independent risk factor for other systemic metabolic diseases. Also, another study has suggested that NAFLD is associated with insulin resistance, independent of obesity. Numerous studies have reported that the presence of NAFLD independently exacerbates associated systemic metabolic disease.

We retrospectively reviewed cases diagnosed with NAFLD over a period of 5 years to determine the effects of NAFLD on the development of type 2 diabetes and metabolic parameters.
MATERIALS AND METHODS

1. Subjects

Among the 10,950 male subjects who participated in the health screening program at the Health Promotion Center in Kangbuk Samsung Hospital in 2005, we excluded subjects with a history of drinking 20 g or more alcohol per day (n=1,755), diabetes (n=437), chronic liver diseases such as viral hepatitis B (based on serology test or history) (n=558), viral hepatitis C (n=17) or liver cirrhosis (n=8), those with missing data (n=1,409) and those who had any one of the components of MetS according to the ATP III criteria\(^1\) (n=7,861). As a consequence, the initial cohort comprised 1,558 participants who were followed-up every 2 years until 2009.

The ultrasonography performed in 2005 identified 196 subjects with NAFLD and 1,362 subjects with non-NAFLD. Among these subjects, 107 showed sustained NAFLD both in 2007 and 2009 based on ultrasonography findings (sustained NAFLD, FL), and 1,054 subjects were found to be non-NAFLD on the two consecutive biennial ultrasounds (sustained non-NAFLD, NFL) (Fig. 1).

This study was approved by the Institutional Review Board at Kangbuk Samsung Hospital. The informed consent requirement for this study was exempted by the Institutional Review Board because researchers only accessed the database for analysis purposes, not to obtain personal information.

2. Medical evaluation

All subjects underwent a questionnaire survey, interview, history taking, blood sampling and ultrasonography a total of three times biennially from 2005 to 2009 at the Health Promotion Center in Kangbuk Samsung Hospital.

3. Interview

A questionnaire survey and interview were completed for all subjects to determine the current history of diabetes or hypertension, past medical history, alcohol intake, smoking status, and family history.

Height and body weight were measured (FA-94H; Fanics, Seoul, Korea) with the patient in a light gown with feet bare. The measured height and weight were recorded to the nearest 0.1 cm and 0.1 kg, respectively. The body mass index (BMI) index was calculated as body weight divided by squared height in meters (kg/m\(^2\)).

4. Laboratory assessments

A blood sample was taken from the antecubital vein after a minimum of 12 hours fasting, and serum glucose, uric acid, lipid profile (total cholesterol, triglyceride [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], HbA1c, and insulin levels were measured.

The fasting glucose level was measured using the hexokinase