Is There Any Relation Between the Degree of Fatty Liver Disease and Severity of Lower Urinary Tract Symptoms?

Yun Ah Song, Soon-Sun Kwon, Seung Whan Doo, Jae Heon Kim, Won Jae Yang, and Yun Seob Song

OBJECTIVE To evaluate the association between the degree of fatty liver disease and severity of lower urinary tract symptoms (LUTS) in healthy middle-aged males.

MATERIALS AND METHODS A total of 1943 Korean men aged between 40 and 70 years who had participated in the voluntary health checkup program from January 2012 to December 2014 were enrolled. LUTS were evaluated with the International Prostate Symptom Score (IPSS) questionnaire. Abdominal ultrasonography was performed to assess nonalcoholic fatty liver disease (NAFLD). Trend test was performed to investigate the association between the degree of fatty liver disease and LUTS severity. Differences between the two groups were analyzed by chi-square test, and we adjusted for confounding factors with analysis of covariance and logistic regression test.

RESULTS The mean age was 51.79 ± 7.03 years, and 1026 (52.8%) subjects were determined to have NAFLD. Differences in categorical variables, between NAFLD grades and IPSS grades, were analyzed by Trend test, and no significant difference was observed (Pearson chi-square, $P = .155$; likelihood ratio, $P = .151$; linear-by-linear association, $P = .527$). After adjustment for age, body mass index, metabolic syndrome, C-reactive protein, prostate-specific antigen, prostate volume with analysis of covariance, and multiple logistic regression test, no significant associations were found between IPSS and NAFLD.

CONCLUSION No significant associations were found between NAFLD and LUTS in middle-aged men, and the degree of NAFLD was not significantly associated with the severity of LUTS in trend. The role of NAFLD, in comparison with age, might be too small to change the LUTS. UROLOGY 89: 90–95, 2016. © 2016 Elsevier Inc.

Many elderly men have benign prostatic hyperplasia (BPH) and suffer from lower urinary tract symptoms (LUTS).[1,2] Recent studies have reported that metabolic derangement, including metabolic syndrome (MS) and non-alcoholic fatty liver disease (NAFLD), has an important effect on prostatic hyperplasia, and they showed significant relationships between metabolic derangement and LUTS.[3-5]

There have been ambiguous conclusions on this issue; several studies reported no significant association between MS or obesity and LUTS,[6-8] whereas several other Asian studies showed an inverse correlation between them.[9-11] Although several meta-analyses have concluded that MS has a relation with only prostate size and not with LUTS,[12-14] there is an updated report about the issue of conflicting results.[5]

The main reason for this issue of conflicting results is that there are complex interrelationships among age, obesity, MS, and NAFLD. Another reason is that the past studies focused on only the severe form of obesity, LUTS, MS, and NAFLD. We have focused on the association between LUTS and NAFLD, because this association might explain the conflicting conclusion of the complex interrelationships and there have been only a few studies on this issue.

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

Funding Support: *This work was supported by Soonchunhyang University Research Fund* (2015-0006).

From the Department of Family Medicine, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, Seoul, South Korea; the Department of Mathematics, College of Nature Sciences, Ajou University, Suwon, South Korea; and the Department of Urology, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, Seoul, South Korea

Address correspondence to: Jae Heon Kim, M.D., Ph.D., Department of Urology, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, 59, Daesagwan-ro, Yongsan-gu, Seoul 140-743, South Korea. E-mail: piacekjh@hanmail.net

Submitted: September 4, 2015, accepted (with revisions): November 24, 2015

http://dx.doi.org/10.1016/j.urology.2015.11.030
0090-4295

Moreover, there have been no attempts to investigate this relationship in healthy people.

The above-mentioned issue is important for deciding whether controlling modifiable metabolic factors of MS may prevent LUTS, because MS is a cluster of metabolic abnormalities including visceral obesity, dyslipidemia (high triglyceride, low high-density lipoprotein [HDL] cholesterol), high blood pressure, and glucose intolerance. Similarly, many studies have observed other possible factors, including the five components of MS and multiple laboratory findings including insulin profile, fasting blood glucose, lipid profile, and C-reactive protein (CRP).[11,15-19]

NAFLD is often considered as the hepatic manifestation of MS.[20] Because NAFLD is a prevalent disorder[21] and whole abdominal ultrasonography is frequently conducted as part of the health checkup in Korea, it would be interesting to understand the relationship between NAFLD and LUTS. The aim of this study is to determine the relation between NAFLD and LUTS. This study clarifies the direct association between NAFLD and LUTS by adjustment for known confounding factors including age, MS, obesity, and prostate size in a healthy population.

MATERIALS AND METHODS

Study Populations

A total of 1943 subjects aged between 40 and 70 years who had participated in the voluntary health checkup program at the health promotion center of Soonchunhyang University Hospital from January 2012 to December 2014 were included in this retrospective review. This study was approved by Institutional Review Board of Soonchunhyang University Hospital.

All men were evaluated for the severity of LUTS by the International Prostate Symptom Score (IPSS), which is the most widely used survey tool for the subjective assessment of LUTS. The patients who were taking medications causing LUTS (such as α-adrenergic blockers, anticholinergics, or 5-α-reductase inhibitors) had a serum prostate-specific antigen (PSA) level of >3.0 ng/mL, abnormal findings on digital rectal examination, pyuria, neurogenic bladder dysfunction, confirmed prostate cancer, prostatitis, and who had undergone previous surgical intervention for BPH were excluded from the study.

Definitions of Variables

"Total IPSS" consists of "storage IPSS (urgency, frequency, nocturia)" and "voiding IPSS (incomplete emptying, intermittency, weak stream, straining)". The subgroup of "voiding IPSS" was defined as voiding IPSS divided by total IPSS. LUTS severities were classified as mild (IPSS of 0-7), moderate (IPSS of 8-19), and severe (IPSS of 20-35).

Anthropometric measurements, including height and weight for calculating body mass index (BMI), were determined. The blood samples were obtained for measuring the serum PSA (AxSYM, Abbott Laboratories, Abbott Park, IL) and serum high-sensitivity C-reactive protein (hs-CRP; latex-enhanced immunonephelometry with a model 7600 apparatus, Hitachi, Skisui, Japan) levels. Then, digital rectal examination and transrectal ultrasonography were performed.

The presence of NAFLD was confirmed by abdominal ultrasonography performed by experienced radiologists. It was defined as NAFLD based on standard criteria in the absence of a potential cause of chronic liver disease, such as positive hepatitis B virus surface antigen or anti-hepatitis C virus antibody, excessive alcohol consumption (>20 g/day), intake of medications known to precipitate fatty liver during the previous 6 months, and other causes of liver disease, such as Wilson's disease or hemochromatosis. The degree of fatty liver was graded as follows: grade 1 (mild), echogenicity was slightly increased, with normal visualization of the diaphragm and the intrahepatic vessel borders; grade 2 (moderate), echogenicity was moderately increased, with slightly impaired visualization of the diaphragm or intrahepatic vessels; grade 3 (severe), echogenicity was markedly increased, with poor or no visualization of the diaphragm, the intrahepatic vessels, and posterior portion of the right lobe.

According to the recent consensus report of the National Cholesterol Education Program's Adult Treatment Panel III, MS was defined as the presence of ≥3 of the following risk factors: (1) waist circumference > 90 cm (Asian population); (2) fasting blood sugar > 100 mg/dL; (3) serum triglyceride > 150 mg/dL; (4) hypertension, systolic blood pressure > 130 mmHg or diastolic blood pressure > 85 mmHg; (5) HDL cholesterol level < 40 mg/dL.

Statistical Analysis

Normal distribution was examined using the Kolmogorov-Smirnov test. Patients were divided into the NAFLD group as the study group and the non-NAFLD group as the control group. For analysis of basic characteristics, continuous variables, presented as mean and standard deviation, were computed by the independent t test. Differences in categorical variables were analyzed by the chi-square test. To estimate the association between the severity of LUTS and the degree of NAFLD, trend tests including chi-square test, likelihood ratio, and linear by linear association test were conducted.

To identify the variables affecting LUTS, we adjusted for confounding factors with analysis of covariance (ANCOVA). Furthermore, multiple regression analysis was conducted after adjustment for age, CRP, prostate volume (PV), BMI, MS, and NAFLD to investigate the relation with each dependent variable including storage IPSS, voiding IPSS, voiding IPSS subscore, total IPSS, and IPSS grade. $P < .05$ was considered statistically significant using the SAS test.

RESULTS

Data from 1943 subjects were analyzed. Among them, 1026 (52.8%) subjects had NAFLD and comprised the study group. In the study group, 633 (32.6%) men had grade 1 NAFLD, 196 (10.1%) men had grade 2 NAFLD, and 197 (10.1%) men had grade 3 NAFLD. The 917 (47.2%) subjects who did not have NAFLD comprised the control group.

The characteristics of all subjects are shown in Table 1. The NAFLD group showed a significantly different mean age (52.40 years vs 51.11 years; $P < .01$), CRP (0.16 mg/dL vs 0.14 mg/dL; $P < .01$), PSA (1.08 ng/mL vs 1.11 ng/mL; $P = .033$), PV (25.45 mL vs 23.61 mL; $P < .01$), and BMI (26.01 kg/m^2 vs 23.42 kg/m^2; $P < .01$) (Table 1).

The association between IPSS grade and NAFLD grade is demonstrated in Table 2. The degree of NAFLD was not significantly associated with the severity of LUTS in chi-square test for trend (Pearson chi-square, $P = .155$; likelihood ratio, $P = .151$; linear-by-linear association, $P = .527$).