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Original Article

Neck Circumference as a Predictor of Insulin Resistance in People with Non-alcoholic Fatty Liver Disease

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Background: Insulin resistance is common in individuals with non-alcoholic fatty liver disease (NAFLD). Because insulin resistance is a predictive factor for advanced liver diseases in people with NAFLD, efforts have been made to predict it through anthropometric variables. Recently, neck circumference (NC) has been regarded as a reliable alternative marker for metabolic disorders. This study verified the association between NC and insulin resistance in patients with NAFLD.
Methods: We analyzed data from 847 people with NAFLD who participated in the 2019 Korean National Health and Nutrition Examination Survey. NAFLD was defined by a hepatic steatosis index score of ≥36 points, and insulin resistance was defined by a homeostatic model assessment of insulin resistance score of ≥2.5 points. Participants were divided according to sex-specific NC tertiles (T1, lowest; T2, middle; T3, highest).
Results: In the analysis of the area under the receiver operating characteristic curve (AUC), NC displayed a greater predictive power than body mass index (BMI) for insulin resistance in women (AUC of NC=0.625 vs. AUC of BMI=0.573, P=0.035). NC and the odds ratio (OR) for insulin resistance showed a cubic relationship in both men and women. In the weighted multiple logistic regression analysis, the ORs with 95% confidence intervals for insulin resistance in people with NAFLD in T2 and T3 compared to the reference tertile (T1) were 1.06 (0.47–2.41) and 1.13 (0.41–3.11), respectively, in men and 1.12 (0.64–1.97) and 2.54 (1.19–5.39), respectively, in women, after adjusting for confounding factors.
Conclusion: NC was positively correlated with insulin resistance in women with NAFLD.

Key words: Neck circumference, Non-alcoholic fatty liver disease, Insulin resistance, Korean

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, affecting 25% of people worldwide.[1] The prevalence of NAFLD is approximately 30% in South Korea.[2] Although NAFLD is closely related to the progression of advanced liver diseases, such as non-alcoholic steatohepatitis, liver cirrhosis, or hepatocellular carcinoma, 10.3% of patients with NAFLD die from cardiovascular diseases.[3] Currently, there is no approved pharmacological treatment for NAFLD. Therefore, the management of NAFLD is mainly focused on lifestyle modifications, including weight reduction; caloric restriction; increased physical activity; and the management of risk factors for NAFLD like obesity, type 2 diabetes mellitus (DM), dyslipidemia, and metabolic syndrome.[4]

There is suggestive evidence from several studies that insulin resistance and NAFLD share a common mechanism.[5-7] NAFLD is related to general and intra-abdominal obesity, and circulating excessive free fatty acids may be cytotoxic by inducing lipid peroxidation and hepatocyte apoptosis. Free fatty acid flux from the excessive amount of adipose tissue toward the peripheral tissues then induces the development of insulin resistance, especially when triglyceride storage levels or the concentration of intermediate fat metabolites becomes excessive.[6] Insulin resistance also results in the delivery of fatty acids to the liver, leading to NAFLD.[7] Moreover, because insulin resistance is a predictive factor for non-alcoholic steatohepatitis or advanced liver fibrosis in patients with NAFLD,[8] early prediction and management of insulin resistance in NAFLD are important. There have been efforts to predict insulin resistance by measuring anthropometric variables, such as waist circumference (WC), body mass index (BMI), and neck circumference (NC). WC, one of the most commonly used parameters for predicting insulin resistance, is highly correlated with insulin resistance.[9] However, there are two ways to measure WC, making the definition of WC unclear.[10] In addition, intra- and inter-observer errors may occur when measuring WC.[11] In contrast, there is a unified method for measuring NC,[12] which has also been proven to be an accurate anthropometric parameter for assessing overweight and obesity in a recent meta-analysis.[13] Research has also shown that NC has a better relationship with prediabetes compared to other anthropometric parameters, including WC.[14] Therefore, there has been increased interest in using NC in the assessment of various metabolic disorders, including obesity, insulin resistance, metabolic syndrome, and obstructive sleep apnea.[15,16] However, few studies to date have investigated the relationship between NC and insulin resistance, particularly in the Korean population. Additionally, to the best of our knowledge, no research has compared the predictive power of NC, WC, and BMI for insulin resistance in patients with NAFLD.

If NC measurements are found to have a predictive power comparable to that of WC or BMI measurements for insulin resistance, NC measurement could serve as an alternative method for predicting insulin resistance in patients with NAFLD. Additionally, as NC measurements are less prone than WC measurements to measurement errors, they could offer a more accurate and reliable option for assessing insulin resistance. This study aimed to verify the association between NC and insulin resistance in patients with NAFLD using nationwide, representative cross-sectional data from Korea.

METHODS

Study population

All data in this analysis were obtained from the 2019 Korean National Health and Nutrition Examination Survey (KNHANES). The Korea Centers for Disease Control and Prevention annually conducts this nationwide, representative, and population-based survey to monitor the health and nutritional status of the Korean population.[17] Sampling is designed according to cross-sectional, multistage, stratified probability based on geographic area, sex, and age. Weights are assigned to each participant for generalization of the sampling units to represent the Korean population. Detailed information about the KNHANES initiative is available on the KNHANES website (http://knhanes.cdc.go.kr). All participants provided written informed consent prior to the survey. As the KNHANES is performed for public welfare and personal information is not included in the dataset, approval from an Institutional Review Board (IRB) for data use was not required. This study was approved by the IRB of Nowon Eulji Medical Center (IRB no. 2022-01-016).

The process of study population selection is shown in Fig. 1. Among a total of 8,110 people who participated in the 2019 KNHANES, 1,504 people < 19 years of age were excluded. We then further excluded those who had (1) missing NC data (n = 2,047); (2) missing fasting plasma glucose (FPG) data (n = 118); (3) a chronic hepatitis B viral infection (n = 139); (4) a chronic hepatitis C viral infection (n = 40) as well as (5) men who drank ≥ 30 g/day of alcohol and women who drank ≥ 20 g/day (n = 343); (6) those without adequate information to evaluate hepatic steatosis index (HSI; n = 160); and (7) participants who did not have NAFLD (n = 2,912). A total of 847 participants were finally included in this study (346 men and 501 women).

Anthropometric data collection

NC (cm) was measured three times to the nearest 0.1 cm at the upper edge of the thyroid cricoid cartilage during expiration, and the average value of the three measurements was used. The participants were categorized into three groups according to sex-specific

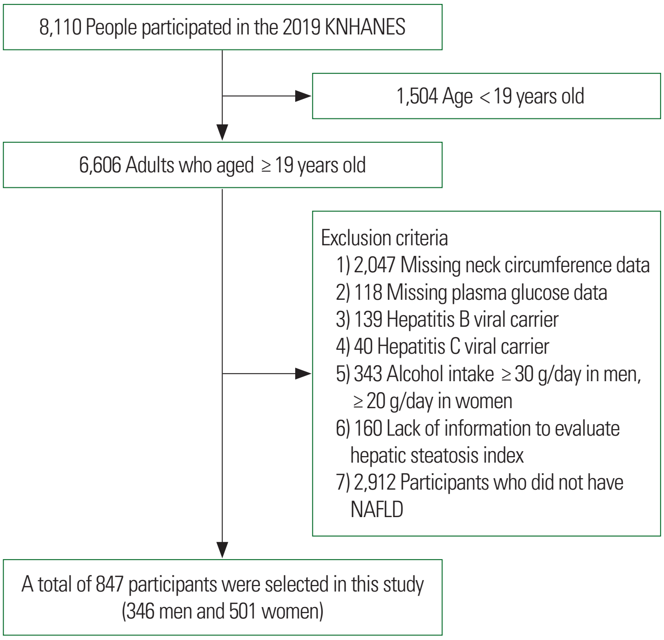

Figure 1. Flowchart of the study population selection. KNHANES, Korean National Health and Nutrition Examination Survey; NAFLD, non-alcoholic fatty liver disease.

tertiles of NC.

WC (cm) was measured in the horizontal plane midway between the iliac crest and the lowest rib. Height (m) and weight (kg) were measured to the nearest 0.001 m and 0.1 kg, respectively. BMI was calculated by dividing the weight by the square of the height (kg/m^2). Participants with BMI values of ≥ 25 kg/m^2 were considered obese according to the definition of the Korean Society for the Study of Obesity.[18]

Assessment of insulin resistance

Blood samples from each participant were collected from the antecubital vein after ≥ 8 hours of fasting. The FPG and serum insulin levels were measured using a Hitachi 7600 analyzer (Hitachi Co.). We calculated the homeostatic model assessment of insulin resistance (HOMA-IR) using the following equation: HOMA-IR = [FPG (mg/dL) × serum insulin (μU/mL)/405]. Participants with HOMA-IR scores of ≥ 2.5 points were regarded as having insulin resistance.[19]

Assessment of NAFLD

The aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were measured using a Hitachi 7600 analyzer (Hitachi Co.). We defined NAFLD using HSI, a validated model for predicting fatty liver.[20,21] The formula of HSI is as follows: HSI = 8/(ALT/AST ratio)+BMI [+2, if DM; +2, if women]. An HSI score ≥ 36 was defined as NAFLD.[20]

Covariates

Participants were categorized into two groups according to their smoking status: current smokers and non-current smokers. We calculated daily alcohol intake (g/day) as 10 (g/per glass of drink) × alcohol consumption (glasses/time) × frequency of alcohol consumption (times/month)/30 (days/month).[22] Men who consumed ≥ 30 g/day of alcohol or women who consumed ≥ 20 g/day of alcohol were defined as heavy drinkers.[23] Based on the Korean version of the Global Physical Activity Questionnaire, physical activity was calculated as the metabolic equivalent of task (MET)-minutes per day.[24] Total calorie intake (kcal/day) was calculated using a well-validated semi-quantitative food frequency questionnaire. Monthly household income was divided into quartiles. Education levels were categorized into four groups: elementary school, middle school, high school, and college/university.

The systolic blood pressure (SBP; mmHg) and diastolic blood pressure (DBP; mmHg) were measured in the sitting position after ≥ 30 minutes of rest. We calculated the mean blood pressure (MBP; mmHg) using the following equation: MBP = (SBP+2 × DBP)/3.[25] Hypertension (HTN) was defined by an SBP of ≥ 140 mmHg, DBP of ≥ 90 mmHg, or treatment with anti-hypertensive medications according to the criteria of the Seventh Joint National Committee.[26] DM was defined by an FPG of ≥ 126 mg/dL, treatment with oral anti-diabetic medications, or treatment with insulin injection therapy according to the 2020 American Diabetes Association criteria.[27] Serum total cholesterol, triglyceride, high-density lipoprotein (HDL)-cholesterol, and low-density lipoprotein (LDL)-cholesterol levels were measured using a Hitachi 7600 analyzer (Hitachi Co.). Dyslipidemia was defined as meeting at least one of the following criteria: (1) total cholesterol ≥ 240 mg/dL; (2) triglycerides ≥ 200 mg/dL; (3) HDL-cholesterol < 40 mg/dL; and (4) LDL-cholesterol ≥ 160 mg/dL.[28]

Statistical analysis

Sampling weights were applied during the analysis of the representative data of the Korean population. The weights were adjusted with the values for the inverse of the response rates and the inverse of the selection probability to the age- and sex-specific values for the Korean population (post-stratification).[17]

All data are presented as mean ± standard error (SE) or percentage (SE) values. For continuous variables, a weighted analysis of variance was used. To compare differences in categorical variables among the groups, a weighted chi-square test was performed.

The predictability of NC, WC, and BMI for the presence of insulin resistance in participants with NAFLD was compared by contrasting areas under the receiver operating characteristic curve (AUCs).

Spline curves were drawn to check whether NC as a continuous variable had a linear relationship with insulin resistance in participants with NAFLD. Using weighted multiple logistic regression analysis, the odds ratio (OR) and 95% confidence interval (CI) values for insulin resistance in the sex-specific medium tertile (T2) and highest tertile (T3) were compared with those of the reference lowest tertile (T1). In model 1, we adjusted for age, WC, total calorie intake, monthly household income, education level, current smoker status, amount of alcohol intake, and physical activity. In model 2, we further adjusted for DM, HTN, and dyslipidemia. Subgroup

Table 1. Characteristics of the study population

Neck circumference	Men				Women			
	T1	T2	T3	*P**	T1	T2	T3	*P**
Unweighted number	118	114	114		167	179	155	
Age (yr)	53.5±0.9	54.9±1.3	52.2±1.1	0.277	59.8±0.8	59.5±1.0	58.2±1.2	0.459
BMI (kg/m^2)	25.6±0.2	27.4±0.2	29.9±0.3	<0.001	26.0±0.2	27.6±0.2	30.6±0.3	<0.001
Waist circumference (cm)	90.7±0.5	95.4±0.7	101.9±0.9	<0.001	87.6±0.5	92.4±0.4	99.0±0.8	<0.001
MBP (mmHg)	95.0±1.1	93.5±1.2	96.4±1.1	0.274	92.9±1.0	91.6±1.0	93.2±1.0	0.467
FPG (mg/dL)	109.7±2.3	111.2±2.5	122.7±4.9	0.058	109.3±2.7	116.3±2.5	115.8±3.0	0.091
HOMA-IR	3.5±0.3	3.7±0.4	4.9±0.5	0.074	3.4±0.4	3.7±0.2	4.5 ±0.2	0.006
Total cholesterol (mg/dL)	188.5±5.2	195.9±4.8	203.0±4.7	0.115	198.2±4.8	196.9±4.1	191.9±4.0	0.592
Triglycerides (mg/dL)	181.8±13.2	183.1±16.4	224.0±17.0	0.134	136.2±6.3	159.9±6.7	160.7±7.7	0.010
HDL-cholesterol (mg/dL)	45.5±1.0	44.3±1.4	41.8±0.9	0.028	51.1±0.9	48.6±0.8	47.5±0.8	0.021
LDL-cholesterol (mg/dL)	116.8±8.4	114.2±7.8	124.4±8.5	0.682	114.2±8.3	130.8±6.0	126.3±7.1	0.303
Monthly household income (%)				0.159				0.252
Lowest quartile	8.0 (2.2)	20.2 (5.3)	14.1 (3.9)		16.1 (3.3)	24.4 (3.5)	26.9 (3.8)	
Second quartile	21.0 (4.2)	21.2 (4.8)	12.4 (3.7)		28.5 (3.9)	23.5 (3.8)	21.8 (3.6)	
Third quartile	34.7 (5.0)	29.9 (5.7)	42.5 (6.3)		28.1 (4.3)	25.6 (3.9)	31.9 (4.7)	
Highest quartile	36.3 (5.5)	28.8 (5.4)	30.9 (5.9)		27.2 (3.8)	26.6 (4.1)	19.3 (3.8)	
Education level (%)				0.364				0.366
Elementary school	10.2 (2.6)	8.9 (3.0)	4.9 (1.8)		35.3 (4.4)	30.6 (4.2)	29.6 (4.5)	
Middle school	7.5 (2.5)	9.2 (2.7)	10.0 (3.7)		12.5 (2.9)	16.5 (4.0)	9.4 (2.8)	
High school	32.6 (5.5)	43.0 (6.2)	29.9 (5.6)		31.7 (4.4)	34.1 (4.4)	45.3 (4.9)	
College or university	49.8 (5.7)	38.8 (6.5)	55.2 (6.5)		20.5 (3.9)	18.7 (3.5)	15.7 (3.7)	
Current smoker (%)	34.3 (4.9)	31.7 (5.9)	28.4 (5.1)	0.701	2.0 (1.4)	7.8 (3.0)	4.9 (2.0)	0.149
Alcohol intake (g/day)	5.3±0.8	5.8±1.0	5.7±0.9	0.917	1.3±0.3	1.1±0.3	2.0±0.6	0.360
Physical activity (METs-min/day)	1,185.0±334.6	854.1±198.6	810.0±148.7	0.602	615.8±80.0	554.9±90.2	717.2±101.8	0.494
Total calorie intake (kcal/day)	2,003.6±79.4	2,183.8±119.1	2,175.6±99.3	0.296	1,529.4±49.3	1,519.9±50.5	1,571.7±56.8	0.802
HTN (%)	47.4 (5.4)	37.5 (5.5)	45.3 (5.5)	0.274	47.7 (4.5)	51.7 (4.7)	56.3 (4.6)	0.360
DM (%)	27.6 (4.5)	29.8 (5.5)	44.8 (5.6)	0.044	31.6 (4.2)	41.9 (4.7)	35.7 (4.4)	0.231
Dyslipidemia (%)	54.3 (6.2)	58.4 (5.5)	72.2 (5.5)	0.083	32.9 (4.6)	38.0 (4.1)	43.1 (4.4)	0.245
HSI score	38.5±0.3	39.6±0.3	42.2±0.4	<0.001	38.1±0.2	39.2±0.2	42.1±0.5	<0.001

Values are presented as mean±standard error or percentage (standard error). Weighted analysis of variance was performed to compare differences in continuous variables. Weighted chi-squared tests were performed to compare differences in categorical variables.
*$P<0.05$ was considered to indicate statistical significance.
BMI, body mass index; MBP, mean blood pressure; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent of task; HTN, hypertension; DM, diabetes mellitus; HSI, hepatic steatosis index.

analysis was also performed based on the presence or absence of DM, although there was no significant effect of the interaction between WC and DM status on insulin resistance (interaction $P=0.546$ in men and $P=0.335$ in women), considering the strong association between DM and insulin resistance.

All statistical analyses were conducted using R version 4.1.3 (R Foundation for Statistical Computing) and the SPSS statistical software program version 23.0 (IBM Corporation). The significance level was set at $P<0.05$.

RESULTS

Demographics of the study population

Table 1 presents the demographics of the study population. In both men and women, the mean values of BMI, WC, and HSI scores increased and the mean HDL-cholesterol value decreased when the sex-specific tertile of NC increased. There were no significant differences among groups in the mean values of age, MBP, FPG, serum total cholesterol level, LDL-cholesterol level, amount of alcohol intake, physical activity, total calorie intake, the proportion of individuals included based on their monthly household income quartiles, the proportion of individuals included based on their education level, the proportion of current smokers, the proportion of patients with HTN, and the proportion of patients with dyslipidemia in both men and women. In men, the proportion of patients with DM was greatest in T3, followed by in T2 and T1, respectively. Among women, the mean HOMA-IR and serum triglyceride levels increased with increasing tertiles of NC.

Comparison of the predictive ability of anthropometric parameters for the presence of insulin resistance

Fig. 2 shows comparisons of the AUC of NC, WC, and BMI for predicting the presence of insulin resistance. In men (Fig. 2A), the AUCs of NC, WC, and BMI were 0.634, 0.669, and 0.640, respectively. Although the predictive ability of NC was the lowest among the three anthropometric parameters, there were no significant differences among the parameters (P for NC vs. WC = 0.208, P for NC vs. BMI = 0.815, P for WC vs. BMI = 0.173, respectively). In women (Fig. 2B), the AUCs of NC, WC, and BMI were 0.625, 0.606, and 0.573, respectively, revealing a significant difference between NC and BMI ($P=0.035$). The optimal cutoff points of NC in predicting insulin resistance were determined to be 41.5 cm in men and 34.5 cm in women, respectively.

Relationship between NC and insulin resistance in participants with NAFLD

A cubic spline curve showing a cubic association between NC and insulin resistance in NAFLD is presented in Fig. 3. As NC in-

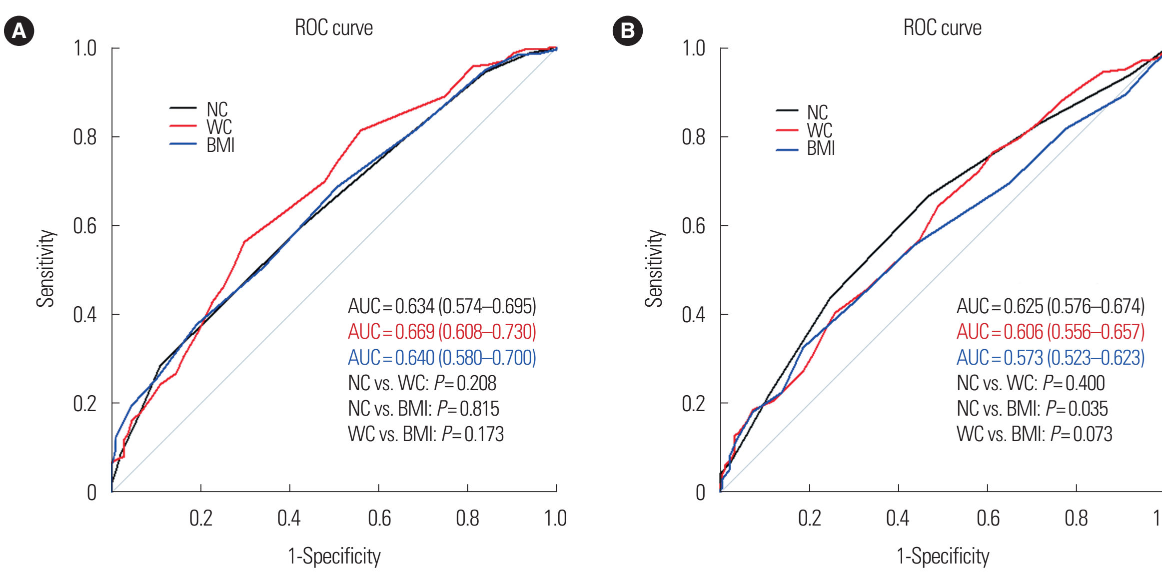

Figure 2. Predictive power for insulin resistance of neck circumference (NC)/waist circumference (WC)/body mass index (BMI). (A) Men and (B) women. ROC, receiver operating characteristic curve; AUC, area under the receiver operating characteristic curve.

creased, the OR for insulin resistance in NAFLD also increased in both men (Fig. 3A) and women (Fig. 3B).

Table 2 shows the relationship between NC and insulin resistance using weighted multiple logistic regression analysis. The OR values for insulin resistance of T2 and T3 compared to the reference T1 were 1.73 (95% CI, 0.82 to 3.64) and 3.37 (95% CI, 1.62 to 6.99) in men and 1.51 (95% CI, 0.93 to 2.45) and 3.32 (95% CI, 1.94 to 5.69) in women, respectively. In model 1, the adjusted OR values for insulin resistance of T2 and T3 were 1.08 (95% CI, 0.50 to 2.32) and 1.38 (95% CI, 0.55 to 3.51) in men and 1.25 (95% CI, 0.71 to 2.21) and 2.62 (95% CI, 1.26 to 5.45) in women. In model 2, the fully-adjusted OR values for insulin resistance of T2 and T3 were 1.06 (95% CI, 0.47 to 2.41) and 1.13 (95% CI, 0.41 to 3.11) in men and 1.12 (95% CI, 0.64 to 1.97) and 2.54 (95% CI, 1.19 to 5.39) in women.

Table 2. Association between neck circumference and insulin resistance in patients with NAFLD

Neck circumference	OR (95% CI)			Overall *P**
	T1	T2	T3	
Men				
Unadjusted	1 (ref.)	1.73 (0.82–3.64)	3.37 (1.62–6.99)	0.006
Model 1	1 (ref.)	1.08 (0.50–2.32)	1.38 (0.55–3.51)	0.786
Model 2	1 (ref.)	1.06 (0.47–2.41)	1.13 (0.41–3.11)	0.971
Women				
Unadjusted	1 (ref.)	1.51 (0.93–2.45)	3.32 (1.94–5.69)	<0.001
Model 1	1 (ref.)	1.25 (0.71–2.21)	2.62 (1.26–5.45)	0.030
Model 2	1 (ref.)	1.12 (0.64–1.97)	2.54 (1.19–5.39)	0.030

Univariable and multivariable logistic analyses were performed to estimate OR and 95% CI values for insulin resistance according to the sex-specific tertiles of neck circumference. Model 1: Adjusted for age, waist circumference, total calorie intake, monthly household income, education level, current smoker, amount of alcohol intake, and physical activity; Model 2: Adjusted for variables included in model 1 plus diabetes mellitus, hypertension, and dyslipidemia.
*$P<0.05$ was considered to indicate statistical significance.
NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; CI, confidence interval.

Fig. 4 shows the results of the subgroup analysis by DM status using a forest plot. There were no significant relationships between NC and insulin resistance in NAFLD in men with or without DM and in women with DM. In women without DM, however, there was a significant association between NC and insulin resistance in NAFLD. The corresponding fully-adjusted OR values for insulin resistance in NAFLD of T2 and T3 compared to T1 were 1.14 (95% CI, 0.59 to 2.19) and 3.16 (95% CI, 1.31 to 7.63), respectively.

DISCUSSION

Given that NAFLD patients with high insulin resistance are at a heightened risk for hepatic complications,[29] early identification and management of insulin resistance in this population is of paramount importance for promoting public health. This study showed that higher NC was independently associated with increased insulin resistance in women with NAFLD, and this relationship persisted even after adjusting for confounding factors.

Boemeke et al.[30] analyzed 82 Brazilian patients with NAFLD and found a significant correlation between NC and insulin resistance in both men and women. They set altered NC cutoff points as 42 cm for men and 36 cm for women. However, in our study, NC was only associated with insulin resistance in women despite the NC cutoff points being similar to those of the previous study.

The differences between our study and the previous study by

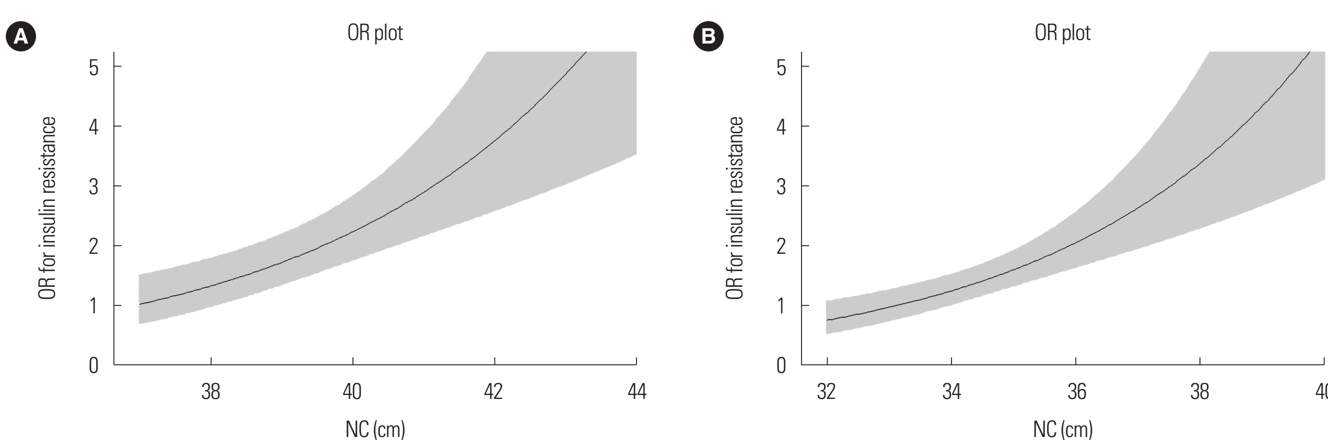

Figure 3. Cubic spline curve for insulin resistance of neck circumference (NC). (A) Men and (B) women. OR, odds ratio.

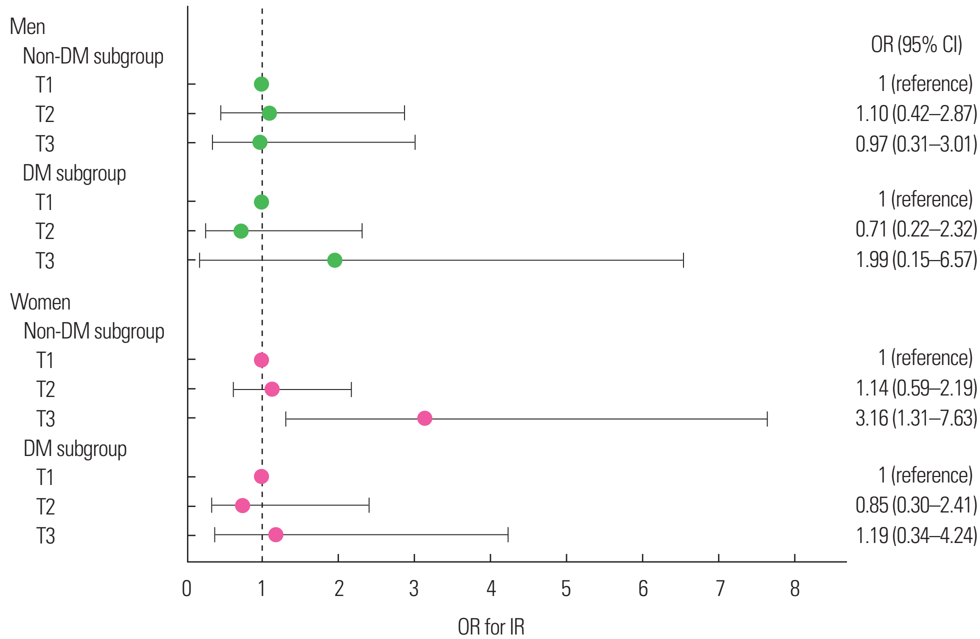

Figure 4. Forest plot for subgroup analysis by diabetes mellitus (DM) status adjusted for age, waist circumference, total calorie intake, monthly household income, education level, smoking status, amount of alcohol intake, physical activity, hypertension, and dyslipidemia. OR, odds ratio; CI, confidence interval; IR, insulin resistance.

Boemeke et al.[30] could be attributed to several factors, including differences in sample size and socioeconomic demographics of the study population. We included a much larger sample size than that of the previous study, which provided greater statistical power and allowed us to more robustly verify the association between NC and insulin resistance in patients with NAFLD. The prevalence of current smokers was strikingly greater in men than in women (31.5% in men vs. 5.0% in women, $P<0.001$). Considering the effect of cigarette smoking on the development of insulin resistance,[31] the higher prevalence of current smokers may be an important confounding factor in the relationship between NC and insulin resistance in men. Our study also found that men had higher levels of alcohol intake than women (5.6 g/day in men vs. 1.4 g/day in women, $P<0.001$). Additionally, men exercised more than women (957.9 METs-min/day vs. 624.4 METs-min/day, $P=0.024$). These differences in the amount of alcohol intake and physical activity levels may have contributed to the attenuation of the association between NC and insulin resistance in men. Previous studies have shown that alcohol intake can improve insulin resistance, possibly by decreasing fasting insulin,[32,33] and regular physical activity has been shown to improve insulin sensitivity and glucose metabolism.[34] These factors could partially explain why the association between NC and insulin resistance was not significant in men. Further studies are needed to investigate the complex interplay among smoking, alcohol intake, physical activity, NC, and insulin resistance in patients with NAFLD. Differences in the distribution of neck fat between men and women could also be a potential mechanism explaining our findings. Torriani et al.[35] measured neck adipose tissue compartments using computed tomography and found that men had higher amounts of posterior cervical and peri-vertebral adipose tissue in the neck, while women had more abundant subcutaneous adipose tissue (SAT) in the neck. Additionally, NC was more strongly correlated with visceral adipose tissue (VAT) in women than in men ($r=0.70$ in women vs. $r=0.61$ in men). The authors suggested that fat accumulation occurs in three neck compartments, with accumulation in posterior cervical neck adipose tissue and subcutaneous neck adipose tissue being more consistently associated with cardiometabolic risk, particularly in women. These findings support our results.

In both men and women, the predictive power for insulin resistance in NC was not significantly different from that of WC. Moreover, it was superior to the predictive power of BMI for insulin resistance in women with NAFLD. A single-center cross-sectional study evaluated the relationship between WC/BMI and insulin resistance as well as NAFLD in healthy Korean participants and found that WC and BMI were highly related to the risk of insulin resistance and NAFLD.[36] These results suggest that both WC and BMI could be used to predict insulin resistance and NAFLD. Our results support those of the previous study. Furthermore, we also determined NC to be a more useful anthropometric variable compared to WC and BMI for the prediction of insulin resistance in women with NAFLD. Our results also fall in line with previous evidence showing the similar degrees of predictability for insulin resistance between NC and WC.[37] Luo et al.[37] reported that AUCs for visceral obesity of NC were 0.781 in men and 0.777 in women, respectively. They also reported the optimal cutoff points of NC to be 38.5 cm in men and 34.5 cm in women, respectively. Our study showed that the predictive power of NC for insulin resistance was lower than that reported in previous studies, and the cutoff point value for men was 10% higher in our study. This may be due to the fact that the previous study analyzed the general population, whereas our study included only NAFLD patients. Additionally, this difference in results could be attributed to genetic differences between the Chinese and Korean populations.

There are possible explanations for our results. First, NC is not only a marker of neck SAT accumulation but also an indicator of excessive VAT.[38,39] SAT accumulation in the neck area has been found to represent whole-body insulin sensitivity.[39] VAT is metabolically active and releases free fatty acids into the portal circulation, contributing to the development of insulin resistance. Moreover, VAT secretes pro-inflammatory adipokines such as interleukin (IL)-1β, IL-6, and tumor necrosis factor-α, which can further exacerbate insulin resistance. Second, sleep apnea is an independent risk factor for insulin resistance; therefore, NC, a surrogate marker of sleep apnea, may show a significant association with insulin resistance.[40] However, we could not include sleep apnea status as a confounding factor because only five individuals responded that they had been diagnosed with sleep apnea by a physician. In future studies, it will be necessary to obtain a larger sample size to confirm the potential impact of sleep apnea on the association between NC and insulin resistance.

Several limitations should be noted. First, a causal relationship was not verified in this study. Therefore, prospective follow-up cohort studies are required. Second, the predictive power of NC was not different from that of WC in both men and women, although it was superior to that of BMI for the prediction of insulin resistance in women with NAFLD. Further studies with larger sample sizes are needed to compare the predictive power of NC, WC, and BMI on insulin resistance in patients with NAFLD. Third, we could not assess dietary information due to a lack of data. Finally, NAFLD was defined through the surrogate marker of HSI, although it has been validated as a predictive marker for identifying NAFLD. Further studies are needed using more precise tools to identify NAFLD, including liver biopsy, controlled attenuation parameter, ultrasonography, computed tomography, or magnetic resonance imaging. Despite these limitations, this study was the first to clarify the role of NC as a predictive marker for insulin resistance in patients with NAFLD and to compare the predictive power of NC with that of other anthropometric variables, such as WC and BMI.

In conclusion, NC is an independent predictor of insulin resistance in women with NAFLD. Due to its simple and reliable method for measuring NC, measuring NC can be a useful alternative method for predicting insulin resistance in patients with NAFLD, considering the potential risk of measurement errors when measuring WC. Early detection of insulin resistance through NC measurement and its management may help delay the progression of liver-related complications. Further studies are needed to determine the usefulness of NC measurement for insulin resistance in disorders other than NAFLD.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Study concept and design: DHS and JHL; acquisition of data: DHS and JHH; analysis and interpretation of data: DHS and JHL; drafting of the manuscript: DHS; critical revision of the manuscript:

JHH and JHL; statistical analysis: DHS and JHL; and study supervision: JHH and JHL.

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