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Original Article

Combined Effect of Obesity and Smoking on the Risk of Subclinical Coronary Artery Disease

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SUMMARY

Background: Smoking and obesity are strongly associated with coronary artery disease (CAD). In this study, we investigated the correlations of obesity (body fat [BF], waist circumference [WC], and body mass index [BMI]) and smoking with subclinical CAD in Taiwanese adults.
Methods: This cross-sectional study included 863 adults. Relevant data were collected through medical history-taking, physical examination, blood tests, and coronary computed tomography angiography (CCTA). Multivariate logistic regression was performed to identify risk factors for subclinical CAD.
Results: The CCTA findings were used to classify participants into three groups: no CAD, probable subclinical CAD, and definite subclinical CAD. WC and BMI were the highest in the definite subclinical CAD group. In the multivariate model, which was adjusted for age, sex, smoking status, fasting plasma glucose, low-density lipoprotein cholesterol (LDL-C), and systolic blood pressure, BF and WC were identified as significant risk factors for definite subclinical CAD. In men, BF and WC were significantly associated with definite subclinical CAD, with odds ratios (ORs) of 1.063 (95% confidence interval [CI]: 1.015–1.114) and 1.030 (95% CI: 1.000–1.062), respectively. Individuals with both obesity and smoking habits had a significantly higher risk of subclinical CAD than those with normal weight and no smoking habits (OR: 2.657; 95% CI: 1.469–4.805).
Conclusion: BF and WC may serve as useful predictors of subclinical CAD in adults. Individuals, particularly men, with both obesity and smoking habits have a substantially higher risk of CAD.

1. Introduction

Coronary artery disease (CAD) remains a leading cause of mortality worldwide, particularly in individuals with asymptomatic cardiovascular conditions. In Taiwan, CAD accounts for more than 17,000 deaths annually and ranks as the second leading cause of death after cancer.[1] Early identification of coronary atherosclerosis is crucial for managing coronary risk factors and decelerating plaque instability. Coronary computed tomography angiography (CCTA) enables high-resolution imaging of plaque morphology and adjacent cardiac structures.[2] CCTA provides the Coronary Artery Calcium Score (CACS), which estimates calcium deposition in coronary arteries. This score serves as a key indicator of CAD development and progression.

Evidence suggests that obesity and smoking considerably elevate the risk of major adverse cardiovascular events, even in individuals with low CACS. Both epicardial and visceral adipose tissues (VATs) have been associated with coronary plaque formation and related events.[3] However, the precise roles of various adipose tissue types in CAD progression are not fully delineated. Bergman et al. identified multiple important indicators of cardiovascular risk, including body mass index (BMI), waist circumference (WC), waist-to-hip ratio, body fat (BF), and visceral adiposity index.[4] Cigarette smoking markedly increases the risk of CAD in both men and women.[5] A CCTA-based study of patients with type 2 diabetes mellitus showed that smokers had higher odds of significant coronary stenosis than nonsmokers.[6]

In the present study, we investigated the correlations of obesity (BF, WC, and BMI) and smoking with the risk of subclinical CAD in Taiwanese adults.

2. Methods

2.1. Study population and data source

For this retrospective cross-sectional study, we assessed the eligibility of 956 asymptomatic individuals (age: 50–75 years) who had undergone CCTA during annual health checkups (between January 1, 2008, and December 31, 2017) at a health examination center in Northern Taiwan. Subclinical CAD was diagnosed through CCTA. Data were obtained through medical history-taking, physical examination, fasting blood tests, and CCTA. Individuals with missing data on lipid profiles, BF, WC, or BMI, as well as those with a history of angina, myocardial infarction, percutaneous coronary intervention, or other cardiac procedures, were excluded. The final study comprised 863

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adults. The study protocol was approved by the Institutional Review Board of MacKay Memorial Hospital (permit number: 18MMHIS137). This study was conducted according to the ethical principles of the Declaration of Helsinki.

2.2. Study design and outcomes

We collected baseline information on age, sex, blood pressure, routine blood test results, DM history, and personal history of alcohol consumption and cigarette smoking. In addition, data were collected for the following obesity indicators: BF, WC, and BMI. BF was assessed using bioelectrical impedance analysis (BIA) under standardized conditions. Measurements were performed in a fasting state, and participants were advised to avoid vigorous exercise and alcohol consumption for at least 24 hours before the assessment. The BIA method estimates BF based on electrical impedance, incorporating variables such as age, sex, height, and weight.

2.3. Diagnostic criteria

CAD was defined in accordance with the 1979 World Health Organization diagnostic criteria.[7] CCTA images were analyzed by an experienced radiologist who was blinded to the study details. The primary outcome was the incidence of definite subclinical CAD, indicated by a CACS of ≥ 100 Agatston Unit (AU) and/or the presence of ≥ 50% coronary luminal stenosis.[8] Probable subclinical CAD was indicated by a CACS of 1–100 AU and the presence of < 50% coronary luminal stenosis.

DM was defined as a fasting plasma glucose level of ≥ 126 mg/dL, a glycated hemoglobin level of ≥ 6.5%, or current use of hypoglycemic agents. Overweight and obesity were defined as a BMI of ≥ 24 kg/m^2 or a WC of ≥ 90 cm for men and ≥ 80 cm for women.

Alcohol consumption was defined as more than 14 standard drinks per week for men and more than 7 for women during the past year. Cigarette smoking was defined as current smoking habits.

2.4. Statistical analysis

On the basis of the CACS, the study was divided into no CAD, probable subclinical CAD, and definite subclinical CAD groups. Continuous variables are presented in terms of mean ± standard deviation values, whereas categorical variables are presented in terms of number and percentage values. ANOVA and chi-square tests were used to compare continuous and categorical variables, respectively. Post hoc analyses were conducted using the least significant difference (LSD) test. Multivariate logistic regression was performed after covariate adjustment. The multivariate model was adjusted for variables included in the 2013 Atherosclerotic Cardiovascular Disease (ASCVD) risk score, namely age, sex, smoking status, fasting plasma glucose, low-density lipoprotein cholesterol (LDL-C), and systolic blood pressure (SBP). Two models were used for analysis: model 1 explored independent predictors of subclinical CAD across the groups, whereas model 2 explored independent predictors of subclinical CAD in the definite subclinical CAD and no CAD groups. To assess the combined effects of obesity and smoking, individuals were grouped by overweight/obesity and smoking status. In addition, subgroup analyses by age and sex were performed. Statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA). Odds ratio (ORs) and 95% confidence intervals (CIs) were calculated. A p value of < 0.05 was considered to be significant.

3. Results

3.1. Baseline clinical and biochemical characteristics

This study included 863 Taiwanese adults. The no CAD, probable subclinical CAD, and definite subclinical CAD groups comprised 413, 325, and 125 individuals, respectively.

Table 1 presents the baseline clinical characteristics and laboratory results of the study population. The mean age ranged from 50 to 75 years, with mean ages of 58.5 ± 5.7, 60.6 ± 6.2, and 62.4 ± 6.4

Table 1
Baseline demographic characteristics of the study population according to the grade of coronary artery stenosis.

	Coronary artery CT stenosis grade				
	No CAD [A] (n = 413)	Probable CAD [B] (n = 325)	Definite subclinical CAD [C] (n = 125)	p value	LSD
Age (years)	58.5 ± 5.7	60.6 ± 6.2	62.4 ± 6.4	< .001*	C > B > A
Sex (%)				< .001*	
Male	197 (47.70%)	218 (67.08%)	94 (75.20%)		
Female	216 (52.30%)	107 (32.92%)	31 (24.80%)		
SBP (mmHg)	126.9 ± 17.6	129.5 ± 17.2	130.6 ± 17.7	0.040*	C > A
DBP (mmHg)	78.2 ± 10.3	78.9 ± 10.1	78.1 ± 11.1	0.681	
ALT (IU/L)	27.2 ± 14.4	29.7 ± 18.8	36.2 ± 60.0	0.002*	C > B, C > A
Cr (mg/dL)	0.87 ± 0.23	0.96 ± 0.37	0.98 ± 0.29	< .001*	C > A, B > A
TG (mg/dL)	129.6 ± 73.3	138.7 ± 67	155.6 ± 93.6	0.002	C > B, C > A
LDL-C (mg/dL)	133.4 ± 33.9	133.9 ± 34.3	135.5 ± 39.4	0.840	
HDL-C (mg/dL)	54.1 ± 15.8	51.6 ± 14.9	49.5 ± 15.5	0.006	A > B, A > C
DM (%)	61 (14.77%)	73 (22.46%)	49 (39.20%)	< .001*	
MetS (%)	132 (31.96%)	146 (44.92%)	67 (53.60%)	< .001*	
Smoking (%)	82 (18.85%)	78 (23.28%)	50 (36.50%)	0.001*	
Alcohol (%)	86 (20.92%)	97 (30.41%)	34 (27.87%)	0.011*	
AC (mg/dL)	101.9 ± 20.3	106.6 ± 26.0	112.0 ± 32.3	< .001*	A > B > C
BF (%)	27.9 ± 6.7	27.3 ± 6.4	27.4 ± 6.8	0.439	
WC (cm)	85.1 ± 9.9	87.3 ± 8.5	89.7 ± 9.0	< .001*	C > B > A
BMI (kg/m^2)	24.5 ± 3.4	25.2 ± 3.1	25.5 ± 3.5	0.003*	C > A, B > A

Data are presented as the number (%) of patients and median ± standard deviation.

* Statistical significance.

Abbreviations: ALT, alanine aminotransferase; BF, body fat; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LSD, least-significant difference; MetS, metabolic syndrome; SBP, systolic blood pressure; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio; γGT, gamma glutamyl transpeptidase.

years in the no CAD, probable subclinical CAD, and definite subclinical CAD groups, respectively, indicating significant between-group differences ($p < 0.001$). Mean WC was highest in the definite subclinical CAD group (89.7 vs. 87.3 and 85.1; $p < 0.001$). Similarly, the mean BMI was significantly higher in the definite subclinical CAD group than in the probable subclinical CAD and no CAD groups (25.5 vs. 25.2 vs. 24.5; $p = 0.003$). The proportions of smokers in the definite subclinical CAD, probable subclinical CAD, and no CAD groups were 36.5%, 23.3%, and 18.9%, respectively, indicating significant between-group differences ($p < 0.001$).

In the definite subclinical CAD group, increases were noted in SBP, fasting plasma glucose level, DM or metabolic syndrome prevalence, and triglyceride level, but reductions were noted in high-density lipoprotein cholesterol level. However, no significant between-group difference was observed in diastolic blood pressure, LDL-C level, or BF level.

3.2. Significant risk factors for subclinical CAD

Because of its clinical relevance, definite subclinical CAD was regarded as the primary outcome. Model 1 (Figure 1) was used to analyze data from all groups, whereas model 2 (Figure 2) was used to analyze data from the no CAD and definite subclinical CAD groups only. Both models indicated upward trends for the correlations of BF and WC with definite subclinical CAD. Subgroup analyses by age and sex yielded additional insights. In men, BF and WC were significantly associated with subclinical CAD, with ORs of 1.063 (95% CI: 1.015–1.114) and 1.030 (95% CI: 1.000–1.062) in model 1, respectively. BMI also showed a significant association only in men in model 2 ($p = 0.017$). However, these associations were not noted in women. Age-based subgroup analysis indicated that BF was significantly associated with definite subclinical CAD only in individuals aged < 65 years, with an OR of 1.053 (95% CI: 1.009–1.099) in model 1. However, none of the overweight/obesity indicators predicted definite subclinical CAD in individuals aged ≥ 65 years.

3.3. Effects of smoking and obesity on the risk of subclinical CAD

Table 1 presents different obesity indicators; interpreting BF measurements was challenging because of the definitions of "healthy individuals" and "individuals with obesity" vary depending on

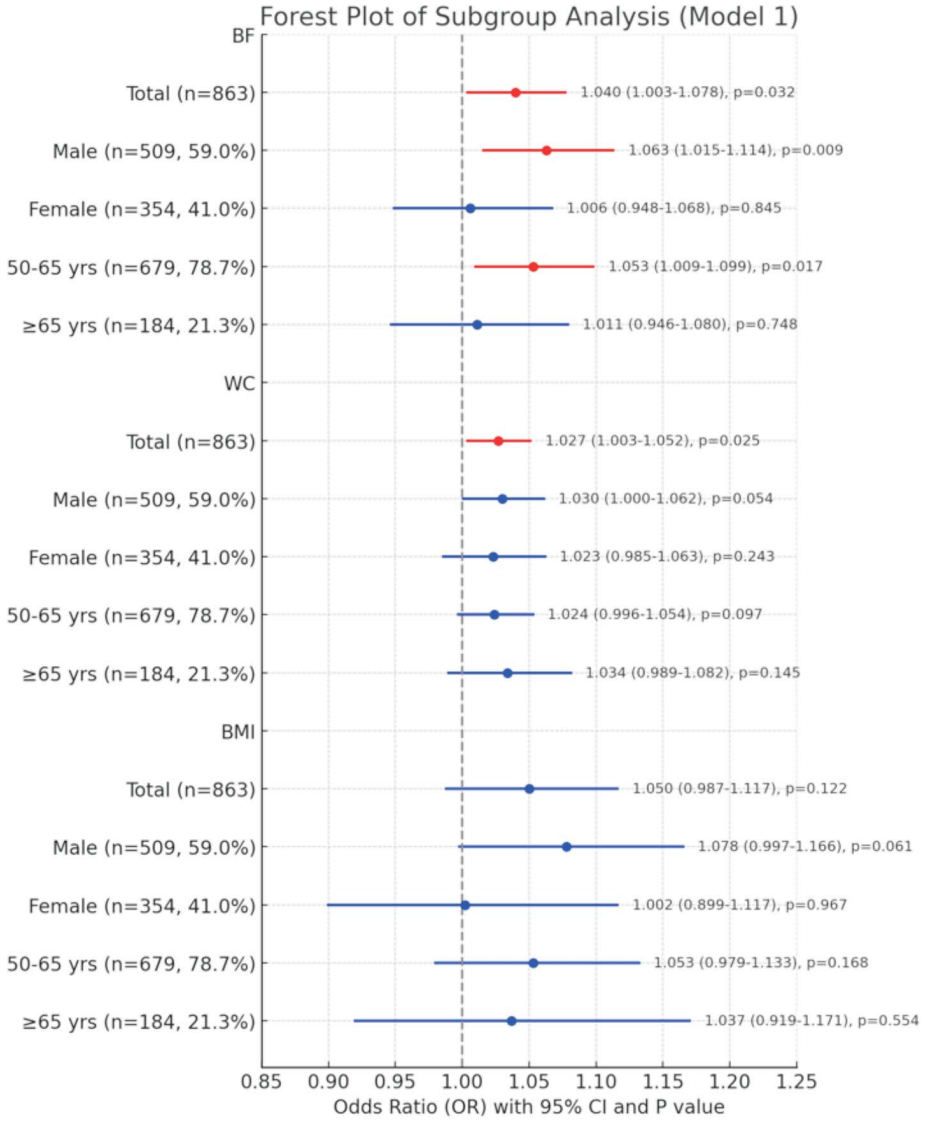

Figure 1. Association between obesity indicators and subclinical coronary artery disease (CAD) in the overall study population. Model 1: adjusted for age, gender, fasting plasma glucose, low-density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP). Abbreviations: BF, body fat; BMI, body mass; index WC, waist circumference.

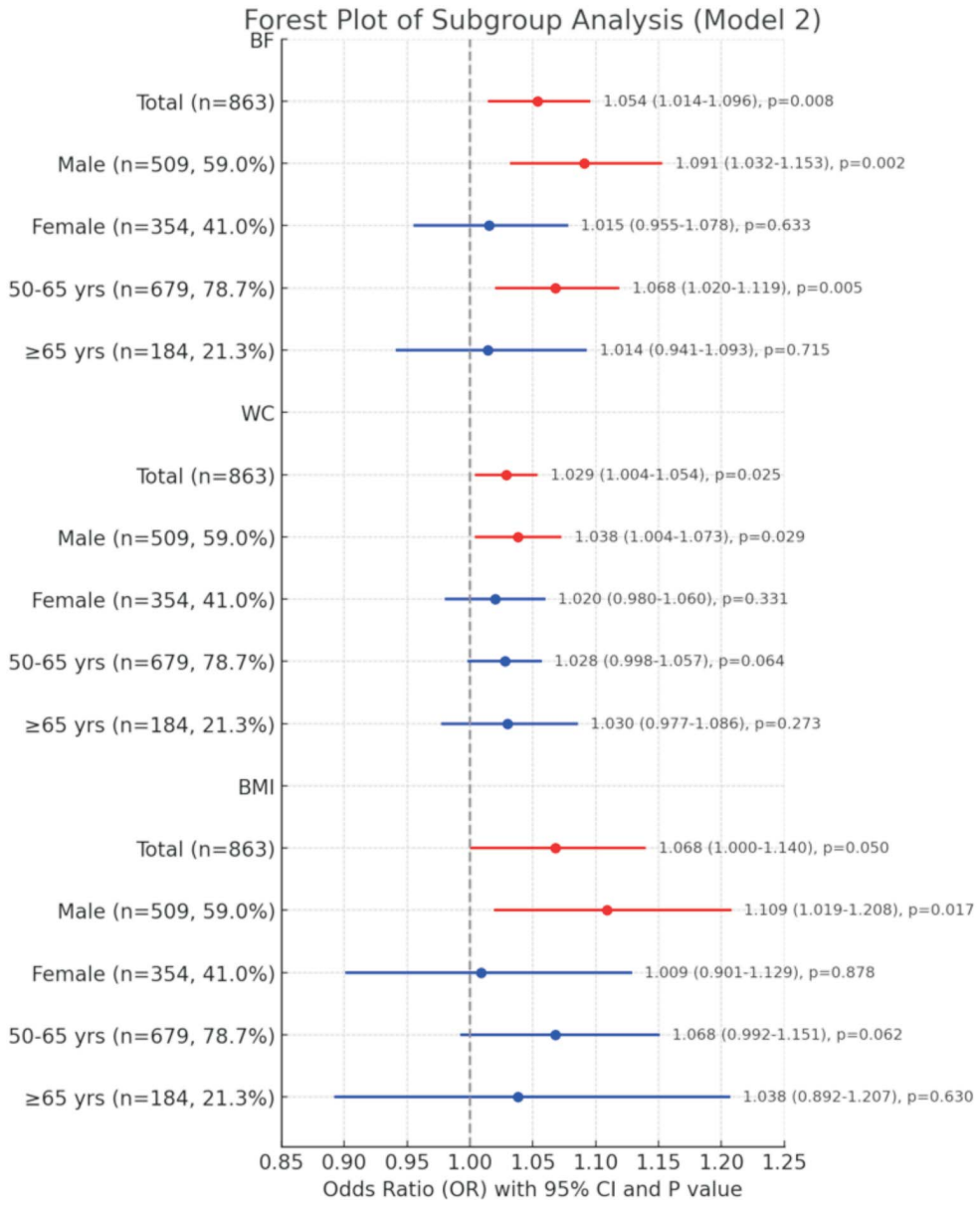

Figure 2. Association between obesity indicators and subclinical CAD in participants with no CAD versus definite subclinical CAD. Model 2 (no CAD vs. definite subclinical CAD): adjusted for age, gender, fasting plasma glucose, LDL-C, SBP. Abbreviations: BF, body fat; BMI, body mass index; WC, waist circumference.

age, sex, and personal factors. As indicated in Figure 3 and Figure 4, BMI and WC were strongly correlated with definite subclinical CAD in individuals with overweight/obesity and smoking habits. The ORs in model 2 were significantly higher than those in model 1, indicating stronger correlations in the no CAD and definite subclinical CAD groups than in the entire study. Specifically, for individuals with obesity and smoking habits, model 2 yielded ORs of 3.219 and 3.816 for BMI and WC, respectively, highlighting a pronounced risk of definite subclinical CAD. By contrast, for individuals with obesity but no smoking habits and those with normal body weight but smoking habits, the ORs were relatively low and not statistically significant.

4. Discussion

Our findings revealed that WC and BMI were higher in individuals with subclinical CAD than in those without it. Significant associations were noted between various obesity indicators (BF, WC, and BMI) and subclinical CAD, particularly among men. These associations were significant in the overall and male populations but non-significant in women and older adults (≥ 65 years), warranting further interpretation. These subgroup-specific null findings may be explained by biological and behavioral differences related to sex and age, such as hormonal profiles, fat distribution, and lifestyle factors, which are discussed in detail in the following section. Some associations were only marginally significant. For instance, in men, the association between WC and subclinical CAD was borderline significant in Model 1 (OR: 1.030; 95% CI: 1.000–1.062; p = 0.054), but reached statistical significance in Model 2 (p = 0.029), suggesting a modest but potentially meaningful effect. Furthermore, multivariate logistic regression identified both BMI and WC as independent predictors of subclinical CAD, particularly in individuals with overweight/obesity and smoking habits. These findings highlight the combined impact of obesity and smoking on subclinical CAD risk, reinforcing the need for integrated prevention strategies.

The sex-based differences observed in the significant associations of obesity indicators with subclinical CAD may be attributable to several factors. First, men and women have distinct patterns of fat distribution.[9] Men are more likely to accumulate abdominal or VAT,

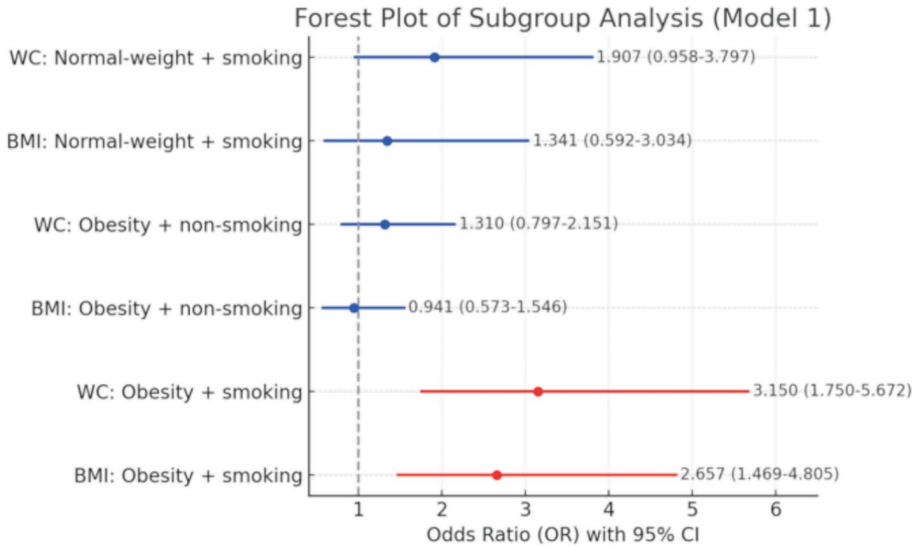

Figure 3. Combined effect of obesity and smoking on subclinical CAD in the overall study population. Model 1: adjusted for age, gender, fasting plasma glucose, LDL-C, SBP. Abbreviations: BMI, body mass index; WC, waist circumference.

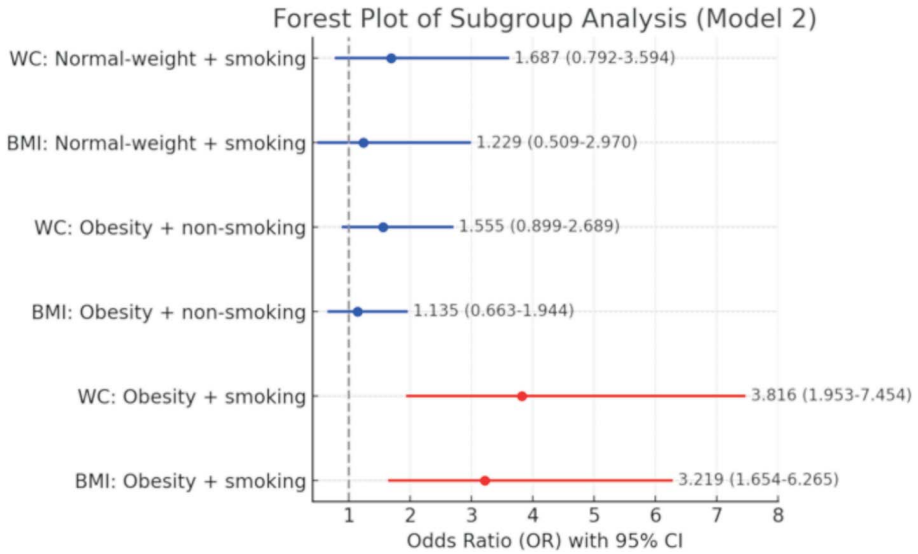

Figure 4. Combined effect of obesity and smoking on subclinical CAD in participants with no CAD versus definite subclinical CAD. Model 2 (no CAD vs. definite subclinical CAD): adjusted for age, gender, fasting plasma glucose, LDL-C, SBP. Abbreviations: BMI, body mass index; WC, waist circumference.

which contributes to CAD through multiple mechanisms, including insulin resistance (IR), dyslipidemia, chronic inflammation, and endothelial dysfunction.[10] Excess VAT increases the release of free fatty acids into the portal circulation, promoting hepatic steatosis and impairing insulin signaling. This leads to both hepatic and peripheral IR, a condition that not only exacerbates metabolic dysfunction but also accelerates atherosclerosis. VAT also promotes vascular inflammation through the secretion of proinflammatory adipokines, such as lipocalin-2 and monocyte chemoattractant protein-1, both of which contribute to atherosclerotic plaque formation. Meanwhile, protective adipokines, such as high-molecular-weight adiponectin, are often reduced in individuals with elevated VAT, further compromising vascular health.[11] Notably, a prospective analysis from the Genetics of Arteriosclerotic Disease (GEA) study indicated that VAT mediates over 50% of the adverse cardiovascular effects associated with systemic IR and adiponectin dysregulation.[12] In contrast, women are more likely to accumulate subcutaneous fat, which may differentially influence the risk of CAD. Second, sex hormones modulate fat metabolism differently: estrogen promotes fat accumulation, whereas testosterone reduces it, resulting in lower BF in men.[13] Hormonal differences may partly explain the sex-specific differences observed in the associations between obesity indicators and subclinical CAD. Finally, men and women often differ in their lifestyle and behavioral habits, such as physical activity levels, sedentary behavior, and smoking habits; these factors can influence the risk of CAD.[14]

A previous cohort study indicated that the combination of obesity and current smoking habits elevates the risk of circulatory disease–related mortality by 6- to 11-fold in individuals aged < 65 years compared with the risk in those with normal body weight and no smoking habits.[15] Our study serves as a pilot investigation into the combined effect of obesity and smoking on subclinical CAD. Several factors may mediate this effect. For example, the combined inflammatory stress from both obesity and smoking can lead to IR, elevate C-reactive protein levels, and increase cytokine secretion. Furthermore, the combined effect of obesity and smoking can adversely alter plasma lipid profiles, which are crucial for coronary artery health.[16] Roos et al. found a strong combined effect of obesity and smoking on the risk of all-cause mortality, although no synergistic interaction was observed.[17] The discrepancies may be explained by the study characteristics, including a higher proportion of women and a younger average age.

Additionally, the method used for BF assessment, BIA, although practical and widely applied in large-scale health examinations, is subject to certain limitations. Its accuracy can be affected by hydration status, recent food intake, and physical activity levels. These potential measurement biases should be considered when interpreting the association between BF and subclinical CAD, particularly in subgroup analyses.

Our study has some limitations. First, the study population predominantly consisted of urban individuals who had voluntarily undergone health checkups, potentially introducing selection bias, as these individuals may have higher health awareness and better access to healthcare. As a result, the prevalence of CAD in the general population may be underestimated. Future studies should include populations with greater geographic and socioeconomic diversity to enhance representativeness and generalizability. Second, the relatively small sample size, especially in women and elderly subgroups, may have reduced the statistical power to detect significant associations. Post hoc power analyses revealed insufficient power in these subgroups, suggesting that the nonsignificant findings should be interpreted with caution. Larger, population-based studies are necessary to validate our results. Although BF measured by BIA is widely used, it is susceptible to factors such as hydration status, recent physical activity, and food intake. Similarly, BMI and WC, while more accessible and standardized, may have limitations in accurately reflecting BF distribution or composition. Nevertheless, due to their simplicity, cost-effectiveness, and broad clinical applicability, BMI and WC were used as the primary indicators of overweight. Finally, critical lifestyle factors, such as dietary habits, physical activity levels, and psychosocial stress, were not assessed, which may confound the observed associations. Future research should incorporate these variables using validated assessment tools to provide a more comprehensive and accurate evaluation of CAD risk.

5. Conclusion

This study examined the effects of age, sex, and the combined impact of smoking and obesity on subclinical CAD risk. Our findings indicate that BF and WC are significantly associated with subclinical CAD, particularly among men and smokers. Notably, individuals with both obesity and smoking behaviors showed the highest risk, with ORs exceeding 3 in both models. These results highlight the importance of integrating BF and WC into cardiovascular risk assessment, especially in asymptomatic adults. Clinically, early screening should prioritize individuals with combined obesity and smoking, who may benefit most from timely lifestyle interventions or imaging-based evaluation to prevent disease progression.

Credit authorship contribution statement

Kai-Hsuan Cheng: Conceptualization, Methodology, Formal Analysis, Writing — Original Draft, Writing — Review & Editing, and Visualization. **Shih-Kai Kao:** Conceptualization, Methodology, Formal Analysis, Writing — Original Draft, Writing — Review & Editing, and Visualization. **Lee-Ching Hwang:** Conceptualization, Methodology, Formal Analysis, Investigation, Resources, and Supervision. **Meng-Ting Tsou:** Conceptualization, Methodology, Formal Analysis, Investigation, Resources, and Supervision. **Yu-Chen Chang:** Investigation, Resources, Writing — Review & Editing, Supervision, and Project Administration. All authors have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgments

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