Association of Body Mass Index with the Risk of Incident Type 2 Diabetes, Cardiovascular Disease, and All-Cause Mortality: A Community-Based Prospective Study

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Background: Type 2 diabetes and cardiovascular disease (CVD) are the most important sequelae of obesity and the leading cause of death. We evaluated the association between body mass index (BMI) and the risk of incident type 2 diabetes, CVD, and all-cause mortality in a prospective study of a Korean population.

Methods: The shapes of the associations were modeled by restricted cubic splines regression analysis. After categorizing all subjects ($n = 8,900$) into octiles based on their BMI levels, we estimated the hazard ratio (HR) for the association of categorized BMI levels with the risk of incident CVD and type 2 diabetes using a Cox's proportional hazard analysis.

Results: The mean age of participants was 52 years and 48% were men. Of the subjects at baseline, 39.0% of men and 45.6% of women were classified as obese (BMI ≥ 25 kg/m^2). Over a mean follow-up of 8.1 years, CVD events occurred in 509 participants; 436 died; and 1,258 subjects developed type 2 diabetes. The increased risk of incident diabetes began to be significant at BMI 23 to 24 kg/m^2 in both sexes (HR, 1.8). For CVD events, the risk began to increase significantly at BMI 26 to 28 kg/m^2 (HR, 1.6). We found a reverse J-shaped relationship between BMI and all-cause mortality, with an increased risk among individuals with BMI values in lower range (BMI <21 kg/m^2).

Conclusion: These results suggest that the BMI cut-off points for observed risk were varied depending on the diseases and that the BMI classification of obesity need to be revised to reflect differential risk of obesity-related diseases.

Keywords: Body mass index; Obesity; Diabetes mellitus; Cardiovascular diseases

INTRODUCTION

Obesity can be defined as an excess of body fat. Obesity raises

the risk for cardiovascular disease (CVD) through other risk factors including dyslipidemia, hypertension, hyperglycemia, and insulin resistance indicating that obesity is an underlying

major risk factor for CVD [1]. The most widely used simple anthropometric measurement to identify obesity in clinical practice is body mass index (BMI) [2].

BMI is a simple index using person's height and weight that is commonly used to identify overweight and obesity in adults. The World Health Organization (WHO) BMI classifications of overweight (defined as BMI $\geq$25 kg/m^2) and obesity (defined as BMI $\geq$30 kg/m^2) are intended for international use; these classifications reflect increased risk for type 2 diabetes and CVD [3]. On the basis of the available data, Asians generally have a higher percentage of body fat than white Westerners with the same BMI, and have increased CVD risks at lower BMI values [4]. There is also accumulating evidence of high prevalence of type 2 diabetes and other major cardiovascular risk factors at the BMI below the level of 25 kg/m^2 that defines overweight in WHO classification [4-6]. For these reasons, the need for developing different BMI cut-off points for different ethnic groups has emerged, but defining obesity for Asian has long been a subject of debate [4,7]. As such, the WHO consultation group decided not to define BMI cut point for Asians separately. Instead, they identified potential public health action points along the BMI continuum ranging from 23.0 to 27.5 kg/m^2 and proposed that each country make decisions regarding the definitions of increased risk for its population [4]. In China, BMIs of 24 and 28 kg/m^2 are recommended as the cut-off points for overweight and obesity, respectively [8]. The Korean Society for the Study of Obesity (KSSO) has established the lower BMI thresholds of 25 kg/m^2 for obesity and 23 kg/m^2 for overweight in Koreans [9].

Type 2 diabetes and CVD are the most important sequelae of obesity and are the leading cause of death in adults [3,10]. We assessed prevalence of obesity and evaluated the association between BMI levels and the risk of incident type 2 diabetes, CVD, and all-cause mortality in a prospective study of a Korean population. The results were also discussed in terms of obesity criteria for Koreans adults.

METHODS

The Korean Genome and Epidemiology Study-Ansan and Ansung study

The Korean Genome and Epidemiology Study (KoGES) is an ongoing prospective population-based cohort study with the support from the National Genome Research Institute. The recruitment of patients, study design, and methods for the KoGES Ansan and Ansung study have been reported previously [10].

Briefly, 10,038 subjects (aged 40 to 69 years) were enrolled in the two different cities of Ansung and Ansan from 2001 to 2002. Since the baseline examination (2001 to 2002), biennial repeated follow-up surveys have been continued. Recently, the eighth follow-up examination (2017 to 2018) has been completed.

Subjects

Initial data were obtained from 10,038 subjects who participated in the KoGES Ansan and Ansung Study. Among these subjects, those who had previous history of CVD ($n=249$) and those who did not undergo any follow-up surveys after the baseline recruitment (2001 to 2002) ($n=908$) were excluded. After applying the above exclusion criteria, the number of participants eligible for the study was 8,900 (4,243 men and 4,657 women with a mean age of 52.3 years). At each visit, investigator obtained informed written consent from all participants. The study protocol was approved by the ethics committee of the Korean Center for Disease Control and Institutional Review Board of the Ajou University School of Medicine (IRB approval No. AJIRB-CRO-07-012).

Study design and statistical analyses

In this study, only data up to the fifth follow-up examination period (2011 to 2012) were analyzed. During a 12 years follow-up period, 9,130 (91%) subjects underwent one or more follow-up examinations, and 6,117 (61%) completed the fifth follow-up survey (2011 to 2012). The spline regression analyses were used to evaluate the association between BMI levels and the risk of incident type 2 diabetes, CVD, and all-cause mortality. Analyses were performed in a separate model by sex. The shapes of the associations between BMI and CVD, and all-cause mortality were modeled by restricted cubic splines (adjusted for age, smoking, alcohol intake, and regular exercise) with four knots set at the 5th, 25th, 75th, and 95th percentiles. In males, knots were equivalent to BMI levels of 19.3, 22.2, 26.1, and 29.1 kg/m^2, respectively, while the values for females were 20.0, 22.6, 26.9, and 30.8 kg/m^2, respectively. We considered the BMI value associated with the lowest risk as the reference value; in the analysis of association with CVD, the BMI of 21.1 and 21.4 kg/m^2 were the reference values for men and women, respectively; for association with all-cause mortality, the reference values were set as the BMI of 27.1 and 22.2 kg/m^2, respectively. The plot was truncated at the 1st and the 99th percentile. After further exclusion of participants with known diabetes ($n=1,250$; 634 men and 616 women) at baseline, spline regression analyses for the association with development of type 2 diabetes was conducted in the same manner as the analy-

sis for the association with incident CVD. The BMI of 21.0 and 21.3 kg/m² were the reference values for men and women, respectively. After categorizing all subjects into octiles based on their BMI levels, we also estimated the hazard ratio (HR) for the association of categorized BMI level with the risk of incident CVD, type 2 diabetes, and all-cause mortality using a Cox's proportional hazard analysis. Statistical data analysis was performed using STATA software version 15.1 (Stata Corp., College Station, TX, USA).

Definition

A CVD event was defined as acute myocardial infarction, coronary-bypass surgery, coronary angioplasty, coronary stent insertion, angina pectoris, acute stroke, and death due to coronary disease or stroke that occurred during the follow-up period. Data on CVD event occurrence were obtained through in-depth interviews with the study participants. These interviews were repeated biennially. There were continuous attempts to contact participants who did not undergo follow-up examination by telephone or by door-to-door visit. Information about the deaths including the dates, places, and causes was obtained from the participants' family members through these contacts. The development of diabetes was assessed from the biennial follow-up examinations and diagnosed according to the criteria of American Diabetes Association (ADA): (1) plasma glucose ≥126 mg/dL in the fasting state; (2) plasma glucose ≥200 mg/dL 2 hours after a 75g oral glucose load; or (3) glycated haemoglobin ≥6.5% [11]. Also, at an in-depth interview conducted at each visit, subjects who had a history of diabetes or currently used insulin or oral anti-diabetic drugs were considered to have developed diabetes. Hypertension was defined as blood pressure greater than or equal to 140/90 mm Hg or use of antihypertensive medication. We defined dyslipidemia as serum low density lipoprotein cholesterol ≥160 mg/dL, high density lipoprotein cholesterol <40 mg/dL, triglycerides ≥200 mg/dL, or use of any medication for dyslipidemia [12]. Regular exercise was defined as doing physical exercise more than three times per week.

Table 1. Baseline Characteristics

Characteristic	Male (n=4,243)	Female (n=4,657)	Total (n=8,900)
Age, yr	51.8±8.8	52.7±9.0	52.3±8.9
Weight, kg	67.4±9.8	58.9±8.6	63.0±10.1
BMI, kg/m²	24.2±2.9	24.9±3.3	24.6±3.1
BMI ≥25 kg/m²	1,656 (39.0)	2,123 (45.6)	3,779 (42.5)
BMI ≥30 kg/m²	121 (2.9)	331 (7.1)	452 (5.1)
Waist circumference, cm	83.6±7.6	81.9±9.7	82.7±8,8
Percentage of body fat, %	21.5±5.1	31.6±5.5	-
Diabetes	634 (14.9)	616 (13.2)	1,123 (12.6)
HbA1c, %	5.81±0.94	5.78±0.91	5.80±0.93
Fasting glucose, mg/dL	91.5±23.9	86.6±19.1	88.9±21.7
HOMA-IR	1.63±1.16	1.77±1.43	1.70±1.31
Hypertension	1,003 (23.6)	1,198 (25.7)	2,201 (24.7)
Systolic blood pressure, mm Hg	117.5±16.5	117.5±19.4	117.5±18.1
Dyslipidemia	2,262 (53.3)	2,187 (47.0)	4,449 (50.0)
LDL-C, mg/dL	118.0±37.5	119.1±33.3	118.6±35.3
Triglyceride, mg/dL	173.4±114.8	144.0±86.3	158.0±101.9
HDL-C, mg/dL	45.1±10.8	47.4±10.9	118.6±35.3
Regular exercise	762 (18.0)	869 (18.7)	1,631 (18.3)
Current drinker	3,005 (70.8)	1,192 (25.6)	4,197 (46.9)
Current smoker	2,082 (49.1)	162 (3.5)	2,244 (25.2)

Values are expressed as mean±standard deviation or number (%).
BMI, body mass index; HbA1c, glycated haemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

RESULTS

The mean age of participants was 52 years and 48% were men. The mean±SD BMI of participants were 24.6±3.1 kg/m² (range, 14.4 to 40.2). Of the subjects at baseline, 39.0% of men and 45.6% of women were classified as obese as defined by the KSSO cut-off (BMI ≥25 kg/m²). The proportion of participants who had diabetes was 12.6% (1,123 of 8,900) (Table 1). Over a mean follow-up of 8.1±2.6 years, CVD events occurred in 509 participants (241 men and 268 women); 436 (293 men and 143 women) died; and 1,258 subjects (665 men and 593 women) developed type 2 diabetes. Restricted cubic spline regression analysis revealed a J-shaped association between BMI levels and incident CVD events (*P* value for nonlinearity=0.045 for men and 0.048 for women) (Fig. 1). The risk for development of CVD was lowest at BMI levels of 20 to 22 kg/m² in men and 21 to 22 kg/m² in women, and BMI levels higher than 26.0 kg/m² in men and 26.5 kg/m² in women were associated with a significantly increased risk. The overall shape of the association between BMI levels and incident diabetes demonstrated an increased risk of incident diabetes at BMI levels higher than 23.7 kg/m², with lowest risk occurring around BMI of 21 kg/m² in men (*P* value for nonlinearity=0.029) (Fig. 2A). On the other hand, the cubic restricted spline model has shown gradually increasing HRs for incident diabetes with increasing BMI levels in women (*P* value for nonlinearity=0.108) (Fig. 2B). Unlike the finding on CVD events, a reverse J-shaped association was seen between BMI and the risk of death from any cause (*P* value for nonlinearity=0.044 for men and 0.082 for women) (Fig. 3). For men, the risk of mortality was lowest at BMI of 25 to 29 kg/m², with inverse association below, and positive association above (Fig. 3A). An increased risk of mortality was more pronounced at lower BMIs than at higher BMIs (Table 2, Fig. 3A). For women, we found inverse association below a BMI of 22.2 kg/m², while there was little evidence of association at higher BMI values (Table 2, Fig. 3B).

In Cox proportional hazards models, as compared with men with a BMI of 20.8 to 22.1 kg/m², men with a BMI of 26.2 to 27.4 kg/m² had a HR for incident CVD of 1.63 (95% confidence interval [CI], 1.06 to 2.50). Among women, the risk of incident CVD increased at a BMI above 28.7 kg/m² with HR of 1.56 (95% CI, 1.03 to 2.35) compared to women with a BMI of 21.3
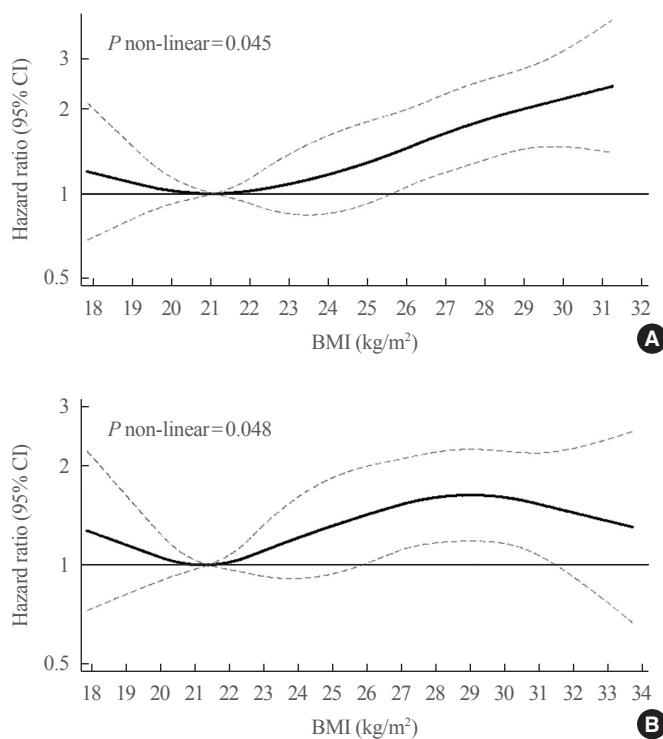
Fig. 1. The association between body mass index (BMI) level and development of cardiovascular disease. (A) Men, (B) Women. The analyses were adjusted for age, smoking, alcohol intake, and regular exercise. Dash line indicates 95% confidence interval (CI).
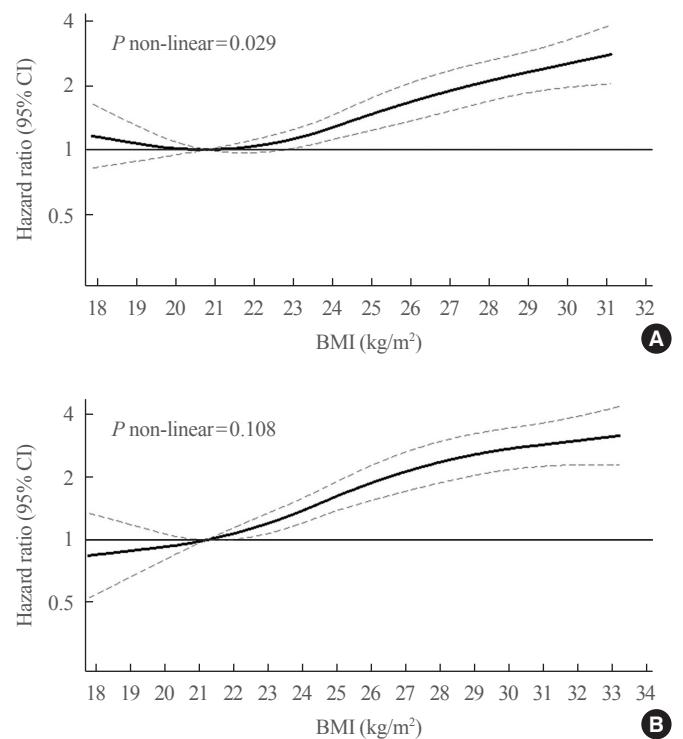

Fig. 2. The association between body mass index (BMI) level and development of type 2 diabetes. (A) Men, (B) Women. The analyses were adjusted for age, smoking, alcohol intake, and regular exercise. Dash line indicates 95% confidence interval (CI).

Table 2. Hazard Ratios for All-Cause Mortality Based on Categorized BMI Levels

BMI categories, kg/m²	Number	No. of subjects who developed diabetes	Incidence rate, %	Hazard ratio (95% CI)[a]	P value[b]
Men	4,243	293	6.9		
≤20.7	528	74	14.0	1.66 (1.06–2.59)	0.026
20.8–22.1	534	50	9.4	1.39 (0.87–2.22)	0.175
22.2–23.2	530	32	6.0	0.98 (0.57–1.60)	0.871
23.3–24.1	531	31	5.8	1.02 (0.61–1.71)	0.944
24.2–25.0	529	30	5.7	1.01 (0.60–1.70)	0.976
25.1–26.1	532	29	5.5	1.02 (0.60–1.72)	0.953
26.2–27.4	532	27	5.1	1	
≥27.5	527	20	3.8	0.87 (0.41–1.34)	0.380
Women	4,657	143	3.1		
≤21.2	583	24	4.1	1.55 (0.81–2.96)	0.182
21.3–22.5	581	15	2.6	1	
22.6–23.5	583	16	2.7	1.05 (0.52–2.12)	0.891
23.6–24.5	584	16	2.7	1.02 (0.50–2.07)	0.952
24.6–25.5	580	17	2.9	1.12 (0.56–2.23)	0.761
25.6–26.6	580	17	2.9	0.98 (0.49–1.95)	0.936
26.7–28.4	584	22	3.8	1.26 (0.69–2.57)	0.396
≥28.5	582	16	2.7	0.99 (0.49–2.04)	0.977

BMI, body mass index; CI, confidence interval.
[a]Adjusted for age, smoking, alcohol intake, and regular exercise; [b]Estimated from Cox proportional-hazard regression model.
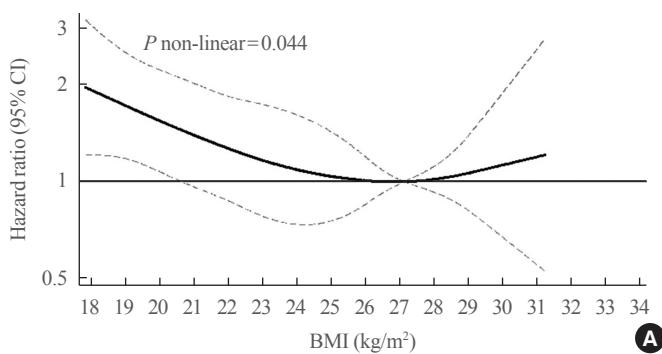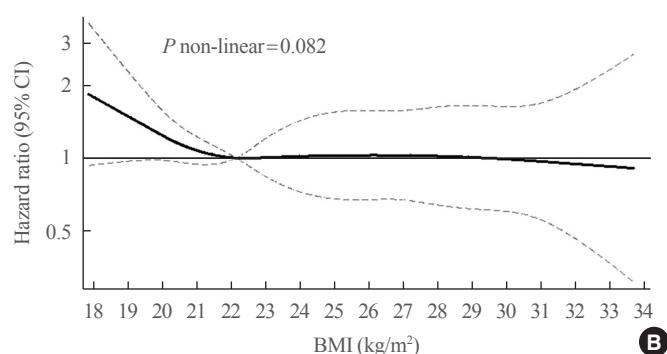
Fig. 3. The association between body mass index (BMI) level and all-cause mortality. (A) Men, (B) Women. The analyses were adjusted for age, smoking, alcohol intake, and regular exercise. Dash line indicates 95% confidence interval (CI).

to 22.5 kg/m² (Table 3). The risk of developing type 2 diabetes began to increase significantly at the BMI category of 24.2 to 25.0 kg/m² for men and 23.6 to 24.5 kg/m² for women, compared to the subjects in the lowest risk group, with HR of 1.81 (95% CI, 1.31 to 2.52) and 1.74 (95% CI, 1.21 to 2.51), respectively (Table 4).

DISCUSSION

Currently, obesity is defined as a BMI ≥25 kg/m² in the Korean population; this criterion was set by the KSSO and recommended by the Western Pacific Regional Office (WPRO) of the WHO in 2000 [7,9]. Applying this criterion, our cohort population had an unexpectedly higher prevalence of obesity, which is close to that of United States adults. In our cohort, 39.0% of

Table 3. Hazard Ratios for Development of Cardiovascular Disease Based on Categorized BMI Levels

BMI categories, kg/m²	Number	No. of subjects who developed diabetes	Incidence rate, %	Hazard ratio (95% CI)[a]	P value[b]
Men	4,243	337	7.9		
≤20.7	528	41	7.8	0.87 (0.56–1.35)	0.526
20.8–22.1	534	38	7.1	1	
22.2–23.2	530	46	8.7	1.28 (0.83–1.97)	0.263
23.3–24.2	531	30	5.6	0.92 (0.57–1.48)	0.718
24.3–25.1	529	42	7.9	1.34 (0.86–2.08)	0.195
25.2–26.1	532	40	7.5	1.29 (0.83–2.02)	0.262
26.2–27.4	532	49	9.2	1.63 (1.06–2.50)	0.026
≥27.5	527	51	9.7	1.80 (1.17–2.77)	0.007
Women	4,657	356	7.6		
≤21.2	583	36	6.2	0.90 (0.57–1.43)	0.653
21.3–22.5	581	37	6.4	1	
22.6–23.6	583	40	6.9	1.09 (0.69–1.70)	0.708
23.7–24.6	584	38	6.5	1.05 (0.67–1.65)	0.839
24.7–25.6	580	54	9.3	1.43 (0.94–2.18)	0.089
25.7–26.8	580	43	7.4	1.04 (0.67–1.61)	0.861
26.9–28.6	584	49	8.4	1.29 (0.84–1.98)	0.243
≥28.7	582	59	10.1	1.56 (1.03–2.35)	0.035

BMI, body mass index; CI, confidence interval.
[a]Adjusted for age, smoking, alcohol intake, and regular exercise; [b]Estimated from Cox proportional-hazard regression model.

men and 45.6% of women were classified as obese as defined by the KSSO cut-off (BMI ≥25 kg/m²) (Supplemental Table S1); in the USA National Health and Nutrition Examination Survey (2015 to 2016), among adults aged 40 to 59 years, 40.8% of men and 44.7% of women were classified as obese based on the global WHO BMI cut-off ≥30 kg/m² [13]. Based on an analysis of nationally representative data from the Korea National Health and Nutrition Examination Survey (2016), the proportion of obese subjects (BMI ≥25 kg/m²) was 34.8% (42.3% of men, 26.4% of women). In particular, the prevalence of obesity among those aged 40 to 59 years was 44% for men and 30% for women [14]. For the European population, the prevalence of obesity (BMI ≥30 kg/m²) was 10% to 27% depending on the country, and the prevalence of obesity was higher in Koreans than in Europeans [15]. Scientific evidence suggests that Asians generally have a higher percentage of body fat than Westerners with the same BMI, and the risk of having CVD increases at a lower BMI value than Westerners [4]. Even so, considering the comparison with prevalence of obesity among United States and European adults, it is worth contemplating whether the current BMI cut-off point for Korean obesi-

ty is too low.

In 2004, the WHO convened an expert consultation on BMI classification for the Asian population as the controversy over whether to develop different BMI cut-off points for different ethnic groups increased [4]. This consultation decided not to define cut-off points for each population separately because the available data did not indicate one clear BMI cut-off point for all Asians [4,6,16]. Instead, the expert consultation group designated BMI levels ≥23 and ≥27.5 kg/m² as potential public health action points along the BMI continuum for Asian populations and proposed that each country define levels of increased risk for its population [4]. In general, BMI ≥25 kg/m² (defined as overweight) is considered a risk factor for diabetes, and therefore the ADA recommends testing for type 2 diabetes in adults of any age with BMI ≥25 kg/m² and who have additional risk factors [11]. However, for Asian American, these BMI values are lower to ≥23 kg/m² because BMI cut points with a sensitivity of 80% fall consistently between 23 and 24 kg/m² for nearly all Asian American subgroups [11,17]. In our study, the increased risk of incident diabetes began to be significant at around BMI 23 to 24 kg/m² in both men and women. These val-

Table 4. Hazard Ratios for Development of Type 2 Diabetes Mellitus Based on Categorized BMI Levels

BMI categories, kg/m²	Number	No. of subjects who developed diabetes	Incidence rate, %	Hazard ratio (95% CI)[a]	P value[b]
Men	3,609	665	18.4		
≤20.7	465	68	14.6	1.08 (0.76–1.54)	0.660
20.8–22.1	469	58	12.4	1	
22.2–23.2	462	74	16.0	1.29 (0.91–1.81)	0.141
23.3–24.1	438	69	15.8	1.29 (0.92–1.82)	0.153
24.2–25.0	438	89	20.3	1.81 (1.31–2.52)	<0.001
25.1–26.1	491	105	21.4	1.83 (1.33–2.51)	<0.001
26.2–27.4	414	92	22.2	1.98 (1.43–2.73)	<0.001
≥27.5	432	110	25.5	2.30 (1.67–3.16)	<0.001
Women	4,041	593	14.7		
≤21.2	517	46	8.9	1	
21.3–22.5	502	43	8.6	0.97 (0.63–1.45)	0.834
22.6–23.5	507	50	9.9	1.16 (0.78–1.72)	0.463
23.6–24.5	504	73	14.5	1.74 (1.21–2.51)	0.003
24.6–25.5	502	80	15.9	1.86 (1.30–2.67)	0.001
25.6–26.6	503	88	17.5	1.99 (1.40–2.83)	<0.001
26.7–28.4	502	90	17.9	2.20 (1.55–3.13)	<0.001
≥28.5	504	123	24.4	3.02 (2.16–4.23)	<0.001

BMI, body mass index; CI, confidence interval.
[a]Adjusted for age, smoking, alcohol intake, and regular exercise; [b]Estimated from Cox proportional-hazard regression model.

ues are close to the 23 kg/m² of BMI suggested by the WHO as a potential public health action point representing increased risk for Asian populations [4] and are also close to the level given by the KSSO and the ADA as overweight (≥23 kg/m²) [9,11].

Meanwhile, the risk of CVD events began to increase significantly at around BMI 26 to 28 kg/m² in both men and women; these values are above the current BMI cut-off (≥25 kg/m²) for obesity in Koreans. Also, our subjects with 25% and 35% body fat (thresholds for obesity among men and women, respectively) [1,18] had a BMI consistent with the median of 25.9 kg/m² (interquartile range, 24.7 to 27.0) in men and 26.7 kg/m² (interquartile range, 25.5 to 28.2) in women, respectively (Supplemental Table S2). In China, BMIs of 28 kg/m² are recommended as the cut-off points for obesity [8]. The Joint Statement by international diabetes organizations recommend that metabolic surgery could be an option to treat type 2 diabetes in patients with class I obesity (BMI 30.0 to 34.9 kg/m²). In this guideline, a public health action point is applied to diabetic patients with obesity in Asian populations, recommending that a BMI value for class I obesity be reduced by 2.5 kg/m² for Asian patients to 27.5 to 32.4 kg/m² [19,20]. Taken together, it may be necessary

to consider raising the BMI cut-off point for Korean obesity to the international criteria of obesity for Asian population.

In our study, we found a reverse J-shaped relationship between BMI and all-cause mortality, with an increased risk among individuals with BMI values in the healthy range (BMI 18.5 to 22.9 kg/m²). This relationship was affected by sex. For men, in particular, BMI was inversely associated with mortality up to 27 kg/m², while there was little association above 22.2 kg/m² in women. Our finding was consistent with those from the general Korean population [21-23]. In a longitudinal analysis of approximately 1.2 million Koreans, the BMI range associated with lowest mortality risk was 21.5 to 27.9 kg/m² [21]. The results from the National Health Insurance Service (NHIS) data has shown that the all-cause mortality of adults aged 45 to75 was lowest at BMI of 24 to 28 kg/m² [22]. A reduced all-cause mortality risk was also found in a large meta-analysis of 141 studies in relation to being overweight (BMI 25 to 30 kg/m²) and being modestly obese (BMI 30 to 35 kg/m²) when compared with normal weight (BMI 18 to 25 kg/m²) [24]. These findings from Korean population and meta-analysis suggest that overweight might be rather protective, indicating that current

classification of obesity by BMI does not reflect the risk of all-cause mortality. Further studies are needed to assess the association with cause-specific mortality.

Self-reported information on CVD events may have been prone to recall bias despite the in-depth nature of interview. Since all participants in our study were aged 40 to 69 years (mean 52.3 ± 8.9) and the KoGES was conducted in two areas in South Korea, the generalizability of our results may be limited. Thus, our findings may not apply to young ages. Indeed, previous studies have shown that the BMI associated with lowest mortality risk was lower in younger individuals than in older individuals [22,23]. We did not consider abdominal adiposity which cannot be sufficiently assessed by BMI measurement. Even with subjects with the same BMI value, those with higher waist circumference may be at higher risk [25]. In addition, the medication data in this group of participants was not reflected in our analysis. The use of statin or antiplatelet drugs may have affected incident CVD events. Similarly, we do not have sufficient behavior data including physical activity and diet because these factors may change during the observation period.

Type 2 diabetes and CVD are the most important sequelae of obesity and the leading cause of death in adults [3,10]. In our study, the risk of incident diabetes increased significantly at BMI 23 to 24 kg/m². For CVD events, the risk began to increase significantly at BMI 26 to 28 kg/m². An increased risk of mortality was more evident at lower BMI range than current cut-point for obesity and this association was sex-specific. The BMI cut-off points for observed risk were varied depending on the diseases and not consistent with universal cut-off values for obesity. These results suggest that the BMI classification of obesity need to be revised to reflect differential risk of obesity-related diseases.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

AUTHOR CONTRIBUTIONS

Conception or design: J.C.B. Acquisition, analysis, or interpretation of data: J.C.B., N.H.C., J.H.K., K.Y.H., S.M.J. Drafting the work or revising: J.C.B. Final approval of the manuscript: N.H.C., J.H.K., K.Y.H., S.M.J., M.K.L.

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