

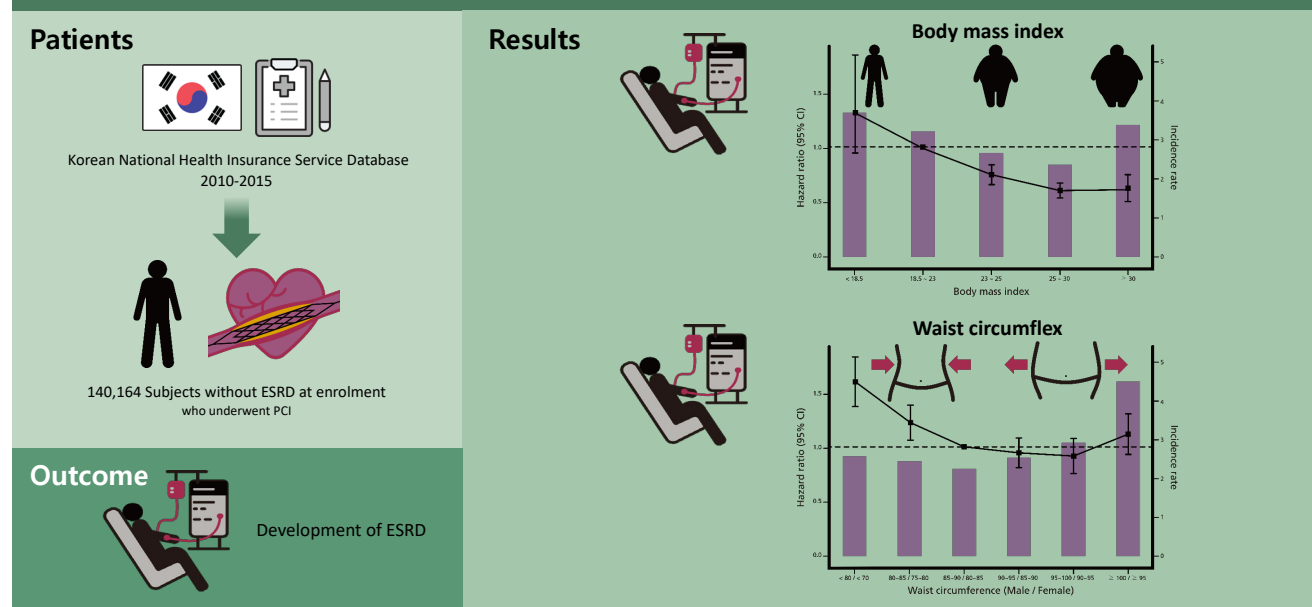


Low waist circumference prior to percutaneous coronary intervention predict the risk for end-stage renal disease: a nationwide Korean population based-cohort study

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Background/Aims: The obesity paradox has been known in end-stage renal disease (ESRD). However, the effect of body mass index (BMI) or waist circumference (WC) prior to percutaneous coronary intervention (PCI) on the development of ESRD is not clear.

Methods: Using nationally representative data from the Korean National Health Insurance System, we enrolled 140,164 subjects without ESRD at enrolment who underwent PCI between 2010 and 2015, and were followed-up until 2017. Patients were stratified into five levels based on their baseline BMI and six levels based on their WC with 5-cm increments. BMI and WC were measured at least 2 years prior to PCI. The primary outcome was the development of ESRD.

Results: During a median follow-up of 5.4 years, 2,082 (1.49%) participants developed ESRD. The underweight group (hazard ratio [HR], 1.331; 95% confidence interval [CI], 0.955 to 1.856) and low WC (< 80/< 75) (HR, 1.589; 95% CI, 1.379 to 1.831) showed the highest ESRD risk and the BMI 25 to 30 group showed the lowest ESRD risk (HR, 0.604; 95% CI, 0.542 to 0.673) in all participants after adjusting for all covariates. In the subgroup analysis for diabetes mellitus (DM) duration, WC < 85/80 cm (men/women) increased ESRD risk in only the DM group (DM < 5 years and DM ≥ 5 years) compared to the reference group (85–90/80–85 of WC), but not the normal or impaired fasting glucose group.

Conclusions: Low WC prior to PCI showed an increased ESRD risk in patients with DM undergoing PCI as compared to those without DM.

Keywords: Body mass index; Kidney failure, chronic; Percutaneous coronary intervention; Waist circumference

INTRODUCTION

The prevalence of obesity has been steadily and significantly increasing worldwide [1,2]. Because of its impact on cardiovascular diseases (CVDs), obesity is becoming one of the most serious global health issues [3]. The risk factors associated with obesity and ischemic heart disease (IHD) are well-established, and obesity itself has been thought to be a risk factor for IHD and can worsen its prognosis regardless of the metabolic status [4,5]. There is less evidence showing obesity as an independent risk factor of end-stage renal disease (ESRD), regardless on the presence of type 2 diabetes mellitus (DM) [6], and observational studies have shown positive associations between obesity and chronic kidney disease (CKD) or ESRD [7,8]. However, some studies showed that obesity did not increase the risk of ESRD in patients with moderate to advanced CKD [9]. Therefore, whether obesity is associated with the development of ESRD remains unclear.

Percutaneous coronary intervention (PCI) is an essential treatment modality for coronary artery disease. Although PCI is mainly performed in patients with underlying diseases such as DM, CKD, and hypertension, resulting in ESRD, there is insufficient data on the association between PCI and ESRD. In addition, the impact of obesity prior to PCI on ESRD risk has not been evaluated.

Therefore, we conducted this study to verify the relationship between obesity prior to PCI and ESRD risk using the National Health Insurance Service (NHIS) health checkup data.

METHODS

Because of the confidentiality of the data used for this study and strict privacy policy from the data holder that the data can be kept among the designated research personnel only, the data cannot be provided to others, even if the data are made anonymous.

Study design and database

The Korean National Health Insurance Service (KNHIS) comprises a complete set of health information pertaining to 50 million Koreans, which includes an eligibility database, medical treatment database, health examination database, and medical care institution database [10,11]. The National Health Insurance Corporation (NHIC) is the single insurer, managed by the Korean government, to which approximately 97% of the Korean population subscribes. Enrollees in the NHIC are recommended to undergo a standardized medical examination at least every 2 years. Among 270,237 subjects who underwent PCI in 2010 to 2015 (index year),

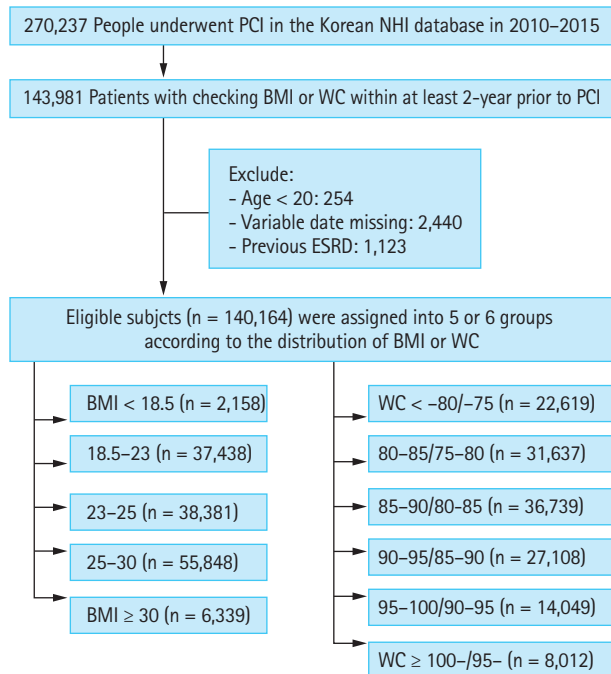


Figure 1. Flow diagram of the study. PCI, percutaneous coronary intervention; NHI, National Health Insurance; BMI, body mass index; WC, waist circumference; ESRD, end-stage renal disease.

143,727 subjects were followed up to 31 December 2017. We excluded 2,440 subjects with missing data for at least one variable. To avoid confounders by pre-existing diseases and minimize the possible effects of reverse causality, those who had a history of ESRD before the index year were also excluded ($n = 1,123$). Ultimately, the study population consisted of 140,164 subjects (Fig. 1). We registered only de novo PCI and excluded patients with a history of PCI to avoid the effects of past coronary intervention due to coronary artery disease, including angina pectoris or MI.

The study protocol adhered to the ethical guidelines of the 2013 Declaration of Helsinki and was approved by the Chonnam National University Hospital (study approval number: CNUH-EXP-2020-187) and NHIS (NHIS-2019-1-379). The need for written informed consent was waived by our review board.

Definitions of body mass index and waist circumference

For each participant, the body mass index (BMI) was calculated by dividing the weight (in kg) by the square of the

height (in m^2). We defined obesity as a BMI ≥ 25 kg/m^2 . Participants were then categorized by the definition of obesity as follows: underweight (BMI < 18.5 kg/m^2), normal (≥ 18.5 to < 23 kg/m^2), overweight (≥ 23 to < 25 kg/m^2), stage 1 obesity (≥ 25 to 30 kg/m^2), and stage 2 obesity (≥ 30 kg/m^2) according to the World Health Organization recommendations for Asian populations [12].

The waist circumference (WC) of each participant was also measured at the midpoint between the rib cage and iliac crest by a trained examiner. Patients were divided into six categories based on 5-cm WC increments: $< 80/< 75$, $80-85/75-80$, $85-90/80-85$ (reference group), $90-95/85-90$, $95-100/90-95$, and $\geq 100/\geq 95$ cm in men/women. Central obesity was defined as a WC ≥ 90 cm in men and ≥ 85 cm in women according to the definition of the Korean Society for the Study of Obesity [13].

Glycemic status and definition of chronic disease

All participants were categorized into four groups based on their glycemic status: normal, impaired fasting glucose (IFG), DM < 5 years, and DM ≥ 5 years. IFG was defined as a fasting plasma glucose level of 100 to 125 mg/dL. Type 2 DM was defined as an FPG level ≥ 126 mg/dL or at least one claim per year for the prescription of hypoglycemic drug under International Classification of Diseases, 10th Revision (ICD-10) codes E11-14 [14]. Patients with type 1 DM who had claims under ICD-10 code E10 were excluded from this study [15,16]. The group with DM < 5 years was defined as who had type 2 DM with 5 years on the date of the health checkup. The group with DM ≥ 5 years was defined as those who had type 2 DM 5 years before the date of the health checkup. Comorbidities were identified using information gathered in the 1 year before the index date. Hypertension was defined as a previous hypertension diagnosis ICD-10 codes (I10–13, I15) and a history of taking at least one anti-hypertensive drug, or a recorded systolic blood pressure (BP) of ≥ 140 mmHg or diastolic BP of ≥ 90 mmHg in the health examination database. Dyslipidemia was identified using the appropriate diagnostic code (E78) and a history of lipid-lowering drug use, or a total serum cholesterol concentration of ≥ 240 mg/dL in the health examination database. CKD was defined as an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73 m^2 calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and as a combination of ICD-10 codes (N18–19). Participants'

fasting blood glucose (mg/dL), total cholesterol (mg/dL), triglyceride (mg/dL), high density lipoprotein cholesterol (mg/dL), and low density lipoprotein cholesterol (mg/dL) concentrations were measured in a fasting state. The quality of the laboratory tests has been validated by the Korean Association for Laboratory Medicine, and hospitals participating in the NHI health checkup programs are certified by the NHIS.

Study outcomes and follow-up

The study population was followed from baseline to the date of ESRD diagnosis or until 31 December 2017, whichever came first. The primary end point was incident ESRD, which was defined using a combination of ICD-10 codes (Z49, Z94.0, and Z99.2) and a special code (V code) that was assigned in the initiation of renal replacement therapy (hemodialysis [HD], V001; peritoneal dialysis [PD], V003) and/or kidney transplantation (KT, V005) during hospitalization. All medical expenses for dialysis are reimbursed using the Korean Health Insurance Review and Assessment Service database. These patients are also registered as special medical aid beneficiaries. Therefore, we were able to identify every patient with ESRD in the entire South Korean population and to analyze the data for all patients with ESRD who started dialysis. Codes for treatment or medical expense claims included V005 for KT, V001 for HD, and V003 for PD. We excluded individuals without previous CKD who had a transplant or dialysis code on the same date as an acute renal failure code. Subjects on continuous renal replacement therapy or acute PD were also excluded.

General health behaviors and sociodemographic variables

Smoking history was categorized as nonsmokers, former smokers, and current smokers. Alcohol drinking was categorized into 0, 1–2, or ≥ 3 times/week by frequency (none, mild, and heavy, respectively), and regular exercise, defined as vigorous physical activity for at least 20 min/day, was categorized into 0, 1–4, and ≥ 5 times/week by frequency. Income level was divided by quartile: Q1 (lowest), Q2, Q3, and Q4 (highest).

Statistical analysis

We report the mean \pm standard deviation with intervals for continuous variables and the numbers (with percentages) for categorical variables. The hazard ratios (HRs) with 95% confidence intervals (CIs) for ESRD by BMI and WC category was

obtained using multivariable Cox proportional hazard models using the normal BMI (BMI 18.5 to 23 kg/m²) and normal WC (85–90/80–85 cm) as a reference after adjustment using four models: Model 1: crude model; Model 2: adjusted for Model 1 plus age, sex, income, DM, dyslipidemia, and hypertension; Model 3: adjusted for Model 2 plus smoking, alcohol drinking, physical activity, and eGFR; and Model 4: adjusted for Model 3 plus previous CVD, heart failure, and cancer. For the Cox proportional hazard regression model, we did not subtract the deceased from the data itself to minimize possible bias when excluding mortality and morbidity.

The cumulative ESRD incidence was estimated by constructing Kaplan-Meier curves for the mean 5.4-year follow-up period, and we used the log-rank test to examine differences in ESRD development by the level of BMI and WC. We also performed subgroup analysis for DM status. A $p < 0.05$ was considered to reflect statistical significance. SAS version 9.3 software and SAS survey procedures (SAS Institute Inc., Cary, NC, USA) were used for all statistical analyses.

RESULTS

Baseline characteristics

Among all the participants, 2,082 (1.49%) developed ESRD during a median follow-up duration of 5.4 years. The mean age was higher among individuals who developed ESRD than among those who did not. The proportions of low income were higher in the incident ESRD than in the non-ESRD groups. Comorbidities such as DM, hypertension, dyslipidemia, CKD, proteinuria, CVD, heart failure, and cancer were more prevalent in the ESRD group than in the non-ESRD group. eGFR and BMI were lower, and BP and glucose levels were higher, in the ESRD group than in the non-ESRD group (Supplementary Table 1).

The characteristics of participants classified by BMI levels and WC are presented in Tables 1 and 2, respectively. Subjects in the underweight group (BMI < 18.5 kg/m²) were older; had a lower income; exercised less; and had a lower prevalence of DM, hypertension, dyslipidemia, and CKD, and a higher prevalence of CVD, heart failure, and cancer. The mortality rate was highest in the underweight group. BP, fasting glucose, and total cholesterol were lower in the underweight group (Table 1). Table 2 shows that the patients in the central obesity group were older; mostly wom-

Table 1. Baseline characteristics of participants by level of body mass index

Variable	Distribution of BMI, kg/m ²					p value
	< 18.5 (n = 2,158)	18.5–23 (n = 37,438)	23–25 (n = 38,381)	25–30 (n = 55,848)	> 30 (n = 6,339)	
Age, yr	70.41 ± 10.29	65.66 ± 10.34	63.63 ± 10.17	61.97 ± 10.50	59.22 ± 12.06	< 0.0001
Male sex	1,451 (67.24)	26,075 (69.65)	27,869 (72.61)	40,061 (71.73)	3,892 (61.4)	< 0.0001
Smoking						< 0.0001
None	964 (44.67)	17,835 (47.64)	18,202 (47.42)	26,619 (47.66)	3,280 (51.74)	
Ex-	359 (16.64)	7,580 (20.25)	9,044 (23.56)	13,411 (24.01)	1,157 (18.25)	
Current	835 (38.69)	12,023 (32.11)	11,135 (29.01)	15,818 (28.32)	1,902 (30)	
Drinking						< 0.0001
None	1,563 (72.43)	24,789 (66.21)	24,162 (62.95)	34,628 (62)	4,168 (65.75)	
Mild	468 (21.69)	10,413 (27.81)	11,883 (30.96)	17,347 (31.06)	1,709 (26.96)	
Heavy	127 (5.89)	2,236 (5.97)	2,336 (6.09)	3,873 (6.93)	462 (7.29)	
Regular exercise	281 (13.02)	7,284 (19.46)	8,370 (21.81)	11,695 (20.94)	1,111 (17.53)	< 0.0001
Income ^a	546 (25.3)	8,295 (22.16)	8,250 (21.5)	11,883 (21.28)	1,424 (22.46)	< 0.0001
DM	513 (23.77)	11,254 (30.06)	12,264 (31.95)	18,979 (33.98)	2,630 (41.49)	< 0.0001
HTN	515 (23.86)	9,342 (24.95)	10,416 (27.14)	17,636 (31.58)	2,593 (40.91)	< 0.0001
CVD	491 (22.75)	7,705 (20.58)	7,710 (20.09)	11,075 (19.83)	1,352 (21.33)	0.0002
Heart failure	250 (11.58)	3,199 (8.54)	3,165 (8.25)	4,852 (8.69)	772 (12.18)	< 0.0001
Cancer	137 (6.35)	1,738 (4.64)	1,430 (3.73)	1,779 (3.19)	180 (2.84)	< 0.0001
Dyslipidemia	863 (39.99)	17,527 (46.82)	19,405 (50.56)	30,177 (54.03)	3,812 (60.14)	< 0.0001
CKD (eGFR < 60 mL/min/1.73 m ²)	343 (15.89)	5,606 (14.97)	5,644 (14.71)	8,527 (15.27)	1,101 (17.37)	< 0.0001
15 ≤ eGFR < 30 mL/min/1.73 m ²	17 (0.79)	332 (0.89)	248 (0.65)	380 (0.68)	61 (0.96)	0.0002
eGFR < 15 mL/min/1.73 m ²	18 (0.83)	296 (0.79)	293 (0.76)	385 (0.69)	60 (0.95)	0.1272
Weight, kg	44.76 ± 5.85	56.18 ± 6.97	63.58 ± 6.92	71.2 ± 8.54	83.67 ± 11.56	< 0.0001
Height, cm	159.97 ± 9.39	161.65 ± 8.88	162.63 ± 8.71	162.85 ± 9.08	161.9 ± 10.21	< 0.0001
WC, cm	70.48 ± 6.32	78.78 ± 5.84	84.15 ± 5.25	89.65 ± 5.93	98.89 ± 7.31	< 0.0001
BMI, kg/m ²	17.42 ± 0.94	21.43 ± 1.14	23.96 ± 0.57	26.77 ± 1.29	31.8 ± 1.92	< 0.0001
SBP, mmHg	126.2 ± 18.15	128.13 ± 16.43	129.72 ± 15.76	131.55 ± 15.56	134.97 ± 16.29	< 0.0001
DBP, mmHg	76.27 ± 11.39	77.45 ± 10.28	78.65 ± 10.1	80.13 ± 10.22	82.58 ± 11.09	< 0.0001
Glucose, mg/dL	108.75 ± 48.03	110.81 ± 40.57	111.96 ± 38.22	113.44 ± 37.2	119.25 ± 41.15	< 0.0001
TC, mg/dL	195.07 ± 42.04	201.89 ± 45.56	205.07 ± 44.36	207.25 ± 47.38	211.09 ± 53.45	< 0.0001
HDL, mg/dL	55.16 ± 15.07	51.77 ± 23.21	49.24 ± 18.74	48.16 ± 23.68	47.83 ± 20.99	< 0.0001
LDL, mg/dL	116.46 ± 36.95	123.1 ± 51.12	125.31 ± 70.69	125.38 ± 66.65	126.07 ± 57.03	< 0.0001
TG, mg/dL ^b	103.54 (101.51–105.62)	123.97 (123.33–124.61)	139.77 (139.05–140.5)	154.47 (153.81–155.14)	170.72 (168.54–172.92)	< 0.0001
eGFR, mL/min/1.73 m ²	82.38 ± 33.54	82.26 ± 40.94	81.2 ± 40.88	80.55 ± 41.04	80.46 ± 42.62	< 0.0001
Hemoglobin, g/dL	13.11 ± 1.69	13.78 ± 1.65	14.16 ± 1.6	14.38 ± 1.61	14.45 ± 1.72	< 0.0001
Death	768 (35.59)	6,108 (16.31)	4,075 (10.62)	4,763 (8.53)	480 (7.57)	< 0.0001

Values are presented as mean ± standard deviation, number (%), or median (range).

BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipid; LDL, low density lipoprotein; TG, triglyceride.

^aLow income 25%.

^bGeometric mean.

Table 2. Baseline characteristics of participants by level of waist circumference

Variable	Distribution of WC, cm						p value
	< 80/ (n = 22,619)	80–85/75–80 (n = 31,637)	85–90/80–85 (n = 36,739)	90–95/85–90 (n = 27,108)	95–100/90–95 (n = 214,049)	≥ 100/≥ 95 (n = 8,012)	
Age	63.95 ± 11.04	62.79 ± 10.45	63.14 ± 10.42	63.50 ± 10.43	64.09 ± 10.70	64.22 ± 11.24	< 0.0001
Male sex	16,240 (71.8)	23,800 (75.23)	26,479 (72.07)	19,216 (70.89)	9,065 (64.52)	4,548 (56.76)	< 0.0001
Smoking							< 0.0001
None	10,461 (46.25)	14,116 (44.62)	17,527 (47.71)	12,932 (47.71)	7,339 (52.24)	4,525 (56.48)	
Ex-	4,425 (19.56)	7,285 (23.03)	8,552 (23.28)	6,606 (24.37)	3,106 (22.11)	1,577 (19.68)	
Current	7,733 (34.19)	10,236 (32.35)	10,660 (29.02)	7,570 (27.93)	3,604 (25.65)	1,910 (23.84)	
Drinking							< 0.0001
None	14,698 (64.98)	19,388 (61.28)	23,061 (62.77)	17,130 (63.19)	9,379 (66.76)	5,654 (70.57)	
Mild	6,593 (29.15)	10,234 (32.35)	11,315 (30.8)	8,116 (29.94)	3,699 (26.33)	1,863 (23.25)	
Heavy	1,328 (5.87)	2,015 (6.37)	2,363 (6.43)	1,862 (6.87)	971 (6.91)	495 (6.18)	
Regular exercise	4,611 (20.39)	6,957 (21.99)	7,768 (21.14)	5,488 (20.24)	2,622 (18.66)	1,295 (16.16)	< 0.0001
Income ^a	5,100 (22.55)	6,810 (21.53)	7,878 (21.44)	5,731 (21.14)	3,064 (21.81)	1,815 (22.65)	< 0.0001
DM	5,539 (24.49)	9,148 (28.92)	11,772 (32.04)	9,727 (35.88)	5,643 (40.17)	3,811 (47.57)	< 0.0001
HTN	5,183 (22.91)	8,223 (25.99)	10,482 (28.53)	8,478 (31.27)	4,925 (35.06)	3,211 (40.08)	< 0.0001
CVD	4,218 (18.65)	5,628 (17.79)	7,300 (19.87)	5,755 (21.23)	3,323 (23.65)	2,109 (26.32)	< 0.0001
Heart failure	1,677 (7.41)	2,346 (7.42)	3,050 (8.3)	2,460 (9.07)	1,581 (11.25)	1,124 (14.03)	< 0.0001
Cancer	1,049 (4.64)	1,165 (3.68)	134 (3.66)	946 (3.49)	475 (3.38)	284 (3.54)	< 0.0001
Dyslipidemia	10,036 (44.37)	15,205 (48.06)	18,954 (51.59)	14,696 (54.21)	8,124 (57.83)	4,769 (59.52)	< 0.0001
CKD (eGFR < 60 mL/min/1.73 m ²)	2,796 (12.36)	4,110 (12.99)	5,338 (14.53)	4,473 (16.5)	2,716 (19.33)	1,788 (22.32)	< 0.0001
15 ≤ eGFR < 30 mL/min/1.73 m ²	171 (0.76)	221 (0.7)	214 (0.58)	201 (0.74)	122 (0.87)	109 (1.36)	< 0.0001
eGFR < 15 mL/min/1.73 m ²	143 (0.63)	249 (0.79)	279 (0.76)	194 (0.72)	116 (0.83)	71 (0.89)	0.1383
Weight, kg	55.1 ± 7.86	61.6 ± 7.9	65.51 ± 8.58	69.67 ± 9.3	72.94 ± 10.47	78.84 ± 12.83	< 0.0001
Height, cm	160.65 ± 8.51	162.39 ± 8.48	162.69 ± 8.89	163.26 ± 9.2	162.75 ± 9.76	162.26 ± 10.19	< 0.0001
WC, cm	73.82 ± 4.26	80.86 ± 2.59	85.54 ± 2.66	90.29 ± 2.63	94.86 ± 2.77	101.64 ± 4.84	< 0.0001
BMI	21.29 ± 2.08	23.3 ± 1.84	24.68 ± 1.91	26.06 ± 2	27.43 ± 2.19	29.81 ± 2.97	< 0.0001
SBP, mmHg	127.11 ± 16.38	129.04 ± 15.77	130.28 ± 15.61	131.48 ± 15.78	132.74 ± 16.02	134.5 ± 16.65	< 0.0001
DBP, mmHg	77.33 ± 10.39	78.54 ± 10.15	79.14 ± 10.19	79.75 ± 10.24	80.25 ± 10.51	81.2 ± 11.05	< 0.0001
Glucose, mg/dL	107.95 ± 39.05	110.63 ± 37.86	112.27 ± 37.95	114.09 ± 37.53	116.73 ± 40.34	121.38 ± 44.48	< 0.0001
TC, mg/dL	201.31 ± 43.9	204.93 ± 46.96	206.13 ± 44.04	206.52 ± 47.9	206.47 ± 45.42	206.43 ± 56.28	< 0.0001
HDL, mg/dL	52.89 ± 21.07	49.96 ± 20.62	48.88 ± 20.61	48.26 ± 26.72	47.94 ± 19.86	48.14 ± 23.04	< 0.0001

Table 2. Continued

Variable	Distribution of WC, cm					p value
	< 80/< 75 (n = 22,619)	80-85/75-80 (n = 31,637)	85-90/80-85 (n = 36,739)	90-95/85-90 (n = 27,108)	95-100/90-95 (n = 214,049)	
LDL, mg/dL	122.81 ± 46.42	125.23 ± 50.17	125.79 ± 88.22	124.89 ± 55.73	123.99 ± 51.77	122.61 ± 56.17 < 0.0001
TG, mg/dL ^b	115.58 (114.82-116.36)	134.29 (133.52-135.06)	145.47 (144.7-146.25)	154.47 (153.52-155.43)	159.17 (157.84-160.52)	164.02 (162.24-165.83) < 0.0001
eGFR, mL/min/1.73 m ²	83.91 ± 42.09	82.22 ± 38.07	81.42 ± 45.09	79.9 ± 38.77	78.57 ± 38.59	77.65 ± 39.06 < 0.0001
Hemoglobin, g/dL	13.8 ± 1.65	14.16 ± 1.61	14.22 ± 1.63	14.28 ± 1.63	14.21 ± 1.68	14.1 ± 1.74 < 0.0001
Death	3,423 (15.13)	3,572 (11.29)	3,793 (10.32)	2,818 (10.4)	1,568 (11.16)	1,020 (12.73) < 0.0001

Values are presented as mean ± standard deviation, number (%), or median (range).

WC, waist circumference; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride.

^aLow income 25%.

^bGeometric mean.

en; had a lower income; exercised less; and had a higher prevalence of DM, hypertension, dyslipidemia, CKD, CVD, and heart failure. Apart from eGFR, BP, fasting glucose, and lipid levels were also higher in the central obesity group. The mortality rate was highest in the WC of < 80/< 75 (Table 2).

Association of BMI and WC with the risk of ESRD

The underweight group (HR, 1.331; 95% CI, 0.955 to 1.856) and the WC < -80/-75 group (HR, 1.589; 95% CI, 1.379 to 1.831) showed the highest ESRD risk, while the BMI 25 to 30 group showed the lowest ESRD risk (HR, 0.604; 95% CI, 0.542 to 0.673) in all participants after adjusting for age, sex, income, presence of DM, dyslipidemia, hypertension, smoking, alcohol drinking, physical activity, glomerular filtration rate, previous CVD, heart failure, and cancer (Table 3 and Fig. 2). Central obesity prior to PCI tended to show a risk factor for ESRD development, but it was not statistically significant (Table 3 and Fig. 2B).

Subgroup analyses

Subgroup analyses for DM and DM duration were performed. The DM group showed a reverse linear relationship with ESRD risk at BMI values below 28.9 kg/m² (Fig. 3A) and WC values below 94 cm (Fig. 3C). However, this reverse linear relationship with ESRD risk was not statistically significant for the non-DM group (Fig. 3B and 3D).

In the DM duration subgroup analysis, the BMI level prior to PCI was not a risk factor for ESRD in all four groups after adjustment with all variables (Table 4). A WC < 85/80 cm (men/women) increased ESRD risk in only DM group (DM < 5 years and DM ≥ 5 years) compared to the reference group (85-90/80-85 of WC), but not the normal or IFG groups (Table 5).

DISCUSSION

The present study demonstrated that low WC prior to PCI was associated with a higher risk of ESRD during a 5.4-year follow-up period after PCI. Moreover, this phenomenon was more obvious in the DM group than in the non-DM group. This association persisted after multivariable adjustment for important potential confounders.

Generally, BMI, an internationally accepted standard anthropomorphic measurement, is used to define obesity in research settings [17]. Several studies have examined the as-

Table 3. Multivariate cox analysis for incident ESRD by level of BMI and WC in underwent percutaneous coronary intervention patients

Group	Total no.	No. of ESRD	Duration, PY	IR, /1,000 PY	HR (95% CI)			
					Model 1	Model 2	Model 3	Model 4
BMI								
< 18.5	2,158	37	9,899.1	3.74	1.136 (0.815–1.582)	1.336 (0.958–1.861)	1.331 (0.955–1.856)	1.347 (0.966–1.878)
18.5–23	37,438	633	197,473.99	3.21	1 (ref)	1 (ref)	1 (ref)	1 (ref)
23–25	38,381	565	211,034.25	2.68	0.842 (0.752–0.943)	0.765 (0.682–0.857)	0.754 (0.672–0.845)	0.800 (0.714–0.896)
25–30	55,848	729	311,221.44	2.34	0.738 (0.664–0.821)	0.610 (0.547–0.679)	0.604 (0.542–0.673)	0.627 (0.562–0.698)
> 30	6,339	118	34,578.16	3.41	1.070 (0.879–1.302)	0.746 (0.611–0.911)	0.618 (0.506–0.755)	0.641 (0.525–0.783)
<i>p</i> for trend				< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
WC								
< 80/< 75	22,619	323	119,092.41	2.71	1.136 (0.986–1.308)	1.502 (1.304–1.731)	1.589 (1.379–1.831)	1.532 (1.330–1.766)
80–85/75–80	31,637	442	172,675.72	2.56	1.08 (0.949–1.229)	1.230 (1.081–1.400)	1.215 (1.067–1.383)	1.176 (1.033–1.338)
85–90/80–85	36,739	479	202,452.23	2.37	1 (ref)	1 (ref)	1 (ref)	1 (ref)
90–95/85–90	27,108	400	150,018.41	2.67	1.128 (0.988–1.288)	1.011 (0.885–1.154)	0.938 (0.821–1.072)	0.960 (0.840–1.096)
98–100/90–95	14,049	237	77,138.12	3.07	1.297 (1.110–1.516)	1.031 (0.882–1.205)	0.915 (0.783–1.070)	0.913 (0.781–1.067)
≥ 100/≥ 95	8,012	201	42,830.04	4.69	1.97 (1.671–2.323)	1.357 (1.150–1.601)	1.103 (0.934–1.302)	1.081 (0.915–1.277)
<i>p</i> for trend				< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Model 1: crude model; Model 2: adjusted for age, sex, income, diabetes mellitus, dyslipidemia, hypertension; Model 3: adjusted for Model 2 plus smoking, alcohol drinking, regular exercise, glomerular filtration rate; Model 4: adjusted for Model 3 plus previous cardiovascular disease, heart failure, cancer.

ESRD, end-stage renal disease; BMI, body mass index; WC, waist circumference; PY, person-years; IR, incidence rate; HR, hazard ratio; CI, confidence interval.

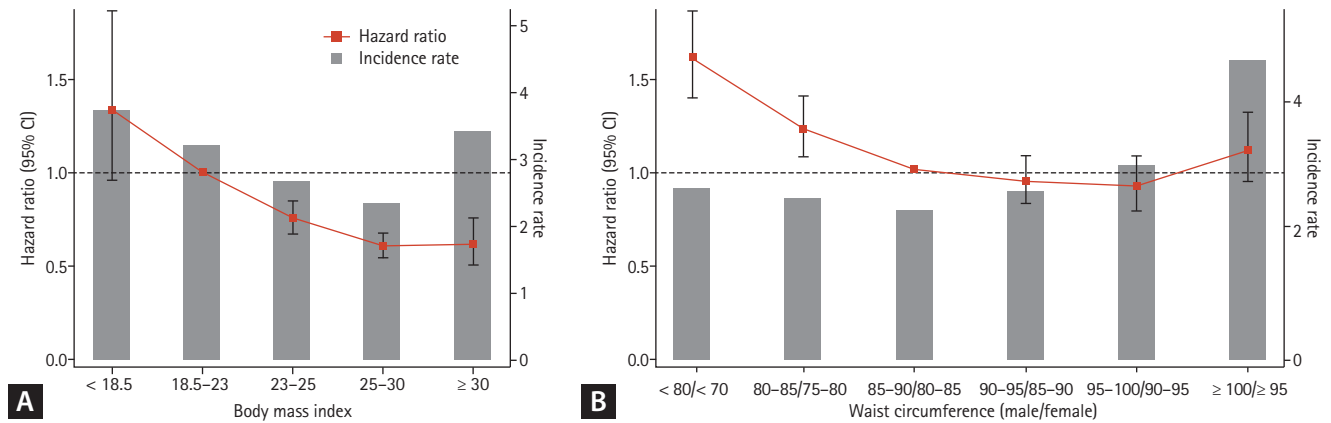


Figure 2. Incidence rates, hazard ratios, and 95% confidence intervals (CIs) of end-stage renal disease by (A) body mass index and (B) waist circumference. Adjusted for age, sex, income-low 25%, diabetes mellitus, hypertension, dyslipidemia, current smoker, alcohol consumption, regular exercise, and estimated glomerular filtration rate.

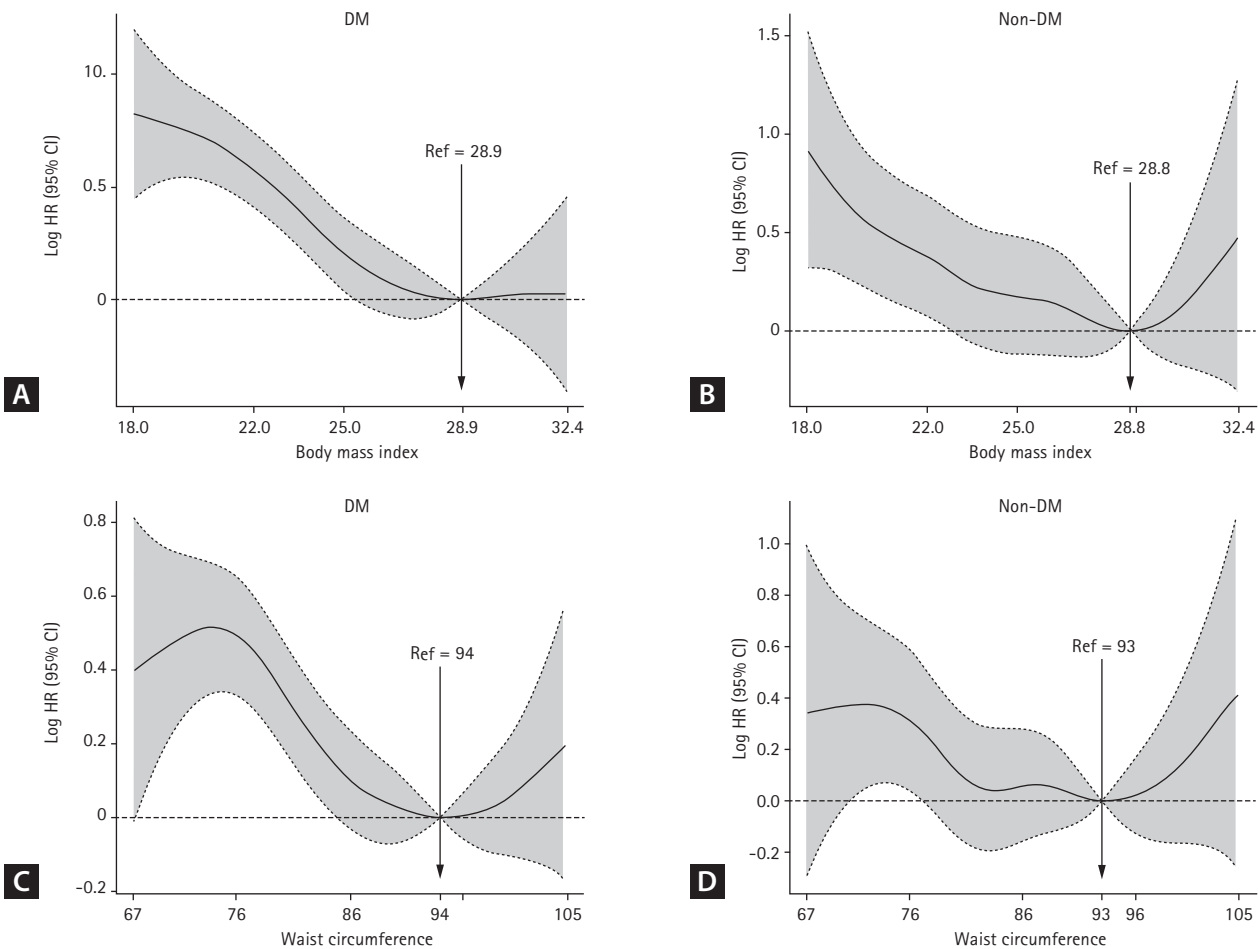


Figure 3. Cubic spline curves depicting the relationship between body mass index or waist circumference and end-stage renal disease risk in (A, C) diabetes mellitus (DM), and (B, D) non-DM subgroup. Adjusted for age, sex, income, DM, dyslipidemia, hypertension, smoking, alcohol drinking, physical activity, and estimated glomerular filtration rate. HR, hazard ratio; CI, confidence interval.

Table 4. Multivariate Cox analysis for incident ESRD by level of BMI in underwent percutaneous coronary intervention patients (subgroup analysis for DM)

Group	BMI group	Total no.	No. of ESRD	Duration, PY	IR, /1,000 PY	HR (95% CI)		
						Model 1	Model 2	Model 3
Normal	< 18.5	1,184	13	5,571.95	2.3331	1.944 (1.095–3.452)	1.636 (0.918–2.916)	1.642 (0.922–2.927)
	18.5–23	17,675	113	95,838.72	1.1791	1 (ref)	1 (ref)	1 (ref)
	23–25	16,446	82	92,519.63	0.8863	0.754 (0.568–1.003)	0.785 (0.589–1.047)	0.796 (0.597–1.061)
	25–30	21,698	112	123,647.66	0.9058	0.772 (0.595–1.003)	0.794 (0.608–1.038)	0.846 (0.648–1.105)
	> 30	1,936	13	10,808.38	1.2028	1.025 (0.577–1.820)	0.89 (0.496–1.597)	0.983 (0.548–1.761)
IFG	< 18.5	461	6	2,100.27	2.8568	2.078 (0.898–4.806)	1.977 (0.848–4.611)	1.883 (0.803–4.416)
	18.5–23	8,509	61	45,194.58	1.3497	1 (ref)	1 (ref)	1 (ref)
	23–25	9,671	51	53,667.81	0.9503	0.709 (0.489–1.028)	0.812 (0.557–1.184)	0.869 (0.596–1.267)
	25–30	15,171	56	85,116.8	0.6579	0.492 (0.342–0.707)	0.615 (0.423–0.894)	0.640 (0.440–0.931)
	> 30	1,773	13	9,686.64	1.3421	0.996 (0.548–1.813)	1.356 (0.731–2.515)	1.457 (0.782–2.713)
DM < 5 years	< 18.5	180	3	816.72	3.6732	0.850 (0.269–2.685)	0.891 (0.281–2.824)	0.855 (0.269–2.713)
	18.5–23	4,135	91	21,667.89	4.1998	1 (ref)	1 (ref)	1 (ref)
	23–25	5,244	84	28,794.88	2.9172	0.700 (0.520–0.942)	0.634 (0.470–0.856)	0.651 (0.483–0.879)
	25–30	8,925	95	50,123.92	1.8953	0.456 (0.342–0.609)	0.385 (0.286–0.518)	0.399 (0.297–0.538)
	> 30	1,364	13	7,634.05	1.7029	0.410 (0.229–0.733)	0.271 (0.150–0.493)	0.282 (0.155–0.513)
DM ≥ 5 years	< 18.5	333	15	1,410.16	10.6371	0.971 (0.579–1.627)	0.939 (0.559–1.575)	1.047 (0.624–1.756)
	18.5–23	7,119	368	34,772.81	10.583	1 (ref)	1 (ref)	1 (ref)
	23–25	7,020	348	36,051.93	9.6527	0.920 (0.794–1.065)	0.838 (0.723–0.971)	0.918 (0.792–1.065)
	25–30	10,054	466	52,333.06	8.9045	0.851 (0.742–0.976)	0.739 (0.644–0.848)	0.761 (0.663–0.874)
	> 30	1,266	79	6,449.09	12.2498	1.164 (0.913–1.485)	0.839 (0.656–1.074)	0.871 (0.680–1.114)
<i>p</i> for trend						0.0031	< 0.0001	0.0004

Model 1: crude model; Model 2: adjusted for age, sex, income, diabetes mellitus, dyslipidemia, hypertension, smoking, alcohol drinking, regular exercise, glomerular filtration rate; Model 3: adjusted for Model 2 plus previous cardiovascular disease, heart failure, cancer. ESRD, end-stage renal disease; BMI, body mass index; DM, diabetes mellitus; PY, person-years; IR, incidence rate; HR, hazard ratio; CI, confidence interval; IFG, impaired fasting glucose.

sociation between BMI and future risk of ESRD. Although the results are conflicting, most epidemiologic studies showed that a higher BMI was associated with an increased risk of kidney disease. Two large epidemiologic studies in the United States reported a positive association between BMI and ESRD, and these studies analyzed a broad spectrum of BMI among a large, diverse sample of participants with long-term follow-up for ESRD [7,8]. It is presumed that a higher BMI is an independent risk factor for ESRD in any ethnic group.

However, the association between BMI with future risk for ESRD tends to be discordant in patients with renal impairment, and this population thus exhibits a so-called “obesity

paradox.” Specifically, although a high BMI is associated with all-cause mortality and decreased renal function in patients with earlier stages of CKD, this association is attenuated in patients with advanced CKD [18,19]. In addition, a few studies also showed that patients with obesity paradoxically exhibited more favorable clinical outcomes with respect to in-hospital, short-, and long-term mortality than those without obesity after PCI [20-23]. Therefore, there are still controversies between BMI and the risk for future ESRD in PCI patients. We therefore considered that longitudinal studies are required to explore the actual relationship between BMI and the risk of ESRD. To the best of our knowledge, this is the

Table 5. Multivariate Cox analysis for incident ESRD by level of WC in underwent percutaneous coronary intervention patients (subgroup analysis for DM)

Group	WC group	Total no.	No. of ESRD	Duration, PY	IR, /1,000 PY	HR (95% CI)		
						Model 1	Model 2	Model 3
Normal	< 80/< 75	11,889	46	59,606.12	0.77	0.912 (0.626–1.329)	1.211 (0.879–1.669)	1.142 (0.829–1.573)
	80–85/75–80	14,446	46	74,122.92	0.62	0.736 (0.505–1.072)	0.813 (0.59–1.12)	0.803 (0.583–1.107)
	85–90/80–85	15,430	66	78,377.69	0.84	1 (ref)	1 (ref)	1 (ref)
	90–95/85–90	10,243	35	51,201.19	0.68	0.812 (0.539–1.224)	0.867 (0.621–1.211)	0.900 (0.644–1.256)
	98–100/90–95	4,689	20	22,694.35	0.88	1.047 (0.635–1.726)	0.814 (0.534–1.239)	0.885 (0.581–1.346)
IFG	≥ 100/≥ 95	2,242	18	10,218.99	1.76	2.084 (1.238–3.510)	1.482 (0.961–2.285)	0.803 (0.583–1.107)
	< 80/< 75	5,191	22	22,482.26	0.98	1.164 (0.679–1.997)	1.321 (0.832–2.097)	1.257 (0.793–1.995)
	80–85/75–80	8,043	28	33,992.97	0.82	0.986 (0.596–1.632)	1.156 (0.77–1.737)	1.128 (0.750–1.698)
	85–90/80–85	9,537	33	39,475.19	0.84	1 (ref)	1 (ref)	1 (ref)
	90–95/85–90	7,138	18	28,657.83	0.63	0.754 (0.424–1.338)	0.888 (0.566–1.394)	0.913 (0.581–1.433)
DM < 5 years	98–100/90–95	3,717	8	14,123.92	0.57	0.676 (0.312–1.463)	0.721 (0.408–1.276)	0.736 (0.416–1.301)
	≥ 100/≥ 95	1,959	11	6,982.17	1.58	1.87 (0.945–3.701)	1.319 (0.723–2.407)	1.390 (0.762–2.537)
	< 80/< 75	2,225	60	19,074.79	3.15	1.717 (1.234–2.387)	2.026 (1.378,2.98)	1.996 (1.356–2.939)
	80–85/75–80	3,926	89	35,726.35	2.49	1.368 (1.017–1.84)	1.499 (1.067,2.105)	1.434 (1.020–2.016)
	85–90/80–85	5,143	86	47,325.53	1.82	1 (ref)	1 (ref)	1 (ref)
DM ≥ 5 years	90–95/85–90	4,352	73	40,502.6	1.80	0.992 (0.726–1.355)	0.906 (0.629–1.306)	0.943 (0.655–1.359)
	98–100/90–95	2,532	47	23,253.69	2.02	1.114 (0.781–1.590)	0.906 (0.599–1.370)	0.912 (0.602–1.382)
	≥ 100/≥ 95	1,670	23	14,219.43	1.62	0.888 (0.561–1.407)	0.738 (0.441,1.234)	0.740 (0.441–1.239)
	< 80/< 75	3,314	195	17,929.24	10.88	1.363 (1.137–1.633)	1.431 (1.187–1.726)	1.392 (1.153–1.681)
	80–85/75–80	5,222	279	28,833.48	9.68	1.22 (1.035–1.437)	1.245 (1.050–1.477)	1.197 (1.009–1.420)
p for trend	85–90/80–85	6,629	294	37,273.82	7.89	1 (ref)	1 (ref)	1 (ref)
	90–95/85–90	5,375	274	29,656.79	9.24	1.169 (0.992–1.379)	0.948 (0.800–1.124)	0.960 (0.810–1.138)
	98–100/90–95	3,111	162	17,066.15	9.50	1.201 (0.991–1.455)	1.068 (0.877–1.300)	1.043 (0.857–1.271)
	≥ 100/≥ 95	2,141	149	11,409.45	13.06	1.645 (1.351–2.003)	1.141 (0.930–1.400)	1.120 (0.912–1.376)
						0.3804	0.0361	0.0086

Model 1: crude model; Model 2: adjusted for age, sex, income, diabetes mellitus, dyslipidemia, hypertension, smoking, alcohol drinking, regular exercise, glomerular filtration rate; Model 3: adjusted for Model 2 plus previous cardiovascular disease, heart failure, cancer.
 ESRD, end-stage renal disease; WC, waist circumference; DM, diabetes mellitus; PY, person-years; IR, incidence rate; HR, hazard ratio; CI, confidence interval; IFG, impaired fasting glucose.

first nationwide cohort study that examines the relationship between lower BMI and ESRD risk in the Korean population prior to PCI. Our findings were inconsistent with most previous published studies, showing that BMI prior to PCI was not associated with risk for ESRD.

Recently, measures of central or abdominal obesity, defined by the WC and waist-hip ratio, have been used as more important predictors to assess the mortality risk than BMI [24,25]. WC, a representative marker of visceral body fat, was found to correlate with inflammation, whereas subcutaneous body fat may be an indicator of the nutritional status [26]. In patients with ESRD, multiple studies identified WC as a direct and strong predictor of mortality and incident cardiovascular events, even after adjusting for the BMI and other risk factors [27,28]. In fact, many studies have shown that central obesity or abdominal adiposity measured by the WC was linearly associated with a higher risk of mortality after PCI [29]. However, our findings show that a WC under $< -80 / < -75$ cm showed the highest risk for future ESRD development as well as higher mortality. Increasing WC was also linearly associated with a lower risk of future ESRD development. However, unlike BMI, low WC prior to PCI was a risk for ESRD, especially in the DM group, suggesting that WC maybe more accurate than BMI to estimate the risk for ESRD in prior to PCI. In our study, there was tendency of a WC of $\geq 100 / \geq 95$ cm (men/women) to increase the risk of ESRD in the DM and non-DM groups. More research on central obesity as a risk factor is needed.

The exact mechanisms by which a low WC presents a high risk for ESRD development in PCI patients are not known. High adiposity itself has been reported as a predictor of good prognosis among patients with coronary artery disease. Lavie et al. [30] reported that a high percentage of body fat, which was measured using the sum of the skinfold method, was associated with a low mortality rate among patients with stable angina. However, more systematic studies are needed to confirm this hypothesis.

Our study has several limitations. First, we did not collect relevant information on the food habits or other comorbidities that might affect weight. Second, this study did not consider use of medications such as hypoglycemic agents or lipid lowering agents, and adherence to treatment. Third, we were unable to obtain more information about the causes of ESRD. Fourth, we used data from the NHIS checkup program in a Korean population; therefore, we cannot generalize the results to other ethnic groups. Fifth, although we

monitored the subjects for 5.4 years, the time of follow-up is short for patients to develop ESRD. Sixth, because of the nature of the claim data, we were unable to evaluate the indication or purpose of the PCI.

In conclusion, to the best of our knowledge, this is the first study on the relationship between BMI and WC prior to PCI and ESRD development in a large general population using a well-established and validated longitudinal national database for around 5.4 years. Our study demonstrated that low WC prior to PCI, which showed the increased ESRD risk in patients undergoing PCI, especially in those with DM.

KEY MESSAGE

1. This is the first study on the relationship between body mass index (BMI) and waist circumference (WC) prior to percutaneous coronary intervention (PCI) and end-stage renal disease (ESRD) development.
2. The BMI prior to PCI was not a risk factor for ESRD with or without diabetes mellitus (DM).
3. Low WC prior to PCI showed an increased ESRD risk in patients undergoing PCI, especially in those with DM.

Conflict of interest

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

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Supplementary Table 1. Baseline characteristics of subjects according to the incident ESRD

Group	None ESRD (n = 138,082)	ESRD (n = 2,082)	p value
Age, yr	63.39 ± 10.63	65.39 ± 9.87	< 0.0001
Male sex	97,897 (70.9)	1,451 (69.69)	0.2296
Current smoker	41,174 (29.82)	539 (25.89)	< 0.0001
Heavy drinker	8,958 (6.49)	76 (3.65)	< 0.0001
Physical activity-regular	28,386 (20.56)	355 (17.05)	< 0.0001
Income-low	29,846 (21.61)	552 (26.51)	< 0.0001
Diabetes mellitus	44,078 (31.92)	1,562 (75.02)	< 0.0001
HTN	95,743 (69.34)	1,945 (93.42)	< 0.0001
CVD	27,635 (20.01)	698 (33.53)	< 0.0001
Heart failure	11,879 (8.60)	359 (17.24)	< 0.0001
Cancer	5,164 (3.74)	100 (4.80)	0.0113
Dyslipidemia	70,411 (50.99)	1,373 (65.95)	< 0.0001
CKD (eGFR < 60 mL/min/1.73 m ²)	19,562 (14.17)	1,659 (79.68)	< 0.0001
15 ≤ eGFR < 30 mL/min/1.73 m ²	439 (0.32)	599 (28.77)	< 0.0001
eGFR < 15 mL/min/1.73 m ²	802 (0.58)	250 (12.01)	< 0.0001
Proteinuria			< 0.0001
Negative	125,014 (91.21)	728 (35.34)	
Trace	4,326 (3.16)	88 (4.27)	
1+	4,361 (3.18)	296 (14.37)	
2+	2,407 (1.76)	482 (23.4)	
3+	805 (0.59)	369 (17.91)	
4+	152 (0.11)	97 (4.71)	
eGFR, mL/min/1.73 m ²	81.81 ± 40.81	41.3 ± 27.69	< 0.0001
BMI, kg/m ²	24.66 ± 3.01	24.51 ± 3.19	0.0251
Glucose, mg/dL	112.17 ± 38.1	136.02 ± 67.9	< 0.0001
Total cholesterol, mg/dL	205.23 ± 46.21	203.61 ± 57.21	0.113
SBP, mmHg	130.1 ± 15.94	137.51 ± 19.57	< 0.0001
DBP, mmHg	79.04 ± 10.33	80.1 ± 12.12	< 0.0001
F/U duration, person-years	5.5 ± 1.93	2.54 ± 1.96	< 0.0001

Values are presented as mean ± standard deviation or number (%).

ESRD, end-stage renal disease; HTN, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; F/U, follow-up.