Underweight and low waist circumference prior to percutaneous coronary intervention increase the risk for end-stage renal disease: A Nationwide Population Based-cohort Study

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Abstract

Background

The effect of obesity prior to percutaneous coronary intervention (PCI) on the development of end-stage renal disease (ESRD) is not clear.

Methods

Using nationally representative data from the Korean National Health Insurance System, we enrolled 140,164 subjects without renal disease 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 body mass index (BMI) and six levels based on their waist circumference (WC; 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 (HR 1.331, 95%CI: 0.955–1.856) and low WC (< 80/<75) (HR 1.589, 95%CI: 1.379–1.831) showed the highest ESRD risk and the BMI 25 ~ 30 group showed the lowest ESRD risk (HR 0.604, 95%CI: 0.542–0.673) in all participants after adjusting for all covariates. In the subgroup analysis for diabetes mellitus (DM), BMI showed a U-shape relationship with ESRD risk at a baseline of 28.8 for BMI in the none-DM group and a reverse linear relationship in the DM group. However, low WC prior to PCI was risk factor in only DM group.

Conclusions

Underweight and low WC prior to PCI, which showed the increased ESRD risk in patients undergoing PCI, especially in those with DM.

Trial Registration:

Retrospectively registered

Background

The prevalence of obesity has been steadily and significantly increasing worldwide [1, 2]. Because of its impact on cardiovascular diseases, 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 [4–7]. 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) [8], and observational studies have shown positive associations between obesity and chronic kidney disease or ESRD [9–12]. However, some studies showed that obesity did not increase the risk of ESRD in patients with moderate to advanced chronic kidney disease (CKD) [13]. 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 other else, whether or not 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, a medical treatment database, a health examination database, and a medical care institution database [14–16]. The National Health Insurance Corporation (NHIC) is the single insurer, managed by the Korean government, to which approximately 97% of the Korean population subscribes. Enrolees in the NHIC are recommended to undergo a standardised medical examination at least every 2 years.

Among 270,237 subjects who underwent PCI in 2010–2015 (index year), 143,727 subjects follow 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 minimise 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. We also excluded patients with cerebrovascular disease, heart failure, or cancer.

This study was approved by the Chonnam National University Hospital (study approval number: CNUH-EXP-2020-187) and National Health Insurance Service (NHIS-2019-1-379), and it was conducted according to the principles of the Declaration of Helsinki. The need for written informed consent was waived by our review board.

Definitions of BMI and WC

For each participant, the BMI was calculated by dividing the weight (in kg) by the square of the height (in m^2). We defined obesity as a BMI $\geq 25 \text{ kg}/m^2$. The participants were then categorized by the definition of obesity as follows: underweight (BMI $< 18.5 \text{ kg}/m^2$), normal (≥ 18.5 to $< 23 \text{ kg}/m^2$), overweight (≥ 23 to $< 25 \text{ kg}/m^2$), stage 1 obesity (≥ 25 to $30 \text{ kg}/m^2$), and stage 2 obesity ($\geq 30 \text{ kg}/m^2$) according to the World Health Organization recommendations for Asian populations [17].

The WC of each participant was also measured at the midpoint between the rib cage and iliac crest by a trained examiner. The patients were divided into 6 categories based on 5-cm WC increments: < 80 cm in men and < 75 cm in women, 80–85 cm in men and 75–80 cm in women, 85–90 cm in men and 80–85 cm in women (reference group), 90–95 cm in men and 85–90 cm in women, 95–100 cm in men and 90–95 cm in women, and ≥ 100 cm in men and ≥ 95 cm in women. Abdominal 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 [18].

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 $100 \sim 125 \text{ mg}/dL$. Type 2 DM was defined as an FPG level $\geq 126 \text{ mg}/dL$ or at least one claim per year for the prescription of hypoglycemic drug under ICD-10 codes E11–14.[19] Patients with type 1 DM who had claims under ICD-10 code E10 were excluded from this study.[20, 21] 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–I13, I15) and a history of taking at least 1 antihypertensive drug, or a recorded systolic blood pressure of $\geq 140 \text{ mmHg}$ or diastolic blood pressure of $\geq 90 \text{ mmHg}$ 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 $\geq 240 \text{ mg}/dL$ in the health examination database.

Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) of $< 60 \text{ ml}/\text{min}/1.73 \text{ m}^2$ calculated using CKD epidemiology collaboration (CKD-EPI) equation and as a combination of ICD-10 codes (N18–N19). The 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 warranted by the Korean Association for Laboratory Medicine, and the 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 peritoneal dialysis 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 to ~ 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 to ~ 4 , and ≥ 5 times/week by frequency. Income level was divided by quartile: Q1 (the lowest), Q2, Q3, and Q4 (the highest).

Statistical Analysis

We report the mean ± SD 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(BMI18.5-23 kg/m²) and normal WC (85–90/80–85 cm) as a references after adjustment using 3 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. 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-value < 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

Table 1 shows the baseline characteristics of the participants regarding the development of ESRD. Among all the participants, 2082 (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 was higher in the incident ESRD than in the non-ESRD groups. Comorbidities such as DM, HTN, dyslipidemia, CKD, and proteinuria were more prevalent in the ESRD group than in the non-ESRD group. GFR and BMI were lower, and BP and glucose levels were higher in the ESRD group than in the non-ESRD group (Table 1).

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

Group	None ESRD (N = 138,082)	ESRD (N = 2,082)	P
Age	63.39 ± 10.63	65.39 ± 9.87	< .0001
Sex, male(%)	97897(70.9)	1451(69.69)	0.2296
Current smoker	41174(29.82)	539(25.89)	< .0001
Heavy drinker	8958(6.49)	76(3.65)	< .0001
Physical activity-regular	28386(20.56)	355(17.05)	< .0001
Income-low	29846(21.61)	552(26.51)	< .0001
Diabetes mellitus	44078(31.92)	1562(75.02)	< .0001
HTN	95743(69.34)	1945(93.42)	< .0001
dyslipidemia	70411(50.99)	1373(65.95)	< .0001
CKD (GFR < 60)	19562(14.17)	1659(79.68)	< .0001
Proteinuria			< .0001
Negative	125014(91.21)	728(35.34)	
Trace	4326(3.16)	88(4.27)	
1+	4361(3.18)	296(14.37)	
2+	2407(1.76)	482(23.4)	
3+	805(0.59)	369(17.91)	
4+	152(0.11)	97(4.71)	
GFR	81.81 ± 40.81	41.3 ± 27.69	< .0001
BMI	24.66 ± 3.01	24.51 ± 3.19	0.0251
Glucose	112.17 ± 38.1	136.02 ± 67.9	< .0001
Total cholesterol	205.23 ± 46.21	203.61 ± 57.21	0.113
SBP	130.1 ± 15.94	137.51 ± 19.57	< .0001
DBP	79.04 ± 10.33	80.1 ± 12.12	< .0001
F/U duration	5.5 ± 1.93	2.54 ± 1.96	< .0001
Abbreviations, ESRD, end-stage renal disease; HTN, hypertension; CKD, chronic kidney disease; GFR, glomerular filtration rate; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; F/U, follow up.			

The characteristics of participants classified by BMI levels and WC are presented in Tables 2 and 3, respectively. Subjects in the underweight group (BMI < 18.5) were older; had a lower income; exercised less; and had a lower prevalence of DM, HTN, dyslipidemia, and CKD (Table 2). BP, fasting glucose, and total cholesterol were also lower in the underweight group (Table 2). Table 3 shows that the central obesity group patients were older; included mostly women; had a lower income; exercised less; and had a higher prevalence of DM, HTN, dyslipidemia, and CKD (Table 3). Apart from eGFR, BP, fasting glucose, and lipid level were also higher in the central obesity group (Table 3).

Table 2
Baseline characteristics of participants by level of body mass index

Variable	Distribution of body mass index					<i>P</i>
	< 18.5 (N = 2158)	18.5 ~ 23 (N = 37438)	23 ~ 25 (N = 38381)	25 ~ 30 (N = 55848)	30~ (N = 6339)	
Age	70.41 ± 10.29	65.66 ± 10.34	63.63 ± 10.17	61.97 ± 10.50	59.22 ± 12.06	< .0001
Sex(male)	1451(67.24)	26075(69.65)	27869(72.61)	40061(71.73)	3892(61.4)	< .0001
Smoking	< .0001					
None	964(44.67)	17835(47.64)	18202(47.42)	26619(47.66)	3280(51.74)	
Ex-	359(16.64)	7580(20.25)	9044(23.56)	13411(24.01)	1157(18.25)	
Current	835(38.69)	12023(32.11)	11135(29.01)	15818(28.32)	1902(30)	
Drinking	< .0001					
None	1563(72.43)	24789(66.21)	24162(62.95)	34628(62)	4168(65.75)	
Mild	468(21.69)	10413(27.81)	11883(30.96)	17347(31.06)	1709(26.96)	
Heavy	127(5.89)	2236(5.97)	2336(6.09)	3873(6.93)	462(7.29)	
Regular Exercise	281(13.02)	7284(19.46)	8370(21.81)	11695(20.94)	1111(17.53)	< .0001
Income*	546(25.3)	8295(22.16)	8250(21.5)	11883(21.28)	1424(22.46)	< .0001
DM	513(23.77)	11254(30.06)	12264(31.95)	18979(33.98)	2630(41.49)	< .0001
HTN	515(23.86)	9342(24.95)	10416(27.14)	17636(31.58)	2593(40.91)	< .0001
Dyslipidemia	863(39.99)	17527(46.82)	19405(50.56)	30177(54.03)	3812(60.14)	< .0001
CKD	343(15.89)	5606(14.97)	5644(14.71)	8527(15.27)	1101(17.37)	< .0001
Weight (Kg)	44.76 ± 5.85	56.18 ± 6.97	63.58 ± 6.92	71.2 ± 8.54	83.67 ± 11.56	< .0001
Height (cm)	159.97 ± 9.39	161.65 ± 8.88	162.63 ± 8.71	162.85 ± 9.08	161.9 ± 10.21	< .0001
WC (cm)	70.48 ± 6.32	78.78 ± 5.84	84.15 ± 5.25	89.65 ± 5.93	98.89 ± 7.31	< .0001
BMI	17.42 ± 0.94	21.43 ± 1.14	23.96 ± 0.57	26.77 ± 1.29	31.8 ± 1.92	< .0001
SBP (mmHg)	126.2 ± 18.15	128.13 ± 16.43	129.72 ± 15.76	131.55 ± 15.56	134.97 ± 16.29	< .0001
DBP (mmHg)	76.27 ± 11.39	77.45 ± 10.28	78.65 ± 10.1	80.13 ± 10.22	82.58 ± 11.09	< .0001
Glucose (mg/dL)	108.75 ± 48.03	110.81 ± 40.57	111.96 ± 38.22	113.44 ± 37.2	119.25 ± 41.15	< .0001
TC (mg/dL)	195.07 ± 42.04	201.89 ± 45.56	205.07 ± 44.36	207.25 ± 47.38	211.09 ± 53.45	< .0001
HDL (mg/dL)	55.16 ± 15.07	51.77 ± 23.21	49.24 ± 18.74	48.16 ± 23.68	47.83 ± 20.99	< .0001
LDL (mg/dL)	116.46 ± 36.95	123.1 ± 51.12	125.31 ± 70.69	125.38 ± 66.65	126.07 ± 57.03	< .0001
**TG (mg/dL)	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)	< .0001
GFR (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	< .0001
Hg (g/dL)	13.11 ± 1.69	13.78 ± 1.65	14.16 ± 1.6	14.38 ± 1.61	14.45 ± 1.72	< .0001
Abbreviations. M, male; DM, diabetes mellitus; HTN, hypertension; CKD, chronic kidney disease; WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipid; LDL, low density lipoprotein; TG, triglyceride; GFR, glomerular filtration rate; Hg, hemoglobin; * low income 25%, **geometric mean.						

Table 3
Baseline characteristics of participants by level of waist circumference

Variable	Distribution of waist circumference						P
	< 80/<75 (N = 22619)	80 ~ 85/75 ~ 80 (N = 31637)	85 ~ 90/80 ~ 85 (N = 36739)	90 ~ 95/85 ~ 90 (N = 27108)	95 ~ 100/90 ~ 95 (N = 214049)	100~/95~ (N = 8012)	
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	< .0001
Sex(male)	16240(71.8)	23800(75.23)	26479(72.07)	19216(70.89)	9065(64.52)	4548(56.76)	< .0001
Smoking							< .0001
None	10461(46.25)	14116(44.62)	17527(47.71)	12932(47.71)	7339(52.24)	4525(56.48)	
Ex-	4425(19.56)	7285(23.03)	8552(23.28)	6606(24.37)	3106(22.11)	1577(19.68)	
Current	7733(34.19)	10236(32.35)	10660(29.02)	7570(27.93)	3604(25.65)	1910(23.84)	
Drinking							< .0001
None	14698(64.98)	19388(61.28)	23061(62.77)	17130(63.19)	9379(66.76)	5654(70.57)	
Mild	6593(29.15)	10234(32.35)	11315(30.8)	8116(29.94)	3699(26.33)	1863(23.25)	
Heavy	1328(5.87)	2015(6.37)	2363(6.43)	1862(6.87)	971(6.91)	495(6.18)	
Regular Exercise	4611(20.39)	6957(21.99)	7768(21.14)	5488(20.24)	2622(18.66)	1295(16.16)	< .0001
Income*	5100(22.55)	6810(21.53)	7878(21.44)	5731(21.14)	3064(21.81)	1815(22.65)	< .0001
DM	5539(24.49)	9148(28.92)	11772(32.04)	9727(35.88)	5643(40.17)	3811(47.57)	< .0001
HTN	5183(22.91)	8223(25.99)	10482(28.53)	8478(31.27)	4925(35.06)	3211(40.08)	< .0001
Dyslipidemia	10036(44.37)	15205(48.06)	18954(51.59)	14696(54.21)	8124(57.83)	4769(59.52)	< .0001
CKD	2796(12.36)	4110(12.99)	5338(14.53)	4473(16.5)	2716(19.33)	1788(22.32)	< .0001
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	< .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	< .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	< .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	< .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	< .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	< .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	< .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	< .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	< .0001
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	< .0001
**TG (mg/dL)	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)	< .0001
GFR (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	< .0001
Hg (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	< .0001
Abbtrations. M, male; DM, diabetes mellitus; HTN, hypertension; CKD, chronic kidney disease; WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipid; LDL, low density lipoprotein; TG, triglyceride; GFR, glomerular filtration rate; Hg, hemoglobin;* low income 25%, **geometric mean.							

Association of BMI and WC with the Risk of ESRD

The underweight group (HR 1.331, 95%CI: 0.955–1.856) and the WC < ~ 80/~75 group (HR 1.589, 95% CI: 1.379–1.831) showed the highest ESRD risk, while the BMI 25 ~ 30 group showed the lowest ESRD risk (HR 0.604, 95%CI: 0.542-0.673) in all participants after adjusting for age, sex, income, presence of DM, dyslipidemia, hypertension, smoking, alcohol drinking, physical activity, and glomerular filtration rate (Fig. 2A & 2B, Fig. 3A&B and Table 4). Central obesity prior to PCI tended to show a risk factor for ESRD development, but it was not statistically significant (Fig. 2B).

Table 4
Multivariate cox analysis for incident ESRD by level of BMI and WC in underwent PCI patients.

Group	Total (n)	ESRD (n)	Duration	IR	HR (95% Confidence interval)		
					Model1	Model2	Model3
Body mass index							
< 18.5	2158	37	9899.1	3.74	1.136(0.815–1.582)	1.336(0.958–1.861)	1.331(0.955–1.856)
18.5 ~ 23	37438	633	197473.99	3.21	1(ref.)	1(ref.)	1(ref.)
23 ~ 25	38381	565	211034.25	2.68	0.842(0.752–0.943)	0.765(0.682–0.857)	0.754(0.672–0.845)
25 ~ 30	55848	729	311221.44	2.34	0.738(0.664–0.821)	0.610(0.547–0.679)	0.604(0.542–0.673)
30~	6339	118	34578.16	3.41	1.070(0.879–1.302)	0.746(0.611–0.911)	0.618(0.506–0.755)
P for trend				< 0.0001	< 0.0001	< 0.0001	< 0.0001
Waist circumference							
< 80/<75	22619	323	119092.41	2.71	1.136(0.986–1.308)	1.502(1.304–1.731)	1.589(1.379–1.831)
80 ~ 85/75 ~ 80	31637	442	172675.72	2.56	1.08(0.949–1.229)	1.230(1.081-1.400)	1.215(1.067–1.383)
85 ~ 90/80 ~ 85	36739	479	202452.23	2.37	1(ref.)	1(ref.)	1(ref.)
90 ~ 95/85 ~ 90	27108	400	150018.41	2.67	1.128(0.988–1.288)	1.011(0.885–1.154)	0.938(0.821–1.072)
98 ~ 100/90 ~ 95	14049	237	77138.12	3.07	1.297(1.110–1.516)	1.031(0.882–1.205)	0.915(0.783–1.070)
100~/95~	8012	201	42830.04	4.69	1.97(1.671–2.323)	1.357(1.150–1.601)	1.103(0.934–1.302)
P for trend				< 0.0001	< 0.0001	< 0.0001	< 0.0001
Abbtrations, IR, incidence rate (per 1000 person-years); ESRD, end-stage renal disease; HR, hazard ratio. 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.							

Subgroup Analyses

Subgroup analyses for DM and DM duration were performed. The DM group showed a reverse linear relationship with ESRD risk at a baseline BMI value of 28.9 kg/m² (Fig. 3C) and a U-shape relationship with ESRD risk at a baseline WC of 94 cm (Fig. 3D). However, the non-DM subgroup analysis, both showed a U-shape relationship with ESRD risk at a baseline BMI value of 28.8 kg/m² and baseline WC of 93 cm (Fig. 3E&F).

In the DM duration subgroup analysis, being underweight was a risk factor in all four groups (normal, IFG patients, DM < 5 years, and DM ≥ 5 years) (Table 5). WC < 80 ~ 85/75 ~ 80 cm increased ESRD risk in only DM group (DM < 5 years and DM ≥ 5 years), not normal or IFG group (Table 6).

Table 5
Multivariate cox analysis for incident ESRD by level of BMI in underwent PCI patients (subgroup analysis for DM)

Group	BMI group	Total (n)	ESRD (n)	Duration	IR	HR (95% Confidence interval)	
						Model1	Model2
Normal	< 18.5	1184	13	5571.95	2.3331	2.518(1.418–4.473)	1.925(1.072–3.456)
	18.5 ~ 23	17675	113	95838.72	1.1791	1.295(0.997–1.682)	1.182(0.905–1.544)
	23 ~ 25	16446	82	92519.63	0.8863	0.977(0.735–1.299)	0.952(0.715–1.266)
	25 ~ 30	21698	112	123647.66	0.9058	1(ref.)	1(ref.)
	30~	1936	13	10808.38	1.2028	1.327(0.747–2.357)	1.195(0.67–2.129)
IFG	< 18.5	461	6	2100.27	2.8568	4.226(1.821–9.808)	3.052(1.292–7.211)
	18.5 ~ 23	8509	61	45194.58	1.3497	2.034(1.415–2.923)	1.529(1.052–2.224)
	23 ~ 25	9671	51	53667.81	0.9503	1.442(0.987–2.107)	1.348(0.92–1.977)
	25 ~ 30	15171	56	85116.8	0.6579	1(ref.)	1(ref.)
	30~	1773	13	9686.64	1.3421	2.027(1.108–3.705)	2.291(1.246–4.213)
DM < 5yrs	< 18.5	180	3	816.72	3.6732	1.862(0.590–5.879)	1.985(0.623–6.318)
	18.5 ~ 23	4135	91	21667.89	4.1998	2.191(1.643–2.921)	2.464(1.832–3.315)
	23 ~ 25	5244	84	28794.88	2.9172	1.534(1.144–2.057)	1.629(1.211–2.191)
	25 ~ 30	8925	95	50123.92	1.8953	1(ref.)	1(ref.)
	30~	1364	13	7634.05	1.7029	0.898(0.503–1.603)	0.739(0.411–1.326)
DM ≥ 5yrs	< 18.5	333	15	1410.16	10.6371	1.141(0.682–1.908)	1.369(0.817–2.294)
	18.5 ~ 23	7119	368	34772.81	10.583	1.175(1.025–1.347)	1.327(1.156–1.523)
	23 ~ 25	7020	348	36051.93	9.6527	1.081(0.941–1.242)	1.181(1.027–1.358)
	25 ~ 30	10054	466	52333.06	8.9045	1(ref.)	1(ref.)
	30~	1266	79	6449.09	12.2498	1.368(1.078–1.737)	1.178(0.925–1.498)
P for trend						0.0031	< 0.0001
Abbreviations, BMI, body mass index; ESRD, end-stage renal disease; IR, incidence rate (per 1000 person-years); HR, hazard ratio; DM, diabetes mellitus BP; IFG, impaired fasting glucose; Model 1: crude model. Model 2: adjusted for age, sex. Income, diabetes mellitus, dyslipidemia, hypertension, smoking, alcohol drinking, regular exercise, glomerular filtration rate.							

Table 6
Multivariate cox analysis for incident ESRD by level of WC in underwent PCI patients (subgroup analysis for DM)

Group	WC group	Total (n)	ESRD (n)	Duration	IR	HR (95% Confidence interval)	
						Model1	Model2
Normal	< 80/<75	11889	46	59606.12	0.77	0.912(0.626–1.329)	1.211(0.879–1.669)
	80 ~ 85/75 ~ 80	14446	46	74122.92	0.62	0.736(0.505–1.072)	0.813(0.59–1.12)
	85 ~ 90/80 ~ 85	15430	66	78377.69	0.84	1(ref.)	1(Ref.)
	90 ~ 95/85 ~ 90	10243	35	51201.19	0.68	0.812(0.539–1.224)	0.867(0.621–1.211)
	98 ~ 100/90 ~ 95	4689	20	22694.35	0.88	1.047(0.635–1.726)	0.814(0.534–1.239)
	100~/95~	2242	18	10218.99	1.76	2.084(1.238–3.510)	1.482(0.961–2.285)
IFG	< 80/<75	5191	22	22482.26	0.98	1.164(0.679–1.997)	1.321(0.832–2.097)
	80 ~ 85/75 ~ 80	8043	28	33992.97	0.82	0.986(0.596–1.632)	1.156(0.77–1.737)
	85 ~ 90/80 ~ 85	9537	33	39475.19	0.84	1(ref.)	1(Ref.)
	90 ~ 95/85 ~ 90	7138	18	28657.83	0.63	0.754(0.424–1.338)	0.888(0.566–1.394)
	98 ~ 100/90 ~ 95	3717	8	14123.92	0.57	0.676(0.312–1.463)	0.721(0.408–1.276)
	100~/95~	1959	11	6982.17	1.58	1.87(0.945–3.701)	1.319(0.723–2.407)
DM < 5yrs	< 80/<75	2225	60	19074.79	3.15	1.717(1.234–2.387)	2.026(1.378,2.98)
	80 ~ 85/75 ~ 80	3926	89	35726.35	2.49	1.368(1.017–1.84)	1.499(1.067,2.105)
	85 ~ 90/80 ~ 85	5143	86	47325.53	1.82	1(ref.)	1(Ref.)
	90 ~ 95/85 ~ 90	4352	73	40502.6	1.80	0.992(0.726–1.355)	0.906(0.629–1.306)
	98 ~ 100/90 ~ 95	2532	47	23253.69	2.02	1.114(0.781–1.590)	0.906(0.599–1.370)
	100~/95~	1670	23	14219.43	1.62	0.888(0.561–1.407)	0.738(0.441,1.234)
DM ≥ 5yrs	< 80/<75	3314	195	17929.24	10.88	1.363(1.137–1.633)	1.431(1.187–1.726)
	80 ~ 85/75 ~ 80	5222	279	28833.48	9.68	1.22(1.035–1.437)	1.245(1.050–1.477)
	85 ~ 90/80 ~ 85	6629	294	37273.82	7.89	1(ref.)	1(Ref.)
	90 ~ 95/85 ~ 90	5375	274	29656.79	9.24	1.169(0.992–1.379)	0.948(0.800-1.124)
	98 ~ 100/90 ~ 95	3111	162	17066.15	9.50	1.201(0.991–1.455)	1.068(0.877-1.300)
	100~/95~	2141	149	11409.45	13.06	1.645(1.351–2.003)	1.141(0.930–1.400)
P for trend						0.3804	0.0361
Abbreviations, BMI, body mass index; ESRD, end-stage renal disease; IR, incidence rate (per 1000 person-years); HR, hazard ratio; DM, diabetes mellitus BP; IFG, impaired fasting glucose; Model 1: crude model. Model 2: adjusted for age, sex. Income, diabetes mellitus, dyslipidemia, hypertension, smoking, alcohol drinking, regular exercise, glomerular filtration rate.							

Discussion

The present study demonstrated that underweight and low WC prior to PCI were 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 subgroup than in the non-DM group, especially in low WC case. 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 [22]. Several studies have examined the association between BMI and the 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 U.S. 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 [11, 12]. 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 [23, 24]. 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 [25–28]. 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 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 underweight had the highest risk for ESRD in PCI patients.

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 [29, 30]. 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 [31]. 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 [32, 33]. 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 [34]. However, our findings show that a WC under ~ 85/~80 cm showed the highest risk for future ESRD development. 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 in the only DM group, suggesting that WC maybe more accurate than BMI to estimate the risk for ESRD in prior to PCI. Central obesity could be a risk factor for ESRD development in all the total, DM and non-DM groups, as well as the low WC group in our study.

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. 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 [35].

Study Limitations

There are some limitation in this study. 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.

Conclusions

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 Underweight and low WC prior to PCI, which showed the increased ESRD risk in patients undergoing PCI, especially in those with DM.

Abbreviations

BMI

Body mass index

CKD

Chronic kidney disease

DM

Diabetes mellitus

eGFR

Estimated glomerular filtration rate

ESRD

End-stage renal disease

NHIS

National health insurance service

PCI

Percutaneous coronary intervention

IHD

Ischemic heart disease

WC

Waist circumference

WHO

World health organization

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

All authors gave their consent for publication of this manuscript

Availability of data and materials

Not applicable.

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Figures

Figure 1

Flow diagram of the study. Abbreviations: PCI, Percutaneous coronary intervention. NHI, National health insurance; ESRD, End-stage renal disease; BMI, body mass index; WC, Waist circumference.

Figure 2

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

Figure 3

Cubic spline curves depicting the relationship between body mass index or waist circumference and end-stage renal disease risk in total (A&B), DM (C&D), and none-DM (D&F) subgroup. Abbreviations: DM, Diabetes mellitus. Adjusted for age, sex, income, DM, dyslipidemia, and hypertension, smoking, alcohol drinking, physical activity, and eGFR.