Journal of Cardiology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Impact of body mass index on long-term outcomes in Japanese patients following percutaneous coronary intervention: The Juntendo PCI Registry

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ARTICLE INFO

Article history:
Received 6 November 2017
Received in revised form 20 January 2018
Accepted 2 February 2018
Available online xxx

Keywords:
Obesity paradox
Lean
Coronary artery disease

ABSTRACT

Background: The prognostic long-term impact of body mass index (BMI) on East Asian patients with coronary artery disease remains unclear.
Methods: An observational retrospective cohort study was carried out involving 3571 patients who had undergone percutaneous coronary intervention (PCI) from 2000 to 2013. Patients were divided into the following five groups according to baseline BMI: Group 1 (underweight 1, BMI $\leq$20.0 kg/m^2); Group 2 (underweight 2, BMI = 20.1–22.5 kg/m^2); Group 3 (normal weight, BMI = 22.6–25.0 kg/m^2); Group 4 (overweight 1, BMI = 25.1–27.5 kg/m^2); and Group 5 (overweight 2, BMI $\geq$27.6 kg/m^2). We then evaluated the association between BMI and both all-cause and cardiac death after PCI.
Results: The ratio of patients in the five groups was as follows: Group 1, 9.2%; Group 2, 21.6%; Group 3, 34.1%; Group 4, 21.1%; and Group 5, 14.5%. A decrease in age was observed from underweight to overweight, as was an increased prevalence of hypertension, diabetes mellitus, dyslipidemia, and smoking. The median follow-up period was 6.3 years (interquartile range, 3.2–9.6 years). In total, 473 deaths (frequency, 13.2%) were identified, including 183 (5.1%) cardiac deaths during follow-up. In unadjusted Cox proportional hazard analysis, using normal weight as the reference, underweight, but not overweight, was associated with a greater risk of both all-cause and cardiac death. In an adjusted model, Group 1 had the highest risk for all-cause death (hazard ratio, 1.58; 95% confidence interval, 1.19–2.10; $p = 0.0019$); however, no significant differences were found for the risk of all-cause and cardiac death between normal weight and overweight patients.
Conclusion: The results of the present long-term follow-up study do not support the so-called "obesity paradox," but rather, suggest that underweight Japanese patients are at greater risk for all-cause mortality following PCI.

Introduction

Obesity is a metabolic disorder associated with cardiovascular disease and increased morbidity and mortality, and has been shown to be a risk factor for the development of coronary artery disease (CAD) [1–3]. Obesity increases insulin resistance, which can lead to type 2 diabetes mellitus, worsens plasma lipid profiles, and increases arterial blood pressure (BP) [4]. Furthermore, obesity is associated with obstructive sleep apnea and sleep-disordered breathing [5]. Nevertheless, numerous studies over the years have shown the so-called "obesity paradox," whereby obesity is related to better clinical outcomes [6–8]. This paradox suggests that being overweight as measured by body mass index (BMI) is associated with lower mortality and morbidity from chronic heart failure and

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https://doi.org/10.1016/j.jjcc.2018.02.007
0914-5087/

CAD [3,9,10]. However, there are few contemporary data regarding the effect of BMI on long-term outcomes after percutaneous coronary intervention (PCI). Therefore, in the present study, we examined the association between BMI and adverse cardiac events up to 10 years following first-time PCI in Japanese patients with CAD.

Methods

Study population and data collection

The present study was a single-center, observational, retrospective cohort study. Among consecutive patients with CAD who underwent first-time PCI at Juntendo University Hospital from 2000 to 2013, we included only those for whom preprocedural BMI values were available. Patients were then divided into the following five groups according to baseline BMI: Group 1 (underweight 1, BMI $\leq$20.0 kg/m^2); Group 2 (underweight 2, BMI = 20.1–22.5 kg/m^2); Group 3 (normal weight, BMI = 22.6–25.0 kg/m^2); Group 4 (overweight 1, BMI = 25.1–27.5 kg/m^2); and Group 5 (overweight 2, BMI $\geq$27.6 kg/m^2).

Demographic data, coronary risk factors, and medication use at the time of PCI were collected from our institutional database. Blood samples were collected in the early morning after overnight fasting, and BP was measured on admission. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m^2, as calculated using the Modification of the Diet in Renal Disease study equation modified with a Japanese coefficient using baseline serum creatinine [11]. Patients with BP >140/90 mmHg or who were receiving antihypertensive agents were regarded as hypertensive. Dyslipidemia was defined as low-density lipoprotein cholesterol (LDL-C) $\geq$140 mg/dL, high-density lipoprotein (HDL-C) $\leq$40 mg/dL, triglyceride (TG) $\geq$150 mg/dL, or receiving treatment with statins and/or lipid-lowering agents. Diabetes mellitus was defined as either hemoglobin A1c $\geq$6.5% or receiving treatment with insulin or oral hypoglycemic agents. Written informed consent was obtained from all patients prior to PCI. This study proceeded in accordance with the Declaration of Helsinki and with approval from our institutional review board. The ethics application approval number was 17-206.

Study endpoints

The study endpoints were all-cause and cardiac death, including CAD, cardiogenic shock, and sudden death. We classified the cause of death into five groups, cardiac death, stroke, cancer, infectious disease, and others. Clinical follow-up included a review of medical charts, telephone contact, and questionnaires sent to patients or their families. Mortality data were collected from the medical records of patients who died or who had been treated at our institution, and the details and cause of death were requested from other hospitals to which patients had been admitted.

Statistical analysis

Continuous variables are expressed as mean $\pm$ standard deviation (SD) or median (interquartile range; IQR). Categorical variables are expressed as a percentage. Patients were divided into five groups based on preprocedural BMI values and then analyzed. Continuous variables were compared using one-way analysis of variance or the Kruskal–Wallis test. Categorical variables (presented as frequencies) were compared using the chi-square test. Unadjusted cumulative event rates were estimated using Kaplan–Meier curves and compared across groups. The association between BMI and all-cause or cardiac death after PCI was determined using multivariate Cox proportional hazard regression analysis. All variables showing values of $p < 0.05$ in univariate analyses were included in multivariate analyses. The variables showing values of $p < 0.05$ in univariate analysis were acute coronary syndrome (ACS), age, CKD, diabetes mellitus, multivessel disease, use of drug-eluting stents, and use of statins. BMI values were included in the multivariate model, and hazard ratios (HR) and 95% confidence intervals (CI) were calculated. Values of $p < 0.05$ were considered to indicate statistical significance. All data were analyzed using JMP version 12.0 for Windows (SAS Institute, Cary, NC, USA).

Results

Baseline and procedural characteristics

Of the 3579 patients who underwent first-time PCI, preprocedural BMI values were available for 3571 (99.8%). For these patients, the median and mean BMI values were 23.9 (IQR: 22.0, 26.2) and 24.2 $\pm$ 3.4, respectively. The ratio of patients in the five groups was as follows: Group 1, 9.2%; Group 2, 21.6%; Group 3, 34.1%; Group 4, 21.1%; and Group 5, 14.5%. The clinical and procedural characteristics of the patients, stratified by preprocedural BMI, are shown in Tables 1 and 2. A decrease in age was observed from underweight to overweight, as was an increased prevalence of hypertension, diabetes mellitus, dyslipidemia, and smoking. No significant differences were found in the proportions of patients having a family history of CAD. Meanwhile, patients with lower BMI exhibited a significantly higher incidence of ACS, CKD, and hemodialysis. The number of patients taking renin–angiotensin–aldosterone system (RAAS) inhibitors, β-blockers, and statins increased with increasing BMI, as did baseline levels of LDL-C, TG, hemoglobin A1c, and BP.

Clinical outcomes

The median follow-up period was 6.3 years (IQR, 3.2–9.6 years). In total, 473 deaths (frequency, 13.2%) were identified during follow-up. The cause of death was as follows: cardiac death, 38.7% (183 deaths); stroke, 7.2% (34 deaths); cancer, 32.4% (153 deaths); infectious disease, 8.7% (41 deaths); and others, 13.1% (62 deaths). On cause-specific death, underweight patients (Group 1 and Group 2) had a higher rate of infectious disease than normal-weight and overweight patients (Groups 3, 4, and 5); 6.2% (29 deaths) vs. 2.5% (12 deaths), $p < 0.001$.

All-cause and cardiac death in patients, stratified by preprocedural BMI, are presented in Figs. 1 and 2. Kaplan–Meier curves revealed that underweight patients had a significantly higher incidence of both all-cause and cardiac death (log-rank test, both $p < 0.0001$).

Tables 3 and 4 show the results of Cox proportional hazard analysis for all-cause and cardiac death (normal weight, BMI = 22.6–25.0 kg/m^2, as a reference). In unadjusted Cox modeling, the risk of all-cause and cardiac death progressively elevated with decreasing BMI (both $p < 0.001$, for trend). However, this relation diminished substantially after adjustment for the other important variables. Interestingly, a J-shaped association was observed between preprocedural BMI and the risk of all-cause death (Fig. 3). In the adjusted model, Group 1 (underweight 1) had the highest risk for all-cause death (HR, 1.58; 95%CI, 1.19–2.10; $p = 0.0019$). Furthermore, no statistically significant differences were seen in the rate of all-cause or cardiac death between normal and overweight patients (Groups 4 and 5).

Table 4 summarizes the findings of multivariate Cox hazard regression analysis with BMI as the continuous variable. Increasing BMI values were significantly associated with all-cause death (per

Please cite this article in press as: Endo H, et al. Impact of body mass index on long-term outcomes in Japanese patients following percutaneous coronary intervention: The Juntendo PCI Registry. J Cardiol (2018), https://doi.org/10.1016/j.jjcc.2018.02.007