Original Article

# Impact of body mass index on repeat coronary revascularization rates in patients with LDL-C below 55 mg/dL and LDL-C below 70 mg/dL: a 42-month cohort study in Korea

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**Background:** Previous studies revealed a linear relationship between body mass index (BMI) and repeat coronary revascularization rate in patients who underwent percutaneous coronary intervention (PCI). However, this relationship has not been demonstrated in Korean patients who meet old and new target low-density lipoprotein cholesterol (LDL-C) levels of Korean dyslipidemia guidelines. Therefore, we conducted this study to find out the effect of BMI on repeat coronary revascularization rate in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL.

**Methods:** This cohort study was followed for 42 months in Daegu Catholic Medical Center, Korea. We included 429 patients with LDL-C <70 mg/dL 1 year after PCI. We compared repeat revascularization rates using Kaplan-Meier survival curves between the normal weight group (18.5 kg/m$^2$ ≤ BMI < 23 kg/m$^2$) and the pre-obesity and obesity group (23 kg/m$^2$ ≤ BMI) in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL.

**Results:** During a follow-up period, there was no significant difference in repeat coronary revascularization-free survival between a group with LDL-C <55 mg/dL and a group with LDL-C <70 mg/dL (79.6% *vs.* 76.2%, P=0.32). In normal weight patients, LDL-C <55 mg/dL group showed higher repeat coronary revascularization-free survival than LDL-C <70 mg/dL group (89.3% *vs.* 77.1%, P=0.05). There was no significant difference in repeat revascularization-free survival between the normal weight group and the pre-obesity and obesity group in patients with LDL-C <70 mg/dL (77.1% *vs.* 75.7%, P=0.67). However, the normal weight group showed significantly higher repeat revascularization-free survival compared to the pre-obesity and obesity group in patients with LDL-C <55 mg/dL (89.3% *vs.* 74.3%, P=0.03). Normal body weight and LDL-C <55 mg/dL [hazard ratio (HR): 0.421, 95% confidence interval (CI): 0.193–0.916, P=0.02] was the only independent predictor for repeat revascularization.

**Conclusions:** In Korean PCI patients with normal body weight whose LDL-C level is less than 70 mg/dL, but more than 55 mg/dL, should be treated with more intensive therapy to lower LDL-C to less than 55 mg/dL. For obese patients who have succeeded in reducing LDL-C below 55 mg/dL, it seems that weight loss should be attempted to a normal body weight level.

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**Keywords:** Coronary artery disease (CAD); low-density lipoprotein cholesterol (LDL-C); obesity; pre-obesity; revascularization

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## Introduction

### *Background*

The "obesity paradox" refers to the observations that obese patients with a particular disease such as cardiovascular disease and cancer may have better outcomes than their normal weight or underweight patients (1). This observation has been also elucidated in patients who underwent percutaneous coronary intervention (PCI) (2-5).

### *Rationale and knowledge gap*

However, most previous studies of the obesity paradox have focused on its impact on survival outcomes (1-4), whereas other studies focusing on repeat revascularization have revealed a linear relationship between body mass index (BMI) and repeat coronary revascularization rates (6-9). Influenced by 2019 European Society of Cardiology (ESC)/ European Atherosclerosis Society (EAS) dyslipidemia guidelines, the recent Korean dyslipidemia guidelines changed the target low-density lipoprotein cholesterol (LDL-C) levels of coronary artery disease (CAD) patients from less than 70 mg/dL to less than 55 mg/dL (10,11). However, there are not enough studies on Korean CAD patients to support this change. In addition, the relationship between obesity and repeat coronary revascularization rate has not been demonstrated in Korean CAD patients who meet old and new target LDL-C level of Korean dyslipidemia guidelines.

### *Objectives*

Therefore, we conducted this study to find out the effect of BMI on repeat coronary revascularization rate in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL after PCI. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-27/rc).

**Highlight box**

**Key findings**

- In Korean patients whose low-density lipoprotein cholesterol (LDL-C) level was less than 55 mg/dL at 1 year after percutaneous coronary intervention (PCI), the normal body weight patients showed significantly higher repeat revascularization-free survival compared to the pre-obesity and obesity patients.

**What is known and what is new?**

- The recent Korean dyslipidemia guidelines changed the target LDL-C levels of coronary artery disease (CAD) patients from less than 70 mg/dL to less than 55 mg/dL. The "obesity paradox" has been elucidated in patients who underwent PCI. However, other studies revealed a linear relationship between body mass index (BMI) and repeat coronary revascularization rate in patients who underwent PCI.
- The results of the present study on Korean patients who underwent PCI showed a linear relationship between BMI and repeat coronary revascularization rate in patients with LDL-C <55 mg/dL.

**What is the implication, and what should change now?**

- The recent changes in the target LDL-C level of the Korean dyslipidemia guidelines for CAD patients may benefit normal-weight patients who underwent PCI.

## Methods

### *Study population and data collection*

We included 1,361 patients from the PCI registry at the Daegu Catholic Medical Center (Daegu, Korea). All patients underwent first PCI using drug-eluting stents (DES) between October 2005 and February 2018 and started statin treatment. Among 1,361 patients, 465 patients who were followed up with an LDL-C level of less than 70 mg/dL one year after PCI were investigated. Of 465 patients, 18 patients who had end-stage renal disease (ESRD) and 18 patients whose BMI was below 18.5 kg/m$^2$ were excluded. Finally, we included 429 patients. The flow of the study is shown in *Figure 1*. Major adverse cardiovascular events (MACEs) evaluation began from the time of the LDL-C follow-up.

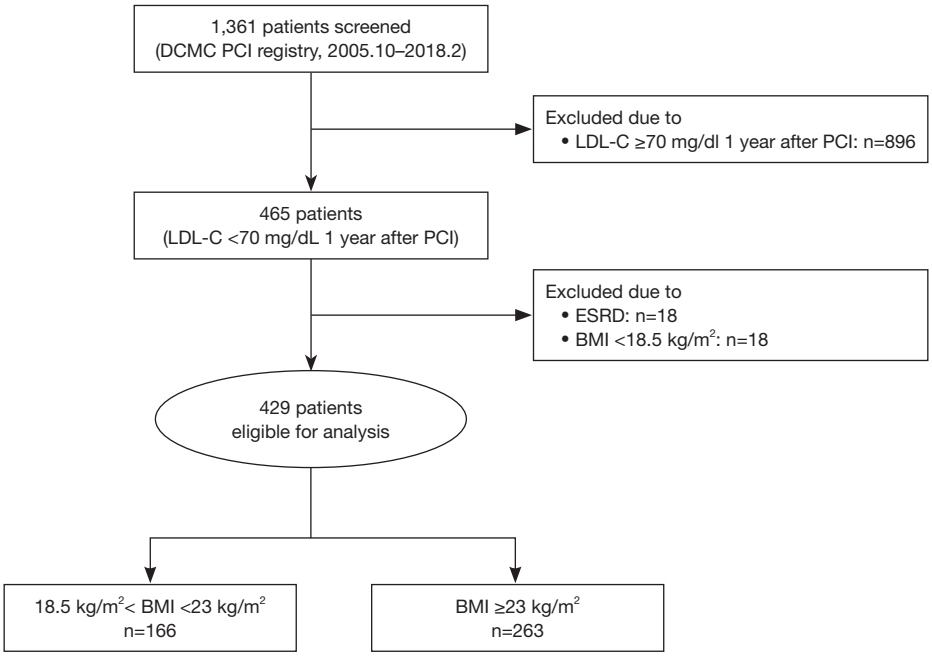


**Figure 1** Progress of study. DCMC, Daegu Catholic Medical Center; PCI, percutaneous coronary intervention; LDL-C, low-density lipoprotein cholesterol; ESRD, end-stage renal disease; BMI, body mass index.

We defined MACEs as cardiac death, non-fatal myocardial infarction (MI), repeat coronary revascularization, and ischemic stroke. We followed the MI definition as the third universal definition (12). The lipid profile of participant at the time of index PCI and at the time of follow-up was investigated. The lipid profiles included measurements of lipoprotein (a) [Lp(a)], triglyceride (TG), total cholesterol (TC), LDL-C, high density lipoprotein cholesterol (HDL-C), apolipoprotein B (Apo B), apolipoprotein A1 (Apo A1). We also evaluated clinical and angiographical data. Prescribed statins were investigated at baseline and follow-up. Statins were classified as high intensity statin, moderate intensity statin, low intensity statin based on the American College of Cardiology (ACC) guideline (13). Other essential medications including antiplatelet, β-blockers, calcium channel blockers, and renin-angiotensin system (RAS) blockers were also prescribed and associated data were collected. We classified coronary lesions into three groups (A, B, and C), with group B (intermediate risk) further divided into class B1 and B2 according to the presence of 1 or 2 adverse characteristics (14). Patients were divided into normal weight group, pre-obesity group and obesity group according to their BMI. Regarding the definition and classification of obesity, we followed the 2022 Korean Obesity Guidelines for the definition of obesity (underweight: BMI <18.5 kg/m$^2$, normal weight: 18.5 kg/m$^2$ ≤ BMI <23 kg/m$^2$, pre-obesity: 23 kg/m$^2$ ≤ BMI <25 kg/m$^2$, obesity: 25 kg/m$^2$ ≤ BMI) (15). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Daegu Catholic Medical Center (No. CR-22-180) and the requirement for patient informed consent was waived due to the study's retrospective nature.

### *PCI procedure and statin usage*

PCI was performed by conventional methods and the type of DES was selected by attending physician. Dual oral antiplatelet therapy (100 mg aspirin and 75 mg clopidogrel, 180 mg ticagrelor, or 10 mg prasugrel) was maintained to patients for at least 12 months after PCI. Every patient was discharged with a statin, and the type of statin was selected by attending physician.

### *Statistical analysis*

Quantitative data were presented as the number (%), mean ± standard deviation. We compared categorical data using the chi-square test or Fisher's exact test. We compared continuous variables using a student's *t*-test when normally

 

distributed and Kruskal-Wallis *H* test when non-normally distributed. Kaplan-Meier survival curves were used for the analysis of repeat revascularization-free survival and compared using the log-rank test between different groups. We performed univariate and multivariate Cox proportional hazards regression to determine the independent predictors for repeat revascularization. Variables were fully included in the multivariate analysis and the stepwise regression method was used. To compare the predicting performance of BMI for repeat revascularization, receiver operating characteristic curves were presented in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL, and area under the curve (AUC) was measured. The optimal cut-off value was determined by Youden index. P (two-sided) <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY, USA).

## Results

### *Comparison of clinical characteristics between LDL-C <55 mg/dL group and LDL-C <70 mg/dL group*

There were 157 patients in the LDL-C <55 mg/dL group and 429 patients in the LDL-C <70 mg/dL group (*Table 1*). In LDL-C <70 mg/dL group, the mean age was 63.00±10.51 years, 73.4% were men. The mean BMI was 23.92±2.87 kg/m$^2$. There was no significant difference in clinical characteristics comparing the two groups. Procedural characteristics including multi-vessel disease (MVD), usage of 1$^{st}$ generation DES, and type b2/c lesions also showed no significant difference. At the time of lipid profile follow-up, the mean LDL-C level was 44.64±7.68 mg/dL in LDL-C <55 mg/dL group and 56.11±10.54 mg/dL in LDL-C <70 mg/dL group (P<0.001). There were also significant differences in TC, TG, Apo B and LDL-C % reduction between LDL-C <55 mg/dL group and LDL-C <70 mg/dL group.

### *Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL*

During a median follow-up period of 42.0 months, there was no significant difference in repeat revascularization-free survival between LDL-C <55 mg/dL group and LDL-C <70 mg/dL group [79.6% *vs.* 76.2%, hazard ratio (HR) 1.221, 95% confidence interval (CI): 0.8211–1.814, P=0.32, *Figure 2A*]. In normal weight patients, LDL-C <55 mg/dL group showed higher repeat coronary revascularization-free survival than LDL-C <70 mg/dL group (89.3% *vs.* 77.1%, HR: 2.225, 95% CI: 1.134–4.364, P=0.05, *Figure 2B*). In the pre-obesity group, there were no significant differences of repeat coronary revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL (77.5% *vs.* 80.9%, HR: 0.8635, 95% CI: 0.4140–1.801, P=0.67, *Figure 2C*). In the obesity group, there were no significant differences of repeat coronary revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL (71.1% *vs.* 70.8%, HR: 1.060, 95% CI: 0.5901–1.904, P=0.83, *Figure 2D*).

### *Comparison of repeat revascularization-free survival between the normal body weight group and the pre-obesity and obesity group in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL*

There was no significant difference in repeat revascularization-free survival between the normal weight group and the pre-obesity and obesity group in patients with LDL-C <70 mg/dL (77.1% *vs.* 75.7%, HR: 1.157, 95% CI: 0.7835–1.709, P=0.67, *Figure 3A*). However, the normal weight group showed significantly higher repeat revascularization-free survival compared to the pre-obesity and obesity group in patients with LDL-C <55 mg/dL (89.3% *vs.* 74.3%, HR: 2.405, 95% CI: 1.167–4.957, P=0.03, *Figure 3B*).

### *Comparison of characteristics between normal body weight vs. pre-obesity and obesity in patients with LDL-C <55 mg/dL and in patients with LDL-C <70 mg/dL*

We compared the clinical characteristics and lipid profiles between the normal body weight group and the pre-obesity and obesity group in patients with LDL-C <70 mg/dL and in patients with LDL-C <55 mg/dL (*Table 2*). In patients with LDL-C <70 mg/dL, the pre-obesity and obesity groups were significantly younger than normal body weight group. The mean BMI was 21.27±1.21 kg/m$^2$ in the normal body weight group, 25.60±2.30 kg/m$^2$ in the pre-obesity and obesity group (P<0.001). At lipid profile follow-up, TG, Apo B were significantly lower in the normal body weight group (TG: P<0.001, Apo B: P<0.001). HDL-C was significantly higher in the normal body weight group (P=0.001). In patients with LDL-C <55 mg/dL, the mean BMI was 20.95±1.28 kg/m$^2$ in the normal body weight group, 25.33±1.79 kg/m$^2$ in the pre-obesity and obesity group (P<0.001). At lipid profile follow-up, Apo B was significantly lower in normal body weight patients (P=0.01).

 

**Table 1** Comparison of clinical characteristics between LDL-C <55 mg/dL and LDL-C <70 mg/dL

| Clinical characteristics | LDL-C <70 mg/dL (n=429) | LDL-C <55 mg/dL (n=157) | P |
|---|---|---|---|
| Age (years) | 63.00±10.51 | 64.15±10.30 | 0.24 |
| Male | 315 (73.4) | 114 (72.6) | 0.84 |
| Diabetes | 213 (49.7) | 86 (54.8) | 0.27 |
| Hypertension | 233 (54.3) | 91 (58.0) | 0.43 |
| Smoking | 190 (44.3) | 64 (40.8) | 0.44 |
| MI at index PCI | 253 (59.0) | 92 (58.6) | 0.93 |
| eGFR (mL/min/1.73 $m^2$) | 85.50±18.89 | 82.58±18.81 | 0.09 |
| BMI (kg/$m^2$) | 23.92±2.87 | 23.77±2.65 | 0.55 |
| EF (%) | 56.02±11.24 | 55.90±11.18 | 0.91 |
| Beta blocker | 369 (86.0) | 137 (87.3) | 0.69 |
| ACEi or ARB | 374 (87.2) | 135 (86.0) | 0.70 |
| CCB | 62 (14.5) | 29 (18.5) | 0.23 |
| High intensity statin | 223 (52.0) | 88 (56.1) | 0.38 |
| MVD | 222 (51.7) | 81 (51.6) | 0.97 |
| Type b2/c lesions | 218 (50.8) | 82 (52.2) | 0.76 |
| 1$^{st}$ generation DES | 52 (12.1) | 20 (12.7) | 0.84 |
| Lipid profile at PCI | | | |
| TC (mg/dL) | 169.93±35.27 | 162.36±37.45 | 0.02 |
| TG (mg/dL) | 160.24±118.27 | 153.26±120.37 | 0.53 |
| HDL-C (mg/dL) | 43.58±12.01 | 43.52±11.77 | 0.95 |
| LDL-C (mg/dL) | 103.03±30.87 | 97.50±30.36 | 0.05 |
| Lp(a) (mg/dL) | 24.96±26.19 | 21.17±21.23 | 0.10 |
| Apo B (mg/dL) | 88.29±22.92 | 83.82±22.46 | 0.03 |
| Apo A1 (mg/dL) | 124.08±26.75 | 123.60±26.63 | 0.84 |
| Lipid profile at follow-up | | | |
| TC (mg/dL) | 113.52±18.17 | 99.77±14.76 | <0.001 |
| TG (mg/dL) | 115.41±74.33 | 101.14±63.30 | 0.03 |
| HDL-C (mg/dL) | 44.39±13.06 | 43.11±12.72 | 0.29 |
| LDL-C (mg/dL) | 56.11±10.54 | 44.64±7.68 | <0.001 |
| Lp(a) (mg/dL) | 25.17±26.68 | 21.67±21.82 | 0.14 |
| Apo B (mg/dL) | 57.94±12.19 | 48.81±10.10 | <0.001 |
| Apo A1 (mg/dL) | 125.81±27.10 | 121.23±27.83 | 0.07 |
| LDL-C % reduction | 40.48±21.82 | 49.44±19.67 | <0.001 |

Data are given as mean ± standard deviation or number (%). LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; BMI, body mass index; EF, ejection fraction; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; MVD, multivessel disease; DES, drug-eluting stent; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; Lp(a), lipoprotein (a).

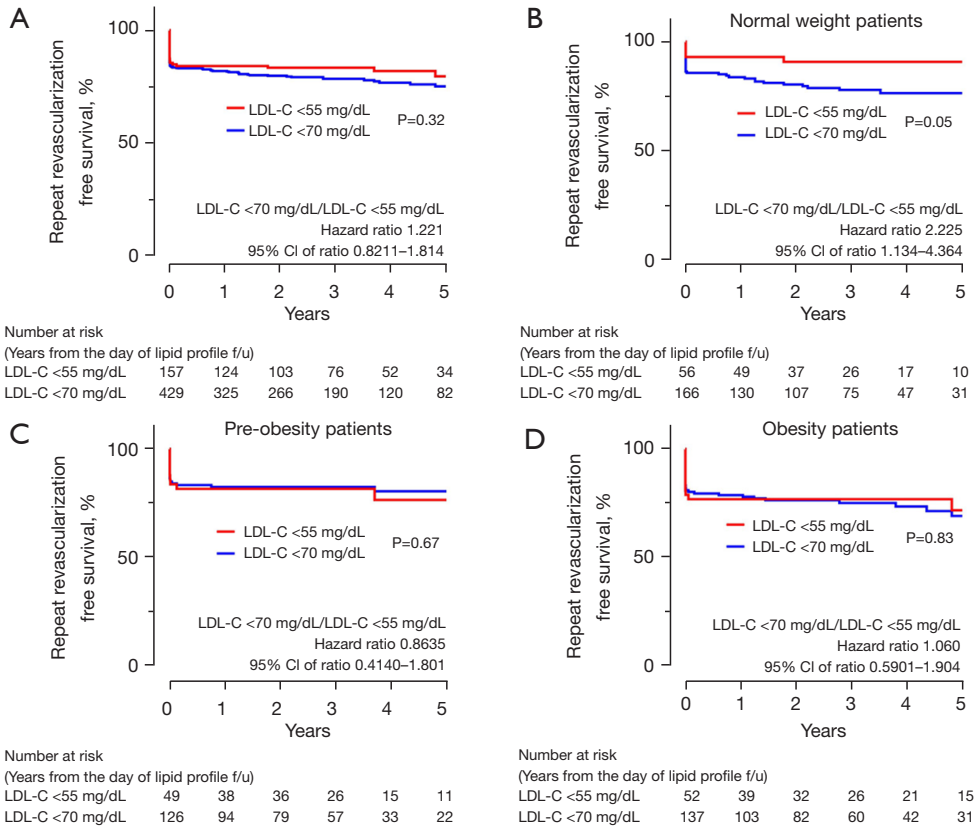


**Figure 2** Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL. (A) Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL. (B) Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL in normal weight patients. (C) Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL in pre-obesity patients. (D) Comparison of repeat revascularization-free survival between LDL-C <55 mg/dL and LDL-C <70 mg/dL in obesity patients. CI, confidence interval; LDL-C, low-density lipoprotein cholesterol.

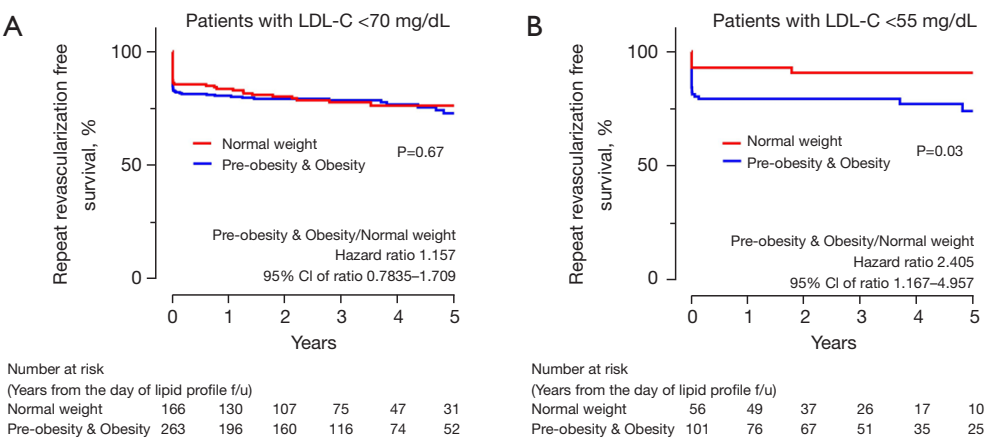


**Figure 3** Comparison of repeat revascularization-free survival between the normal body weight group and the pre-obesity and obesity group. (A) Comparison of repeat revascularization-free survival between the normal body weight group and the pre-obesity and obesity group in patients with LDL-C <70 mg/dL. (B) Comparison of repeat revascularization-free survival between the normal body weight group and the pre-obesity and obesity group in patients with LDL-C <55 mg/dL. LDL-C, low-density lipoprotein cholesterol; CI, confidence interval.

**Table 2** Comparison of characteristics between normal body weight *vs.* pre-obesity and obesity in patients with LDL-C <70 mg/dL and in patients with LDL-C <55 mg/dL

| Clinical characteristics | LDL-C <70 mg/dL | | | LDL-C <55 mg/dL | | |
|---|---|---|---|---|---|---|
| | Normal body weight (n=166) | Pre-obesity and obesity (n=263) | P | Normal body weight (n=56) | Pre-obesity and obesity (n=101) | P |
| Age, years | 65.81±10.40 | 61.23±10.21 | <0.001 | 65.89±11.01 | 63.18±9.81 | 0.11 |
| Male | 114 (68.7) | 201 (76.4) | 0.07 | 43 (76.8) | 71 (70.3) | 0.38 |
| Diabetes | 77 (46.4) | 136 (51.7) | 0.28 | 30 (53.6) | 56 (55.4) | 0.82 |
| Hypertension | 83 (50.0) | 150 (57.0) | 0.15 | 28 (50.0) | 63 (62.4) | 0.13 |
| Smoking | 71 (42.8) | 119 (45.2) | 0.61 | 25 (44.6) | 39 (38.6) | 0.46 |
| MI at index PCI | 101 (60.8) | 152 (57.8) | 0.53 | 33 (58.9) | 59 (58.4) | 0.95 |
| eGFR (mL/min/1.73 $m^2$) | 85.45±18.38 | 85.54±19.24 | 0.96 | 85.25±18.35 | 81.10±19.00 | 0.18 |
| BMI (kg/$m^2$) | 21.27±1.21 | 25.60±2.30 | <0.001 | 20.95±1.28 | 25.33±1.79 | <0.001 |
| EF (%) | 55.40±12.18 | 56.40±10.61 | 0.36 | 54.48±12.02 | 55.69±10.68 | 0.23 |
| Beta blocker | 140 (84.3) | 229 (87.1) | 0.42 | 45 (80.4) | 92 (91.1) | 0.05 |
| ACEi or ARB | 142 (85.5) | 232 (88.2) | 0.42 | 51 (91.1) | 84 (83.2) | 0.17 |
| CCB | 27 (16.3) | 35 (13.3) | 0.39 | 12 (21.4) | 17 (16.8) | 0.47 |
| High intensity statin | 82 (49.4) | 141 (53.6) | 0.39 | 32 (57.1) | 56 (55.4) | 0.83 |
| MVD | 94 (56.6) | 128 (48.7) | 0.10 | 31 (55.4) | 50 (49.5) | 0.48 |
| Type b2/c lesions | 89 (53.6) | 129 (49.0) | 0.35 | 32 (57.1) | 50 (49.5) | 0.35 |
| 1$^{st}$ generation DES | 24 (14.5) | 28 (10.6) | 0.23 | 7 (12.5) | 13 (12.9) | 0.94 |
| Lipid profile at PCI | | | | | | |
| TC (mg/dL) | 170.35±35.40 | 169.66±35.25 | 0.84 | 156.76±36.37 | 165.46±37.86 | 0.16 |
| TG (mg/dL) | 135.44±87.72 | 175.90±131.7 | 0.001 | 138.48±94.99 | 161.46±132.10 | 0.25 |
| HDL-C (mg/dL) | 46.21±12.78 | 41.92±11.20 | <0.001 | 45.86±12.99 | 42.22±10.88 | 0.06 |
| LDL-C (mg/dL) | 103.66±33.10 | 102.64±29.43 | 0.74 | 93.74±33.31 | 99.58±28.56 | 0.25 |
| Lp(a) (mg/dL) | 24.87±24.41 | 25.01±27.29 | 0.95 | 19.84±16.70 | 21.90±23.42 | 0.56 |
| Apo B (mg/dL) | 87.47±24.20 | 88.81±22.10 | 0.55 | 82.23±25.31 | 84.70±20.80 | 0.51 |
| Apo A1 (mg/dL) | 126.66±27.86 | 122.46±25.95 | 0.11 | 127.66±30.22 | 121.35±24.29 | 0.15 |
| Lipid profile at follow-up | | | | | | |
| TC (mg/dL) | 113.68±18.97 | 113.42±17.69 | 0.88 | 96.69±16.47 | 101.48±13.51 | 0.05 |
| TG (mg/dL) | 99.70±65.02 | 125.32±78.16 | <0.001 | 90.92±73.55 | 106.81±56.43 | 0.13 |
| HDL-C (mg/dL) | 46.91±13.85 | 42.80±12.29 | 0.001 | 44.20±14.93 | 42.50±11.34 | 0.42 |
| LDL-C (mg/dL) | 55.30±11.82 | 56.62±9.63 | 0.20 | 43.26±8.56 | 46.51±6.47 | 0.12 |
| Lp(a) (mg/dL) | 25.44±25.97 | 25.00±27.17 | 0.86 | 23.99±23.74 | 20.38±20.69 | 0.32 |
| Apo B (mg/dL) | 56.29±12.07 | 58.99±12.17 | 0.02 | 46.05±10.10 | 50.34±9.83 | 0.01 |
| Apo A1 (mg/dL) | 128.58±28.95 | 124.06±25.77 | 0.09 | 122.22±32.83 | 120.68±24.79 | 0.74 |
| LDL-C % reduction | 41.30±22.60 | 39.96±21.35 | 0.53 | 50.64±19.90 | 48.77±19.61 | 0.57 |

Data are given as mean ± standard deviation or number (%). LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; BMI, body mass index; EF, ejection fraction; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; MVD, multivessel disease; DES, drug-eluting stent; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; Lp(a), lipoprotein (a).

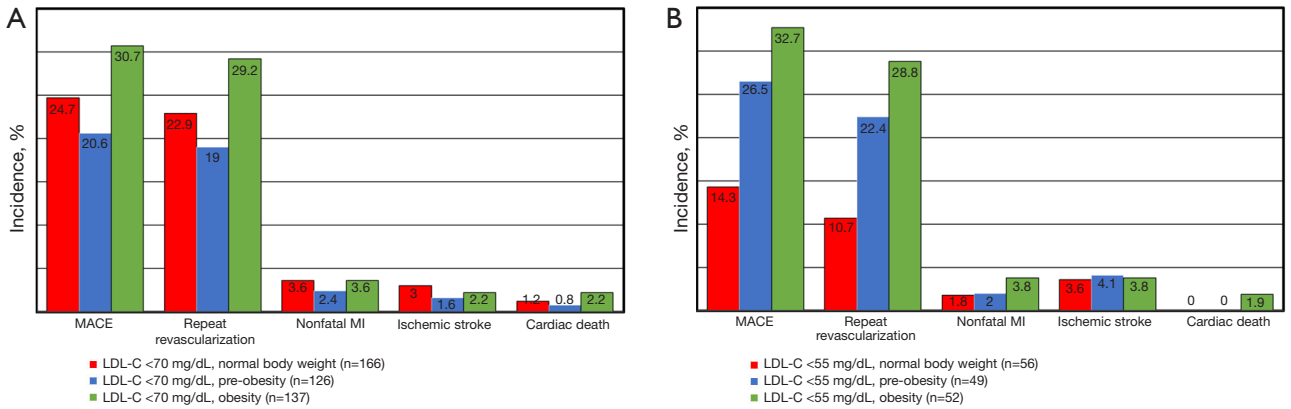


**Figure 4** Comparison of MACEs rate among the normal body weight group, the pre-obesity group, and the obesity group. (A) Comparison of MACEs rate among the normal body weight group, the pre-obesity group, and the obesity group in patients with LDL-C <70 mg/dL. (B) Comparison of MACEs rate among the normal body weight group, the pre-obesity group, and the obesity group in patients with LDL-C <55 mg/dL. MACE, major adverse cardiovascular event; MI, myocardial infarction; LDL-C, low-density lipoprotein cholesterol.

### *Comparison of MACEs rate among the normal body weight group, the pre-obesity group, and the obesity group in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL*

In patients with LDL-C less than 70 mg/dL, there was no linear relationship between BMI and MACE rate and between BMI and repeat revascularization rate (*Figure 4A*). However, in patients with LDL-C less than 55 mg/dL, the MACE rate and repeat revascularization rate tended to increase with increasing BMI (*Figure 4B*). The repeat revascularization rate in normal weight patients was 22.9% when LDL-C was less than 70 mg/dL, but it decreased to 10.7% when LDL-C was less than 55 mg/dL. On the other hand, there was no similar decrease of repeat revascularization rate in pre-obesity and obesity patients.

### *Predicting performance of BMI for repeat revascularization in patients with LDL-C <55 mg/dL and patients with LDL-C <70 mg/dL*

BMI showed better predictability for repeat revascularization in patients with LDL-C <55 mg/dL (AUC: 0.622, 95% CI: 0.531–0.712, P=0.025, *Figure 5A*) than in patients with LDL-C <70 mg/dL (AUC: 0.525, 95% CI: 0.460–0.589, P=0.454, *Figure 5B*). The cutoff BMI for repeat revascularization in patients with LDL-C <55 mg/dL was 22.0 kg/m$^2$.

### *Independent predictors for MACE and repeat revascularization*

We analyzed independent predictors for repeat revascularization by using univariate and multivariate Cox proportional hazards regression (*Table 3*). Normal body weight and LDL-C <55 mg/dL (HR: 0.421, 95% CI: 0.193–0.916, P=0.02) was the only independent predictor for repeat revascularization.

## Discussion

### *Key findings*

The primary findings of our study are as follows: (I) In Korean patients, there was no significant difference in repeat coronary revascularization-free survival between a group with LDL-C <55 mg/dL and a group with LDL-C <70 mg. (II) In patients with LDL-C <55 mg/dL, there was significantly higher repeat coronary revascularization-free survival in the normal weight group compared to the pre-obesity and obesity group. While, there was no significant difference of repeat coronary revascularization-free survival between the normal weight group compared to the pre-obesity and obesity group in patients with LDL-C <70 mg/dL. (III) In patients with LDL-C <55 mg/dL, the MACE rate and repeat revascularization rate showed linear relationship with BMI. (IV) Normal body weight and LDL-C <55 mg/dL was the only independent predictor for repeat revascularization in patients with LDL-C <70 mg/dL.

### *Comparison with similar researches*

2019 ESC/EAS dyslipidemia guideline recommended LDL-C goal of <55 mg/dL and LDL-C reduction of ≥50% from baseline in patients with atherosclerotic cardiovascular

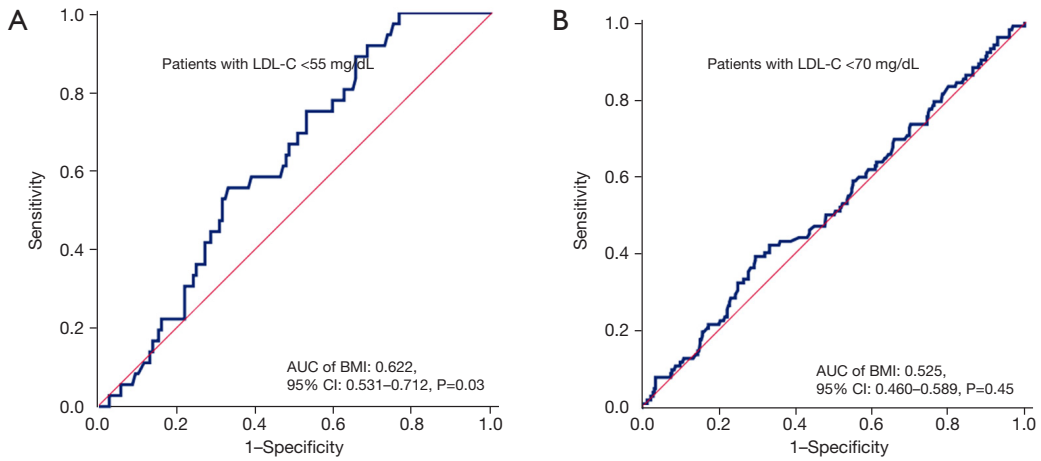


**Figure 5** ROC curves for repeat revascularization. (A) ROC curve for repeat revascularization in patients with LDL-C <55 mg/dL, (B) ROC curve for repeat revascularization in patients with LDL-C <70 mg/dL. LDL-C, low-density lipoprotein cholesterol; ROC, receiver operating characteristic; AUC, area under the ROC curve; BMI, body mass index; CI, confidence interval.

**Table 3** Independent predictors for repeat revascularization

| Variance | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | P | HR | 95% CI | P |
| Normal body weight and LDL-C <55 mg/dL | 0.459 | 0.223–0.946 | 0.03 | 0.421 | 0.193–0.916 | 0.02 |
| Pre-obesity, obesity and LDL-C <55 mg/dL | 1.149 | 0.696–1.899 | 0.58 | | | |
| Normal body weight and 70 mg/dL > LDL-C ≥55 mg/dL | 1.450 | 0.880–2.388 | 0.14 | | | |
| Pre-obesity, obesity and 70 mg/dL > LDL-C ≥55 mg/dL | 0.966 | 0.607–1.537 | 0.88 | | | |
| LDL-C % reduction ≥50% | 0.942 | 0.632–1.404 | 0.76 | | | |
| Age | 1.003 | 0.984–1.021 | 0.78 | | | |
| Male | 1.124 | 0.720–1.754 | 0.60 | | | |
| Diabetes | 0.782 | 0.528–1.158 | 0.22 | | | |
| Hypertension | 1.029 | 0.697–1.521 | 0.88 | | | |
| Smoking history | 0.975 | 0.659–1.444 | 0.90 | | | |
| eGFR | 1.004 | 0.994–1.015 | 0.41 | | | |
| Multi-vessel disease at index PCI | 1.068 | 0.723–1.578 | 0.74 | | | |
| Type b2/c lesion at index PCI | 1.112 | 0.753–1.642 | 0.59 | | | |
| High intensity statin | 0.841 | 0.570–1.241 | 0.38 | | | |
| First-generation DES | 1.101 | 0.615–1.973 | 0.74 | | | |
| ACEi or ARB | 0.728 | 0.388–1.366 | 0.32 | | | |
| Beta blocker | 1.029 | 0.540–1.960 | 0.93 | | | |
| CCB | 1.137 | 0.613–2.108 | 0.68 | | | |

HR, hazard ratio; CI, confidence interval; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; DES, drug-eluting stent; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor antagonist; CCB, calcium channel blocker.

disease (ASCVD) (9). The LDL-C target for patients with ASCVD in the ESC/EAS dyslipidemia guideline is based primarily on recent large-scale trials of proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors which mainly conducted in Western populations (16,17). Influenced by 2019 ESC/EAS dyslipidemia guidelines, the recent Korean dyslipidemia guidelines changed the target LDL-C level of CAD patients from less than 70 mg/dL to less than 55 mg/dL (11). There were prior studies about optimal LDL-C levels of CAD patients in Korea and Japan. However, they did not demonstrate the benefit of lowering target LDL-C level from 70 to 55 mg/dL. Ahn *et al.* compared MACE incidence between LDL-C <55 mg/dL and LDL-C <70 mg/dL in Korean acute myocardial infarction (AMI) patients. There was no significant difference of MACE incidence between the two groups (18). Sakuma *et al.* demonstrated that cardiovascular risk is maintained even when LDL-C is lowered to less than 70 mg/dL in Japanese CAD patients (19). As in the previous studies, there was no significant difference in clinical outcomes between LDL-C less than 55 mg/dL and LDL-C less than 70 mg/dL in present study. However, we found that in patients with normal body weight, LDL-C <55 mg/dL have higher repeat coronary revascularization-free survival compared to LDL-C <70 mg/dL. The results of the present study are consistent with previous studies which demonstrated that more LDL-C lowering with intensive lipid lowering therapy (LLT) is more effective in normal body weight patients than in obese patients. Nylén *et al.* showed that in type 2 diabetic male veterans, statin therapy removed the increased mortality associated with BMI <25 kg/m$^2$ (20). Khan *et al.* also demonstrated intensive LLT derived the highest cardiovascular risk reduction in patients with BMI <25 kg/m$^2$ compared with patients with BMI ≥30 kg/m$^2$. They concluded that normal weight patients may have a larger clinical benefit (cardiovascular mortality, all-cause mortality, MI, revascularization, MACE) from intensive LLT compared with obese patients. Khan *et al.* explained their research results with the following three mechanism (21). First, characteristics of the dyslipidemia of obese patients include elevated TC, TG, and very low-density lipoprotein cholesterol with lower HDL-C levels. Statins only slightly lower TG and do not completely correct the characteristic dyslipidemia seen in obesity, which poses a residual risk after statin treatment. Second, increased levels of inflammation in obese patients may pose a residual cardiovascular risk even after LLT. Third, obesity is associated with decreased expression of LDL receptors, which may modulate the efficacy of LLT.

The "obesity paradox" has been elucidated in patients who underwent PCI. Most previous studies on the obesity paradox have concentrated on its impact on survival (2-5). The main mechanism of the obesity paradox has been suggested to be the low incidence of post-procedural bleeding complications and the long-term, intensive use of medication in obese patients (22,23). The present study differs from previous obesity paradox studies in the following ways: First, we investigated the MACE rate that occurred 1 year after PCI excluding the MACE rate within 1 year of PCI. Second, we included patients whose LDL-C remained very low for a long time. Therefore, this study is unique in that it included patients who were discharged without complications after PCI and satisfied LDL-C levels of the Korean dyslipidemia guidelines for a long time. Third, Tan *et al.* demonstrated that long-term intensive drug use was the cause of the obesity paradox after PCI (23). Biswas also showed that obese patients tend to have increased use of guideline-based medical therapy, in particular β-blockers, renin-angiotensin-system blockers, and statins (5). However, there were no differences of medication use between the normal body weight group and pre-obesity, obesity group in our study (*Table 2*). Therefore, we believe that this study showed that obesity has an independent impact on prognosis after PCI by eliminating factors such as acute complications or medication use. Other studies that focused on repeat revascularization revealed a linear relationship BMI and repeat coronary revascularization rate (6-9). Nikolsky *et al.* suggested that the linear relationship between BMI and repeat coronary revascularization rate may be related to insulin resistance of obese patients (8). Insulin resistance is a well-known risk factor of in-stent restenosis. Previous studies have reported that insulin resistance causes the proliferation of vascular smooth muscle cells after stent implantation (24-26).

### *Explanations of findings, implications and actions needed*

The results of the present study also showed the linear relationship between BMI and repeat coronary revascularization rate in patients with LDL-C <55 mg/dL. The repeat revascularization rate in normal weight patients was 22.9% when LDL-C was less than 70, but it decreased to 10.7% when LDL-C was less than 55. On the other hand, there was no similar decrease of repeat revascularization rate in pre-obesity and obesity patients. It seems that lowering the LDL-C level from less than 70 to less than

 

55 did not reduce the repeat coronary revascularization rate of obese patients due to insulin resistance. In the present study, normal body weight and LDL-C <55 mg/dL was the only independent predictor for repeat revascularization. Therefore, Korean PCI patients with normal body weight whose LDL-C level is less than 70 mg/dL, but more than 55 mg/dL, should be treated with more intensive LLT to lower LDL-C to less than 55 mg/dL. For obese patients who have succeeded in reducing LDL-C below 55 mg/dL after LLT, it seems that weight loss should be attempted to a normal body weight level. We excluded underweight patient in our study with following reasons. First, underweight has been reported as an important risk factor for cardiac death after MI (27-29). Second, underweight patients are more likely to have old age, a higher prevalence of most comorbidities and measures of frailty (27). We excluded underweight patients from this study because these clinical findings related to underweight could bias the results of the present study.

### *Strength and limitations*

Our study had several limitations. First, because this study was retrospective, the blood test period and clinical follow-up period for each patient were different, and statin use was also inconsistent. However, since this study targeted patients whose LDL-C decreased to less than 70 mg/dL one year after PCI, the patient's compliance was excellent and the clinical follow-up period was sufficiently long. Second, the recent Korean dyslipidemia guidelines also recommended reducing LDL-C by ≥50% from the baseline level. However, we did not include a ≥50% reduction in LDL-C as an inclusion criterion. In this respect, our study did not fully meet the Korean dyslipidemia guidelines. To date, the relationship between obesity and repeat coronary revascularization rate has not been demonstrated in Korean patients who meet old and new target LDL-C level of Korean dyslipidemia guidelines. Therefore, this study is significant as it is the first study to investigate the relationship between obesity and clinical outcomes in Korean patients who satisfied the new target LDL-C level of Korean dyslipidemia guidelines after PCI.

## Conclusions

In Korean PCI patients with normal body weight whose LDL-C level is less than 70 mg/dL, but more than 55 mg/dL, should be treated with more intensive therapy to lower LDL-C to less than 55 mg/dL. For obese patients who have succeeded in reducing LDL-C below 55 mg/dL, it seems that weight loss should be attempted to a normal body weight level.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-27/rc

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-27/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board at Daegu Catholic Medical Center (No. CR-22-180) and the requirement for patient informed consent was waived due to the study's retrospective nature.



 

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