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The obesity paradox: effect of body mass index on 2-years clinical outcome after primary percutaneous coronary intervention in Indonesia

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Abstract. – OBJECTIVE: Several studies demonstrated that a high body mass index (BMI) might actually benefit patients with cardiovascular disease, including coronary heart disease. However, other studies were unable to confirm this paradoxical phenomenon in all populations. Therefore, this study aims to determine the association between BMI and long-term clinical outcomes in ST-segment elevation myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI).

PATIENTS AND METHODS: This was a retrospective cohort study of 400 STEMI patients undergoing PCI. Clinical outcome evaluation was done by face-to-face or phone interview and collecting objective data. Statistical analysis was performed to compare the outcomes between underweight-normal group with overweight-obese group.

RESULTS: The incidence of major adverse cardiovascular events (MACE) was lower in patients with higher BMI group in 2-years evaluation (24.1% *vs*. 39.9%; $p < 0.001$). Multivariate analysis showed that BMI was an independent predictor of MACE and the incidence of recurrent infarction (OR 2.322 [CI 95% 1.505-3.584; $p < 0.001$]). The risk of MACE reduces as the weight increases, with a nadir of risk reduction for MACE at 28 to 29.0 kg/m^2, in which the curve rises after, but remained below the risk associated with BMI of 23 kg/m^2.

CONCLUSIONS: In our population, patients with high BMI have a lower incidence of long-term MACE, especially recurrent myocardial infarction, in patients with STEMI undergoing PCI.

Key Words:
STEMI, Percutaneous coronary intervention, Obesity, Body mass index.

Abbreviations
ACS: Acute Coronary Syndrome; BMI: Body Mass Index; CABG: Coronary Artery Bypass Surgery; CAD: Coronary Artery Disease; PCI: Percutaneous Coronary Intervention; STEMI: ST-segment Elevation Myocardial Infarction; MACE: Major Adverse Cardiovascular Events; NSTEMI: Non ST-segment Elevation Myocardial Infarction.

Introduction

Obesity is a known risk factor for various diseases, including cardiovascular disease (CVD)[1]. Worldwide, obesity has become an epidemic. In 2015, there were more than 800 million people diagnosed with obesity, and a high body mass index (BMI) is responsible for 4 million deaths globally[2]. These patients may develop coronary artery disease (CAD), which in later stages can manifest as an acute coronary syndrome (ACS), including acute myocardial infarction with ST-segment elevation (STEMI) or acute myocardial infarction without ST-segment elevation (NSTEMI)[3]. Percutaneous coronary intervention (PCI) is currently the most recommended strategy for such cases to reduce mortality[4].

On the other hand, numerous studies showed the protective effect of obesity in several diseases. This phenomenon is often known as "paradoxical obesity"[5]. From a cardiovascular point of view, this phenomenon was first reported by Ellis et al[6] in 1996, who reported a better prognosis in higher BMI group in CAD patients undergoing PCI. Recently, several published meta-analysis support the existence of

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paradoxical obesity in CAD populations undergoing PCI[7,8]. The meta-analysis conducted by Ma et al[9] also provides a similar conclusion. The report indicates that patients who underwent PCI or coronary artery bypass surgery (CABG) and had high BMI had fewer mortality and cardiovascular events.

However, there is heterogeneity in this study that may be caused by variations in gender, race, and several different population groups. One of the conflicting results was found in some Asian countries, such as China, where high BMI has no protective effect on mortality than normal BMI. It is suspected because the average BMI of Asian populations is significantly lower compared to Western countries[9,10]. Study in Germany obtained that when STEMI patients with the inclusion of cardiogenic shock, no evidence of paradoxical obesity can be found[11]. Majority of these studies did not differentiate the individual spectrum of CAD (stable CAD, NSTEMI, or STEMI). This needs to be studied further because STEMI patients have different basic characteristics, pathophysiology, and atherosclerosis complexity than stable CAD or STEMI[12]. This study aims to determine the association between BMI and long-term clinical outcomes in STEMI patients undergoing PCI.

Patients and Methods

Study Design and Sample

This was a non-randomized, single-center, observational, retrospective cohort study evaluating the 2-year clinical outcomes of STEMI patients who underwent primary PCI (PPCI) in the National Cardiovascular Center Harapan Kita hospital between January 2016-October 2017. We compared the outcomes between underweight-normal group and overweight-obese group. Two-year clinical follow-up were acquired by face-to-face or phone call interviews, or medical record tracing. We excluded the subjects which: 1) Fibrinolytic strategy was chosen; 2) Undergoing only coronary angiography, plain old balloon angioplasty (POBA) or PPCI using *Bare Metal Stent* (BMS); 3) No data of body height and weight during hospitalization; 4) Unavailable to contact or data regarding follow-up evaluation of clinical outcomes cannot be obtained. The study protocol was approved by the Ethics Committee at the National Cardiovascular Center Harapan Kita hospital.

The diagnosis of STEMI was based on the patient presented with chest pain with ST-segment elevation in at least two contiguous leads of $\geq$ 2 mm in men or $\geq$ 1.5 mm in women in leads V2-V3 and/or of $\geq$ 1 mm in other contiguous chest leads or limb leads, or new-onset left bundle branch block on admission electrocardiogram[13]. For this analysis, patients were classified into two groups following the classification of World Health Organization for Asia-Pacific population[14]: underweight-normal (BMI <23.0 kg/m^2, n=188); and overweight-obese (BMI $\geq$23.0 kg/m^2, n=212). Patients characteristics consisted of medical history (diabetes mellitus, hypertension, smoking, dyslipidemia, history of coronary artery disease, family history of heart disease); presentation characteristics (blood pressure, heart rate, symptom-to-door time, Killip class, left ventricular ejection fraction); laboratory findings (glucose, creatinine, cardiac enzymes); angiography and procedural findings; and medical treatment. Long-term MACEs, including re-infarction, total repeat revascularization, cardiovascular mortality, and all-cause mortality, were compared between the two groups.

Statistical Analysis

Data analysis was performed using IBM SPSS 20.0 (IBM Corp., Armonk, NY, USA) and STATA 14 for Windows. Kolmogorov-Smirnov normality test was performed on numerical data. Numerical data with normal distribution were expressed in mean ± standard deviation, while numerical data with abnormal distribution are expressed in the median and minimum-maximum range. Categorical data were described in frequency (percentage). The statistical test for categorical data was Chi-square test, then Fisher's exact test was performed if the requirements were not met. Multivariate analysis was performed using logistic regression test with stepwise backward LR method. Various clinical outcomes were estimated with Kaplan-Meier curve analysis and differences between groups were compared with log-rank test. *p*-value (probability) of less than 0.05 was considered as statistically significant.

Results

Baseline Characteristics

The 400 subjects included in this study were divided into two groups based on BMI accord-

ing to the Asia Pacific classification, namely BMI < 23.0 (underweight and normal; N = 188; 47%) and BMI ≥ 23.0 (overweight and obese; N = 212; 53%). The majority of research subjects were male in both groups. The age distribution was normal in both groups, with mean age being slightly younger in the overweight-obese group but not statistically significant (55.7 ± 10.55 *vs.* 57.2 ± 10.7; $p = 0.164$). The prevalence of comorbidities such as hypertension, dyslipidemia, and diabetes mellitus was slightly higher in the overweight-obese group, but not statistically significant.

Mean creatinine clearance in underweight-normal group was lower than the overweight-obese group (65.99 *vs.* 82.28; $p < 0.001$). Prevalence of renal insufficiency based on creatinine clearance was also significantly higher in underweight-normal group (10.6% and 3.8%; $p = 0.007$). The onset of STEMI during arrival at the hospital was not statistically significant in both groups. The proportion of patients who arrived more than 12 hours since onset was also not significantly different in the two groups (43.6% *vs.* 37.7%; $p = 0.232$). The mean left ventricular ejection fraction was lower in the underweight-normal group than the overweight-obese group (43.82% *vs.* 46.59%, $p = 0.02$). Both groups already received guideline-based therapy for STEMI patients post PPCI. Baseline characteristics of both groups are listed in Table I.

Coronary Angiography and PCI Profile

As shown in Table II, both groups showed no significant differences in the number of coronary lesions, LM involvement, infarct-related artery (IRA). Mean diameter and length of stent used during the procedures did not significantly differ. The proportion of LAD lesions was greater in the overweight-obese group than underweight-normal group (86.3% *vs.* 78.7%, $p = 0.032$). Meanwhile, lesions in RCA, LCX, and LM did not show significant differences in both groups.

Table I. Baseline clinical characteristics.

Variable	Underweight-normal (BMI < 23.00; N = 188)	Overweight-obese (BMI ≥ 23.00; N = 212)	*p*-value
Sex			
Male	166 (88.3%)	177 (83.5%)	0.170
Female	22 (11.7%)	35 (16.5%)	
Age (years)	57.2 (±10.7)	55.7 (±10.55)	0.164
Cardiovascular Risk Factor			
Smoking	134 (71.3%)	144 (67.9%)	0.467
Dyslipidemia	54 (28.7%)	78 (36.8%)	0.087
Hypertension	120 (63.8%)	160 (70.8%)	0.140
Diabetes mellitus	70 (37.2%)	95 (44.8%)	0.124
Family history of heart disease	32 (17%)	18 (8.5%)	0.01
Renal Function			
CCT (ml/mins)	65.99 (11.39-161.39)	82.28 (12.9-234.72)	< 0.001
Renal Insufficiency (CCT < 30 ml/mins)	20 (10.6%)	8 (3.8%)	0.007
Onset (hours)	6.0 (0.5-12)	6.0 (0.13-12)	0.602
Killip Class			
I	131 (69.7%)	169 (79.7%)	0.09
II	40 (21.3%)	26 (12.3%)	
III	6 (3.2%)	5 (2.4%)	
IV	11 (5.9%)	12 (5.7%)	
Left Ventricle Ejection Fraction (%)	43.82 (±12.20)	46.59 (±11.44)	0.02
LVEF < 35%	40 (18.9%)	45 (23.9%)	0.216
Medication			
Aspirin	166 (88.3%)	189 (89.2%)	0.788
Clopidogrel	143 (76.1%)	159 (75%)	0.805
Ticagrelor	22 (11.7%)	30 (14.2%)	0.467
Statin	162 (86.2%)	185 (87.3%)	0.747
Beta-blocker	158 (84%)	176 (83%)	0.783
ACE-inhibitor	117 (62.2%)	141 (66.5%)	0.372

BMI: Body Mass Index, CCT: Creatinine Clearance Test, ml/mins: milliliters per minutes, LVEF: Left Ventricle Ejection Fraction, ACE: Angiotensin Converting Enzyme.

Table II. Coronary angiogram and PCI.

Variable	Underweight-normal (BMI < 23.00; N = 188)	Overweight-obese (BMI ≥ 23.00; N = 212)	*p*-value
Coronary lesions			
1VD	55 (29.3%)	62 (29.2%)	0.476
2VD	56 (29.8%)	74 (34.9%)	
3VD	77 (41%)	76 (35.8%)	
LM Disease	18 (9.7%)	21 (10.1%)	0.891
Location			
LAD	148 (78.7%)	184 (86.8%)	0.032
LCx	102 (54.3%)	108 (50.9%)	0.508
RCA	123 (65.4%)	132 (62.3%)	0.512
LM	17 (9.0%)	18 (8.5%)	0.845
Infarct Related Artery (IRA)			
LAD	100 (53.2%)	107 (50.5%)	0.798
LCx	24 (12.8%)	26 (12.3%)	
RCA	64 (34%)	79 (37.3%)	
Stent Diameters (mm)	3.0 (2.25-4.0)	3.0 (2.0-4.0)	0.181
Stent Length (mm)	28.0 (13.0-44.0)	28.0 (12.0-39.0)	0.122

BMI: Body Mass Index, 1VD: one vessel disease, 2VD: two vessel disease, 3VD: three vessel disease, LM: Left Main, LAD: Left Anterior Descending, LCx: Left Circumflex, RCA: Right Coronary Artery, mm: milimeters.

MACE Differences in BMI Groups

The comparison of MACE in both BMI groups can be seen in Table III. Incidence of MACE in overweight-obese group was significantly lower than underweight-normal group after the 3 months of evaluation post PPCI. This number included in-hospital events (1.4% *vs.* 4.8%; *p* 0.048). This difference was seen more prominently in the 2 years follow-up post-initial procedure (24.1% *vs.* 39.9%; *p* 0.001). The long-term evaluation

Table III. Incidence of mace in BMI groups.

Clinical outcomes	Underweight-normal (SBMI < 23.00; N = 188)	Overweight-obese (BMI ≥ 23.00; N = 212)	*p*-value
3 months post PPCI			
MACE (%)	4.8	1.4	0.048
Re-infarction (%)	4.3	0	0.002
Total Repeat Revascularization (%)	1.1	0	0.22
Cardiac mortality (%)	2.1	0.5	0.192
6 months post PPCI			
MACE (%)	6.4	1.9	0.022
Re-infarction (%)	4.3	0	0.002
Total Repeat Revascularization (%)	2.1	0.5	0.192
Cardiac mortality (%)	2.7	0.5	0.104
1 year post PPCI			
MACE (%)	14.4	7.1	0.018
Re-infarction (%)	8.0	0.9	< 0.001
Total Repeat Revascularization (%)	4.3	1.9	0.166
Cardiac mortality (%)	5.3	3.3	0.318
2 years follow-up			
MACE (%)	39.9	24.1	< 0.001
Re-infarction (%)	20.7	6.6	< 0.001
Total Repeat Revascularization (%)	12.2	9.9	0.458
Cardiac mortality (%)	16.0	9.4	0.049
All-cause mortality (%)	25.5	18.4	0.084

BMI: Body Mass Index, PPCI: Primary Percutaneous Coronary Intervention, MACE: Major Adverse Cardiovascular Events.

also found the incidence of recurrent myocardial infarction, as one of the MACE composites, was lower in subjects with overweight-obese (6.6%) compared to underweight-normal group (20.7%) with a *p*-value <0.001. This results also can be seen since 3 months post PPCI.

In both groups, the incidence of cardiovascular mortality did not significantly differ at the 3 months, 6 months, and 1 year after the initial procedure. However, in 2 years follow-up, there was a noticeable increase of events in both groups and resulted in a significant difference where the cardiovascular mortality rate in the Underweight-normal group was greater than overweight-obese (16.0% *vs.* 9.4%; *p* 0.049). Meanwhile, other MACE composites, total repeat revascularization, did not significantly differ in both groups in all evaluation phases.

The dose-response relationship between BMI and MACE is demonstrated in Figure 1. The risk of MACE reduces as the weight increases, with the nadir of risk reduction for MACE at 28 to 29.0 kg/m^2, in which the curve rises after but remained below the risk of patients with BMI of 23 kg/m^2 or less.

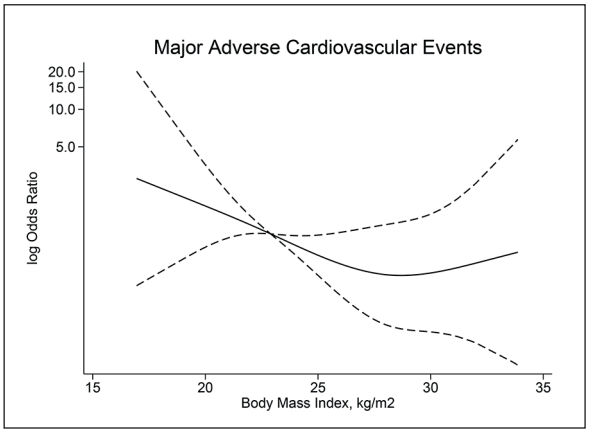

Figure 1. Dose-response relationship between body mass index and MACE outcome.

Multivariate Analysis and Survival Curve for MACE

For the long-term outcomes of MACE, bivariate analysis showed that the variables that had the potential to influence the incidence of MACE were BMI group, diabetes mellitus, Killip class during admission, and LVEF during initial hospitalization. From the multivariate analysis (Table IV), we found that the variable most associated with MACE events is underweight-normal group (OR 2.322 [CI 95% 1.505-3.584; $p < 0.001$]), and Killip class 2-4. (OR 2.088 [CI 95% 1.007-4.332; $p = 0.048$]).

The Kaplan-Meier curve was created to analyze the time course of the clinical outcomes assessed in this study. Based on the curve, it can be seen that there are significant differences in the survival rate analysis of MACE incidence between both BMI groups (Figure 2A, log-rank $p <$ 0.001). In the first year post initial procedure, the incidence of MACE in overweight-obese group was 7%, and underweight-normal group was 14%, whereas in two years, the difference of MACE incidence between those two BMI groups diverged even more. The analysis on recurring myocardial infarction resulted in similar results, that there is a significant difference in the incidence with a log-rank *p* of <0.001 (Figure 2B). The difference was also more prominent in 2 years follow-up in comparison to 1 year follow-up. On the other hand, Figures 2C and 2D showed that the BMI groups did not significantly associate with the clinical outcome of total repeat revascularization and cardiovascular death within the time course (log-rank $p = 0.452$ and 0.052, respectively).

Discussion

Our study revealed several interesting aspectss. Although not statistically significant, the overweight-obese group has a slightly younger

Table IV. Multivariate analysis for MACE within 2 years.

Variable	OR (CI 95%)	*p*-value
BMI < 23 kg/m^2	2.322 (1.505-3.584)	< 0.001
Killip class II-IV	2.088 (1.007-4.332)	0.048
Diabetes mellitus	1.514 (0.978-2.344)	0.063
LVEF < 35%	1.161 (0.683-1.973)	0.58

BMI: Body Mass Index, PPCI: Primary Percutaneous Coronary Intervention, MACE: Major Adverse Cardiovascular Events.

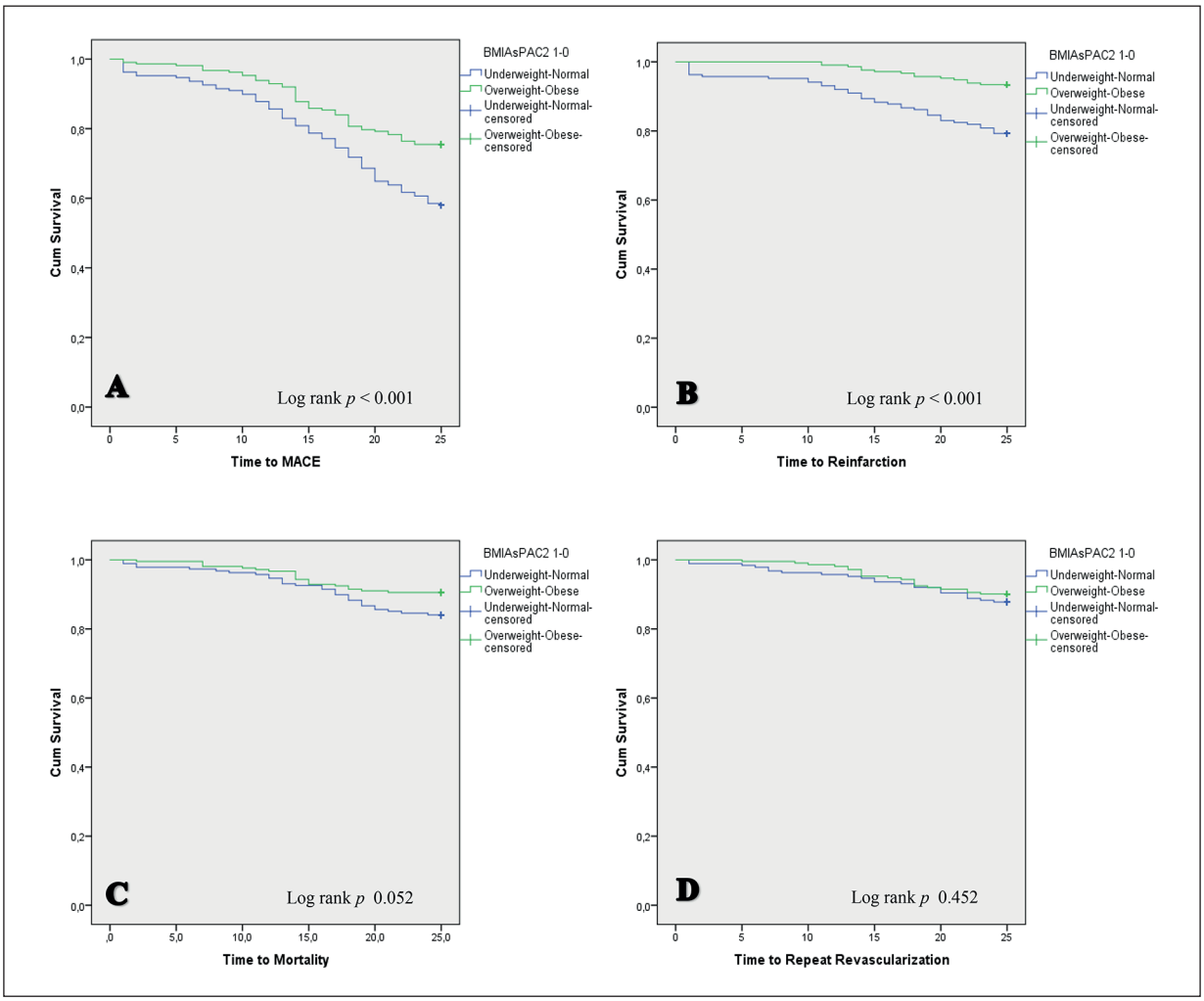

Figure 2. A, Kaplan-Meier survival analysis for MACE outcome. **B,** Kaplan-Meier survival analysis for recurrent myocardial infarction outcome. **C,** Kaplan-Meier survival analysis for cardiovascular death outcome. **D,** Kaplan-Meier survival analysis for total repeat revascularization outcome.

mean age than the underweight-normal group (55.7 *vs.* 57.2). Younger age is one of the hypotheses proposed as one of the mechanisms that lead to better prognosis in higher BMI patients with CAD[15]. Similar result was also reported by Kang et al[16] comparing BMI group to clinical outcomes in STEMI patients. The study found significant age differences between underweight, normal, overweight, and obese subjects (mean age 69.7 years, 64.7 years, 59.4 years, and 56.5 years, respectively; p <0.001). Azhari et al[5] in studies in populations CHD in general also obtained significantly younger age (p <0.001) in the higher BMI group[5].

In theory, obesity predisposes to other metabolic syndromes including dyslipidemia, diabetes mellitus, and hypertension[17]. Neeland et al[18] in studies with STEMI subjects, reported that the prevalence of these metabolic comorbidities is equivalent with a higher BMI group and was statistically significant (p <0.001). This was confirmed by studies of Kang et al[16] and Azhari et al[5], who reported similar results. In our study, the proportion of these metabolic disorders was found to be higher in the overweight-obese group, including Diabetes mellitus (44.8% *vs.* 37.2%), hypertension (70.8% *vs.* 63.8%), and dyslipidemia (36.8% *vs.* 28.7 %). However, the difference is not statistically significant. In addition, subjects with renal insufficiency, measured by serum creatinine levels, were found more in underweight-normal group (10.6% *vs.* 3.8%; p = 0.007). The study by Akin et al[11] also reported that the group with a BMI ≤ 24.9 had a higher proportion of renal

insufficiency (29.3%) than the BMI 25-30 (18.7%) and BMI> 30 (11.5%) with a *p*-value <0.001. These findings also supported the hypothesis that in lower BMI, comorbidities including organ dysfunction is more common and has an influence on clinical outcomes[19].

Previous studies also mentioned that better LVEF in the higher BMI group could be one of the mechanisms that provide better clinical outcomes[19]. This is evidenced in the Kang et al[16] study which showed a higher mean LVEF in higher BMI (48.3% in underweight, 50.3% in normal, 51.3% in overweight, and 52.6% in obesity; p <0.001). Joyce et al[20] also showed the similar relationship between BMI and LVEF with a mean for the BMI group <25, 25-30, and > 30 was 43%, 46%, and 52%, respectively. Likewise, our study obtained that the mean LVEF was slightly better in the overweight-obese group compared to underweight-normal group (46.59% *vs.* 43.82%; p = 0.02).

From the characteristics of PCI procedure, Kang et al[16] research showed that the mean diameter of the stent required for the PCI is directly proportional to the BMI. They were 3.11 mm for underweight, 3.18 mm for normal weight, 3.24 mm for overweight, and 3.28 mm for obesity (p <0.001). Likewise, studies by Simoni et al[21] reported mean stent diameter in the normal BMI group, overweight and obesity of 2.98 mm, 3.05 mm, and 3.143 mm, respectively. The larger diameter of the stent used, which represents the IRA's diameter, is theoretically a possible mechanism that supports the occurrence of obesity paradox phenomenon[22,23]. However, our study did not find significant differences in median stent diameter between both groups (3.0 mm *vs.* 3.0 mm; p = 0.181). Probably, it is because of the number of samples that are not big enough to provide normal data distribution. Meanwhile, if the data distribution is assumed to be normal, the mean diameter of the stent used in the overweight-obese group is slightly larger than the underweight-normal group (3.10 mm *vs.* 3.02 mm).

Almost all published systematic reviews and meta-analyses support the existence of a paradoxical obesity phenomenon in clinical outcomes in CAD subjects undergoing PCI[9,10]. Nevertheless, there are not many specifically study on this phenomenon in STEMI subjects. Kang et al[16], who conducted the study in this subset, reported that the MACE outcome by BMI groups did not significantly differ on 1 and 6 months post PCI evaluation. However, a significant difference was observable in the 1-year post-procedure evaluation with the proportion of 28.2% in underweight, 15.2% in normal, 13.0% in overweight and 14.8% in obesity (p = 0.031)[16]. In our study, MACE incidence rate was already significantly higher in lower BMI group even from 3 months post PCI up to 2 years. The survival analysis with the Kaplan-Meier curve also showed that MACE events occurred more in underweight-normal group than the overweight-obese (Log rank p <0.001) and the curve was even more diverge along the time course.

For clinical outcomes of recurrence of myocardial infarction, this study also showed a significant difference in the proportions between two BMI groups since 3 months post initial PCI. A higher incidence of recurrent myocardial infarction events was found in lower BMI. This is different from the study of Kang et al[16], which reported no significant differences in the incidence of recurring myocardial infarction up to 1 year evaluation after the PCI procedure, i.e. 2.6% in underweight, 1.1% in normal, 0.5% in overweight, and 1.1% in obese (p = 0.246). Our survival analysis showed a significant difference in two BMI groups for recurrence of myocardial infarction (log-rank p <0.001). In the first year, the incidence of recurring myocardial infarction in the overweight-obese group was 1%, while the underweight-normal group was 7%. The more striking difference only appeared in 2 years follow-up, which are 7% in overweight-obese group *vs.* 21% in underweight-normal group. It is possible that if the study of Kang et al[16] was continued for a more extended period, then the difference in the incidence of recurrent myocardial infarction could be more significant.

Among the proposed hypotheses for paradoxical obesity, one that could explain the protective effect on the incidence of recurrent acute myocardial infarction might be adipose tissue regulation in the regulation of inflammatory factors such as TNF-α and others. These inflammatory agents play a role in all phases of atherosclerosis[24,25]. Another possible explanation is, although not statistically significant in our population, higher proportion of comorbidities such as diabetes, hypertension, and dyslipidemia were found in overweight-obese groups than underweight-normal groups. Secondary prevention and management of these comorbidities may be one of the factors supporting the paradoxical obesity phenomenon in this study[19].

Cardiovascular death is the most studied clinical outcome in STEMI subjects in relation to BMI groups. The systematic review conducted by Romero-Corral et al[15] concluded that underweight status increases RR for cardiovascular death by 1.45 (95% CI 1.16-1.81) compared to normal weight. In contrast, the lowest RR was found in the overweight group at 0.88 (95% CI 0.75-1.02) compared to normal weight. Kang et al[16] also reported significantly lower cardiovascular mortality rates at higher BMI, even since the 1-month evaluation post PCI. At 1-year evaluation, they reported a 9% cardiovascular mortality rate in the underweight group, 2.6% in the normal group, 1.5% in the overweight group, and 0.8% in the obese group ($p < 0.001$). In sub-analysis of our study the 2-year cardiovascular mortality rate also higher in the underweight-normal group with OR 1.823 (95% CI 0.997-3.333; $p = 0.049$). However, in a multivariate analysis, it was found that lower BMI is not an independent predictor of this clinical outcome.

This study is focused on STEMI and found that the nadir of risk reduction for MACE was at 28 to 29.0 kg/m^2, in which the curve rises after but remained below the risk at 23 kg/m^2. This further strengthens the findings of a meta-analysis that indicate lower mortality in obese patients[26]. The meta-analysis found that the benefit was highest in the obese, followed by overweight and severely obese compared to normal BMI, which supports that the nadir point in our study falls in the obese category. This finding is further supported by the NCDR ACTION Registry-GWTG, highlighting that mild obesity has lower long-term risk in older patients with STEMI[12]. The finding is also supported by the GULF COAST registry which both peripheral and central obesity were associated with reduction in 1-year mortality among patients with ACS[27]. Previously, a registry from Australia showed a U-shaped relationship between BMI and adverse events in ACS patients and the highest event rate is in most obese (>60 kg/m^2)[28], unfortunately we do not have patients >60 kg/m^2 BMI; thus, the higher end of BMI in our sample still has lower MACE compared to patients with normal weight. A study on 6978 patients in Korea showed that obesity had a protective effect on MACE, especially in patients without diabetes[29]. Although there is no dose-response graph and identifiable nadir, the benefit in terms of MACE was most observed in patients with 25 to 29.0 kg/m^2, which supports our finding.

Study Limitations

This is a retrospective cohort study, hence, recall bias remains a possibility. However, we can minimize it by confirming the interview results with the medical records and objective data. If the clinical outcomes occurred outside our center, we requested the patient's resume and report on the actions taken. Failure to contact some of the patients is another problem that leads to the loss of follow-up. Additionally, the choice of using BMI as an anthropometric index in some literature is less representative of the composition of fat mass and non-fat mass, which are considered to be more associated with the risk of cardiovascular events.

Conclusions

This study indicates that higher BMI positively affects long-term clinical outcomes in STEMI patients undergoing Primary PCI. The benefit is mostly observed in patients with mild obesity. However, as primary prevention of cardiovascular disease itself, maintain a healthy BMI should still be prioritized. Future prospective study was suggested to determine the possible mechanism for this phenomenon from all proposed hypotheses.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval and Consent to Participate

This study was performed in compliance with the guidelines for good clinical practice and the Declaration of Helsinki and was approved by the institutional ethical review board of National Cardiovascular Center Harapan Kita, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, ethical clearance reference number: LB.02.01/VII/388/KEP.083/2019. Informed consent was not required by the institutional ethical review board because this is a retrospective study.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article. Corresponding author (D.F) can be contacted for more information.

Authors' Contribution

DGA, DF and AAA conceived and designed the study. DGA, DF, AMA, AAA drafted the manuscript. DGA, DF, AAA, BR, SI, SNS, and RP interpreted the data, and per-

formed extensive research on the topic. ASM, NI and RP reviewed the draft and provide critical revision for the manuscript. DGA, DF, and RP performed the statistical analysis. All authors contributed to the writing of the manuscript. All authors have read and approved the manuscript.

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