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ORIGINAL ARTICLE

Prognostic impact of body mass index and culprit lesion calcification in patients with acute myocardial infarction

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Abstract

Patients with acute myocardial infarction (AMI) with low body mass index (BMI) have worse outcomes than obese patients, and this phenomenon is recognized as "obesity paradox." Coronary calcification is associated with cardiac events. However, the association between BMI and calcification and their involvement in the mortality of AMI patients remain unknown. This study consecutively enrolled 517 patients with AMI who underwent emergent coronary intervention within 24 h after onset. Patients were divided into four groups according to the baseline BMI interquartile ranges: Q1 (BMI < 21.9 kg/m^2), Q2 (21.9 ≤ BMI < 24.0 kg/m^2), Q3 (24.0 ≤ BMI < 26.0 kg/m^2), and Q4 (BMI ≥ 26.0 kg/m^2). Calcification in the culprit lesion was also evaluated. The Q1 group was older and had a lower frequency of coronary risk factors. Moderate/severe calcification was most frequently observed in Q1, followed by Q2, Q3, and Q4. The Q1 group had the highest all-cause mortality, and patients with moderate/severe calcification had a higher all-cause mortality than that in patients without calcification. The highest all-cause mortality was observed in Q1with calcification, and the lowest was in Q4 without calcification. Q1 and the presence of moderate/severe calcification were independently associated with all-cause mortality. Although low-BMI patients with AMI had a lower frequency of coronary risk factors, they had a worse all-cause mortality than that in high-BMI patients. Our findings suggest that lesion calcification and its possible association with low BMI are involved in the higher mortality rate in these patients.

Keywords Acute myocardial infarction · Body mass index · Coronary calcification

Introduction

Obesity is closely associated with the incidence of cardiovascular diseases and mortality [1–5]. However, some controversial studies have demonstrated that obese patients with concomitant cardiovascular disease have better outcomes than those in normal- or low-body-weight patients. This phenomenon has been recognized as the "obesity paradox" [6–8]. Regarding patients with acute myocardial infarction (AMI), several studies have demonstrated that patients with a lower body mass index (BMI) have worse in-hospital and long-term mortality rates than those of normal- or high-BMI patients [9–15]. However, the underlying mechanisms remain unclear.

Previous studies have suggested that calcified target coronary lesions are associated with higher risks of all-cause mortality and target lesion revascularization in patients treated with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). A pooled analysis of the HORIZON-AMI and ACUITY trials revealed that patients with moderate/severe target lesion calcification were older and had a higher incidence of 1-year mortality after PCI [16]. In a cohort of patients who underwent CABG, subjects with severe lesion calcification were older, had a

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lower BMI, and were associated with increased mortality in comparison to those without lesion calcification [17]. These studies indicate that there are possible associations between aging or low BMI and coronary calcification.

However, the association between BMI and coronary artery calcification and their involvement in the outcomes of patients with AMI remain unknown. The aim of the present study was to evaluate the association between BMI and coronary artery calcification and their involvement in the incidence of all-cause mortality in patients with AMI treated with emergent PCI.

Materials and methods

Study patients

This study enrolled consecutive patients with AMI who presented to Hirosaki University Hospital between December 2008 and March 2013 and underwent emergent PCI within 24 h after symptom onset. Exclusion criteria were cardiac arrest on arrival ($n=2$) and AMI resulting from stent thrombosis ($n=13$). Finally, 517 patients [405 males (78%); mean age, 65 ± 13 years] were enrolled. The diagnosis of AMI was established using the universal definition of myocardial infarction based on clinical symptoms, changes in electrocardiographic readings, and the elevation of cardiac biomarkers [18]. BMI was calculated as body weight (kg) divided by the square of height (m^2) at the time of AMI presentation. Patients were divided into four groups according to the baseline BMI interquartile ranges: Q1 group (BMI < 21.9 kg/m^2, $n=123$), Q2 group ($21.9 \leq$ BMI < 24.0 kg/m^2, $n=126$), Q3 group ($24.0 \leq$ BMI < 26.0 kg/m^2, $n=134$), and Q4 group (BMI ≥ 26.0 kg/m^2, $n=134$). This study was conducted according to the principles of the Declaration of Helsinki and approved by the ethics committee of our institution.

Severity of calcification in the culprit lesion

The severity of calcification in the culprit lesion was evaluated using coronary angiography according to the criteria from a previous report [16], and this grading was performed by two physicians blinded to the outcomes of all patients in this study. Patients were divided into three groups according to the severity of calcification in the culprit lesion as follows: no/mild, moderate, and severe calcification groups. Moderate calcification was defined as radiopaque densities that were noted only during the cardiac cycle and that typically involved only one side of the vascular wall. Severe calcification was defined as radiopaque densities that were noted without cardiac motion prior to contrast injection and that generally involved both sides of the arterial wall. The interobserver variability kappa values for the degree of culprit lesion calcification were also evaluated.

Endpoints

The primary endpoint of this study was all-cause mortality. Follow-up was initiated on the day of admission. The patients were followed up for a median of 2.7 years with optimal medical treatment.

Statistical analysis

All continuous variables were expressed as mean ± standard deviation or median (interquartile range), and categorical variables were expressed as numbers and percentages. Continuous variables were compared using one-way analysis of variance, and the statistical significance of differences was calculated using the Tukey–Kramer test. The Mann–Whitney *U* test was used for nonparametric variables. The chi-square analysis was used to compare categorical variables. Furthermore, we examined the frequency of calcification in the culprit lesion evaluated by coronary angiography stratified by BMI categories using Cochran–Armitage trend test. Mortality was estimated using the Kaplan–Meier method and compared using the log-rank test. Multivariate analysis for the predictors of all-cause mortality was performed using Cox proportional hazards regression. The variables used for analysis included age, male gender, coronary risk factors [including hypertension, dyslipidemia, diabetes mellitus (DM), and smoking habits], CKD (chronic kidney disease), multi-vessel or left main trunk (LMT) disease, Killip classification IV at presentation, left ventricular ejection fraction in an acute phase, BMI categories (four groups), and the presence of moderate/severe coronary calcification. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. Receiver operating characteristic (ROC) curve analysis for predicting all-cause mortality was also performed. Statistical analyses were performed using JMP 13 software (SAS, Cary, NC, USA). A p value of < 0.05 was considered statistically significant.

Results

Patient characteristics

The baseline patient characteristics stratified by BMI categories are listed in Table 1. The mean age significantly decreased with increasing BMI. The patients in the Q1 group had a lower prevalence of coronary risk factors, including hypertension, dyslipidemia, and DM. The prevalence of smoking habits did not differ among the four groups. Patients in the Q1 group had a higher prevalence of cardiogenic shock

Table 1 Patient profiles stratified by BMI categories

	Q1 group ($n=123$)	Q2 group ($n=126$)	Q3 group ($n=134$)	Q4 group ($n=134$)	p value
Age, years	72 ± 11	66 ± 11	65 ± 12	60 ± 14	< 0.01
Male gender, *n* (%)	87 (71)	101 (80)	110 (82)	107 (80)	0.13
BMI, kg/m^2	19.5 ± 1.7	22.9 ± 0.6	24.9 ± 0.5	29.0 ± 2.6	< 0.01
Coronary risk factors					
Hypertension, *n* (%)	78 (63)	88 (70)	93 (69)	109 (81)	< 0.05
Dyslipidemia, *n* (%)	75 (61)	97 (77)	100 (75)	110 (82)	< 0.01
Diabetes mellitus, *n* (%)	36 (29)	57 (45)	61 (46)	72 (54)	< 0.01
Smoking, *n* (%)	80 (65)	79 (63)	80 (60)	85 (63)	0.83
Previous MI, *n* (%)	9 (7)	16 (13)	16 (12)	12 (9)	0.45
Previous CABG, *n* (%)	0 (0)	1 (1)	0 (0)	0 (0)	0.38
Multi-vessel or LMT, *n* (%)	80 (65)	71 (56)	70 (52)	68 (51)	0.096
CKD	62 (50)	48 (38)	39 (29)	31 (23)	< 0.01
Hemodialysis, *n* (%)	8 (7)	2 (2)	4 (3)	1 (1)	< 0.05
Killip classification, *n* (%)					< 0.05
I	88 (72)	104 (83)	115 (86)	111 (83)	
II	14 (11)	12 (10)	11 (8)	10 (7)	
III	6 (5)	7 (6)	5 (4)	7 (5)	
IV	15 (12)	3 (2)	3 (2)	6 (4)	
Forrester classification, *n* (%)	($n=107$)	($n=101$)	($n=120$)	($n=116$)	0.29
I	46 (43)	51 (51)	64 (53)	53 (46)	
II	14 (13)	7 (7)	10 (8)	16 (14)	
III	23 (22)	21 (21)	32 (27)	25 (22)	
IV	24 (22)	22 (22)	14 (12)	22 (19)	
Culprit lesion, *n* (%)					0.22
LMT	7 (6)	3 (2)	1 (1)	3 (2)	
RCA	51 (41)	42 (33)	43 (32)	47 (35)	
LAD	45 (37)	62 (49)	70 (52)	64 (48)	
LCx	20 (16)	19 (15)	20 (15)	20 (15)	
Blood chemistry at admission					
Total cholesterol (mg/dL)	190 ± 41	193 ± 43	202 ± 45	205 ± 46	< 0.05
Triglyceride (mg/dL)	106 ± 86	143 ± 116	135 ± 96	153 ± 101	< 0.01
LDL cholesterol (mg/dL)	119 ± 36	119 ± 39	128 ± 40	129 ± 38	< 0.05
HDL cholesterol (mg/dL)	51 ± 14	46 ± 13	47 ± 11	44 ± 10	< 0.01
Admission glucose (mg/dL)	167 ± 72	166 ± 72	161 ± 60	174 ± 74	0.49
HbA1c (%)	5.7 ± 1.2	5.9 ± 1.1	6.0 ± 1.1	6.4 ± 1.5	< 0.01
BNP (pg/mL)	84 (34–229)	40 (19–172)	45 (16–105)	47 (18–116)	< 0.01
eGFR (mL/min/1.73 m^2)	59 (41–77)	69 (51–84)	71 (56–83)	76 (60–89)	< 0.01
Time to admission (hours)	3.6 (2.2–6.0)	3.4 (2.3–6.4)	3.5 (2.3–6.2)	3.3 (2.1–7.3)	0.89
LVEF at acute phase (%)	45 ± 12	44 ± 11	47 ± 10	45 ± 10	0.28

Values are expressed as mean ± standard deviation, median (interquartile range), or *n* (%)

BMI indicates body mass index, *CABG* coronary artery bypass grafting, *CKD* chronic kidney disease, *CPK* creatinine phosphokinase, *eGFR* estimate glomerular filtration rate, *LMT* left main trunk, *MI* myocardial infarction, *RCA* right coronary artery, *LAD* left ascending artery, *LCx* left circumflex, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *HbA1c* hemoglobin A1c, *BNP* brain natriuretic peptide, *LVEF* left ventricular ejection fraction

Q1 group: BMI < 21.9 kg/m^2; Q2 group: 21.9 ≤ BMI < 24.0 kg/m^2; Q3 group: 24.0 ≤ BMI < 26.0 kg/m^2; Q4 group: BMI ≥ 26.0 kg/m^2

(Killip classification IV) on admission than that of patients in other groups. Although the prevalence of multi-vessel or LMT disease tended to be higher in patients in the Q1 group, there was no significant difference in this prevalence among patients in other groups ($p=0.096$). Patients in the Q1 group had lower levels of total cholesterol, low-density

lipoprotein cholesterol, and triglycerides and higher levels of high-density lipoprotein cholesterol compared with those in patients in the Q4 group. The levels of hemoglobin A1c increased with the BMI. Brain natriuretic peptide levels on admission were significantly higher in patients in the Q1 group than in those in other groups. Estimate glomerular filtration rate (eGFR) was better in the Q4 group, followed by the Q3, Q2, and Q1 groups [76 (60–89), 71 (56–83), 69 (51–84), and 59 (41–77) mL/min/1.73 m^2, respectively; $p < 0.01$]. Moreover, there were more patients with hemodialysis in the Q1 group compared with those in other groups ($p < 0.01$). The time from symptom onset to admission did not differ among the four groups.

Severity of calcification in the culprit lesion

Moderate/severe coronary calcification was observed in 41% of all study patients. The interobserver variability yielded acceptable concordance for no/mild (kappa = 0.90), moderate (kappa = 0.83), and severe (kappa = 0.95) calcifications. As shown in Fig. 1, moderate/severe calcification in the culprit lesion was most frequently observed in the Q1 group, followed by the Q2, Q3, and Q4 groups (72%, 55%, 28%, and 14%, respectively; $p < 0.01$). There was a significant increase in the severity of calcification in the culprit lesion with decrease in BMI level ($p < 0.01$). Patients with moderate/severe coronary calcification were more likely to have a proximal culprit lesion (i.e., in coronary segment 1, 6, or 11, classified according to the definition of the American Heart Association), including LMT, than patients with no/mild calcification (54% versus 33%, respectively; $p < 0.01$) (Table 2). Next, we evaluated the association between renal function and the severity of calcification in the culprit lesion. Patients with CKD ($n = 180$) had more moderate/severe calcification in the culprit compared with those without CKD (58% in patients with CKD vs 33% without CKD, $p < 0.01$).

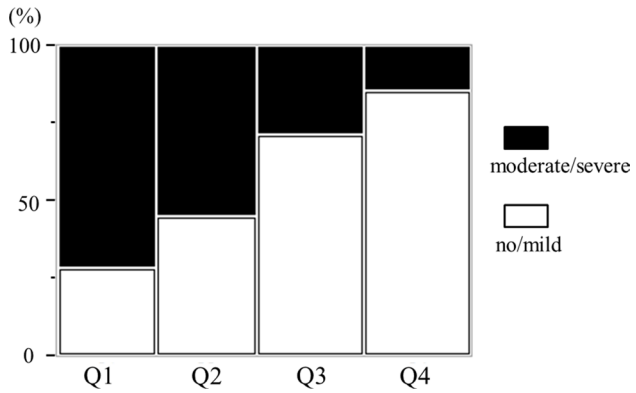

Fig. 1 Prevalence of calcification in the culprit lesion evaluated by coronary angiography stratified by BMI categories

Long-term mortality

The rate of incidence of long-term all-cause mortality is shown in Fig. 2. The Q1 group had the worst all-cause mortality rate, followed by the Q2, Q3, and Q4 groups ($p < 0.01$ by log-rank test) (Fig. 2A). The number of all-cause deaths in the Q1, Q2, Q3, and Q4 groups was 32/123 (26%), 22/126 (18%), 9/134 (7%), and 6/134 (4%), respectively (Table 3). Furthermore, we performed a landmark analysis at 1 month after emergent PCI, because Killip classification IV has a great impact on the short-term mortality in patients with AMI. A landmark analysis revealed that the Q1 group had the worst all-cause mortality rate, followed by the Q2, Q3, and Q4 groups ($p < 0.01$ by log-rank test) (Supplementary Figure). Moreover, patients with moderate/severe coronary calcification had a higher all-cause mortality rate in comparison to those with no/mild calcification ($p < 0.01$ by log-rank test) (Fig. 2B). The number of all-cause deaths in the no/mild and moderate/severe calcification groups was 18/303 (6%) and 51/214 (24%), respectively (Table 3).

We further evaluated impact of the renal function on the all-cause mortality. All-cause mortality was higher in patients with CKD compared with those without CKD (47% in patients with CKD vs 6% without CKD, $p < 0.01$ by log-rank test).

Table 2 Location of the culprit lesion

	No/mild calcification ($n = 303$)	Moderate/severe calcification ($n = 214$)	p value
Proximal culprit lesion, n (%)	101 (33)	115 (54)	< 0.01
LMT	4 (1)	10 (5)	
RCA segment 1	28 (9)	24 (11)	
LAD segment 6	60 (20)	73 (34)	
LCx segment 11	9 (3)	8 (4)	

Values are expressed as n (%)

LMT left main trunk, *RCA* right coronary artery, *LAD* left ascending artery, *LCx* left circumflex

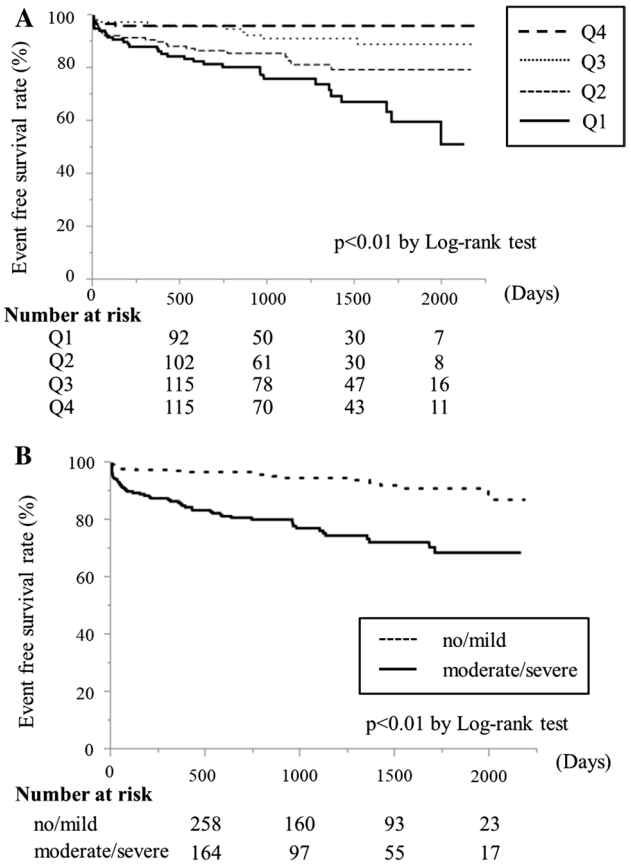

Fig. 2 Kaplan–Meier survival curves in AMI patients. **a** All-cause mortality stratified by BMI categories. **b** All-cause mortality stratified by the severity of calcification in the culprit lesion

Table 3 Mortality stratified by BMI categories and severity of calcification in the culprit lesion

	All-cause death	Cardiovascular death	Non-cardiovascular death
BMI subgroup			
Q1 ($n=123$)	32 (26)	13 (11)	19 (15)
No/mild ($n=35$)	3 (9)	2 (6)	1 (3)
Moderate/severe ($n=88$)	29 (33)	11 (13)	18 (20)
Q2 ($n=126$)	22 (18)	16 (13)	6 (5)
No/mild ($n=57$)	5 (9)	2 (4)	3 (5)
Moderate/severe ($n=69$)	17 (25)	14 (20)	3 (4)
Q3 ($n=134$)	9 (7)	5 (4)	4 (3)
No/mild ($n=96$)	5 (5)	1 (1)	4 (4)
Moderate/severe ($n=38$)	4 (11)	4 (11)	0 (0)
Q4 ($n=134$)	6 (4)	5 (4)	1 (1)
No/mild ($n=115$)	5 (4)	4 (3)	1 (1)
Moderate/severe ($n=19$)	1 (5)	1 (5)	0 (0)
Calcification			
No/mild ($n=303$)	18 (6)	9 (3)	9 (3)
Moderate/severe ($n=214$)	51 (24)	30 (14)	21 (10)

Values are expressed as n (%). Q1 group: BMI < 21.9 kg/m^2; Q2 group: 21.9 ≤ BMI < 24.0 kg/m^2; Q3 group: 24.0 ≤ BMI < 26.0 kg/m^2; Q4 group: BMI ≥ 26.0 kg/m^2

Cardiovascular and non-cardiovascular mortalities

Cardiovascular and non-cardiovascular mortalities were separately analyzed (Table 3). The number of cardiovascular deaths in the Q1, Q2, Q3, and Q4 groups was 13/123 (11%), 16/126 (13%), 5/134 (4%), and 5/134 (4%), respectively, and the number of non-cardiovascular deaths in these groups was 19/123 (15%), 6/126 (5%), 4/134 (3%), and 1/134 (1%), respectively. The number of cardiovascular deaths in the no/mild and moderate/severe calcification groups was 9/303 (3%) and 30/214 (14%), respectively, and the number of non-cardiovascular deaths in these groups was 9/303 (3%) and 21/214 (10%), respectively.

Predictors of all-cause mortality

Owing to a significant association between the presence of coronary calcification and BMI, these valuables were separately analyzed. The results of multivariate Cox proportional hazard analyses for elucidating the predictors of all-cause mortality are shown in Table 4. Even after adjusting for covariates, Q1 and Q2 were associated with all-cause mortality (HR for Q1 3.11, 95% CI 1.34–8.49 and HR for Q2 3.23, 95% CI 1.32–9.13, both $p < 0.01$) (Table 4A). Furthermore, the presence of moderate/severe coronary calcification was associated with all-cause mortality (HR: 1.77, 95% CI: 1.00–3.25, $p < 0.05$) (Table 4B). In both analyses, CKD had the highest HR for all-cause mortality. Moreover, we performed multivariate analysis for the predictor of cardiovascular mortality. When BMI was added in the analysis, age, CKD, Killip classification IV, and LVEF were the independent predictors for cardiovascular mortality, but BMI was not. When the presence of coronary calcification was added in the analysis, age, CKD, DM, Killip classification IV, LVEF, and coronary calcification were the independent predictors for cardiovascular mortality.

To further investigate these associations, the patients were divided into eight groups according to the baseline BMI interquartile ranges and the presence of moderate/severe coronary calcification. Detailed results of mortality are shown in Table 3. The HRs (95% CI) for all-cause mortality in the Q1, Q2, Q3, and Q4 groups with no/mild or moderate/severe calcification were evaluated using the Q4 group with no/mild calcification as a reference. The highest incidence of all-cause mortality was observed in

Table 4 Adjusted hazard ratios for all-cause mortality

	Adjusted HR (95% CI)	*p* value
A		
BMI		
Q4	Reference	
Q3	1.31 (0.47–3.94)	0.61
Q2	3.23 (1.32–9.13)	< 0.01
Q1	3.11 (1.34–8.49)	< 0.01
Age	1.05 (1.02–1.09)	< 0.01
Male gender	1.92 (0.90–4.24)	0.09
Hypertension	0.95 (0.55–1.71)	0.85
Dyslipidemia	0.58 (0.34–0.98)	< 0.05
Diabetes mellitus	1.51 (0.88–2.58)	0.13
Smoking	1.17 (0.64–2.23)	0.62
CKD	3.78 (2.06–7.33)	< 0.01
Multi-vessel or LMT disease	2.14 (1.11–4.56)	< 0.05
Killip classification IV	2.79 (1.41–5.20)	< 0.01
LVEF at acute phase	0.95 (0.93–0.97)	< 0.01
B		
Calcification in culprit lesion		
No/mild	Reference	
Moderate/severe	1.77 (1.00–3.25)	< 0.05
Age	1.05 (1.02–1.08)	< 0.01
Male gender	1.85 (0.88–4.05)	0.11
Hypertension	0.97 (0.56–1.74)	0.91
Dyslipidemia	0.55 (0.32–0.93)	< 0.05
Diabetes mellitus	1.49 (0.89–2.48)	0.13
Smoking	1.28 (0.71–2.42)	0.42
CKD	4.46 (2.45–8.57)	< 0.01
Multi-vessel or LMT disease	1.73 (0.90–3.69)	0.11
Killip classification IV	2.93 (1.49–5.39)	< 0.01
LVEF at acute phase	0.95 (0.93–0.97)	< 0.01

Q1 group: BMI < 21.9 kg/m^2; Q2 group: 21.9 ≤ BMI < 24.0 kg/m^2; Q3 group: 24.0 ≤ BMI < 26.0 kg/m^2; Q4 group: BMI ≥ 26.0 kg/m^2

BMI body mass index, *CKD* chronic kidney disease, *LVEF* left ventricular ejection fraction, *LMT* left main trunk, *HR* hazard ratio, *CI* confidence interval

the Q1 group with moderate/severe calcification, followed by the Q2 group with moderate/severe calcification, both of which were statistically significant (Fig. 3).

ROC curve for predicting all-cause mortality

The optimal cutoff value of BMI for long-term all-cause mortality derived from the ROC curve was 23.6 kg/m^2 (C-statistic = 0.73, $p < 0.01$). The use of this cutoff value indicated a sensitivity, specificity, positive predictive value, and negative predictive value of 78%, 60%, 23%, and 95%, respectively.

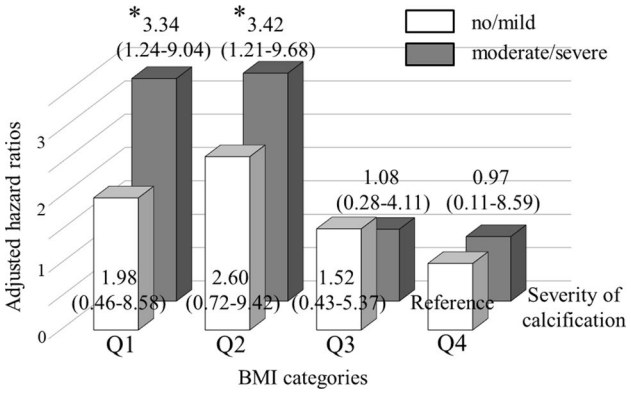

Fig. 3 Adjusted hazard ratios of all-cause mortality stratified by BMI categories and the severity of calcification in the culprit lesion using the Q4 group with no/mild calcification as a reference. Data are shown as hazard ratios and 95% confidence intervals. *$p < 0.05$

Discussion

In the present study, we demonstrated that (1) patients with AMI with a low BMI had a higher mortality rate in comparison to those with a high BMI; (2) patients with AMI with moderate/severe calcification in the culprit lesion had a higher mortality rate in comparison to those with no/mild calcification; (3) moderate/severe calcification in the culprit lesion was most frequently observed in low-BMI patients; (4) the highest mortality was observed in low-BMI patients with moderate/severe calcification in the culprit lesion, and the lowest mortality was observed in high-BMI patients with no/mild calcification; and (5) both BMI and moderate/severe calcification in the culprit lesion were independent predictors of long-term all-cause mortality. Although low-BMI patients with AMI had a lower incidence of coronary risk factors, they had a higher incidence of moderate/severe calcification in the culprit lesion and the highest long-term all-cause mortality. These findings indicate that low BMI and moderate/severe coronary calcification in patients with AMI are likely to be associated with higher mortality.

Associations among BMI, coronary calcification, and mortality

Obesity reduces insulin sensitivity, enhances free fatty acid turnover, increases basal sympathetic tone, induces a hypercoagulable state, and promotes systemic inflammation, all of which contribute to the development and progression of cardiovascular diseases [5]. In the present study, we observed that high-BMI patients with AMI had a higher prevalence of coronary risk factors (i.e., hypertension, dyslipidemia, and DM), which is consistent with the results of other studies [2–4, 15, 19, 20]. Despite such adverse clinical profiles, high-BMI patients with

AMI had a lower long-term all-cause mortality in comparison to low-BMI patients with AMI. These findings are recognized as the "obesity paradox," and our findings support previous reports [6–15]. Moreover, in this study, patients in the Q1 group had a higher prevalence of cardiogenic shock (Killip classification IV) on admission than patients in other groups. Although there was no difference in the culprit lesions among the 4 groups, the prevalence of multi-vessel or LMT disease tended to be higher in patients in the Q1 group ($p = 0.096$). Patients with multi-vessel or LMT disease were known to have worse outcomes compared with those without. Therefore, we think that the higher prevalence of multi-vessel or LMT disease in patients in the Q1 group may contribute to the higher prevalence of cardiogenic shock on admission compared with those in other groups.

Several studies have reported an association between coronary calcification and clinical outcomes in patients undergoing PCI and have revealed that coronary calcification is a predictor of target vessel failure and major adverse events [21–23]. Similarly, patients undergoing CABG who had severe calcification in the lesion exhibited increased mortality [17, 24]. Genereux et al. reported that PCI in patients with AMI with moderately or severely calcified lesions was associated with higher 1-year rates of major adverse cardiac events, including all-cause mortality, myocardial infarction, and target lesion revascularization [16]. These studies support our results that low-BMI patients with AMI had a higher prevalence of moderate/severe calcification in the culprit lesion and higher mortality. Calcified coronary lesions represent an advanced stage in the atherosclerotic process, wherein a soft plaque is converted to a fibrocalcific plaque. It has been reported that coronary calcification is associated with systemic atherosclerosis [25], which might affect mortality. Moreover, our subjects with moderate/severe coronary calcification were more likely to have proximal culprit lesions than those with no/mild calcification, and this association may be related to the increased mortality. Therefore, our finding that patients with AMI with moderate/severe coronary calcification had a higher mortality may be reasonable. However, it remains unclear whether there is a direct association between low BMI and coronary calcification. We compared BMI among the 3 groups divided by the severity of coronary calcification in the culprit lesion. BMI was the highest in the patients with no/mild coronary calcification in the culprit, followed by those with moderate calcification and those with severe calcification (25.5 ± 3.6, 22.8 ± 2.8, and 21.7 ± 3.4 kg/m^2, respectively; $p < 0.01$). These finding suggests a possible association between low BMI and coronary calcification. However, our results were derived from a single-center retrospective analysis, and to the best of our knowledge, there has been no study to clarify the relationship between low BMI and coronary calcification in patients with AMI. Further studies are required to elucidate its underlying mechanisms.

Cardiovascular and non-cardiovascular mortalities

Brian et al. reported that low BMI is a marker of systemic illness in patients treated with PCI, and these patients had a higher prevalence of tumors, leukemia, and lymphoma [3]. Furthermore, other studies have reported that low-BMI patients with cardiovascular disease had higher rates of cachexia-related comorbidities, including cancer, dementia, and hypoalbuminemia [6, 10]. Our study demonstrating that the incidence of non-cardiovascular mortality was the highest in low-BMI patients also supports their results. Moreover, we observed that low- or normal-BMI patients had a higher incidence of cardiovascular death in comparison to high-BMI patients. Thus, both cardiovascular and non-cardiovascular deaths are responsible for higher mortality rates in low-BMI patients with AMI.

Limitations

There are several limitations in the present study. First, our results were derived from a single-center retrospective analysis. Therefore, the generalization of our results would be limited. However, we studied consecutive patients admitted during the study period, which may minimize the biases involved in a retrospective study. Second, the changes in BMI occurring during the follow-up period, which might have impacted long-term mortality, were not assessed [26]. Finally, we evaluated the severity of calcification only in the culprit lesion and did not assess the presence of calcification in segments with non-culprit lesions, which might have affected the outcomes.

Conclusions

Although low-BMI patients with AMI had a lower frequency of coronary risk factors, they had a higher incidence of moderate/severe calcification in the culprit lesion and the highest long-term all-cause mortality in comparison to high-BMI patients. We suggest that calcification in the culprit lesion and its possible association with low BMI are involved in the higher mortality of these patients.

Compliance with ethical standards

Conflict of interest None.

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