Body mass index as a tool for optimizing surgical care in coronary artery bypass grafting through understanding risks of specific complications

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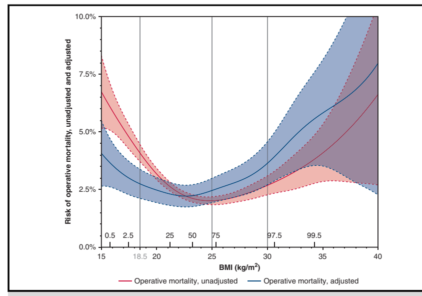
ABSTRACT

Objectives: To investigate the relationship between body mass index (BMI) and early outcomes, and specific types of morbidities associated with low and high BMI, in patients undergoing coronary artery bypass grafting.

Methods: This was a retrospective study on isolated coronary artery bypass grafting patients (aged $\geq$60 years) between 2008 and 2017 in the Japan Cardiovascular Surgery Database. The primary end point was defined as operative mortality. The secondary end point was combined morbidity (ie, operative mortality, reoperation for bleeding, stroke, new onset of hemodialysis, mediastinitis, and prolonged ventilation). Patient characteristics and outcomes were compared among BMI groups. Spline curves were fit between BMI and outcomes. Multivariable logistic regression models with categorized BMI and generalized additive models with spline-transformed BMI were used to estimate and visualize the effect of BMI adjusted for other covariates.

Results: A total of 96,058 patients were included in the analysis. Low (<18.5) and high ($\geq$30) BMI were both associated with a higher risk of mortality (low: adjusted odds ratio, 1.34; 95% confidence interval, 1.16-1.54; $P < .0001$, and high: adjusted odds ratio, 2.10; 95% confidence interval, 1.70-2.59; $P < .0001$) and combined morbidity (low: adjusted odds ratio, 1.18; 95% confidence interval, 1.08-1.29; $P = .0002$ and high: adjusted odds ratio, 1.82; 95% confidence interval, 1.63-2.03; $P < .0001$). Low and high BMI were associated with different types of morbidities. In models using spline transformation, the deviation of BMI from a proximately 21 to 23 was proportionally associated with increased risk.

Conclusions: In patients undergoing coronary artery bypass grafting, low and high BMI were risk factors of mortality associated with different types of morbidities, which may warrant tailored preventive approaches. (J Thorac Cardiovasc Surg 2020;160:409-20)



Correlation between BMI and operative mortality.

Central Message

In patients undergoing CABG, a deviation of BMI from 21 to 23 was proportionally associated with increased adjusted risk of mortality. Low and high BMI were associated with different types of morbidity.

Perspective

The effect of BMI on surgical outcomes in patients undergoing CABG procedure remains controversial. Both high and low BMI increased risk of mortality and were associated with different types of morbidity. These results highlight the importance of preoperative rehabilitation to prevent pneumonia in low BMI and strict blood sugar control and proper graft selection to avoid mediastinitis and leg wound infection in high BMI.

See Commentaries on pages 421 and 423.

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Abbreviations and Acronyms

BITA	= bilateral internal thoracic artery
BMI	= body mass index
BSA	= body surface area
CABG	= coronary artery bypass grafting
ITA	= internal thoracic artery
JCVSD	= Japan Cardiovascular Surgery Database
STS	= Society of Thoracic Surgeons
SVG	= saphenous vein graft

Scanning this QR code will take you to the article title page to access supplementary information.

The effect of relative body weight of patients undergoing cardiac surgery on early and late outcomes has been the subject of major long-standing debate. Multiple studies reported high operative risk associated with high body mass index (BMI) in cardiac surgery.[1-3] In contrast, the concept of the obesity paradox has been described in surgery, and indicates a relationship between obesity and decreased mortality and morbidity compared to normal weight.[4-6] It remains unclear whether high BMI is a risk factor for adverse outcomes after cardiac surgery.

Low BMI is also a risk factor for mortality and adverse outcomes in cardiac surgery.[1,7,8] Despite this, several studies found that low BMI patients are not worse off than normal BMI patients in terms of mortality and morbidity after cardiac surgery.[2,9] Most of these studies were based on a single-institutional experience and dealt with a relatively small sample size. Accordingly, no definitive answers have been obtained regarding the influences of low BMI and high BMI on operative mortality and specific morbidities after cardiac surgery, and even less clear is how such BMI-sensitive risks can be mitigated in patients undergoing cardiac surgery. The objective of this study was to investigate the relationship between body mass index and early mortality and morbidity in patients (aged ≥60 years) who underwent isolated coronary artery bypass grafting (CABG) using a Japanese nationwide database.

METHODS

The Institutional Review Board of The Jikei University approved this study (No. 28-103[8346]) and issued a waiver for obtaining patient consent because of the unconsolidated access to the original data. Clinical trial registry No. UMIN000025042.

Study Population

Data were obtained from a Japanese nationwide clinical database, the Japan Cardiovascular Surgery Database (JCVSD). The JCVSD was established in 2000 to be comparable to the Society of Thoracic Surgeons (STS) National Database in North America.[10,11] The JCVSD Adult Section contains clinical data for cardiovascular surgery from all Japanese hospitals, and included approximately 550,000 cases from 584 institutions as of April 2018. The data collection form contains 255 variables that are nearly identical to those in the STS database. Through the JCVSD web-based system, each participating hospital enters data and uses a feedback report in real time that includes risk-adjusted outcomes based on a comparison with all participating hospitals.

CABG cases of patients aged 60 years or older from January 1, 2008, through December 31, 2017, registered in the JCVSD were included in the analysis. Surgical cases for patients who had undergone previous cardiac operations were excluded, as were salvage operations and surgeries with concomitant procedures, including valve surgery, aortic surgery, and other cardiac and noncardiac surgery. Surgical cases with missing values in any of the following were also excluded: the patient's body weight, height, age at the time of surgery, or operative mortality (Figure 1).

In this study, patients were divided into 4 groups: BMI <18.5 (group 1, low BMI group), 18.5 to 24.9 (group 2), 25 to 29.9 (group 3), and ≥30 (group 4, high BMI group) on the basis of World Health Organization guidelines.[12-14]

Study End Points

The primary end point was defined as operative mortality, and the secondary end point was defined as combined morbidity: operative mortality, reoperation for bleeding, stroke, new onset of hemodialysis, mediastinitis, and prolonged ventilation (more than 24 hours). The definitions of variables including pre- and postoperative morbidity are shown in Tables E1 and E2.

Statistical Analysis

Among BMI groups, Pearson χ^2 test was used to compare categorical variables, and Mann-Whitney-Wilcoxon test was used to compare continuous variables. To visualize the relationship between BMI and outcomes (unadjusted risk), a spline curve was fit to a logit-transformed binary indicator of outcomes. To estimate the effect of BMI adjusted for other covariates, multivariable logistic regression was fit using categorized BMI along with other relevant clinical variables. To visualize the relationship of BMI on outcomes adjusted for other covariates, the adjusted risk of events (mortality and combined morbidity) was calculated as follows. First, generalized additive models of outcomes were developed with spline-transformed BMI using the same covariates as in the aforementioned logistic regression models with categorized BMI. Then, the risk of events was simulated through BMI values of 15.0 through 40.0 using the above generalized additive model assuming the other covariates are either mode (in cases of categorical variables) or median (continuous variables). The adjusted risk of events for each patient was calculated as the simulated risk described above multiplied by the ratio of the observed proportion of patients with events to the mean simulated risk, both in the study cohort. In multivariable modeling, independent variables were selected based on existing literature, and no variable selection method (eg, stepwise selection) was applied.[11,15] A similar analysis was performed with body surface area (BSA).

The frequency of missing values was <0.1% in the majority of variables. Cases with missing values were excluded for the summary of distribution and comparison between groups. For multivariable regression, missing values were replaced with the median (for continuous variables) or mode (for categorical variables). The distribution of categorical variables was presented as proportions of specific levels among cases with a valid recording of the variable. The distribution of continuous variables

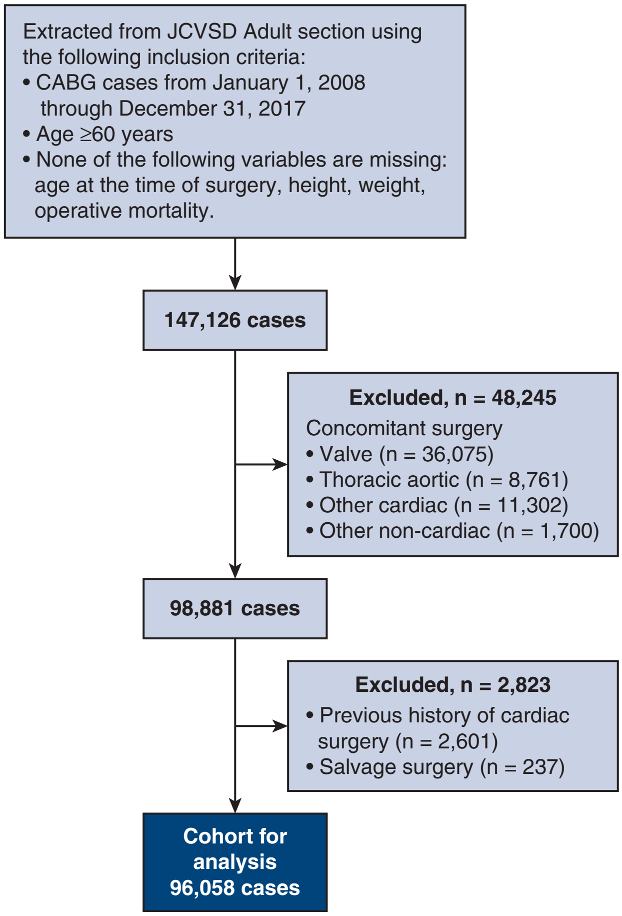

FIGURE 1. Flowchart of patient selection for this study. Data were obtained from the Japan Cardiovascular Surgery Database (*JCVSD*) Adult section. There were 147,126 patients (aged ≥60 years) who underwent coronary artery bypass grafting (*CABG*) from January 1, 2008, through December 31, 2017, and did not have missing values in any of the following variables: age at the time of surgery, height, weight, and operative mortality. Patients who underwent surgeries with concomitant procedures (n = 48,245) were excluded. Then, those with history of previous cardiac surgery (n = 2601) and those who underwent salvage operations (n = 237) were also excluded. The remaining 96,058 patients were included in the analysis.

was presented as the median and quartiles, because most of them had non-normal distribution.

For modeling with generalized additive model with spline transformation, R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria) running package *mgcv* version 1.8-28 was used. For the other statistical analysis, JMP Pro, version 14.2.0 (SAS Institute Inc, Cary, NC) was used.

RESULTS

As in Figure 1, 96,058 patients were included in the study. Patient characteristics stratified by BMI are shown in Table 1 (note that these are crude results, not adjusted for other covariates). Group 1 and 4 contained 5451 (5.7%) and 3242 (3.4%) patients, respectively.

The proportion of hypertension, hyperlipidemia, and diabetes was significantly higher in the high BMI group. In contrast, the low BMI group had a higher proportion of patients with current smoking, congestive heart failure, respiratory failure, and chronic renal failure, lower ejection fraction, urgent or emergent surgery, and preoperative intra-aortic balloon pump support compared with the other groups.

Intraoperative factors are shown in Table 2. Off-pump CABG was performed in more than 60% of all cases. The other CABG group included on-pump beating CABG and CABG with cardiac arrest. There were significant differences among the 4 groups in terms of cardiopulmonary bypass time. The left internal thoracic artery (ITA) was used for approximately 90% of patients, and the right ITA was also used for approximately 30% of patients. The proportion of patients who received intraoperative transfusion was highest in the low BMI group. Postoperative mortalities and morbidities are shown in Table 3. Operative mortality rates were 5.0%, 2.5%, 2.1%, and 3.5% for groups 1, 2, 3, and 4, respectively ($P < .0001$). The proportion of patients with combined morbidity were 14.1%, 10.0%, 10.3%, and 14.5%, respectively ($P < .0001$).

As for a contingency analysis, low BMI (<18.5) and high BMI (≥30) were associated with a higher risk of operative mortality (low BMI: unadjusted odds ratio [uOR], 2.05; 95% confidence interval [95% CI], 1.79-2.33; $P <$. 0001 and high BMI: uOR, 1.41; 95% CI, 1.16-1.71; $P = .0009$) and combined morbidity (low BMI: uOR, 1.49; 95% CI, 1.37-1.61; $P < .0001$ and high BMI: uOR, 1.54; 95%CI, 1.39-1.70; $P < .0001$) compared to reference (18.5≤ BMI <25) (Tables 4 and 5). As for multivariable logistic regression analysis, low (<18.5) BMI was associated with significantly higher operative mortality (adjusted odds ratio [aOR], 1.34; 95% CI, 1.16–1.54; $P < .0001$) and combined morbidity (aOR, 1.18; 95% CI, 1.08-1.29; $P = .0002$). Likewise, high (≥30) BMI was also associated with significantly higher operative mortality (aOR, 2.10; 95% CI, 1.70-2.59; $P < .0001$) and combined morbidity (aOR, 1.82; 95% CI, 1.63-2.03; $P < .0001$) (Tables 4 and 5). To visualize the relative importance of BMI in risk prediction of individual patients, bubble plots were drawn whose *x*- and *y*-axes represent uORs and aORs, respectively, of BMI and the other variables on the outcomes (Figures E1 and E2). Both low (<18.5) and high (≥30) BMI were located near the diagonal line along with conventional risk factors, suggesting that the effects of both low and high BMI were largely not explained by the other variables. The results of spline fit and generalized additive models with spline transformation of BMI are shown in Figures 2 and 3. Spline fit of operative mortality and combined morbidity (unadjusted risk) showed that a BMI of approximately 23 to 25 was associated with the lowest risk. Generalized additive models with a spline transformation of BMI

TABLE 1. Preoperative patient characteristics

Variable	Total	Body mass index <18.5	18.5-24.9	25.0-29.9	≥30.0	*P* value
No. of patients	96,058	5451	63,403	23,962	3242	
Year of surgery						<.0001
2008-2009	12,023 (12.5)	640 (11.7)	7980 (12.6)	3057 (12.8)	346 (10.7)	
2010-2011	15,102 (15.7)	841 (15.4)	10,040 (15.8)	3769 (15.7)	452 (13.9)	
2012-2013	23,538 (24.5)	1341 (24.6)	15,556 (24.5)	5813 (24.3)	828 (25.5)	
2014-2015	23,245 (24.2)	1312 (24.1)	15,408 (24.3)	5743 (24.0)	782 (24.1)	
2016-2017	22,150 (23.1)	1317 (24.2)	14,419 (22.7)	5580 (23.3)	834 (25.7)	
Age (y)						<.0001
60-64	15,793 (16.4)	629 (11.5)	9479 (15.0)	4794 (20.0)	891 (27.5)	
65-59	21,525 (22.4)	1018 (18.7)	13,954 (22.0)	5753 (24.0)	800 (24.7)	
70-74	23,397 (24.4)	1182 (21.7)	15,654 (24.7)	5842 (24.4)	719 (22.2)	
75-79	21,364 (22.2)	1341 (24.6)	14,525 (22.9)	4943 (20.6)	555 (17.1)	
≥80	13,979 (14.6)	1281 (23.5)	9791 (15.4)	2630 (11.0)	277 (8.5)	
Female sex	22,111 (23.0)	1814 (33.3)	13,890 (21.9)	5277 (22.0)	1130 (34.9)	<.0001
Body height (cm)	161 (155-166)	160 (152-165)	161 (155-166)	162 (155-167)	160 (151-166)	<.0001
Body weight (kg)	60.0 (53.0-67.0)	44.0 (40.0-48.0)	57.5 (52.0-62.8)	69.5 (64.0-74.5)	81.0 (73.8-87.8)	<.0001
Body surface area (m^2)	1.63 (1.51-1.74)	1.42 (1.32-1.51)	1.60 (1.50-1.69)	1.74 (1.63-1.83)	1.84 (1.70-1.95)	<.0001
Body mass index	23.2 (21.2-25.4)	17.6 (16.8-18.1)	22.4 (20.9-23.6)	26.5 (25.7-27.7)	31.5 (30.6-33.0)	<.0001
Current smoker	14,336 (14.9)	893 (16.4)	9471 (14.9)	3536 (14.8)	436 (13.4)	.0016
Diabetes mellitus						<.0001
No diabetes	45,527 (47.4)	2902 (53.2)	30,877 (48.7)	10,709 (44.7)	1039 (32.0)	
Noninsulin dependent	36,148 (37.6)	1758 (32.3)	23,341 (36.8)	9519 (39.7)	1530 (47.2)	
Insulin dependent	14,382 (15.0)	791 (14.5)	9185 (14.5)	3733 (15.6)	673 (20.8)	
Hyperlipidemia	58,747 (61.2)	2530 (46.4)	37,533 (59.2)	16,316 (68.1)	2368 (73.0)	<.0001
Chronic renal failure (eGFR)						<.0001
≥60	55,527 (57.8)	3073 (56.4)	36,494 (57.6)	14,012 (58.5)	1948 (60.1)	
45-59	18,389 (19.1)	766 (14.1)	11,961 (18.9)	5067 (21.1)	595 (18.4)	
30-44	8812 (9.2)	475 (8.7)	5699 (9.0)	2341 (9.8)	297 (9.2)	
15-29	3708 (3.9)	216 (4.0)	2472 (3.9)	889 (3.7)	131 (4.0)	
≤14	1038 (1.1)	75 (1.4)	718 (1.1)	204 (0.9)	41 (1.3)	
Hemodialysis	8584 (8.9)	846 (15.5)	6059 (9.6)	1449 (6.0)	230 (7.1)	
Serum creatinine (mg/dL)	0.9 (0.75-1.1)	0.86 (0.69-1.11)	0.9 (0.74-1.1)	0.9 (0.77-1.1)	0.9 (0.75-1.13)	<.0001
eGFR (mL/min/1.73 m^2)	67.6 (52.7-87.4)	73.5 (52.7-101.2)	67.8 (52.8-87.2)	66.5 (52.5-85.0)	69.3 (53.0-91.9)	<.0001
Hypertension	75,807 (78.9)	3924 (72.0)	49,131 (77.5)	19,926 (83.2)	2826 (87.2)	<.0001
Chronic lung disease						<.0001
No	82,896 (86.3)	4430 (81.3)	54,710 (86.3)	20,950 (87.4)	2806 (86.6)	
Mild	10,619 (11.1)	718 (13.2)	6994 (11.0)	2551 (10.6)	356 (11.0)	
Moderate or severe	2543 (2.6)	303 (5.6)	1699 (2.7)	461 (1.9)	80 (2.5)	
Immunosuppressive treatment	1662 (1.7)	145 (2.7)	1122 (1.8)	339 (1.4)	56 (1.7)	<.0001
Peripheral vascular disease	16,627 (17.3)	1336 (24.5)	11,297 (17.8)	3506 (14.6)	488 (15.1)	<.0001
CVD*						<.0001
None	77,603 (80.8)	4273 (78.4)	50,995 (80.4)	19,620 (81.9)	2715 (83.7)	
CVD, no CVA	9305 (9.7)	596 (10.9)	6261 (9.9)	2176 (9.1)	272 (8.4)	
CVA	9147 (9.5)	581 (10.7)	6145 (9.7)	2166 (9.0)	255 (7.9)	
PCI ≤6 h	892 (1.0)	56 (1.1)	563 (1.0)	236 (1.1)	37 (1.3)	.2626
Myocardial infarction						<.0001
≤6 h	1547 (1.6)	104 (1.9)	1037 (1.6)	355 (1.5)	51 (1.6)	

(Continued)

TABLE 1. Continued

Variable	Total	Body mass index				P value
		<18.5	18.5-24.9	25.0-29.9	≥30.0	
6-24 h	2652 (2.8)	185 (3.4)	1767 (2.8)	623 (2.6)	77 (2.4)	
1-21 d	4840 (5.0)	303 (5.6)	3298 (5.2)	1080 (4.5)	159 (4.9)	
21 d or none	87,019 (90.6)	4859 (89.1)	57,301 (90.4)	21,904 (91.4)	2955 (91.1)	
CHF and NYHA functional class						<.0001
No CHF	75,087 (78.2)	3841 (70.5)	49,427 (78.0)	19,333 (80.7)	2486 (76.7)	
NYHA I-III	15,743 (16.4)	1142 (21.0)	10,503 (16.6)	3522 (14.7)	576 (17.8)	
NYHA IV	5223 (5.4)	466 (8.5)	3470 (5.5)	1107 (4.6)	180 (5.6)	
Angina pectoris and CCS						<.0001
No angina pectoris, CCS I or II	63,149 (65.7)	3331 (61.1)	41,611 (65.6)	16,118 (67.3)	2089 (64.4)	
CCS III	18,386 (19.1)	1104 (20.3)	12,128 (19.1)	4490 (18.7)	664 (20.5)	
CCS IV	12,947 (13.5)	905 (16.6)	8612 (13.6)	2983 (12.4)	447 (13.8)	
Angina pectoris and type						<.0001
No angina pectoris	13,037 (13.6)	939 (17.2)	8650 (13.6)	3038 (12.7)	410 (12.6)	
Stable angina pectoris	50,873 (53.0)	2581 (47.3)	33,309 (52.5)	13,229 (55.2)	1754 (54.1)	
Unstable angina pectoris	32,130 (33.4)	1929 (35.4)	21,431 (33.8)	7692 (32.1)	1078 (33.3)	
Cardiogenic shock	3668 (3.8)	272 (5.0)	2486 (3.9)	802 (3.3)	108 (3.3)	<.0001
Atrial fibrillation or atrial flutter	3870 (4.0)	251 (4.6)	2515 (4.0)	959 (4.0)	145 (4.5)	.0715
Sustained VT or VF	1466 (1.5)	107 (2.0)	989 (1.6)	321 (1.3)	49 (1.5)	.0047
Inotropic agents	1709 (2.9)	133 (3.9)	1151 (3.0)	375 (2.6)	50 (2.7)	.0005
Status						<.0001
Elective	78,462 (81.7)	4270 (78.3)	51,689 (81.5)	19,811 (82.7)	2692 (83.0)	
Urgent	10,765 (11.2)	700 (12.8)	7169 (11.3)	2550 (10.6)	346 (10.7)	
Emergent	6828 (7.1)	480 (8.8)	4543 (7.2)	1601 (6.7)	204 (6.3)	
No. of obstructed coronary arteries						.2337
≤1	7103 (7.4)	420 (7.7)	4687 (7.4)	1748 (7.3)	248 (7.6)	
2	24,195 (25.2)	1386 (25.4)	16,018 (25.3)	6037 (25.2)	754 (23.3)	
3	64,760 (67.4)	3645 (66.9)	42,698 (67.3)	16,177 (67.5)	2240 (69.1)	
Left main disease	40,906 (42.6)	2362 (43.3)	27,475 (43.3)	9838 (41.1)	1231 (38.0)	<.0001
LVEF (%)						<.0001
≥61	47,481 (49.4)	2103 (38.6)	31,118 (49.1)	12,602 (52.6)	1658 (51.1)	
30-60	42,521 (44.3)	2689 (49.3)	28,116 (44.3)	10,303 (43.0)	1413 (43.6)	
≤29	6056 (6.3)	659 (12.1)	4169 (6.6)	1057 (4.4)	171 (5.3)	
Moderate or severe aortic insufficiency	853 (0.9)	73 (1.3)	587 (0.9)	172 (0.7)	21 (0.6)	<.0001
Aortic stenosis	3376 (3.5)	265 (4.9)	2236 (3.5)	765 (3.2)	110 (3.4)	<.0001
Moderate or severe mitral insufficiency	2297 (2.4)	250 (4.6)	1617 (2.6)	385 (1.6)	45 (1.4)	<.0001
Moderate or severe tricuspid insufficiency	977 (1.0)	144 (2.6)	680 (1.1)	136 (0.6)	17 (0.5)	<.0001
Preoperative IABP	16,333 (17.0)	1049 (19.2)	10,947 (17.3)	3812 (15.9)	525 (16.2)	<.0001

Values are presented as n (%) or median (interquartile range). *eGFR*, Estimated glomerular filtration rate; *CVD*, cerebrovascular disease; *CVA*, cerebrovascular attack; *PCI*, percutaneous coronary intervention; *CHF*, congestive heart failure; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *VT*, ventricular tachycardia; *VF*, ventricular fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump. *CVD includes noninvasive arterial imaging test demonstrating ≥75% stenosis of any of the major extracranial or intracranial vessels to the brain.

(adjusted risk) showed that, both for mortality and morbidity, a BMI of approximately 21 to 23 was associated with the lowest risk. For comparison, the results of a similar analysis with BSA are shown in Figures E3 and E4. In contrast to the correlation between BMI and outcomes, which was observed throughout the range of BMI in the study population, the correlation between BSA and outcomes was clearly observed only with the outlier values; that is, approximately <2.5 and >97.5 percentiles of BSA.

DISCUSSION

The major findings of the present study based on a nationwide surgical registry are as follows: in patients undergoing isolated CABG, both low (<18.5) BMI and high (≥30.0)

TABLE 2. Intraoperative patient characteristics

Variable	Total	Body mass index <18.5	Body mass index 18.5-24.9	Body mass index 25.0-29.9	Body mass index ≥30.0	*P* value
No. of patients	96,058	5451	63,403	23,962	3242	
Use of CPB*						
On pump	34,104 (35.5)	1951 (35.8)	22,491 (35.5)	8469 (35.3)	1193 (36.8)	.4115
Off pump	61,954 (64.5)	3500 (64.2)	40,912 (64.5)	15,493 (64.7)	2049 (63.2)	
Intraoperative transfusion	57,901 (60.3)	4159 (76.3)	39,234 (61.9)	12,702 (53.0)	1806 (55.7)	<.0001
Graft harvested						<.0001
No ITA	11,504 (12.0)	754 (13.8)	7688 (12.1)	2685 (11.2)	377 (11.6)	
Only LITA	53,934 (56.1)	3226 (59.2)	35,588 (56.1)	13,244 (55.3)	1876 (57.9)	
Only RITA	1815 (1.9)	141 (2.6)	1254 (2.0)	370 (1.5)	50 (1.5)	
Bilateral ITA	28,805 (30.0)	1330 (24.4)	18,873 (29.8)	7663 (32.0)	939 (29.0)	
Left radial	8687 (9.0)	335 (6.1)	5581 (8.8)	2451 (10.2)	320 (9.9)	<.0001
Right radial	1480 (1.5)	61 (1.1)	954 (1.5)	401 (1.7)	64 (2.0)	.0033
GEA	6668 (6.9)	291 (5.3)	4224 (6.7)	1917 (8.0)	236 (7.3)	<.0001
No. of grafts harvested - SVG						<.0001
0	27,323 (28.4)	1471 (27.0)	17,852 (28.2)	7074 (29.5)	926 (28.6)	
1	41,887 (43.6)	2340 (42.9)	27,584 (43.5)	10,533 (44.0)	1430 (44.1)	
≥2	26,811 (27.9)	1637 (30.0)	17,945 (28.3)	6344 (26.5)	885 (27.3)	
No. of anastomoses by graft						
LITA						<.0001
0	7301 (7.6)	579 (10.6)	4902 (7.7)	1590 (6.6)	230 (7.1)	
1	82,978 (86.4)	4614 (84.6)	54,793 (86.4)	20,790 (86.8)	2781 (85.8)	
≥2	5779 (6.0)	258 (4.7)	3708 (5.8)	1582 (6.6)	231 (7.1)	
RITA						<.0001
0	64,463 (67.1)	3931 (72.1)	42,539 (67.1)	15,760 (65.8)	2233 (68.9)	
1	29,309 (30.5)	1415 (26.0)	19,326 (30.5)	7638 (31.9)	930 (28.7)	
≥2	2286 (2.4)	105 (1.9)	1538 (2.4)	564 (2.4)	79 (2.4)	
Lt radial						<.0001
0	87,002 (90.6)	5098 (93.5)	57,581 (90.8)	21,415 (89.4)	2908 (89.7)	
1	6009 (6.3)	245 (4.5)	3813 (6.0)	1721 (7.2)	230 (7.1)	
≥2	3047 (3.2)	108 (2.0)	2009 (3.2)	826 (3.4)	104 (3.2)	
Rt radial						.0183
0	94,461 (98.3)	5386 (98.8)	62,374 (98.4)	23,525 (98.2)	3176 (98.0)	
1	995 (1.0)	40 (0.7)	641 (1.0)	270 (1.1)	44 (1.4)	
≥2	602 (0.6)	25 (0.5)	388 (0.6)	167 (0.7)	22 (0.7)	
GEA						<.0001
0	88,825 (92.5)	5129 (94.1)	58,807 (92.8)	21,902 (91.4)	2987 (92.1)	
1	5850 (6.1)	265 (4.9)	3699 (5.8)	1680 (7.0)	206 (6.4)	
≥2	1383 (1.4)	57 (1.0)	897 (1.4)	380 (1.6)	49 (1.5)	
SVG						<.0001
0	21,781 (22.7)	1140 (20.9)	14,211 (22.4)	5680 (23.7)	750 (23.1)	
1	28,228 (29.4)	1599 (29.3)	18,545 (29.2)	7165 (29.9)	919 (28.3)	
≥2	46,049 (47.9)	2712 (49.8)	30,647 (48.3)	11,117 (46.4)	1573 (48.5)	
No. of anastomosis by coronary artery						
LAD						.0474
0	3404 (3.5)	174 (3.2)	2189 (3.5)	907 (3.8)	134 (4.1)	
1	90,108 (93.8)	5140 (94.3)	59,538 (93.9)	22,418 (93.6)	3012 (92.9)	
≥2	2546 (2.7)	137 (2.5)	1676 (2.6)	637 (2.7)	96 (3.0)	
Dx						.0008
0	64,860 (67.5)	3698 (67.8)	42,544 (67.1)	16,340 (68.2)	2278 (70.3)	
1	29,383 (30.6)	1658 (30.4)	19,623 (30.9)	7194 (30.0)	908 (28.0)	
≥2	1815 (1.9)	95 (1.7)	1236 (1.9)	428 (1.8)	56 (1.7)	

(Continued)

TABLE 2. Continued

Variable	Total	Body mass index <18.5	18.5-24.9	25.0-29.9	≥30.0	*P* value
LCx						<.0001
0	23,094 (24.0)	1583 (29.0)	15,108 (23.8)	5604 (23.4)	799 (24.6)	
1	56,042 (58.3)	3096 (56.8)	37,082 (58.5)	14,028 (58.5)	1836 (56.6)	
≥2	16,922 (17.6)	772 (14.2)	11,213 (17.7)	4330 (18.1)	607 (18.7)	
RCA						<.0001
0	32,830 (34.2)	1936 (35.5)	21,922 (34.6)	7965 (33.2)	1007 (31.1)	
1	53,016 (55.2)	3034 (55.7)	34,855 (55.0)	13,256 (55.3)	1871 (57.7)	
≥2	10,212 (10.6)	481 (8.8)	6626 (10.5)	2741 (11.4)	364 (11.2)	
No. of anastomoses - Total						<.0001
1	6803 (7.1)	490 (9.0)	4562 (7.2)	1524 (6.4)	227 (7.0)	
2	22,793 (23.7)	1436 (26.3)	14,920 (23.5)	5705 (23.8)	732 (22.6)	
3	35,527 (37.0)	1972 (36.2)	23,372 (36.9)	8943 (37.3)	1240 (38.2)	
4	21,769 (22.7)	1127 (20.7)	14,485 (22.8)	5424 (22.6)	733 (22.6)	
≥5	7235 (7.5)	345 (6.3)	4799 (7.6)	1840 (7.7)	251 (7.7)	
Aorta nontouch	21,706 (22.6)	1279 (23.5)	14,239 (22.5)	5489 (22.9)	699 (21.6)	.0948
Aorta crossclamp	18,047 (18.8)	916 (16.8)	11,840 (18.7)	4659 (19.4)	632 (19.5)	<.0001
Aorta sideclamp	21,794 (22.7)	1192 (21.9)	14,397 (22.7)	5437 (22.7)	768 (23.7)	.2678
Aorta suture device	34,494 (35.9)	2063 (37.9)	22,916 (36.1)	8372 (34.9)	1143 (35.3)	.0001
Operative time (min)	310 (250-377)	300 (240-370)	307 (250-374)	316 (256-384)	330 (269-402)	<.0001
Perfusion time (min)	135 (105-171)	130 (100-168)	134 (104-170)	138 (108-174)	143 (108-181)	<.0001

Values are presented as n (%) or median (interquartile range). *CPB*, Cardiopulmonary bypass; *ITA*, internal thoracic artery; *LITA*, left internal thoracic artery; *RITA*, right internal thoracic artery; *GEA*, gastroepiploic artery; *SVG*, saphenous vein graft; *Lt radial*, left radial artery; *Rt radial*, right radial artery; *LAD*, left anterior descending coronary artery; *Dx*, diagonal branch; *LCx*, left circumflex artery; *RCA*, right coronary artery. *Perfusion time was only determined for patients who had on-pump CABG.

BMI were associated with an increased risk of operative mortality and combined morbidity, the increased risk associated with low BMI and high BMI was independent from other covariates, deviation of BMI from 21 to 23 was proportionally associated with increased risk of mortality and morbidity, and specific types of morbidities associated with low BMI and high BMI were different.

Obesity is a well-known risk factor for adverse health outcomes[16-18] and has become an important issue in Western countries.[19] It has also been widely assumed that obesity has a strong influence on the development of cardiovascular disease and increases the risk for major complications after cardiac operations. Van Straten and colleagues[1] reported that morbid obesity is an independent predictor of late mortality after CABG. Devarajan and colleagues[2] reported that obesity was associated with increased pulmonary morbidity after CABG. In contrast, some recent reports have indicated that obese patients have better short- and long-term outcomes after cardiac surgery, which is well known as the obesity paradox in Western countries.[4-6] The mechanism of this paradox remains unclear.

Regarding mortality, previous studies have shown that patients with low BMI have a higher mortality: Engelman and colleagues[7] reported that low (<20) BMI and low (<2.5 g/dL) albumin level were risk factors of postoperative mortality for CABG, valve surgery, or combined CABG/valve surgery. Thourani and colleagues[8] also reported that patients with BMI ≤24 were at significantly increased risk of in-hospital and long-term mortality after valvular surgery. Both of those studies were based on single-institutional experiences including CABG and different types of valve surgery. In contrast, our current study is based on more than 96,000 patients undergoing isolated CABG extracted from a Japanese national surgical registry.

Different multiple mechanisms may be involved in the increased risk of operative mortality in patients with low or high BMI undergoing CABG. A higher rate of low BMI patients (group 1) had worse preoperative conditions compared to the other patients (groups 2, 3, and 4) (Table 1). For example, they had a higher proportion of preoperative intra-aortic balloon pump, low ejection fraction, congestive heart failure, chronic lung disease, chronic renal failure, and emergent situations. They also had a higher incidence of intraoperative transfusion, which is well known as a risk factor of adverse outcomes in cardiac surgery.[20] These factors are likely to explain the high mortality in low BMI patients to some degree, but not entirely (Tables 4 and 5, Figures E1 and E2).

In contrast, high BMI (ie, obese) patients had a higher prevalence of hypertension, hyperlipidemia, and diabetes.[21] The combination of hypertension with obesity may cause a synergetic effect on the sympathetic nerve system, renal and

TABLE 3. Postoperative mortalities and morbidities

Variable	Total	Body mass index <18.5	18.5-24.9	25.0-29.9	≥30.0	*P* value
Number of patients	96,058	5451	63,403	23,962	3242	
Operative mortality	2469 (2.6)	271 (5.0)	1581 (2.5)	504 (2.1)	113 (3.5)	<.0001
Combined morbidity	10,013 (10.4)	770 (14.1)	6316 (10.0)	2456 (10.3)	471 (14.5)	<.0001
Intubation time (h)	12 (5-18)	13 (6-20)	12 (5-18)	12 (5-18)	15 (6-24)	<.0001
Prolonged ventilation	4764 (5.0)	387 (7.1)	2899 (4.6)	1237 (5.2)	241 (7.4)	<.0001
ICU stay (d)	3 (2-4)	3 (2-5)	3 (2-4)	3 (2-4)	3 (2-5)	<.0001
ICU stay ≥8 d	8103 (8.4)	687 (12.6)	5136 (8.1)	1887 (7.9)	393 (12.1)	<.0001
Stroke	1587 (1.7)	96 (1.8)	1053 (1.7)	378 (1.6)	60 (1.9)	.565
TIA	1181 (1.2)	94 (1.7)	790 (1.2)	261 (1.1)	36 (1.1)	.0015
Postoperative renal failure	3455 (3.6)	230 (4.2)	2157 (3.4)	891 (3.7)	177 (5.5)	<.0001
New onset of hemodialysis	2084 (2.2)	144 (2.6)	1297 (2.0)	533 (2.2)	110 (3.4)	<.0001
Perioperative MI	719 (0.7)	38 (0.7)	481 (0.8)	176 (0.7)	24 (0.7)	.9508
AV block/PMI	403 (0.4)	30 (0.6)	275 (0.4)	89 (0.4)	9 (0.3)	.1427
New onset atrial fibrillation	13,295 (13.8)	786 (14.4)	8573 (13.5)	3441 (14.4)	495 (15.3)	.0005
Cardiac arrest	1252 (1.3)	106 (1.9)	813 (1.3)	270 (1.1)	63 (1.9)	<.0001
Anticoagulant complication	359 (0.4)	31 (0.6)	229 (0.4)	84 (0.4)	15 (0.5)	.0762
Tamponade	824 (0.9)	61 (1.1)	515 (0.8)	212 (0.9)	36 (1.1)	.0358
Reoperation for bleeding	1442 (1.5)	114 (2.1)	975 (1.5)	316 (1.3)	37 (1.1)	<.0001
Pulmonary embolism	87 (0.1)	5 (0.1)	52 (0.1)	23 (0.1)	7 (0.2)	.1015
Gastrointestinal complication	1238 (1.3)	133 (2.4)	805 (1.3)	261 (1.1)	39 (1.2)	<.0001
Postoperative infection (mediastinitis, leg wound infection, pneumonia, or septicemia)	5698 (5.9)	471 (8.6)	3525 (5.6)	1394 (5.8)	308 (9.5)	<.0001
Mediastinitis	1412 (1.5)	87 (1.6)	828 (1.3)	396 (1.7)	101 (3.1)	<.0001
Leg wound infection	1769 (1.8)	100 (1.8)	1042 (1.6)	500 (2.1)	127 (3.9)	<.0001
Pneumonia	2356 (2.5)	298 (5.5)	1511 (2.4)	460 (1.9)	87 (2.7)	<.0001
Septicemia	1087 (1.1)	85 (1.6)	674 (1.1)	275 (1.1)	53 (1.6)	.0003
MOF	945 (1.0)	80 (1.5)	620 (1.0)	200 (0.8)	45 (1.4)	<.0001
Readmission	1914 (2.0)	115 (2.1)	1209 (1.9)	503 (2.1)	87 (2.7)	.0071

Values are presented as n (%) or median (interquartile range). These are crude results. *ICU*, Intensive care unit; *TIA*, transient ischemic attack; *MI*, myocardial infarction; *AV*, atrioventricular; *PMI*, pace maker implantation; *MOF*, multiple organ failure.

adrenal function, the adipokines, endothelium, and insulin resistance.[22] Obesity and hypertension may also cause alterations in artery structure and function. In this study, a higher proportion of patients with triple-vessel coronary diseases were recognized in the high BMI group. Hyperlipidemia and a high level of blood sugar are well known risk factors of atherosclerosis. It is also accepted that inadequate blood sugar control during the pre-, intra-, and immediate postoperative period has a negative influence on wound healing. Patients with diabetes also tend to be vulnerable to infections, including mediastinitis. These factors are likely to contribute to the high mortality in high BMI patients, but do not fully explain the effect of high BMI on mortality (Tables 4 and 5, Figures E1 and E2).

Although the current analysis showed that both low (<18.5) and high (≥30) BMI were associated with operative mortality and combined morbidity, low and high BMI may differ regarding the degree to which their correlation with outcomes are explained by the other preoperative patient features. As shown in Figures E1 and E2, the aORs of high BMI were higher than the uORs, whereas the aORs of low BMI were lower than the uORs. Although those findings are insufficient to conclude the relative contribution of the other preoperative patient features to the crude correlation between BMI and outcomes, the correlation between low BMI and outcomes may be explained to some extent by other preoperative conditions, such as congestive heart failure

TABLE 4. Unadjusted and adjusted odds ratios for operative mortality (for each body mass index [BMI] group)

BMI	Estimate (95% Confidence interval)	*P* value
Unadjusted odds ratio		
<18.5	2.05 (1.79-2.33)	<.0001
18.5-24.9	Reference	
25.0-29.9	0.84 (0.76-0.93)	.0006
≥30.0	1.41 (1.16-1.71)	.0009
Adjusted odds ratio		
<18.5	1.34 (1.16-1.54)	<.0001
18.5-24.9	Reference	
25.0-29.9	1.15 (1.03-1.28)	.0137
≥30.0	2.10 (1.70-2.59)	<.0001

Adjusted odds ratios of the other covariates are presented in Table E3.

and chronic lung disease, whereas that of high BMI may be more independent from other preoperative comorbidities, including hypertension and diabetes. This may reflect the negative influence of typical features of high BMI patients; for example, a large physique and fat accumulation, as discussed earlier.

Whereas both low and high BMI were associated with a high risk of combined morbidity compared with the reference group, the risk of specific postoperative morbidities differed between the low and high BMI groups. For example, pneumonia was more common among low BMI patients, whereas leg wound infection was more common among high BMI patients. The mechanism underlying why low BMI patients are prone to pneumonia may be partly explained by a decrease in nutritional intake. The functional reserve as well as recovery of respiratory function after operation may be limited in low BMI patients.[23] Pneumonia can be caused not only by compromised immunity but also by difficulty in expectoration of discharge as a result of respiratory muscle atrophy.[24] Thus, more attention should be paid to low BMI patients in terms of their perioperative nourishment, inflammatory reactions, and respiratory condition. The high risk of postoperative pneumonia in low BMI patients highlights the importance of preoperative preventive measures such as cessation of smoking, training of respiratory muscles, and omission of the nasogastric tube.[25,26]

TABLE 5. Unadjusted and adjusted odds ratios for combined morbidity (for each body mass index [BMI] group)

BMI	Estimate (95% Confidence interval)	*P* value
Unadjusted odds ratio		
<18.5	1.49 (1.37-1.61)	<.0001
18.5-24.9	Reference	
25.0-29.9	1.03 (0.98-1.08)	.2074
≥30.0	1.54 (1.39-1.70)	<.0001
Adjusted odds ratio		
<18.5	1.18 (1.08-1.29)	.0002
18.5-24.9	Reference	
25.0-29.9	1.21 (1.15-1.27)	<.0001
≥30.0	1.82 (1.63-2.03)	<.0001

Adjusted odds ratios of the other covariates are presented in Table E4.

The reasons underlying the higher prevalence of leg infection in high BMI patients remain unclear. Terada and colleagues[27] reported that infection risk was 3 times higher in BMI ≥40 patients compared with normal BMI patients after CABG in a Canadian registry of 7560 patients (aOR, 3.29; 95% CI, 2.30-4.71; $P < .001$). In the highly obese group (BMI ≥40), the incidence of complications within 1 month after operation was 56% higher than that of the normal-weight group (BMI, 18.5-24.9) (aOR, 1.56; 95% CI, 1.21-2.01; $P = .001$), and was elevated by 35% over the moderately obese group (BMI, 35-39.9) (aOR, 1.35; 95% CI, 1.11-1.63; $P = .002$).[27] It is also well known that a higher prevalence of wound infection and delayed traumatic healing may be partly explained by insufficient blood sugar control. Although we do not have detailed data on blood sugar levels, the higher prevalence of diabetes might at least partly explain the reason why high BMI patients tend to have skin wound infections as well as mediastinitis.

Although all arterial grafts might be an additional risk factor for sternal complications in patients with obesity, this is controversial. A recent randomized trial by Taggart and colleagues[28] indicated that bilateral ITA (BITA) increased the risk of sternal wound complication as well as sternal wound reconstruction. On the other hand, Vrancic and colleagues[29] suggested that "BITA did not increase the risk of mediastinitis in the total population or in the propensity score matched subgroups." In the current study, there were no significant differences in the incidence of mediastinitis among patients undergoing CABG with no ITA grafts, single ITA, and BITAs (data not shown).

For high BMI patients with diabetes mellitus, strict control of preoperative, intraoperative, and immediate postoperative blood sugar level may be important to avoid mediastinitis and leg wound infection.[30] Shortening operative time may also be effective in reducing the incidence of surgical site infection.[31] A strategy of all arterial graft CABG (ie, avoidance of SVG harvesting) may also reduce the risk of leg wound infection.[32] Although all arterial grafts might increase operative time, our data indicated that there was no significant difference in operative time between patients with all arterial grafts and those with arterial and venous grafts (data not shown). In each BMI group of our study cohort, 2 or more harvested SVGs had a significant correlation with a higher incidence of leg would infection (Figure E5), which highlights the probable effectiveness of minimizing the number of SVG harvesting sites in avoiding leg wound infection, even in the case that a SVG is necessary for complete revascularization.

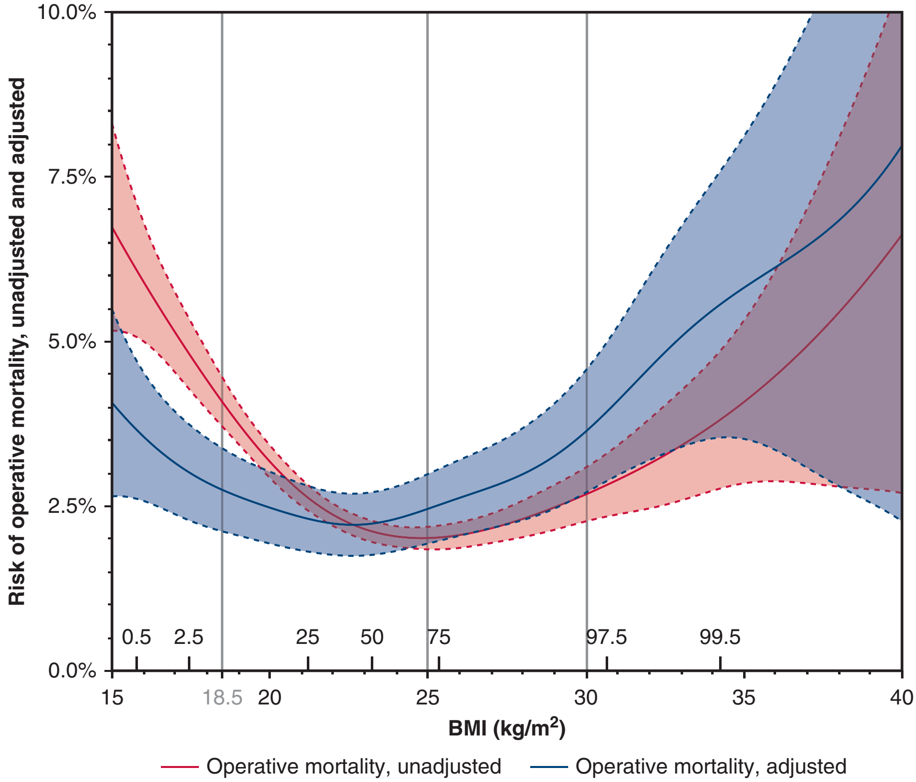

FIGURE 2. Correlation between body mass index (*BMI*) and operative mortality (unadjusted and covariate adjusted mortality). The results of spline fit and a generalized additive model with spline transformation of BMI are shown for mortality. The *red line* indicates unadjusted mortality, and the *blue line* indicates adjusted mortality. *Shaded areas* represent 95% confidence intervals. *Ticks* on the *x*-axis indicate percentiles of BMI in the study population. As for unadjusted mortality, a BMI of approximately 25 was associated with the lowest risk. Regarding adjusted mortality, a BMI of approximately 21 to 23 was associated with the lowest risk.

Existing risk prediction scores in cardiovascular surgery (eg, European System for Cardiac Operative Risk Evaluation II and STS predicted risk of mortality score) can be possibly improved in terms of accuracy in both patients with low and high BMI and the overall patient population by incorporating the nonlinear correlation of BMI on outcomes as demonstrated in this study.[33] European System for Cardiac Operative Risk Evaluation II does not include BMI, BSA, or any other variable to reflect a patient's body habitus. While STS predicted risk of mortality score uses BSA as a predictor, using BMI may allow for improved accuracy in both overall population and low and high BMI groups.

Study Limitations

This study is a retrospective cohort study, which has inherent limitations due to its observational nature. Moreover, important preoperative laboratory findings, including albumin or prealbumin, which may provide a more definitive objective assessment of malnutrition, were not available. Other factors including preoperative frailty and intraoperative techniques of saphenous vein harvesting were also not available. Because JCVSD does not contain items representing frailty, we were unable to analyze its role in relation to BMI in this study.

Most importantly, long-term outcomes were not available in the current study. This was a limitation of JCVSD shared with the STS Adult Cardiac Surgery Database and the database on which European System for Cardiac Operative Risk Evaluation II is based. In a real clinical setting, it may be difficult to improve the preoperative status of low BMI patients who are frequently associated with congestive heart failure, low ejection fraction, and respiratory dysfunction. Accordingly, these patients may not tolerate preoperative rehabilitation. For high BMI patients, although it may also be important to reduce their weight and perform preoperative rehabilitation, some patients may not tolerate performing loaded exercise. Although we focused on patients with isolated first-time CABG who were aged 60 years or older, further studies are warranted to investigate whether a similar relationship between BMI and surgical outcomes is observed in other populations (eg, among redo or younger

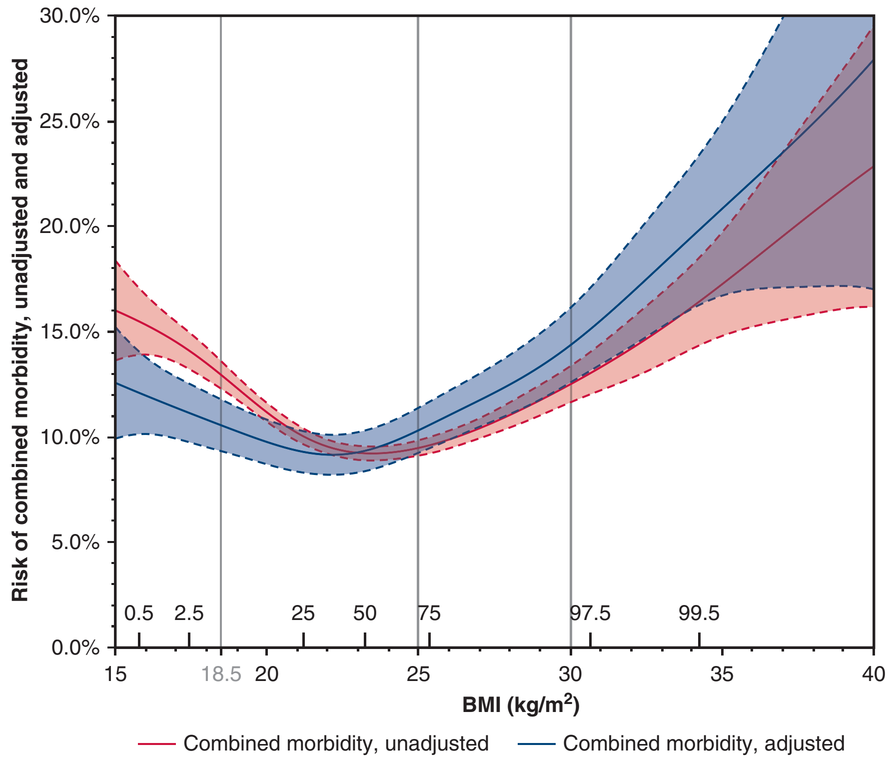

FIGURE 3. Correlation between body mass index (*BMI*) and combined morbidity (unadjusted and covariate adjusted combined morbidity). The results of spline fit and a generalized additive model with spline transformation of BMI are shown for combined morbidity. The *red line* indicates unadjusted combined morbidity, and the *blue line* indicates adjusted combined morbidity. *Shaded areas* represent 95% confidence intervals. *Ticks* on the *x*-axis indicate percentiles of BMI in the study population. As for unadjusted combined morbidity, a BMI of approximately 23 to 24 was associated with the lowest risk. Regarding adjusted combined morbidity, a BMI of approximately 21-23 was associated with the lowest risk.

CABG patients, those with combined CABG and other surgical procedures, and those with different types of cardiovascular surgery). The population of this study did not allow for a conclusive analysis on patients with extremely high BMI because there were only 308 patients (0.32%) in the 35≤ BMI <40 range and only 40 (0.04%) in the BMI ≥40 range (Figure E6). Because this Japanese nationwide database study represents a homogeneous population with a small number of extremely high BMI patients, future research is warranted that examines patient populations with other races and a larger number of extremely high BMI patients.

CONCLUSIONS

In patients undergoing isolated CABG, low and high BMI are risk factors of mortality associated with different types of morbidity. This highlights importance of tailored approaches to address the BMI-sensitive risks in reducing mortality and morbidity among low and high BMI patients.

Conflict of Interest Statement

Dr Kohsaka has received a grant from Daiichi-Sankyo and Bayer Yakuhin and personal fees from Bayer Yakuhin, Bristol-Myer Squibb, and Pfizer. All other authors have nothing to disclose with regard to commercial support.

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Key Words: body mass index, coronary artery bypass grafting, operative mortality, morbidity

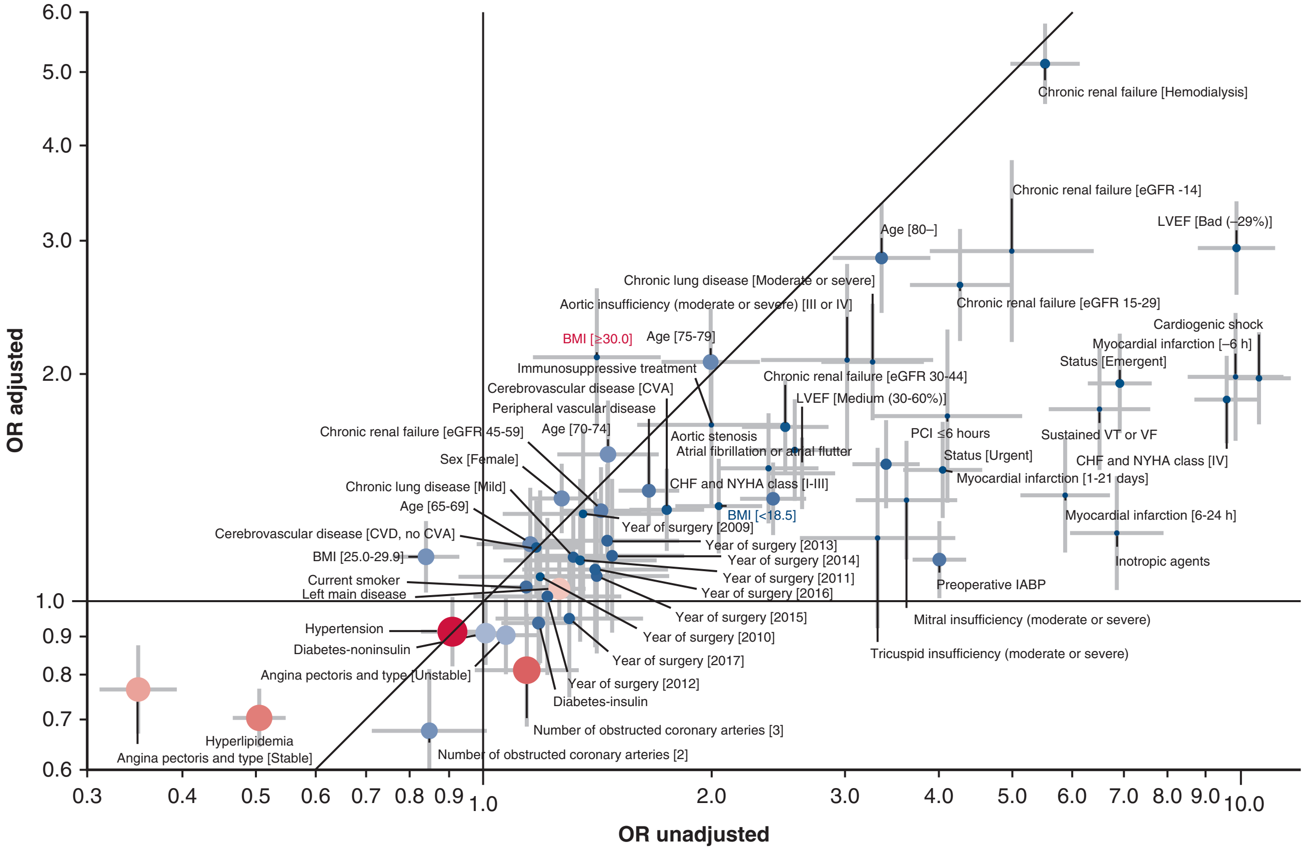

FIGURE E1. Unadjusted and adjusted odds ratios of body mass index (*BMI*) groups and other patient features for operative mortality. The *x*- and *y*-axes represent unadjusted and adjusted odds ratios, respectively, of BMI and other patient feature variables on operative mortality. Size and color of *bubbles* represent number of patients with the feature. A feature might have a large number of patients (*large, red bubble*), or a small number of patients (*small, blue bubble*). Both low (<18.5) and high (≥30) BMI are located near the *diagonal line* along with conventional risk factors, suggesting that the effects of both low and high BMI are largely independent from the other variables. The unadjusted and adjusted odds ratios of BMI and other variables for operative mortality are presented also in Table E3. *eGFR*, Estimated glomerular filtration rate; *LVEF*, left ventricular ejection fraction; *CVA*, cerebrovascular attack; *PCI*, percutaneous coronary intervention; *VT*, ventricular tachycardia; *Vf*, ventricular fibrillation; *CHF*, congestive heart failure; *NYHA*, New York Heart Association; *CVD*, cerebrovascular disease; *IABP*, intra-aortic balloon pump.

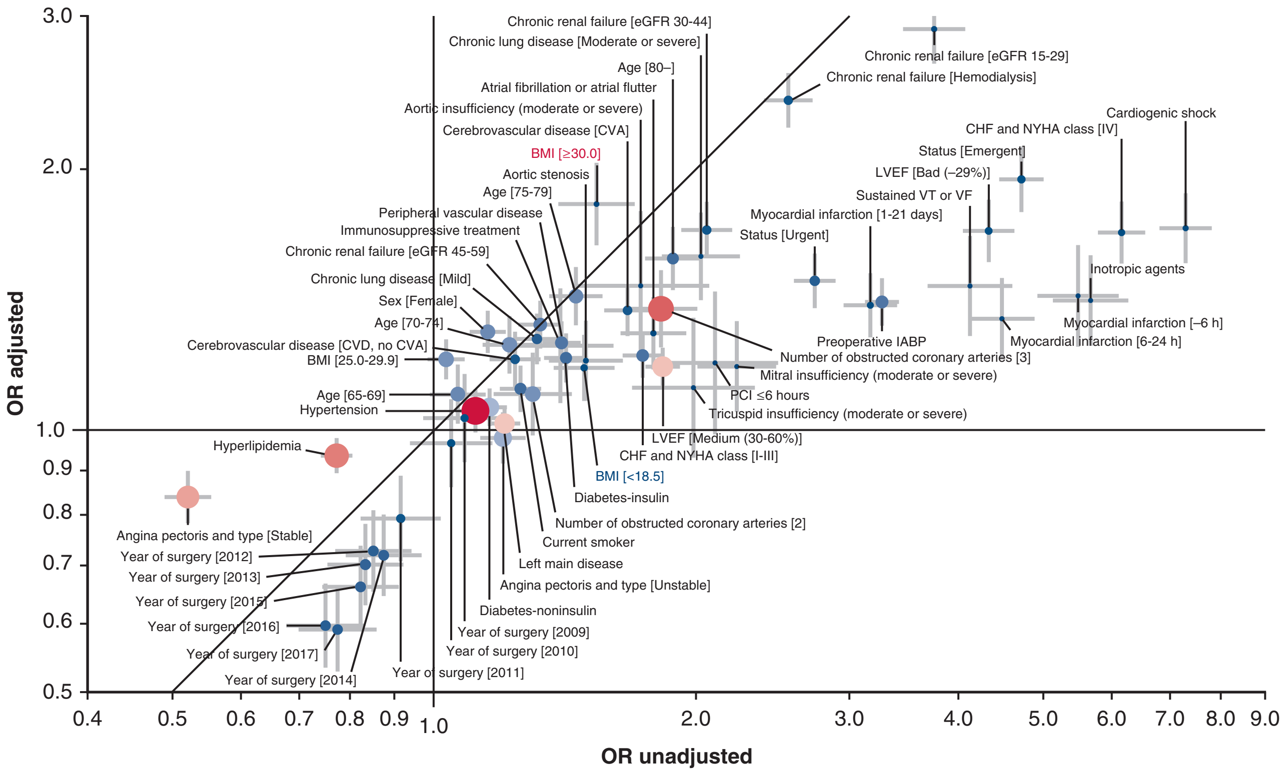

FIGURE E2. Unadjusted and adjusted odds ratios of body mass index (*BMI*) groups and other patient features for combined morbidity. The *x*- and *y*-axes represent unadjusted and adjusted odds ratios, respectively, of BMI and other patient feature variables on combined morbidity. Size and color of bubbles represent number of patients with the feature. A feature might have a large number of patients (*large, red bubble*), or a small number of patients (*small, blue bubble*). Both low (<18.5) and high (≥30) BMI are located near the diagonal line along with conventional risk factors, suggesting that the effects of both low and high BMI are largely independent from the other variables. The unadjusted and adjusted odds ratios of BMI and other variables for operative mortality are presented also in Table E4. *eGFR*, Estimated glomerular filtration rate; *CVA*, cerebrovascular attack; *CHF*, congestive heart failure; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *VT*, ventricular tachycardia; *Vf*, ventricular fibrillation; *CVD*, cerebrovascular disease; *IABP*, intra-aortic balloon pump; *PCI*, percutaneous coronary intervention.

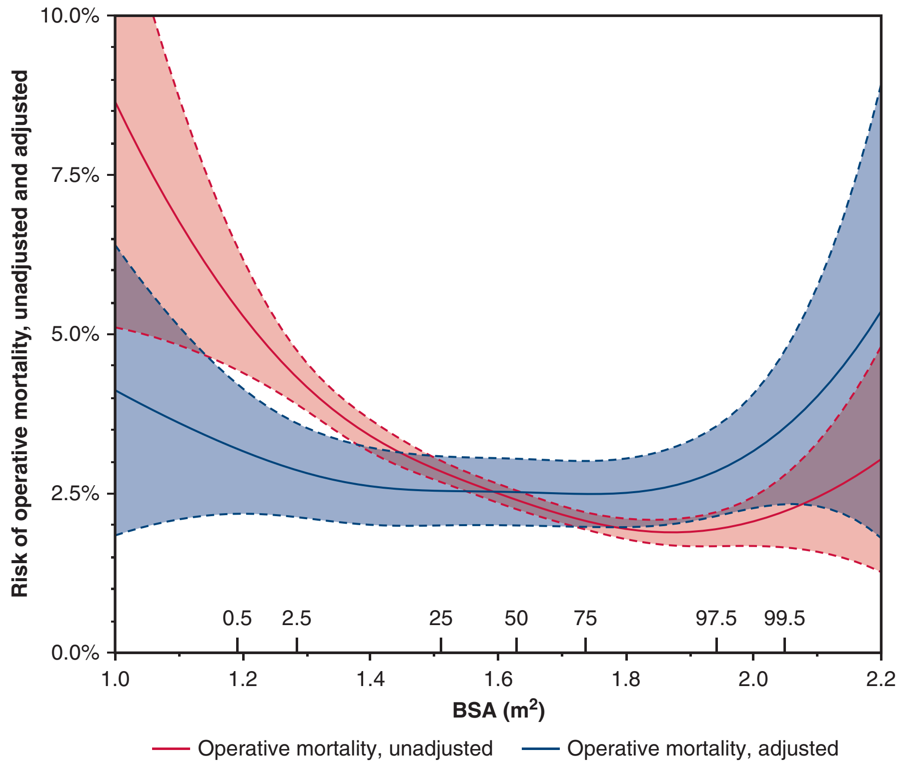

FIGURE E3. Correlation between body surface area (*BSA*) and operative mortality (unadjusted and covariate adjusted mortality). The results of spline fit and a generalized additive model with spline transformation of BSA are shown for mortality. The *red line* indicates unadjusted mortality, and the *blue line* indicates adjusted mortality. *Shaded areas* represent 95% confidence intervals. *Ticks* on the *x*-axis indicate percentiles of BSA in the study population. In contrast to the relationship between body mass index (BMI) and operative mortality (Figure 2), which was observed throughout the range of BMI, the relationship between BSA and outcomes was observed only in the outlier values, approximately <2.5 and >97.5 percentiles.

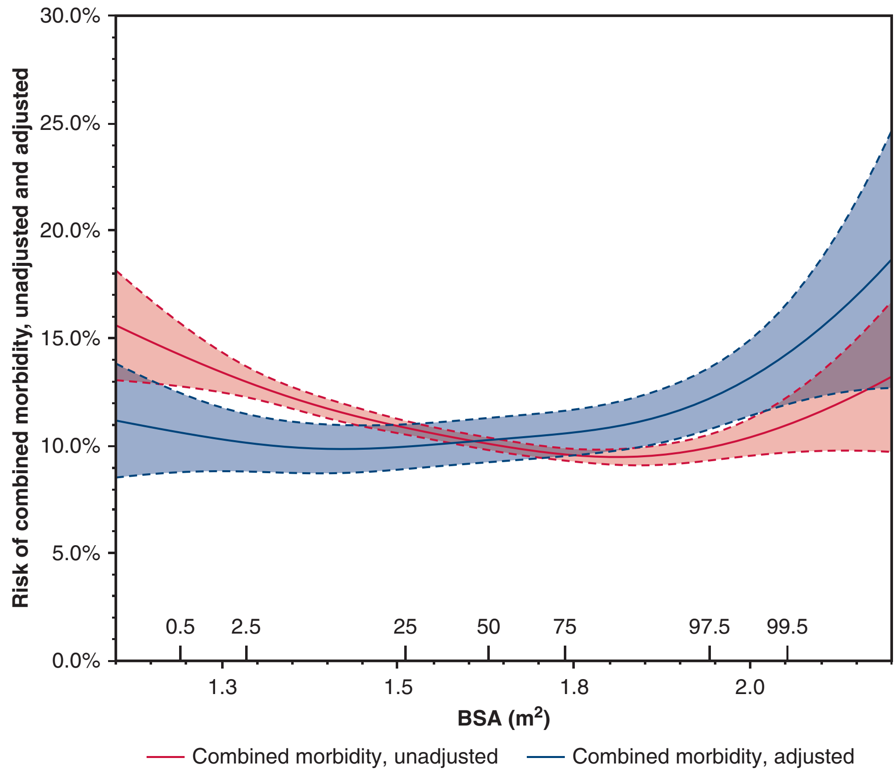

FIGURE E4. Correlation between body surface area (*BSA*) and combined morbidity (unadjusted and covariate adjusted morbidity). The results of spline fit and a generalized additive model with spline transformation of BSA are shown for combined morbidity. The *red line* indicates unadjusted combined morbidity, and the *blue line* indicates adjusted combined morbidity. *Shaded areas* represent 95% confidence intervals. *Ticks* on the *x*-axis indicate percentiles of BSA in the study population. In contrast to the relationship between body mass index (BMI) and combined morbidity (Figure 3), which was observed throughout the range of BMI, the relationship between BSA and outcomes was observed only in the outlier values, approximately >97.5 percentile.

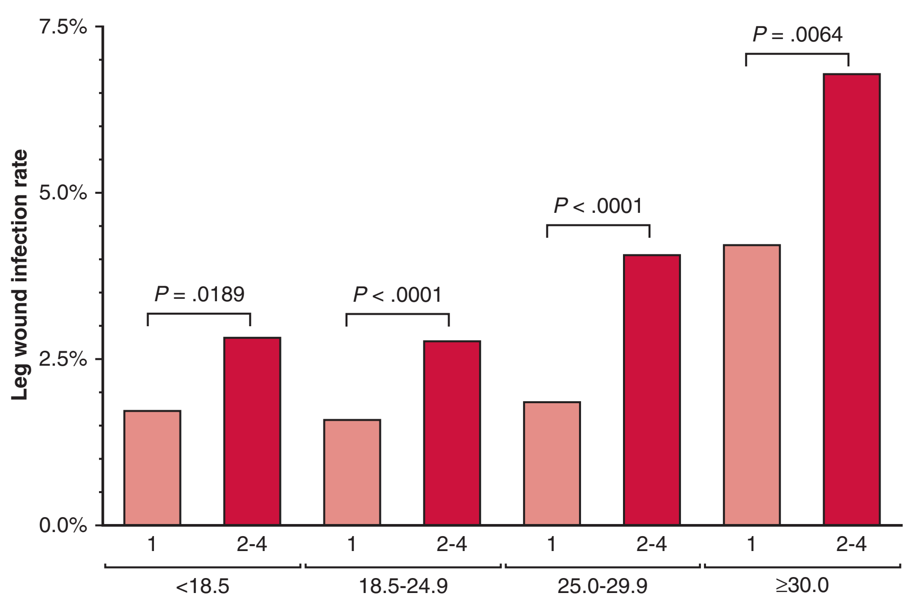

FIGURE E5. Leg wound infection rate by body mass index (*BMI*) and number of saphenous vein graft (*SVG*) harvesting sites.

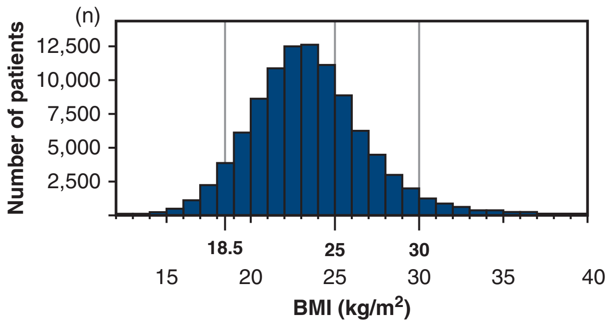

FIGURE E6. Distribution of body mass index (*BMI*) in the current study cohort.

TABLE E1. Definitions of variables including pre- and postoperative morbidity

Variable	Definition
Hypertension	Indicated if the patient has a current diagnosis of hypertension defined by any one of the following: • History of hypertension diagnosed and treated with medication, diet, and/or exercise • Prior documentation of blood pressure >140 mm Hg systolic and/or 90 mm Hg diastolic on at least 2 occasions for patients • Currently undergoing pharmacological therapy for treatment of hypertension
Dyslipidemia	Indicated if the patient has a fasting blood level that includes the following: • Low-density lipoprotein cholesterol ≥140 mg/dL, or • High-density lipoprotein cholesterol <40 mg/dL, or • Triglyceride ≥150 mg/dL
Diabetes mellitus	Indicated if the patient satisfies 1 of the following conditions: • Fasting plasma glucose ≥126 mg/dL • A random plasma glucose ≥200 mg/dL • Hemoglobin A1c ≥6.5% • 2-h plasma glucose ≥200 mg/dL during an oral glucose tolerance test • Using an oral antihyperglycemic drug, insulin injection, or incretin enhancers
Current smoker	Having smoked any type of cigarette in the most recent year
Chronic lung disease	Including chronic obstructive pulmonary disease Mild: Forced expiratory volume in 1 s 60%-75% and/or the medication except for steroid; moderate: Forced expiratory volume in 1 s 50%-59% and/or steroid; severe: Forced expiratory volume in 1 s <50% and/or oxygen tension <60 or carbon dioxide tension >50
Chronic renal failure	Proteinuria or serum creatinine ≥1.3 mg/dL or estimated glomerular filtration rate ≤60 mL/min/1.73 m^2
Myocardial infarction	Indicated if the patient satisfies the criteria within 1 mo before surgery: Lasting symptom of myocardial ischemia with elevation of myocardial marker (more than twice the normal level of creatine kinase and creatine kinase myocardial band, and >99 percentile value of tropnin T)
Status - urgent	Surgery started within 24 h after decision for operation
Status - emergent	Surgery started immediately
Operative mortality	All deaths occurring, regardless of the postoperative survival period, during the hospitalization in which the operation was performed and all deaths, regardless of occurring after discharge from the hospital, but before the end of the thirtieth postoperative day. (Cases for which the cause of death was not related to the operation were excluded.)
Combined morbidity	Operative mortality, reoperation for bleeding, stroke, new onset of hemodialysis, mediastinitis, and prolonged ventilation
Stroke	A new symptom of paralysis of the central nervous system that lasted for >72 h before discharge
Cerebrovascular disease	Defined as transient ischemic attack, reversible ischemic neurological deficit, and cerebrovascular attack Transient ischemic attack: Transient disorder for central nervous system within 24 h Reversible ischemic neurological deficit: Transient disorder for central nervous system more than 24 h and within 72 h Cerebrovascular attack: Disorder for central nervous system more than 72 h
Cerebrovascular attack	Disorder for central nervous system more than 72 h
Transient ischemic attack	Transient disorder for central nervous system within 24 h
Reversible ischemic neurological deficit	Transient disorder for central nervous system more than 24 h and within 72 h
Prolonged ventilation	More than 24 h postoperative intubation time for respiratory failure, including acute respiratory distress syndrome, pulmonary edema, and pneumonia
Postoperative renal failure	A rise in creatinine concentration of 2 mg/dL or a requirement of new dialysis
Atrioventricular block	The situation requiring permanent pacemaker implantation

(Continued)

TABLE E1. Continued

Variable	Definition
Cardiac arrest	Indicated when the patient had an acute cardiac arrest documented by one of the following: • Ventricular fibrillation • Ventricular tachycardia with unstable hemodynamic parameters • Asystole
Anticoagulant complication	Bleeding and thromboembolism with anticoagulant therapy
Infections	Mediastinitis, pneumonia, septicemia, and leg wound infection
Multiple organ failure	The failure of ≥ 2 vital organ systems
Readmission	Indicated when the patient was readmitted to the hospital within 30 d after this surgery

Based on JCVSD Adult Section Data Specifications version 2016.a (https://center6.umin.ac.jp/islet/jacvsd/old/index.html; accessed on June 30, 2019) and translated into English by the authors. Combined morbidity and infections were defined for this study.

TABLE E2. Definitions of major items in the Japan Cardiovascular Surgery Database (JCVSD) and Society of Thoracic Surgeons Adult Cardiac Surgery Database (STS-ACSD)

Item	JCVSD	STS-ACSD
Hypertension	Indicate if the patient has a current diagnosis of hypertension defined by any 1 of the following: • History of hypertension diagnosed and treated with medication, diet, and/or exercise • Prior documentation of blood pressure >140 mm Hg systolic and/or 90 mm Hg diastolic on at least 2 occasions for patients • Currently undergoing pharmacologic therapy for treatment of hypertension	Indicate if the patient has a current diagnosis of hypertension defined by any 1 of the following: • History of hypertension diagnosed and treated with medication, diet, and/or exercise • Prior documentation of blood pressure >140 mm Hg systolic and/or 90 mm Hg diastolic for patients without diabetes or chronic kidney disease, or prior documentation of blood pressure >130 mm Hg systolic or 80 mm Hg diastolic on at least 2 occasions for patients with diabetes or chronic kidney disease • Currently undergoing pharmacologic therapy for treatment of hypertension
Dyslipidemia	Indicate if the patient has the fasting blood level, including the following: • Low-density lipoprotein cholesterol ≥140 mg/dL; or • High-density lipoprotein cholesterol <40 mg/dL; or • Triglyceride ≥150 mg/dL	Indicate if the patient has a history of dyslipidemia that was diagnosed and/or treated by a physician. National Cholesterol Education Program* criteria include documentation of the following: • Total cholesterol >200 mg/dL (5.18 mmol/L); or • Low-density lipoprotein cholesterol ≥130 mg/dL (3.37 mmol/L); • High-density lipoprotein cholesterol <40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.30 mmol/L) in women; • Currently receiving antilipidemia treatment
Diabetes mellitus	Indicate if the patient has the fasting blood level, including 1 of the following: • Fasting plasma glucose ≥126 mg/dL • A random plasma glucose ≥200 mg/dL • Hemoglobin A1c ≥6.5% • 2-h Plasma glucose ≥200 mg/dL during an oral glucose tolerance test • Using oral antihyperglycemic drug, insulin injection, or incretin enhancers	History of diabetes diagnosed and/or treated by a health care provider. The American Diabetes Association criteria include documentation of the following: • Hemoglobin A1c ≥6.5%; or • Fasting plasma glucose ≥126 mg/dL (7.0 mmol/L); or • 2-h Plasma glucose ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test; or • In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L)
Cerebrovascular disease	Cerebrovascular disease is defined as transient ischemic attack, reversible ischemic neurologic deficit, and cardiovascular accident Transient ischemic attack: Transient disorder for central nervous system within 24 h Reversible ischemic neurologic deficit: Transient disorder for central nervous system over 24 h and within 72 h Cerebrovascular attack: Disorder of the central nervous system lasting longer than 72 h	Stroke is an acute episode of focal or global neurologic dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction, where the neurologic dysfunction lasts >24 h Defined as a transient episode of focal neurologic dysfunction caused by brain, spinal cord, or retinal ischemia, without acute infarction, where the neurologic dysfunction resolves within 24 h Noninvasive or invasive arterial imaging test demonstrating ≥50% stenosis of any of the major extracranial or intracranial vessels to the brain Previous cervical or cerebral artery revascularization surgery or percutaneous intervention This does not include chronic (nonvascular) neurologic diseases or other acute neurologic insults such as metabolic and anoxic ischemic encephalopathy
Cerebrovascular attack	Disorder of the central nervous system lasting longer than 72 h	Indicate whether the patient has a history of stroke. Stroke is an acute episode of focal or global neurologic dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction, where the neurologic dysfunction lasts >24 h

(Continued)

TABLE E2. Continued

Item	JCVSD	STS-ACSD
Myocardial infarction	Indicate if the patient is equal to below criteria within 1 mo before surgery. • Lasting symptom of myocardial ischemia with elevation of myocardial marker (ie, more than twice the normal level of creatine kinase and creatine kinase-myocardial bank, and more than 99 percentile value of tropnin T)	Indicate if the patient has had at least 1 documented previous myocardial infarction at any time before this surgery
Peripheral vascular disease	There is no mention about the criteria for peripheral vascular disease in JCVSD data specifications version 2016.a. However, there is an item to select the presence or absence of ''the history of peripheral vascular surgery including abdominal aortic surgery''	Indicate whether the patient has a history of peripheral arterial disease (eg, upper and lower extremity, renal, mesenteric, and abdominal aortic systems) This can include • Claudication, either with exertion or at rest • Amputation for arterial vascular insufficiency • Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping) • Documented abdominal aortic aneurysm with or without repair • Positive noninvasive test (eg, ankle brachial index $\leq$0.9, ultrasound, magnetic resonance or computed tomography imaging >50% diameter stenosis in any peripheral artery, such as renal, subclavian, femoral, or iliac) or angiographic imaging • Peripheral arterial disease excludes disease in the carotid artery, cerebrovascular arteries, or thoracic aorta • Peripheral vascular disease does not include deep vein thrombosis
Clinical status of a patient before entering the operating room	Elective: Surgery not included in any of the following criteria Urgent: Surgery started within 24 h after decision for operation Emergent: Surgery started immediately Salvage: Resuscitation was needed during transfer or before induction of anesthesia in an operating room	Elective: The patient's cardiac function has been stable in the days or weeks before the operation. The procedure could be deferred without increased risk of compromised cardiac outcome Urgent: Procedure required during same hospitalization in order to minimize chance of further clinical deterioration. Examples include but are not limited to: worsening, sudden chest pain, congestive heart failure, acute myocardial infarction, intra-aortic balloon pump, unstable angina with intravenous nitroglycerin, or rest angina Emergent: Patients requiring emergency operations will have ongoing, refractory (ie, difficult, complicated, and/or unmanageable), unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except cardiac surgery. An emergency operation is one in which there should be no delay in providing operative intervention Emergent salvage: The patient is undergoing cardiopulmonary resuscitation en route to an operating room or before anesthesia induction or has ongoing extracorporeal membrane oxygenation to maintain life

(Continued)

TABLE E2. Continued

Item	JCVSD	STS-ACSD
Cardiac arrest	Indicate whether the patient had an acute cardiac arrest documented by 1 of the following: • Ventricular fibrillation • Ventricular tachycardia with unstable hemodynamics • Asystole	Indicate whether the patient had an acute cardiac arrest documented by 1 of the following: • Ventricular fibrillation • Rapid ventricular tachycardia with hemodynamic instability • Asystole • Implantable cardioverter defibrillator shocks
Postoperative renal failure	A rise in serum creatinine level $\geq$2.0 mg/dL and more than 2$\times$ preoperative serum creatinine level; or a requirement of new dialysis	Indicate whether the patient had acute renal failure or worsening renal function resulting in 1 or both of the following: Increase in serum creatinine level 3.0$\times$ greater than baseline, or serum creatinine level $\geq$4 mg/dL; acute rise must be at least 0.5 mg/dL Or, a new requirement for dialysis postoperatively
Readmission	Indicate whether the patient was readmitted to the hospital within 30 d after this surgery	Indicate whether the patient was readmitted to the hospital within 30 d of discharge from hospitalization for this surgery

Based on JCVSD Adult Section Data Specifications version 2016.a (https://center6.umin.ac.jp/islet/jacvsd/old/index.html; accessed on June 30, 2019) and translated into English by the authors and refered to by Nawata K, D'Agostino RS, Habib RH, Kumamaru H, Hirahara N, Miyata H, et al. First database comparison between the United States and Japan: coronary artery bypass grafting. *Ann Thorac Surg*. 2020;109:1159-1164. *Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-2497.

TABLE E3. Unadjusted and adjusted odds ratios (ORs) for operative mortality (except for each body mass index group)*

Variable	Unadjusted		Adjusted	
	OR (95% Confidence interval)	*P* value	OR (95% Confidence interval)	*P* value
Year of surgery				
2008	Reference		Reference	
2009	1.35 (1.06-1.73)	.0141	1.31 (1.01-1.69)	.0432
2010	1.19 (0.93-1.52)	.1706	1.08 (0.83-1.40)	.5714
2011	1.34 (1.06-1.69)	.0119	1.13 (0.89-1.45)	.3191
2012	1.22 (0.97-1.52)	.0854	1.02 (0.80-1.29)	.8948
2013	1.46 (1.17-1.81)	.0005	1.20 (0.95-1.52)	.1181
2014	1.48 (1.19-1.84)	.0003	1.15 (0.91-1.45)	.2413
2015	1.41 (1.13-1.76)	.0017	1.08 (0.85-1.37)	.5152
2016	1.40 (1.13-1.75)	.0021	1.10 (0.87-1.40)	.4166
2017	1.30 (1.04-1.63)	.0201	0.95 (0.75-1.21)	.6756
Age (y)				
60-64	Reference		Reference	
65-69	1.15 (0.98-1.36)	.0843	1.19 (1.00-1.41)	.0452
70-74	1.46 (1.25-1.70)	<.0001	1.56 (1.33-1.84)	<.0001
75-79	2.00 (1.72-2.32)	<.0001	2.07 (1.76-2.44)	<.0001
≥80	3.36 (2.89-3.89)	<.0001	2.84 (2.41-3.36)	<.0001
Female sex	1.27 (1.16-1.39)	<.0001	1.37 (1.23-1.52)	<.0001
Current smoker	1.14 (1.02-1.27)	.0192	1.05 (0.93-1.18)	.4656
Diabetes mellitus				
Noninsulin dependent	1.01 (0.92-1.10)	.8752	0.91 (0.83-1.00)	.0525
Insulin dependent	1.18 (1.06-1.32)	.0040	0.94 (0.82-1.07)	.3205
Hyperlipidemia	0.51 (0.47-0.55)	<.0001	0.70 (0.64-0.77)	<.0001
Chronic renal failure (eGFR)				
≥60	Reference		Reference	
45-59	1.43 (1.27-1.62)	<.0001	1.32 (1.16-1.51)	<.0001
30-44	2.50 (2.20-2.86)	<.0001	1.70 (1.47-1.97)	<.0001
15-29	4.26 (3.66-4.96)	<.0001	2.62 (2.21-3.10)	<.0001
≤14	4.98 (3.89-6.40)	<.0001	2.90 (2.20-3.83)	<.0001
Hemodialysis	5.52 (4.96-6.13)	<.0001	5.13 (4.54-5.80)	< .0001
Hypertension	0.91 (0.83-1.00)	.0565	0.91 (0.82-1.01)	.0905
Chronic lung disease				
Mild	1.31 (1.17-1.48)	<.0001	1.14 (1.01-1.30)	.0403
Moderate or severe	3.27 (2.79-3.82)	<.0001	2.07 (1.74-2.47)	< .0001
Immunosuppressive treatment	2.00 (1.60-2.51)	<.0001	1.71 (1.34-2.19)	< .0001
Peripheral vascular disease	1.65 (1.51-1.81)	<.0001	1.40 (1.26-1.56)	< .0001
CVD†				
CVD, no CVA	1.17 (1.03-1.34)	.0190	1.18 (1.02-1.36)	.0239
CVA	1.75 (1.56-1.96)	<.0001	1.32 (1.17-1.50)	<.0001
PCI ≤6 h	4.10 (3.27-5.14)	<.0001	1.76 (1.35-2.29)	<.0001
Myocardial infarction				
≤6 h	9.84 (8.51-11.38)	<.0001	1.98 (1.63-2.41)	<.0001
6-24 h	5.86 (5.12-6.72)	<.0001	1.38 (1.16-1.64)	.0003
1-21 d	4.04 (3.58-4.56)	<.0001	1.49 (1.29-1.73)	<.0001
CHF and NYHA class				
NYHA I-III	2.41 (2.18-2.67)	<.0001	1.37 (1.22-1.53)	<.0001
NYHA IV	9.58 (8.68-10.57)	<.0001	1.85 (1.62-2.11)	<.0001

(Continued)

TABLE E3. Continued

Variable	Unadjusted OR (95% Confidence interval)	Unadjusted *P* value	Adjusted OR (95% Confidence interval)	Adjusted *P* value
Angina pectoris and type				
Stable	0.35 (0.31-0.39)	<.0001	0.77 (0.67-0.88)	.0001
Unstable	1.07 (0.96-1.19)	.2012	0.90 (0.80-1.02)	.0933
Cardiogenic shock	10.57 (9.59-11.64)	<.0001	1.97 (1.71-2.27)	<.0001
Atrial fibrillation or atrial flutter	2.58 (2.24-2.96)	<.0001	1.59 (1.36-1.85)	<.0001
Sustained VT or VF	6.51 (5.58-7.59)	<.0001	1.80 (1.49-2.16)	<.0001
Inotropic agents	6.86 (5.95-7.91)	<.0001	1.23 (1.04-1.47)	.0181
Status				
Urgent	3.40 (3.07-3.77)	<.0001	1.52 (1.33-1.74)	<.0001
Emergent	6.92 (6.28-7.63)	<.0001	1.94 (1.67-2.26)	<.0001
No. of obstructed coronary arteries				
2	0.85 (0.71-1.01)	.0696	0.68 (0.56-0.81)	<.0001
3	1.14 (0.97-1.34)	.0953	0.81 (0.68-0.96)	.0174
Left main disease	1.26 (1.16-1.36)	<.0001	1.04 (0.95-1.14)	.3848
LVEF (%)				
≥61	Reference		Reference	
30-60	2.64 (2.38-2.91)	<.0001	1.48 (1.33-1.65)	<.0001
≤29	9.87 (8.78-11.10)	<.0001	2.93 (2.54-3.38)	<.0001
Moderate or severe aortic insufficiency	3.02 (2.33-3.93)	<.0001	2.08 (1.56-2.79)	<.0001
Aortic stenosis	2.38 (2.04-2.77)	<.0001	1.50 (1.27-1.77)	<.0001
Moderate or severe mitral insufficiency	3.62 (3.10-4.22)	<.0001	1.36 (1.14-1.63)	.0008
Moderate or severe tricuspid insufficiency	3.32 (2.62-4.20)	<.0001	1.21 (0.92-1.60)	.1663
Preoperative IABP	4.00 (3.69-4.34)	<.0001	1.14 (1.01-1.28)	.0323

Adjusted odds ratios are based on multivariable logistic regression. Odds ratios for BMI groups, unadjusted and adjusted, are presented in Table 4. Odds ratios of BMI and other variables, unadjusted and adjusted, are also presented in Figure E1. *eGFR*, Estimated glomerular filtration rate; *CVD*, cerebrovascular disease; *CVA*, cerebrovascular attack; *PCI*, percutaneous coronary intervention; *CHF*, congestive heart failure; *NYHA*, New York Heart Association; *VT*, ventricular tachycardia; *VF*, ventricular fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pumping. *AUC, 0.839. †CVD includes noninvasive arterial imaging test demonstrating ≥75% stenosis of any of the major extracranial or intracranial vessels to the brain.

TABLE E4. Unadjusted and adjusted odds ratios and upper and lower limits of 95% confidence interval (CI) for combined morbidity (except for each body mass index group)*

Variable	Unadjusted Odds ratio (95% CI)	Unadjusted *P* value	Adjusted Odds ratio (95% CI)	Adjusted *P* value
Year of surgery				
2008	Reference		Reference	
2009	1.08 (0.97-1.21)	.1491	1.03 (0.92-1.16)	.5813
2010	1.05 (0.94-1.17)	.4175	0.97 (0.86-1.09)	.5717
2011	0.92 (0.82-1.02)	.1029	0.79 (0.71-0.89)	<.0001
2012	0.85 (0.77-0.94)	.0019	0.73 (0.65-0.81)	<.0001
2013	0.83 (0.75-0.92)	.0004	0.70 (0.63-0.78)	<.0001
2014	0.88 (0.79-0.97)	.0096	0.72 (0.64-0.80)	<.0001
2015	0.82 (0.74-0.91)	.0002	0.66 (0.59-0.74)	<.0001
2016	0.75 (0.68-0.83)	<.0001	0.60 (0.53-0.67)	<.0001
2017	0.77 (0.70-0.86)	<.0001	0.59 (0.53-0.66)	<.0001
Age (y)				
60-64	Reference		Reference	
65-69	1.06 (0.99-1.15)	.0955	1.10 (1.02-1.19)	.0159
70-74	1.22 (1.14-1.31)	<.0001	1.26 (1.16-1.35)	<.0001
75-79	1.45 (1.36-1.56)	<.0001	1.43 (1.32-1.54)	<.0001
≥80	1.88 (1.75-2.02)	<.0001	1.58 (1.45-1.72)	<.0001
Female sex	1.15 (1.10-1.21)	<.0001	1.30 (1.23-1.37)	<.0001
Current smoker	1.26 (1.19-1.33)	<.0001	1.12 (1.05-1.19)	.0004
Diabetes mellitus				
Noninsulin dependent	1.16 (1.11-1.21)	<.0001	1.06 (1.01-1.12)	.0156
Insulin dependent	1.42 (1.34-1.50)	<.0001	1.21 (1.14-1.29)	<.0001
Hyperlipidemia	0.77 (0.74-0.81)	<.0001	0.94 (0.89-0.98)	.0052
Chronic renal failure (eGFR)				
≥60	Reference		Reference	
45-59	1.32 (1.25-1.40)	<.0001	1.32 (1.24-1.41)	<.0001
30-44	2.06 (1.92-2.20)	<.0001	1.70 (1.58-1.83)	<.0001
15-29	3.75 (3.46-4.07)	<.0001	2.90 (2.64-3.18)	<.0001
≤14	8.23 (7.24-9.35)	<.0001	6.83 (5.93-7.86)	<.0001
Hemodialysis	2.55 (2.39-2.72)	<.0001	2.40 (2.23-2.58)	<.0001
Hypertension	1.12 (1.06-1.18)	<.0001	1.05 (0.99-1.12)	.0751
Chronic lung disease				
Mild	1.31 (1.23-1.40)	<.0001	1.27 (1.19-1.36)	<.0001
Moderate or severe	2.02 (1.83-2.24)	<.0001	1.59 (1.41-1.78)	<.0001
Immunosuppressive treatment	1.40 (1.21-1.61)	<.0001	1.25 (1.08-1.46)	.0038
Peripheral vascular disease	1.40 (1.33-1.47)	<.0001	1.26 (1.19-1.34)	<.0001
Cerebrovascular disease†				
No CVA	1.24 (1.16-1.33)	<.0001	1.21 (1.12-1.30)	.0001
CVA	1.67 (1.57-1.77)	<.0001	1.37 (1.28-1.47)	<.0001
PCI ≤6 h	2.10 (1.78-2.48)	<.0001	1.20 (0.99-1.45)	.0636
Myocardial infarction				
≤6 h	5.49 (4.93-6.11)	<.0001	1.43 (1.25-1.63)	<.0001
6-24 h	4.49 (4.12-4.89)	<.0001	1.34 (1.21-1.50)	<.0001
1-21 d	3.17 (2.95-3.40)	<.0001	1.39 (1.28-1.52)	<.0001
CHF and NYHA functional class				
I-III	1.74 (1.65-1.83)	<.0001	1.22 (1.15-1.29)	<.0001
IV	6.16 (5.78-6.55)	<.0001	1.69 (1.56-1.83)	<.0001

(Continued)

TABLE E4. Continued

Variable	Unadjusted		Adjusted	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Angina pectoris and type				
Stable	0.52 (0.49-0.55)	<.0001	0.84 (0.78-0.90)	<.0001
Unstable	1.20 (1.13-1.27)	<.0001	0.98 (0.92-1.05)	.5717
Cardiogenic shock	7.29 (6.81-7.82)	<.0001	1.71 (1.56-1.88)	<.0001
Atrial fibrillation or atrial flutter	1.79 (1.64-1.95)	<.0001	1.29 (1.18-1.42)	<.0001
Sustained VT or VF	4.12 (3.69-4.61)	<.0001	1.47 (1.28-1.67)	<.0001
Inotropic agents	5.67 (5.13-6.27)	<.0001	1.41 (1.25-1.59)	<.0001
Status				
Urgent	2.74 (2.59-2.89)	<.0001	1.49 (1.38-1.60)	<.0001
Emergent	4.73 (4.46-5.01)	<.0001	1.95 (1.78-2.12)	<.0001
No. of obstructed coronary arteries				
2	1.30 (1.17-1.44)	<.0001	1.10 (0.99-1.23)	.0840
3	1.82 (1.65-2.01)	<.0001	1.38 (1.25-1.53)	<.0001
Left main disease	1.20 (1.16-1.26)	<.0001	1.02 (0.97-1.07)	.4275
LVEF (%)				
≥61	Reference		Reference	
30-60	1.83 (1.75-1.92)	<.0001	1.18 (1.13-1.25)	<.0001
≤29	4.33 (4.05-4.64)	<.0001	1.70 (1.56-1.84)	<.0001
Moderate or severe aortic insufficiency	1.73 (1.44-2.07)	<.0001	1.47 (1.20-1.79)	.0002
Aortic stenosis	1.49 (1.35-1.65)	<.0001	1.20 (1.08-1.34)	.0006
Moderate or severe mitral insufficiency	2.23 (2.01-2.47)	<.0001	1.18 (1.05-1.34)	.0058
Moderate or sever tricuspid insufficiency	1.99 (1.69-2.34)	<.0001	1.12 (0.93-1.35)	.2298
Preoperative IABP	3.27 (3.12-3.42)	<.0001	1.41 (1.32-1.50)	<.0001

Adjusted odds ratios are based on multivariable logistic regression. Odds ratios for body mass index groups, unadjusted and adjusted, are presented in Table 5. Odds ratios of body mass index and other variables, unadjusted and adjusted, are also presented in Figure E2. *CI*, Confidence interval; *eGFR*, estimated glomerular filtration rate; *CVA*, cerebrovascular attack; *PCI*, percutaneous coronary intervention; *CHF*, congestive heart failure; *NYHA*, New York Heart Association; *VT*, ventricular tachycardia; *VF*, ventricular fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pumping. *AUC, 0.745. †CVD includes noninvasive arterial imaging test demonstrating ≥75% stenosis of any of the major extracranial or intracranial vessels to the brain.