



Outcomes of Thoracic Aortic Surgery in Patients With Coronary Artery Disease

— Based on the Japan Adult Cardiovascular Surgery Database —

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Background: Coronary artery disease (CAD) is associated with increased morbidity and mortality after open repair of thoracic aorta. Nevertheless, the efficacy of preoperative coronary angiography (CAG) and revascularization is controversial. The aim of this study was to clarify the effect of preoperative CAD on surgical outcome by reviewing the Japan Adult Cardiovascular Database.

Methods and Results: This study involved 4,596 patients who underwent open surgery for true thoracic aortic aneurysm between 2004 and 2009. After excluding patients with concomitant cardiac operation, except coronary artery bypass grafting (CABG), the remaining 1,904 patients with coronary artery stenosis included 995 cases of simultaneous CABG. The prevalence of CAD was significantly higher in patients with diabetes, renal dysfunction, hyperlipidemia, cerebrovascular disorders, peripheral artery lesions, old myocardial infarction (MI), and coronary intervention. Patients with simultaneous CABG had severe CAD compared with those without, with no other major differences in patient background noted. Thirty-day postoperative and in-hospital mortalities were higher in CAD patients. Incidence of perioperative MI was higher in patients who underwent open aortic repair with simultaneous CABG, but simultaneous CABG did not affect operative mortality.

Conclusions: In patients with surgically treated true aortic aneurysm, CAD was frequently observed, suggesting that aggressive preoperative coronary evaluation is needed.

Key Words: Coronary artery disease; Database; Thoracic aortic disease; Thoracic aortic surgery

Coronary artery disease (CAD) is currently seen in approximately 10–30% of patients with thoracic aortic disease.^{1–5} When undergoing open repair for aortic disease without coronary intervention for CAD, there are risks of developing perioperative myocardial infarction (MI), cardiac dysfunction due to insufficient intraoperative myocardial protection or myocardial ischemia, and fatal arrhythmia. Therefore, CAD is a known risk factor for early death after surgery for thoracic aortic disease.^{6–8} Especially in patients with unstable CAD, coronary revascularization before or during surgery is useful in significantly reducing the risk of cardiac complications such as perioperative MI or operative mortality.^{1,2,4} According to ACCF/AHA guidelines however, the benefit of coronary revascularization before or during surgery still remains a controversial subject. Furthermore, the usefulness of actively performing coronary screening and treatment, especially in patients with stable CAD, is unclear.⁹ A number of studies have investigated treatments for CAD and the relationship

of such treatments to surgical outcome in patients with aortic disease or peripheral artery disease. Many of these studies, however, were limited by the small numbers of subjects involved; this is one of the reasons for the low evidence level in the guidelines. We therefore used the Japan Adult Cardiovascular Surgery Database (JACVSD), a national registry in Japan, to investigate the presence of CAD on preoperative coronary angiography (CAG) and its relationship to patient background and outcome of open aortic repair in patients with thoracic aortic disease.

Methods

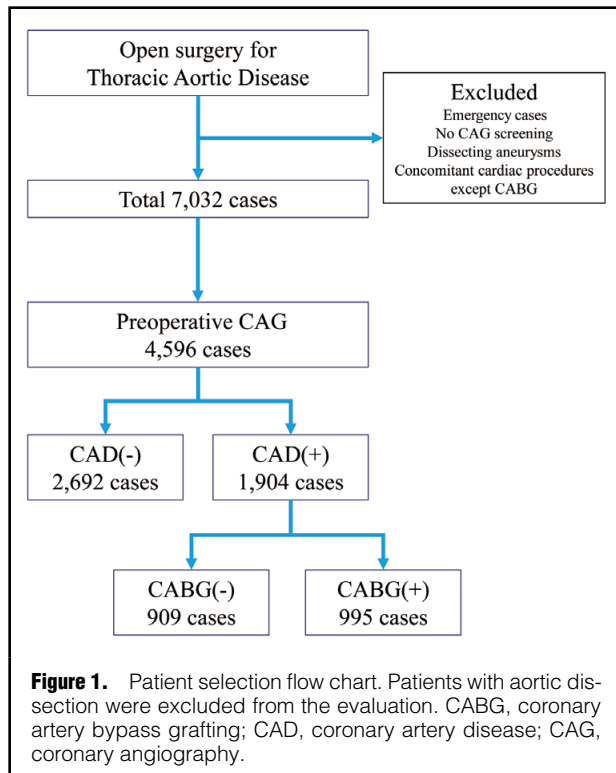
The JACVSD is a Japanese clinical database that was introduced in 2000 as a multicenter database of cardiovascular surgery; approximately 500 institutions (99%) were enrolled in this database as of 2017.¹⁰ Investigation items were defined as being equivalent to those of the Society of Thoracic Surgeons database for comparison purposes; there are

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approximately 250 such items. Although enrollment in JACVSD is voluntary, the vast majority of institutions are currently enrolled in this database and the completeness of the data is high. Furthermore, careful checking of the consistency between registered data and clinical records by visiting randomly selected institutions regularly maintains the accuracy of data at a high level. The use of data was approved by the JACVSD Data Utilization Committee.

Of the patients registered in JACVSD who received elective open repair for thoracic aortic disease (ascending, arch, descending, and thoracoabdominal), 4,596 patients who underwent preoperative CAG were selected for the study. Patients who underwent emergency surgery or simultaneously received other open heart surgery, except coronary artery bypass grafting (CABG), were excluded (**Figure 1**). Based on the presence or absence of CAD, patients were divided into 2 groups, namely CAD (+) and CAD (–), respectively. CAD (+) patients were further divided into 2 groups based on the presence and absence of concomitant CABG, namely CABG (+) and CABG (–), respectively. Patient background (age, sex, body mass index [BMI], smoking history, hypertension, hyperlipidemia, cerebral infarction, chronic obstructive pulmonary disease [COPD], diabetes mellitus [DM], MI, renal insufficiency, dialysis, peripheral vascular disease, etiology and location of major vessel disease, presence or absence of angina, past history of coronary artery intervention, number of affected branches of coronary artery, presence or absence of left main trunk [LMT] lesion, and left ventricular function) and early post-operative outcomes of aortic surgery were retrospectively reviewed. CAD was defined as $\geq 50\%$ stenosis at the LMT and $\geq 75\%$ stenosis at the 3 major branches. Thirty-day mortality was defined as death in the 30 days after surgery irrespective of hospitalization; and in-hospital mortality

was defined as death during hospitalization in the 30 days after surgery. Complications included new-onset cerebral infarction, transient ischemic attack, perioperative MI, cardiac arrest including fatal arrhythmia, pneumonia, gastrointestinal complications, induction of dialysis due to renal insufficiency, and infection.

Statistical Analysis

Statistical analysis was done using SPSS for Windows. Continuous variables are expressed as mean, and categorical variables are expressed as absolute number or percentage. Univariate comparisons of categorical and continuous variables were made using chi-squared test or Fisher's exact test and Student t-test, as appropriate. All reported P-values are 2-sided, and $P < 0.05$ was considered statistically significant. Stepwise logistic regression analysis was performed to identify independent risk factors for operative mortality. Predictors included in the multivariate analysis were as follows: age category (5-year age group), sex, BMI ($\geq 30 \text{ kg/m}^2$), smoking, DM, COPD, renal dysfunction, dialysis, hypertension, hyperlipidemia, cerebrovascular disease, peripheral vascular disease, angina pectoris, CAD, previous MI, congestive heart failure, valvular disease, New York Heart Association (NYHA) functional class (≥ 3), true aneurysm, aortic lesion (ascending, arch, descending, and thoracoabdominal), rupture, and redo surgery. Moreover, multivariate analysis was performed to identify risk factors for operative mortality in the CAD (+) group. Predictors included in the subgroup analysis were as follows: age category (5-year age group), sex, renal dysfunction, dialysis, peripheral vascular disease, triple-vessel disease, congestive heart failure, NYHA functional class (≥ 3), true aneurysm, aortic lesion, rupture, and concomitant CABG. Results are expressed using odds ratios (OR) and 95% CI.

Results

Patient background according to the presence of CAD is given in **Table 1**. Overall, 58.4% of patients had a history of smoking. In addition, hypertension and hyperlipidemia were found in 81.7% and 35.8% of patients, respectively. Patients with renal dysfunction accounted for 9.8%, of whom 2.3% were receiving dialysis. A relatively small number of patients (0.8%) had ejection fraction $< 30\%$. Of 4,596 patients who underwent preoperative CAG, 1,904 (41.4%) had a significant stenosis in the coronary artery.

A history of coronary intervention was noted in 151 patients (5.6%) without CAD prior to thoracic aortic surgery. Furthermore, 995 patients with CAD received concomitant CABG; such patients were frequently observed among those who underwent open surgical repair of aortic root, ascending aorta, and aortic arch via a midsternotomy. According to the Japan System for Cardiac Operative Risk Evaluation (SCORE), a system for predicting operative risk based on JACVSD data, the CAD (+) group had a higher predicted 30-day and in-hospital mortality than the CAD (–) group, while the CABG (+) and CABG (–) groups had the same level of risk.

Of 1,904 patients with CAD, lesions were detected in single ($n=856$), double ($n=498$), and triple coronary arteries ($n=436$), or in the LMT alone ($n=114$). In addition, patients with stable angina comprised 32.9% of the CAD (+) patients (i.e., $n=627$), and 39 patients (2.1%) had unstable CAD (**Figure 2A,B**). Concomitant CABG was performed in 326 patients (38.1%) with a single coronary artery lesion, 275

Table 1. Preoperative Patient Characteristics

Variables	CAD (–), n=2,692	CAD (+)		P-value
		CABG (–), n=909	CABG (+), n=995	
Age (years)	70.3±11.0	72.2±7.4	72.4±7.4	<0.0001
Male	74.4	83.4	82.9	<0.0001
BMI (kg/m ²)	23.3±7.8	23.7±3.4	23.5±3.2	0.332
Smoking	55.9	65.7	64.8	<0.0001
Smoking in ≤1 month	17.3	15.5	18.8	0.116
Hypertension	79.8	88	85.8	<0.0001
Hyperlipidemia	32.4	45.5	44.6	<0.0001
Cerebrovascular disease	13.9	19.7	20.7	<0.0001
COPD (≥moderate)	5.8	5.9	5.2	0.741
DM	14.3	19.8	20.4	<0.0001
MI	2.5	12.1	11.1	<0.0001
Renal failure	8.5	13.8	12.7	<0.0001
Hemodialysis	2.1	3.4	2.5	0.052
PAD	17	28.9	28.8	<0.0001
Coronary intervention	5.6	29.6	12.8	<0.0001
Arrhythmia	5.7	6.8	6.6	0.295
NYHA class ≥3	1.2	1.3	3.8	<0.0001
LVEF<30%	0.7	1.3	0.8	0.132
Extent of graft replacement				
Aortic root	3.2	0.6	1.6	<0.0001
Ascending	23.8	17.8	27.8	<0.0001
Arch	49.3	47.4	66.6	<0.0001
Descending	28.9	31.5	8.4	<0.0001
Thoracoabdominal	10.8	14.7	0.8	<0.0001
JapanSCORE				
30-day operative mortality	3.4±2.5	4.7±4.1	5.1±5.3	<0.0001
In-hospital mortality	4.9±4.3	6.4±5.5	6.6±5.9	<0.0001

Data given as mean±SD or %. BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral artery disease; SCORE, System for Cardiac Operative Risk Evaluation.

(55.2%) with double coronary artery lesions, 280 (64.2%) with triple coronary artery lesions, and 114 (100%) with a lesion in the LMT alone. It is notable that all patients with a lesion in the LMT received CABG (**Figure 2C**). In the CABG (+) group, angina was detected in 479 (48.1%), of whom 31 (3.1%) presented with unstable angina (**Figure 2D**). A trend was noted for concomitant CABG to be more frequently selected as the number of affected coronary arteries and the severity of symptoms increased.

Postoperative complications in CAD (–) and CAD (+) groups are listed in **Table 2A**. Patients in the CAD (+) group had a higher incidence of many complications, except for paraparesis or paraplegia, atrioventricular block, cardiac arrest, perioperative MI, and pulmonary embolism. The incidence of postoperative complications in the CABG (–) and CABG (+) groups is given in **Table 2B**. The CABG (+) group had a significantly higher incidence of perioperative MI, postoperative atrial fibrillation, and prolonged ventilation, although there was no significant difference in the incidence of 30-day or in-hospital mortality. Perioperative MI was observed in 13 CAD (–) patients (0.5%), in 2 CABG (–) patients (0.2%), and in 13 CABG (+) patients (1.3%), showing a significantly higher incidence of MI in the CABG (+) group ($P=0.008$). There was no significant difference, however, in the incidence of postoperative cardiac arrest including fatal arrhythmia, which was observed in 32 CAD

(–) patients (1.2%), 13 CABG (–) patients (1.4%), and 9 CABG (+) patients (0.9%). Complications due to anticoagulant therapy were frequently observed in the CAD (+) group.

Operative mortality after aortic surgery was noted in 5.3% ($n=244$) of all patients. Postoperative 30-day mortality was seen in 70 CAD (–) patients (2.6%), and in 99 CAD (+) patients (5.0%), showing a higher incidence in patients with CAD. In comparison, the in-hospital mortality rate was 4.3% in the CAD (–) group, and 8.0% in the CAD (+) group, showing a higher incidence in CAD (+). In-hospital mortality, however, was not significantly different between the CABG (–) and CABG (+) groups ($P=0.130$; **Figure 3**).

On multivariate analysis CAD was identified as an independent risk factor for operative mortality (OR, 1.53; 95% CI: 1.138–2.062, $P=0.005$; **Table 3**). The area under the curve for the discrimination of risk model was 0.741 (95% CI: 0.708–0.774). In the CAD (+) group, on logistic regression analysis the independent risk factors for operative mortality were age, renal dysfunction, dialysis, rupture, aortic arch repair and thoracoabdominal repair, whereas concomitant CABG was not identified as a risk factor (**Table 4**).

Discussion

Although there have been some studies investigating the outcomes of surgery for aortic disease in CAD patients, the

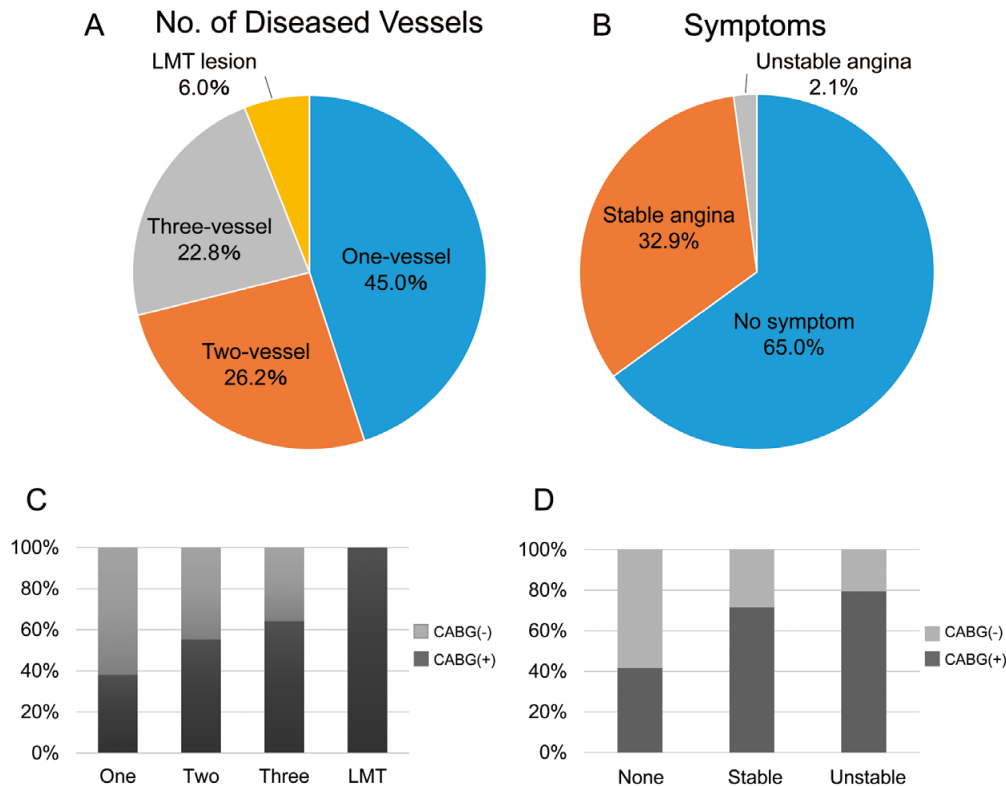


Figure 2. Clinical and angiography characteristics in patients with coronary artery disease (CAD). **(A)** No. diseased vessels of the coronary artery. **(B)** Percentage of patients with CAD and symptoms of angina pectoris. **(C)** Percentage of concomitant coronary artery bypass grafting (CABG) cases according to the number of diseased vessels of the coronary artery. **(D)** Percentage of patients with angina symptoms and concomitant CABG. LMT, left main trunk.

subjects in most of these studies were patients with abdominal aortic disease or peripheral vascular disease.^{11–14} In the field of thoracic aortic disease, there are few studies on the incidence of CAD in patients with electively operable aortic disease or on surgical outcomes in these patients; furthermore, many of these studies were conducted in a limited number of patients in a single institution. We therefore used an accurate Japanese database to investigate differences in patient background and surgical outcome in accordance with the presence or absence of CAD, in a large patient cohort.

In this analysis, approximately 23% of patients who underwent CAG were found to have CAD before surgery for thoracic aortic disease. CAG is performed routinely in all patients before surgery for thoracic artery disease in some institutions; in other institutions, however, it is performed only in patients at high risk of CAD; thus, the detection rate of CAD differed between institutions. The incidence of CAD in patients with thoracic aortic disease, however, is 10–30%.^{1–5} In this study, a relatively high prevalence of CAD was observed. This may be attributable to limiting the study to true aortic aneurysms by excluding aortic dissection, which sometimes may not be caused by arteriosclerosis. Considering that some patients who were preoperatively judged to not have a significant coronary artery stenosis received a prior coronary intervention, it is highly possible that CAD occurs more frequently in patients with a true aortic aneurysm. Furthermore, approximately

65% of patients with CAD did not complain of symptoms of angina, suggesting difficulty in judging the presence or absence of coronary stenosis by symptoms alone. Therefore, we believe preoperative screening for CAD should be performed in patients with a true aortic aneurysm even when they are asymptomatic.

The incidence of cardiac complications directly related to CAD, incorporating perioperative MI and cardiac arrest including ventricular fibrillation, was very low and additionally, there was no significant increase in the incidence of cardiac complications in CAD patients as compared with patients without CAD. This suggests that aortic surgery is performed in association with almost no cardiac complications including perioperative MI in patients with relatively mild CAD. As described in the ACCF/AHA guidelines, limiting the group of patients who require treatment for CAD before or during aortic surgery to patients with severe CAD could reduce the incidence of perioperative cardiac complications.

Operative mortality and the incidence of major complications, however, were significantly higher (approximately 2-fold increase) when aortic surgery alone was performed in patients with significant coronary stenosis. Furthermore, on multivariate analysis CAD was an independent risk factor for operative mortality. These findings raise the possibility that perioperative myocardial ischemia caused by CAD, or myocardial damage due to insufficient intra-

Table 2. Outcome of Open Aortic Surgery vs. Presence of CAD, and vs. Presence of Simultaneous CABG in CAD Patients

Parameters	CAD (-), n=2,692	CAD (+), n=1,904	OR	95% CI	P-value
A. CAD (+) vs. CAD (-)					
Reoperation for any reasons	6.3	9.9	1.635	1.318–2.029	<0.001
Re-exploration for bleeding	3.7	5.9	1.635	1.242–2.153	<0.001
Stroke	5.0	8.0	1.655	1.303–2.101	<0.001
Continuous coma	1.8	3.8	2.196	1.521–3.170	<0.001
Temporary CNS disorder	3.0	4.4	1.506	1.106–2.052	0.010
Paraparesis or paraplegia	4.0	5.1	1.284	0.971–1.699	0.082
Complete AV block	0.5	0.6	1.309	0.606–2.818	0.545
Cardiac arrest	1.2	1.1	0.972	0.566–1.667	1.000
Perioperative MI	0.5	0.8	1.636	0.789–3.392	0.248
Cardiac tamponade	1.6	2.7	1.696	1.128–2.548	0.015
Atrial fibrillation	13.5	20.0	1.600	1.367–1.873	<0.001
Pneumonia	5.6	8.8	1.628	1.297–2.045	<0.001
Pulmonary embolism	0.2	0.3	1.699	0.550–5.248	0.379
Prolonged ventilation >24 h	13.6	20.1	1.600	1.368–1.872	<0.001
Acute renal failure requiring dialysis	3.1	5.3	1.761	1.310–2.366	<0.001
Complication related to anti-coagulant Tx	0.5	1.0	2.188	1.100–4.350	0.032
	CABG (-), n=909	CABG (+), n=995			
B. CABG (+) vs. CABG (-) in CAD patients					
Reoperation for any reason	8.6	11.1	1.324	0.977–1.795	0.077
Re-exploration for bleeding	5.0	6.8	1.408	0.958–2.702	0.098
Stroke	7.0	9.0	1.313	0.941–1.831	0.111
Continuous coma	3.3	4.3	1.323	0.826–2.120	0.283
Temporary CNS disorder	4.7	4.2	0.888	0.576–1.367	0.657
Paraparesis or paraplegia	6.2	4.1	0.655	0.434–0.987	0.047
Complete AV block	0.4	0.8	1.834	0.585–5.741	0.392
Cardiac arrest	1.4	0.9	0.629	0.274–1.445	0.293
Perioperative MI	0.2	1.3	6.004	1.509–23.854	0.008
Cardiac tamponade	2.2	3.1	1.429	0.814–2.509	0.256
Atrial fibrillation	17.5	22.2	1.347	1.073–1.690	0.011
Pneumonia	9.2	8.5	0.917	0.670–1.257	0.629
Pulmonary embolism	0.3	0.3	0.913	0.210–3.966	1.000
Prolonged ventilation >24 h	18.2	21.9	1.265	1.010–1.585	0.045
Acute renal failure requiring dialysis	4.7	5.9	1.269	0.850–1.896	0.263
Complication related to anti-coagulant Tx	1.1	1.0	0.913	0.388–2.147	1.000

AV, atrioventricular; CI, confidence Interval; CNS, central nervous system; OR, odds ratio; Tx, therapy. Other abbreviations as in Table 1.

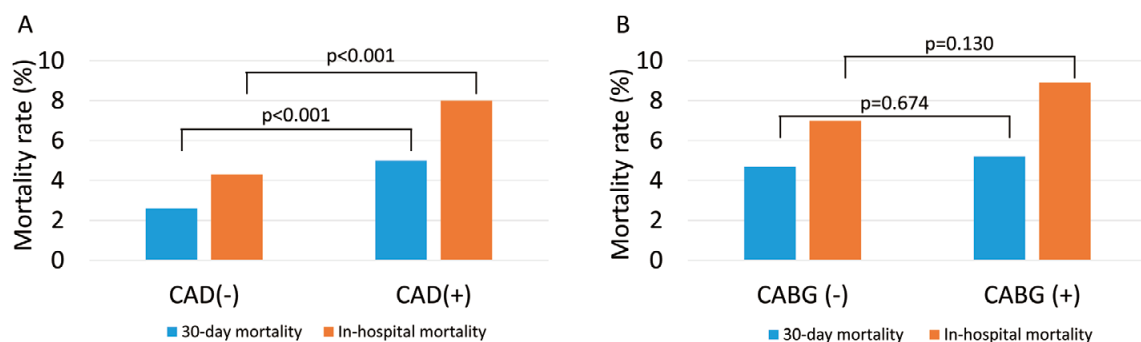


Figure 3. Thirty-day and in-hospital mortality after open thoracic aortic repair in (A) patients with vs. without coronary artery disease (CAD), and (B) patients with CAD with or without concomitant coronary artery bypass grafting (CABG).

Table 3. Multivariate Risk Factors for Death After Aortic Surgery

Risk factors	OR	95% CI	P-value
Age (5-year intervals)	1.25	1.136–1.384	<0.0001
Diabetes mellitus	1.92	1.316–2.787	0.001
Renal dysfunction	2.05	1.381–3.036	<0.0001
Hemodialysis	2.89	1.592–5.251	<0.0001
Cerebrovascular disease	1.38	0.970–1.969	0.073
CAD	1.53	1.138–2.062	0.005
PAD	1.314	0.955–1.806	0.093
Redo surgery	1.64	1.114–2.403	0.012
NYHA class >3	7.27	3.725–14.176	<0.0001
Rupture	4.1	1.646–10.21	0.002
Ascending aorta	1.40	0.986–1.996	0.060
Aortic arch	1.99	1.402–2.832	<0.0001
Thoracoabdominal	3.40	2.283–5.064	<0.0001

Abbreviations as in Tables 1,2.

Table 4. Multivariate Risk Factors for Death After Aortic Surgery in CAD Patients

Risk factors	OR	95% CI	P-value
Age (5-year intervals)	1.330	1.141–1.549	<0.001
Diabetes mellitus	0.924	0.574–1.486	0.744
Renal dysfunction	1.964	1.177–3.276	0.010
Hemodialysis	3.922	1.818–8.460	<0.001
Cerebrovascular disease	1.474	0.961–2.263	0.076
Triple-vessel disease	0.904	0.576–1.418	0.661
PAD	1.017	0.664–1.559	0.937
Redo surgery	1.740	0.954–3.175	0.071
NYHA class >3	1.959	0.801–4.793	0.141
Concomitant CABG	1.355	0.896–2.049	0.150
Rupture	7.644	2.783–21.001	<0.001
Ascending aorta	1.065	0.673–1.685	0.790
Aortic arch	1.772	1.084–2.897	0.023
Thoracoabdominal	4.605	2.425–8.747	<0.001

Abbreviations as in Tables 1,2.

operative myocardial protection, would affect surgical outcome, although CAD was not directly related to the occurrence of perioperative MI or fatal arrhythmia. Thus, when severe coronary stenosis is detected prior to surgery, coronary revascularization, including CABG, may possibly improve outcome.

On univariate analysis the incidence of perioperative MI and prolonged ventilation was significantly higher in the CABG (+) group. According to the JACVSD definitions, regardless of electrocardiogram changes, the elevation of biochemistry cardiac markers, such as creatine kinase (CK) or CK-MB more than twice the upper limit of normal, or positive troponin test, is defined as perioperative MI. This definition may partly affect the higher incidence of perioperative MI in the CABG (+) group. It has also been reported that biochemistry cardiac markers increase after bypass surgery for coronary stenosis.¹⁵ Moreover, issues associated with combined procedures, such as a prolonged duration of operation and extracorporeal circulation, may negatively affect these outcomes. No significant difference in operative death, however, was observed

between the CABG (–) and CABG (+) groups. Moreover, simultaneous CABG was not a risk factor for operative mortality in the CAD patients. Thus, simultaneous CABG should be considered if patients have severe CAD, such as triple-vessel disease or LMT stenosis.

Study Limitations

This was a retrospective study with a number of limitations. First, it was not possible to simply compare the difference in surgical outcome for thoracic aortic disease in the presence or absence of CAD because patient background differed according to the presence of CAD. Although several techniques exist, such as propensity matching, for adjusting preoperative patient background, we decided to present real-world data on the prevalence of CAD, patient background, and postoperative outcome in patients who underwent open surgery for true aneurysms of the thoracic aorta, obtained from a relatively large cohort. Second, the severity of CAD was not evaluated because detailed information regarding the severity or location of coronary stenosis was not available from the registry. Third, detailed information on the surgical procedure and the method of organ protection for each patient was unknown. The fourth limitation is that the registry data did not provide information on any relationship to postoperative cardiac complications, such as perioperative MI or cardiac arrest, and the cause of death. Although perioperative MI may be a cause of postoperative cardiac death, there were only a limited number of perioperative MI cases, irrespective of the presence of significant coronary artery stenosis, in this study. Notably, higher mortality was observed in CAD (+) patients, despite the lower number of perioperative MI cases compared with the CAD (–) patients. Therefore, we infer that the direct contribution of perioperative MI to mortality is very small.

Conclusions

We have investigated the current status of preoperative CAG in patients with thoracic aortic disease using the Japanese national registry database (JACVSD). Approximately 40% of patients who underwent CAG were found to have CAD. Although the incidence of cardiac complications related to CAD was very low, such as MI or ventricular fibrillation, CAD was identified as an independent risk factor for operative mortality. In patients with aortic disease having risk factors for CAD, aggressive evaluation of CAD should be carried out before surgery. Once severe CAD is detected, preoperative coronary intervention or simultaneous CABG should be considered.

Acknowledgments

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Disclosures

The authors declare no conflicts of interest.

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