syndrome, and improved antibiotic alternatives with newer, broad-spectrum medications [1]. However, most modern case series of secondary peritonitis with severe sepsis or septic shock have reported an average mortality rate of ~30 % [3].

Knowledge regarding the predictive factors and arrival at a consensus scoring system for the risk of mortality after surgery for ADP would be useful. Many hospitals and surgeons have tried to clarify these factors and develop scoring systems in their own units [1, 3, 9–13]. Although nationwide data regarding the quality of emergency surgical care using the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) have been reported in several studies [14–17], to date, there has been no report of a nationwide study focused on ADP.

The National Clinical Database (NCD) in Japan, which commenced patient registration in January 2011, is a nationwide project linked to the surgical board certification system. Submitting cases to the NCD is a prerequisite for all member institutions of both the Japan Surgical Society and the Japanese Society of Gastroenterological Surgery (JSGS), and only registered cases can be used for board certification. The NCD collaborates with the ACS-NSQIP [12], which shares a similar goal of developing a standardized surgery database for quality improvement. The NCD contains >1,200,000 surgical cases collected from >3,500 hospitals in 2011, and risk models of some of the procedures (total gastrectomy, right hemicolectomy, hepatectomy, pancreaticoduodenectomy, hepatectomy, etc.) have been created using these data [18–21]. In this study, a risk model was developed using 8,482 surgical cases of ADP from 1,285 hospitals throughout Japan. This risk model will hopefully contribute to the future improvement in the quality control of surgery for ADP.

Methods

Data acquisition

The NCD continuously recruits individuals to approve the inputted data from members of various departments in charge of annual cases, as well as data entry officers, through a web-based data management system to assure the traceability of the data. Furthermore, the project managers consecutively and consistently validate the data by inspection of randomly chosen institutions.

In this study, we focused on ADP cases in the GI surgery section of the NCD that were characterized by variables and definitions that were almost identical to those applied in the ACS-NSQIP [14–17, 22]. In the GI surgery section, all of the surgical cases are registered and require detailed input items for the eight procedures representing the performance of surgery in each specialty (low anterior resection, right hemicolectomy, hepatectomy, total gastrectomy, partial gastrectomy, pancreatoduodenectomy, esophagectomy, and ADP). All variables, definitions and inclusion criteria regarding the NCD are accessible from the website (http://www.ncd.or.jp/) to participate institutions, and are also intended to support an E-learning system in order for participants to input consistent data. The NCD provides answers to all queries regarding data entry (~80,000 inquiries in 2011) and regularly includes the responses to some of the queries as Frequently Asked Questions on the website.

Patient selection

A total of 8,482 patients who underwent surgery for ADP were identified from the NCD in 2011. Most of the patients who underwent surgery for ADP required emergency surgery within 24 h after admission, because the condition of the patients would otherwise have proven fatal or would have caused severe damage to the patients. This is differentiated from localized intra-abdominal abscess, which allows for a time-rich detailed exploration. Surgery for ADP (i.e., surgical debridement and/or drainage) is a procedure representing the performance of a surgery that has been allowed by the national Japanese insurance system. To reduce the bacterial load, the abdominal cavity is lavaged, with particular attention to areas prone to abscess formation (e.g., the paracolic gutters and subphrenic areas). When surgery is performed to address underlying diseases or resection of a perforated viscus with reanastomosis or the creation of a fistula, supplemental procedures, such as resection of the small intestine, colorectal resection and enterostomy, are also recorded. The NCD allows the inclusion of up to eight ICD-10 codes for the preoperative/postoperative diagnosis of each case. Possible causative diseases necessitating surgery in the NCD include peritonitis, intestinal perforation, appendicitis, gastroduodenal ulcer/perforation, intestinal obstruction and vascular insufficiency, etc.

Pre- and perioperative variables

The potential independent variables included the patient demographics, pre-existing comorbidities, preoperative laboratory values, and perioperative data. The demographic variables of age, gender, smoking status, and drinking status were considered. Patients were categorized on the basis of whether they were transferred directly by ambulance or not. General factors, such as the preoperative functional status [independent, partially dependent, and totally dependent with regard to a patient's ability to perform activities of daily living (ADL) 30 days and immediately before surgery] and the body mass index (BMI), were also considered. The ASA physical status classification was evaluated. We also considered preexisting comorbidities, including the cardiovascular status (congestive heart failure, coronary diseases, hypertension, previous cardiac surgery, and peripheral vascular disease), respiratory status (dyspnea, ventilator dependence, pneumonia, and chronic obstructive pulmonary disease), renal status (acute renal failure and dialysis), hematological status (bleeding disorders and preoperative blood transfusion), oncological status (disseminated cancer, chemotherapy and radiotherapy), preoperative blood transfusion, chronic steroid use, ascites, sepsis, diabetes, open wound, and pregnancy. The laboratory parameters included in the analysis were the white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate amino transferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A1c, and C-reactive protein (CRP). The length of the surgery, intraoperative blood loss and relaparotomy within 30 days after surgery for ADP were also considered. A total of 4,192 supplemental procedures for source control were also included.

Endpoints

The outcome measures of this study were the 30-day and surgical mortality rates. The former was defined as death within 30 days of surgery regardless of the patient's geographical location, even if the patient had been discharged from the hospital. The latter was defined as death within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), as well as any patient who died after being discharged, up to 30 days from the date of surgery.

Statistical analysis

Data were randomly assigned into two subsets that were split 80/20, the first for model development, and the second for validation. The two sets of logistic models (30-day mortality and surgical mortality) were constructed for dataset development using stepwise selection of the predictors with a probability (P) value for inclusion of 0.05. A "goodness-of-fit" test was performed to assess how efficiently the model could discriminate between surviving and deceased patients. Model calibration (the degree to which the observed outcomes were similar to the predicted outcomes from the model across patients) was examined by comparing the observed with the predicted average within each of 10 equally sized subgroups arranged in increasing order of patient risk [6, 23].

Results

Outcomes

Among the data for the 8,482 patients stored in the NCD for 2011, the 30-day and postoperative mortality rates for ADP were 9.0 and 14.1 %, respectively. The causative diseases leading to the need for surgery are listed in Table 1. The development dataset (test set) included 6,759 records, and the validation dataset (validation set) included 1,723 records (Table 2). The rates of relaparotomy and readmission within 30 days in all records were 8.1 and 1.7 %, respectively, in these datasets.

Risk profile for the study population

The patient population that underwent surgery for ADP had an average age of 64.7 years (SD 18.6), 59.8 % of whom were males, and 38.7 % of patients were taken to the hospital by ambulance, 93.1 % of whom required emergency surgery. An abbreviated risk profile of the study population is shown in Table 3. The patients with partially/totally dependent and totally dependent evaluations of the ADL within 30 days before surgery comprised 20.7 and 7.7 % of the patients, respectively. Only 0.6 % of the patients had a BMI $\geq$35 kg/m^2. Of the included patients, 43.2 %

Table 1 The causative disease leading to the need for surgery

Diagnosis	Number	30-Day mortality		Surgical mortality	
		Number	Percent (%)	Number	Percent (%)
Acute peritonitis	4,378	429	9.8	652	14.9
Appendicitis	1,183	4	0.3	10	0.8
Intestinal perforation	1,576	148	12.9	222	19.3
Gastroduodenal ulcer/perforation	833	63	7.3	64	9.7
Intestinal obstruction	396	50	12.6	80	20.2
Cholecystitis/cholangitis	218	18	9.0	26	13.1
Vascular insufficiency	121	21	17.4	35	28.9
All cases	8,482	762	9.0	1,195	14.1

The listed diseases were not mutually exclusive

Causative diseases with fewer than 100 cases were not listed

Table 2 The outcomes of surgery for acute diffuse peritonitis

Outcomes	Test set ($n = 6{,}759$)		Validation set ($n = 1{,}723$)		Overall incidence ($n = 8{,}482$)	
	Number	Percent (%)	Number	Percent (%)	Number	Percent (%)
30-Day mortality	604	8.9	158	9.2	762	9.0
In-hospital mortality	938	13.9	241	14.0	1,179	13.9
Surgical mortality	950	14.1	245	14.2	1,195	14.1
Relaparotomy within 30 days	546	8.1	145	8.4	691	8.1
Readmission within 30 days	107	1.6	39	2.3	146	1.7

were ASA class 3–5. Regarding preexisting comorbidities, 20.5 % of patients had received preoperative blood transfusions, 22.7 % had ascites, 31.8 % had sepsis, and 13.5 % had diabetes.

The types of supplemental surgical procedures ($n = 4{,}192$) performed for source control are listed in Table 4. The primary surgical procedures were enterostomy (30.4 %), colorectal resection (19.9 %), closure of a perforated stomach/duodenum (13.0 %), appendectomy (12.4 %), resection of the small intestine (8.2 %), the Hartmann procedure (6.5 %), cholecystectomy/cholecystotomy (3.5 %), closure of a perforated small intestine (3.3 %), and surgery for intestinal obstruction (2.5 %).

Model results

Two different risk models were developed, and the final logistic model with odds ratios and 95 % confidence intervals are presented in Table 5. The scoring system for the mortality risk models according to the logistic regression equation was as follows:

Predicted mortality $= e(\beta 0 + \Sigma\beta i\, Xi)/1 + e(\beta 0 + \Sigma\beta i\, Xi)$, where βi is the coefficient of the variable Xi in the logistic regression equation provided in Table 5 for the 30-day mortality and surgical mortality. $Xi = 1$ if a categorical risk factor is present and 0 if it is absent. For the age category, $Xi = 1$ if the patient age is <59 years old; 2 if the patient age is between 60 and 64; 3 if 65 and 69; four if 70 and 74; 5 if 75–79 and the $Xi = 6$ if the age was ≥80 years old. Between the two models, there were 16 overlapping variables: the age, ASA class 5, ASA class 4, ASA class 3, disseminated cancer, nontumor-bearing, preoperative transfusion, chronic steroid use, serum albumin <2.0 g/dL, serum total bilirubin ≥3.0 mg/dL, serum AST ≥35 U/L, serum ALP ≥600 U/L, serum urea nitrogen ≥20 or 25 mg/dL, serum Na <130 mEq/L and serum CRP ≥10.0 mg/dL.

The important variables (odds ratio >2.0) affecting the 30-day mortality were ASA class 3 (OR, 2.69; 95 % CI, 2.05–3.54), ASA class 4 (OR, 4.28; 95 % CI, 3.11–5.87), ASA class 5 (OR, 8.65; 95 % CI, 6.14–12.18), previous PCI (OR, 2.05; 95 % CI, 1.26–3.31), previous PVD surgery (OR, 2.45; 95 % CI, 1.16–5.17) and disseminated cancer (OR, 2.16; 95 % CI, 1.53–3.05), whereas those affecting the surgical mortality were ASA Class 3 (OR, 2.27; 95 % CI, 1.83–2.82), ASA Class 4 (OR, 4.67; 95 % CI, 3.61–6.05), ASA class 5 (OR, 6.54; 95 % CI, 4.83–8.84) and disseminated cancer (OR, 2.09; 95 % CI, 1.54–2.83).

Model performance

To evaluate the model performance, both a C-index (a measure of model discrimination) with a 95 % CI, which is the area under the receiver operating characteristic curve, and the model calibration across risk groups were evaluated. As a performance parameter of the risk model, the C-indices of the 30-day and surgical mortality were 0.851 (95 % CI, 0.822–0.880) and 0.852 (95 % CI, 0.828–0.875), respectively (Fig. 1). Figure 2 demonstrates the calibration of the models and how well the rates for the predicted events matched those of the observed events among the patient risk subgroups.

Discussion

Systemic sepsis is a life-threatening condition that may occur as a result of intra-abdominal infections of all types [1, 3]. In complicated intra-abdominal infections, the infection spreads beyond the organ of origin and causes either localized or diffuse peritonitis [2, 10]. Complicated intra-abdominal infections represent an important cause of morbidity, and are frequently associated with a poor prognosis [2, 10]. The mortality is reportedly reduced by 50 % following the introduction of the basic concepts of surgery for intra-abdominal infections by: (1) elimination of the septic foci, (2) removal of necrotic tissue and (3) drainage of purulent material. Advances that have provided a better understanding of the pathophysiology, the role of damage control, the prevention of intra-abdominal

Table 3 Key risk profiles and outcomes

	Records for the entire study population ($n = 8{,}482$)		Outcome groups			
			30-Day mortality ($n = 762$)		Surgical mortality ($n = 1{,}195$)	
	Number	Percent	Number	Percent	Number	Percent
Characteristics						
Demographics						
Age, mean (SD), years	64.7 (18.6)		74.8 (13.7)		74.5 (13.2)	
Males	5,072	59.8	416	8.2	667	13.2
Ambulance transportation	3,283	38.7	364	11.1	511	15.6
Preoperative risk assessment						
General						
ADL within 30 days before surgery						
Partially/totally dependent	1,756	20.7	342	19.5	535	30.5
Totally dependent	653	7.7	149	22.8	231	35.4
ADL immediately before surgery						
Partially/totally dependent	2,358	27.8	427	18.1	654	27.7
Totally dependent	1,162	13.7	258	22.2	375	32.3
Body mass index ≥35 kg/m^2	51	0.6	11	20.8	14	28.3
Weight loss over 10 %	442	5.2	77	17.4	134	30.3
ASA class 3, ASA class 4, or ASA class 5	3,664	43.2	641	17.5	976	26.6
Cardiovascular						
Congestive heart failure	237	2.8	71	30.0	103	43.4
Previous myocardial infarction	51	0.6	14	27.5	18	35.3
Angina pectoris	110	1.3	20	18.2	26	23.6
Hypertension without therapy	271	3.2	27	10.0	45	16.7
Previous PCI	170	2	37	22.0	44	26.2
Previous cardiac surgery	119	1.4	28	23.3	35	29.3
Previous surgery for PVD	51	0.6	14	28.3	24	47.2
Pulmonary						
Dyspnea	712	8.4	192	27.0	267	37.4
Ventilator-dependent	331	3.9	98	29.6	147	44.3
Pneumonia	305	3.6	84	27.6	125	40.9
COPD	288	3.4	46	15.8	71	24.6
Renal						
Acute renal failure	407	4.8	127	31.1	177	43.5
Dialysis	322	3.8	79	24.4	118	36.7
Oncological						
Non-tumor-bearing	7,490	88.3	618	8.3	947	12.6
Disseminated cancer	450	5.3	95	21.2	161	35.8
Chemotherapy	297	3.5	49	16.6	101	33.9
Radiotherapy	51	0.6	9	17.0	14	27.7
Hematological						
Bleeding disorder without therapy	560	6.6	159	28.5	214	38.2
Preoperative blood transfusion	1,739	20.5	351	20.2	535	30.8
Other						
Previous cerebrovascular disease	450	5.3	76	17.0	119	26.4
Chronic steroid use	365	4.3	71	19.4	109	29.9
Ascites without therapy	1,925	22.7	259	13.4	412	21.4
Sepsis	2,697	31.8	453	16.8	661	24.5

Table 3 continued

	Records for the entire study population (n = 8,482)		Outcome groups			
			30-Day mortality (n = 762)		Surgical mortality (n = 1,195)	
	Number	Percent	Number	Percent	Number	Percent
Diabetes	1,145	13.5	152	13.3	241	21.0
Preoperative laboratory value						
White blood cell count <4,500/μL	1,993	23.5	253	12.7	382	19.2
White blood cell count <4,000/μL	1,789	21.1	230	12.9	345	19.3
Hemoglobin <13.5 g/dL in males; <12.5 g/dL in females	4,419	52.1	541	12.3	886	20.1
Hemoglobin < 10.0 g/dL	1,734	20.4	268	15.5	442	25.5
Hematocrit <30 %	1,671	19.7	264	15.8	440	26.3
Platelet count <15,000/μL	1,484	17.5	297	20.0	406	27.4
Platelet count <12,000/μL	771	9.1	192	24.9	260	33.7
Platelet count <8,000/μL	288	3.4	104	36.1	137	47.6
Serum albumin <2.0 g/dL	619	7.3	141	22.8	225	36.4
Serum albumin <2.5 g/dL	1,612	19	291	18.1	491	30.5
Serum albumin <3.0 g/dL	2,943	34.7	450	15.3	746	25.3
Serum total bilirubin ≥3.0 mg/dL	365	4.3	76	20.9	113	31.0
Serum AST ≥35 U/L	2,036	24	331	16.2	483	23.8
Serum ALP ≥340 U/L	1,442	17	199	13.8	317	22.0
Serum ALP ≥600 U/L	407	4.8	76	18.8	113	27.8
Serum urea nitrogen ≥20 mg/dL	3,868	45.6	596	15.4	898	23.2
Serum urea nitrogen ≥25 mg/dL	2,748	32.4	503	18.3	736	26.8
Serum creatinine ≥1.2 mg/dL	2,171	25.6	401	18.5	591	27.2
Serum creatinine ≥2.0 mg/dL	984	11.6	216	22.0	320	32.5
Serum Na <130 mEq/L	475	5.6	78	16.5	135	28.3
Serum Na <13 5 mEq/L	1,976	23.3	245	12.4	398	20.1
Serum Na ≥145 mEq/L	314	3.7	71	22.5	95	30.2
Serum CRP ≥10.0 mg/dL	3,927	46.3	369	9.4	611	15.6
Operation						
Length of operation ≥6 h	51	0.6	12	24.0	16	32.0
Intraoperative blood loss ≥2,000 mL	161	1.9	40	24.5	62	38.2
Relaparotomy within 30 days	687	8.1	81	11.7	163	23.7

SD standard deviation, *ADL* activities of daily living, *ASA class* American Society of Anesthesiologists Physical Status Classification, *PCI* percutaneous coronary intervention, *PVD* peripheral vascular disease, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *Na* sodium, *CRP* C-reactive protein

compartment syndrome and antibiotic administration have collectively helped to reduce the mortality rate below 20 % [1].

In this study, the 30-day and surgical mortality rates after surgery for all acute types of primary, secondary and tertiary peritonitis [1–3] were 9.0 and 14.1 %, respectively. Recently, published studies reported that the 30-day mortality rate after surgery for ADP was 8–9 % [24, 25], whereas the surgical mortality rate was 12.8–33.3 % (12.8 % [26], 14 % [5], 19 % [24], 22 % [27], 21.8 % [12], 23.1 % [11] and 33.3 % [28]). For reference, the 30-day mortality rate of the patients in the ACS-NSQIP study of 5,083 patients who underwent emergency colorectal operations was 15.4 % [17]. Thus, although the 30-day mortality rate in this study was similar to that in previous studies, the surgical mortality rates in the previous studies from western countries was higher than that in the current study. We believe that our results were satisfactory for a nationwide outcome of surgery for ADP.

Early prognostic evaluation of complicated intra-abdominal infections is important to assess the severity and prognosis of disease [10]. A number of factors influencing the prognosis of patients with complicated intra-abdominal infections, as well as scoring systems to evaluate these

Table 4 Supplemental surgical procedures performed for source control and the outcomes

Surgical	Surgical procedures		Outcome groups			
			30-Day mortality		Surgical mortality	
	Number	Percent	Number	Percent	Number	Percent
Gastro-duodenum						
Closure of perforated stomach and/or duodenum	545	13.0	35	6.4	46	8.4
Gastrectomy	75	1.8	7	9.3	8	10.7
Postduodenal small intestine						
Resection of small intestine	345	8.2	35	10.1	67	19.4
Closure of perforated intestine	138	3.3	10	7.2	22	15.9
Surgery for intestinal obstruction	106	2.5	21	19.8	30	28.3
Enterostomy	1,276	30.4	185	14.5	280	21.9
Appendix						
Appendectomy	519	12.4	4	0.8	11	2.1
Colon and rectum						
Right-sided colon resection	177	4.2	19	10.7	32	18.1
Left-sided colon resection	326	7.8	47	14.4	68	20.9
Anterior resection	22	0.5	2	9.1	2	9.1
Hartmann procedure	273	6.5	32	11.7	44	16.1
Total colectomy	19	0.5	4	21.1	5	26.3
Hepato-biliary-pancreatic						
Hepatic resection/suturing the liver	8	0.2	1	12.5	2	25.0
Cholecystectomy/cholecystostomy	151	3.6	12	8.1	20	13.4
Choledocholithotomy/choledochoduodenostomy (-jejunostomy)/choledochostomy	29	0.7	7	25.0	7	25.0
Surgery for acute pancreatitis/resection of the pancreas/Drainage of pancreatic duct or cyst, %	8	0.2	2	22.2	4	44.4
Others						
Abdominoperineal resection/total pelvic exenteration	17	0.4	4	22.2	4	22.2
Splenectomy	13	0.3	3	21.4	4	28.6

A total of 4,192 supplemental surgical procedures were included. Surgical procedures performed fewer than eight times were not listed. Some patients underwent more than one surgical procedure

factors, have been reported [3, 10–13, 24]. From our risk model, the important variables identified to affect the 30-day mortality rate were ASA class 3, ASA class 4, ASA class 5, previous percutaneous coronary intervention (PCI), previous surgery for peripheral vascular disease (PVD) and disseminated cancer, whereas those affecting the surgical mortality rate were ASA class 3, ASA class 4, ASA class 5 and disseminated cancer. Although the ASA classification of fitness for surgery was not devised as a risk prediction score, several studies have reported the association between the ASA class and observed postoperative mortality in elderly patients following emergency GI surgery [13, 29]. In univariate and multivariate analyses of the mortality of emergency surgical patients, the ASA class has been consistently shown to be a good predictor of postoperative death, although this is despite its subjective nature and the inter-observer variations in measuring the ASA class [13].

Other significant factors identified by our risk assessment model, including age, ambulance transportation, the ADL, respiratory distress, preoperative pneumonia, bleeding disorders, preoperative blood transfusion and long-term steroid use, were also significant risk factors for the 30-day and/or surgical mortality. Several risk factors (age, dyspnea, previous PCI, disseminated cancer, long-term steroid use, bleeding disorder without therapy and preoperative blood transfusion) have been reported in previous studies [31, 32], although ambulance transportation and the ADL have not been previously reported. The rate of ambulance transport among the elderly is continually increasing along with the rapidly aging population in Japan [33]. In this study, 38.7 % of the 8,482 patients who underwent surgery for ADP were admitted to a hospital by direct ambulance transport. Among the critical components of health care systems, ambulance services play an important

Table 5 The odds ratios with 95 % confidence intervals for the risk models of surgery for acute diffuse peritonitis

Variables	30-Day mortality				Surgical mortality			
	β coefficient	OR	95 % CI	P value	β coefficient	OR	95 % CI	P value
Demographics								
Age category[a]	0.211	1.24	1.17–1.31	<0.001	0.234	1.26	1.20–1.33	<0.001
Ambulance transport	0.317	1.37	1.12–1.68	0.002				
Respiratory distress	0.462	1.59	1.22–2.06	<0.001				
ADL, totally dependent immediately before surgery	0.337	1.4	1.11–1.77	0.005				
ADL, totally dependent within 30 days before surgery					0.465	1.59	1.22–2.07	0.001
ADL, partially/totally dependent immediately before surgery,					0.303	1.35	1.12–1.64	0.002
Preoperative pneumonia					0.342	1.41	1.01–1.97	0.045
ASA class 5	2.157	8.65	6.14–12.18	<0.001	1.877	6.54	4.83–8.84	<0.001
ASA class 4	1.453	4.28	3.11–5.87	<0.001	1.542	4.67	3.61–6.05	<0.001
ASA class 3	0.99	2.69	2.05–3.54	<0.001	0.822	2.27	1.83–2.82	<0.001
Preexisting comorbidity								
Previous PCI	0.715	2.05	1.26–3.31	0.004				
Previous surgery for PVD	0.897	2.45	1.16–5.17	0.018				
Disseminated cancer	0.769	2.16	1.53–3.05	<0.001	0.735	2.09	1.54–2.83	<0.001
Non tumor-bearing	−0.436	0.65	0.48–0.87	0.003	−0.69	0.5	0.4–0.64	<0.001
Bleeding disorder without therapy	0.499	1.65	1.24–2.19	0.001	0.484	1.62	1.31–2.01	<0.001
Preoperative blood transfusion	0.472	1.6	1.13–2.28	0.009	0.595	1.81	1.32–2.49	<0.001
Chronic steroid use	0.552	1.74	1.21–2.50	0.003	0.651	1.92	1.39–2.65	<0.001
Weight loss over 10 %					0.331	1.39	1.02–1.90	0.036
Preoperative laboratory value								
White blood cell count <4,500/μL					0.404	1.5	1.25–1.8	<0.001
White blood cell count <4,000/μL	0.336	1.4	1.12–1.75	0.003				
Hemoglobin <13.5 g/dL in males; <12.5 g/dL in females					0.273	1.31	1.07–1.62	0.01
Hemoglobin <10.0 g/dL	0.254	1.29	1.03–1.61	0.024				
Hematocrit <30 %					0.209	1.23	1.01–1.51	0.044
Platelet count <15,000/μL	0.413	1.51	1.19–1.92	0.001				
Platelet count <12,000/μL					0.356	1.43	1.13–1.8	0.003
Platelet count <8,000/μL	0.424	1.53	1.03–2.26	0.033				
Serum albumin <2.0 g/dL	0.51	1.67	1.25–2.22	<0.001	0.394	1.48	1.14–1.93	0.003
Serum albumin <3.0 g/dL					0.316	1.37	1.13–1.67	0.002
Serum total bilirubin ≥3.0 mg/dL	0.532	1.7	1.16–2.49	0.006	0.676	1.97	1.40–2.76	<0.001
Serum AST ≥35 U/L	0.3	1.35	1.09–1.67	0.006	0.358	1.43	1.19–1.72	<0.001
Serum ALP ≥600 U/L	0.545	1.73	1.18–2.51	0.005	0.474	1.61	1.15–2.24	0.005
Serum urea nitrogen ≥20 mg/dL	0.569	1.77	1.28–2.43	0.001	0.563	1.76	1.35–2.29	<0.001
Serum urea nitrogen ≥25 mg/dL	0.343	1.41	1.06–1.88	0.02				
Serum creatinine ≥2.0 mg/dL					0.405	1.5	1.2–1.89	<0.001
Serum Na <130 mEq/L	0.521	1.68	1.21–2.35	0.002	0.56	1.75	1.31–2.33	<0.001
Serum Na ≥145 mEq/L	0.526	1.69	1.16–2.46	0.006				
Serum CRP ≥10.0 mg/dL	0.397	1.49	1.21–1.83	<0.001	0.423	1.53	1.27–1.83	<0.001
Intercept (β0)	−5.449			<0.001	−4.83			<0.001

ADL activities of daily living, *ASA class* American Society of Anesthesiologists Physical Status Classification, *PCI* percutaneous coronary intervention, *PVD* peripheral vascular disease, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *Na* sodium, *CRP* C-reactive protein, *OR* odds ratio, *CI* confidence interval

[a] Age, years, <59, 60–64, 65–69, 70–74, 75–79, ≥80

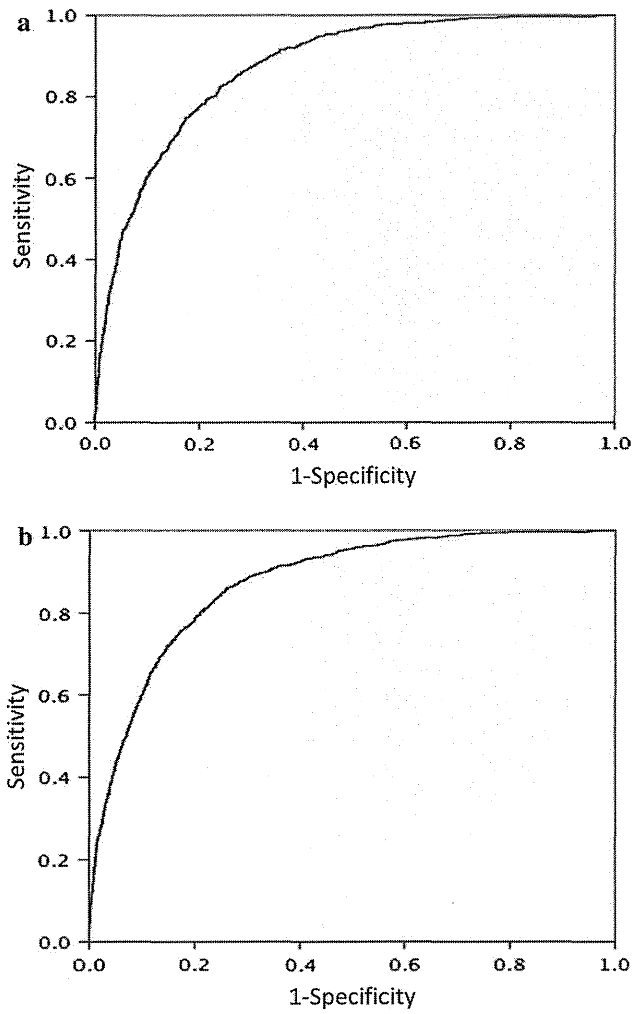

Fig. 1 The receiver operating characteristics (ROC) curves for the 30-day mortality (**a**) and surgical mortality (**b**) in the validation set

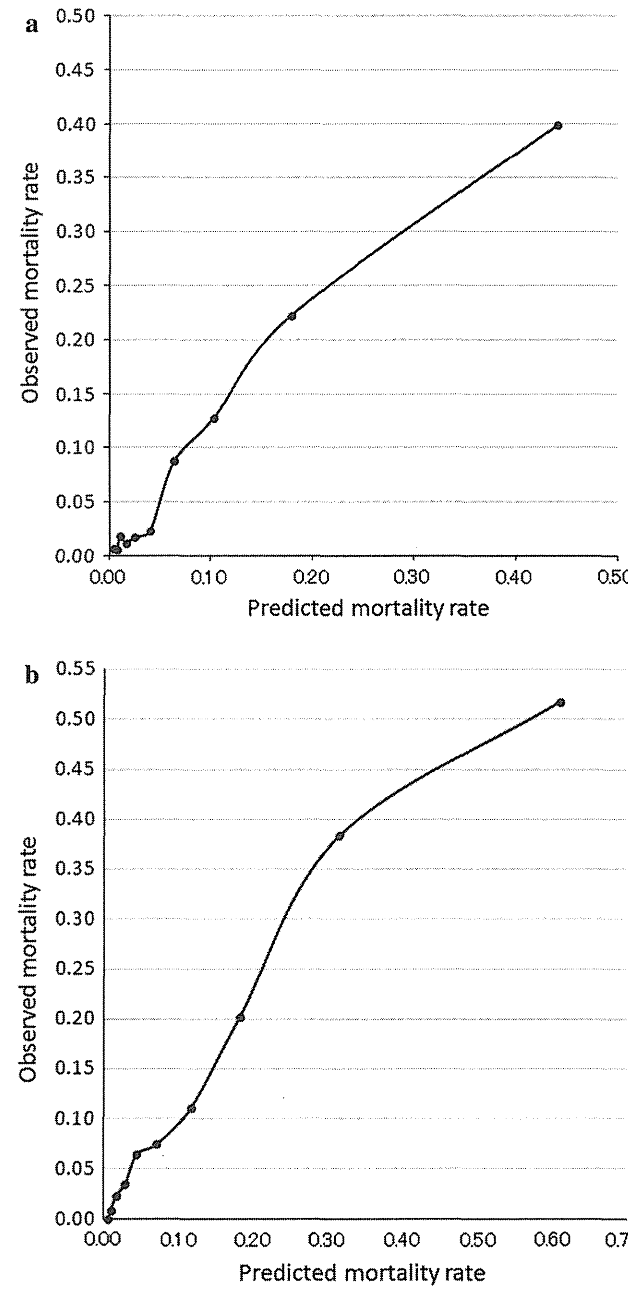

Fig. 2 The model calibration for the 30-day (**a**) and surgical (**b**) mortality models

part in the continuum of health care by providing prehospital care and transport in emergency situations [33]. The ADL describes the essential activities that a person needs to perform to be able to live independently. Particularly in the aging individual, the combination of acute and chronic diseases often results in disabilities and limitations in the ADL [34]. Functional limitations are particularly associated with mortality in patients with hip fractures and pulmonary infections, and in acute medical patients [34, 35]. In this risk model, not only the ADL (totally dependent) immediately before surgery, but also the ADL (totally/partially dependent) within 30 days before surgery was a significant risk factor for surgical mortality. These data suggest that assessment of the ADL within 30 days before surgery should be considered for the clinical management of ADP.

From our risk model, 12 laboratory factors (white blood cell count, hemoglobin, hematocrit, platelet count, and the serum levels of albumin, total bilirubin, aspartate amino transferase, alkaline phosphatase, urea nitrogen, creatinine, sodium and CRP) were significant risk factors for the 30-day and surgical mortality. These laboratory data may reflect the degree of physiological derangement due to the intra-abdominal infection and preexisting critical illness, and have been reported in previous studies.

The C-indices of the models for the 30-day and surgical mortality in this study were 0.851 and 0.852, respectively. These data indicate that our models were reliable. Although the usefulness of several scoring systems, such as the Acute Physiology and Chronic Health Evaluation (APACHE) score and the Mannheim Peritonitis Index, have been reported [13], they are not specific for Japanese patients who undergo surgery for ADP. The reliability of existing scores or indices for ADP surgery may be improved by including our risk model. The NCD collects data obtained before admission and during the hospitalization period. On the other hand, the APACHE database is a collection of data obtained only after the patient has been admitted to the intensive care unit [14]. Some NCD preoperative data were predictive of the patient outcomes, which may allow for the earlier identification of potential complications.

This study was associated with several potential limitations. First, except for the ASA class, the other scoring systems to potentially predict the mortality after surgery for ADP, such as the APACHE score and Mannheim Peritonitis Index [13], could not be determined from this database. Second, we could not distinguish between the two different types of intra-abdominal infections (community- and healthcare-acquired), from this database. Third, the risk of mortality differed between ADP due to upper gastrointestinal perforation and that caused by colon perforation, as shown in Table 1. The lack of information regarding the details of the causative diseases in some patients was another limitation of this study. Fourth, the effects of surgical procedures on certain causative disease should be analyzed in a future study.

In conclusion, this report is the first risk stratification study of surgery for ADP to use a nationwide NCD. By analyzing 8,482 patients from 1,285 surgical units throughout Japan, the 30-day and surgical mortality rates were determined to be 9.0 and 14.1 %, respectively. The results of this series are satisfactory regarding the nationwide outcome of surgery for ADP, and this system can be useful in predicting the outcome of surgery for ADP, and may be useful to evaluate and benchmark performance.

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Conflict of interest The authors report no conflicting financial interests.

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Off-pump versus on-pump coronary artery bypass grafting in patients with left ventricular dysfunction

Chikara Ueki, MD,[a,b] Hiroaki Miyata, PhD,[b] Noboru Motomura, MD, PhD,[b] Genichi Sakaguchi, MD, PhD,[a,b] Takehide Akimoto, MD, PhD,[a,b] and Shinichi Takamoto, MD, PhD[b]

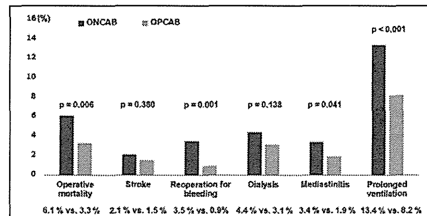
ABSTRACT

Objective: Using data from the Japan Adult Cardiovascular Surgery Database, we evaluated the prognostic influence of off-pump technique in patients with low ejection fraction who underwent coronary artery bypass grafting.

Methods: We analyzed 2187 patients with an ejection fraction <0.30 who underwent primary, nonemergency, isolated coronary artery bypass grafting between 2008 and 2012, as reported in the Japan Adult Cardiovascular Surgery Database. Patients were divided into on-pump (n = 1134; 51.1%) and off-pump (n = 1053; 48.9%) coronary artery bypass grafting groups. Propensity-score matching for 20 preoperative variables was performed, and early mortality and morbidity were compared between matched groups.

Results: Propensity-score matching created 918 pairs. Of the 918 patients in the off-pump group, conversion to an on-pump procedure occurred in 56 (6.1%). Compared with on-pump, off-pump technique was associated with significantly lower incidences of 30-day death (1.7% vs 3.7%; $P = .01$), operative death (3.3% vs 6.1%; $P = .006$), mediastinitis (1.9% vs 3.4%; $P = .041$), reoperation for bleeding (0.9% vs 3.5%; $P < .001$), and prolonged ventilation (8.2% vs 13.4%; $P < .001$). Comparison of patients undergoing off-pump versus on-pump procedures demonstrated no significant differences in the incidence of stroke (1.5% vs 2.1%; $P = .38$), renal failure (6.1% vs 7.4%; $P = .26$), and postoperative dialysis (3.1% vs 4.4%; $P = .14$). Institutional volume-adjusted analysis confirmed most of these results.

Conclusions: Off-pump coronary artery bypass grafting is associated with significantly reduced early mortality and morbidity in patients with an ejection fraction <0.30. (J Thorac Cardiovasc Surg 2015;■:1-7)



Postoperative outcomes of off-pump versus on-pump coronary artery bypass grafting in propensity-matched pairs.

Central Message

Off-pump technique may improve operative outcomes in patients with low ejection fraction undergoing coronary artery bypass grafting.

Perspective

The clinical benefit of off-pump technique in patients with low ejection fraction is still unclear. In this large, retrospective study with risk adjustment, off-pump coronary artery bypass grafting was associated with significantly reduced early mortality and morbidity in patients with low ejection fraction. These findings will help to establish the best operative strategy in this high-risk population.

ACD

Although the clinical benefits of off-pump coronary artery bypass (OPCAB) have not been demonstrated in large randomized trials,[1,2] multiple observational studies have shown the mortality and/or morbidity benefit of OPCAB versus on-pump coronary artery bypass (ONCAB), especially in high-risk subgroups.[3-6] In addition to other representative risk factors, including advanced age, diabetes, and renal dysfunction, left ventricular dysfunction has been shown to be a predictor of early mortality after coronary artery bypass grafting (CABG).[7]

Recent large randomized trials—the Randomized On/Off Bypass (ROOBY) trial and the CABG Off or On Pump Revascularization Study (CORONARY)—included only a small number of patients with low ejection fraction (EF).[1,2] Hence, these randomized trials could not evaluate the prognostic benefit of OPCAB in patients with low EF. Moreover, most retrospective studies from single centers also have significant limitations such as a relatively low sample size and a strong bias in treatment choice. Considering this situation, a risk-adjusted retrospective study of a large database, such as the Society of Thoracic Surgeons (STS) national database, plays an important role in establishing the best strategy for patients with low EF undergoing CABG.[8]

From the [a]Department of Cardiovascular Surgery, Shizuoka General Hospital, Shizuoka, Japan; and [b]Japan Cardiovascular Surgery Database Organization, Tokyo, Japan.

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Address for reprints: Chikara Ueki, MD, Department of Cardiovascular Surgery, Shizuoka General Hospital, 4-27-1 Kita-Ando Aoi-ku, Shizuoka 420-8527, Japan (E-mail: uekichikara@gmail.com).

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CORONOARY	= CABG Off or On Pump Revascularization Study
EF	= ejection fraction
ICU	= intensive care unit
JACVSD	= Japan Adult Cardiovascular Surgery Database
MACE	= major adverse cardiovascular events
NCD	= National Clinical Database
ONCAB	= on-pump coronary artery bypass
OPCAB	= off-pump coronary artery bypass
ROOBY	= Randomized On/Off Bypass trial
STS	= Society of Thoracic Surgeons

The purpose of this study was to evaluate the prognostic influence of OPCAB in patients with an EF <0.30 using a large sample from the Japan Adult Cardiovascular Surgery Database (JACVSD).

PATIENTS AND METHODS

The institutional review board of our institution approved this study. Informed consent was obtained from each patient to allow his or her data to be entered into the database.

The JACVSD

JACVSD, which was created to enable evaluation of surgical outcomes after cardiovascular procedures in hospitals throughout Japan, currently captures clinical information from most Japanese hospitals.

The 255 variables in the data collection form are nearly identical to those of the STS national database. The content of the JACVSD (http://www.jacvsd.umin.jp) and STS databases (http://sts.org) can be viewed online. The JACVSD has developed software for web-based data collection that allows data managers at participating hospitals to submit data electronically to the central office. Participation in JACVSD is voluntary, but there is a high degree of completeness of the data. In addition, the accuracy of submitted data is maintained by regular data auditing in which monthly visits are made to participating hospitals to check the reported data against clinical records. Data validity is further confirmed by independent comparison of specific hospitals' volume of cardiac surgeries entered in JACVSD with that reported in the annual survey of the Japanese Association for Thoracic Surgery. Further, in 2010 and later, the JACVSD served as a part of the National Clinical Database (NCD) in Japan, which includes clinician-initiated databases reflecting all surgical. The NCD covers 95% of total surgical procedures.

Study Population

We examined the data for patients included in the JACVSD from January 1, 2008, to December 31, 2012. Records with missing age (or out of range), sex, or 30-day status (see Study End Points for an explanation) were excluded. With the exception of body surface area, and preoperative creatinine value, all missing or out-of-range values were imputed using the variable-specific median value. After this data cleaning, patients with an EF <0.30 who underwent isolated CABG were included. In the JACVSD, echocardiography, left ventriculography, radionucleotide scan, physician estimation, and other methods (including magnetic resonance imaging) were permitted for the evaluation of EF. The distribution of determination was equivalent between the 2 groups ($P = .089$) and for most of patients was evaluated by echocardiography (62.6%) and left ventriculography gram (21.5%). Missing evaluation method occurred in 14.3% of all patients, and radionucleotide scan (1.0%), physician estimation (0.4%), and other methods (0.1%) were used in only a small portion of patients. Exclusion criteria were emergency or salvage status and redo surgery. Thus, 2187 consecutive patients were included in the analysis. Because intention-to-treat principle was applied to all statistical analyses, patients were divided into those intended for ONCAB (n = 1134; 51.1%) and OPCAB (n = 1053; 48.9%) procedure. Patients intended for OPCAB were included in the OPCAB group even if they were converted intraoperatively to ONCAB.

Study End Points

The study end points were 30-day mortality, operative mortality, and postoperative morbidity. Thirty-day mortality was defined as death within 30 days after surgery. Operative mortality was defined as death occurring within 30 days after surgery and death during the index hospitalization. Major adverse cardiovascular events (MACEs) were defined as a combined end point that included operative mortality, perioperative myocardial infarction, and stroke. Renal failure was defined as an increase in serum creatinine concentration to twice preoperative levels or to >2.0 mg/dL, or new requirement for dialysis or hemofiltration. Perioperative myocardial infarction was defined as at least 2 of the following: continuous angina for >20 minutes regardless of nitrite treatment or rest, elevation of cardiac enzyme levels (creatine kinase-myocardial band) >1/20 of the total creatine kinase level or double the preoperative level and/or lactate dehydrogenase isozyme subtype 1 > subtype 2 and/or positive troponin-I and/or troponin-T), new cardiac wall-motion abnormalities, and Q waves or ST-segment elevation/T-wave changes in >2 serial 12-lead electrocardiograms.

Propensity Matching and Statistical Analysis

Propensity-score matching was used to adjust differences in baseline characteristics because patients were not randomly assigned to receive ONCAB or OPCAB. Each patient's estimated propensity score, which is the likelihood of the patient being intended to undergo OPCAB, was calculated using a multivariate logistic model that included 20 preoperative variables: age, presence of unstable angina, extracardiac vascular disease, cerebrovascular disease (ie, presence of stroke or a history of transient ischemic attack), hypertension, hyperlipidemia, diabetes, preoperative hemodialysis, chronic lung disease (mild, moderate, or severe), arrhythmia, aortic stenosis greater than grade 1, aortic regurgitation greater than grade 2, mitral regurgitation greater than grade 2, tricuspid regurgitation greater than grade 2, cardiogenic shock, history of myocardial infarction, congestive heart failure, New York Heart Association functional class III or IV, triple-vessel disease, and left main disease. The Hosmer-Lemeshow test result was not significant ($P = .292$) and the c-statistic for this propensity model was 0.599 (0.576-0.623; 95% confidence interval). We then performed a 1-to-1 matched analysis on the basis of the estimated propensity score of each patient. The propensity scores were compared between ONCAB and OPCAB patients, with a match occurring when 1 patient in the ONCAB group had an estimated score within 0.6 standard deviations of a patient in the OPCAB group. If 2 or more patients in the ONCAB group met this criterion, we randomly selected 1 patient for matching. We also performed univariate comparisons of patient characteristics and outcome variables between the propensity-score-matched groups of ONCAB and OPCAB patients using Fisher exact test and Student t test as appropriate. In addition, an institutional-volume adjusted analysis was performed by using a mixed-effects logistic regression model. In this model, the annual isolated CABG case volumes of hospitals were included as a covariate.

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TABLE 1. Patient characteristics of the original and matched cohorts

	Original cohort			Matched cohort		
Variable	ONCAB (n = 1134)	OPCAB (n = 1053)	P value	ONCAB (n = 918)	OPCAB (n = 918)	P value
Ejection fraction (%)	26.6 ± 10.4	27.2 ± 7.9	.159	26.8 ± 11.1	27.0 ± 7.8	.734
Age (yrs)	65.7 ± 10.2	67.4 ± 10.1	.002	66.7 ± 9.8	66.2 ± 10.0	.281
Male sex	978 (86.2)	903 (85.8)	.742	784 (85.4)	786 (85.6)	.895
Body mass index	23.0 ± 3.7	22.9 ± 3.8	.417	22.9 ± 3.7	23.0 ± 3.8	.557
Smoking history	742 (65.4)	701 (66.6)	.574	592 (64.5)	610 (66.4)	.377
Diabetes	731 (64.5)	633 (60.1)	.036	574 (62.5)	581 (63.3)	.735
Hyperlipidemia	669 (59.0)	571 (54.2)	.025	517 (56.3)	520 (56.6)	.888
Hypertension	835 (73.6)	758 (72.0)	.387	668 (72.8)	669 (72.9)	.958
Serum creatinine (mg/dL)	2.19 ± 3.42	1.96 ± 2.47	.072	2.13 ± 3.54	2.01 ± 2.53	.403
Preoperative eGFR (mL/min/1.73 m^2)	39.0 ± 21.0	39.9 ± 21.5	.333	39.3 ± 20.6	40.1 ± 22.0	.381
Preoperative dialysis	160 (14.1)	128 (12.2)	.177	117 (12.7)	120 (13.1)	.835
Cerebrovascular disease	150 (13.2)	182 (17.3)	.008	133 (14.5)	131 (14.3)	.894
Carotid stenosis	73 (6.4)	94 (8.9)	.028	61 (6.6)	78 (8.5)	.134
Chronic lung disease	120 (10.6)	148 (14.1)	.013	105 (11.4)	95 (10.3)	.454
Extracardiac vascular disease	212 (18.7)	223 (21.2)	.146	176 (19.2)	174 (19.0)	.905
Prior percutaneous coronary intervention	279 (24.6)	263 (25.0)	.840	229 (24.9)	225 (24.5)	.829
Prior myocardial infarction	693 (61.1)	615 (58.4)	.197	543 (59.2)	547 (59.6)	.849
Congestive heart failure	511 (45.1)	426 (40.5)	.030	385 (41.9)	386 (42.0)	.962
Unstable angina	355 (31.3)	321 (30.5)	.678	282 (30.7)	285 (31.0)	.880
Preoperative shock	74 (6.5)	58 (5.5)	.318	55 (6.0)	54 (5.9)	.921
Preoperative arrhythmia	155 (13.7)	127 (12.1)	.262	115 (12.5)	115 (12.5)	1.000
New York Heart Association functional class III or IV	506 (44.6)	392 (37.2)	<.001	370 (40.3)	377 (41.1)	.739
Left main disease ≥50%	405 (35.7)	355 (33.7)	.326	320 (34.9)	326 (35.5)	.769
Triple-vessel disease	955 (84.2)	840 (79.8)	.007	757 (82.5)	764 (83.2)	.665
Aortic stenosis ≥ grade 1	20 (1.8)	32 (3.0)	.05	15 (1.6)	11 (1.2)	.429
Mitral stenosis ≥ grade 1	13 (1.1)	10 (0.9)	.652	11 (1.2)	6 (0.7)	.223
Aortic insufficiency ≥ grade 2	87 (7.7)	108 (10.3)	.034	77 (8.4)	71 (7.7)	.607
Mitral insufficiency ≥ grade 2	326 (28.7)	361 (34.3)	.005	275 (30.0)	272 (29.6)	.878
Tricuspid insufficiency ≥ grade 2	131 (11.6)	144 (13.7)	.135	113 (12.3)	107 (11.7)	.666
Urgent status	191 (16.8)	165 (15.7)	.458	154 (16.8)	148 (16.1)	.706

Data are presented as n (%) or mean ± standard deviation. *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *eGFR*, estimated glomerular filtration rate.

RESULTS

Patient Characteristics of All Unmatched Patients

Patient characteristics of the entire unmatched cohort are presented in Table 1. The OPCAB group was significantly older and had significantly higher prevalence of cerebrovascular disease, carotid stenosis, respiratory disease, aortic valve insufficiency, and mitral valve insufficiency. However, the ONCAB group had significantly higher prevalence of diabetes mellitus, hyperlipidemia, congestive heart failure, New York Heart Association functional class III or IV, and triple-vessel disease.

Operative Data and Clinical Outcome for the Original, Unmatched Cohort

Table 2 shows operative data for the entire unmatched cohort. The OPCAB group had significantly fewer distal anastomoses but employed both the right and left internal thoracic arteries significantly more frequently. Unplanned conversion from OPCAB to ONCAB occurred in 64 patients (6.1%). Aortic crossclamping was performed in 406 patients (35.8%) in the ONCAB group. In 72.2% of the OPCAB group, proximal anastomosis was performed without aortic clamping (326 patients [31.0%] with aortic no-touch technique and 434 patients [41.2%] with a suture device). Operative durations were significantly shorter in the OPCAB group (316.0 vs 376.3 minutes; $P < .001$).

Several early outcomes were significantly better in the OPCAB group (Table 3), which had significantly lower 30-day mortality and operative mortality and significantly lower incidence of reoperation for bleeding, deep sternal wound infection, prolonged (>24 hours) mechanical ventilation, prolonged (≥8 days) intensive care unit (ICU) stay, and perioperative transfusion. Although the incidence of MACEs was significantly lower in the OPCAB group, the

ACD

TABLE 2. Operative data for the original cohort

Variable	ONCAB (n = 1134)	OPCAB (n = 1053)	P value
Operative duration (min)	376.3 ± 105.5	316.0 ± 101.3	<.001
CPB time (min)	153.5 ± 59.1	—	—
Distal anastomoses	3.35 ± 1.05	3.15 ± 1.27	<.001
Proximal anastomosis			
Aortic no-touch	114 (10.1)	326 (31)	<.001
Partial clamp	327 (28.8)	269 (25.5)	.084
Suture device	286 (25.2)	434 (41.2)	<.001
Total clamp	406 (35.8)	24 (2.3)	<.001
ITA use			
Left	1031 (90.9)	978 (92.9)	.094
Right	264 (23.3)	404 (38.4)	<.001
Bilateral	245 (21.6)	383 (36.4)	<.001
None	87 (7.7)	57 (5.4)	.033

Data are presented as mean ± standard deviation or n (%). *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *CPB*, cardiopulmonary bypass; *ITA*, internal thoracic artery.

TABLE 4. Operative data in propensity-matched pairs

Variable	ONCAB (n = 918)	OPCAB (n = 918)	P value
Operative duration (min)	375.4 ± 103.8	322.5 ± 101.8	<.001
CPB time (min)	152.1 ± 59.2	—	—
Distal anastomoses	3.34 ± 1.05	3.21 ± 1.26	.019
Proximal anastomosis			
Aortic no-touch	97 (10.6)	278 (30.3)	<.001
Partial clamp	268 (29.2)	235 (25.6)	.084
Suture device	228 (24.8)	381 (41.5)	<.001
Total clamp	325 (35.4)	24 (2.6)	<.001
ITA use			
Left	826 (90.0)	856 (93.2)	.012
Right	208 (22.7)	366 (39.9)	<.001
Bilateral	193 (21.0)	348 (37.9)	<.001
None	80 (8.7)	47 (5.1)	.002

Data are presented as n (%) or mean ± standard deviation. *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *CPB*, cardiopulmonary bypass; *ITA*, internal thoracic artery.

incidence of stroke, perioperative myocardial infarction, renal failure, and renal failure requiring dialysis did not differ between groups.

Outcomes of Propensity Score-Matched Patients

Baseline characteristics of the matched cohort are shown in Table 1. There were no significant differences in any preoperative factor between the 2 groups.

Table 4 shows operative data for the matched cohort, in which the OPCAB group had slightly fewer distal anastomoses but received bilateral internal thoracic artery grafting significantly more frequently. Aortic crossclamping was performed in 325 patients (35.4%) in the ONCAB group. In 71.8% of the OPCAB group, proximal anastomosis was performed without aortic clamping (278 patients [30.3%] with aortic no-touch technique and 381 patients [41.5%] with a suture device). After matching, operative durations were still significantly shorter in the OPCAB group. Unplanned conversion from OPCAB to ONCAB occurred in 56 patients (6.1%), among whom operative mortality was 12.5% (7 patients). Of these patients with unplanned conversion, 40 (71.4%) were converted to ONCAB because of hemodynamic instability.

TABLE 3. Postoperative outcomes in the original cohort

Outcome	ONCAB (n = 1134)	OPCAB (n = 1053)	P value
30-d Mortality	42 (3.7)	20 (1.9)	.011
Operative mortality	67 (5.9)	36 (3.4)	.006
Perioperative myocardial infarction	7 (0.6)	6 (0.6)	.885
Stroke	23 (2.0)	20 (1.9)	.828
Major adverse cardiovascular events*	90 (7.9)	54 (5.1)	.008
Reoperation for bleeding	38 (3.4)	8 (0.8)	<.001
Renal failure	81 (7.1)	61 (5.8)	.201
Dialysis	49 (4.3)	30(2.8)	.065
Mediastinitis	39 (3.4)	20 (1.9)	.026
Septicemia	25 (2.2)	17 (1.6)	.315
Atrial fibrillation	143 (12.6)	135 (12.8)	.883
Perioperative transfusion	898 (79.2)	667 (63.3)	<.001
Prolonged ventilation†	153 (13.5)	84 (8.0)	<.001
ICU stay ≥8 d	200 (17.6)	125 (11.9)	<.001
Readmission within 30 d	28 (2.5)	28 (2.7)	.779

Data are presented as n (%). *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *ICU*, intensive care unit. *Includes operative mortality, myocardial infarction, and stroke. †Defined as ≥24 hours.

After propensity-score matching, several clinical outcomes were still better in the OPCAB group, which had significantly lower 30-day mortality and operative mortality as well as significantly lower incidences of reoperation for bleeding, deep sternal wound infection, prolonged ventilation, prolonged ICU stay, and perioperative transfusion (Table 5). Although the incidence of MACE was lower in the OPCAB group ($P = .008$), the incidence of stroke, perioperative myocardial infarction, renal failure, and renal failure requiring dialysis did not differ between groups. Institutional volume-adjusted analysis confirmed most of the results of primary analysis (Table 6).

DISCUSSION

The benefit of OPCAB technique in patients with a low EF is still unclear. The recent large randomized controlled trials (the ROOBY and CORONARY trials) did not show improved mortality in the OPCAB groups.[1,2] However, in both studies, patients with an EF <0.35 comprised only a small portion of the entire cohort. In the ROOBY trial patients with a low EF accounted for only 5.7% of the entire cohort,[1] whereas in the CORONARY trial patients with a low EF accounted for only 5.4% of OPCAB group and 5.6% of ONCAB group.[2] Therefore, these randomized controlled trials could not reach definite conclusions about the best strategy for surgical coronary revascularization in

TABLE 5. Postoperative outcomes in propensity-matched pairs

Outcome	ONCAB (n = 918)	OPCAB (n = 918)	P value
30-d Mortality	34 (3.7)	16 (1.7)	.010
Operative mortality	56 (6.1)	30 (3.3)	.006
Perioperative myocardial infarction	7 (0.8)	6 (0.7)	.781
Stroke	19 (2.1)	14 (1.5)	.380
Major adverse cardiovascular event*	76 (8.3)	43 (4.7)	.002
Reoperation for bleeding	32 (3.5)	8 (0.9)	.001
Renal failure	68 (7.4)	56 (6.1)	.264
Dialysis	40 (4.4)	28 (3.1)	.138
Mediastinitis	31 (3.4)	17 (1.9)	.041
Septicemia	22 (2.4)	14 (1.5)	.178
Atrial fibrillation	119 (13.0)	114 (12.4)	.726
Perioperative transfusion	727 (79.2)	578 (63.0)	<.001
Prolonged ventilation†	123 (13.4)	75 (8.2)	<.001
ICU stay ≥8 d	159 (17.3)	111(12.1)	.002
Readmission within 30 d	27 (2.9)	26 (2.8)	.889

Data are presented as n (%). *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *ICU*, intensive care unit. *Includes operative mortality, myocardial infarction, and stroke. †Defined as ≥24 hours.

low-EF patients. In this context, large retrospective studies using appropriate risk-adjustment methods are still required to establish a sound treatment strategy for patients with a low EF undergoing CABG.

The Japanese Association for Thoracic Surgery reported that intended OPCAB is performed in more than 60% of all patients undergoing CABG in Japan.[9] As shown in our analysis, even among CABG patients with left ventricular dysfunction, intended OPCAB accounted for approximately half of this high-risk group. We found that in patients with low EF, OPCAB was associated with significant reductions in 30-day mortality and operative mortality, and with a significantly lower incidence of reoperation for bleeding, mediastinitis, perioperative transfusion, prolonged mechanical ventilation, and prolonged ICU stay. The largest retrospective study of OPCAB in patients with low EF was recently conducted using data from the STS national database and demonstrated the clinical benefit of OPCAB.[8] The present study, which is from Japan, where OPCAB is performed more frequently than in other countries, is the second-largest retrospective study comparing OPCAB and ONCAB in patients with low EF.

TABLE 6. Institutional-volume adjusted odds ratios (ORs) of on-pump coronary artery bypass versus off-pump coronary artery bypass

Outcome	OR (95% confidence interval)	P value
30-d Mortality	0.447 (0.238-0.839)	.012
Operative mortality	0.521 (0.326-0.832)	.006
Stroke	0.723 (0.355-1.475)	.373
Reoperation for bleeding	0.247 (0.112-0.546)	.001
Renal failure	0.878 (0.605-1.275)	.264
Dialysis	0.740 (0.447-1.225)	.242
Mediastinitis	0.547 (0.297-1.007)	.053
Prolonged ventilation*	0.582 (0.427-0.793)	.001

*Defined as ≥24 hours.

First, OPCAB significantly reduced 30-day mortality (1.7% in OPCAB vs 3.7% in ONCAB; odds ratio [OR], 0.48) and operative mortality (3.3% in OPCAB vs 6.1% in ONCAB; OR, 0.52) in patients with low EF. This is consistent with the results of the meta-analysis of retrospective studies and the report from the STS national database. In their meta-analysis of 13 retrospective studies that included only patients with poor left ventricular function, Jarral and colleagues[10] reported a 39% reduction in the risk of 30-day mortality in the OPCAB cohort (OR, 0.61). Based on propensity-score analysis using the STS national database, Keeling and colleagues[8] reported that OPCAB was associated with significantly lower in-hospital mortality (adjusted OR, 0.82 in all centers and 0.63 in high-volume centers) in patients with an EF <0.30. Other studies have suggested that the benefit of OPCAB may be more apparent in high-risk patients. Puskas and colleagues[3] reported that there was a significant mortality benefit for OPCAB in patients with STS predicted risk of mortality >0.025 (OR, 0.45; 95% confidence interval, 0.33-0.63). In addition, a report using data from the STS national database to compare outcomes of OPCAB and ONCAB showed that OPCAB was associated with a greater reduction in mortality and morbidity in patients with higher STS predicted risk of mortality scores.[11] These results may explain the risk-reduction benefit of OPCAB in patients with low EF. Preoperative renal function, which is 1 of the strongest prognostic factors, should also be considered when interpreting the risk-reduction benefit of OPCAB that we have demonstrated in the present study. Our cohort had a lower preoperative median estimated glomerular filtration rate value (41.3 mL/min/1.73 m^2 in ONCAB and 41.6 mL/min/1.73 m^2 in OPCAB) and a higher prevalence of preoperative hemodialysis (12.7% in ONCAB and 13.1% in OPCAB) than those reported for the STS database (median estimated glomerular filtration rate, 71.2 mL/min/1.73 m^2 in ONCAB and 69.2 mL/min/1.73 m^2 in OPCAB; prevalence of hemodialysis, 4.5% in ONCAB and 5.4% in OPCAB).[8] Using data from the STS national database, Chawla and colleagues[12] showed that OPCAB was associated with lower mortality in patients with poor preoperative renal function. The high prevalence of chronic kidney disease in our cohort could explain the strong reduction in mortality in OPCAB despite a smaller sample size than that from the STS database.

OPCAB was also associated with a significantly lower incidence of reoperation for bleeding, perioperative transfusion, mediastinitis, prolonged ventilation, and prolonged ICU stay in this high-risk cohort. Avoidance of transfusion is thought to be among the most important benefits of eliminating extracorporeal circulation. Numerous studies have reported the association of OPCAB with

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reduced requirement for transfusion in patients with a low EF[8,13,14]; in particular, the well-designed randomized trial of Puskas and colleagues[13] demonstrated that OPCAB reduced the incidence of coagulopathy. Other recent studies have shown that perioperative blood transfusion was significantly associated with increased mortality after CABG.[15,16] This evidence suggests that a reduction in transfusion requirement might explain the reduced mortality in our OPCAB cohort.

In the present study, the OPCAB group had a significantly lower incidence of mediastinitis despite the increased use of bilateral internal thoracic arteries in this group. There are several explanations for this reduction of deep sternal wound infection in OPCAB. First, extracorporeal circulation itself can increase the incidence of mediastinitis. In their multivariate analysis of CABG cases from the STS database, Fowler and colleagues[17] showed that perfusion time longer than 100 minutes was an independent risk factor for major infection. In the present study, both mean perfusion time longer than 150 minutes and perioperative transfusion could explain the increased incidence of mediastinitis in the ONCAB group. Risnes and colleagues[18] reported that the amount of blood transfused was an independent risk factors for mediastinitis (>10 units; OR, 3.96; 95% confidence interval, 1.60-9.60). This could be explained by a decrease in immune function after transfusion.[19]

Although many large, retrospective studies have shown that OPCAB may decrease the incidence of stroke compared with ONCAB,[11,20-23] there was no significant difference in the incidence of stroke between OPCAB and ONCAB in the present study. In a large, prospective study of perioperative stroke in CABG, Tarakji and colleagues[24] reported that intraoperative stroke rates were lowest in OPCAB (0.14%) and on-pump beating-heart CABG (0%) and statistically higher with on-pump arrested-heart CABG (0.50%). In the present study, about 65% of the ONCAB cohort underwent the procedure using the on-pump beating-heart technique, which might reduce the incidence of stroke in the ONCAB cohort. In addition, the rates of stroke in our study (2.1% in ONCAB and 1.5% in OPCAB) are similar to those in the recent study using data from the STS national database (1.9% in ONCAB and 1.3% in OPCAB), but the number of patients with OPCAB in the present study is about one-fifth of those in the study using the STS database.[8] This suggests that the relatively small effect of stroke prevention in our study could not reach significance because of a lack of statistical power. This may partially explain why the previous randomized controlled trials could not show a preventive effect on perioperative stroke, even in high-risk patients.[25,26]

OPCAB patients received slightly but statistically significantly fewer distal anastomoses per patient than ONCAB patients, which is consistent with results of the CORONARY and ROOBY trials.[1,2] Furthermore, in the present study, OPCAB patients received bilateral internal thoracic arteries more frequently than ONCAB patients. This might be explained by the effort in the OPCAB cohort to minimize aortic manipulation as much as possible. In fact, aortic no-touch technique was used in about 30% of the OPCAB cohort in the present study. Siamak and colleagues[27] reported that the use of bilateral internal thoracic arteries had no significant influence on short-term mortality after CABG in patients with low-EF. Hence, more frequent use of bilateral internal thoracic arteries in OPCAB patients would not significantly affect the short-term outcome in the present study. Because long-term follow-up data were not available in the present study, we could not estimate the prognostic effect of slightly fewer distal anastomoses and more frequent use of bilateral internal thoracic arteries in the OPCAB cohort.

In the present study, 56 patients (6.1%) converted from OPCAB to ONCAB. Although this conversion rate was higher than the conversion rate (2.1%) in the general population reported from a national survey in Japan,[9] this was similar to the conversion rate (5.2%) for patients with low EF reported from the STS database.[8] Operative mortality in patients who were converted from OPCAB to ONCAB was very high. Solving the problem of this high mortality with conversion will be necessary to reduce early mortality in OPCAB patients.

The present study has several limitations. First, because of the retrospective nature of this study, propensity-score matching could not completely adjust for potential selection bias. Second, our data on left ventricular function were limited to left ventricular EF, which represents systolic function. No data on left ventricular dimension and diastolic function, which might affect postoperative mortality, were available. Third, because of the lack of long-term data in the present study, our analysis of the clinical benefit of OPCAB technique is limited to short-term outcomes. Finally, we performed the institutional-volume-adjusted analysis but we could not perform the surgeon-volume-adjusted analysis because during 2010 and later (during our study period), the JACVSD served as a part of the NCD and the method of connecting the surgeons and their procedures changed. This change made it impossible to gain data about surgeon volume during the study period. In the previous study from the JACVSD, institutional volume index was significantly associated with 30-day mortality and operative mortality, but on the other hand, the surgeon-volume index was not significantly associated with these outcomes.[28] Therefore we believe the effect of surgeon volume is more limited than the effect of institution volume.

CONCLUSIONS

In patients with an EF <0.30, OPCAB is associated with significantly reduced early mortality and morbidity. Despite the relatively high mortality accompanying unplanned conversion to ONCAB and the importance of solving this problem, OPCAB technique may improve operative outcomes in this high-risk cohort.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: off-pump coronary artery bypass grafting, on-pump coronary artery bypass grafting, left ventricular dysfunction, propensity score

000 Off-pump versus on-pump coronary artery bypass grafting in patients with left ventricular dysfunction

Chikara Ueki, MD, Hiroaki Miyata, PhD, Noboru Motomura, MD, PhD, Genichi Sakaguchi, MD, PhD, Takehide Akimoto, MD, PhD, and Shinichi Takamoto, MD, PhD, Shizuoka and Tokyo, Japan

Off-pump technique may improve operative outcomes in patients with low ejection fraction undergoing coronary artery bypass grafting.

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ORIGINAL ARTICLE
Cardiovascular Intervention

Outcomes of Percutaneous Coronary Intervention Performed With or Without Preprocedural Dual Antiplatelet Therapy

Yukinori Ikegami, MD, PhD; Shun Kohsaka, MD, PhD; Hiroaki Miyata, PhD; Ikuko Ueda, PhD; Jun Fuse, MD; Munehisa Sakamoto, MD; Yasuyuki Shiraishi, MD; Yohei Numasawa, MD; Koji Negishi, MD; Iwao Nakamura, MD; Yuichiro Maekawa, MD, PhD; Yukihiko Momiyama, MD, PhD; Keiichi Fukuda, MD, PhD

Background: Preprocedural dual antiplatelet therapy (DAPT) in percutaneous coronary interventions (PCI) has been shown to improve outcomes; however, the efficacy of the procedure and its complications in Japanese patients remain largely unexplored, so we examined the risks and benefits of DAPT before PCI and its association with in-hospital outcomes.

Methods and Results: We analyzed data from patients who had undergone PCI at 12 centers within the metropolitan Tokyo area between September 2008 and September 2013. Our study group comprised 6,528 patients, of whom 2,079 (31.8%) were not administered preprocedural DAPT. Non-use of preprocedural DAPT was associated with death, postprocedural shock, or heart failure (odds ratio [OR]: 1.47, 95% confidence interval [CI]: 1.10–1.96, P=0.009), and postprocedural myocardial infarction (OR: 1.41, 95% CI: 1.18–1.69, P<0.001) after adjusting propensity scores for known predictors of in-hospital complications. Non-use of DAPT was not associated with procedure-related bleeding complications (OR: 0.98, 95% CI: 0.71–1.59, P=0.764).

Conclusions: Approximately one-third of the patients who underwent PCI did not receive preprocedural DAPT despite guideline recommendations. Our results indicate that patients undergoing PCI with DAPT have a lower risk of postprocedural cardiac events without any increased bleeding risk. Further studies are needed to implement the use of DAPT in real-world PCI. (*Circ J* 2015; **79:** 2598–2607)

Key Words: Bleeding; Dual antiplatelet therapy; Japanese; Percutaneous coronary intervention

Dual antiplatelet therapy (DAPT) improves outcomes in patients undergoing percutaneous coronary interventions (PCI), mainly owing to the therapy's antiplatelet effects on different stages of the platelet activation process. Previous studies have shown that preprocedural DAPT significantly reduces major cardiovascular events in patients with ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and planned PCI cases, compared with patients receiving single antiplatelet therapy.[1–3] As a consequence, although there are slight differences in antiplatelet regimens in different guidelines, the guidelines of the American College of Cardiology, American Heart Association, European Society of Cardiology, and Japanese Circulation Society all recommend pre-PCI DAPT as class I.[4–10]

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Although, the enhanced antithrombotic effects of DAPT should provide additional protection against thrombotic events for patients undergoing PCI, DAPT could also increase the risk of bleeding complications. Particularly, the safety of DAPT in an East Asian population vulnerable to bleeding is unknown.[11,12] The current guidelines from the Japanese Circulation Society are based solely on evidence from Western coun-

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Department of Cardiology, National Hospital Organization, Tokyo Medical Center, Tokyo (Y.I., J.F., M.S., Y. Momiyama); Department of Cardiology, Keio University School of Medicine, Tokyo (S.K., I.U., Y.S., Y. Maekawa, K.F.); Department of Healthcare Quality Assessment, The University of Tokyo, Tokyo (H.M.); Department of Cardiology, Ashikaga Red Cross Hospital, Ashikaga (Y.N.); Department of Cardiology, Yokohama Municipal Hospital, Yokohama (K.N.); and Department of Cardiology, Hino Municipal Hospital, Hino (I.N.), Japan

Mailing address: Shun Kohsaka, MD, PhD, Department of Cardiology, Keio University, School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. E-mail: kohsaka@cpnet.med.keio.ac.jp

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Table 1. Baseline Clinical Characteristics of Each Group Based on Preprocedural Antiplatelet Therapy

	Non-DAPT (n=2,079), % (n)	DAPT (n=4,449), % (n)	P value
Age, years (median)	66.5±11.7	67.1±11.7	0.032
50–59	15.2 (315)	18.9 (842)	<0.001
60–69	28.3 (589)	33.7 (1,501)	<0.001
70–79	27.9 (581)	33.9 (1,510)	<0.001
>80	13.6 (282)	13.8 (614)	0.796
Female	24.5 (509)	19.3 (857)	<0.001
BMI	24.1±3.7	24.2±3.3	<0.001
Coronary risk factors			
DM	37.2 (1,642)	37.7 (175)	0.840
DM with insulin	5.3 (111)	5.9 (264)	0.336
Hypertension	63.5 (1,320)	64.7 (2,877)	0.356
Hyperlipidemia	53.3 (1,108)	57.5 (2,557)	0.002
Smoking	35.2 (732)	34.5 (1,534)	0.564
Comorbidities			
CVD	8.4 (175)	7.7 (343)	0.324
COPD	3.0 (62)	2.3 (101)	0.086
CKD stage ≥3	8.8 (182)	12.0 (535)	<0.001
PAD	6.0 (124)	6.0 (267)	0.953
History			
Prior MI	6.6 (137)	6.7 (300)	0.871
Prior HF	6.5 (136)	5.0 (223)	0.012
Prior CABG	4.3 (89)	2.9 (127)	0.003
Presenting status			
CCS class 3/4	24.1 (502)	20.7 (922)	0.002
CCS class 4	12.7 (265)	8.7 (388)	<0.001
HF	14.8 (308)	11.6 (517)	<0.001
NYHA class 3/4	8.3 (172)	6.9 (306)	0.044
Coronary status			
2-vessel disease	33.6 (669)	43.1 (1,916)	<0.001
3-vessel disease	18.9 (392)	23.3 (1,037)	<0.001
LMT stenosis	6.7 (140)	8.4 (372)	0.023
PCI indication			
STEMI <12h	23.6 (491)	20.5 (913)	0.005
STEMI >12h, unstable	5.8 (121)	5.3 (236)	0.393
NSTEMI/UA	31.6 (656)	28.4 (1,265)	0.045
Stable angina	18.2 (379)	24.1 (1,073)	<0.001
Puncture site			
Radial artery	21.0 (437)	35.3 (1,569)	<0.001
Femoral artery	76.2 (1,584)	62.5 (4,449)	<0.001
Drug-eluting stent	52.1 (1,083)	63.0 (2,802)	<0.001
Bare metal stent	29.8 (619)	26.7 (1,186)	0.023
Single stent	41.5 (863)	56.5 (2,513)	<0.001
Multiple stents	40.4 (840)	33.2 (1,447)	<0.001
Single stent length (mm)	20.5±6.1	20.6±6.1	0.791
Multiple stent length (mm)	31.2±6.5	32.8±6.4	0.703

BMI, body mass index; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; CKD, chronic kidney disease; CVD, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; HF, heart failure; LMT, left main trunk; MI, myocardial infarction; NSTEMI, non-ST-elevation MI; PCI, percutaneous coronary intervention; PAD, peripheral artery disease; STEMI, ST-elevation MI; UA, unstable angina.

tries, and few trial results from studies focusing on East Asian populations are available. Furthermore, the actual bleeding complication rate in Japanese patients who undergo PCI has not yet been determined. Consequently, despite the Japanese guidelines, the use of preprocedural DAPT still varies among Japanese institutions; a single multicenter study from Japan showed that only 66.7% of Japanese patients who had undergone primary PCI for STEMI received preprocedural DAPT.[13]

To the best of our knowledge, no studies have specifically evaluated the risks and benefits of pre-PCI DAPT and the association with in-hospital outcomes in Japan. Therefore, we investigated the prevalence of DAPT use in a multicenter