TABLE 1. Demographic and clinical characteristics of patients who underwent low anterior resection in Japan during 2011 and outcome

		Operative mortality (n = 144, 0.9%)	
Clinical characteristics		*Mortality*	*p*
Age, y, mean (SD, median)	66.2 (11.7, 67.0)	–	–
Sex			
Male	10,772 (64.5)	110	<0.003
Female	5923 (35.5)	44	
Indication for surgery			
Malignant tumor	16,440 (99.7)	–	–
Appendix cancer	8 (0.05)	0	1.000
Colorectal cancer	16,032 (96.0)	140	0.666
Anal canal cancer	149 (0.9)	1	1.000
Carcinoid	96 (0.6)	1	0.566
GIST	18 (0.1)	0	1.000
Cancer metastases or relapse[a]	583 (3.5)	8	0.168
Benign tumor	71 (0.4)	2	1.000
No tumor[b]	184 (1.1)	2	0.674
Disseminated cancer[c]	733 (4.4)	25	<0.001
ASA-PS grade			
5	6 (0)	–	–
4	22 (0.1)	2[d]	0.024
3	1201 (7.2)	–	–
ADL (preoperative)			
Totally dependent	97 (0.6)	7	<0.001
Partially dependent	652 (3.9)	35	<0.001
COPD	424 (2.5)	12	<0.001
Previous PVD surgery	56 (0.3)	4	0.001
Bleeding disorder without treatment	72 (0.4)	6	<0.001
Cerebrovascular disease	579 (3.5)	13	0.002
Preoperative transfusions	249 (1.5)	17	<0.001
Smoked within the past year	3440 (20.6)	26	0.531
Habitual alcohol consumption	3938 (23.6)	35	0.850
BMI, kg/m^2 (N = 16,564)			
Mean (SD)	23.5 (70.6)	–	–
Distribution			
<25	13,192 (79.6)	–	–
25–30	2988 (18.0)	–	–
30–35	325 (2.0)	–	–
>35	59 (0.4)	–	–

N = 16,695. Values are numbers of patients with percentage in parentheses, unless otherwise noted.
–, not applicable; ADL = activities of daily living; ASA-PS = American Society of Anesthesiologists Physical Status classification; COPD = chronic obstructive pulmonary disease; GIST = gastrointestinal stromal tumor; PVD = peripheral vascular disease.
[a]Cancer metastases or relapse may overlap the headings of malignant tumors.
[b]Lower anterior resection performed for reasons other than malignant or benign tumor.
[c]Surgery resulted in incomplete resection.
[d] ASA-PS grade 4 and 5.

which may be the largest clinical data collection to date for surgery within 1 year. Most of the patients (96%) underwent low anterior resection for colorectal cancer. The 30-day mortality after low anterior resection in this series was 0.4%, which was much lower than results reported in other countries, for example, in 20,150 colorectal surgeries on nonelderly patients (<70 years) in NSQIP (2005–2007), the mortality was 2.0%.[8] In other multicenter studies, 30-day mortality was 5.8% to 6.8% (colorectal surgery; England), 2.4% to 7.0% (anterior resection; Norway), 2.1% (anterior resection; Sweden), 2.3% (rectal surgery; Belgium), 3.1% (rectal surgery; Spain), and 5.5% (elective colorectal surgery; United Kingdom).[9–13] The surgical mortality probability model exhibited reasonable discrimination and excellent calibration in the validation data set.

Differences exist between Japan and Western countries in the surgical management and neoadjuvant treatment of rectal cancers, including differences in the use of lymph node dissection and preoperative chemoradiation.[14] Lateral lymph node dissection, in addition to TME, is the standard operative procedure for lower rectal cancer in Japan.[15] However, the precise number of cases with lateral lymph node dissection in the current NCD data set is not known. The principle of complete lymph node dissection in rectal cancer surgery in Japan is to make a high central ligation up to the root of the inferior mesenteric artery. In

TABLE 2. Preoperative and operative characteristics and outcome

Characteristic	n/N (%)[a]	Operative mortality (n/N = 144/16,695, 0.9%) Mortality	p
Emergency operation	178/16517 (1.1)	7	0.001
Preoperative treatment			
Radiotherapy	254/16,695 (1.5)	1	0.729
Chemotherapy	299/16,695 (1.8)	5	0.117
Bleeding, mL, median (range), N = 16,403	160.0 (0–16,300)	3[b]	0.494
Blood transfusion, mL, median (range), N = 16,568	2441 (0–40,000)	27[c]	<0.001
Operation time, min, median (range), N = 16,580	237 (16–1199)	22[d]	0.990
Surgical procedure			
Handsewn anastomosis	677/16,695 (4.1)	4	0.668
Laparoscopic surgery	6541/16,695 (39.2)	38	0.002
Stoma creation	771/16,695 (4.6)	7	0.841

[a]Unless otherwise noted.
[b]Bleeding over 2000 mL.
[c]Blood transfusion over 5 units.
[d]Operation time over 6 hours.

contrast, the standard operative strategy for rectal cancer in Western countries is TME without lateral lymph node dissection; instead, preoperative chemoradiation treatment is added.[16] Neoadjuvant radiation was performed in only 1.5% of our patients. A randomized controlled trial is being conducted to compare TME alone with TME plus lateral lymph node dissection in stage II or III lower rectal cancer,[15] and we need a few more years to answer the question of whether lateral lymph node dissection provides an oncological benefit to the patients with low rectal cancer. Nevertheless, both lateral lymph node dissection and preoperative chemoradiation treatment may increase operative morbidity and mortality.[15]

It is interesting that a BMI greater than 30 kg/m^2 had the highest odds ratio (7.1) for 30-day mortality in our risk models. The relatively low BMI in our series (mean, 23.5; SD, 70.6 kg/m^2) might explain our relatively low operative mortality. Only 2.3% of our patients had a BMI greater than 30 kg/m^2. Reports have suggested that obese patients undergoing colectomy have higher postoperative morbidity and mortality.[17,18] However, according to an ACS-NSQIP report, 30-day mortality did not differ significantly by BMI in colectomy for cancer.[19] Another study showed that lateral lymph node dissection increased morbidity,[15] and this procedure may also have affected the mortality of the patients with obesity.[20,21]

The quality of a database depends on the robustness of data collected.[14] It is interesting that significant differences in colorectal procedures were observed between the ACS-NSQIP and ACS case log systems in risk factor and outcome data.[14] Although the spectrum of procedures presented was remarkably similar between the 2 programs, the case log system enabled surgeons to self-report patient

TABLE 3. Outcome of low anterior resection and operative mortality.

Outcome	n (%)[a]	Operative mortality Mortality	p
Mortality			
30-day	75 (0.4)	75	<0.001
Operative	144 (0.9)		
Readmission within 30 days	353 (2.1)	4	0.551
Reoperation			
Within 30 days	1195 (7.2)	45	<0.001
Any	1348 (8.1)	54	<0.001
Complications include all grades	4393 (26.3)	114	<0.001
Complications of grade 3 or higher	1487 (8.90)	95	<0.001
Surgical complications			
Superficial incisional SSI	763 (4.6)	17	<0.001
Deep incisional SSI	254 (1.5)	15	<0.001
Organ space SSI	1285 (7.7)	33	<0.001
Anastomotic leak	1700 (10.2)	50	<0.001
Pulmonary embolism	14 (0.1)	2	0.006
Urinary tract infection	229 (1.4)	13	<0.001
SIRS	194 (1.2)	8	<0.001

[a]N = 16,695.
SIRS = systemic inflammatory response syndrome; SSI = surgical site infection.

TABLE 4. Low anterior resection risk models: 30-day mortality

Characteristic	30-day mortality, OR (95% CI)
Older age category	1.34 (1.13–1.58)
Previous surgery for PVD	6.24 (1.39–28.00)
Disseminated cancer	4.89 (2.52–9.49)
Preoperative transfusions	5.36 (2.45–11.74)
BMI >30 kg/m^2	7.01 (2.79–17.62)
Platelet count <120 × 10^3/μL	5.02 (2.20–11.44)
Serum albumin <40 g/L	3.41 (1.75–6.63)
Na <138 mmol/L	3.58 (2.06–6.22)
Bleeding disorder without treatment	5.22 (1.54–17.68)
Serum urea nitrogen >25 mg/dL	3.58 (2.06–6.22)

PVD = peripheral vascular disease.

TABLE 5. Low anterior resection risk models: operative mortality

Characteristic	*Operative mortality, OR (95% CI)*
Older age category	1.41 (1.24–1.60)
Sex, male	1.92 (1.18–3.15)
Respiratory distress, any	2.91 (1.48–5.70)
ADL (preoperative), totally dependent	2.92 (1.22–7.01)
ADL (preoperative), partially dependent	2.5 (1.42–4.40)
Ascites, any	4.04 (1.82–9.00)
Previous surgery for PVD	5.79 (1.84–18.18)
Disseminated cancer	2.80 (1.55–5.07)
Preoperative transfusions	2.58 (1.26–5.29)
BMI > 30kg/m^2	1.522 (0.428–12.625)
Serum creatinine >265.2 μmol/L	4.00 (1.59–10.05)
Low hemoglobin (men <135 g/L, women <125 g/L)	2.60 (1.51–4.47)
High hematocrit (men >0.48, women >0.42)	3.56 (1.39–9.10)
Platelet count <120×10^3/μL	3.44 (1.67–7.06)
Serum albumin <25 g/L	2.71 (1.26–5.82)
AST >0.67 μkat/L	1.89 (1.07–3.32)
Na <138 mmol/L	2.54 (1.65–3.90)

ADL = activities of daily living; AST = aspartate aminotransferase; Na = sodium; PVD = peripheral vascular disease.

risk factors and the NSQIP used trained data abstractors for recording, with strict data collection methods. In this regard, the NCD pays much attention to keeping the quality of the data high. Although it is a surgeon's self-reported data, participating hospitals are obligated to designate data managers for data entry. The NCD regularly holds training sessions for data managers and ensures traceability of the data, strict definitions of variables, 30-day follow-up of outcomes, and regular audits for data validation.

A unique feature of the NCD database is that patients are registered from all types of hospitals throughout the country. Under the national health care system, most patients do not have to travel to the large hospitals in metropolitan areas, but go to the hospitals nearby. Thus, the patient population of NCD was not limited to the large, high-volume hospitals or academic centers but includes many small hospitals. Also the patient population consists of almost a single ethnicity. In addition, the environment of the health care system may influence the outcome of surgical care. In Japan, patients can stay in hospital relatively longer than in Western countries. Actually, the length of hospital stay of the patients (n = 16,282, missing value was 413) undergoing low anterior resection during the year of 2011 was 21 days (median), and the length of postoperative stay was 16 days (median). Thus, patients can receive thorough postoperative care and treatment of comorbidities during the hospital stay. Accordingly, our rate of readmission within 30 days is 2.1%, whereas reoperation within 30 days is 7.2%.

TABLE 6. Risk model performance metrics for low anterior resection

Risk model	*p*	*C-index*	*95% CI*
30-day mortality	<0.001	0.75	0.64–0.86
Operative mortality	<0.0001	0.77	0.67–0.86

C-index = concordance index.

The 30-day mortality rate is the most common definition of postoperative mortality in the surgical literature, probably because it is easy to follow up patients for this short duration. However, 30-day mortality may underestimate the true risk for death after colorectal surgery.[14,22] In fact, in the literature, the 90-day mortality rate is recommended as a standard outcome measure after colorectal surgery. Therefore, we assessed all operative mortality (90-day mortality) in addition to 30-day mortality. Although operative mortality was more than double the 30-day mortality, it was still satisfactory.

This study had several limitations. First, the NCD is a newly established, self-selected set of programs, and data entry is dependent on each hospital. Although training programs for data managers have been set up, mistakes in data entry may be made due to inexperience. Second, we cannot separate out other trends or programs and influences (local or national) that affect the quality of surgical care.[23] Other factors not included in our variables (for example, the extent of the surgeon's specialization or case volume[24] or subjective bias in evaluation of the patient's condition)[25] may be better predictors of the outcome of the surgical care. Third, the frequency of laparoscopic surgery in low anterior resection (39.2% in this study) has recently been increasing. Low operative mortality was observed in laparoscopic techniques compared with open techniques; however, operative procedure (open or laparoscopic) itself was not the independent risk factor for mortality. Further precise analysis of laparoscopic techniques on morbidity and mortality will be needed. Fourth, low anterior resection consists of a mixture of low-risk and high-risk procedures. For example, the anastomosis level (distance from the anal verge) was not included in our database. Thus, rectosigmoid colon cancer and low rectal cancer may both be included in the analysis. Fifth, although most hospitals nationwide participate in the NCD program, this was not a population-based study.

Nonetheless, studies such as this provide information about risks and benefits that are particularly relevant in surgery, where patients must make decisions as to whether to proceed with an operation and where and from whom they will seek care. Our results facilitate comparisons among surgeons and institutions within Japan, as well as comparison with other countries, thus serving as a catalyst for quality improvement and as a basis for accurate counseling of patients regarding operative risk.

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ORIGINAL ARTICLE

Nomogram Prediction of Metachronous Colorectal Neoplasms in Patients With Colorectal Cancer

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Objective: To construct a predictive model of postoperative colorectal neoplasm development using a nomogram.

Background: Although patients with colorectal cancer (CRC) are known to be at high risk of developing metachronous adenoma or CRC, no statistical model for predicting the incidence of postoperative colorectal lesions has been reported.

Methods: A total of 309 CRC patients who underwent surgical resection received regular endoscopic follow-up to detect the development of metachronous adenoma or adenocarcinoma. The patients were divided into the derivation set (n = 209) and the validation set (n = 100). The nomogram to predict the 3- and 5-year adenoma-free survival rates was constructed using the derivation set, and a calibration plot and concordance index (c-index) were calculated. The predictive utility of the nomogram was validated in the validation set.

Results: Sex, age, and number of synchronous lesions at the time of surgery for primary CRC were adopted as variables for the nomogram. The nomogram showed moderate calibration, with a c-index of 0.709 in the derivation set and 0.712 in the validation set.

Conclusions: A nomogram based on sex, age, and number of synchronous lesions at the time of surgery has the ability to predict postoperative adenoma-free survival.

Keywords: colonoscopy, colorectal adenoma, colorectal cancer, nomogram, postoperative surveillance

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Colorectal cancer (CRC) is one of the most common malignancies in Japan and in Western countries.[1] Furthermore, those with a history of CRC are at a higher risk for developing second metachronous adenomas or CRC recurrence during the follow-up period.[2–5] Chen et al[6] reported that 0.7% of patients develop metachronous CRC during the 3 years after surgical resection for the initial CRC.

It is generally accepted that most CRCs develop through a continuous process, transforming from normal mucosa to adenoma to carcinoma,[7–9] a process known as the adenoma-carcinoma sequence. Therefore, the early detection and endoscopic resection of newly developed adenomas constitute an important preventive strategy, especially in patients who have undergone surgical resection for primary CRC. However, there are no definite guidelines for adenoma surveillance after the surgical resection of primary CRC. The 2006 guidelines issued by the American Cancer Society indicate that a postoperative colonoscopy should be performed 1, 4, and 9 years after the initial surgical procedure,[10] but these guidelines also state that the currently available evidence does not fully address any clinical, genetic, or biologic markers that may predict the development of metachronous CRC. Therefore, the development of a prediction model of metachronous colorectal lesions after resection of initial CRC is very important.

Several studies have previously attempted to identify risk factors for the development of metachronous adenomas after resection of initial CRC. The location of CRC in the proximal colon and previous or synchronous adenoma presence were reported to be risk factors for the early development of metachronous lesions.[5,11] However, there have been no previous studies investigating the time course of adenoma formation after surgery using the log-rank test or Cox proportional hazard model. Recently, we demonstrated that age, presence of a synchronous lesion, and diabetes mellitus were independent predictive variables affecting the development of postoperative colorectal neoplasms.[11] By extending the previously reported regression results, we have designed the present study to construct a predictive model of postoperative colorectal neoplasm development using a nomogram, a tool widely used among clinicians because of its utility as a prediction model and its user-friendly interface.[12,13]

MATERIALS AND METHODS

Patient Selection

We retrospectively evaluated the medical records of 552 consecutive patients with colorectal adenocarcinoma, diagnosed between January 2004 and December 2007, who underwent surgical resection at the Department of Surgical Oncology, the University of Tokyo Hospital. Patients with adenomatous polyposis (>30 lesions at the time of surgery or familial adenomatous polyposis), those with hereditary non-polyposis colon cancer, and those with inflammatory bowel disease were excluded from the study. After surgical resection, all specimens were histopathologically reviewed, and the pathological TNM class and stage were determined according to the classification established by the American Joint Committee on Cancer.[14] In cases of multifocal disease, the histopathological variables were determined by assessing the dominant lesion (the most extensive lesion based on tumor invasion or size). Primary colon cancer located proximal to the splenic flexure was defined as right-sided, and the distally located one was defined as left-sided; all variables were assessed at the time of surgery. This study was approved by the institutional review board, and all patients gave written informed consent.

The first colonoscopy was scheduled at 1 year after surgery, and adenomas detected during the first colonoscopy were treated as synchronous lesions. Polyps larger than 5 mm were removed by endoscopic mucosal resection and were histopathologically analyzed. Hyperplastic polyps and other nonneoplastic colorectal lesions were recorded but not included in the analysis. After confirming the absence of colonic lesions (clean colon) by perioperative colonoscopy, endoscopic surveillance was conducted every 1 to 2 years. Patients who failed to undergo the second colonoscopy, which was usually scheduled 2 years after surgery, were excluded from the study; the final number of patients enrolled in this surveillance program was

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309. The patients were divided into 2 groups: the derivation and validation groups. The derivation group consisted of 209 patients who underwent surgery from January 2004 to June 2006, and the validation group consisted of 100 patients who underwent surgery from July 2006 to December 2007. The nomogram was constructed on the basis of derivation group data, and its predictive utility was validated in the validation group.

Statistical Analysis

The Kaplan-Meier method was used to estimate overall survival and recurrence-free survival, and the log-rank test was used to analyze differences in survival between groups. For the derivation group, the following potential prognostic variables were assessed: sex, age, and sex (general characteristics); tumor location, depth of invasion, regional lymph node metastasis, distant metastasis, lymphatic invasion, venous invasion, histologic differentiation, and the presence of concomitant CRCs and/or adenomas at the time of surgery (cancer-related variables); and smoking, body mass index greater than 25 kg/m^2, history of previous malignancies (CRC or extracolic malignancy), first-degree family history of CRC, hypertension, hyperlipidemia, and diabetes mellitus (patient background variables). A multivariate Cox proportional hazards analysis was performed using variables whose P value was less than 0.2 in univariate analysis. By following the method of Wang et al,[15] we built nomograms for predicting the probability of 3- and 5-year adenoma-free survival rates after surgery. The nomogram was subjected to 100 bootstrap resamples for calculating the estimated Harrell concordance index (c-index) as an index of model performance.[16] The c-index estimates the probability of concordance between predicted and observed outcomes in rank order and is equivalent to the area under the receiver operating characteristic curve, if there are no censored cases.[16] It represents the ability of the model to discriminate between patients who survived without adenoma development and those who did not. Higher values indicate better discrimination: a value of 0.5 indicates no predictive discrimination, whereas a value of 1.0 indicates perfect separation of patients with different outcomes.

We also performed calibration using a calibration curve, a graphic representation of the relationship between the observed outcome frequencies and the predicted probabilities, with both the derivation and validation groups. Using the constructed nomogram, the score of predicting the 5-year adenoma-free survival rate was calculated for both groups. All statistical analyses were performed using the statistical software program R 3.0.1 with rms and Hmisc packages (http://www.r-project.org/).

RESULTS

Of the 552 patients enrolled in the study, 243 were excluded for the following reasons: 227 patients did not undergo colonoscopic surveillance (CRC progression in 108 patients, other disease progression in 64 patients, and a move or change of hospital in 55 patients), 4 patients had colitic cancers, 3 patients had polyposis, and 3 patients died during the perioperative period. The differences between the included and excluded patients are presented in Table 1. Because a large proportion of the patients excluded from the analysis had residual cancer or recurrence, and most of the remaining excluded patients failed to receive surveillance because of the development of diseases other than CRC, the age and stage of initial CRC were higher in the excluded group than in the included group. General characteristics related to adenoma formation are also presented in Table 2. The characteristics of patients in the derivation and validation groups were comparable. The incidence of CRC formation per year was 0.0064 in both groups, and that of adenoma formation was approximately 0.084 in both groups. Although the 5-year adenoma-free rate was a little lower in the validation group, this difference was not statistically significant ($P = 0.077$).

TABLE 1. Differences Between Included and Excluded Patients

	Included	Excluded	P
Total, n	309	243	
Sex, n			
Male	199	149	
Female	110	94	0.4564
Age, mean ± SD, yr	63.2 ± 10.3	68.0 ± 11.7	<0.001
Location, n (%)			
Right hemicolon	68 (22.0)	78 (32.1)	
Left hemicolon	112 (36.2)	76 (31.3)	
Rectum	129 (41.7)	89 (36.6)	0.0288
Stage, n (%)			
0/I	99 (32.0)	45 (18.5)	
II	105 (34.0)	69 (28.4)	
III	84 (27.2)	70 (28.8)	
IV	21 (6.8)	59 (24.3)	<0.001

TABLE 2. Patient Characteristics

	Derivation Data Set	Validation Data Set
No. patients	209	100
Sex, n (%)		
Male	134 (64.1)	64 (64)
Female	75 (35.9)	36 (36)
Median follow-up time, yr	5.57	5.04
Total follow-up time, yr	1097.0	466.5
Total colorectal cancer cases developed during follow-up time, n	7	3
Incidence per year	0.00638	0.00643
Total colorectal adenoma cases developed during follow-up time, n	93	39
Incidence per year	0.08470	0.08359
Cumulative 5-yr adenoma-free rate	75.35%	71.71%
95% CI	68.31–81.25	61.30–80.22

CI indicates confidence interval.

Development of the Nomogram

The results of the univariate and multivariate analyses of the association between variables and the 5-year adenoma-free survival rate are shown in Table 3. In the univariate analysis, male patients and older patients had a significantly shorter adenoma-free survival time. The variables associated with progression of the primary cancer, such as T stage and presence of lymph node or distant metastasis, showed no correlation with postoperative adenoma development, consistent with our previous report. Although the presence of second or additional primary CRC showed no correlation, if both synchronous CRC and adenomas were included in the category sublesions, the presence of sublesions was strongly associated with postoperative adenoma development. We previously reported that the presence of diabetes mellitus correlated with postoperative development[11]; however, in this study, no variables concerning patient background, including diabetes mellitus, correlated with adenoma development.

Therefore, we performed multivariate analysis using the variables of sex, age, and the presence of concomitant colorectal

TABLE 3. Univariate and Multivariate Analyses of the Association Between Clinicopathological Factors and Postoperative Adenoma-Free Intervals

	Univariate Analysis		Multivariate Analysis		
	5-yr Adenoma-Free Survival	*P*	Hazard Ratio	95% CI	*P*
Sex					
Female	84.5%				
Male	68.2%	0.0404	1.75	0.89–3.71	0.1102
Age					
<70 yr	76.6%				
≥70 yr	62.4%	0.0188	1.95	1.04–3.54	0.0387
Cancer-related variables					
Tumor location					
Right-sided colon	74.9%				
Left-sided colon	74.6%				
Rectum	73.1%	0.7888			
Depth of invasion					
T1/2	72.7%				
T3/4	74.1%	0.9003			
Regional lymph node metastasis					
N0	72.2%				
≥N1	76.9%	0.3909			
Distant metastasis					
M0	73.3%				
M1	80.9%	0.503			
Lymphatic invasion					
Absent	74.5%				
Present	71.4%	0.8254			
Venous invasion					
Absent	73.9%				
Present	74.3%	0.957			
Histopathology					
Well or moderate	73.0%				
Other	90.9%	0.106	2.54	0.54–45.43	0.2874
Concomitant colorectal cancers at the time of surgery					
Absent	75.0%				
Present	64.0%	0.1367	1.45	0.66–2.93	0.3394
Concomitant colorectal cancers and adenomas at the time of surgery					
Absent	84.2%				
Present	61.0%	<0.0001	1.95	1.04–3.54	0.0387
Patient background variables					
Smoking					
Absent	77.6%				
Present	69.2%	0.1768	1.23	0.69–2.23	0.4825
Body mass index ≥25 kg/m^2					
Absent	72.2%				
Present	77.2%	0.5937			
History of malignancies					
Absent	74.8%				
Present	64.6%	0.1307	1.39	0.60–2.81	0.4158
Family history of colorectal cancer					
Absent	72.6%				
Present	83.8%	0.2803			
Hypertension					
Absent	77.2%				
Present	66.8%	0.0994	1.03	0.57–1.91	0.9314
Hyperlipidemia					
Absent	74.3%				
Present	69.6%	0.6153			
Diabetes mellitus					
Absent	75.4%				
Present	66.9%	0.399			

CI indicates confidence interval.

sublesions. Because the latter 2 variables were independent predictive factors in the prediction of adenoma development and sex also showed a trend toward correlation, we constructed the nomogram with point scales of these 3 variables (Fig. 1). The sum of the each variable point was plotted on the total point axis, and the estimated median 3- and 5-year adenoma-free survival rates were obtained by drawing a vertical line from the plotted total point axis straight down to the outcome axis. The c-index of this model was 0.709, indicating good discrimination. Figure 2A shows the calibration graph for the nomogram, in which the probability of 5-year adenoma-free survival as predicted by the nomogram is plotted against the corresponding observed survival rates obtained by the Kaplan-Meier method. This illustration demonstrates good calibration of the nomogram. Furthermore, the derivation group was further stratified into 3 groups according to the score calculated using the nomogram: the high-risk (>75th percentile of the group), low-risk (<25th percentile), and intermediate-risk (25th–75th percentile) groups. Figure 3A demonstrates that scoring with the nomogram effectively discriminated the risk of postoperative adenoma development.

Validation

To validate whether the nomogram would be applicable to other data sets, we conducted a validation study using data from the 100 CRC patients in the validation group. The c-index of the validation group was 0.712, demonstrating that the nomogram also showed good prediction in the validation patient group. Moreover, the calibration plot of the validation group demonstrated good calibration (Fig. 2B). Patients in the validation group were also stratified by percentile into

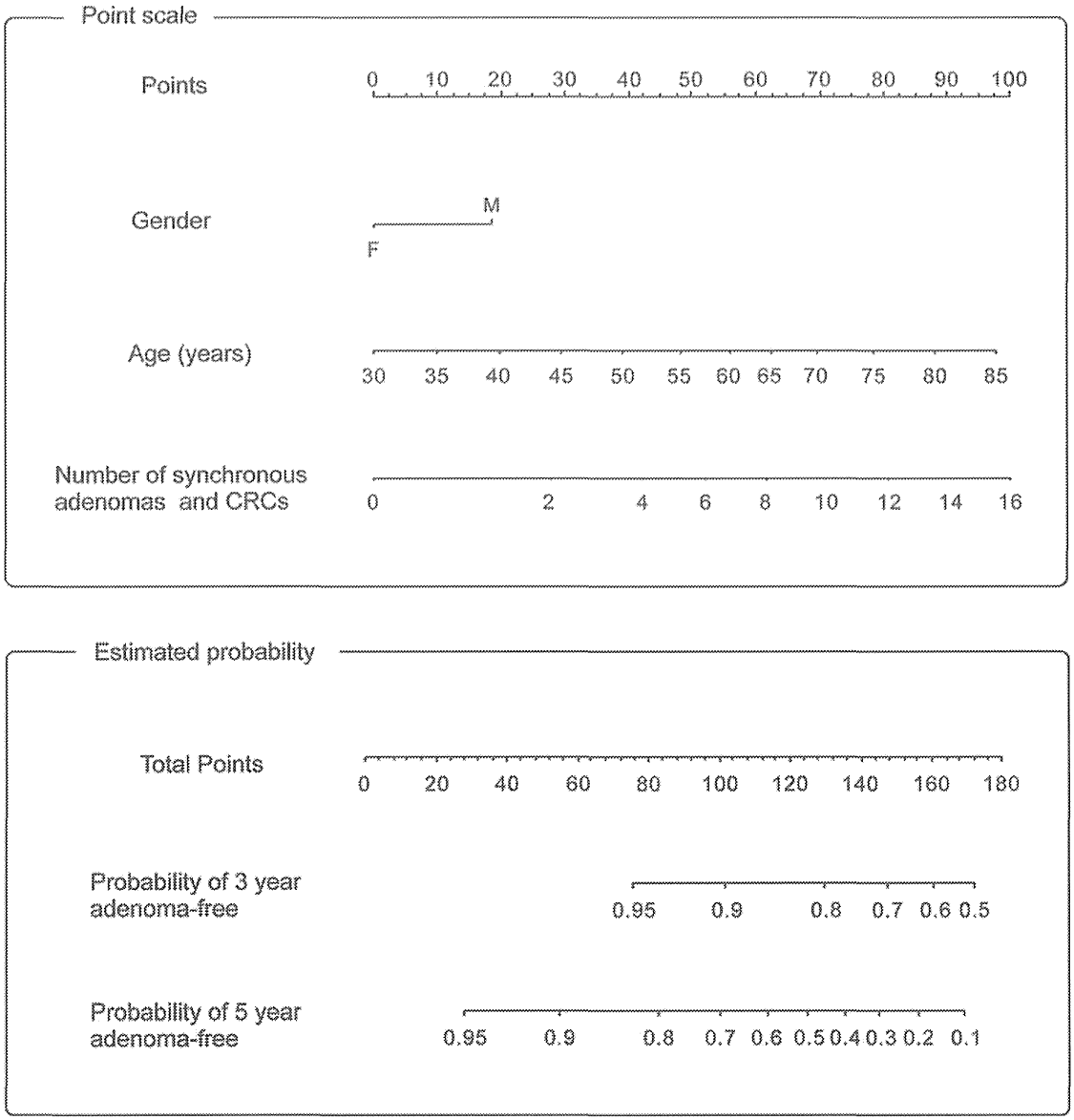

FIGURE 1. Nomogram for predicting postoperative adenoma-free survival after surgery for colorectal cancer. The 3- and 5-year probabilities of survival without adenoma or CRC development is estimated by summing the score of the 3 variables, that is, sex, age, and the number of synchronous adenomas and CRCs at the time of surgery.

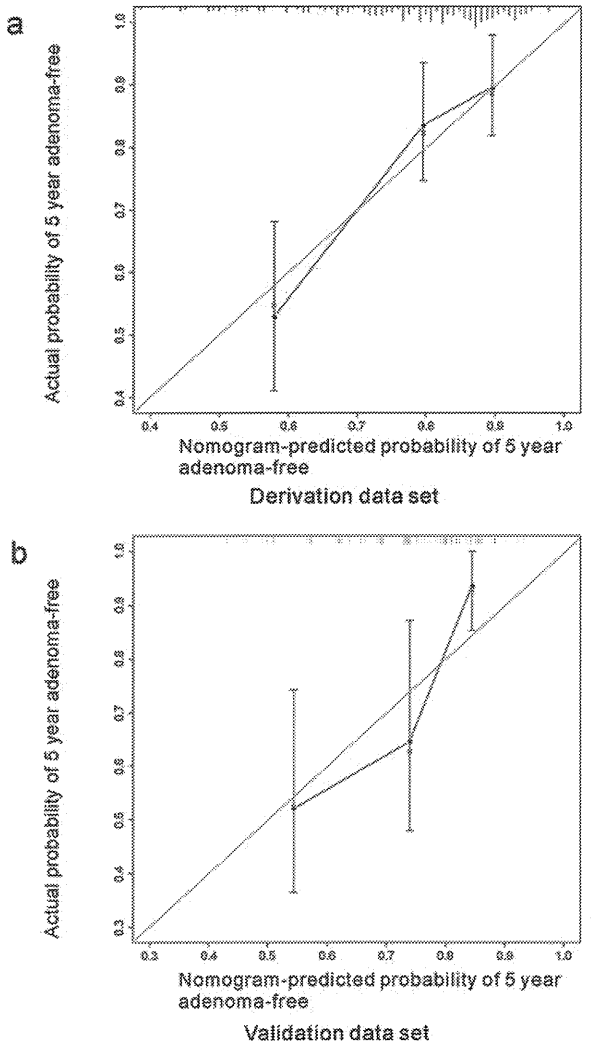

FIGURE 2. Calibration of the nomogram in the derivation (A) and validation (B) data sets. The horizontal axis is the nomogram-predicted probability of adenoma-free survival at 5 years, and the vertical axis is the actual adenoma-free survival rate estimated at 5 years using the Kaplan-Meier method. The line from the lower left to the upper right corner of the plot area is the reference line that indicates ideal prediction. Bars indicate 95% confidence intervals.

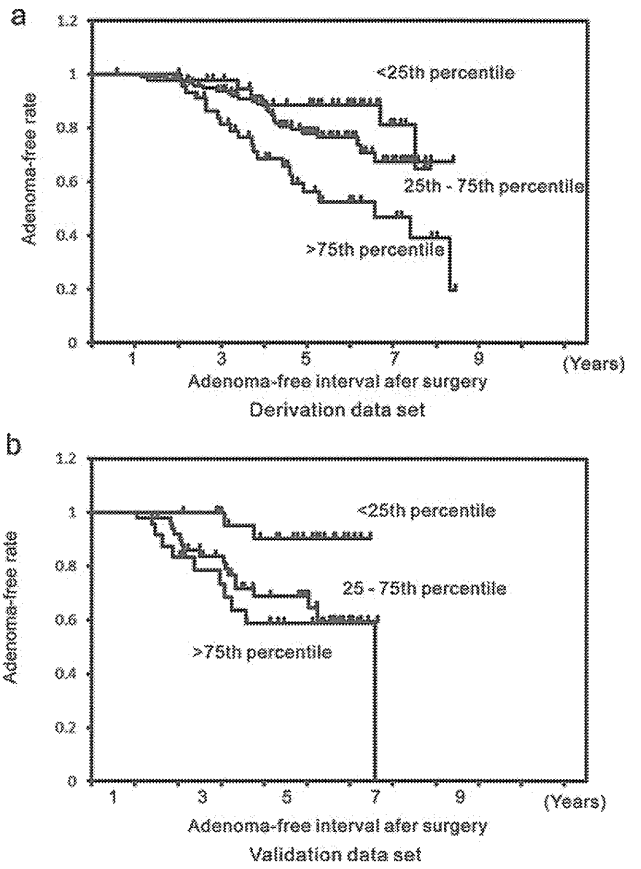

FIGURE 3. Actual adenoma-free survival curves of patients in the derivation (A) and validation (B) sets stratified by quartiles of the nomogram-predicted score. The patients were stratified into 3 groups according to their percentile of the nomogram-predicted score: <25th, 25th–75th, and >75th percentile.

3 groups (<25th, 25th–75th, >75th percentile), and the adenoma-free survival in each group was found to increase in this order of patient groups, similar to the result of the derivation group (Fig. 3B).

DISCUSSION

Because CRC patients are at high risk for developing metachronous colorectal adenoma or carcinoma after resection of the primary tumor,[5,17] many studies have attempted to identify the risk factors predicting the development of postoperative neoplasms, but only a few factors have been reported. In the present study, we evaluated possible risk factors by dividing them into sex, age, cancer-related variables, and patient background variables. Initially, in our analysis, male sex was a higher risk factor for postoperative neoplasm development, but the correlation was not strong in the multivariate analysis. This may be explained by the fact that the male patients were on average older than the female patients and advanced age was a strong risk factor. Moon et al[18] also reported that male sex correlated with postoperative adenoma development in a univariate analysis; however, similar to our study, the correlation was not statistically significant by multivariate analysis. Furthermore, they found that age was a risk factor for adenoma development,[18–20] also corroborating our results.

The variables related to cancer progression or malignant potential, such as depth of invasion or presence of metastasis, showed no correlation with postoperative adenoma development. Although several studies have reported that the location of the primary CRC in the proximal colon is a risk factor for metachronous adenoma,[21,22] we failed to find any correlation between primary CRC location and the incidence of postoperative adenoma development. On the contrary, similar to the results of this study, the presence of synchronous colorectal adenomas has been reported to be a risk factor in many studies.[3,11,17,22,23] Chu et al[24] reported that 6.5% of patients with synchronous polyps had metachronous large bowel cancer whereas 3.4% of those without polyps developed metachronous large bowel cancer. Moreover, multiple polyps are associated with a higher risk of metachronous colorectal cancer than single polyps.[25] Correlations between other variables related to patient background and postoperative polyp development were also investigated. We evaluated a variety of

factors reported to be associated with adenoma formation, including previous cancer history, family history of CRC, hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking habits,[20,26–30] but no correlations were observed with any of these variables. In our previous study, we reported that diabetes was an independent predictive factor for adenoma development[11]; however, there was no correlation in the present study.

Because the nomogram is intended to be used for pragmatic postoperative surveillance in municipal hospitals, the variables included in the nomogram should be limited. Too many variables can make calculating the predictive score cumbersome, and variables with a lopsided risk group distribution will be less useful in clinical application, even if the variables are statistically significant. Although expression of MUC-5 in the initial CRC has been reported to have a protective effect,[22] and microsatellite instability has been reported to be a possible risk factor for the development of metachronous colorectal neoplastic lesions,[31] variables that require experimental techniques such as immunohistochemistry or gene analysis are inappropriate as parameters for a nomogram. Furthermore, a nomogram has an advantage over other statistic models because continuous variables can be directly converted to a prognosis-predicting score and therefore continuous variables are more desirable than categorized ones. From these perspectives, the variables we adopted for the nomogram in the present study are ideal (sex, age, and number of synchronous lesions).

Chung et al[32] evaluated the cumulative incidence of colorectal neoplasia development by stratifying patients according to risk factors. They recommended extending the surveillance interval beyond 5 years for the low-risk group, in which the 5-year incidence of adenoma development was 45.8%. A 3-year colonoscopic follow-up period was recommended for the high-risk group, in which the 5-year incidence of adenoma development as 57.8%. Similarly, a number of guidelines for polyp surveillance have been published and most of these recommend 3-year intervals for high-risk patients and intervals of 5 or more years for low-risk patients.[33–35] Further to these previous reports, we recommend extending the colonoscopic surveillance interval to 5 years for those whose probability of 5-year adenoma-free survival is more than 50%, that is, for those with fewer than 120 points according to the nomogram. Conversely, those with a probability of 5-year adenoma-free survival less than 50%, that is, with more than 120 points according to the nomogram, should undergo a colonoscopy at least every 3 years. However, there have been no published guidelines concerning the ideal colonoscopic interval after CRC resection. Therefore, the validity of the intervals recommended by our nomogram should be prospectively evaluated in the future.

The c-indexes of nomograms previously reported were approximately 0.7. For example, c-indexes were 0.68 to 0.73 for predicting the prognosis of rectal cancer,[36] 0.69 for predicting recurrence after surgery for breast cancer,[37] and 0.66 to 0.70 for predicting recurrence of desmoid fibromatosis.[38] The nomogram we constructed showed moderate prediction capability in the derivation set, comparable with these previous reports, as shown in both the calibration plot and the Kaplan-Meyer adenoma-free survival plot. The calibration plot showed a similar distribution to the ideal reference line, and the survival plot showed good stratification of metachronous lesion-free intervals by nomogram scoring. Because application of the nomogram to the validation set also showed moderate prediction capabilities in the calibration and survival plots, the nomogram may be applicable in other hospitals.

CONCLUSIONS

This nomogram is the first statistical model for predicting the development of metachronous colorectal lesions, and it may be of great assistance during postoperative surveillance after CRC surgery.

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Operative Mortality and Complication Risk Model for All Major Cardiovascular Operations in Japan

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Background. The Japan Cardiovascular Surgery Database (JCVSD) is a nationwide benchmarking project to improve the quality of cardiovascular surgery in Japan. This study aimed to develop new JACVD risk models not only for operative mortality but also for each postoperative complication for coronary artery bypass grafting (CABG) operations, valve operations, and thoracic aortic operations.

Methods. We analyzed 24,704 isolated CABG operations, 26,137 valve operations, and 18,228 thoracic aortic operations. Risk models were developed for each operation for operative death, permanent stroke, renal failure, prolonged ventilation (>24 hours), deep sternal wound infection, and reoperation for bleeding. The population was divided into an 80% development sample and a 20% validation sample. The statistical model was constructed by multiple logistic regression analysis. Model discrimination was tested using the area under the receiver operating characteristic curve (C index).

Results. The 30-day mortality rates for isolated CABG, valve, and thoracic aortic operations were 1.5%, 2.5%, and 6.0%, respectively, and operative mortality rates were 2.4%, 3.8%, and 8.4%, respectively. The C indices for the end points of isolated CABG, valve, and aortic thoracic operations were 0.6358 for (deep sternal infection) to 0.8655 (operative mortality), 0.6114 (reoperation for bleeding) to 0.8319 (operative death), and 0.6311 (gastrointestinal complication) to 0.7591 (operative death), respectively.

Conclusions. These risk models increased the discriminatory power of former models. Thus, our models can be said to reflect the current state of Japan. With respect to major complications, useful feedback can now be provided through the Japan Cardiovascular Surgery Database Web-based system.

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The evaluation of patient outcomes has become increasingly accepted as a first step in assessing and improving the quality of patient care. Because baseline patient variables influence outcomes of cardiovascular operations, risk adjustment based on clinical risk factors is required to understand quality improvement. Risk models of isolated coronary artery bypass grafting (CABG) have been reported from several series, especially in Western countries [1]. The Society of Thoracic Surgeons (STS) National Adult Cardiac Database (NCD) and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) have contributed much to this field [2–6].

To assess daily clinical practice in the context of Japan, rather than relying on systems such as the STS NCD or the EuroSCORE, a Japan-specific database is needed. To this end, the Japan Cardiovascular Surgery Database (JCVSD) was established in 2000 as a benchmarking project to improve the quality of cardiovascular operations. As of 2013, the JCVSD has accumulated clinical information from more than 500 hospitals across Japan and is considered a national representative quality improvement initiative. The JCVSD data collection form has more than 300 variables, the definitions of which (available at: http://www.jacvsd.umin.jp) are based on those of the STS NCD (available at: http://www.sts.org).

Our previous reports using data from the JCVSD identified risk factors for isolated CABG [7], valve operations [8], and thoracic aortic operations [9]. However, these risk models only assessed mortality and composite morbidity. To improve the quality of cardiovascular operations, it is also important to identify risk factors for each postoperative complication. Thus, this study aimed to develop risk models not only for operative mortality but also for each postoperative complication.

Material and Methods

Study Population

We identified all cardiovascular procedures performed between January 1, 2005, and December 31, 2009. The

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present study included 24,704 isolated CABG operations, 26,137 valve operations, and 18,228 thoracic aortic operations from 177 hospitals.

Data Collection

Through the JCVSD Web-based system, each participating hospital enters data and uses a real-time feedback report system that includes risk-adjusted outcomes, which are compared among all participating hospitals. Although participation in the JCVSD is voluntary, submissions tend to be thorough, with overall preoperative risk factors used in risk models missing in less than 3% of entries. The definitions of JCVSD variables are almost identical to those of the STS NCD (available online at http://sts.org).

The accuracy of submitted data is verified through monthly visits to each participating hospital by the site visit working group. Members of the group verify that the number of procedures from the original operative record listed for the hospital matches the number in the JACVSD. Members also examine each clinical record and compare it with that inputted into the JACVSD. In addition to source document verification, all hospital data are confirmed by independent comparisons of hospital adult cardiovascular surgical volume submitted to the JCVSD against that reported to the annual survey of the Japanese Association for Thoracic Surgery. This study was approved by the Institutional Review Board in each participating hospital. Informed consent was obtained from each patient to allow his or her data to be entered into this database.

End Points

The primary outcome measure of the JCVSD analysis was 30-day operative mortality, defined as death at 30 days or before hospital discharge. The other end points were operative death, and postoperative complications, including stroke, reoperation for bleeding, postoperative mechanical ventilation required for greater than 24 hours, renal failure, deep sternal wound infection, paraparesis, perioperative myocardial infarction, intensive care unit stay exceeding 7 days, and gastrointestinal complication. Also, using these outcomes, major morbidity was defined as any of the following postoperative complications: stroke, reoperation for bleeding, postoperative mechanical ventilation required for greater than 24 hours, renal failure, or deep sternal wound infection which occurred in hospital or within 30 days of an operation, regardless of the patient's geographic location after discharge.

Statistical Analysis

Data were randomly assigned into two subsets that were split 80/20, one for model development and the other for validation. The number of cases for isolated CABG, valve, and thoracic aortic operations were 19,762/4,942, 20,878/5,259, and 14,570/3,658, respectively. The Fisher exact test and two-sample t test were used to compare the validation and test data sets. To develop a risk model for each outcome, multiple logistic regression analysis using step-wise selection (backward method) of predictors with a p value for inclusion of less than 0.05 was conducted.

A goodness-of-fit test was performed to assess how well the model could discriminate between survivors vs nonsurvivors. When all statistically nonsignificant variables were eliminated from the model, goodness-of-fit testing was performed to assess the discrimination between survivors and nonsurvivors, and the area under the receiver operating characteristic curve was used to assess how well the model could discriminate between survivors and nonsurvivors. In our risk models, we did not consider intrainstitutional correlations and time trends with generalized estimating equations with empirical standard error estimates to account for patient clustering within institutions because these may be potential confounding factors when estimating regression coefficients for variables of primary interest [1–3]. We used SPSS 20.0 software (IBM Corp, Armonk, NY) for data analyses.

Results

Risk Profile of Study Population

The patient risk profile for each procedure is summarized in the Appendix. Patients in the isolated CABG group were a mean age of 68.3 years, 77.5% were men, and 18.5% required emergency operations. Preoperative comorbidities were chronic lung disease (mild, moderate, and severe; 7.1%) and renal failure (13.3%). Patients in the group with valve operations were a mean age of 66.4 years, 55.3% were men, and 6.0% required emergency operations. Preoperative comorbidities were chronic lung disease (mild, moderate, and severe; 9.6%) and renal failure (11.1%). Patients in the group with thoracic aortic operations were a mean age of 66.8 years. 65.6% were men, and 32.7% required emergency operations. Preoperative comorbidities were chronic lung disease (mild, moderate, and severe; 12.3%) and renal failure (8.8%).

Outcome Rates

Outcomes of each operation are summarized in Table 1. The 30-day mortality rates for isolated CABG, valve, and thoracic aortic operations were 1.5%, 2.5%, and 6.0%, respectively, and operative mortality rates were 2.4%, 3.8%, and 8.4%, respectively.

Model Results and Performance

Risk models were developed and final logistic models and model performance metrics are presented in Tables 2–4. Risk factors for isolated CABG were age, renal failure, prior CABG operation, cardiogenic shock, arrhythmia, and others. Risk factors for valve operations were age, renal failure, cerebrovascular disease, prior valve operation, and others. Risk factors for aortic thoracic operations were body mass index, noncardiac vascular lesion, acuity status, main reason for the indication of operation, location of the operation, and others.

Table 1. Outcomes for Patients Who Underwent Isolated Coronary Artery Bypass Grafting, Valve Operations, and Thoracic Aortic Operations

	Isolated CABG (n = 24,704)		Valve Operation (n = 26,137)		Thoracic Aortic Operation (n = 18,228)	
Outcome	No.	%	No.	%	No.	%
Death ≤30 days after operation	380	1.5	649	2.5	1,097	6.0
Operative death	582	2.4	1,000	3.8	1,523	8.4
Death or main complication[a]	2,893	11.7	3,776	14.4	5,397	29.6
Reoperation for bleeding	443	1.8	1,050	4.0	1,044	5.7
Stroke	373	1.5	471	1.8	1,233	6.8
Newly required dialysis	630	2.6	801	3.1	1,028	5.6
Deep sternal wound infection	456	1.8	404	1.5	371	2.0
Paraplegia/paraparesis	66	0.3	100	0.4	766	4.2
Prolonged ventilation	1,781	7.2	2,194	8.4	4,002	22.0
Perioperative MI	294	1.2	176	0.7	187	1.0
Gastrointestinal complication	403	1.6	494	1.9	688	3.8
Length of ICU stay ≥7 days	1,500	6.1	2,157	8.3	3,502	19.2

[a] Stroke, newly required dialysis, prolonged ventilation >24 hours, deep sternal wound infection, or reoperation for bleeding.

CABG = coronary artery bypass grafting; ICU = intensive care unit; MI = myocardial infarction.

The C indices for end points ranged from 0.6358 (deep sternal infection) to 0.8655 (operative mortality) for isolated CABG, from 0.6114 (reoperation for bleeding) to 0.8319 (operative mortality) for valve operations, and from 0.6311 (gastrointestinal complication) to 0.7591 (operative mortality) for aortic thoracic operations.

Comment

JCVSD is a database initiative that was started in 2000 with the aim of increasing the quality of cardiovascular operations in Japan. The first risk model was based on data up through 2005 [9] and was widely used for inter-institutional benchmarking with risk-adjusted outcomes, patient case conferences at each hospital, and informed consent before operations. The risk models developed in the present study include cases added to the database since 2005. As the number of participating facilities increased, so did the number of available cases in the database. This increased the discriminatory ability of the models and also allowed for more accurate assessments by the inclusion of a validation group. Thus, our models can be said to reflect the current state of Japan.

With respect to major complications, more useful feedback for use in the clinical context can now be provided with the development of individual risk models. In addition, we could assess characteristics and variations of clinical performance among institutions by use of risk models. In the future, we anticipate that identifying issues that differ among institutions, such as the rate of developing infectious diseases and bleeding, will work toward improving the quality of health care.

In addition to the presently developed models, other countries also have risk models for isolated CABG, valve operations, and thoracic aortic operations. Discussions on how to consider differences in countries and in race in the development and use of risk models are warranted. That patient background and disease incidence differ by country and race [10] highlights the importance of developing risk models that target Asian populations, such as Japanese people. Highlighting the usefulness of a Japan-specific risk model is that compared with other countries, the obese population is small in Japan, the rate of operations for thoracic aortic aneurysms is higher, and preoperative risk and the distribution of operative procedures greatly differ in Japan relative to other countries [11]. Moving forward, it will be useful to build a framework for sharing the significance of our findings in the international context through international collaborations and by considering racial, environmental, and institutional factors.

The rate of postoperative complications of isolated CABG, such as death and stroke, are not largely different from comparable data reported by the STS, although in Japan, renal and respiratory failure tend to be less frequent and infectious diseases are more frequent. On one hand, Japanese patients tend to be younger, have a lower body mass index, have a lower incidence of chronic respiratory failure, and have less history of myocardial infarction compared with patients of other countries [1]. On the other hand, when compared with data from the STS NCD, there are more patients with diabetes, a history of renal failure, angina, left main disease, and aortic valve stenosis in Japan. Although more patients have a history of diabetes in Japan compared with the United States, only a few models have identified diabetes history and therapy as risk factors. Despite the lower incidence of renal failure in Japan, the odds ratio for preoperative renal failure is markedly higher compared with that in the United States.

Table 2. Description of Risk Models for Isolated Coronary Artery Bypass Grafting

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Prolonged Ventilation >24 Hours	Gastrointestinal Complication	ICU Stay >7 Days
Age category, y	<60, 60–65, 65–70, 70–75, 75–80, ≥80	1.28	1.13	1.09	1.15	1.14		1.16	1.23	1.19
Body surface area, m2				0.93						
Gender	Male				1.44					0.88
Body mass index, kg/m^2	≥30		1.38					1.53		1.65
Past or present smoker	Yes							1.16	1.77	
Current smoker ≤1 month	Yes		1.23					1.20		1.17
Diabetes mellitus	Yes		1.18			1.78				
Diabetes treatment	Yes						1.27			
Renal failure	Yes	2.15	2.16	1.94		7.55	1.77	1.65	1.57	2.11
Chronic dialysis	Yes	1.98							1.55	
Hypertension	Yes		1.12		1.32		1.26			
Chronic lung disease	Moderate, severe									1.70
	Mild, moderate, severe	2.08	1.59			1.89	1.94	1.99	1.68	1.41
Noncardiac vascular lesion	Yes	1.72	1.31		1.37			1.26		
	Thoracic aorta					1.94				1.48
	Peripheral vessel (including abdominal aorta)						1.46			1.21
Cerebrovascular disease (TIA, RIND, CVA, coma)	Yes		1.28		1.98			1.23		1.29
Cerebrovascular disease if yes	Within 2 weeks before operation	2.89			2.59			1.61		
History of psychoneurotic disorder	Yes								1.91	
Prior CABG	Yes	2.46	2.26	5.17		1.70	2.06	1.81	1.85	2.37
Myocardial infarction	Yes		1.11					1.34		
Congestive heart failure	Yes	1.80	1.32			1.43	1.45	1.36		1.38
Angina	Unstable		1.15					1.25		
Cardiogenic shock	Yes	1.75	1.76	1.46		1.61	1.65	1.81	2.11	1.91
Arrhythmia	Yes	2.02	1.23			1.61		1.55	1.37	1.61
CCS Angina Grading Scale	≥II									1.23
NYHA Functional Classification	III		1.22					1.38	1.88	1.35
	IV	1.43	1.90		1.70	1.56		2.23	1.93	1.59
Medication ≤48 hours before operation	Yes	1.63				1.47				1.28
Aortic stenosis	Yes							1.42		
Mitral stenosis	Yes								3.44	
Diseased coronary vessels, No.	3		1.22	1.29			1.52	1.29	1.30	1.30

(*Continued*)

Table 2. Continued

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Prolonged Ventilation >24 Hours	Gastrointestinal Complication	ICU Stay >7 Days
Left ventricular function	Medium		1.12							1.26
	Bad	2.60	1.63	1.71		1.81		1.48		2.32
Mitral insufficiency	≥III	2.04								1.48
Acuity status	Urgent, emergency, salvage	2.05	1.68		1.40	2.05		2.12		2.11
	Emergency, salvage	3.38	2.33	1.75	2.13	2.33		2.76		3.17
Unplanned CABG	Yes	2.08	1.42		2.29	1.75		1.61		1.59
C statistics		0.8655	0.7294	0.6360	0.6744	0.8531	0.6358	0.7714	0.6756	0.7938

CABG = coronary artery bypass grafting; CCS = Canadian Cardiovascular Society; CVA = cerebrovascular accident; ICU = intensive care unit; NYHA = New York Heart Association; RIND = reversible ischemic neurologic deficit; TIA = transient ischemic attack.

It is important to note that Japan has a relatively high frequency of aortic diseases compared with other countries. In particular, Japan has a high incidence of aortic dissection, and this relates to patient characteristics such as high blood pressure and the presence of many elderly patients. One reason for this may be that computed tomography examinations are performed very often in Japan, thus presenting more opportunities to detect aortic diseases [12].

In the risk models of the present study, there were no exclusion criteria for the highly difficult thoracic aortic operations, and even if CABG or valve operations had been performed, if a thoracic aortic operation was also performed, and all of these were categorized as thoracic aortic operations. The characteristics of the operation were considered by including as risk factors whether rupturing was the reason the operation was indicated, type of valve operation (aortic valve, mitral valve, or multiple valve operations), type of aortic aneurysm, and the main reason that the operation was indicated. The International Registry of Acute Aortic Dissection has developed a risk model for thoracic aortic operations that targets only acute type A aortic dissection.

Although direct comparisons of the models are difficult, Japanese patients are evidently older and tend to have a higher incidence of diabetes. However, it should be noted that the risk factors used in the models are very different due to the characteristics of the database. Although our risk models have high discriminatory ability, improving the database's structure and methods for risk evaluation will be important to increase the quality of thoracic aortic operations throughout the world.

This study has some limitations. To improve the risk models, the risk factors to consider must be determined. Operative mortality tends to have high discriminatory ability, but some complications lack this ability. Although the STS has reported similar results regarding the limited discriminatory ability for the risk model of reoperation, we believe this should be improved. With respect to renal failure, there is much discussion in the field regarding which variables to use as indicators; for example, estimated glomerular filtration rate, creatinine clearance, and preoperative creatinine cutoff value. Although we simply used renal failure impairment and dialysis as risk factors related to renal dysfunction because they did not have a major effect, it will be necessary to continuously consider this aspect with usefulness for clinical interpretation about renal dysfunction.

In conclusion, the risk-adjustment models for isolated CABG, valve, and thoracic aortic operations in Japan were updated, and we developed additional risk models of not only operative mortality, 30-day morality, and composite morbidity but also of postoperative complications, including stroke, reoperation for bleeding, postoperative mechanical ventilation required for more than 24 hours, renal failure, deep sternal wound infection, paraparesis, perioperative myocardial infarction, intensive care unit stay exceeding 7 days, and gastrointestinal complications. Our new risk models will contribute to

Table 3. Description of Risk Models for Valve Operations

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Prolonged Ventilation >24 Hours	Gastrointestinal Complication	ICU Stay >7 Days
Age category, y	<60, 60–65, 65–70, 70–75, 75–80, ≥80	1.28	1.17	1.13	1.10	1.17	1.15	1.18	1.19	1.23
Body surface area, m^2				0.93						
Gender	Male		1.19	1.44	1.21					
Body mass index, kg/m^2	≥30		1.87			1.87	2.19	2.30		1.71
Current smoker ≤1 month	Yes			1.23						
Diabetes mellitus	Yes					1.70		1.12		
Diabetes treatment	Yes	1.21	1.18				1.28			1.28
Renal failure	Yes	2.27	2.16			4.82	1.53	1.69	1.79	2.05
Chronic dialysis	Yes	1.88			1.65		1.54	1.26	1.84	1.36
Hypertension	Yes		1.09			1.18		1.13		
Infective endocarditis	Yes		1.37		1.59	1.39		1.52		
	Active	1.70								1.59
Chronic lung disease	Moderate, severe								1.93	
	Mild, moderate, severe	1.48	1.48		1.44	1.35		1.74		1.44
Carotid artery lesion	Yes	1.44	1.30		2.12		1.69	1.55		
Noncardiac vascular lesion	Yes			1.37						
	Thoracic aorta	1.94	1.53			1.52		1.74		1.41
	Peripheral vessel (including abdominal aorta)	1.55	1.17						1.58	
Cerebrovascular disease	Yes		1.38		2.02			1.39		1.36
Cerebrovascular disease if yes	≤2 weeks									
History of psychoneurotic disorder	Yes	1.84	1.43	1.59		1.71	2.49		2.02	1.37
Prior valve operation	Yes	1.54	1.79	2.25		1.54	1.69	1.64	1.53	1.47
Prior PCI	Yes	1.39							1.43	
Myocardial infarction	Yes		1.19		1.37			1.37		1.29
Congestive heart failure	Yes	1.34	1.13	1.37	1.41					1.19
Angina	Yes									1.20
	Unstable	1.41								
Cardiogenic shock	Yes	1.74	1.67	1.66			1.80	1.64		1.33
Arrhythmia	Yes		1.15			1.24	1.28	1.15		1.14
NYHA Functional Class	II							1.23	1.52	1.27
	III	1.60	1.28			1.61		1.86	2.16	1.72
	IV	2.54	2.58			3.24		3.81	2.94	3.51
Medication ≤48 hours before operation	Yes	1.66			1.75	1.44	1.83			

(*Continued*)

Table 3. Continued

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Prolonged Ventilation >24 Hours	Gastrointestinal Complication	ICU Stay >7 Days
Mitral stenosis	Yes			1.28						
Aortic stenosis	Yes		1.26		1.40			1.24		
Diseased coronary vessels, No.	2		1.19			1.49		1.37		1.41
	3	1.49	1.48		1.91	1.67	1.59	1.50		1.62
Left ventricular function	Medium	1.21	1.13					1.22		1.23
	Bad	2.30	1.37					1.46		1.93
	Medium, bad					1.27				
Aortic insufficiency	≥II								1.26	
Mitral insufficiency	≥II				1.25		1.22			
Tricuspid insufficiency	≥II	1.27	1.23	1.29	1.26	1.30		1.13		1.34
	≥III	1.44				1.38		1.18	1.44	
Acuity status	Urgent	1.45	1.47					1.69		
	Emergency, salvage	1.65	1.70		2.05			1.90		
	Urgent, emergency, salvage					1.41			1.91	1.93
CABG	Yes		1.26	1.24			1.59	1.26		
Unplanned CABG	Yes	2.59	2.60		3.09	2.33		3.32		4.24
Aortic procedure	Yes	1.46		1.32		1.18			1.52	1.32
	Repair							1.48		
Mitral procedure	Yes									1.26
	Replacement	1.72	1.35		1.25	1.45		1.59		1.47
Multiple valve operation	Yes		1.20	1.21				1.19	1.55	
C-statistics		0.8319	0.7278	0.6144	0.6736	0.8083	0.6352	0.7882	0.7280	0.7837

CABG = coronary artery bypass graft surgery; ICU = intensive care unit; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

Table 4. Description of Risk Models for Thoracic Aortic Operations

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Paraparesis	Prolonged Ventilation >24 Hours	Perioperative MI	ICU Stay >7 Days	Gastrointestinal Complication
Age category, y	<60, 60–65, 65–70, 70–75, 75–80, ≥80	1.18	1.10	1.07	1.11	1.10		1.08	1.11		1.06	1.09
Body surface area, m^2						1.05			1.03			
Gender	Male	1.23	1.22	1.27	1.20	1.38		1.65			1.11	1.37
Body mass index, kg/m^2	≥30	2.00	2.01		1.34	1.80	2.66	1.44	1.96		1.81	1.41
Past or present smoker	Yes						1.51	1.34	1.16			1.26
Current smoker ≤1 month	Yes	1.20	1.17		1.22	1.34						
Diabetes mellitus	Yes							1.38			1.18	
Diabetes treatment	Yes						1.44					
Renal failure	Yes	1.79	1.63			4.17		1.36	1.44		1.79	1.82
Chronic dialysis	Yes	1.76										2.00
Hypertension	Yes		1.24		1.31	1.20		1.54	1.18		1.18	
Infective endocarditis	Yes		2.20			2.92	2.53		2.48		1.77	
	Active	2.59		1.93								
Chronic lung disease	Moderate, severe	1.45										
	Mild, moderate, severe	1.27	1.41			1.43	1.74		1.52		1.27	1.67
Carotid artery lesion	Yes		1.33		1.69				1.43			
Noncardiac vascular lesion	Peripheral vessel (including abdominal aorta)	1.48	1.51	1.28	1.28	1.60		1.46	1.61	1.57	1.35	1.32
Cerebrovascular disease	Yes	1.23	1.14		1.40				1.16		1.34	
Cerebrovascular disease if yes	≤2 weeks before operation		1.35		1.65			1.82				
History of psychoneurotic disorder	Yes	1.73	1.33		1.44	1.34		1.40	1.24		1.33	
Prior thoracic aortic operation	Yes	1.49	1.70	2.13		1.54	1.76		1.55		1.43	1.50
MI	Yes	1.44								2.46		
Congestive heart failure	Yes					1.50					1.46	1.42
Angina	Yes								1.20	1.90		
	Unstable											1.86
Cardiogenic shock	Yes	1.56	1.21	1.43					1.24		1.37	
Arrhythmia	Yes	1.29										1.40
CCS Angina Grading Scale	≥II							1.41				
	IV			1.79								
NYHA Functional Class	III		1.28						1.38			
	IV		1.22			1.52			1.28	1.81		

(*Continued*)

Table 4. Continued

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Paraparesis	Prolonged Ventilation >24 Hours	Perioperative MI	ICU Stay >7 Days	Gastrointestinal Complication
	III, IV	1.49										
Medication ≤48 hours before operation	Inotropic agents		1.31				1.80					
Aortic stenosis	Yes					1.43			1.25			
Diseased coronary vessels, No.	2		1.27								1.28	
	3		1.60						1.47		1.41	
	≥2				1.44		1.95					1.38
Left main disease ≥50%	Yes	1.55								2.31		
Left ventricular function	Medium	1.33		1.16	1.14					1.68		
	Bad	3.29			1.57					2.52		
	Medium, bad										1.10	
Aortic insufficiency	≥II			1.24								
Mitral insufficiency	≥II									1.96		
	≥III					1.54						
Tricuspid insufficiency	≥II					1.27					1.24	
	≥III											
Acuity status	Urgent	1.41	1.54			1.46			1.80	1.91	1.93	
	Emergency, salvage	2.13	1.82	1.43	1.29	1.51		1.73	2.02	1.91	2.27	1.58
	Urgent, emergency, salvage						1.78					
CABG	Yes	1.86	1.58	1.81	1.42	1.84			1.55		1.61	1.30
Unplanned CABG	Yes	2.24								9.55		
Aortic procedure	Yes		1.25				1.39		1.21			
	Replacement			1.59							1.16	1.48
Mitral procedure	Yes		1.69						1.75		1.60	
Aortic aneurysm type	Dissection	1.38	1.31	1.38		1.25		1.37	1.48		1.32	
	Pseudoaneurysm	1.61	1.24				2.09		1.32		1.54	
Aortic dissection	≤2 weeks before operation		1.39		1.83	1.81			1.19		1.45	1.58
Main reason for the operative indication	Rupture	2.37	1.77	1.62	1.62	1.88	1.40		1.75		1.62	1.61
Location of operation	Arch	1.46	1.77	1.40	1.45	1.40	2.12	1.25	1.81		1.66	1.70
	Root						1.45			1.74		
	Ascending		1.25				1.47		1.35	1.68		
	Descending	1.38						2.10	1.16			1.60
	Abdominal										1.64	

(*Continued*)