Risk Model for Distal Gastrectomy When Treating Gastric Cancer on the Basis of Data From 33,917 Japanese Patients Collected Using a Nationwide Web-based Data Entry System

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Objective: To establish a risk model for distal gastrectomy in Japanese patients with gastric cancer.

Background: Risk stratification for distal gastrectomy in Japanese patients with gastric cancer improves surgical outcomes.

Methods: The National Clinical Database was constructed for risk determination in gastric cancer-related gastrectomy among Japanese individuals. Data from 33,917 gastric cancer cases (1737 hospitals) were used. The primary outcomes were 30-day and operative mortalities. Data were randomly assigned to risk model development (27,220 cases) and test validation (6697 cases) subsets. Stepwise selection was used for constructing 30-day and operative mortality logistic models.

Results: The 30-day, in-hospital, and operative mortality rates were 0.52%, 1.16%, and 1.2%, respectively. The morbidity was 18.3%. The 30-day and operative mortality models included 17 and 21 risk factors, respectively. Thirteen variables overlapped: age, need for total assistance in activities of daily living preoperatively or within 30 days after surgery, cerebrovascular disease history, more than 10% weight loss, uncontrolled ascites, American Society of Anesthesiologists score (≥ class 3), white blood cell count more than 12,000/μL or 11,000/μL, anemia (hemoglobin: males, <13.5 g/dL; females, <12.5 g/dL; or hematocrit: males, <37%; females <32%), serum albumin less than 3.5 or 3.8 g/dL, alkaline phosphatase more than 340 IU/L, serum creatinine more than 1.2 mg/dL, serum Na less than 135 mEq/L, and prothrombin time-international normalized ratio more than 1.25 or 1.1. The C-indices for the 30-day and operative mortalities were 0.785 (95% confidence interval, 0.705–0.865; $P < 0.001$) and 0.798 (95% confidence interval, 0.746–0.851; $P < 0.001$), respectively.

Conclusions: The risk model developed using nationwide Japanese data on distal gastrectomy in gastric cancer can predict surgical outcomes.

Keywords: distal gastrectomy, gastric cancer, National Clinical Database, risk model of mortality, surgical outcome

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Age-adjusted mortality of gastric cancer has decreased in most countries; however, it remains the fourth most common cause of cancer death worldwide.[1] Treatment for gastric cancer has received special consideration in East Asia because of its high incidence.[2] Surgery is the most effective treatment approach for gastric cancer. According to the Japanese gastric cancer treatment guidelines, standard surgery for curable advanced gastric cancer is more than two-thirds (subtotal) gastrectomy with D2 dissection.[3] This procedure has been performed without pancreatosplenectomy, which has been shown to be responsible for high mortality and morbidity.[4] In general, the gastrectomy procedures, including lymphadenectomy for early and advanced gastric cancer, have been accepted and performed as standard procedures in most hospitals that participate in the Japanese Gastric Cancer Association.[5] The Japanese Gastric Cancer Association collected data regarding the survival outcomes of 13,626 patients with primary gastric cancer treated at 208 participating hospitals in 2002 and showed that the direct death rate (30-day mortality) was 0.48%.[5] In addition, a nationwide survey by the Japanese Society of Gastrointestinal Surgery (JSGS), which included 24,100 cases treated at 1775 institutions in 2006 and 2007, found that the mortality rates varied from 0.4% to 1.1% depending on the hospital volume.[6] The outcomes appear to be better than those reported in Western countries[7–10]; however, further improvement is still possible.

The National Clinical Database (NCD), which commenced patient registration in January 2011, is a web-based data entry system linked to the surgical board certification in Japan. In this study, we focused on the NCD division of gastrointestinal surgery,[11–13] which uses patient variables and definitions that are almost identical to those used by the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).[14] Traditionally, various governing bodies, including ACS-NSQIP, have used the 30-day patient mortality as a benchmark to assess the quality of both hospital and surgeon performances in virtually all major surgical procedures. However, we recently reported that mortality based only on known data at 30 days is misleading, and it greatly underestimates the actual perioperative mortality by up to 50% compared with that at 90 days for various procedures (eg, pancreaticoduodenectomy, hepatectomy, and total gastrectomy).[11–13] Thus, the risks for 30- and 90-day in-hospital mortalities should be analyzed together with parameters similar to those used in ACS-NSQIP for patients undergoing distal gastrectomy. To formulate risk models for the 30-day and operative mortalities associated with distal gastrectomy, we evaluated data from 33,917 gastric cancer cases entered in NCD and tested the performance of the model for open and laparoscopic gastrectomy.

METHODS

Study Population

NCD is a nationwide project performed with the cooperation of the board certification system for surgery in Japan. Submission of cases to NCD is a prerequisite for all member institutions of both the Japan Surgical Society and the JSGS, and only registered cases can be used for board certification.[15] Information related to more than 1,200,000 surgical cases treated at more than 3500 hospitals was

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collected in 2011. The common input items in the JSGS guidelines have been registered from 2045 institutions. To ensure data traceability, NCD staff work with individuals who approve the data, those in the departments responsible for the annual reporting of case data, and individuals who enter the data via a web-based data management system. The staff also validates data consistency consecutively based on random inspections of the institutions.

In this study, we focused on the specific NCD section for gastrointestinal surgery, which uses variables and definitions that are almost identical to those employed by ACS-NSQIP (http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf#search = 'user+guide+for+the+2012+ACS+NSQIP'). Briefly, potential independent variables included patient demographics, pre-existing comorbidities, preoperative laboratory values, and operative data. The demographic variables of age, sex, smoking status, and alcohol drinking status were considered. The patients were categorized according to whether they were transferred directly by ambulance or not. General factors such as preoperative functional status [independent, partially dependent, and totally dependent based on a patient's ability to perform activities of daily living (ADL) at 30 days and immediately before surgery] and body mass index were also considered. The American Society of Anesthesiologists (ASA) physical status classification system was evaluated. We also considered pre-existing comorbidities, including cardiovascular status (eg, congestive heart failure, coronary diseases, hypertension, previous cardiac surgery, and peripheral vascular disease), respiratory status (eg, dyspnea, ventilator dependence, pneumonia, and chronic obstructive pulmonary disease), renal status (eg, acute renal failure and dialysis), hematological status (eg, bleeding disorders and preoperative blood transfusion), oncological status (eg, disseminated cancer, chemotherapy, and radiotherapy), preoperative blood transfusion, chronic corticosteroid use, ascites, sepsis, diabetes, presence of an open wound, and pregnancy. The laboratory parameters included in the analysis were white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time-international normalized ratio, and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A_{1c}, and C-reactive protein.

This study focused on 30-day outcomes (if a patient had been discharged after their initial admission) based on a direct 30-day time point assessment. The outcomes included 23 rigorously defined morbidities (including the following categories: wound, respiratory system, urinary tract, central nervous system, cardiac, and other preoperative conditions) as well as mortality. NCD registered the surgical cases from each department in the gastroenterological surgery section, which required the detailed input of items for 8 procedures that represented the performance of surgery in each specialty. All the variables and definitions, as well as the inclusion criteria for NCD, are accessible on the NCD Web site (http://www.ncd.or.jp/). NCD supports an E-learning system to ensure consistent data entry by participants. The NCD staff also answers all inquiries regarding data entry (approximately 80,000 inquiries in 2011) and regularly lists some of these as "Frequently Asked Questions" on the Web site.

The presence of distal gastrectomy in patients with gastric cancer was performed between January 1, 2011 and December 31, 2011 at 1737 institutions in Japan. The NCD records of patients who did not give permission to use their records were excluded from this analysis. Records with missing data in terms of age, sex, or status at 30 days after surgery were also excluded. We selected patients who had undergone distal gastrectomy for gastric cancer, including those who underwent cholecystectomy during the same operation. The exclusion criteria were any other associated surgeries that affected the outcomes based on the surgical criteria for distal gastrectomy applied in Japan after distal gastrectomy and/or gall bladder cancer (Fig. 1). Data were excluded for 41 patients who had undergone simultaneous distal pancreatectomy and 87 patients who had undergone splenectomy (30-day mortalities, 0% and 3.4%, respectively). After data cleaning, the data from 33,917 patients with gastric cancer treated at 1737 hospitals throughout Japan were used to develop the risk model (Fig. 1).

End Points

The primary outcome measures were the 30-day and operative mortalities. "Operative mortality" was defined as death during the index hospitalization, regardless of the length of hospital stay (≤90 days), as well as death after hospital discharge and 30 days or less from the surgery date.

Statistical Analysis

We used SPSS (version 20; IBM Corp., Armonk, NY) for the data analyses. Data were randomly divided into 2 subsets with a split of 80/20, where 1 set was used for model development (27,220 cases) and the other for validation (6697 cases). There were no significant differences in the profiles of the variables between the model development and validation sets, according to univariate analysis using Fisher exact tests and unpaired Student *t* tests. The 2 sets of logistic models (30-day mortality and operative mortality) were constructed for data set development using forward stepwise selection of predictors with a $P < 0.05$ for inclusion. A goodness-of-fit test was performed to assess how well the model could discriminate between patient survival and death. The receiver operating characteristic (ROC) curves for 30-day and operative mortalities were created for the validation data set. An ROC curve is a plot of a test's true positive rate (sensitivity) versus its false-positive rate (1 − specificity). Each point on the ROC curve indicates a pair of false- and true-positive rates that is achieved using a particular threshold to dichotomize the predicted probabilities. Model calibration (the degree to which the observed outcomes matched the predicted outcomes from the model across a group of patients) was

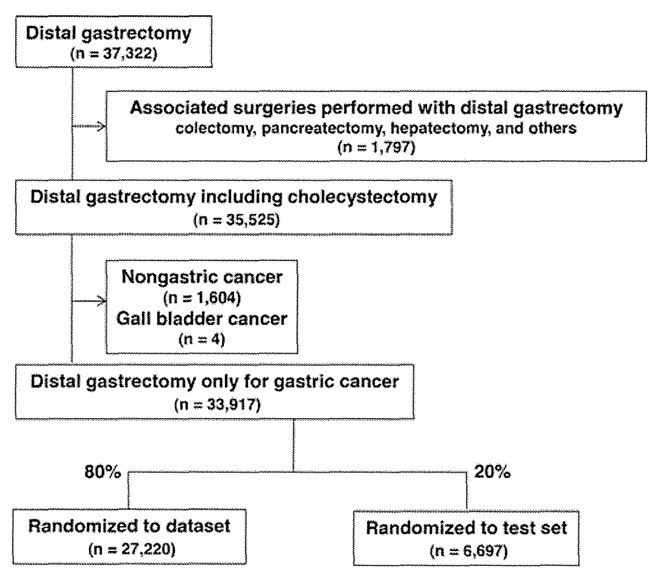

FIGURE 1. Study population selection process. We selected cases where the patients underwent distal gastrectomy for gastric cancer, including patients who simultaneously underwent cholecystectomy. The exclusion criteria were any other associated surgery that could affect the outcomes after distal gastrectomy and/or gall bladder cancer.

examined by comparing the observed and predicted averages with each of 10 equally sized subgroups, which were arranged in order of increasing patient risk.

RESULTS

Risk Profile of the Study Population

The NCD patient population (patients with gastric cancer who underwent distal gastrectomy: n = 33,917) had a mean age of 69.0 (standard deviation = 11.8) years, and 66.5% of the patients were males. Among this population, 1.4% of the patients arrived at the hospital by ambulance and 0.9% required emergency surgery. An abbreviated risk profile of the study population is shown in Table 1. In brief, 8.9% of the patients had an ASA classification of 3 to 5; 0.7% and 0.8% had total dependency during ADLs within 30 days after surgery or preoperatively, respectively; 4.7% needed some assistance with ADLs before surgery; 18.2% had a body mass index more than 25 kg/m^2; and 4.7% had experienced weight loss more than 10%. In terms of pre-existing comorbidities, 33.3% of the patients had hypertension, 15.1% had diabetes mellitus, 3.6% had chronic obstructive pulmonary disease, 0.8% required preoperative dialysis, 3.9% had cerebrovascular disease, 1.1% had ascites, and 2.8% required blood transfusion. Distal gastrectomy with associated cholecystectomy was performed in 10.3% of the patients.

Outcome Rates

The 30-day, in-hospital, and operative mortality rates for distal gastrectomy in the treatment of gastric cancer among the 2011 NCD population were 0.52%, 1.16%, and 1.2%, respectively.

The postoperative morbidities are summarized in Table 2. The overall morbidity in the distal gastrectomy population was 18.3%, and grade II or higher complications, as defined by the Clavien–Dindo Classification of Surgical Complications system,[16] were observed in 11.5% of the patients. Surgical complications included surgical site infection in 4.3% of the patients, anastomotic leakage in 2.1%, and pancreatic fistula (grades A, B, and C) in 1.6%. Nonsurgical complications included pneumonia in 2.0% of the patients, acute renal failure in 0.3%, central nervous system events in 0.5%, and cardiac events in 0.3%.

The following variables were significantly more frequent in the 30-day and operative mortality groups compared with the nonmortality group: reoperation within 30 days, overall complications, surgical complications (except bile leakage in the 30-day mortality group), and nonsurgical complications. In the 30-day mortality group, the incidences of unplanned intubation, pulmonary embolism, cardiac events, and septic shock were increased compared with those in the operative mortality group. In contrast, the incidence of postoperative infectious complications (ie, surgical site infection, bile leakage, pneumonia, and urinary tract infection) increased in the operative mortality group.

Model Results and Performance

Two different risk models were developed. The final logistic models with odds ratios (ORs) and 95% confidence intervals (CIs) are shown in Table 3. The scoring system for the mortality risk models based on the logistic regression equation was as follows:

$$\text{Predicted mortality} = e(\beta 0 + \sum \beta i Xi)/1 + e(\beta 0 + \sum \beta i Xi),$$

where βi is the coefficient of the variable Xi in the logistic regression equation provided in Table 3 for 30-day mortality and 90-day in-hospital mortality. Xi = 1 if a categorical risk factor is present and 0 if it is absent. For the age categories, Xi = 1, if the patient age is less than 59 years; Xi = 2, for 60 to 64 years; Xi = 3, for 65 to 69 years; Xi = 4, for 70 to 74 years; Xi = 5, for 75 to 79 years; and Xi = 6, for 80 years or more. The 2 groups shared 13 overlapping variables: age, need for total assistance in ADL before surgery or within 30 days after surgery, history of cerebrovascular disease, weight loss more than 10%, uncontrolled ascites, ASA score class 3 or more, white blood cell count more than 12,000/μL or 11,000/μL, anemia (hemoglobin: males, <13.5 g/dL; females, <12.5 g/dL; or hematocrit: males <37%; females <32%), serum albumin less than 3.5 or 3.8 g/dL, alkaline phosphatase more than 340 IU/L, serum creatinine more than 1.2 mg/dL, serum Na less than 135 mEq/L, and prothrombin time-international normalized ratio more than 1.25 or 1.1. The independent variables for only 30-day mortality were habitual alcohol consumption, preoperative pneumonia, history of myocardial infarction, and untreated bleeding disorder. The independent variables for only operative mortality were the presence of respiratory distress, disseminated cancer, chronic corticosteroid use, emergency surgery, low platelet count (<$12 \times 10^4/\mu$L), aspartate aminotransferase more than 40 IU/L, increased level of total bilirubin (>2 mg/dL), and activated partial thromboplastin time more than 40 seconds.

Model Performance

To evaluate the model performance, we evaluated the area under the ROC curve (AUC) and the model calibration across risk groups. The ROC curves for both models are shown in Figure 2. The AUC was 0.785 for the 30-day mortality [95% confidence interval (CI), 0.705–0.865; $P < 0.001$] and 0.798 for the overall operative mortality (95% CI, 0.746–0.851; $P < 0.001$). Figure 3 shows the calibration of the models, which illustrates how well the rates for the predicted events matched those of the observed events among the patient risk subgroups.

We evaluated the model performance in open and laparoscopic distal gastrectomy cases (n = 22,039 and 11,878 cases, respectively). The preoperative risk factors were significantly higher in open cases than those in laparoscopic cases (Table 4; Supplemental Digital Content available at http://links.lww.com/SLA/A750). The 30-day and operative mortalities in the open cases were significantly high than those in the laparoscopic cases (Table 5; Supplemental Digital Content available at http://links.lww.com/SLA/A751). This was also the case with morbidity. The ROC curves obtained when both models were applied to the open and laparoscopic cases are shown in Figure 4 (Supplemental Digital Content available at http://links.lww.com/SLA/A752). The AUC was 0.746 for the 30-day mortality (95% CI, 0.628–0.863; $P < 0.001$) and 0.787 for the overall operative mortality (95% CI, 0.717–0.856; $P < 0.001$) in the laparoscopic cases. The AUC was 0.791 for the 30-day mortality (95% CI, 0.756–0.827; $P < 0.001$) and 0.831 for the overall operative mortality (95% CI, 0.808–0.853; $P < 0.001$) in the open cases.

DISCUSSION

The nationwide database used in this study was constructed from the data related to 33,917 cases treated at 1737 hospitals, which comprise most of the Japanese institutions that perform gastric cancer surgery. In this study, the postoperative morbidity, 30-day mortality, and postoperative mortality were 18.3%, 0.52%, and 1.2%, respectively. This is the first report in Japan to present 30-day and operative mortality risk models for distal gastrectomy, which were developed using data from the nationwide web-based data entry system of NCD. The variables examined were selected from among those considered in ACS-NSQIP. The 30-day and operative mortality models included 17 and 21 significant variables, respectively, and the C-indices for the 30-day and operative mortalities in the validation sets were 0.785 and 0.798, respectively, thereby supporting the good predictive abilities of the models.

TABLE 1. Key Preoperative Risk Factors and Surgical Outcomes

			Distal Gastrectomy Outcome Groups					
	Entire Study Population (n = 33,917)		30-d Mortality (n = 176)			Operative Mortality (n = 409)		
Characteristics	n	%	n	%	*P*	n	%	*P*
Demographics								
Age, mean (SD), yr	69 (11.8)		76.4 (11.2)		<0.001	76.4 (11.2)		<0.001
Males	22,558	66.5	130	73.9	0.039	301	73.6	0.002
Ambulance transport	474	1.4	12	6.8	<0.001	33	8.1	<0.001
Preoperative risk assessment								
General								
ADL before 30 d: total assistance	227	0.7	12	6.8	<0.001	27	6.6	<0.001
Preoperative ADL: total assistance	264	0.8	14	8.0	<0.001	33	8.1	<0.001
Preoperative ADL: any assistance	1604	4.7	45	25.6	<0.001	121	29.6	<0.001
Body mass index >25 kg/m^2	6153	18.2	28	15.9	0.49	60	14.7	0.07
Habitual alcohol consumption	8113	23.9	41	23.3	0.92	75	18.3	0.008
Current smoker (within a year)	6721	19.8	32	18.2	0.63	75	18.3	0.49
Brinkman index >400	9201	27.1	43	24.4	0.44	104	25.4	0.47
Diabetes	5131	15.1	43	24.4	0.001	84	20.5	0.003
Pulmonary								
Preoperative pneumonia	147	0.4	9	5.1	<0.001	17	4.2	<0.001
Chronic obstructive pulmonary disease	1206	3.6	14	8.0	0.006	41	10.0	<0.001
Respiratory distress	743	2.2	18	10.2	<0.001	51	12.5	<0.001
Cardiac								
Congestive heart failure	262	0.8	8	4.5	<0.001	15	3.7	<0.001
Myocardial infarction	188	0.6	7	4.0	<0.001	13	3.2	<0.001
Angina pectoris	442	1.3	9	5.1	<0.001	20	4.9	<0.001
Previous percutaneous coronary intervention	846	2.5	16	9.1	<0.001	30	7.3	<0.001
Previous cardiac surgery	408	1.2	6	3.4	0.02	13	3.2	0.002
Previous peripheral vascular disease surgery	169	0.5	5	2.8	0.002	9	2.2	<0.001
Hypertension	11,293	33.3	75	42.6	0.010	165	40.3	0.003
Renal								
Acute renal failure	23	0.1	0	0.0	1.00	2	0.5	0.003
Preoperative dialysis	268	0.8	7	4.0	<0.001	15	3.7	<0.001
Central nervous system								
Previous cerebrovascular disease	1329	3.9	28	15.9	<0.001	53	13.0	<0.001
Nutritional/immune/other								
Weight loss >10%	1599	4.7	34	19.3	<0.001	80	19.6	<0.001
Ascites	372	1.1	15	8.5	<0.001	34	8.3	<0.001
Ascites without control	298	0.9	13	7.4	<0.001	29	7.1	<0.001
Disseminated cancer	584	1.7	16	9.1	<0.001	46	11.2	<0.001
Chronic steroid use	287	0.8	1	0.6	1.00	13	3.2	<0.001
Bleeding disorder without treatment	148	0.4	7	4.0	<0.001	13	3.2	<0.001
Preoperative transfusions	944	2.8	26	14.8	<0.001	51	12.5	<0.001
Chemotherapy	453	1.3	4	2.3	0.30	8	2.0	0.27
Radiotherapy	45	0.1	0	0.0	1.00	1	0.2	0.42
Sepsis	57	0.2	3	1.7	0.003	7	1.7	<0.001
Emergent surgery	316	0.9	16	9.1	<0.001	35	8.6	<0.001
ASA ≥Grade 3	3008	8.9	62	35.2	<0.001	152	37.2	<0.001
ASA Grade 5	33	0.1	2	1.1	0.013	3	0.7	0.007
Cholecystectomy	3499	10.3	15	8.5	0.528	43	10.5	0.879
Preoperative laboratory data								
White blood cells								
>9000/mL	1933	5.7	29	16.5	0.015	66	16.1	<0.001
>11,000/mL	601	1.8	16	9.1	<0.001	32	7.8	<0.001
Hemoglobin, males: <13.5 g/dL; females: <12.5 g/dL	14,642	43.2	129	73.3	<0.001	294	71.9	<0.001
Hematocrit, males: <37% females: <32%	10,467	30.9	108	61.4	<0.001	250	61.1	<0.001
Platelets								
<8 × 10^4/mL	175	0.5	5	2.8	0.029	9	2.2	<0.001
<12 × 10^4/mL	932	2.7	13	7.4	0.001	38	9.3	<0.001
Serum albumin <3.8 g/dL	8730	25.7	99	56.3	<0.001	255	62.3	<0.001

(Continues)

TABLE 1. Key Preoperative Risk Factors and Surgical Outcomes (*Continued*)

			Distal Gastrectomy Outcome Groups					
	Entire Study Population (n = 33,917)		30-d Mortality (n = 176)			Operative Mortality (n = 409)		
Characteristics	n	%	n	%	*P*	n	%	*P*
AST >40 IU/L	2064	6.1	20	11.4	0.007	56	13.7	<0.001
ALP >340 IU/L	2540	7.5	30	17.0	<0.001	61	14.9	<0.001
Total bilirubin >2 mg/dL	285	0.8	2	1.1	0.66	10	2.4	0.003
BUN >20 mg/dL	5201	15.3	52	29.5	<0.001	135	33.0	<0.001
Creatinine >1.2 mg/dL	2231	6.6	32	18.2	<0.001	76	18.6	<0.001
Serum Na								
<130 mEq/L	179	0.5	11	6.3	0.061	19	4.6	<0.001
<135 mEq/L	1068	3.1	32	18.2	<0.001	70	17.1	<0.001
Hemoglobin A_{1c} >6.5%	2035	6.0	8	4.5	0.520	20	4.9	0.40
CRP >1.0 mg/dL	2696	7.9	44	25.0	<0.001	118	28.9	<0.001
PT-INR								
>1.1	4748	14.0	63	35.8	<0.001	142	34.7	<0.001
>1.25	966	3	21	12	<0.001	42	10	<0.001
APTT > 40 seconds	902	2.7	13	7.4	<0.001	39	9.5	<0.001

ALP indicates alkaline phosphatase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; PT-INR, prothrombin time-international normalized ratio; SD, standard deviation.

TABLE 2. Prevalence of Morbidity With Distal Gastrectomy Outcomes

			Distal Gastrectomy Outcome Groups					
	Entire Study Population (n = 33,917)		30-d Mortality (n = 176, 0.52%)			Operative Mortality (n = 409, 1.2%)		
Postoperative Outcomes	n	%	n	%	*P*	n	%	*P*
Readmission within 30 d	553	1.6	3	1.7	0.765	7	1.7	0.843
Reoperation within 30 d	633	1.9	29	16.9	<0.001	80	19.6	<0.001
Postoperative complications								
Overall	6193	18.3	148	84.1	<0.001	329	80.4	<0.001
≥Grade II	3893	11.5	138	78.4	<0.001	303	74.1	<0.001
Surgical complications								
Surgical site infection	1458	4.3	31	17.6	<0.001	89	21.8	<0.001
Superficial incisional	668	2.0	9	5.1	0.008	42	10.3	<0.001
Deep incisional	288	0.8	8	4.5	<0.001	35	8.6	<0.001
Organ space	910	2.7	27	15.3	<0.001	72	17.6	<0.001
Wound dehiscence	182	0.5	6	3.4	<0.001	26	6.4	<0.001
Anastomotic leak	696	2.1	25	14.2	<0.001	73	17.8	<0.001
Pancreatic fistula	542	1.6	17	9.7	<0.001	37	9.0	<0.001
Bile leakage	102	0.3	2	1.1	0.099	13	3.2	<0.001
Nonsurgical complications								
Pneumonia	687	2.0	35	19.9	<0.001	122	29.8	<0.001
Unplanned intubation	293	0.9	77	43.8	<0.001	136	33.3	<0.001
Prolonged ventilation >48 hr	299	0.9	59	33.5	<0.001	129	31.5	<0.001
Pulmonary embolism	26	0.1	4	2.3	<0.001	5	1.2	<0.001
Acute renal failure	89	0.3	25	14.2	<0.001	55	13.4	<0.001
Urinary tract infection	150	0.4	5	2.8	0.001	21	5.1	<0.001
Events in central nervous system	164	0.5	32	18.2	<0.001	60	14.7	<0.001
Cardiac events	118	0.3	75	42.6	<0.001	88	21.5	<0.001
Septic shock	138	0.4	38	21.6	<0.001	75	18.3	<0.001

Many studies have aimed to develop methods that predict the risk of perioperative mortality following gastric resection in the Western hemisphere[17–20] and in Asian countries.[21] All these previous studies used data from either a single institution or a nationwide database.[17–21] The most commonly used nationwide databases in the Western hemisphere are the population-based National Inpatients Sample[17,18] and ACS-NSQIP.[20] However, the National Inpatients Sample data set is an administrative data set, which lacks operative factors such as the procedure duration, bleeding volume, and extent of lymph node resection, and it also lacks other important factors such as ASA status, preoperative nutritional status, extent of weight loss, palliative versus curative resection, and use of neoadjuvant therapy. The risk models created using ACS-NSQIP variables have been shown to be quite effective for predicting mortality in

TABLE 3. Risk Models for 30-Day Mortality and Operative Mortality After Distal Gastrectomy

	30-d Mortality					Operative Mortality				
Variables	b Coefficient	Odds Ratio	95% CI		*P*	b Coefficient	Odds Ratio	95% CI		*P*
Age category	0.184	1.202	1.062	1.361	0.004	0.283	1.327	1.217	1.446	<0.001
ADL										
Before 30 d: total assistance	1.083	2.955	1.418	6.159	0.004					
Preoperative: total assistance						1.099	3.001	1.856	4.852	<0.001
Habitual alcohol consumption	0.453	1.573	1.047	2.362	0.029					
Preoperative pneumonia	1.019	2.769	1.171	6.549	0.02					
Respiratory distress						0.869	2.385	1.634	3.482	<0.001
Myocardial infarction	1.14	3.127	1.282	7.63	0.012					
Previous cerebrovascular disease	0.734	2.084	1.248	3.48	0.005	0.575	1.777	1.228	2.572	0.002
Weight loss >10%	0.82	2.271	1.437	3.589	<0.001	0.785	2.192	1.592	3.018	<0.001
Ascites without control	1.091	2.978	1.404	6.315	0.004	1.018	2.767	1.638	4.674	<0.001
Disseminated cancer						1.063	2.896	1.897	4.42	<0.001
Chronic steroid use						1.026	2.789	1.454	5.35	0.002
Bleeding disorder without treatment	1.17	3.223	1.205	8.622	0.02					
Emergent surgery						0.618	1.856	1.026	3.357	0.041
ASA ≥class 3	0.668	1.95	1.288	2.953	0.002	0.648	1.912	1.453	2.518	<0.001
White blood cells										
>11,000/mL						0.934	2.545	1.591	4.071	<0.001
>12,000/mL	1.299	3.666	1.837	7.314	<0.001					
Hemoglobin										
Males: <13.5 g/dL females: <12.5 g/dL	0.596	1.814	1.136	2.897	0.013					
Hematocrit										
Males: <37% females: <32%						0.364	1.439	1.089	1.901	0.01
Platelets <12 × 10^4/mL						0.696	2.006	1.3	3.093	0.002
Serum albumin										
<3.5 g/dL	0.395	1.485	0.979	2.252	0.063					
<3.8 g/dL						0.555	1.741	1.303	2.326	<0.001
Aspartate aminotransferase >40 IU/L						0.416	1.516	1.06	2.169	0.023
Alkaline phosphatase >340 IU/L	0.772	2.164	1.384	3.386	0.001	0.442	1.556	1.113	2.173	0.01
Total bilirubin >2 mg/dL						0.969	2.634	1.204	5.764	0.015
Creatinine >1.2 mg/dL	0.573	1.773	1.124	2.796	0.014	0.59	1.803	1.328	2.448	<0.001
Serum Na <135 mEq/L	0.908	2.48	1.528	4.025	<0.001	0.812	2.251	1.612	3.146	<0.001
PT-INR										
>1.1						0.423	1.527	1.175	1.985	0.002
>1.25	0.708	2.03	1.162	3.549	0.013					
APTT > 40 seconds						0.455	1.576	1.05	2.366	0.028
Intercept	− 7.393				<0.001	− 6.996				<0.001

APTT indicates activated partial thromboplastin time; PT-INR, prothrombin time-international normalized ratio.

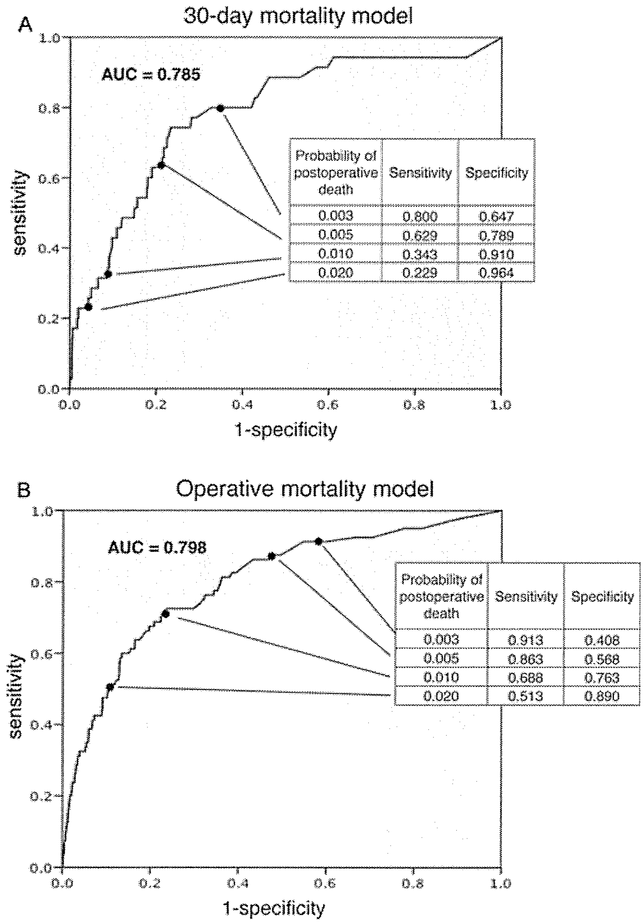

FIGURE 2. ROC curves of the (A) 30-day mortality model and (B) operative mortality model. The AUC was 0.785 for the 30-day mortality (95% CI, 0.705–0.865; $P < 0.001$) and 0.798 for the overall operative mortality (95% CI, 0.746–0.851; $P < 0.001$).

various procedures and for improving surgical quality in participating hospitals.[14] However, Borja-Cacho et al[22] showed that the current ACS-NSQIP variables do not have a good predictive capacity for major complications after major oncological resection, and thus they advocated the use of additional disease-specific and operation-specific variables to obtain more accurate predictions of the 30-day postoperative outcome. NCD uses variables similar to those employed in ACS-NSQIP but with some modifications that allow it to represent not only the 30-day mortality but also the in-hospital mortality 90 days or less after surgery. The Japanese system of universal health care allows most patients who undergo surgery to be cared for in the same hospital that performed the operation until the patient can independently function in terms of ADL.[23,24] With this adjustment to include longer-term mortality, the operative mortality rate of patients treated by distal gastrectomy increased to twice the 30-day mortality rate (1.2% vs 0.52%, respectively).

There are 2 major distinct gastrectomy procedures: distal and total gastrectomy. The surgical procedures for resection and anastomosis are quite different, and the outcomes of the respective procedures are reported in the JSGS annual report (30-day mortality/operative mortality: subtotal gastrectomy, 0.6%/1.3%; total gastrectomy, 1.0%/2.3%).[25] In this study, we focused only on patients who had undergone distal gastrectomy for gastric cancer. Out of the 17 and 21 risk factors in the 30-day and operative mortality models, respectively, 13 variables shared similar characteristics. Previously, many of these factors have been shown to affect perioperative mortality in patients who undergo gastric resections for malignancy.[17–22] The results of our study clearly showed that common and independent variables affected the mortality risk in the early (30-day mortality) and late (90-day in-hospital mortality) postoperative periods. The variables that predicted the 30-day mortality only and not the operative mortality comprised those that influence relatively early death after surgery, such as habitual alcohol consumption, preoperative pneumonia, myocardial infarction, and untreated bleeding disorder. The variables that predicted operative mortality only are those that influence late death after surgery, such as any respiratory distress, disseminated cancer, chronic corticosteroid use, emergency surgery, low platelet count, and high levels of aspartate aminotransferase, total bilirubin, and activated partial thromboplastin time. The variables that predicted both the 30-day and operative mortalities are those that influence both early and late death after surgery. In particular, the laboratory variables (eg, white blood cell count, serum albumin, and prothrombin time-international normalized ratio) that captured the risk of both early and late mortality appeared to be related to substantially abnormal levels in the 30-day mortality group. Further analysis is needed to determine the variables that are relevant to the respective morbidities leading to mortality, but these results provide insight into the specific preoperative risk variables responsible for the early or late mortality of patients who undergo distal gastrectomy.

This study had several limitations, which need to be addressed in future studies. First, the reported mortality and morbidity rates in our study would have been influenced by cancer stage, extent of lymphadenectomy (eg, D1, D1, and D2),[8,9,10,26–28] curative ability of the surgery,[29,30] hospital volume,[31,32] and institutional experience.[33] In addition, we only analyzed the variables that could be obtained before surgery. Although these risk models predicted the mortality well for open or laparoscopic approaches, the effects of these variables on outcomes should be assessed in a future study using a propensity score matching system. Second, some reports have described preoperative scoring systems that predict surgical risks, such as the Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity and the Estimation of Physiologic Ability and Surgical Stress for general surgery.[34,35] However, although these systems are useful for general surgery, some modifications would be required for specific operative procedures.[36] The NCD is currently being used to investigate the accuracy of these models for Japanese patients who undergo gastrectomy. Third, although our analysis used the nationwide database, the study population was limited to a single race. Therefore, our results should be evaluated on the basis of comparisons with patients from other countries using the same variables and definitions. Thus, we are currently planning a mutual collaboration with ACS-NSQIP.

CONCLUSIONS

We report the first risk stratification study based on the NCD for distal gastrectomy in cancer treatment. The NCD database allowed us to determine interinstitutional differences in outcomes and the factors that affect these differences. This system will contribute to an improved quality control in surgical practice and it should also be useful in counseling and for obtaining informed consent from patients.

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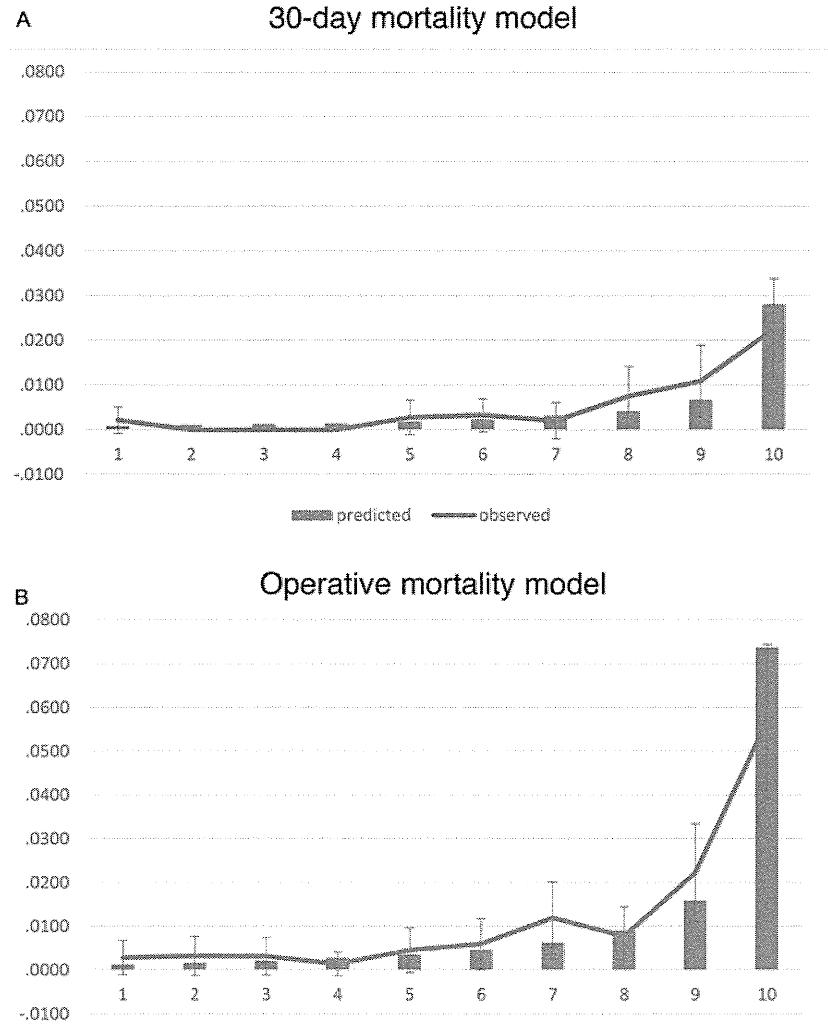

FIGURE 3. Calibrations of the 30-day mortality model (A) and operative mortality model (B). The calibrations of the models illustrate how well the rates of the predicted events matched those of the observed events among the patient risk subgroups. The error bar represents 95% confidence interval.

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Total Gastrectomy Risk Model

Data From 20,011 Japanese Patients in a Nationwide Internet-Based Database

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Objective: To construct a risk model for total gastrectomy outcomes using a nationwide Internet-based database.

Background: Total gastrectomy is a very common procedure in Japan. This procedure is among the most invasive gastrointestinal procedures and is known to carry substantial surgical risks.

Methods: The National Clinical Database was used to retrieve records on more than 1,200,000 surgical cases from 3500 hospitals in 2011. After data cleanup, 20,011 records from 1623 hospitals were analyzed for procedures performed between January 1, 2011, and December 31, 2011.

Results: The average patient age was 68.9 years; 73.7% were male. The overall morbidity was 26.2%, with a 30-day mortality rate of 0.9%, in-hospital mortality rate of 2.2%, and overall operative mortality rate of 2.3%. The odds ratios for 30-day mortality were as follows: ASA (American Society of Anesthesiologists) grade 4 or 5, 9.4; preoperative dialysis requirement, 3.9; and platelet count less than 50,000 per microliter, 3.1. The odds ratios for operative mortality were as follows: ASA grade 4 or 5, 5.2; disseminated cancer, 3.5; and alkaline phosphatase level of more than 600 IU/L, 3.1. The C-index of 30-day mortality and operative mortality was 0.811 (95% confidence interval [CI], 0.744–0.879) and 0.824 (95% CI, 0.781–0.866), respectively.

Conclusions: We have performed the first reported risk stratification study for total gastrectomy, using a nationwide Internet-based database. The total gastrectomy outcomes in the nationwide population were satisfactory. The risk models that we have created will help improve the quality of surgical practice.

Keywords: National Clinical Database, risk factors of mortality, total gastrectomy, 30-day mortality, risk model

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Gastric cancer is currently the fourth most common malignancy worldwide[1] and is among the most prevalent types of cancer in Eastern Asia, including Japan, Korea, and China.[2] Surgical resection is often the only curative treatment, although some early gastric cancers limited to the mucosa may be treated endoscopically.[3] Total gastrectomy is usually indicated for tumors located in the upper third of the stomach or advanced gastric cancer extending to the cardia.

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Total gastrectomy is among the most invasive gastrointestinal procedures and is known to carry substantial surgical risks. Patients with gastric cancer frequently have anemia, malnutrition, or organ dysfunction due to tumor extension.[4] Major complications of total gastrectomy can be fatal; these complications include esophagojejunal anastomotic leakage, duodenal stump leakage, and pancreatic fistula related to suprapancreatic lymphadenectomy.[5] In addition, the proportion of patients with gastric cancer who are elderly is increasing.[6] Although all of these factors may affect mortality, and several additional factors influence the incidence of gastric cancer itself, there are few studies that have used a large patient cohort to describe a risk model of mortality for total gastrectomy.

The National Clinical Database (NCD), which commenced patient registration in January 2011, is a nationwide project that is linked to the surgical board certification system in Japan. In this study, we focused on the NCD division of gastrointestinal surgery that uses patient variables and definitions almost identical to those used by the American College of Surgeons National Surgical Quality Improvement Program.[7] Using this database, we created a risk model of mortality for Japanese patients undergoing total gastrectomy.

METHODS

Data Collection

In 2011, the NCD collected data on more than 1,200,000 surgical cases from 3500 hospitals. In the gastroenterological surgery section, the database registered all surgical cases that fell into this category; in addition, it required detailed input items for the 8 procedures, including total gastrectomy, that were determined to represent the performance of surgery in each specialty. Patients who declined to have their records entered in the NCD were excluded from our analysis. Records with missing data on patient age, sex, or status, 30 days after surgery were also excluded. A total of 20,011 patients who underwent total gastrectomy at 1623 institutions between January 1, 2011, and December 31, 2011, were eligible for analysis.

The NCD constructed software for an Internet-based data collection system, and the data managers of participating hospitals were responsible for forwarding their data to the NCD office. The NCD ensures traceability of its data by maintaining continuity in the staff who approve data, the staff of the departments in charge of annual cases, and the data-entry personnel. It also validates data consistency via random inspections by participating institutions. All variables, definitions, and inclusion criteria for the NCD are accessible to participating institutions on its Web site (http://www.ncd.or.jp); the database administrators also provide e-learning systems to teach participants how to input consistent data. The administrators answer all inquiries regarding data entry, answering approximately 80,000 inquiries in 2011, and Frequently Asked Questions are displayed on the Web site.

Endpoint

The primary outcome measure of this study was 30-day mortality and overall operative mortality. The calculation of operative mortality included all patients who died during the index hospitalization, including hospital stays up to 90 days, and any patient who died after hospital discharge within 30 days of the operation date.

Statistical Analysis

Data were randomly assigned to 2 subsets, with 80% allocated for model development and 20% for validation testing. The development data set comprised 16,036 records, and the validation data set comprised 3975 records. The 2 sets of logistic models, 30-day mortality and operative mortality, were constructed for the development data set using a stepwise selection of predictors, with the P value for inclusion set at 0.05. A goodness-of-fit test was performed to assess how well the model could discriminate between survivors and deceased patients. Model calibration, the degree to which the observed outcomes were similar to the predicted outcomes, was examined by comparing the observed with the predicted average within each of the 10 equal-sized subgroups, arranged in increasing order of patient risk.

RESULTS

Study Population Risk Profile

The total gastrectomy patient population represented in the NCD had an average age of 68.9 years; 73.7% of the population was male. The mean body mass index of the study population was 22.4 kg/m^2. Only 2.0% required emergency surgery. Furthermore, 4.6% of the patients needed assistance in activities of daily life. Weight loss of more than 10% was observed in 8.7% of patients. American Society of Anesthesiologists (ASA) scores of grade 3 and grade 4/5 were seen in 8.9% and 0.6% of patients, respectively. Preoperative comorbidities included diabetes mellitus in 8.9% of patients, preoperative respiratory distress in 2.4% of patients, disseminated cancer in 3.7% of patients, and ascites in 2.0% of patients. An abbreviated demographic and risk profile of the study population is shown in Table 1.

Morbidity

The overall morbidity in the total gastrectomy NCD population was 26.2%; grade II or higher complications, as defined by the Clavien-Dindo Classification of Surgical Complications system,[8] were observed in 18.3% of patients. Surgical complications included surgical site infection in 8.4% of patients, anastomotic leakage in 4.4% of patients, and pancreatic fistula (grades B, C) in 2.6% of patients. Nonsurgical complications included pneumonia in 3.6% of patients, renal failure in 1.3% of patients, central nervous system events in 0.7% of patients, and cardiac events in 0.6% of patients. The postoperative morbidities are presented in Table 2.

TABLE 1. Key Descriptive Data

Variables	N = 20,011
Age, mean, yr	68.9
Males, %	73.7
Body mass index, mean, kg/m^2	22.4
Status (emergent), %	2.0
ADL (any assistance), %	4.6
Weight loss, >10%, %	8.7
ASA score, %	
Grade 3	8.9
Grade 4 or 5	0.6
Diabetes, %	15.7
Previous cardiac surgery, %	1.1
Preoperative respiratory distress, %	2.4
Preoperative dialysis, %	0.5
Cerebrovascular accident, %	2.2
Disseminated cancer, %	3.7
Ascites, %	2.0

ADL indicates activities of daily life.

Outcomes

Total gastrectomy outcomes are presented in Table 3. The 30-day mortality was 0.9%, the in-hospital mortality was 2.2%, and the overall operative mortality was 2.3%.

Model Results

Risk models for 30-day mortality and operative mortality were developed; the final logistic models with the odds ratios and 95% confidence intervals are presented in Tables 4 and 5. The ASA score (grade 4 or 5) was the most significant factor in both models. In addition, there were 11 variables that appeared in both models: a preoperative dialysis requirement; a total bilirubin level of more than 2 mg/dL; the presence of disseminated cancer; an alkaline phosphatase level of more than 600 IU/L; an aspartate aminotransferase level of more than 35 IU/L; a prothrombin time–international normalized ratio of more than 1.25; any assistance needed for preoperative activities of daily living; the presence of ascites; a serum albumin level of less than 3.5 g/dL; and the patient's age category (see Tables 4 and 5 for the definition of age category).

Model Performance

To assess the performance of the models, both the C-index and the model calibration across risk groups were evaluated. The receiver operating characteristic curves of both models are shown in Figure 1. The C-index, a measure of model discrimination represented by the area under the receiver operating characteristic curve, was 0.811 for 30-day mortality (95% confidence interval, 0.744–0.879) (Fig. 1A) and 0.824 for overall operative mortality (95% confidence interval, 0.781–0.866) (Fig. 1B). Figure 2 demonstrates the calibration of the models or how well the rates for the predicted event matched those of observed event among patient risk subgroups. (Figure 2A, 30-day mortality risk model; and Figure 2B, operative mortality risk model)

DISCUSSION

Although mortality due to gastric cancer has been steadily decreasing in recent years,[9] the incidence of this cancer in Japan is still the highest of all solid tumors,[10] probably due to the high incidence of *Helicobacter pylori* infection in the Japanese population.[11] Gastric cancer is one of the most commonly encountered diseases in Japanese surgical units; Japanese surgeons are therefore very familiar with gastric cancer surgery, which explains why our study cases were collected from such a large number of institutes.

Although numerous studies have reported the morbidity and mortality rates for gastrectomy in general, few have described these rates for total gastrectomy alone. Moreover, it is still unknown whether total gastrectomy should be considered a more invasive procedure than distal gastrectomy. A randomized controlled trial comparing D1 subtotal gastrectomy with D3 total gastrectomy for cancers located in the gastric antrum revealed that significantly more abdominal abscesses are observed in patients undergoing total gastrectomy; this is attributed to the extended lymphadenectomy involved in the latter procedure.[12] In contrast, an Italian study demonstrated that postoperative morbidity rates are comparable between subtotal gastrectomy and total gastrectomy,[13] although postoperative quality of life is significantly better after subtotal gastrectomy.[14] Both studies

TABLE 2. Morbidities in the NCD Total Gastrectomy Population

Complications	Test Set (n = 16,036)	Validation Set (n = 3975)	Overall Incidence (N = 20,011)
Overall complications	4216 (26.3)	1033 (26.0)	5249 (26.2)
Grade II or higher*	2965 (18.5)	708 (17.8)	3668 (18.3)
Surgical complications			
Surgical site infection	1355 (8.4)	331 (8.3)	1686 (8.4)
Superficial incisional	503 (3.1)	128 (3.2)	631 (3.2)
Deep incisional	244 (1.5)	66 (1.7)	310 (1.5)
Organ space	1024 (6.4)	251 (6.3)	1275 (6.4)
Anastomotic leak	711 (4.4)	170 (4.3)	881 (4.4)
Pancreatic fistula (grade B, C)	419 (2.6)	110 (2.8)	529 (2.6)
Bile leak	81 (0.5)	15 (0.4)	96 (0.5)
Wound dehiscence	161 (1.0)	37 (0.9)	198 (1.0)
Nonsurgical complications			
Pneumonia	589 (3.7)	137 (3.4)	726 (3.6)
Unplanned intubation	282 (1.8)	57 (1.4)	339 (1.7)
Prolonged ventilation >48 h	308 (1.9)	70 (1.8)	378 (1.9)
Pulmonary embolism	25 (0.2)	3 (0.1)	28 (0.1)
Renal failure	213 (1.3)	46 (1.2)	259 (1.3)
CNS events	121 (0.8)	28 (0.7)	149 (0.7)
Cardiac events	90 (0.6)	23 (0.6)	113 (0.6)
Sepsis	138 (0.9)	24 (0.6)	162 (0.8)

The values given are number (percentage).
*Clavien-Dindo classification.
CNS indicates central nervous system.

TABLE 3. Outcome Rates in the NCD Total Gastrectomy Population

Outcomes	Test Set (n = 16,036)	Validation Set (n = 3975)	Overall Incidence (N = 20,011)
30-d mortality	153 (1.0)	34 (0.9)	187 (0.9)
In-hospital mortality	358 (2.2)	89 (2.2)	447 (2.2)
Operative mortality	367 (2.3)	90 (2.3)	457 (2.3)
Reoperation within 30 d	542 (3.4)	122 (3.1)	664 (3.3)
Readmission within 30 d	311 (1.9)	86 (2.2)	397 (2.0)

The values given are number (percentage).

TABLE 4. Risk Model of 30-Day Mortality

Variables	Status	Hazard Ratio	95% Confidence Interval
ASA score	Grade 4 or 5	9.383	4.85–18.152
Preoperative dialysis	Present	3.906	1.546–9.867
Platelet count	<50,000/μL	3.064	1.256–7.473
Total bilirubin	>2.0 mg/dL	2.919	1.189–7.17
Disseminated cancer	Present	2.641	1.603–4.35
Alkaline phosphatase	>600 IU/L	2.457	1.153–5.232
Previous cardiac surgery	Present	2.346	0.997–5.518
Aspartate aminotransferase	>35 IU/L	2.340	1.549–3.537
Diabetes	Insulin use	2.182	1.116–4.266
PT-INR	>1.25	2.182	1.318–3.613
Preoperative ADL	Any assistance	2.086	1.329–3.272
Ascites	Present	2.018	1.11–3.669
Preoperative transfusion	Present	1.936	1.208–3.102
Blood urea nitrogen	>25 mg/dL	1.886	1.201–2.961
Albumin	<3.5 g/dL	1.714	1.167–2.517
Alkaline phosphatase	>340	1.682	1.032–2.739
Hemoglobin	Male, <13.5 g/dL; female, <12.5 g/dL	1.659	1.03–2.675
Age category		1.194	1.067–1.337

Age category is defined as follows: category 1, <60 years; category 2, ≤60 to <65 years; category 3, ≤65 to <70 years; category 4, ≤70 to <75 years; category 5, ≤75 years.
ADL indicates activities of daily living; PT-INR, prothrombin time–international normalized ratio.

TABLE 5. Risk Model of Operative Mortality

Variables	Status	Hazard Ratio	95% Confidence Interval
ASA score	Grade 4 or 5	5.248	2.735–10.07
Disseminated cancer	Present	3.458	2.514–4.757
Alkaline phosphatase	>600 IU/L	3.116	1.812–5.356
Total bilirubin	>2.0 mg/dL	2.751	1.355–5.587
Preoperative dialysis	Present	2.583	1.146–5.819
Pancreaticosplenectomy	Present	2.219	1.177–4.185
White blood cell count	>11,000/μL	2.037	1.368–3.033
Preoperative ADL	Any assistance	2.015	1.469–2.764
PT-INR	>1.25	1.880	1.292–2.737
Cerebrovascular accident	Present	1.858	1.136–3.037
ASA score	Grade 3	1.819	1.37–2.417
Ascites	Present	1.752	1.133–2.71
Respiratory distress	Present	1.719	1.139–2.594
Aspartate aminotransferase	>35 IU/L	1.685	1.252–2.266
Status	Emergent	1.656	1.031–2.662
White blood cell count	<3500/μL	1.629	1.172–2.265
Weight loss	>10%	1.584	1.185–2.119
Sodium	<138 mEq/L	1.429	1.104–1.85
Albumin	<3.5 g/dL	1.411	1.045–1.905
Albumin	<3.0 g/dL	1.353	0.974–1.88
Hematocrit	<30%	1.339	1.025–1.75
Age category		1.294	1.199–1.396

Age category is defined as follows: category 1, <60 years; category 2, ≤60 to <65 years; category 3, ≤65 to <70 years; category 4, ≤70 to <75 years; category 5, ≤75 years.

ADL indicates activities of daily living; PT-INR, prothrombin time–international normalized ratio.

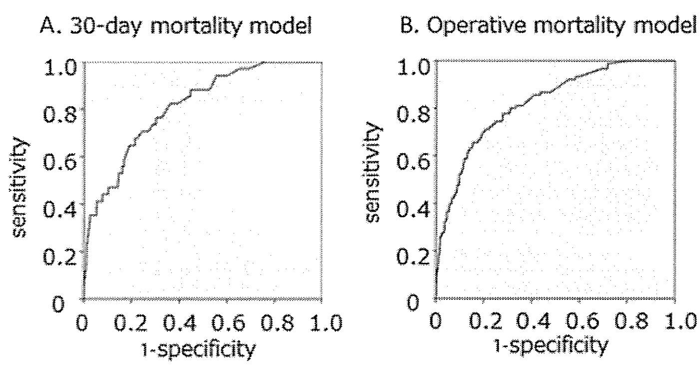

FIGURE 1. Receiver operating characteristic curves of each model. The C-index, a measure of model discrimination represented by the area under the receiver operating characteristic curve, was (A) 0.811 for 30-day mortality (95% CI, 0.744–0.879) and (B) 0.824 for overall operative mortality (95% CI, 0.781–0.866). CI indicates confidence interval.

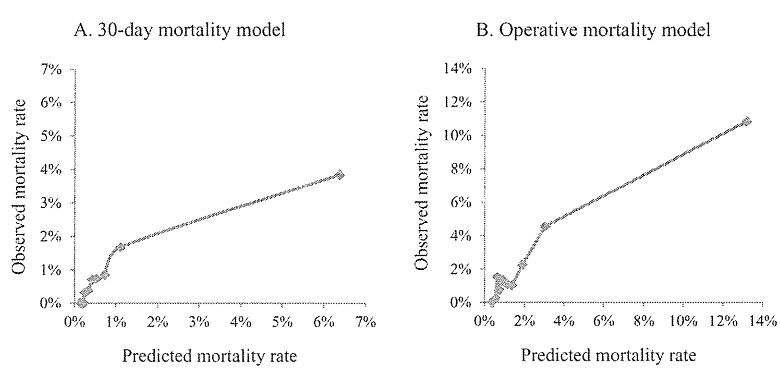

FIGURE 2. The calibration of (A) 30-day mortality model, and (B) operative mortality model.

report that mortality is similar between subtotal gastrectomy and total gastrectomy.[12,13] These results suggest that morbidity experienced after gastrectomy may depend on the extent of lymphadenectomy rather than the extent of gastrectomy. Several randomized controlled trials performed in Western countries have demonstrated that morbidity is significantly higher after D2 or greater lymphadenectomy than after D1 dissection.[15–17]

Although the operative outcomes for gastrectomy have been reported from several high-volume centers,[18] the nationwide outcomes in Japan remain unknown. The advent of the NCD enables the analysis of these nationwide outcomes for several operative procedures, including total gastrectomy. In addition, the database allows researchers to determine interinstitutional differences in the outcomes and factors affecting these differences. Most importantly, development of a risk model using this database is expected to contribute to improved quality control for several procedures.

In this study, we observed an overall morbidity of 26.2% in NCD patients undergoing total gastrectomy. Morbidity in the aforementioned randomized trials ranged from 16.8% to 28% in the D1 groups and 33% to 46% in the D2 or greater groups.[15–17] The 30-day mortality and overall postoperative mortality rates in the NCD total gastrectomy population were 0.9% and 2.3%, respectively. Mortality rates in the other trials ranged from 1.8% to 6.5% in the D1 groups and 3.7% to 13% in the D2 or greater groups. According to a recent report conducted by the Japanese Gastric Cancer Association using a nationwide registry, D2 lymph node dissection is performed in 49.2% of patients and extended D1 dissection is performed in 20.9% of patients whereas D0 or D1 lymphadenectomy is performed in 27.2% of patients.[18] When we consider the fact that such a high percentage of patients undergo D2 lymph node dissection at many institutions, the morbidity and mortality rates for total gastrectomy are satisfactorily low in Japan.

According to our risk models, the most important variable affecting both 30-day and overall operative mortality rates is the ASA score. The ASA classification is among the most commonly used scoring systems, although it is subjective and prone to interobserver variability.[19] The ASA grade has the advantages of simplicity and of universal use[20] and is known to be an effective risk indicator when used either alone[21] or in combination with other parameters.[22,23] Other factors affecting mortality can be divided into 2 groups, with the first group including factors related to patients' general condition such as the need for preoperative dialysis and laboratory test abnormalities and the second group including variables related to tumor extension such as the presence of disseminated cancer and ascites. It is reasonable to presume that a poor preoperative general condition correlates with postoperative mortality. As an example of the impact of the second group of variables, peritoneal dissemination is a progression pattern distinctive for gastric cancer; curative resection is usually impossible in this situation, and palliative resection is often performed for symptom relief. High morbidity and mortality rates have been reported for noncurative gastric cancer surgery.[24]

In our risk model, body mass index was not a significant factor affecting the mortality. Overweight is a well-known risk of postoperative complications after gastrectomy. Tsujinaka et al[25] investigated influence of overweight on surgical complications after gastrectomy using data from Japan Clinical Oncology Group study 9501, which explored survival benefit of para-aortic D3 dissection over standard D2 dissection. They revealed that being overweight increased the risk for surgical complications in patients who underwent D2 dissection.[25] Kulig et al[26] conducted a multicenter study to evaluate the effects of overweight on surgical outcomes in a Western patient population and demonstrated that higher body mass index was associated with a higher rate of cardiopulmonary complications and intra-abdominal abscess. Despite the increase in postoperative complications in overweight patients, obesity did not affect the mortality in both studies, as observed in this study.

Preoperative treatment may also affect the occurrence of mortality after total gastrectomy. In the European countries, perioperative chemotherapy is the standard treatment approach for patients with resectable gastroesophagel cancer.[27] In contrast, postoperative chemotherapy using S-1 is the standard therapy for patients with stage II/III gastric cancer in Japan.[28] Only 4.3% and 0.1% of the NCD total gastrectomy population underwent neoadjuvant chemotherapy and radiotherapy, respectively, and therefore neoadjuvant therapy was not a significant factor affecting the mortality.

The C-indices of the models for 30-day mortality and operative mortality indicate that our models are reliable. Although the usefulness of several scoring systems, such as the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM)[29] and the Estimation of Physiologic Ability and Surgical Stress (E-PASS),[30,31] in predicting the risks associated with gastrectomy has been reported, these systems are not specific to Japanese patients undergoing total gastrectomy. Using our risk model results, we may be able to create a novel scoring system suitable for total gastrectomy in Japanese patients.

It is unclear whether all total gastrectomy cases all over Japan are really enrolled in the NCD. Basically, the data manager in each participating hospital is responsible for the data enrollment. However, as the NCD is linked to the surgical board certification system, we assume that almost all cases are enrolled in this system. Indeed, the number of cases in this study is almost 5 times higher than that of the nationwide registry maintained by the Japan Gastric Cancer Association.[18]

CONCLUSIONS

We have reported the first risk stratification study on total gastrectomy in Japan by using a nationwide Internet-based database. The nationwide mortality rates after total gastrectomy are quite satisfactory. We have developed risk models for total gastrectomy that will contribute to improving the quality of this procedure.

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ORIGINAL ARTICLE—ALIMENTARY TRACT

Risk model for right hemicolectomy based on 19,070 Japanese patients in the National Clinical Database

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Abstract
Background Right hemicolectomy is a very common procedure throughout the world, although this procedure is known to carry substantial surgical risks. The present study aimed to develop a risk model for right hemicolectomy outcomes based on a nationwide internet-based database.
Methods The National Clinical Database (NCD) collected records on over 1,200,000 surgical cases from 3,500 Japanese hospitals in 2011. After data cleanup, we analyzed 19,070 records regarding right hemicolectomy performed between January 2011 and December 2011.
Results The 30-day and operative mortality rates were 1.1 and 2.3 %, respectively. The 30-day mortality rates of patients after elective and emergency surgery were 0.7 and 6.0 %, respectively ($P < 0.001$). The odds ratios of preoperative risk factors for 30-day mortality were: platelet <50,000/μl, 5.6; ASA grade 4 or 5, 4.0; acute renal failure, 3.2; total bilirubin over 3 mg/dl, 3.1; and AST over 35 U/l, 3.1. The odds ratios for operative mortality were: previous peripheral vascular disease, 3.1; cancer with multiple metastases, 3.1; and ASA grade 4 or 5, 2.9. Sixteen and 26 factors were selected for risk models of 30-day and operative mortality, respectively. The c-index of both models was 0.903 [95 % confidence interval (CI) 0.877–0.928; $P < 0.001$] and 0.891 (95 % CI 0.873–0.908; $P < 0.001$), respectively.
Conclusion We performed the first reported risk stratification study for right hemicolectomy based on a nationwide internet-based database. The outcomes of right hemicolectomy in the nationwide population were satisfactory. The risk models developed in this study will help to improve the quality of surgical practice.

Keywords Right hemicolectomy · Colorectal cancer · Mortality · Risk model · National Clinical Database

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Introduction

The rate of colorectal cancer in Japan is rapidly increasing [1, 2]. Although the extent of lymphadenectomy for colorectal cancer differs according to institutions, operative procedures such as bowel resection and anastomosis have been established. Right hemicolectomy is one of the standard approaches to treating colorectal diseases. Although an established procedure, some risks of postoperative mortality and morbidity are associated with hemicolectomy. The risk of intraoperative bleeding is higher after more aggressive lymphadenectomy such as D3 lymph node

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dissection or complete mesocolic excision with central ligation [3, 4].

Written informed consent is essential before patients undergo invasive medical procedures in light of medical ethics. In particular, operative mortality and morbidity risks should be explained. However, a nationwide prospective database has not yet been used to analyze post-surgical rates of mortality and morbidity in Japan, and data applied during the informed consent process have depended on each institution.

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) collects data from many institutions in the United States of America and uses them to prevent postoperative mortality and morbidity. The National Clinical Database (NCD) in Japan started to prospectively collect data about surgical procedures in January 2011. The quality of surgical procedures in Japan has previously been investigated within individual institutions or by study groups. However, these studies could not investigate the nationwide quality of surgery in Japan. The NCD has now enabled such an analysis. The distribution of diseases and the difference in mortality and morbidity rates by regions can be investigated using this database. It will also help to improve treatment outcomes by comparing those at individual institutions with others across the country. The NCD also collaborates with the certification system of each surgical society in Japan. Patients registered in the NCD will only be approved if each surgical society in Japan applies for certification. Detailed information is required for the following surgical procedures: oesophagectomy, distal gastrectomy, total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and surgery for acute diffuse peritonitis.

Here, we used NCD data to clarify and establish a risk model for 30-day and operative mortality after right hemicolectomy.

Methods

Data collection

The National Clinical Database (NCD) is a nationwide project in cooperation with the board certification system of surgery in Japan in which data from over 1,200,000 surgical patients at over 3,500 hospitals were collected in 2011. The NCD continuously identifies individuals who approve data, departmental personnel in charge of annual patients and data entry personnel via a web-based data management system and can thus assure data traceability. It also consecutively validates data consistency by randomly inspecting institutions.

Here, we focused on gastrointestinal surgery data in the NCD, the variables and definitions for which are almost identical to those of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). The program focuses on 30-day outcomes (whether a patient has been discharged from initial admission) via direct determination of the 30-day time point. Outcomes include morbidity (including respiratory, urinary tract, central nervous system and cardiac pathologies and other types), as well as mortality. The gastroenterological surgery section registers all surgical patients in a department and requires detailed input items for the eight procedures that represent surgical performance within each specialty. All variables and definitions of inclusion criteria regarding NCD are accessible to participating institutions on the website (http://www.ncd.or.jp/) and it supports E-learning so that participants can upload consistent data. It answers all inquiries regarding data entry (about 80,000 inquiries in 2011) and regularly opens some of them as Frequently Asked Questions on the website.

Endpoint

This study focuses on right hemicolectomies performed between January 1, 2011 and December 31, 2011 in Japan. Any NCD records that were denied entry by patients were excluded from this analysis. Records with missing information about age, sex or status at 30 days post-operation were also excluded. The primary outcome measure of this study was 30-day and operative mortality rates. Operative mortality includes all patients who died within the index hospitalization, regardless of the length of hospital stay (up to 90 days), as well as any patients who died after hospital discharge within 30 days from the date of the procedure.

Statistical analysis

Data were randomly assigned to two subsets that were split 80/20, one for model development (cohort 1) and the other for validation testing (cohort 2). Two sets of logistic models (30-day mortality and operative mortality) were constructed for a development dataset using step-wise selection of predictors with a P value for inclusion of 0.05. The 'goodness-of-fit' was tested to assess how well the model could discriminate between survivors and deceased patients. Model calibration (the degree to which observed and predicted outcomes were similar from the model across patients) was examined by comparing the observed with the predicted averages within each of 10 equally sized subgroups arranged in increasing order of patient risk.

Results

Right hemicolectomy

The number of registered patients who underwent right hemicolectomy was 19,507. Among these, 437 were

Table 1 Patient characteristics

	Cohort 1 $N = 15{,}275$ (25 percentile to 75 percentile)	Cohort 2 $N = 3{,}795$ (25 percentile to 75 percentile)	*P* value	Total Number (25 percentile to 75 percentile)
Age	73 (65–80)	73 (65–80)	0.628	73 (65–80)
Gender				
Male	7,684 (50.3 %)	1,901 (50.1 %)	0.828	9,585 (50.3 %)
Female	7,591 (49.7 %)	1,894 (49.9 %)		9,485 (49.7 %)
BMI	21.9 (19.6–24.1)	21.9 (19.6–24.2)	0.663	21.9 (19.6–24.2)
Length of hospital stay	19 (14–29)	20 (14–29)	0.602	19 (14–29)
Surgery				
Operation time (min)	180 (138–232)	178 (135–235)	0.548	180 (138–233)
Anesthesia time (min)	235 (190–294)	235 (186–295)	0.763	235 (189–295)
Bleeding (ml)	100 (36–245)	100 (38–258)	0.406	100 (37–250)
Preoperative blood test				
WBC (/μl)	6,000 (4,775–7,600)	5,990 (4,700–7,600)	0.653	6,000 (4,770–7,600)
Hemoglobin (g/dl)	11.2 (9.6–13.0)	11.2 (9.7–13.0)	0.328	11.2 (9.6–13)
Platelet (×10,000/μl)	25.8 (20.3–33.3)	25.6 (20.3–33.2)	0.656	25.7 (20.3–33.3)
Albumin (g/dl)	3.8 (3.3–4.2)	3.8 (3.3–4.1)	0.808	3.8 (3.3–4.2)
Total bilirubin (mg/dl)	0.5 (0.4–0.7)	0.5 (0.4–0.7)	0.13	0.5 (0.4–0.7)
AST (U/l)	20 (16–26)	20 (16–26)	0.943	20 (16–26)
ALT (U/l)	15 (11–21)	14 (10–21)	0.575	14 (11–21)
Creatinine (mg/dl)	0.73 (0.6–0.9)	0.73 (0.6–0.9)	0.852	0.73 (0.6–0.9)
Blood urea nitrogen (mg/dl)	14 (11–18)	14 (11–17.8)	0.663	14 (11–18)
Sodium (mEq/l)	140 (138–142)	140 (138–142)	0.281	140 (138–142)
PT-INR	1.03 (0.97–1.10)	1.03 (0.97–1.10)	0.306	1.03 (0.97–1.1)

BMI body mass index, *WBC* white blood cell, *PT* prothrombin time

excluded because of the lack of information and the simultaneous surgical procedure such as pancreaticoduodenectomy that were more complicated than right hemicolectomy. The development dataset (cohort 1) included 15,275 records and the validation dataset (cohort 2) included 3,795 records.

The median age at surgery was 73 years and 50.3 % were male. The median surgical duration was 180 min, the median blood loss was 100 ml (Table 1) and 7.4 % of the patients in this population underwent surgery because of diseases other than cancer. Table 1 shows the main results of preoperative blood tests. The findings did not significantly differ between the two cohorts.

Risk profile of study population

In this population, 8.4 % of patients underwent emergency surgery. Preoperative comorbidities included hypertension, diabetes mellitus, smoking (within 1 year), activities of daily living (ADL) with any type of assistance and other in 36, 17.1, 12.9, 10.2 and 24.8 %, respectively (Table 2). These preoperative risk factors did not significantly differ between the two cohorts.

Outcomes

The overall 30-day and operative mortality rates were 1.1 and 2.3 %, respectively (Table 3), and those of patients who underwent elective and emergency surgery were 0.7 and 6.0 %, respectively ($P < 0.001$). The rates of readmission and reoperation within 30 days were 2.4 and 3.2 %, respectively. The total complication rate after right hemicolectomy was 22.1 % and most of them were classified as grades I to III. The rates of grade IV and V complications were 0.7 and 0.9 %, respectively. The rates of major complications after right colectomy were surgical site infection (SSI), anastomotic leak, pulmonary embolism and cardiac events in 7.8, 1.7, 0.2 and 0.5 %, respectively (Table 3). Unfavorable perioperative events included blood loss of >1,000 ml in 2.9 % and a surgical duration that exceeded 6 h in 3.7 %.

Model results

Two risk models were developed and Tables 4 and 5 show the final logistic model with odds ratios (ORs) and 95 % confidence intervals (CIs) for logistic regression analyses. Sixteen and 26 factors were selected as risk models for 30-day and

Table 2 Preoperative risk and frequency

Preoperative risk	Cohort 1 (N = 15,275)		Cohort 2 (N = 3,795)		P value	Total (N = 19,070)		
	Number	Percent	Number	Percent		Number	Percent	30-day mortality rate (%)
Ambulance transport	771	5	191	5	0.997	962	5	6.4
Emergency operation	1,285	8.4	313	8.2	0.766	1,598	8.4	6
Diabetes mellitus	2,597	17	660	17.4	0.564	3,257	17.1	1.4
Smoking (within a year)	1,974	12.9	479	12.6	0.644	2,458	12.9	1.3
Alcohol	6,374	41.7	1,590	41.9	0.854	7,964	41.8	0.9
Respiratory distress	451	3	97	2.6	0.213	548	2.9	6.2
ADL with any assistance	1,580	10.3	370	9.7	0.295	1,950	10.2	5.3
COPD	427	2.8	116	3.1	0.384	543	2.8	2.6
Pneumonia	117	0.8	24	0.6	0.456	141	0.7	11.3
Ascites	560	3.7	135	3.6	0.769	695	3.6	7.3
Hypertension	5,507	36.1	1,365	36	0.939	6,872	36	1.4
Congestive heart failure	254	1.7	60	1.6	0.771	314	1.6	8.9
Myocardial infarction	108	0.7	28	0.7	0.838	136	0.7	4.4
Angina	257	1.7	61	1.6	0.827	318	1.7	2.8
Previous PCI	414	2.7	88	2.3	0.194	502	2.6	2.6
Previous cardiac surgery	215	1.4	44	1.2	0.273	259	1.4	2.7
Acute renal failure	54	0.4	10	0.3	0.53	64	0.3	29.7
Preoperative dialysis	157	1	40	1.1	0.865	197	1	8.6
Cerebrovascular disease	748	4.9	167	4.4	0.108	915	4.8	3.3
Cancer with multiple metastases	959	6.3	254	6.7	0.353	1,213	6.4	3.7
Chronic use of steroid	176	1.2	42	1.1	0.858	218	1.1	3.2
Weight loss over 10 %	881	5.8	212	5.6	0.694	1,093	5.7	3
Bleeding disorder	703	4.6	164	4.3	0.485	867	4.5	5.7
Preoperative blood transfusion	793	5.2	170	4.5	0.076	963	5	2.7
Preoperative chemotherapy	110	0.7	38	1	0.076	148	0.8	0.7
Preoperative radiotherapy	14	0.1	7	0.2	0.165	21	0.1	4.8
Sepsis	289	1.9	69	1.8	0.836	358	1.9	17
Previous PVD surgery	75	0.5	16	0.4	0.685	91	0.5	8.8
Pregnancy	1	0.007	1	0.03	0.358	2	0.01	0
Other than cancer surgery	1,154	7.6	263	6.9	0.201	1,417	7.4	5.2
ASA performance status								
Grade 3	1,944	12.7	461	12.1	0.336	2,405	12.6	3.2
Grade 4	155	1	34	0.9	0.511	189	1	14.8
Grade 5	59	0.4	16	0.4	0.783	75	0.4	30.7

ADL activity of daily living, *COPD* chronic obstructive pulmonary disease, *PCI* percutaneous coronary intervention, *PVD* peripheral vascular disease, *ASA* American Society of Anesthesiologists

operative mortality, respectively. Among the independent risk factors of 30-day mortality, those with odds ratios of >3 were <5 × 10^4 platelets/μl (OR 5.59), ASA grade 4 and 5 (OR 3.99), acute renal failure (OR 3.23), total bilirubin >3 mg/dl (OR 3.12) and AST >35 U/l (OR 3.08, Table 4). Among the independent risk factors for operative mortality, those with odds ratios of >2 were previous peripheral vascular disease (PVD), surgery (OR 3.13), cancer with multiple metastases (OR 3.08), American Society of Anesthesiologists (ASA) grades 4 or 5 (OR 2.91), AST >40 U/l (OR 2.66), <8 × 10^4 platelets/μl (OR 2.55), ADL with any type of assistance (OR 2.51), preoperative dialysis (OR 2.51), blood urea nitrogen over 60 mg/dl (OR 2.42), congestive heart failure (OR 2.16), and chronic steroid use (OR 2.01, Table 5). The Nagelkerke R^2 was 0.336 in the 30-day mortality model and 0.322 in the operative mortality model.

The scoring system for the mortality risk models according to the logistic regression equation was as follows:

$$\text{Predicted mortality} = e^{(\beta_0+\Sigma\beta_i X_i)}/1+e^{(\beta_0+\Sigma\beta_i X_i)}.$$

Table 3 Outcome of right hemicolectomy

Outcome	Cohort 1 ($N = 15{,}275$)		Cohort 2 ($N = 3{,}795$)		P value	Total ($N = 19{,}070$)	
	Number	Percent	Number	Percent		Number	Percent
30-day mortality							
All	175	1.1	43	1.1	0.99	218	1.1
Elective	92	0.7	30	0.9	0.2	122	0.7
Emergency	83	6.5	13	4.2	0.14	96	6
30-day operative mortality							
All	342	2.2	88	2.3	0.76	430	2.3
Elective	209	1.5	61	1.8	0.27	270	1.5
Emergency	133	10.4	27	8.6	0.36	160	10
Readmission within 30 days	348	2.3	114	3	0.01	462	2.4
Postoperative complication (Clavian–Dindo)							
Grade I	1,344	8.8	349	9.2	0.44	1,693	8.9
Grade II	1,195	7.8	329	8.7	0.085	1,524	8
Grade III	552	3.6	130	3.4	0.58	682	3.6
Grade IV	113	0.7	30	0.8	0.75	143	0.7
Grade V	148	1	29	0.8	0.26	177	0.9
Total	3,352	21.9	867	22.8	0.24	4,219	22.1
Reoperation within 30 days	491	3.2	119	3.1	0.83	610	3.2
Postoperative complication							
SSI	1,168	7.6	310	8.2	0.28	1,478	7.8
Anastomotic leak	250	1.6	79	2.1	0.068	329	1.7
Pneumonia	293	1.8	77	2	0.65	370	1.9
Pulmonary embolism	24	0.2	9	0.2	0.28	33	0.2
Acute renal failure	97	0.6	22	0.6	0.81	119	0.6
Central nervous system event	122	0.8	27	0.7	0.67	149	0.8
Cardiac event	79	0.5	24	0.6	0.39	103	0.5
SIRS	107	0.7	36	0.9	0.11	143	0.7
Sepsis	112	0.7	41	1.1	0.038	153	0.8
Surgery							
Bleeding from 1,000 to 2,000 ml	328	2.1	87	2.3	0.58	415	2.2
Bleeding over 2,000 ml	110	0.7	31	0.8	0.53	141	0.7
Transfusion	445	2.9	117	3.1	0.59	562	2.9
Operation over 6 h	536	3.5	168	4.4	0.008	704	3.7

SIRS systemic inflammatory response syndrome

β_i is the coefficient of the variable X_i in the logistic regression equation provided in Table 4 for 30-day mortality, and Table 5 for operative mortality. $X_i = 1$ if a categorical risk factor is present and 0 if it is absent. For age category, $X_i = 1$ if patient age is <59; 60–64 $X_i = 2$; 65–69 $X_i = 3$; 70–74 $X_i = 4$; 75–79 $X_i = 5$; and ≥ 80 $X_i = 6$.

Model performance

To evaluate model performance, both the concordance c-index (a measure of model discrimination) with 95 % CIs, which is the area under the receiver operating characteristics (ROC) curve, and model calibration across the risk groups were evaluated. Table 6 shows details of model performance indicators. The c-indices were 0.903 and 0.891 for the 30-day and operative mortality risk models, respectively (Fig. 1a, b), and the c-indices in the validation datasets for these two models were 0.836 and 0.854, respectively (Fig. 1c, d). Figure 2 demonstrates the calibration of the models or how well the rates for the predicted event matched those of the observed event among patient risk subgroups.

Discussion

The present study investigated short-term outcomes after right hemicolectomy using data from the NCD. The 30-day