of resection has been shown to be an important risk factor for mortality in many reports. Indeed, various criteria have been used to predict the success of hepatectomy procedures; for example, laparoscopic radiofrequency ablation or enucleation, wedge resection, and lobectomy in the Nationwide Inpatient Sample database[16]; minor, intermediate, and major resection ($\geq$3 segments) in a nationwide French database;[17] hepatectomy (partial lobe, extensive, left, and right) in the ACS-NSQIP database;[21] and limited resection, segmentectomy, lobectomy, and extended lobectomy with or without reconstruction in the Japanese DPC database.[14] Because a variety of operative procedures are currently performed,[2,22-25] it is difficult to categorize each according to the variables described herein. So, in this NCD analysis, we included variables that indicate the specific resected liver subsegments (S1 to S8), which makes it possible to identify which type of hepatectomy was performed. For the first time, we present a model that clearly demonstrated that resection, including S1, S7, or S8, is a risk factor for 90-day in-hospital mortality.

With these variables, our model performed very well in its discriminatory ability in both the development and validation datasets. The C-indices of the validation datasets for 30-day mortality and 90-day in-hospital mortalities were 0.714 and 0.761, respectively. Although the usefulness of the Portsmouth-Physiological and Operative Severity Score for enumeration of Mortality and Morbidity[26] and the Estimation of Physiologic Ability and Surgical Stress[27] has been established for predicting the risk of hepatectomy, they seem to be unsuitable to rate the prognoses of patients who undergo hepatectomy because these models frequently overestimate postoperative mortality.[28] To overcome this problem, we are currently creating a novel scoring system suitable for hepatectomy according to these risk models, which will be made available in each participating cancer center in the near future.

Limitations

Although this analysis included more than 7,000 hepatectomy cases registered in a single year, there were still several limitations. First, the use of nationally collected data, derived from all types of patients and hospitals, would be expected to contribute to improving the quality control of the surgical procedures; however, outcomes obtained in this study may have been influenced by several factors characteristic of each hospital, such as case volume, training status, compliance, surgical specialization, resource use, and procedure-specific variables (ie, portal vein embolization, inflow occlusion to liver, and laparoscopic approach).[29-34] Second, our risk models to predict hepatectomy complications were not evaluated according to the Clavien–Dindo criteria in this analysis, although they will be included in a future study. Third, this analysis used a nationwide database, but it was limited to a single race. Therefore, our results should be evaluated in comparison with those of other countries using the same variables and definitions. To this end, we are currently planning a mutual collaboration with ACS-NSQIP.

CONCLUSIONS

In conclusion, the Japanese NCD, which is similar to the American ACS-NSQIP database, has collected data from virtually all hepatectomy cases covered by the universal health care system of Japan. Among this population, the 30-day mortality and 90-day in-hospital mortality rates were 2.0% and 4.0%, respectively, which were quite satisfactory. We also developed risk models for hepatectomy that will contribute to improved quality control of procedures and may be useful to evaluate and benchmark performance.

Author Contributions

Study conception and design: Kenjo, Miyata, Gotoh, Kitagawa, Shimada, Baba, Tomita, Kimura, Sugihara, Mori
Acquisition of data: Miyata
Analysis and interpretation of data: Kenjo, Miyata, Gotoh
Drafting of manuscript: Kenjo, Miyata, Gotoh, Kitagawa, Shimada, Baba, Tomita, Kimura
Critical revision: Tomita, Sugihara, Mori

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A Pancreaticoduodenectomy Risk Model Derived From 8575 Cases From a National Single-Race Population (Japanese) Using a Web-Based Data Entry System

The 30-Day and In-hospital Mortality Rates for Pancreaticoduodenectomy

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Objective: To create a mortality risk model after pancreaticoduodenectomy (PD) using a Web-based national database system.

Background: PD is a major gastroenterological surgery with relatively high mortality. Many studies have reported factors to analyze short-term outcomes.

Subjects and Methods: After initiation of National Clinical Database, approximately 1.2 million surgical cases from more than 3500 Japanese hospitals were collected through a Web-based data entry system. After data cleanup, 8575 PD patients (mean age, 68.2 years) recorded in 2011 from 1167 hospitals were analyzed using variables and definitions almost identical to those of American College of Surgeons–National Surgical Quality Improvement Program.

Results: The 30-day postoperative and in-hospital mortality rates were 1.2% and 2.8% (103 and 239 patients), respectively. Thirteen significant risk factors for in-hospital mortality were identified: age, respiratory distress, activities of daily living within 30 days before surgery, angina, weight loss of more than 10%, American Society of Anesthesiologists class of greater than 3, Brinkman index of more than 400, body mass index of more than 25 kg/m^2, white blood cell count of more than 11,000 cells per microliter, platelet count of less than 120,000 per microliter, prothrombin time/international normalized ratio of more than 1.1, activated partial thromboplastin time of more than 40 seconds, and serum creatinine levels of more than 3.0 mg/dL. Five variables, including male sex, emergency surgery, chronic obstructive pulmonary disease, bleeding disorders, and serum urea nitrogen levels of less than 8.0 mg/dL, were independent variables in the 30-day mortality group. The overall PD complication rate was 40.0%. Grade B and C pancreatic fistulas in the International Study Group on Pancreatic Fistula occurred in 13.2% cases. The 30-day and in-hospital mortality rates for pancreatic cancer were significantly lower than those for nonpancreatic cancer.

Conclusions: We conducted the reported risk stratification study for PD using a nationwide surgical database. PD outcomes in the national population were satisfactory, and the risk model could help improve surgical practice quality.

Keywords: in-hospital mortality, National Clinical Database (NCD), pancreaticoduodenectomy, risk factor, risk model

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The number of pancreatic surgical procedures has been increasing both in several Western countries and in Japan.[1,2] Pancreaticoduodenectomy (PD) is one of the most complex procedures in gastroenterological surgery and is often indicated for various diseases; thus, surgical techniques are continuously being improved.[3–6] Although the perioperative mortality rate of PD in high-volume centers is reportedly 1% to 2%,[7–9] population-based studies have reported a range of 4% to 8%.[10,11] However, the post-PD morbidity rate remains relatively high at 20% to 50%.[12–14] The curability of disease, whether malignant or nonmalignant, is typically anticipated after PD, although the long-term outcome differs depending on the original disease status.[2,6] Essentially, both surgeons and patients require precise risk information of the procedure before surgery; hence, many hospitals and surgeons have attempted to elucidate these factors and have consequently developed several scoring systems.[15–17] Are et al[18] reported that renal failure, hypothyroidism, liver disease, and hypertension were associated with post-PD mortality. Although several studies have contributed to a nationwide database regarding the quality of pancreatic resection using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) criteria, they have focused only on 30-day mortality.[18,19] However, mortality associated with pancreatic resection is reported more often after 30 days.[15,16,20] This report proposes a risk stratification system for post-PD mortality based on data from a single nation, including in-hospital postoperative outcomes, to complement the National Clinical Database (NCD) of Japan, thereby further defining its stratification criteria. We believe that this risk model will contribute to improvement in PD quality control not only in Japan but also worldwide.

METHODS

The NCD is a nationwide project in cooperation with the certification board of the Japan Surgical Society. In 2011, data from more than 1.2 million surgical cases were collected from more than 3500 hospitals. The NCD is continuously updated by data management departments from participating institutions and is evaluated annually using a Web-based data management system to ensure data

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traceability. Moreover, it validates data consistency through inspections of randomly selected institutions.

In this study, we focused on a data subset of gastroenterological surgery derived from the NCD using variables and definitions almost identical to those of the ACS-NSQIP. Indications for benign and malignant tumors were identified using the Union for International Cancer Control classification system. For this study, we selected cases with the exclusion criterion of simultaneous major hepatectomy. For subgroup analysis of PD procedures, lymph node dissection, vascular reconstruction, other organ excision, and gallbladder cancer surgery were included as variables. The present models focused on 30-day postoperative outcomes, regardless of whether the patient was discharged after initial hospital admission, through direct assessment of both the 30-day and in-hospital postoperative outcomes. In-hospital mortality was defined as death before postoperative day 30 and death among patients who were hospitalized for 30 days or more after surgery and died during that time. PD outcomes included mortality and rigorously defined morbidities categorized as wound, respiratory, urinary tract, central nervous system, cardiac, and others. All variables, definitions, and inclusion criteria are accessible on the NCD Web site (http://www.ncd.or.jp/), which is monitored to respond to inquiries regarding data entries (~80,000 inquiries in 2011), and responses are regularly posted under the heading "Frequently Asked Questions."

This research focused on PD surgical procedures performed from January 1, 2011, to December 31, 2011, in Japan. The NCD records of patients who refused access were excluded from this analysis. In addition, records with missing data regarding age, sex, or 30-day postoperative status were also excluded. Most Japanese hospitals performing surgery were included in this study, and a number of methods were used to verify the collected data. Because deterrents for input omissions are used in applications for specialist institutions, input was mandatory to apply for specialist status. To examine data reliability, randomly selected institutions were visited to confirm record consistency in the hospital registries. A well-known method was applied in which the input rate was calculated on the basis of recorded pre-2011 cases to ascertain that there were no omitted data from the records of each institution. Some of the surgical procedures were compared with the number of reported cases to verify the consistency in the number of submitted cases.

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

RESULTS

Preoperative Risk Profiles and Laboratory Data of the Study Population

The NCD patient population had a mean age of 68.2 ± 10.6 years, and 61.4% were men (Table 1). The following primary diagnoses were made: pancreatic carcinoma in 51.6% of the patients, extrahepatic bile duct carcinoma in 19.5%, carcinoma of the ampulla of Vater in 12.7%, perihilar bile duct carcinoma in 3.7%, metastatic tumors or recurrence in 1.9%, carcinoma of the gallbladder in 1.0%, and lesions other than cancer, including intraductal papillary mucinous neoplasm (IPMN), serous cystadenoma, solid pseudo-papillary neoplasm, and pancreatic neuroendocrine tumor in 8.6%.

The following significant preoperative risk factors related to both 30-day and in-hospital mortalities were observed: male sex, activities of daily living, body mass index of more than 25 kg/m^2, American Society of Anesthesiologists (ASA) class of greater than 3, angina, myocardial infarction, hypertension, chronic obstructive pulmonary disease, hemoglobin levels of less than 10.0 g/dL, serum albumin levels of less than 2.5 g/dL, total bilirubin levels of more than 2.0 mg/dL, creatinine levels of more than 3.0 mg/dL, and C-reactive protein levels of more than 1.0 mg/dL. On the contrary, significant risk factors for 30-day mortality alone included previous cardiac surgery and extrahepatic bile duct carcinoma. However, in subgroups of PD procedures, none of the following risk factors showed any significant difference in in-hospital mortality: lymph node dissection, vascular reconstruction, other organ excision, and gallbladder cancer surgery. Interestingly, lymph node dissection was associated with significantly lower 30-day mortality than the other variables.

Perioperative Risk Profile and Prevalence of Morbidity in the Study Population

The mean post-PD hospital length of stay was 29 days [interquartile range (IQR), 21–42 days] and post-PD length of stay in the 30-day and in-hospital mortality subgroups was 15 days (IQR, 7–23 days) and 31 days (IQR, 15–57 days), respectively (Table 2). The 30-day postoperative mortality rate was 1.2% (103 patients), whereas the in-hospital mortality rate was 2.8% (239/8575 patients).

Overall morbidities occurred in 40.0% of patients. Grade B or C pancreatic fistulas were reported in 13.2% of the patients. Furthermore, other significant operative risk factors associated with both 30-day and in-hospital mortalities included intraoperative estimated blood loss of more than 2000 mL and transfusion of more than 5 units. In addition, reoperations performed for any reason within 30 days were also significant risk factors; however, operation time of more than 6 hours was not a significant risk factor.

Postoperative complications were highly significant risk factors for 30-day and in-hospital mortalities and included surgical complications (bile leakage, anastomotic leakage, pancreatic fistula, and wound dehiscence), infection [surgical site infections (SSIs), urinary tract infection, standardized infection ratio, systemic sepsis, and septic shock], respiratory issues (pneumonia, unplanned intubation, pulmonary embolism, and prolonged ventilation >48 hours), renal failure, central nervous system complications, and cardiac issues.

Prevalence of Morbidity Associated With Vascular Reconstruction

The cases that underwent vascular reconstruction (n = 953; 11.1%) (Table 1) were characterized by higher blood loss and longer operation times than those in nonreconstruction cases (n = 7622; 88.9%); however, these cases had low complication rates for pancreatic fistulas (grade B or C; 6.8% vs 14.0%; $P < 0.001$) and SSIs (organ space with leakage, 4.5% vs 9.0%; $P < 0.001$). Pancreatic cancer was reported in 847 cases (88.9%) within the vascular reconstruction subgroup (n = 953).

Model Results and Performance

We developed 2 different risk models of preoperative factors for 30-day and operative mortalities. The final logistic model with the odds ratios and 95% confidence intervals is presented in Table 3. All risk model data were derived from multivariate analysis. There were 4 overlapping variables between the 2 groups: preoperative comorbidities (age, ASA class >3, and body mass index >25 kg/m^2) and

TABLE 1. Key Preoperative Risk Profiles and Outcomes

		Outcome Groups			
	Entire Study Population (N = 8575), Positive Rate %	30-d Mortality (n = 103; 1.2%)		In-hospital Mortality (n = 239; 2.8%)	
Characteristics		**%**	***P***	**%**	***P***
Demographics					
Age, mean (SD), yr	68.2 (10.6)	72.2 (8.1)		72.8 (7.9)	
Male sex, %	61.4	1.4	0.01	3.1	0.022
Emergency surgery	0.9	6.4	0.002	12.8	<0.001
ADL within 30 d before surgery: Partially/totally dependent	3.2	3.3	0.005	11.8	<0.001
BMI >25 kg/m^2, %	14.8	2.1	0.005	3.8	0.026
ASA class >3	9.1	3.1	<0.001	8.6	<0.001
Habitual alcohol consumption	22.9	1.4	0.410	2.7	0.876
Smoking within a year	19.1	1.3	0.707	2.9	0.678
Brinkman index >400	25.6	1.5	0.140	3.3	0.115
Weight loss >10%	7.3	1.9	0.087	5.8	<0.001
Preexisting comorbidity					
Cardiovascular					
Congestive heart failure	0.4	2.8	0.353	19.4	<0.001
Angina	1.1	4.2	0.028	9.4	0.001
Myocardial infarction	0.4	8.8	0.008	20.6	<0.001
Hypertension	34.0	1.6	0.016	3.6	0.001
Previous PCI	2.4	2.4	0.100	7.3	<0.001
Previous cardiac surgery	1.1	4.3	0.025	6.5	0.045
Pulmonary					
COPD	2.6	4.5	<0.001	7.7	<0.001
Respiratory distress	1.0	5.6	0.004	17.8	<0.001
Renal					
Acute renal failure	0.1	42.9	<0.001	71.4	<0.001
Preoperative dialysis	0.6	5.8	0.024	13.5	<0.001
Bleeding disorder	3.2	3.3	0.006	6.2	0.002
Other					
Previous cerebrovascular disease	3.1	3.0	0.015	5.9	0.004
Chronic steroid use	1.0	4.7	0.020	7.0	0.033
Disease					
Ampulla of Vater carcinoma	12.7	1.5	0.371	3.2	0.374
Extrahepatic bile duct carcinoma	19.5	1.7	0.032	3.5	0.046
Perihilar bile duct carcinoma	3.7	2.2	0.110	4.4	0.084
Gallbladder cancer	1.0	0.0	0.629	1.1	0.521
Pancreatic cancer	51.6	0.9	0.017	2.4	0.018
Cancer metastasis/recurrence	1.9	1.2	1.000	3.7	0.467
Duodenal cancer	3.5	1.0	1.000	3.3	0.590
Other than cancer surgery	8.6	1.0	0.722	2.4	0.640
Preoperative laboratory results					
WBC count >11,000/μL	1.9	3.1	0.013	11.2	<0.001
Hemoglobin levels <10 g/dL	8.5	0.7	0.594	5.0	<0.001
Platelet count <120,000/μL	3.3	1.7	0.086	3.8	0.001
PT/INR >1.1	22.0	0.3	0.055	4.6	<0.001
APTT >40 s	4.6	1.3	<0.001	7.7	<0.001
Serum albumin levels <2.5 g/dL	2.1	2.7	<0.001	9.8	<0.001
Serum total bilirubin levels >2.0 mg/dL	23.4	0.2	0.014	3.9	<0.001
Serum AST ≥100 U/L	11.9	0.5	0.760	4.1	<0.001
Serum ALT ≥100 U/L	20.4	0.3	0.713	2.9	0.871
Serum urea nitrogen levels <8.0 mg/dL	7.1	0.8	0.079	3.0	0.797
Serum urea nitrogen levels ≥25 mg/dL	4.0	1.5	0.304	6.2	<0.001
Serum creatinine levels ≥3.0 mg/dL	0.9	3.9	0.054	13.0	<0.001
Serum CRP levels >1.0 mg/dL	18.5	0.3	0.095	4.5	<0.001

(continued)

TABLE 1. *(Continued)*

Characteristics	Entire Study Population (N = 8575), Positive Rate %	Outcome Groups: 30-d Mortality (n = 103; 1.2%) %	30-d Mortality P	In-hospital Mortality (n = 239; 2.8%) %	In-hospital Mortality P
Lymph node dissection	40.8	0.9	0.015	2.5	0.229
Vascular reconstruction	11.1	1.5	0.429	2.9	0.754
Excision with inclusion of other organs	4.1	1.7	0.321	2.5	1.000

The variables of the Japanese NCD were almost identical to those of the ACS-NSQIP, other than alcohol consumption, which was divided into 3 categories: no alcohol consumption, occasional alcohol consumption, and habitual alcohol consumption. Hemoglobin content was not included as a variable by the ACS-NSQIP but was included in the NCD. Descriptive statistics were compared using the Fisher exact test for categorical data of 30-day and in-hospital mortalities of patients in the mortality and nonmortality groups. All statistical tests were 2-sided, and statistical significance was set as $P < 0.05$.

ADL indicates activities of daily living; ALT, alanine transaminase; APTT, activated partial thromboplastin time; ASA class, American Society of Anesthesiologists Physical Status Classification; AST, aspartate aminotransferase; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; PCI, percutaneous coronary intervention; PT/INR, prothrombin time/international normalized ratio; WBC, white blood cell.

TABLE 2. Prevalence of Morbidity With PD Outcomes

Characteristics	Entire Study Population (N = 8575), Positive Rate %	Outcome Groups: 30-d Mortality (n = 103; 1.2%) %	30-d Mortality P	In-hospital Mortality (n = 239; 2.8%) %	In-hospital Mortality P
Operation time >6 h	78.6	1.2	0.629	2.9	0.471
Intraoperative estimated blood loss >2000 mL	11.0	3.4	<0.001	6.9	<0.001
Intraoperative blood transfusion >5 units	35.9	2.1	<0.001	4.7	<0.001
Reoperation for any reason	5.1	7.7	<0.001	16.9	<0.001
Perioperative accident	0.8	11.8	<0.001	16.2	<0.001
Complications	40.0	2.9	<0.001	6.0	<0.001
Transfusion	7.5	11.0	<0.001	22.1	<0.001
Infectious complications:					
SSI	18.7	2.1	<0.001	6.2	<0.001
Wound dehiscence	2.1	5.4	<0.001	15.8	<0.001
Anastomotic leakage	13.0	2.9	<0.001	8.3	<0.001
Pancreatic fistula, grade B or C	13.2	2.4	<0.001	7.4	<0.001
Bile leakage	3.0	4.2	<0.001	9.7	<0.001
Pneumonia	2.6	11.8	<0.001	27.7	<0.001
Unplanned intubation	2.3	30.8	<0.001	52.3	<0.001
Pulmonary embolism	0.2	10.0	0.024	20.0	0.002
Prolonged ventilation >48 h	2.7	24.1	<0.001	46.1	<0.001
Acute renal failure	1.0	27.1	<0.001	56.5	<0.001
Urinary tract infection	0.8	2.9	0.205	10.0	0.003
SIRS	2.6	3.6	0.005	8.9	<0.001
Systemic sepsis	5.7	8.8	<0.001	21.6	<0.001
Septic shock	1.4	23.3	<0.001	55.2	<0.001
CNS complications	1.0	26.2	<0.001	41.7	<0.001
Cardiac complications	0.9	74.7	<0.001	85.3	<0.001

Wound dehiscence, anastomosis leakage, and pancreatic fistula grade B or C were not included as variables in the ACS-NSQIP but have been added to the Japanese NCD. Descriptive statistics were compared using the Fisher exact test for categorical data of 30-day and operative mortalities of patients in the mortality and nonmortality groups. All statistical tests were 2-sided, and statistical significance was set as $P < 0.05$.

CNS indicates central nervous system; SIRS, systemic inflammatory response syndrome.

preoperative laboratory data (activated partial thromboplastin time >40 seconds).

Male sex, emergency surgery, bleeding disorders, chronic obstructive pulmonary disease, and serum urea nitrogen levels of less than 8.0 mg/dL were independent variables in the 30-day mortality group. There were 6 independent variables in the in-hospital mortality subgroup: respiratory distress, activities of daily living within 30 days before surgery, angina, weight loss of more than 10%, Brinkman index more than 400, white blood cell count of more than 11,000 cells per microliter, platelet count of less than 120,000 per microliter, prothrombin time/international normalized ratio of more than 1.1, and serum creatinine levels of more than 3.0 mg/dL.

To evaluate model performance, the C-index (a measure of model discrimination), which was the area under the receiver operating characteristic curve, was calculated for the validation sets. The C-indices of the 30-day and in-hospital mortalities were 0.675 ($P < 0.006$; range, 0.551–0.799) and 0.725 ($P < 0.001$; range, 0.657–0.793), respectively, thereby indicating good performance for in-hospital mortality in the low-risk group. Details of model performance metrics for in-hospital mortality are displayed in Figure 1.

DISCUSSION

PD patients (N = 8575) from 1167 hospitals were used to construct the models in this study. Of 239 deaths, 103 occurred within 30 days and 136 after 30 days. The 30-day and in-hospital mortality rates after PD were 1.2% and 2.8%, respectively. Moreover, the overall morbidity rate was 40.0% and the grade B or C pancreatic fistula rate was 13.2%. These results indicated that the morbidity rates were comparable with those of previous study

TABLE 3. Risk Models of Preoperative Factors for Mortality Rates (30-Day and In-hospital) After PD

	30-d Mortality			In-hospital Mortality		
Variables	Odds Ratio	95% Confidence Interval	*P*	Odds Ratio	95% Confidence Interval	*P*
Age*	**1.260**	1.109–1.486	0.001	**1.283**	1.159–1.420	<0.001
Male sex	**1.971**	1.171–3.319	0.011			
Emergency surgery	**4.309**	1.364–13.618	0.013			
COPD	**2.446**	1.078–5.549	0.032			
Respiratory distress				**2.438**	1.197–4.963	0.014
ADL within 30 d before surgery				**2.479**	1.510–4.070	<0.001
Angina				**2.583**	1.199–5.562	0.015
Bleeding disorder	**4.436**	1.363–14.434	0.013			
Weight loss >10%				**2.102**	1.367–3.232	0.001
ASA grade ≥3	**2.207**	1.290–3.777	0.004	**2.124**	1.461–3.087	<0.001
Brinkman index >400				**1.609**	1.163–2.226	0.004
BMI >25 kg/m^2	**2.401**	1.444–3.992	0.001	**1.866**	1.289–2.703	0.001
WBC count >11,000/μL				**3.101**	1.645–5.843	<0.001
Platelet count <120,000/μL				**2.122**	1.190–3.784	0.011
PT-INR >1.1				**1.507**	1.093–2.078	0.012
APTT >40 s	**3.220**	1.716–6.043	<0.001	**2.001**	1.232–3.251	0.005
Serum urea nitrogen levels <8.0 mg/dL	**2.268**	1.144–4.498	<0.001			
Serum creatinine levels >3.0 mg/dL				**3.462**	1.450–8.266	0.005

*Less than 60, 60 to 65, 65 to 70, 70 to 75, 75 to 80, and more than 80 years.

Odds ratios and 95% confidence intervals for the associations of variables with mortality were calculated using logistic regression models.

ADL indicates activities of daily living; APTT, activated partial thromboplastin time; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PT-INR, prothrombin time/international normalized ratio; WBC, white blood cell.

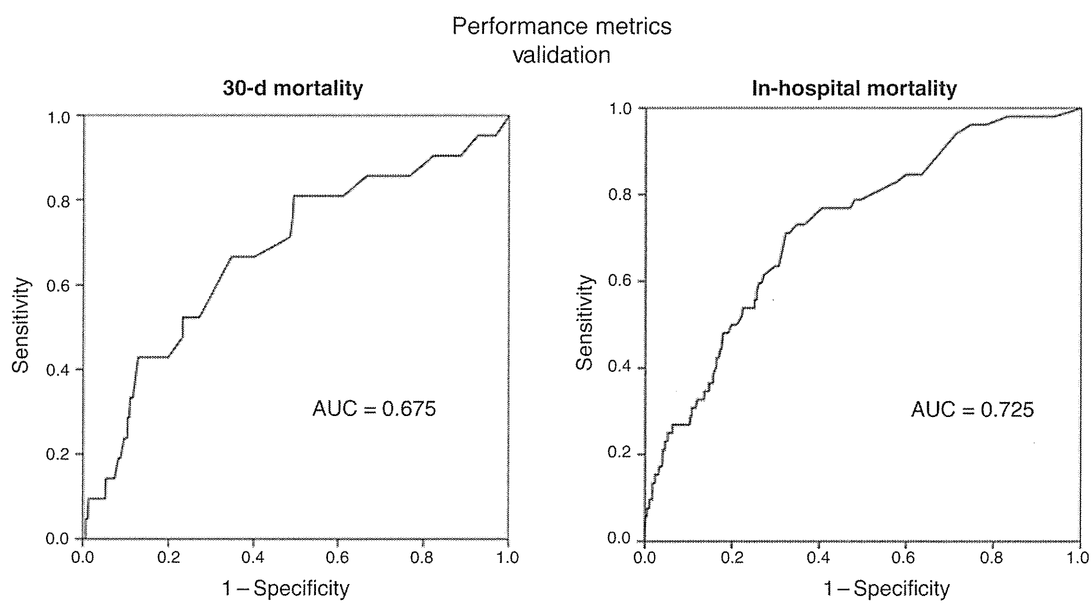

FIGURE 1. Calibration of the 30-day and in-hospital mortality risk models. The C-indices for 30-day and in-hospital mortalities are 0.675 (range, 0.551–0.799; $P < 0.006$) and 0.725 (range, 0.657–0.793; $P < 0.001$), respectively. AUC indicates area under the receiver operating characteristic curve.

results, regardless of whether they were from single-institution or nationwide studies.[12–14] The 30-day and in-hospital mortality rates in this analysis were considerably good compared with those in previous reports from single institutions.[7–9,15] Our risk models suggested that 13 variables were significant risk factors for in-hospital mortality.

The aforementioned parameters could prove useful to surgeons and patients in PD risk clarification as a potential therapeutic approach. In this report, we present our analysis of PD risk stratifications using a nationwide surgical database.

Risk stratification for PD was performed using the ACS-NSQIP database.[18,19] Parikh et al[19] reported that the 30-day mortality and complication rates after pancreatic resection using data of 7571 patients (2005–2008) after proximal (PD) (n = 4621), distal pancreatectomy (DP) (n = 2552), or total pancreatectomy (n = 177) and those who underwent enucleation (n = 221) were 2.5% and 32%, respectively; they also observed that the risk factors associated with 30-day mortality were age, sex, obesity, sepsis, functional status, ASA class, coronary heart disease, dyspnea, bleeding disorders, and extent of surgery. Furthermore, Kelly et al[20] reported overall 30-day complication and mortality rates of 28.1% and 1.2%, respectively, in 2322 DP patients. Moreover, preoperative variables associated with 30-day mortality were esophageal varices, neurological disease, dependent functional status, recent weight loss, elevated alkaline phosphatase levels, and elevated blood urea nitrogen levels. In the present study, in addition to these variables, preoperative laboratory data, including white blood cell count, hemoglobin, platelet count, prothrombin time, activated partial thromboplastin time, serum albumin, serum alanine transaminase, serum creatinine, and serum C-reactive protein, were found to be significant risk factors of in-hospital mortality. The major characteristics of this study were the relatively large number of PD patients and a relatively long postoperative hospitalization period of 29 days (IQR range, 21–42 days) compared with those among studies conducted in Western countries. Table 4 shows the differences in disease, 30-day mortality rates, in-hospital mortality rates, and complication rates between Japanese and Western cases retrieved from the literature.

Overall complications occurred in 40.0% of PD patients, and intraoperative variables and various complications were associated with 30-day and in-hospital mortalities, although the effects on mortality differed between the categories. Intraoperative variables, including blood loss of more than 2000 mL and intraoperative transfusion, were associated with mortality. Unplanned intubation, prolonged ventilation of more than 48 hours, renal failure, septic shock, and central nervous system and cardiac complications were very severe and contributed to the high mortality rates. In addition, SSIs and anastomotic leakage of pancreatic fistulas and bile were also associated with mortality. Because the cause of death was not identified in the NCD system, it was unclear whether these complications resulted in patient death. Regardless of either situation, prevention of surgical complications has been considered crucial for successful surgical treatment.[21–23]

PD is applicable to the treatment of pancreatic cancer and other conditions, such as carcinoma of the extrahepatic bile duct or the papilla of Vater.[24] However, carcinomas of the extrahepatic bile duct are often associated with a soft pancreas; thus, complication rates tend to be higher.

In the NCD system, indications for PD were included as variables (Table 1). In fact, the 30-day and in-hospital mortality rates for pancreatic cancer were 0.9% and 2.4%, respectively, which were significantly lower than those for nonpancreatic cancer. PD with combined portal vein resection has been reported as a treatment option for advanced pancreatic cancer. In this analysis, 953 vascular reconstruction cases (11.1%) were included. Despite the greater intraoperative blood loss and longer operation time, the 30-day and in-hospital mortality rates were 1.5% and 2.9%, respectively, which were not significantly different from those of nonreconstruction cases (1.2% and 2.8%, respectively) (Table 1). In contrast, complication rates for the incidence of pancreatic fistula and SSIs in organ spaces with leakage were significantly low. Most of the patients indicated for PD were recommended to undergo PD for the treatment of pancreatic cancer (847/953 cases; 88.9%). A similar report[25] documented that combined vascular resection for pancreatic adenocarcinoma had no adverse effects on postoperative mortality. The complication rate of vascular reconstruction cases was lower than those without reconstruction. Although the reason behind this is not very clear from the statistical analysis, it may be attributable to the fact that vascular resection cases are often typical pancreatic cancer cases associated with portal infiltration and a hard pancreas; however, cases that do not require portal vascular resection are those with a soft pancreas, such as cancer of the lower biliary duct (30-day and in-hospital mortality rates, 1.7% and 3.5%, respectively). Meanwhile, a report of 3582 PD patients added to the American College of Surgeons national database documented a 30-day postoperative mortality rate of 5.7% after vascular resection (n = 281; 7.8%), which was significantly higher than the corresponding 2.9% reported in cases without

TABLE 4. Differences Between This Study and Western Studies

Presenter	Year of Presentation	Study Period/	No. Cases	Surgical Procedure	Rate of (%) Malignancy	Mean Hospitalization Period, d	30-d (%) Mortality	In-hospital (%) Mortality	Rate of (%) Complication
Yeo et al[12]	1997	1990–1996	650	PD	82	—	1.4	1.4	41
Cameron et al[8]	2006	1969–2003	1,000	PD	85	9	1	1	41
Are et al[18]	2009	2000–2005	5,481	PD	—	>10 (61%)	—	5.2–6.3	—
Simons et al[14]	2009	1998–2006	102,417	PD and DP	—	16.5	—	6.3	22.7
Parikh et al[19]	2010	2005–2008	7,571	PD	66.5	—	2.5	—	31.8
Carroll et al[21]	2010	1991–2002	1,847	PD and DP	—	—	7.7	8.1	19.9
Venkat et al[15]	2011	1998–2009	1,976	PD	82	—	1.4	3.8	—
Castleberry et al[27]	2012	2005–2009	3,301	PD	100	—	2.9	—	33.3
	2012	2005–2009	281	PD with VR	100	—	5.7	—	39.9
Kim et al[5]	2012	2005–2008	4,975	PD	100	—	—	2.1	—
Assifi et al[29]	2012	2000–2010	553	PD	—	—	2	—	43.2
This study		2011	8,575	PD	91.7	29	1.2	2.8	40.0

VR indicates vascular resection.

vascular resection.[26] The difference between these 2 studies needs to be clarified and is currently being considered through a mutual collaboration of the ACS-NSQIP and the Japanese NCD. We believe our results present a useful reference for preoperative preparation in high-risk cases, such as recommendation of diets to obese individuals, notifying families and patients of higher risks and obtaining their informed consent, and not performing PD in prominently high-risk cases.

LIMITATIONS

Although this analysis included more than 8000 PD patients registered in 1 year, there were still several limitations. In Japan, PD is performed for cancers of the pancreatic head, lower bile duct, the ampulla of Vater, duodenum, gallbladder, and hilar bile duct, and pancreatic metastasis among others (eg, IPMN, serous cystic neoplasm, solid pseudopapillary neoplasm, pancreatic neuroendocrine tumor) Therefore, the following points should be considered when applying the results of this article to studies originating in other countries.

IPMNs may develop into invasive carcinoma or might be associated with pancreatic adenocarcinoma; therefore, accurate diagnosis and careful follow-up are recommended.[3,24,27,28] However, in the NCD system, detailed pathological information, such as IPMN classification, is not very clear and needs to be included as a variable in future. Moreover, the outcomes may have been influenced by hospital volume, hospital training status, hospital compliance, surgical specialization, resource utilization, and procedure-specific variables, including preoperative biliary drainage, pylorus preservation method, and ante/retrocolic reconstruction of the alimentary tract, among others.[11] These risk variables for mortality and morbidity will be evaluated in a future study using the present basic risk model.

CONCLUSIONS

The present risk stratification study of PD using a nationwide database included 8575 patients from 1167 surgical units throughout Japan, in which the 30-day and in-hospital mortality rates were 1.2% and 2.8%, respectively. The results of this series were sufficient to estimate the nationwide outcome of PD and thus this system will contribute to improvement in quality control of surgical practice in gastroenterological surgical procedures.

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Most of the authors of this study were members of the JSGS Database Committee or working members of the committee, who participated in creating gastroenterological surgery section of the NCD and analyzing data. All cases are input with items representing surgical performance in each specialty for 8 procedures: esophagectomy, partial/total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and operation for acute generalized peritonitis. Risk models for each procedure have been created by these authors under a unified vision. The authors' contribution is as follows:

Wataru Kimura: He made substantial contributions to conception and design, interpretation of data. He participated in drafting the article or revising it critically for important intellectual content. He wrote and submitted the manuscript, and revised and resubmitted the manuscript. He contributed to generally organize and manage the manuscript. He gave final approval of the version to be published.

Hiroaki Miyata: He made substantial contributions to acquisition of data and/or analysis. He contributed to almost all the statistics of the manuscript.

Mitsukazu Gotoh: He is one of the leaders of the NCD of Japan. He participated in creating gastroenterological surgery section of the NCD and analyzing data. With regard to the manuscript, he helped Dr Kimura on various problems and advised him. He participated in drafting the manuscript or revising it critically for important intellectual content.

Ichiro Hirai: He participated in drafting the manuscript or revising it critically for important intellectual content. He helped Dr Kimura in writing and managing the manuscript.

Akira Kenjo: He made substantial contributions to acquisition of data and/or analysis. He helped Drs Kimura and Hirai in writing and managing the manuscript, with special reference to the statistical aspects.

Yuko Kitagawa: He is a member of the JSGS Database Committee, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Mitsuo Shimada: He is a member of the JSGS Database Committee, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Hideo Baba: He is a member of the JSGS Database Committee, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Naohiro Tomita: He is a member of the JSGS Database Committee, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Tohru Nakagoe: He is a member of the JSGS Database Committee, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Kenichi Sugihara: He is a member of the JSGS, who contributed to creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

Masaki Mori: He is a member of the JSGS, who contributed in creating gastroenterological surgery section of the NCD and analyzing data. He made substantial contributions in acquisition of data.

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ORIGINAL ARTICLE

Surgical risk model for acute diffuse peritonitis based on a Japanese nationwide database: an initial report on the surgical and 30-day mortality

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Abstract
Purpose Acute diffuse peritonitis (ADP) is an important surgical complication associated with high morbidity and mortality; however, the risk factors associated with a poor outcome have remained controversial. This study aimed in collecting integrated data using a web-based national database system to build a risk model for mortality after surgery for ADP.
Methods We included cases registered in the National Clinical Database in Japan. After data cleanup, 8,482 surgical cases of ADP from 1,285 hospitals treated between January 1 and December 31, 2011 were analyzed.
Results The raw 30-day and surgical mortality rates were 9.0 and 14.1 %, respectively. The odds ratios (>2.0) for 30-day mortality were as follows: American Society of Anesthesiologists (ASA) class 3, 2.69; ASA class 4, 4.28; ASA class 5, 8.65; previous percutaneous coronary intervention (PCI), 2.05; previous surgery for peripheral vascular disease (PVD), 2.45 and disseminated cancer, 2.16. The odds ratios (>2.0) for surgical mortality were as follows: ASA class 3, 2.27; ASA class 4, 4.67; ASA class 5, 6.54, and disseminated cancer, 2.09. The C-indices of 30-day and surgical mortality were 0.851 and 0.852, respectively.
Conclusion This is the first report of risk stratification after surgery for ADP using a nationwide surgical database. This system could be useful to predict the outcome of surgery for ADP and for evaluations and benchmark performance studies.

Keywords Acute diffuse peritonitis · Risk factor · Mortality · Risk model

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Introduction

Acute diffuse peritonitis (ADP) is an important surgical complication associated with a high incidence of morbidity and mortality [1–4], and is defined as the uncontained rapid spread of an intra-abdominal infection beyond the organ of origin to multiple (2–4) quadrants of the intra-abdominal cavity, regardless of the underlying disease processes, such as a ruptured appendix, ischemic colitis, gastrointestinal (GI) tract perforation, etc. [2–5]. Emergency surgery is defined as a surgery performed on a patient immediately after the diagnosis [6]. Although a definite preoperative diagnosis of a detailed etiology is difficult even using the recently developed imaging modalities [7, 8], the surgical management of ADP involves immediate evacuation of all purulent collections and source control [1–3].

Although the mortality rate from intra-abdominal infections was close to 90 % in the early 1900s, prior to the introduction of the basic principles of surgery, in the modern era, the reduction in mortality to below 20 % has resulted due to the better understanding of the role of damage control, prevention of intra-abdominal compartment

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

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

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

Methods

Data acquisition

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

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

Patient selection

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

Pre- and perioperative variables

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

Endpoints

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

Statistical analysis

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

Results

Outcomes

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

Risk profile for the study population

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

Table 1 The causative disease leading to the need for surgery

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

The listed diseases were not mutually exclusive

Causative diseases with fewer than 100 cases were not listed

Table 2 The outcomes of surgery for acute diffuse peritonitis

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

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

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

Model results

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

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

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

Model performance

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

Discussion

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

Table 3 Key risk profiles and outcomes

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

Table 3 continued

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

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

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

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

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

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

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

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

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

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

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

Variables	30-Day mortality				Surgical mortality			
	β coefficient	OR	95 % CI	*P* value	*β* coefficient	OR	95 % CI	*P* value
Demographics								
Age category[a]	0.211	1.24	1.17–1.31	<0.001	0.234	1.26	1.20–1.33	<0.001
Ambulance transport	0.317	1.37	1.12–1.68	0.002				
Respiratory distress	0.462	1.59	1.22–2.06	<0.001				
ADL, totally dependent immediately before surgery	0.337	1.4	1.11–1.77	0.005				
ADL, totally dependent within 30 days before surgery					0.465	1.59	1.22–2.07	0.001
ADL, partially/totally dependent immediately before surgery,					0.303	1.35	1.12–1.64	0.002
Preoperative pneumonia					0.342	1.41	1.01–1.97	0.045
ASA class 5	2.157	8.65	6.14–12.18	<0.001	1.877	6.54	4.83–8.84	<0.001
ASA class 4	1.453	4.28	3.11–5.87	<0.001	1.542	4.67	3.61–6.05	<0.001
ASA class 3	0.99	2.69	2.05–3.54	<0.001	0.822	2.27	1.83–2.82	<0.001
Preexisting comorbidity								
Previous PCI	0.715	2.05	1.26–3.31	0.004				
Previous surgery for PVD	0.897	2.45	1.16–5.17	0.018				
Disseminated cancer	0.769	2.16	1.53–3.05	<0.001	0.735	2.09	1.54–2.83	<0.001
Non tumor-bearing	−0.436	0.65	0.48–0.87	0.003	−0.69	0.5	0.4–0.64	<0.001
Bleeding disorder without therapy	0.499	1.65	1.24–2.19	0.001	0.484	1.62	1.31–2.01	<0.001
Preoperative blood transfusion	0.472	1.6	1.13–2.28	0.009	0.595	1.81	1.32–2.49	<0.001
Chronic steroid use	0.552	1.74	1.21–2.50	0.003	0.651	1.92	1.39–2.65	<0.001
Weight loss over 10 %					0.331	1.39	1.02–1.90	0.036
Preoperative laboratory value								
White blood cell count <4,500/μL					0.404	1.5	1.25–1.8	<0.001
White blood cell count <4,000/μL	0.336	1.4	1.12–1.75	0.003				
Hemoglobin <13.5 g/dL in males; <12.5 g/dL in females					0.273	1.31	1.07–1.62	0.01
Hemoglobin <10.0 g/dL	0.254	1.29	1.03–1.61	0.024				
Hematocrit <30 %					0.209	1.23	1.01–1.51	0.044
Platelet count <15,000/μL	0.413	1.51	1.19–1.92	0.001				
Platelet count <12,000/μL					0.356	1.43	1.13–1.8	0.003
Platelet count <8,000/μL	0.424	1.53	1.03–2.26	0.033				
Serum albumin <2.0 g/dL	0.51	1.67	1.25–2.22	<0.001	0.394	1.48	1.14–1.93	0.003
Serum albumin <3.0 g/dL					0.316	1.37	1.13–1.67	0.002
Serum total bilirubin ≥3.0 mg/dL	0.532	1.7	1.16–2.49	0.006	0.676	1.97	1.40–2.76	<0.001
Serum AST ≥35 U/L	0.3	1.35	1.09–1.67	0.006	0.358	1.43	1.19–1.72	<0.001
Serum ALP ≥600 U/L	0.545	1.73	1.18–2.51	0.005	0.474	1.61	1.15–2.24	0.005
Serum urea nitrogen ≥20 mg/dL	0.569	1.77	1.28–2.43	0.001	0.563	1.76	1.35–2.29	<0.001
Serum urea nitrogen ≥25 mg/dL	0.343	1.41	1.06–1.88	0.02				
Serum creatinine ≥2.0 mg/dL					0.405	1.5	1.2–1.89	<0.001
Serum Na <130 mEq/L	0.521	1.68	1.21–2.35	0.002	0.56	1.75	1.31–2.33	<0.001
Serum Na ≥145 mEq/L	0.526	1.69	1.16–2.46	0.006				
Serum CRP ≥10.0 mg/dL	0.397	1.49	1.21–1.83	<0.001	0.423	1.53	1.27–1.83	<0.001
Intercept (*β*0)	−5.449			<0.001	−4.83			<0.001

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

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

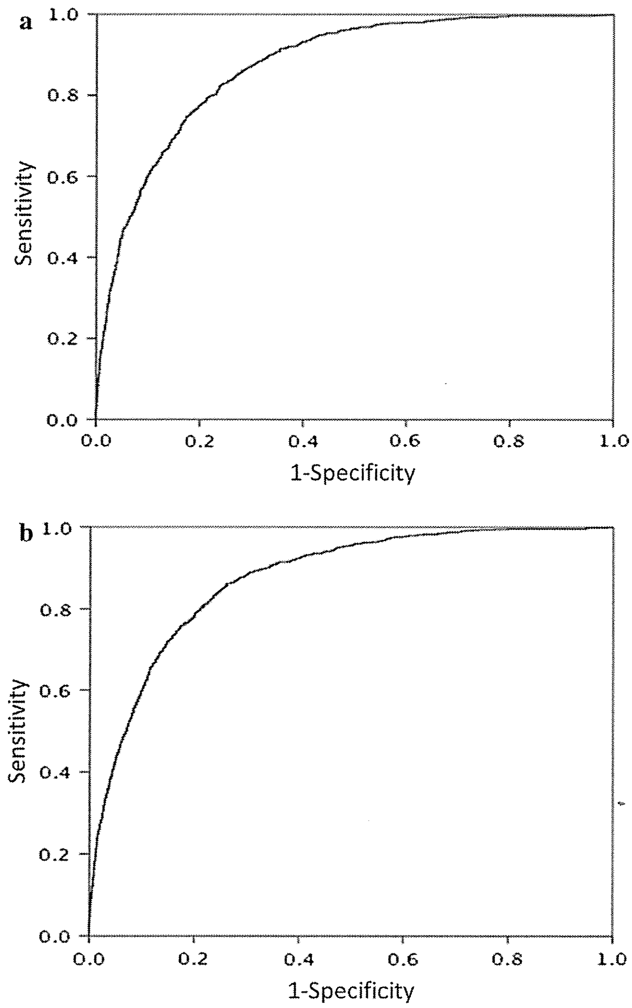

Fig. 1 The receiver operating characteristics (ROC) curves for the 30-day mortality (**a**) and surgical mortality (**b**) in the validation set

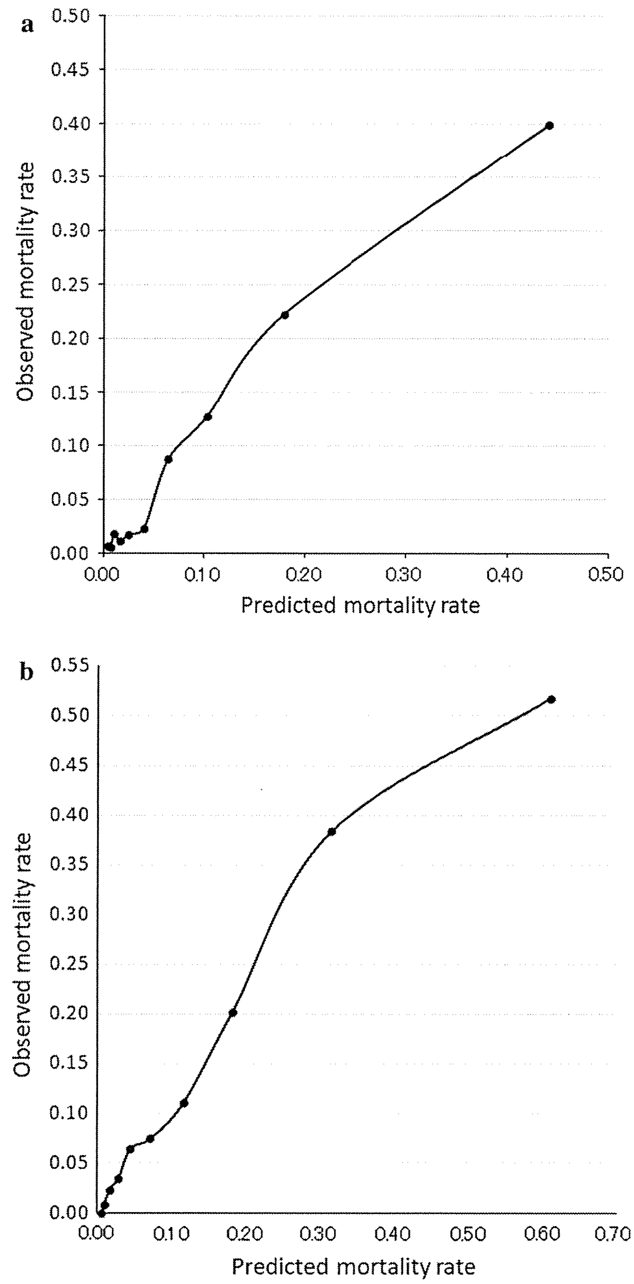

Fig. 2 The model calibration for the 30-day (**a**) and surgical (**b**) mortality models

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

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

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

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

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

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