Abbreviations and Acronyms

ADL	= activities of daily living
ASA	= American Society of Anesthesiologists
JSGS	= Japan Society of Gastroenterological Surgery
LOS	= length of stay
MOS	= more than 1 segment
NCD	= National Clinical Database
PT-INR	= prothrombin time-international normalized ratio
ROC	= receiver operating characteristic
SSI	= surgical site infection

to track surgical cases performed in Japan over 3 years (2006 to 2008), which reported relatively low mortality rates in major surgical procedures.[8,9] The JSGS, realizing the importance of risk-adjusted surgical outcomes for accurate comparisons and quality improvement, created the database as a subset of the National Clinical Database (NCD) of Japan, with significant support from the Japan Surgical Society. Submitting cases to the NCD is a prerequisite for all member institutions of both the Japan Surgical Society and JSGS, and only registered cases can be used for board certification.

The NCD collaborates with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP),[10] which shares a similar goal of developing a standardized surgery database for quality improvement. Traditionally, various governing bodies, including the ACS-NSQIP, have used 30-day patient mortality as a benchmark to assess the quality of both hospital and surgeon performance in virtually all major surgical procedures. However, Mayo and colleagues[11] recently reported that mortality based only on known data at 30 days is misleading and greatly underestimates the actual perioperative mortality by up to 50% compared with data at 90 days. The Japanese system of universal health care allows almost all patients who undergo surgery to be cared for in the hospitals performing the operation until the patients can function independently in activities of daily living (ADL).[12,13] Therefore, the risk for 30- and 90-day in-hospital mortality should be analyzed using parameters similar to those of the ACS-NSQIP for patients undergoing hepatectomy of more than 1 segment (MOS). We evaluated more than 7,000 cases to formulate risk models associated with hepatectomy. This is the first reported hepatectomy risk model of cases derived from a nationwide population recorded through a web-based data entry system.

METHODS

Data collection

The NCD is a nationwide collaborative in association with the Japanese surgical board certification system, in which more than 1.2 million surgical cases from over 3,500 hospitals were collected throughout 2011. The NCD is continuously in communication with hospital personnel who approve data and those in charge of tracking cases annually, as well as those responsible for data entry through the NCD web-based data management system, assuring data traceability. The NCD also consistently validates submitted data through random site visits. Hepatectomy outcomes include rigorously defined morbidities (categorized as wound, respiratory, urinary tract, central nervous system, and cardiac, among others) as well as mortality. Furthermore, the NCD supports an e-learning system for participants to continuously input data, responds to all inquiries regarding data entry (approximately 80,000 inquiries in 2011), and regularly posts some of the queries received via the website under the heading, "Frequently Asked Questions."

This analysis focused on hepatectomy procedures performed in Japan from January 1, 2011 to December 31, 2011. We collected data on 20,455 hepatectomy cases after excluding patients undergoing simultaneous operations including esophagectomy (n = 21), pancreaticoduodenectomy (n = 97), and operations for acute diffuse peritonitis (n = 3). The 30-day mortality and 90-day in-hospital mortality rates for the 20,455 cases were 1.2% and 2.3%, respectively.

The variables and definitions adopted by the NCD are almost identical to those established by ACS-NSQIP. The detailed input of these items for hepatectomy is limited only to procedures in which MOS were resected, excluding the lateral segment. All variables, definitions, and inclusion criteria maintained by the NCD are accessible to participating institutions on their website at http://www.ncd.or.jp/. The numbers of cases of partial hepatectomy, lateral segmentectomy, systemic subsegmentectomy, and S4a/S5 resection were 10,161; 1,489; 1,054; and 225, respectively. Thirty-day and 90-day in-hospital mortality rates for each procedure were 0.7/1.3%; 0.5/1.3%; 0.8/1.4%; and 0.9/1.3%, respectively. These cases were not applicable for this analysis. Although laparoscopic surgery has been widely applied for lateral segmentectomy and partial hepatectomy, laparoscopic surgery for MOS was performed only in a limited number of institutes as clinical trials. These cases were also excluded from this study. The exclusion criteria and the respective number of cases are shown in a flow chart in Figure 1. As a result, 7,732 patients, who underwent MOS hepatectomy in 987 hospitals from January 1 2011 to December 31, 2011, were eligible for inclusion.

Indications for benign and malignant tumors were identified using the Union for International Cancer Control (UICC) classification system. Specific hepatectomy procedures were identified by variables indicating resected

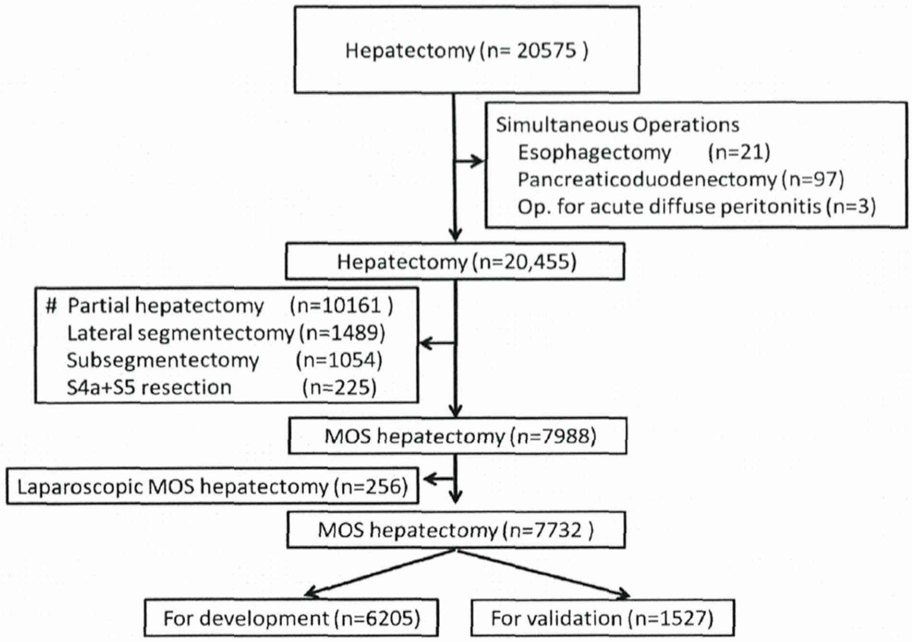

Figure 1. Study population and development and validation of risk stratification. MOS hepatectomy refers to hepatectomy of more than 1 segment, with the exception of lateral segmentectomy.

segments (S1−S8), which were included in the development of the risk model.

Endpoints

The primary endpoints of this analysis were 30-day mortality and 90-day in-hospital mortality. Records with missing patient data regarding age, sex, or 30-day postoperative status were excluded. The 90-day in-hospital mortality included all patient deaths occurring within the hospitalization period regardless of the length of hospital stay (up to 90 days), and all deaths after hospital discharge (up to 30 days postoperatively).

Statistical analysis

We used SPSS (version 20) for data analysis. Univariate analysis of the data was performed using the Fisher's exact test, the unpaired Student's *t*-test, and the Mann−Whitney U test. To develop the risk model, data were randomly assigned to 2 subsets: 80% (6,205 records) for model development and 20% (1,527 records) for validation. The 2 sets of logistic models (30-day mortality and 90-day in-hospital mortalities) were constructed for development dataset using stepwise selection of predictors with p value <0.05 for inclusion. A goodness-of-fit test was performed to assess how well the model could discriminate between patient survival and death. 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 and predicted averages within each of 10 equally sized subgroups arranged in increasing order of patient risk.

RESULTS

Risk profiles and laboratory data of the study population

As shown in Table 1, the NCD patient population had a mean (±SD) age of 66.9 ± 11.8 years (range 0 to 98 years) and 70.6% (n = 5,457) were male. In this population, 1.2% arrived at the hospital by ambulance and 0.8% required emergency surgery. An abbreviated risk profile for the study population is shown in Table 1. In brief, 10.2% of the patient population had an American Society of Anesthesiologists (ASA) classification of III to V; partial/total dependency for ADL was 3.1%; 3% of patients had a body mass index >30 kg/m^2; and weight loss of >10% occurred in 2.7% of patients. With regard to pre-existing comorbidities, 36.3% had hypertension, 24.8% had diabetes mellitus, 2.7% had COPD, 0.8% had preoperative dialysis, 3.6% had cerebrovascular disease, 1.7% had esophageal varices, 2.1% had ascites, and 1.1% required blood transfusion.

Primary diagnoses were hepatocellular carcinoma in 47.0% of the patients, metastatic liver disease in 29.0%, intrahepatic cholangiocarcinoma in 11.9%, perihilar cholangiocarcinoma in 4.4%, gallbladder cancer in

Table 1. Key Preoperative Risk Factors and Surgical Outcomes

Characteristics	Entire study population (n = 7,732)	30-d Mortality (n = 157, 2.0%)		90-d In-hospital mortality (n = 309, 4.0%)	
		Data	p Value	Data	p Value
Demographics					
Age, y, mean (SD)	66.9 (11.8)	70.6 (12.7)		71.1 (11.4)	
Males, %	70.6	2.2	0.11	4.3*	0.048
Ambulance transport, %	1.2	8.9*	<0.001	15.6*	<0.001
Preoperative risk assessment					
General					
ADL within 30 d before surgery	3.1	8.1*	<0.001	16.1*	<0.001
Body mass index >30 kg/m^2, %	3.0	3.0	0.34	5.1	0.39
Alcoholism, %	25.0	1.7	0.46	3.6	0.35
Current smoker (within 1 y), %	19.5	2.1	0.76	4.2	0.71
Diabetes, %	24.8	2.5	0.09	4.9*	0.022
Pulmonary					
Ventilator dependent, %	0.2	14.3*	0.032	28.6*	0.002
Pneumonia, %	0.2	10.5	0.06	31.6*	<0.001
COPD, %	2.7	5.3*	0.003	9.7*	<0.001
Respiratory distress, %	1.7	7.6*	<0.001	16.7*	<0.001
Hepatobiliary					
Ascites, %	2.1	8.6*	<0.001	15.3*	<0.001
Gastrointestinal					
Esophageal varices, %	1.7	3.9	0.19	6.2	0.18
Cardiac					
Congestive heart failure, %	0.6	4.7	0.22	9.3	0.09
Previous PCI, %	2.2	2.3	0.78	3.5	>0.99
Previous cardiac surgery, %	1.4	4.0	0.15	6.0	0.30
Hypertension, %	36.3	2.5*	0.023	6.9*	0.002
Renal					
Acute renal failure, %	0.1	14.3	0.13	14.3	0.25
Dialysis, %	0.8	9.4*	0.002	10.9*	0.013
Central nervous system					
Previous cerebrovascular disease, %	3.6	4.3*	0.014	7.6*	0.004
Nutritional/immune/other					
Disseminated cancer, %	6.2	1.7	0.74	4.6	0.47
Chronic steroid use, %	0.9	2.9	0.40	8.8	0.05
Weight loss >10%	2.7	3.4	0.20	10.2*	<0.001
Bleeding disorder, %	1.1	5.2*	0.001	16.3*	0.002
Preoperative blood transfusion, %	1.1	10.3*	<0.001	18.4*	<0.001
Chemotherapy, %	5.7	1.4	0.39	2.9	0.32
Radiotherapy, %	0.6	3.4	0.45	3.4	>0.99
Sepsis, %	0.4	7.1	0.11	14.3*	0.024
Emergency case, %	0.8	17.5*	<0.001	23.8*	<0.001
ASA classification (III, IV, or V), %	10.2	6.0*	<0.001	10.4*	<0.001
Epidural anesthesia, %	66.7	1.6*	<0.001	3.4*	<0.001
Disease					
Hepatocellular carcinoma, %	47.0	2.3	0.15	4.0	0.95
Intrahepatic cholangiocarcinoma, %	11.9	2.2	0.71	5.2*	0.049
Metastatic liver tumor, %	29.0	0.9*	<0.001	2.0*	<0.001
Gallbladder cancer, %	2.1	7.5*	<0.001	13.8	<0.001

(Continued)

Table 1. Continued

Characteristics	Entire study population (n = 7,732)	30-d Mortality (n = 157, 2.0%)		90-d In-hospital mortality (n = 309, 4.0%)	
		Data	p Value	Data	p Value
Perihilar cholangiocarcinoma, %	4.4	5.0*	0.001	11.2*	<0.001
Other than cancer, %	5.5	1.7	0.72	3.6	0.80
Preoperative laboratory data					
Hemoglobin <10 g/dL, %	7.0	4.6*	<0.001	10.6*	<0.001
Platelet count <120,000 /μL, %	12.4	3.5*	<0.001	5.7*	0.01
Platelet count <80,000/μL, %	2.4	5.9*	0.001	9.7*	<0.001
Serum albumin <3.5 g/dL, %	16.1	5.1*	<0.001	10.4*	<0.001
Serum albumin <3.0 g/dL, %	4.7	8.3*	<0.001	17.1*	<0.001
Serum AST ≥35 IU/L, %	38.8	3.2*	<0.001	6.0*	<0.001
Serum total bilirubin >2.0 mg/dL, %	2.8	6.0*	<0.001	13.0*	<0.001
Serum creatinine ≥2.0 mg/dL, %	1.4	8.2*	<0.001	9.1*	0.012
PT-INR >1.1, %	23.4	3.9*	<0.001	7.1*	<0.001

Descriptive statistics were compared using Fisher's exact test for respective variables between the mortality and nonmortality groups.
*Statistical significance ($p < 0.05$).
ADL, activities of daily living; ALP, alkaline phosphatase; ALT, alanine transaminase; ASA class, American Society of Anesthesiologists Physical Status Classification; AST, aspartate aminotransferase; CRP, C-reactive protein; PCI, percutaneous coronary intervention; PT-INR, prothrombin time–international normalized ratio.

2.1%, and noncancerous lesions in 5.5%. In this population, 0.8% (n = 63) required emergency surgery.

Procedure-related results

All performed hepatectomy procedures are listed in Table 2. As shown, medial segmentectomy and left lobectomy had lower mortality rates; however, hepatectomy with revascularization and for gallbladder cancer, perihilar cholangiocarcinoma, and right-side hepatectomy involving MOS were associated with increased 30-day mortality and 90-day in-hospital mortality. Combined caudate lobe resection and major hepatectomy with caudate lobe resection had poorer in-hospital mortality rates.

Length of stay in hospital and outcome rates

The admission rate to the ICU and length of stay (LOS) in the hospital were examined (Table 3). Fifty-six percent of all patients were admitted to the ICU, with a median LOS of 1 day. The median LOS after surgery was 16.0 days for the entire study population, and the median LOS in the ICU for the mortality population was prolonged to 3.0 days. The outcomes of hepatectomy in the NCD 2011 study population included a 30-day mortality rate of 2.0% and a 90-day in-hospital mortality rate of 4.0%. A total of 203 patients (2.6%) underwent reoperation within 30 days. Overall, postoperative complications of all grades occurred in 30.4% of the patients. Incidence rates for specific major morbidities are presented in Table 4.

The following variables increased in the 30-day mortality and 90-day in-hospital mortality groups: reoperation within 30 days, surgical complications (anastomotic leakage, bile leakage, wound dehiscence, and postoperative transfusion), infectious complications (surgical site infection [SSI], pneumonia, systemic inflammatory response syndrome, and systemic sepsis), respiratory complications (unplanned intubation and prolonged ventilation of >48 hours), renal complications (renal failure and acute renal failure), central nervous system complications, and cardiac complications. In the 30-day mortality group, the incidences of pulmonary embolism and cardiac complications were elevated compared with those of overall in-hospital mortality. By contrast, the incidence of postoperative infectious complications (SSI, bile leakage, sepsis, and systemic inflammatory response syndrome) was elevated in the 90-day in-hospital mortality group.

Model results and performance

Two different risk models were developed; 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:

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

where βi is the coefficient of the variable Xi in the logistic regression equation provided in Table 5 for 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 age category,

Table 2. Surgical Procedures for Hepatectomy

			30-d Mortality			90-d In-hospital mortality		
Hepatectomy	**Involved segments**	**Cases, n**	**Deaths, n**	**%**	**p Value**	**Deaths, n**	**%**	**p Value**
One segment		2,641	43	1.6	0.07	70	2.7	<0.001
Medial	S4	331	1	0.3	0.015	2	0.6	<0.001
Anterior	S5,8	454	10	2.2	0.73	19	4.2	0.81
Posterior	S6,7	681	12	1.8	0.78	19	2.8	0.10
Two segments		4007	74	1.8	0.26	157	3.9	0.73
Left	S2,3,4	797	8	1.0	0.033	11	1.4	<0.001
Right	S5,6,7,8	1359	37	2.7	0.06	75	5.5	0.14
Central	S4,5,8	209	1	0.5	0.13	6	2.9	0.59
More than 2 segments								
Right hepatectomy with S1	S1,5,6,7,8	137	4	2.9	0.36	13	9.5	0.003
Right trisegmentectomy	S4,5,6,7,8	646	16	2.5	0.38	33	5.1	0.14
Right trisegmentectomy with S1	S1,4,5,6,7,8	40	2	5.0	0.20	4	10.0	0.07
Left hepatectomy with S1	S1,2,3,4	356	6	1.7	0.85	15	4.2	0.78
Left trisegmentectomy with S1	S1,2,3,4,5,8	41	2	4.9	0.20	6	14.6	0.005
Procedure								
Isolated S1 resection	S1	53	3	5.7	0.09	3	5.7	0.47
Hepatectomy including S1	S1or S1+other	1182	29	2.5	0.26	75	6.3	<0.001
Hepatectomy including S2	S2+other	2081	30	1.4	0.029	65	3.1	0.018
Hepatectomy including S3	S3+other	2202	31	1.4	0.016	73	3.3	0.05
Hepatectomy including S4	S4+other	3051	45	1.5	0.005	106	3.5	0.07
Hepatectomy including S5	S5+other	3711	96	2.6	0.001	201	5.4	<0.001
Hepatectomy including S6	S6+other	3729	93	2.5	0.006	182	4.9	<0.001
Hepatectomy including S7	S7+other	3593	95	2.6	<0.001	184	5.1	<0.001
Hepatectomy including S8	S8+other	3866	103	2.7	<0.001	209	5.4	<0.001
Hepatectomy with revascularization		203	12	5.9	0.001	25	12.3	<0.001
Hepatectomy for gall bladder cancer		107	7	6.5	0.006	14	13.1	<0.001
Hepatectomy for hilar bile duct cancer		172	6	3.5	0.006	12	7.0	0.071

Descriptive statistics were compared using the Fisher's exact test for categorical data of operative procedures between the mortality and nonmortality groups.

Xi = 1 if patient age is <59 years; Xi = 2 if age is 60−64; Xi = 3 if age is 65−69; Xi = 4 if age is 70−74; Xi = 5 if age is 75 to 79; and Xi = 6 if age is ≥80.

As shown, between the 2 groups there were 13 overlapping variables: age, male sex, status (emergency surgery), preoperative comorbidities (ASA grade ≥3, ADL before 30 days requiring any assistance, and ascites), primary diagnosis (gallbladder cancer), preoperative laboratory data (albumin ≤3.5 g/dL, aspartate transaminase ≥35 IU/L, creatinine ≥2.0 mg/dL, and prothrombin time international normalized

Table 3. Length of Stay in Hospital

		Hepatectomy outcomes groups	
Variable	**Entire study population (n = 7,732)**	**30-d Mortality (n = 157)**	**90-d In-hospital mortality (n = 309)**
LOS in hospital, d			
Mean (SD)	29.2 (23.0)	23.8 (19.0)	46.0 (36.1)
Median (IQR)	22.0 (16−34)	19.0 (11−32)	38.0 (18−66)
LOS after surgery, d			
Mean (SD)	23.7 (57.5)	13.2 (9.3)	35.1 (32.6)
Median (IQR)	16.0 (12−25)	12.0 (4.5−21)	27.0 (12−51)
ICU admission, n (%)	4,299 (55.6)	155 (98.7)	212 (68.6)
LOS in ICU, d			
Mean (SD)	2.5 (8.4)	8.3 (19.7)	9.2 (17.8)
Median (IQR)	1.0 (1−2)	3.0 (1−10)	3.0 (1−9)

IQR, interquartile range; LOS, length of stay.

Table 4. Prevalence of Morbidity with Hepatectomy Outcomes

Postoperative outcomes	Entire study population (n = 7,732)		Hepatectomy outcomes groups: 30-d Mortality (n = 157)		Hepatectomy outcomes groups: 90-d In-hospital mortality (n = 309)	
	n	%	n	%	n	%
30-day mortality	157	2.0				
Operative mortality	309	4.0				
Readmission within 30 d	138	1.8	2	1.3	5	1.6
Reoperation within 30 d	203	2.6	30	19.1	53	17.2
Surgical complication						
Anastomotic leak	137	1.8	6	3.8	32	10.4
Bile leak	620	8.0	19	12.1	69	22.3
Wound dehiscence	90	1.2	8	5.1	24	7.8
Transfusion >5 U	327	4.2	77	49.0	138	44.7
Infectious complication						
Surgical site infection						
Superficial incisional	357	4.6	10	6.4	41	13.3
Deep incisional	148	1.9	12	7.6	31	10.0
Organ space	428	5.5	18	11.5	55	17.8
Organ space with leakage	108	1.4	3	1.9	19	6.1
Pneumonia	183	2.4	34	21.7	82	26.5
Urinary tract infection	41	0.5	3	1.9	10	3.2
SIRS	115	1.5	7	4.5	22	7.1
Systemic sepsis	323	4.2	61	38.9	139	45.0
Respiratory						
Unplanned intubation	175	2.3	67	42.7	130	42.1
Pulmonary embolism	20	0.3	5	3.2	6	1.9
Prolonged ventilation over 48 h	197	2.5	63	40.1	128	41.4
Renal						
Renal failure	193	2.5	61	38.9	115	37.2
Acute renal failure	95	1.2	40	25.5	77	24.9
CNS	87	1.1	32	20.4	59	19.1
Cardiac complication	70	0.9	53	33.8	65	21.0

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

ratio [PT-INR] ≥1.1), resected segment (S8), and operative procedure (revascularization).

Serum creatinine level ≥2.0 mg/dL was an independent variable in the 30-day mortality group. There were 10 independent variables in the 90-day in-hospital mortality group: COPD, preoperative pneumonia, intrahepatic cholangiocarcinoma, perihilar cholangiocarcinoma, hemoglobin ≤10 mg/dL, platelet count ≤80,000 cells/μL, albumin ≤3.0 g/dL, tumor location (S1 or S7), and left trisegmentectomy with S1 resection.

The final models discriminated the development sets with areas under the receiver operating characteristic (ROC) curve of 0.828 and 0.826 for 30-day mortality and 90-day in-hospital mortality, respectively. To evaluate the models' performance, the C-index (a measure of model discrimination), which is the area under the ROC curve, was calculated for each validation set. The C-indices of 30-day mortality and 90-day in-hospital mortalities were 0.714 and 0.761, respectively, indicating good performance for 90-day in-hospital mortality in the low-risk group. Details of models' performance metrics are given in Figure 2.

DISCUSSION

In this study 7,732 cases were enrolled for MOS hepatectomy. Universal health care in Japan allows patients to remain hospitalized for several weeks after surgery if they require additional medical care. The NCD includes variables almost identical to those included in the ACS-NSQIP database and can capture the clinical course of in-hospital patients up to 90 days postoperatively.

This retrospective study evaluated 7,732 cases of MOS hepatectomy, in which the 30-day mortality and 90-day in-hospital mortality rates were 2.0% and 4.0%, respectively,

Table 5. Risk Models for 30-Day Mortality and 90-Day In-Hospital Mortality after Hepatectomy

	30-d Mortality					90-d In-hospital mortality				
Variables	**β coefficient**	**Odds ratio**	**95% CI**		**p Value**	**β coefficient**	**Odds ratio**	**95% CI**		**p Value**
Age category*	0.33	1.38	1.22	1.57	<0.001	0.31	1.36	1.24	1.49	<0.001
Sex, male	0.46	1.58	1.01	2.48	0.047	0.43	1.53	1.11	2.12	0.021
Emergent surgery	1.35	3.84	1.52	9.74	0.008	1.02	2.78	1.18	6.60	0.022
ADL before 30 d	0.73	2.07	1.09	3.93	0.026	1.03	2.79	1.72	4.52	<0.001
COPD						0.7	2.02	1.13	3.61	0.027
Ascites	0.74	2.10	1.03	4.28	0.042	0.62	1.85	1.02	3.36	0.043
Preoperative pneumonia						1.33	3.77	1.20	11.85	0.045
ASA ≥grade 3	0.7	2.02	1.28	3.19	0.004	0.71	2.03	1.44	2.86	<0.001
Intrahepatic cholangiocarcinoma						0.58	1.78	1.19	2.66	0.011
Hilar bile duct carcinoma	0.92	2.52	0.98	6.46	0.05	0.7	2.00	1.25	3.23	0.008
Gallbladder cancer	1.4	4.07	1.64	10.11	0.007	1.18	3.24	1.76	5.99	<0.001
Hemoglobin <10 g/dL						0.59	1.80	1.20	2.72	0.024
Platelet count <120,000/μL	0.56	1.74	1.08	2.80	0.022	0.45	1.57	1.03	2.40	0.035
Platelet count <80,000/μL						0.76	2.15	1.06	4.33	0.001
Serum albumin <3.5 g/dL	0.7	2.01	1.34	3.02	0.007	0.5	1.64	1.16	2.34	0.027
Serum albumin <3.0 g/dL						0.52	1.67	1.04	2.69	0.045
Serum AST ≥35 U/L	0.84	2.31	1.55	3.44	<0.001	0.53	1.69	1.28	2.24	<0.001
Serum creatinine >2.0 mg/dL	1.37	3.94	1.77	8.79	<0.001					
PT-INR >1.1	0.55	1.73	1.17	2.57	0.003	0.35	1.41	1.05	1.90	0.015
Hepatectomy with s1						0.48	1.62	1.12	2.33	0.031
Hepatectomy with s7						0.45	1.56	1.14	2.14	0.009
Hepatectomy with s8	0.77	2.17	1.45	3.24	0.002	0.67	1.96	1.42	2.71	<0.001
Hepatectomy with revascularization	1.35	3.84	1.89	7.82	0.006	1.09	2.96	1.71	5.14	0.001
Left trisegmentectomy with S1 resection						1.36	3.89	1.40	10.82	0.018
Intercept (β0)	−7.22				<0.001	−6.52				<0.001

*Age, y, <59, 60–64, 65–69, 70–74, 75–79, ≥80.
ADL, activities of daily living; ASA class, American Society of Anesthesiologists Physical Status Classification; AST, aspartate aminotransferase; PT-INR, prothrombin time–international normalized ratio.

and complications occurred in 32.1%. Certain preoperative and operative indications, preoperative laboratory data, and the extent and location of resected segments, were stratified for risk of 30-day mortality and 90-day in-hospital mortality after MOS hepatectomy. To the best of our knowledge, this is the first report to convincingly demonstrate the incidence of preoperative comorbidities, postoperative complications, and mortality rates among patients who underwent hepatectomy using the Japanese NCD.

In the NCD, all types of hepatectomy cases (n = 20,455) including MOS hepatectomy were registered as available patient data on mortality. The 30-day mortality and 90-day in-hospital mortality rates for all hepatectomy cases were 1.2% and 2.3%, respectively, which were comparable with the findings from a second nationwide Japanese database, the Diagnosis Procedure Combination (DPC) database,[14] in which the in-hospital patient mortality rate after hepatectomy between July 2007 and December 2008 (n = 5,207) was 2.6%[15] and the in-hospital mortality rate within 30 days of surgery in patients undergoing hepatectomy for various reasons between July 2007 and December 2009 (n = 18,046) was 1.1 %.[14] The DPC database is a discharge abstract and administrative claims database of inpatient admissions only from secondary and tertiary care hospitals in Japan, which represent approximately 40% of all inpatient admissions to these institutes. Importantly, the DPC database does not include some important clinical data that might more accurately reflect the risk of patient death, such as organ failure and a number of other preoperative comorbidities. In contrast, this NCD analysis included detailed data from 987 participating institutes, better representing a nationwide study of risk stratification.

Reporting deaths that occur within a maximum of 30 days of surgery likely underestimates the true mortality rate associated with hepatic resection. For example, Mayo and colleagues[11] showed that the number of patient deaths was underestimated by 36% and 52% after 30

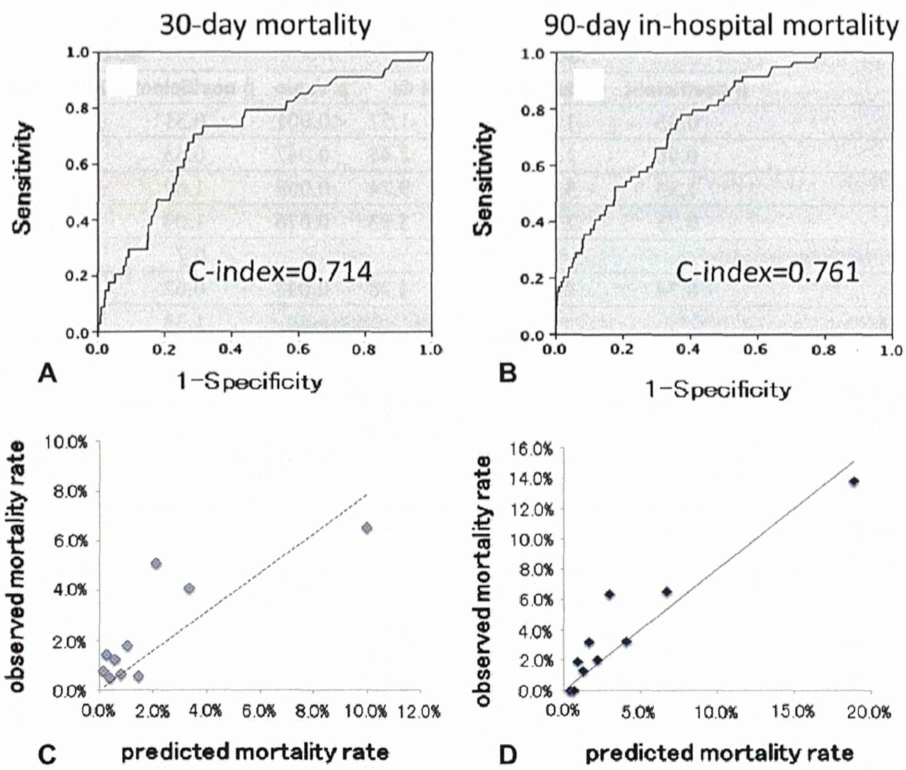

Figure 2. Thirty-day mortality and 90-day in-hospital mortality risk models and calibrations. Receiver operating characteristic (ROC) curves for the prognostic model performance predicting (A) 30-day mortality, (B) 90-day in-hospital mortality, (C) observed vs predicted mortality rates for 30-day mortality, and (D) 90-day in-hospital mortality in the validation set are illustrated. For model calibration, the observed and predicted averages within each of 10 equally sized subgroups were plotted (C, D).

days of hepatectomy for hepatocellular carcinoma and colorectal liver metastasis, respectively, when compared with the number of deaths within 30 days. In this study, we found a similar number of patient deaths after 30 days. Several morbidities occurred more often in association with mortality after 30 days, including organ space SSI and anastomotic leakage. In fact, we identified several risk factors for 90-day in-hospital mortality that were not detected in the risk models of 30-day mortality.

As indicated by the risk models formulated for our analysis, several patient and perioperative factors were significant in both 30-day mortality and 90-day in-hospital mortality rates, including emergency surgery, patient status (age, sex, ADL, and ASA class), and comorbidity (COPD, ascites, and preoperative pneumonia). Our results were in accordance with those of previous analyses using large nationwide databases of Western countries.[16,17] We also found that indications for hepatectomy, including intrahepatic cholangiocarcinoma, perihilar cholangiocarcinoma, and gallbladder cancer (which is usually associated with biliodigestive anastomosis) were significant risk factors of 90-day in-hospital mortality. These findings were also compatible with those of 2 previous single-institution analyses,[18,19] but not with those from a nationwide study.

The NCD variables, which are similar to those established by ACS-NSQIP, were used for the first time to demonstrate that preoperative laboratory variables could be significant risk factors for mortality, which included platelet count (<120,000 or <80,000 cells/μL), prolonged prothrombin time-international normalized ratio (PT-INR) >1.10, and serum levels of hemoglobin (<10 g/dL), albumin (<3.5 and ≥3.0 g/μL), aspartate aminotransferase (≥35 U/L), and creatinine (>2.0 mg/dL). These data indicated that liver function parameters themselves, which deteriorated possibly in association with cirrhosis, could be significant risk factors for mortality. These findings were also comparable with those of Schroeder and associates,[20] who recommended using the Child-Turcotte-Pugh (CTP) score (to assess the prognosis of chronic liver disease) and ASA score to predict treatment outcomes. Notably, our risk score included 3 relevant variables (ascites, serum albumin, and PT-INR) among 5 included in the Child-Turcotte-Pugh criteria (encephalopathy, ascites, serum albumin, serum bilirubin, and PT-INR). The extent 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 (≥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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