published in 1977 defined various issues regarding how to record colorectal cancer surgery and pathological findings including the extent of regional lymph node dissection [12]. The Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines for the treatment of colorectal cancer were then published in 2005 [13]. These guidelines have helped to minimize differences in the care of patients with colorectal cancer in Japanese institutions. On the other hand, a German study group found 30-day mortality rates in low-, medium-, and high-volume centers of 2.6, 2.8, and 3.4 %, respectively [8]. Although outcomes could not be compared among institutions in the present study, some Japanese questionnaires uncovered a similar tendency, which should be clarified in the future (unpublished data; http://www.jsgs.or.jp/modules/en/index.php?content_id=10). The operative mortality rate up to 90 days in the present study was 2.3 %, which was twice the 30-day mortality rate. Visser et al. [5] noted that, "...death after colectomy is later than we think". Their study found that 30-day mortality rates after all, elective and emergency colectomies were 4.3, 1.4 and 15.8 %, respectively. On the other hand, mortality at 90 days increased to 9.1, 4.1 and 28.9 %, respectively [5]. These results indicate that the mortality rate is higher after than before 30 days. This should be a need-to-know item when obtaining written informed consent to undergo right hemicolectomy.

The rate of emergency surgery was 8.4 % in the present study, which is lower than the 18.5–22.5 % rates found in previous studies [5, 7, 9]. One of the reasons for the lower emergency rate might be the prevalence of colonoscopy in Japan. Colonoscopy is commonly applied to patients with positive fecal occult blood tests or with abdominal symptoms. Bowel obstruction caused by colon cancer can be an indication for a temporary stoma. In addition, the rate of emergency operations has decreased because of stents or transanal ileus tubes [14, 15]. The 30-day mortality rate of emergency surgery in this study was 6 % and lower than the 15.8–22.5 % rates identified in reports from other countries [5, 7, 9]. This might be due to a difference in comorbidity rates. A Dutch group reported that two-thirds of patients with gastrointestinal cancers had comorbidities [11]. Hypertension and diabetes mellitus were the major comorbidities in the present study, at rates of 36 and 17 %, respectively. However, considering the rapid increase in the elderly Japanese population, comorbidities in patients with colorectal cancer should be more carefully managed to maintain low mortality and morbidity rates after colectomy.

The morbidity rate was 22 % in the present study. Among these, the morbidity rates of Calvien–Dindo grades ≥III and ≥IV were 5.3 and 1.7 %, respectively. These rates of severe morbidities should be explained when written informed consent to undergo hemicolectomy is obtained. Among patients who underwent right hemicolectomy, 7.8 % developed SSI, which was similar to that in a recent study from Japan [16] and better than previous results [17]. One reason might be the low body mass index (BMI) of the Japanese. From this standpoint, risk models of the surgery should be developed by countries or by ethnic groups with similar lifestyles.

One of the main purposes of the present study was to establish a risk model of mortality after right hemicolectomy in Japan. The 16 and 26 risk factors for 30-day and operative mortality were selected by stepwise logistic regression analysis. The common risk factors for both were emergency surgery, ADL with any type of assistance, congestive heart failure, cancer with multiple metastasis, sepsis, ASA grade ≥3, platelet count, sodium <138 mEq/l, PT-INR over 1.1, and >9,000 white blood cells/μl. Patients with these risk factors should be prudently managed. The c-indices, which are the same as the area under the ROC curves (AUC), were 0.903 using the 16 factors and 0.891 using 26 factors in the 30-day and operative mortality risk models, respectively. The AUC results are considered excellent for AUC values between 0.9–1, good for AUC values between 0.8–0.9, fair for AUC values between 0.7–0.8, poor for AUC values between 0.6–0.7 and failed for AUC values between 0.5–0.6 [18]. Therefore, these risk models are reliable and useful in managing patients with right hemicolectomy. In addition, the c-indices of the 30-day and operative mortality risk models were 0.836 and 0.854, respectively, using the validation dataset. The accuracy of these risk models were validated statistically. This study has been performed as part of a project which aims to improve the quality of medical services. We will open a website through which physicians can get risk predictions (30-day and operative mortality rate) preoperatively, right after they enter a patient's information.

Some excellent risk models for the management of patients with colorectal cancer have been constructed, such as POSSUM, P-POSSUM, CR-POSSUM, and ACPGBI [19–22]. Ferjani et al. [23] reported that the ACPGBI was the most useful in predicting overall mortality among them. The ACPGBI uses the variables of age, ASA grade, cancer stage and operative urgency. The c-index in their study was 0.701. Fazio et al. [24] established the Cleveland Clinic Colorectal Cancer Model (CCCCM) based on patients who underwent surgery at the Cleveland Clinic. Their model included age, ASA grade, TNM stage, operative urgency, cancer resection and hematocrit. The c-index of operative mortality in the CCCCM was 0.801. Some risk factors with high odds ratio in our study were different from those in the previous studies. It might depend on differences of race or medical care system. We plan to establish a user-friendly scoring system that will be helpful for routine clinical use in Japan.

At the same time, the next step of this study will be to compare mortality and morbidity rates among institutions to improve the quality of care for Japanese patients after undergoing right hemicolectomy.

In conclusion, we have reported the first risk stratification study on right hemicolectomy in Japan using a nationwide internet-based database. The nationwide 30-day and operative mortality rates after right hemicolectomy were 1.1 and 2.3 %, respectively. These results were satisfactory. We have developed risk models for right hemicolectomy that will help to improve the management of this procedure.

Acknowledgments We thank all data managers and hospitals participating in this National Clinical Database project for their great efforts in entering the data. We also thank Prof. Hideki Hashimoto and Noboru Motomura, MD for providing direction for the foundation of NCD and the working members of the JSGS database committee (Masayuki Watanabe, MD; Satoru Imura, MD; Fumihiko Miura, MD; Hiroya Takeuchi, MD; Ichiro Hirai, MD; Yoshio Takesue, MD; Hiroyuki Suzuki, MD; Megumi Ishiguro, MD; Hiroyuki Konno, MD; Makoto Gega, MD; Nagahide Matsubara MD; and Akihiko Horiguch, MD). This study was supported by a research grant from the Ministry of Health, Labour and Welfare in Japan.

Conflict of interest All authors declare that there is no conflict of interest in this manuscript.

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ORIGINAL CONTRIBUTION

Mortality After Common Rectal Surgery in Japan: A Study on Low Anterior Resection From a Newly Established Nationwide Large-Scale Clinical Database

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BACKGROUND: The health-care system, homogenous ethnicity, and operative strategy for lower rectal cancer surgery in Japan are to some extent unique compared to those in Western countries. The National Clinical Database is a newly established nationwide, large-scale surgical database in Japan.

OBJECTIVE: To illuminate Japanese national standards of clinical care and provide a basis for efforts to optimize patient care, we used this database to construct a risk model for a common procedure in colorectal surgery—low anterior resection for lower rectal cancer.

DESIGN: Data from the National Clinical Database on patients who underwent low anterior resection during 2011 were analyzed. Multiple logistic regression analyses were performed to generate predictive models of 30-day mortality and operative mortality. Receiver-operator characteristic curves were generated, and the concordance index was used to assess the model's discriminatory ability.

RESULTS: During the study period, data from 16,695 patients who had undergone low anterior resection were collected. The mean age was 66.2 years and 64.5% were male; 1.1% required an emergency procedure. Raw 30-day mortality was 0.4% and operative mortality was 0.9%. The postoperative incidence of anastomotic leakage was 10.2%. The risk model showed the following variables to be independent risk factors for both 30-day and operative mortality: BMI greater than 30 kg/m^2, previous peripheral vascular disease, preoperative transfusions, and disseminated cancer. The concordance indices were 0.77 for operative mortality and 0.75 for 30-day mortality.

LIMITATIONS: The National Clinical Database is newly established and data entry depends on each hospital.

CONCLUSIONS: This is the first report of risk stratification on low anterior resection, as representative of rectal surgery, with the use of the large-scale national surgical database that we have recently established in Japan. The resulting risk models for 30-day and operative mortality from rectal surgery may provide important insights into the delivery of health care for patients undergoing GI surgery worldwide.

KEY WORDS: Colorectal surgery; Epidemiology; Low anterior resection; National database; Risk factor; Risk model.

Financial Disclosure: None reported.

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Dis Colon Rectum 2014; 57: 1075–1081
DOI: 10.1097/DCR.0000000000000176

Large-scale national clinical databases can illuminate national standards of clinical care and provide the necessary data for analyzing problems and evaluating potential solutions, thus serving as a basis for efforts to optimize patient care. Examples in the United States include the Surveillance Epidemiology and End Result–Medicare database[1] and the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).[2] In Japan, a registry for gastroenterological surgery was established as a division of the National Clinical Database (NCD) in 2011 in cooperation with the Japanese Society of Surgery, Japanese Society of Gastroenterological Surgery, Japanese Society of Hepato-Biliary-Pancreatic Surgery, Japan Esophageal Society, Japanese Gastric Cancer Association, Japanese Society for Cancer of the Colon and Rectum, Liver Cancer Society Group of Japan, Japan Pancreas Society, Japan Society for Endoscopic Surgery, and Japanese Society for Abdominal Emergency Medicine. The NCD is a large-scale nationwide database, with data collected through a Web-based data entry system from an ethnically homogeneous population.

We chose a common but rather advanced procedure in colorectal surgery—low anterior resection for lower rectal cancer—as a model for investigating the usefulness of the NCD in the evaluation of surgical care. Colorectal cancer is the third most common malignant disease worldwide.[3] In Japan, colorectal cancer is the second most commonly diagnosed cancer, the third leading cause of cancer death in men, and the first leading cause of cancer death in women.[4] Since the 1980s, both the colon and the rectum have accounted for increasing proportions of cancer incidence in Japan.[4] Surgical intervention remains the primary treatment strategy for rectal cancer, and low anterior resection with preservation of the anal sphincter is a standard surgical procedure worldwide.[5] Thus, this procedure seems to be an appropriate choice for evaluating the levels of surgical care internationally. Because low anterior resection has been associated with relatively high morbidity and mortality,[6] the analysis of risk factors associated with this technique may help to improve the quality of surgical care, particularly in comparisons among countries.[7] We therefore constructed a risk model for prediction of the outcome of low anterior resection based on data from the NCD.

MATERIALS AND METHODS

Data Source

Since the establishment of the NCD, all new applicants for licensure in the surgical specialties accredited by the societies sponsoring the NCD are required to use records from this database to document their surgical experience. Thus, most hospitals, whether large or small, now participate in the NCD. In 2011, 3372 of 4883 (69%) hospitals with surgical departments participated. Although the NCD is basically a self-entry system, close attention is paid to maintaining the high quality of the entry data. Hospitals are advised to designate a data entry person (data manager) who completes the documentation of all cases treated in a given year through the Web-based data management system. Data managers participate in regular training programs at progressive levels. Instructions with definitions of all variables and inclusion criteria for the NCD are available to participating institutions on the NCD Website (http://www.ncd.or.jp/), along with an E-learning system to ensure the consistency of data input. All inquiries regarding data entry (approximately 80,000 inquiries in 2011) are answered, and a list of frequently asked questions is given on the Website.

Current laws, ordinances, and guidelines regarding the confidentiality of data are observed. Names of patients are not included in the database, and patients agree for their data to be included in research projects by using presumed consent with opt-out through the Web page and/or a notice of each hospital, which was approved by individual internal review board of all participating hospitals. A system for ensuring traceability of the data is in place, and regular audits are performed by designated NCD personnel, who visit institutions on a random basis for inspections validation of the data.

All cases of gastroenterological surgery are registered in the database, and detailed information is recorded for representative procedures. The recorded variables are strictly defined and are almost identical to those used in the ACS-NSQIP. Care is taken to ensure 30-day follow-up for outcomes.

Patients

National Clinical Database records for patients who underwent low anterior resection from January 1, 2011, through December 31, 2011, were analyzed for this study. The term low anterior resection limits the procedure to its cut-end (anastomosis) of the large intestine, which is lower than peritoneal reflection, and thus, the level of anastomosis is less than 7cm from the anal verge. Low anterior resection includes ultra-low anterior resection and intersphincteric resection with handsewn coloanal anastomosis. Records from patients who refused use of their data were excluded from the analysis. Records with missing data for age, sex, or status at postoperative day 30 were also excluded.

Outcome Assessment

The primary outcome measures of this study were 30-day mortality and operative mortality. Thirty-day mortality was defined as death within 30 days after the operation date regardless of whether the patient had been discharged from the initial admission. Operative mortality included all deaths occurring during the index hospitalization, regardless of the length of hospital stay (up to 90 days), in addition to deaths occurring after hospital discharge but within 30 days after the operation date.

Morbidity within 30 days after surgery was also analyzed, regardless of whether a patient had been discharged from the initial admission. Morbidity was rigorously defined and categorized as wound, respiratory, urinary tract, central nervous system, cardiac, or other morbidity.

Statistical Analysis

A risk model was developed with patient and perioperative characteristics recorded in the NCD as potential predictor variables. Data were randomly assigned to 2 subsets, which were split 80/20; 1 subset was used for model development, and the other was used for a validation test. Two sets of logistic models (30-day mortality and operative mortality) were constructed for the development data set by using stepwise selection of predictors, with the p value for inclusion set at less than 0.05. A goodness-of-fit test was performed to assess how well the model could discriminate survivors versus deceased patients. Model calibration (the degree to which 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 equal-sized subgroups arranged in increasing order of patient risk. Receiver-operator characteristic curves were generated, and the area under the curve was used to calculate a concordance index (C-index), with a C-index value of >0.7 implying good prediction ability.

RESULTS

Demographic and Clinical Characteristics

From January through December 2011, 1,200,000 surgical cases were collected in the NCD throughout Japan. A total of 16,695 patients who had undergone low anterior resection were included in this study. The development data set included 13,316 records, and the validation data set included 3379 records. The patients' demographic and clinical characteristics are shown in Table 1. The mean age of the study population was 66.2 years; 64.5% were male. For 96% of patients, the indication for surgery was colorectal cancer. Disseminated cancer was diagnosed in 4.4%. The ASA score was grade 3 in 7.2%, and 3.9% required at least some type of assistance in daily life. Other preoperative comorbidities included chronic obstructive pulmonary disease in 2.5%, previous peripheral vascular disease surgery in 0.3%, and cerebrovascular disease in 3.5%.

Perioperative Variables

Preoperative and operative characteristics are given in Table 2. The operation was performed on an emergency basis in 1.1%. Preoperative radiotherapy was performed in 1.5% of the patients, and chemotherapy was performed in 1.8% of the patients. Although most procedures were performed with double-stapled anastomosis, handsewn anastomosis was performed in 4.1%. The rate of laparoscopic surgery was 39.2%, and a stoma was required in 4.6%. The median operative time was 237 minutes (range, 16–1199), and median blood loss was 160 mL (range, 0–16,300 mL).

Outcome Rates

As shown in Table 3, the raw 30-day mortality rate among the 16,695 patients who underwent low anterior resection was 0.4%, and the operative mortality rate (which includes 30-day mortality) was 0.9%. Complications including all grades that occurred within 30 days postoperatively were observed in 26.3% of the patients. Among these complications, 8.90% were grade 3 or higher. The rate of readmission within 30 days was 2.1%. Reoperation was performed within 30 days in 7.2%. Surgical site infections included superficial incisional infection in 4.6%, deep incisional infection in 1.5%, and organ space infection in 7.7%. The postoperative incidence of anastomotic leakage based on purulent discharge from a drain and/or on radiological leakage was 10.2%, whereas the majority of the cases presumably being performed were total mesorectal excision (TME).

Risk Model Results and Performance

Two sets of logistic models (30-day mortality and operative mortality) were constructed for the development data set and model calibration was examined by using a validation data set. Final logistic risk models for 30-day and operative mortality are presented with ORs and 95% CIs in Tables 4 and 5. There were 10 independent variables in the 30-day mortality model and 18 in the operative mortality model. Of these, the following 7 variables overlapped between the 2 models: older age category, previous peripheral vascular disease surgery, disseminated cancer, preoperative transfusions, BMI greater than 30 kg/m^2, platelet number less than $12 \times 10^4/\mu L$, and Na under 138 mEq/mL.

As shown in Table 6, the C-index (a generalization of the area under the curve) was 0.75 for 30-day mortality and 0.77 for operative mortality. The surgical mortality probability model exhibited reasonable discrimination and excellent calibration ($p < 0.001$) in the validation data set.

DISCUSSION

To our knowledge, this is the first report of a probability model of surgical mortality for a common rectal surgical procedure (low anterior resection) from the NCD, with a data set consisting of 16,695 consecutive cases within 1 year. In 2011, NCD collected more than 1,200,000 surgical cases from over 3300 hospitals nationwide in Japan,

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

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

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

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

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

TABLE 2. Preoperative and operative characteristics and outcome

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

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

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

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

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

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

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

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

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

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

PVD = peripheral vascular disease.

TABLE 5. Low anterior resection risk models: operative mortality

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

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

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

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

TABLE 6. Risk model performance metrics for low anterior resection

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

C-index = concordance index.

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

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

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

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Risk Stratification of 7,732 Hepatectomy Cases in 2011 from the National Clinical Database for Japan

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BACKGROUND: There has been no report on risk stratification for hepatectomy using a nationwide surgical database in Japan. The objective of this study was to evaluate mortality and variables associated with surgical outcomes of hepatectomy at a national level.

STUDY DESIGN: We analyzed records of 7,732 patients who underwent hepatectomy for more than 1 segment (MOS) during 2011 in 987 different hospitals, as identified in the National Clinical Database (NCD) of Japan. The NCD captured 30-day morbidity and mortality as well as 90-day in-hospital mortality outcomes, which were submitted through a web-based data entry system. Based on 80% of the population, independent predictors for 30-day mortality and 90-day in-hospital mortality were calculated using a logistic regression model. The risk factors were validated with the remaining 20% of the cohort.

RESULTS: The median postoperative length of hospitalization was 16.0 days. The overall patient morbidity rate was 32.1%. Thirty-day mortality and 90-day in-hospital mortality rates were 2.0% and 4.0%, respectively. Totals of 14 and 23 risk factors were respectively identified for 30-day mortality and 90-day in-hospital mortality. Factors associated with risk for 90-day in-hospital mortality were preoperative condition and comorbidity, operative indication (emergency surgery, intrahepatic/perihilar cholangiocarcinoma, or gallbladder cancer), preoperative laboratory data, and extent and location of resected segments (segment 1, 7, or 8). As a performance metric, c-indices of 30-day mortality and 90-day in-hospital mortality were 0.714 and 0.761, respectively.

CONCLUSIONS: Here we report the first risk stratification analysis of hepatectomy using a Japanese nationwide surgical database. This system would predict surgical outcomes of hepatectomy and be useful to evaluate and benchmark performance. (J Am Coll Surg 2014;218:412–422. © 2014 by the American College of Surgeons)

The safety and efficacy of liver resection have improved dramatically in recent years, allowing broader indications for the procedure in both benign and malignant diseases.[1] Perioperative mortality rates in high volume cancer centers are reportedly 0% to 2%.[2-4] In contrast, population-based analyses using administrative data from Western countries have reported mortality rates of 5% to 10%,[4-7] indicating capacity for further improvement.

In 2006, the Japanese Society of Gastroenterological Surgery (JSGS) formed a committee to devise a database

Disclosure Information: Nothing to disclose.

Dr Gotoh received a research grant from the Ministry of Health, Labor and Welfare in Japan.

National Clinical Database (NCD) and the hospitals participating in NCD are the source of the data used herein and they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Received May 19, 2013; Revised November 5, 2013; Accepted November 11, 2013.

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ISSN 1072-7515/13/$36.00
http://dx.doi.org/10.1016/j.jamcollsurg.2013.11.007

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

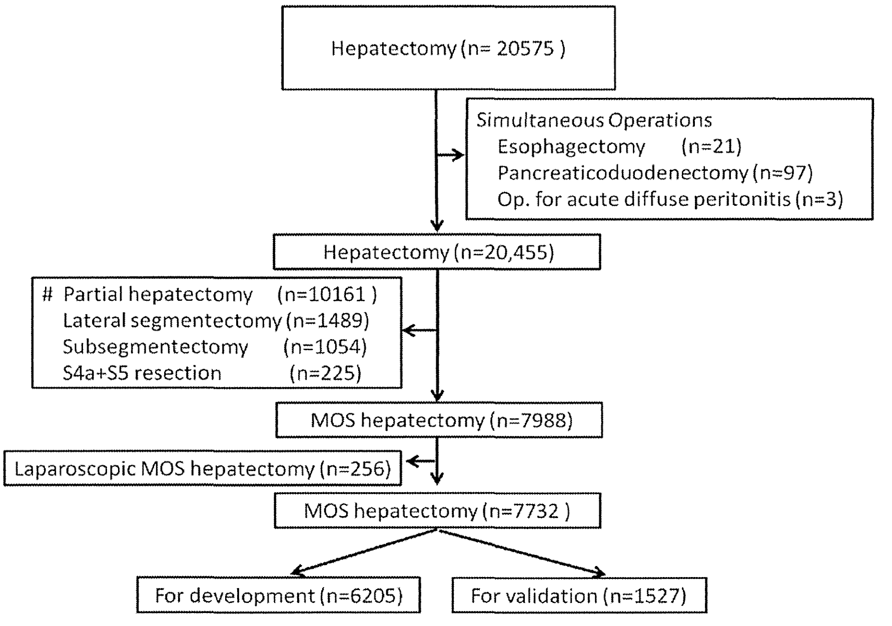

Figure 1. Study population and development and validation of risk stratification. MOS hepatectomy refers to hepatectomy of more than 1 segment, with the exception of lateral segmentectomy.

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

	Entire study population (n = 7,732)		Hepatectomy outcomes groups			
			30-d Mortality (n = 157)		90-d In-hospital mortality (n = 309)	
Postoperative outcomes	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

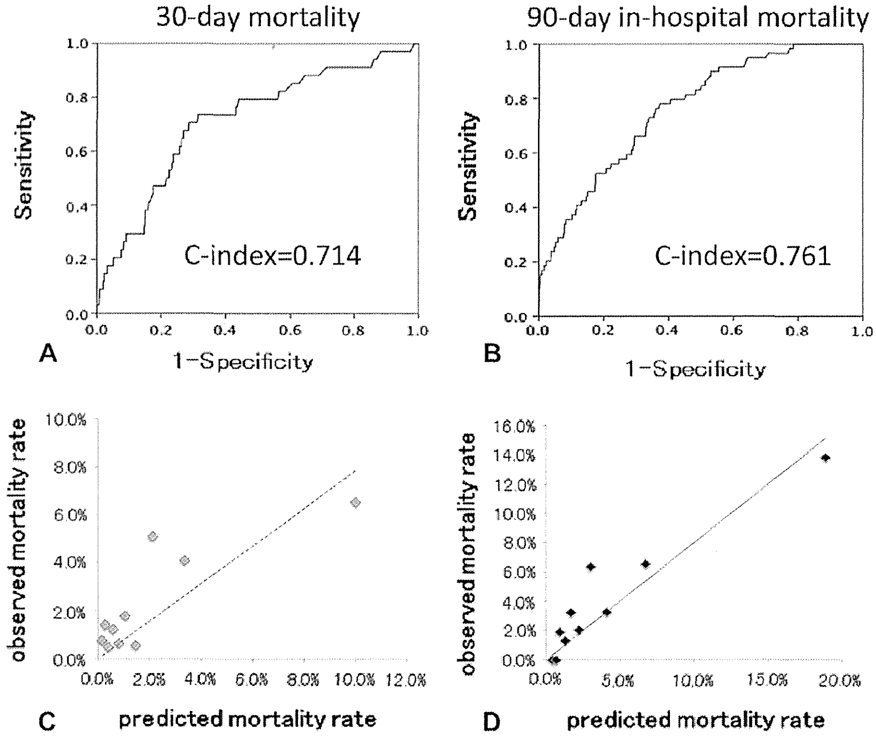

Figure 2. Thirty-day mortality and 90-day in-hospital mortality risk models and calibrations. Receiver operating characteristic (ROC) curves for the prognostic model performance predicting (A) 30-day mortality, (B) 90-day in-hospital mortality, (C) observed vs predicted mortality rates for 30-day mortality, 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 $\geq$3.0 g/μL), aspartate aminotransferase ($\geq$35 U/L), and creatinine ($>$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

Acknowledgment: We wish to thank all of the data managers and hospitals participating in this National Clinical Database project for their continued efforts in entering the data. We also would like to thank Prof Hideki Hashimoto and Noboru Motomura, MD for providing direction for the foundation of NCD and the working members of the JSGS database committee (Masayuki Watanabe, MD; Satoru Imura, MD; Fumihiko Miura, MD; Hiroya Takeuchi, MD; Ichiro Hirai, MD; Yoshio Takesue, MD; Hiroyuki Suzuki, MD; Megumi Ishiguro, MD; Hiroyuki Konno, MD; Makoto Gega, MD; Nagahide Matsubara MD; and Akihiko Horiguch, MD). We would also like to acknowledge Norihiro Kokudo, MD and Kenneth Nollet, MD for their important suggestions regarding this manuscript.

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