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A new scoring system for predicting in-hospital death after lung cancer surgery (the SABCIP score) using a Japanese nationwide administrative database

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Abstract

Background: We aimed to develop and validate a new risk scoring tool for predicting in-hospital mortality after lung cancer surgery.

Methods: We retrospectively identified patients admitted for lung cancer surgery from a nationwide administrative database in Japan and randomly divided them into derivation and validation cohorts. In the derivation cohort, we performed logistic regression analysis to determine predictive variables and developed a risk scoring tool by proportionally weighting the regression coefficients and assigning points to each variable. In both cohorts, we evaluated the predictive performance of the score using the c-index and showed the in-hospital mortality at each risk score.

Results: In total, 64 175 patients (32 170 and 32 005 patients in the derivation and validation cohort, respectively) were enrolled, including 115 (0.4%) and 119 (0.4%) in-hospital patient deaths in the derivation and validation cohorts, respectively. Following the multivariate regression analysis, we selected six variables to create the SABCIP score, a risk scoring tool named after the parameters on which it is based, namely male sex, age ≥ 75 years, body mass index <18.5, clinical stage ≥3, interstitial lung disease, and procedure type (sleeve resection, chest wall resection, or pneumonectomy). The c-index of the score was 0.82 and 0.80 in the derivation and validation cohorts, respectively, which represents a better or equal discrimination performance compared with previous scoring tools. In-hospital mortality increased as the score increased in both cohorts.

Conclusion: The SABCIP score is a simple and useful predictor of in-hospital mortality in patients after lung cancer surgery.

KEYWORDS
in-hospital mortality, lung cancer, lung resection, risk modeling, surgery

INTRODUCTION

Surgical resection is a possible curative treatment for patients with anatomically resectable non-small cell lung cancer (stage I or II[1]) and may provide them with the best chance of long-term survival.[2] The reported postoperative complication rate after lung cancer resection ranges from approximately 30%–40%[3–5] and postoperative mortality is reported to be 0.5%–5.2%[6–10] in patients with lung cancer; therefore, it is important to reduce these postoperative events for lung cancer surgery. Although several scoring models have been developed to estimate the rate of postoperative complications and mortality,[7–9] some may be complicated or require specific expertise. Therefore, a simpler and easier scoring tool for the accurate prediction of postoperative complications can be effective in improving the prognosis of patients with lung cancer after surgical treatment.

The Diagnosis Procedure Combination (DPC), the Japanese national case-mix system database,[11] covers 83% of the Japanese acute care hospitalizations (more than ten million hospitalizations in 2018) and also includes patient information on admissions, such as age, sex, smoking status, and comorbidities (https://www.mhlw.go.jp/index.html). This study was conducted to develop and test a simple and useful scoring tool for predicting in-hospital death after lung cancer surgery using the large DPC database of patients.

METHODS

Source database

We extracted data from the DPC, the Japanese national case-mix system database constructed by the DPC research team under the Ministry of Health, Labor and Welfare in Japan.[11] The DPC is a patient classification system based on the diagnosis of patients and the procedures provided to them during their hospital stay. Most Japanese acute care hospitals are financed with a combination of DPC-based per-diem payments and fee-for-service payments. The DPC database collects data on hospitalization, discharge destination, comorbidities, and complications during hospitalization (written in Japanese text and coded using the International Classification and Related Health Problems 10th Revision codes), as well as the following clinical information: age, sex, height, weight, smoking status, Hugh-Jones grade, tumor, lymph node, metastasis (TNM) classification of cancers, surgery information, and drug

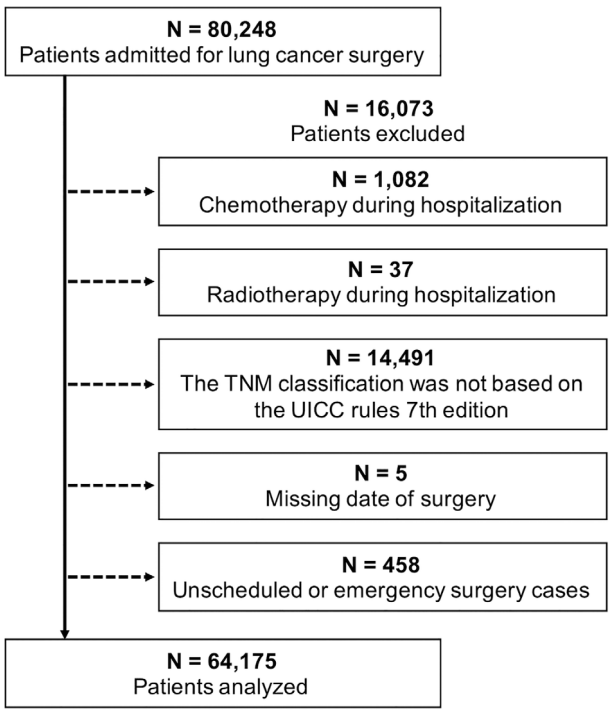

FIGURE 1 Patient flow diagram. TNM, tumor, lymph node, metastasis; UICC, Union for International Cancer Control

TABLE 1 Patient characteristics in the derivation and validation cohorts

Patient characteristics	Derivation cohort $n = 32\,170$	Validation cohort $n = 32\,005$
In-hospital death	115 (0.4%)	119 (0.4%)
Age (years)	69.6 ± 9.5	69.8 ± 9.3
Male	19 348 (60.1%)	19 261 (60.2%)
Body mass index	23.0 ± 3.4	22.9 ± 3.4
Pack-years	12.3 [0.0–45.0]	12.0 [0.0–45.0]
Hugh-Jones grade		
1	25 084 (82.1%)	24 713 (81.4%)
2	3944 (12.9%)	4135 (13.6%)
3	985 (3.2%)	1006 (3.3%)
4	385 (1.3%)	352 (1.2%)
5	148 (0.5%)	154 (0.5%)
Clinical stage		
1	22 764 (76.8%)	22 579 (76.5%)
2	3609 (12.2%)	3632 (12.3%)
3	2343 (7.9%)	2353 (8.0%)
4	942 (3.2%)	947 (3.2%)
Procedure type		
Wedge resection	5758 (17.9%)	5636 (17.6%)
Segmentectomy	3412 (10.6%)	3439 (10.7%)
Lobectomy	22 079 (68.5%)	21 945 (68.5%)
Sleeve resection	311 (1.0%)	365 (1.1%)
Chest wall resection	448 (1.4%)	474 (1.5%)
Pneumonectomy	201 (0.6%)	185 (0.6%)
Hospital stratified by annual volume		
<50	5128 (16.2%)	5242 (16.7%)
50–100	8739 (27.6%)	8794 (27.9%)
≥100	17 764 (56.2%)	17 436 (55.4%)
Comorbidity		
Diabetes	6191 (19.2%)	6321 (19.8%)
Hypertension	8105 (25.2%)	8214 (25.7%)
Ischemic heart disease	2644 (8.2%)	2622 (8.2%)
Chronic heart failure	1218 (3.8%)	1170 (3.7%)
Cerebrovascular disease	1343 (4.2%)	1308 (4.1%)
Dementia	206 (0.6%)	185 (0.6%)
Chronic obstructive pulmonary disease	2341 (7.3%)	2415 (7.5%)
Asthma	1093 (3.4%)	1071 (3.3%)
Interstitial lung disease	1580 (4.9%)	1585 (5.0%)
Liver disease	66 (0.2%)	50 (0.2%)
Neurological disorders	93 (0.3%)	104 (0.3%)
Preoperative treatment		
Dialysis	186 (0.6%)	189 (0.6%)
Oxygen therapy	332 (1.0%)	324 (1.0%)
Corticosteroid therapy	607 (1.9%)	573 (1.8%)

Note: Data are presented as mean ± standard deviation or median (interquartile range) or frequencies (%).

TABLE 2 Independent predictor variables for in-hospital death of the multivariable model in the derivation cohort

Variable	β coefficient	Odds ratio	95% confidence interval	*p*-value
Age (years)				
<75	–	–	–	–
≥75	1.47	4.34	2.86–6.59	<0.001
Sex				
Female	–	–	–	–
Male	1.96	7.13	3.44–14.8	<0.001
Body mass index				
<18.5	1.50	4.47	2.81–7.11	<0.001
≥18.5	–	–	–	–
Clinical stage				
1–2	–	–	–	–
3–4	1.03	2.79	1.77–4.41	<0.001
Procedure type				
Wedge resection or segmentectomy or lobectomy	–	–	–	–
Sleeve resection or chest wall resection or pneumonectomy	1.22	3.39	1.86–6.19	<0.001
Comorbidity				
Interstitial lung disease	1.15	3.16	1.77–4.41	<0.001

Note: Results are presented as β coefficient, odds ratios and 95% confidence intervals.

information. The institutional review board of the University of Occupational and Environmental Health, Japan approved this study (R2-007).

Subjects and outcomes

We retrospectively identified patients admitted for lung cancer surgery (procedure codes: K514-00 [thoracotomy] and [thoracoscopic surgery] K514-02) between January 2016 and December 2018. The exclusion criteria were as follows: chemotherapy during hospitalization; radiotherapy during hospitalization; TNM classification not according to the Union for International Cancer Control (UICC) rules seventh edition,[1] and lack of the date of surgery. Unscheduled or emergency surgery cases were also excluded because our risk score was designed to estimate postoperative events in stable patients with scheduled lung cancer resection. Finally, the patients were randomly divided into derivation and validation cohorts. The allocation of the two groups was carried out randomly using random numbers ranging from 0 to 100, with a cutoff value of 50.

The primary outcome was in-hospital mortality. Secondary outcomes were antibacterial drug use 7–14 days after surgery, blood transfusion use after surgery, and frequency of disseminated intravascular coagulation (DIC) diagnosis after surgery.

Data collection

We extracted the following information on admission from the DPC database: age, sex, body mass index (BMI), smoking status (pack-years), Hugh-Jones grade,[12] clinical stage (based on the TNM classification according to the UICC rules seventh edition[1]), and hospital stratified by annual volume. Surgical procedures included wedge resection, segmentectomy, lobectomy, sleeve resection, chest wall resection, and pneumonectomy. We also extracted the following comorbidities and preoperative treatment on admission: diabetes, hypertension, ischemic heart disease, chronic heart failure, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, asthma, interstitial lung disease, liver disease, neurological disorders, dialysis, oxygen therapy, and corticosteroids. These diagnoses were coded

TABLE 3 The SABCIP score for in-hospital death

Variable	Score
Age (years)	
≥75	1
Sex	
Male	2
Body mass index	
<18.5	1
Clinical stage	
3–4	1
Procedure type	
Sleeve resection, chest wall resection, pneumonectomy	1
Comorbidity	
Interstitial lung disease	1

Note: The SABCIP score is named after the six variables on which it is based: sex, age ≥ 75 years, body mass index <18.5, clinical stage ≥3, interstitial lung disease, and procedure type.

using the International Classification of Diseases and Injuries 10th revision (ICD-10).

Statistical analysis

To determine independent predictive variables for in-hospital death, we first performed a univariate logistic regression analysis in the derivation cohort. We excluded variables with a frequency <2.0% and included variables with a level of significance <0.20, and odds ratio >1.0, from the univariate analysis into the multivariate analysis. We performed multivariate analysis using logistic regression with backward elimination methods with a significance level of <0.05. For the regression analysis, the variables were divided into binary variables: age (<75 years vs. ≥75 years), BMI (<18.5 vs. ≥18.5), clinical stage (1–2 vs. 3–4), procedure type (wedge resection or segmentectomy or lobectomy vs. sleeve resection or chest wall resection or pneumonectomy). The adopted cutoff values of age and BMI were based on a widely used threshold. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit statistics.[13]

To develop a risk-scoring tool for predicting in-hospital death, we assigned each independent predictor with a point score according to the regression coefficient of the multivariate model.[14] We assessed the discrimination of the risk score by the c-index, which is identical to the area under the receiver operating characteristic curve.[15] In addition, we calculated the in-hospital mortality, postoperative antibacterial drug usage rate, postoperative blood transfusion usage rate, and postoperative DIC diagnosis rate at each risk score.

Finally, to assess the external validity of the obtained risk score, we applied the risk score to the validation cohort. We then evaluated the predictive performance of the risk score using the c-index and showed the in-hospital mortality and other postoperative event rates in the validation cohort. All analyses were conducted at a significance level of $\alpha = 0.05$ using STATA 16.1 software (StataCorp).

RESULTS

Among the 80 248 patients who underwent lung cancer surgery, 16 073 were excluded for the following reasons: chemotherapy during hospitalization ($n = 1082$); radiotherapy during hospitalization ($n = 37$); TNM classification not based on the UICC rules seventh edition[1] ($n = 14\,491$), missing date of surgery ($n = 5$), and unscheduled or emergency surgery cases ($n = 458$) (Figure 1). Finally, 64 175 patients were enrolled in the study. Of these, 32 170 patients were randomly assigned to the derivation cohort, and the remainder ($n = 32\,005$) to a validation cohort (Table 1). We identified 115 (0.4%) and 119 (0.4%) patients with in-hospital death after lung cancer surgery in the derivation and validation cohorts, respectively. The mean ± standard deviations of age were 69.6 ± 9.5 years and 69.8 ± 9.3 years, and 60.1% and 60.2% were male patients in the derivation and the validation cohort, respectively. The majority (68.5%) of the patients underwent lobectomy in both cohorts. The proportions of comorbidities and preoperative treatment did not differ markedly between the two cohorts (Table 1).

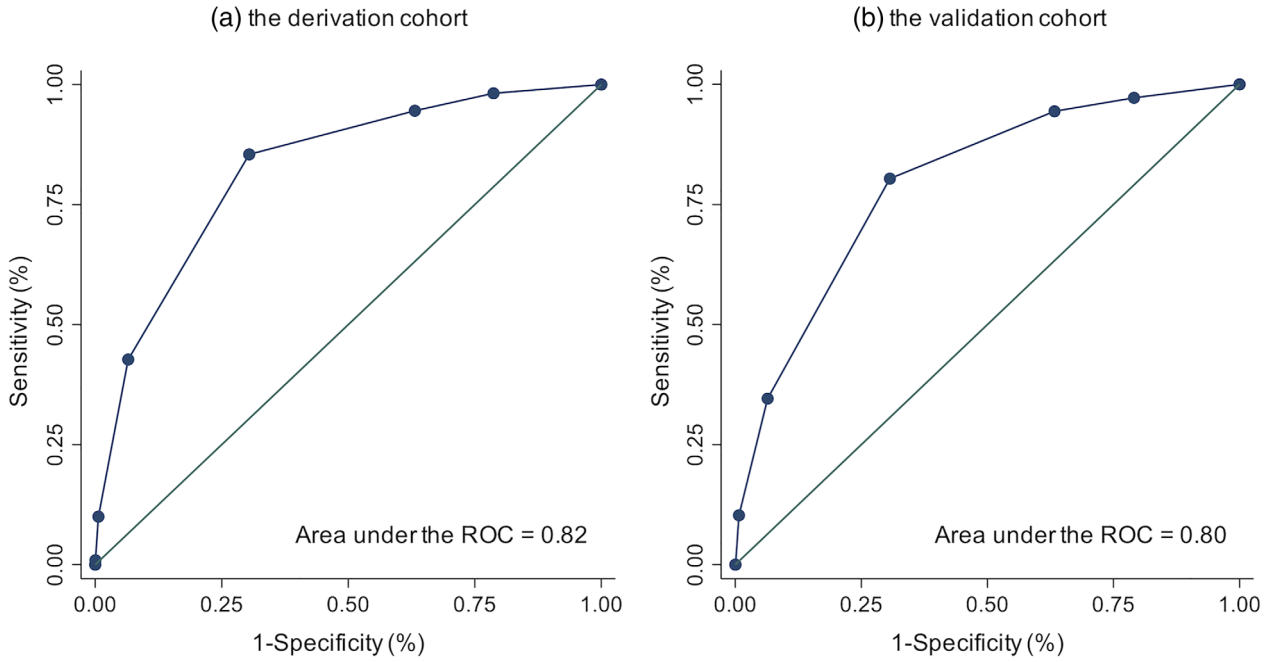

FIGURE 2 Receiver operating characteristic curve in the derivation and validation cohort. The area under the receiver operating characteristic (ROC) curve was 0.82 in the derivation cohort (a) and 0.80 in the validation cohort (b)

TABLE 4 In-hospital mortality and other postoperative event rates at each risk score in the derivation cohort

Score	Total	In-hospital mortality	Antibacterial drug usage rate	Blood transfusion usage rate	DIC diagnosis rate
0	6410	2 (0.03%)	331 (5.2%)	54 (0.8%)	5 (0.08%)
1	4679	4 (0.09%)	312 (6.7%)	85 (1.8%)	3 (0.06%)
2	9855	10 (0.1%)	971 (9.9%)	259 (2.6%)	4 (0.04%)
3	7240	47 (0.6%)	1095 (15.1%)	299 (4.1%)	13 (0.2%)
4	1804	36 (2.0%)	423 (23.4%)	181 (10.0%)	8 (0.4%)
5	188	10 (5.3%)	77 (41.0%)	38 (20.2%)	2 (1.1%)
6	14	1 (7.1%)	3 (21.4%)	3 (21.4%)	0 (0.0%)
7	1	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)

Note: Data presented as frequencies (%).
Abbreviations: DIC: disseminated intravascular coagulation; n/a: not applicable.

As a result of the univariate analysis in the derivation cohort (Supplemental Table 1), the following variables were entered into a backward stepwise multivariate logistic regression analysis: age ≥ 75 years; male sex; BMI <18.5; pack-years >1; Hugh-Jones grade ≥ 3; clinical stage ≥3; sleeve resection, chest wall resection, or pneumonectomy; diabetes; chronic heart failure; cerebrovascular disease; and interstitial lung disease. The independent predictor variables for in-hospital death in the multivariable model of the derivation cohort are shown in Table 2. The Hosmer-Lemeshow goodness-of-fit statistics showed a p-value of 0.24, indicating a good fit.

To develop a risk scoring tool for predicting in-hospital mortality in patients after surgical treatment of lung cancer, the remaining six categorical variables in the stepwise multivariate regression analysis were selected, and relative weights were assigned according to the regression coefficient. Table 3 shows the calculations of the SABCIP score (male sex, age (≥75 years), BMI (<18.5), clinical stage (3, 4), interstitial lung disease, and procedure type [sleeve resection or chest wall resection or pneumonectomy]).

The c-index of the SABCIP score for predicting in-hospital mortality was 0.82 in the derivation cohort (Figure 2a). Table 4 shows the in-hospital mortality and other postoperative event rates in each risk score in the derivation cohort. In-hospital mortality, postoperative antibacterial drug usage rate, blood transfusion usage rate, and DIC diagnosis rate gradually increased as the score points increased (Table 4). The c-index of the validation cohort was 0.80, indicating good external validity (Figure 2b). Similar to the trend in the derivation cohort, the in-hospital mortality and other postoperative event rates in the validation cohort gradually increased as the score points increased (Supplemental Table 2).

DISCUSSION

Using a Japanese nationwide administrative database, we developed the SABCIP score comprising only six variables (sex, age, BMI, clinical stage, interstitial lung disease, and procedure type) for predicting in-hospital death in lung cancer patients after surgical treatment, with a high c-index of 0.82. The validation cohort showed that the SABCIP score accurately predicted in-hospital death (c-index = 0.80), and the mortality increased as the score increased.

Among previous risk scores for lung cancer surgery mortality, the Thoracoscore (c-index = 0.85) showed better discrimination than the SABCIP score (c-index = 0.82), and the reliability of the Thoracoscore was validated externally.[7] However, the SABCIP score comprised fewer variables (6 vs. 11 variables) and was generated from a larger cohort (n = 64 175 vs. n = 15 183) than the Thoracoscore.[7] The other risk models developed from the French Thoracic Surgery database and the European Society of Thoracic Surgeons database comprised 11 variables, with a c-index of 0.78[8] and nine variables with a c-index of 0.65.[9] Compared with these previous risk scoring models, the SABCIP score achieved a higher c-index of 0.82 for in-hospital death after lung cancer surgery, with only six variables immediately available after determination of the surgical procedure type, and had sufficient discriminative performance, as supported by external validation.

Previous reports revealed that preoperative pulmonary rehabilitation and interventions, including education on smoking cessation and nutrition, decrease postoperative pulmonary complications and length of hospital stay after lung resection.[16–18] The SABCIP score allows us to assess postoperative fatal risk at the time the operative procedure is decided (before or immediately after hospitalization for lung cancer surgery); therefore, this score may allow the early identification of high-risk patients who require preoperative interventions. Further prospective studies are needed to elucidate whether the SABCIP score facilitates early preoperative interventions for high-risk patients and contributes to decreased postoperative mortality and complication rates.

Previous reports showed that infectious diseases, such as pneumonia and pleural empyema, accounted for more than half of the leading causes of death after lung resection.[19,20] Although information on the main cause of death was not available from our database, the postoperative antibacterial drug use rate, the frequency of DIC diagnosis, and blood transfusion use rate increased as the score increased, suggesting that

postoperative infection and bleeding were associated with death after lung cancer surgery in this study.

This study had several limitations. Although the large number of patients in the DPC database (83% of the Japanese acute care hospitalizations with approximately 490 000 beds in 1700 acute care hospitals in 2018) allowed a detailed analysis of the utility of the SABCIP Score (https://www.mhlw.go.jp/index.html), this study is limited by its retrospective nature. Second, pathological data and the results of pulmonary function tests were not available in the DPC database. Third, the DPC database did not include the main in-hospital mortality causes; therefore, we estimated them using the rates of antibacterial drugs usage, blood transfusion and diagnosis of DIC. Finally, the DPC data also did not include physiological and radiological data, such as pulmonary function.

In conclusion, the SABCIP score with only six variables that are routinely available and calculable at the time the operative procedure is decided can be a useful predictor of postoperative in-hospital mortality in lung cancer patients.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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