# Machine learning-based prediction of postoperative mortality in emergency colorectal surgery: A retrospective, multicenter cohort study using Tokushukai Medical Database

**Shota Akabane** (akap.sh.3381@gmail.com)
Tokyo Women's Medical University
**Katsunori Miyake**
Shonan Kamakura General Hospital
**Masao Iwagami**
University of Tsukuba
**Kazunari Tanabe**
Shonan Kamakura General Hospital
**Toshio Takagi**
Tokyo Women's Medical University

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**Article**

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# Abstract

## Background

Emergency colorectal surgery may constitute surgical challenges, resulting in high mortality and morbidity rates. Although prognostic factors associated with mortality in patients with emergency colorectal surgery have been identified, an accurate mortality risk assessment is still necessary to determine the range of therapeutic resources in accordance with the severity of patients. We established machine-learning models with nonlinear feature extraction to predict in-hospital mortality for patients who had emergency colorectal surgery using clinical data at admission and attempted to identify prognostic factors associated with in-hospital mortality.

## Methods

This retrospective cohort study included adult patients undergoing emergency colorectal surgery in 42 hospitals between 2012 and 2020. Patients were divided into those hospitalized between July 2010 and June 2018 (training/validation dataset) and those hospitalized between July 2018 and June 2020 (testing dataset). We employed logistic regression and three supervised machine-learning models: random forests, gradient-boosting decision trees (GBDT), and multilayer perceptron (MLP) in the training dataset. The prediction models were tested using all testing datasets, and the area under the receiver operating characteristics curve (AUROC) was calculated for each model. The Shapley additive explanations (SHAP) values are also calculated to identify the significant variables in GBDT.

## Results

There were 8,792 patients who underwent emergency colorectal surgery. The in-hospital mortality rates were 11.9% and 11.3% for the training/validation and testing datasets, respectively. After model training, the AUROC was calculated for in-hospital mortality prediction with each trained machine-learning model. Therefore, the AUROC values of 0.742, 0.782, 0.814, and 0.768 were obtained for logistic regression, random forests, GBDT, and MLP. According to SHAP values, age, colorectal cancer, use of laparoscopy, and some laboratory variables, including serum lactate dehydrogenase serum albumin, and blood urea nitrogen, were significantly associated with in-hospital mortality.

## Conclusion

We successfully generated the machine-learning prediction model, including GBDT, with the best prediction performance and exploited the potential for use in evaluating in-hospital mortality risk for patients who undergo emergency colorectal surgery.

# BACKGROUND

Colorectal surgery is one of the most common types of abdominal surgery [1]. It should be performed as emergency surgery if the lower gastrointestinal tract is perforated, strangulated, or blocked. Compared with elective colorectal surgery, which is associated with 1–3% mortality, emergency colorectal surgery might constitute surgical challenges, resulting in high mortality and morbidity rates [2, 3]. It is estimated that 25% of colorectal surgery is performed on an emergency basis [4], with 10–25% mortality and 30–50% morbidity rate [5, 6]. Thus, the high prevalence of mortality after nonelective colorectal surgery has inspired global authorities involved in quality improvement in surgical care.

Several studies have revealed prognostic factors contributing to mortality in patients with emergency colorectal surgery, and various prediction models have extensively been established to evaluate the severity of the patient's condition and shared with healthcare providers to fulfill collaborative care [7, 8]. Although the Enumeration of Mortality and Morbidity (POSSUM) has been used in patients with emergency colorectal surgery [9, 10], it tends to underestimate mortality when the caseload of emergency cases exceeds 20%. Researchers have subsequently tried to modify POSSUM into a more decent scoring system for colorectal surgery from a series of 6,790 patients [11]. However, only 2.9% of these patients had emergency colorectal surgery, with a mortality rate of 25%. Thus, the objective mortality risk prediction of patients on initiation of treatment is indispensable to determine the range of therapeutic resources in accordance with the severity of patients. A mortality prediction model that encompasses the whole hospitalized population is essential to determine the scale of medical assets needed in the manner of disease severity during hospitalization.

Current machine-learning analyses with nonlinear feature extraction in clinical determination have broadly been demonstrated to boost prediction capacity [12, 13]. Employing these procedures to the issue can generate a precise prediction model for morbidity and mortality. To construct the mortality prediction model, laboratory findings were advantageous in achieving a preferable prediction capacity. They are generally obtained with most patients on initiation of their treatment and are barely repeatable in a short period. Therefore, clinicians can efficiently choose which laboratory values to use for the prediction analyses. Accordingly, the laboratory findings are feasible and have been utilized in previous mortality prediction models [14, 15].

Hereby, we established machine-learning models with nonlinear feature extraction to predict in-hospital mortality for patients who had emergency colorectal surgery using clinical data at admission and compare them with a conventional logistic regression model that has frequently been applied to linear feature extraction, as well as attempted to identify prognostic factors associated with in-hospital mortality.

## METHODS

# Data source

We utilized the Tokushukai Medical Database for this retrospective cohort study, which was generated from the clinical data from 42 hospitals in the Tokushukai Group [16, 17]. The Tokushukai Group is one of the largest Japanese hospital chains, which handles 72 hospitals, including 38 hospitals employing the diagnosis procedure combination (DPC) system in Japan [18]. The Tokushukai Medical Database primarily includes departmental claims data (particularly the DPC inpatient data) in addition to electronic medical notes, including outpatient and inpatient laboratory findings. The DPC inpatient data consist of patients' sex and age; dates of admission and discharge; discharge status (alive or dead); primary diagnoses, preexisting comorbidities on admission, and complications during hospital stay documented by the attending doctors based on the International Classification Disease 10th revision (ICD-10) codes [19]; types of surgery; and medications and interventions, including renal replacement therapy and mechanical ventilation daily.

The study was approved by the Tokushukai Group Joint Ethics Committee and the Research Promotion Center at Tokyo Women's Medical University in accordance with the tenets of the Declaration of Helsinki. Informed consent from individual patients was deferred as all data were anonymized for research purposes.

# Study population

The population of this study includes adult patients (aged ≥ 18 years) who were admitted to one of the 42 hospitals engaging in the Tokushukai Medical Database between July 2010 and June 2020 and underwent emergency colorectal surgery. The compatible surgery was determined according to the Japanese surgery codes K719 (colectomy), K726 or K736 (colostomy), and K740 (rectal resection). Emergency surgery was defined as one performed within three days from admission. If a patient had colorectal surgery more than two times during the period, the analysis was restricted to the initial surgery [17].

Patients were divided into two groups: those hospitalized between July 2010 and June 2018 (training/validation dataset) and those hospitalized between July 2018 and June 2020 (testing dataset). The patient characteristics (i.e., candidate predictors) and in-hospital mortality were described using summary statistics.

# Outcome

The outcome of interest was the in-hospital mortality.

# Predictor variables

According to our literature review [14, 15, 20, 21, 22, 23] and the clinical knowledge of the authors, 46 variables were selected for model training, including baseline characteristics: age, sex, weight, height, body mass index (BMI) upon admission, length of stay to surgery, surgery type, indication for surgery, 10 comorbidities, and 20 laboratory variables on admission.

# Statistical analysis (Machine learning)

We applied conventional logistic regression [24] and three established machine-learning analyses, namely random forests [25], gradient-boosting decision trees (GBDT) [26], and multilayer perceptrons (MLP) [27], to the training/validation dataset to generate prediction models. These machine-learning analyses have been applied to prediction models for in-hospital mortality in previous studies [28, 29]. We used a class-balanced loss to the training phase of machine learning, and all imputed data were utilized to develop the model and adopt the hyperparameters of the model, which are capable of magnifying the mean values of the area under the receiver operating characteristics curve (AUROC) earned from five-fold cross-validation within the training data. The training data were divided into training and validation datasets.

In the logistic regression, we applied a grid search to regulate the hyperparameters of the coefficient. In random forests, we also employed a grid search to utilize the model with 500 decision trees for the maximum depth of each decision tree and explanatory variable applied to classification in the node arrangement. As for the GBDT, we investigated the number of leaves and the needed data in each leaf with a grid search to develop the model. Regarding the MLP, we applied a four-layer neural network with each layer of 256 perceptrons to the stochastic gradient descent. In terms of hyperparameter optimization, learning rate, the dropout ratio of perceptrons, and batch size were tested with a grid search. The validation data were utilized to assess the termination mark of the training with the early stopping protocol in the MLP. The logistic regression and machine-learning analyses were performed with Python (version 3.7.7) and R (version 4.1.3) scripts.

Following the training and hyperparameter optimization, the prediction models were processed using all testing datasets, and we calculated the AUROC for each model. Regarding the output value of the machine-learning model, isotonic regression was applied to the probability calibration with the validation data at each phase of cross-validation to assume the evaluation of predictive capacity for future data. Therefore, the average of the output values of these models created with cross-validation was utilized to calculate the concluding AUROC. We also calculated the area under the precision–recall curve (AUPRC) for each model as per the prediction assignment with imbalanced data. With regard to a precise comparison of prediction analyses in binary classification with imbalanced data, AUPRC is more descriptive than AUROC [30]. Shapley additive explanations (SHAP) values were also calculated for the GBDT to identify the significant variables with the SHAP module of Python [31].

# RESULTS

Between July 2010 and June 2020, 9,304 patients who underwent emergency colorectal surgery were registered in the database. Of these patients, 512 were excluded because they did not undergo surgery within 3 days after admission (n = 109) and/or had missing variables (n = 403). The 8,792 remaining patients were included in the analysis, including 6,564 patients in the training/validation and 2,228 in the testing dataset (Fig. 1). Detailed statistics of the variables in the preprocessed training/validation dataset and the testing dataset are shown (Table 1).

The proportion of in-hospital mortality was 11.9% (778/6,564) for the training/validation dataset and 11.3% (251/2,228) for the testing dataset. Following the model training, the AUROC and the AUPRC were obtained based on the results of the analyses using 46 variables with developed machine-learning models against the testing dataset. Accordingly, the AUROC values of 0.742 [95% CI, 0.718–0.770], 0.782

[95% CI, 0.754–0.817], 0.814 [95% CI, 0.784–0.843], and 0.768 [95% CI, 0.724–0.799] and the AUPRC values of 0.325 [95% CI, 0.299–0.354], 0.396 [95% CI, 0.368–0.428], 0.406 [95% CI, 0.371–0.433], and 0.339 [95% CI, 0.304–0.361] were respectively calculated for the logistic regression, the random forests, the GBDT, and the MLP (Fig. 2a, 2b). Consequently, the prediction model generated with the GBDT demonstrated the best AUROC and AUPRC values; otherwise, other models revealed a modest discrepancy in the values.

We also calculated SHAP values for the GBDT to scrutinize the relevance of the variables and the validity of the prediction model with the internal algorithm. As a result, age, colorectal cancer, laparoscopy use, and some laboratory variables, including serum lactate dehydrogenase (LDH), serum albumin, and blood urea nitrogen (BUN), were listed high (Fig. 3a, 3b).

# DISCUSSION

Management of emergency surgical colorectal diseases is challenging, and the significant discrepancy in postoperative mortality rates between elective colonic resections (1–3%) and procedures emergently performed (12–20%) implies that multiple factors are supposed to be associated with [2, 3].

In the current study, we successfully introduced the machine-learning prediction model of in-hospital mortality after emergency colorectal surgery with an extensive database including 8,792 patients in 42 community hospitals in Japan. In the analyses, we employed the 46 variables, including baseline characteristics, namely, age, sex, weight, height, body mass index at admission, length of stay to surgery, surgery type, indication for surgery, 10 comorbidities, and 20 laboratory variables on admission to generate the prediction model of in-hospital mortality, using the machine-learning models which demonstrated preferable values for AUROC, AUPRC, and capacity of risk stratification. Although several studies have predicted in-hospital mortality using logistic regression with laboratory values on admission [7, 20, 21, 22], comparative studies for machine-learning analyses with linear and nonlinear feature extraction have been unsatisfactory. Our prediction models can achieve high performance by analyzing sufficient data, using machine-learning analyses that can handle nonlinear classification and competent optimization of hyperparameters.

In this study, the assessment of SHAP values for each variable enables us to visualize their significance in the testing dataset, which demonstrated that the patient’s age is a robust predictor of in-hospital mortality after emergency colorectal surgery. Most studies have acknowledged that age is a significant risk factor to be recognized in the preoperative assessment [20, 21, 22]. Since older age is also associated with other comorbidities contributing to postoperative complications, the combination with other risk factors can result in higher mortality rates.

This study also demonstrated that colorectal cancer is relevant to in-hospital mortality. Some preexisting reports have revealed that the dissemination and cancer stage significantly increase mortality in a short period [20, 21, 23]. Despite the lack of data on the cancer stage in this study, it is considered to be a crucial prognosis-related factor.

Moreover, the in-hospital mortality rates are higher in patients who underwent open procedures than in those who underwent laparoscopic procedures. Similarly, previous studies have shown a remarkably lower chance of death in patients with laparoscopic colectomy than those undergoing open colectomy. Although clarifying the rigorous explanation for this significantly lower mortality risk among patients with laparoscopic surgery is complex, underlying factors can exist within the database, including unmeasured selection bias or comorbidities. Regarding other laparoscopic colorectal surgery studies, faster recovery times, a lower rate of complication, and a less frequent necessity for additional surgical intervention can contribute to a reduction in mortality [32, 33].

This study also manifested that LDH, serum albumin, and BUN are essential variables in predicting in-hospital mortality among the data we applied to generate the machine-learning models, which is in accordance with some previous studies enrolling patients with sepsis or emergency colorectal surgery [14, 15, 20, 34]. Although this implies the coherence of the prediction models with internal algorithms with existing studies, the results of this study do not necessarily justify the cause-and-effect relationship between variables and outcomes. Therefore, in actual clinical situations, prioritizing risk assessment with existing prediction models confirmed to be clinically established, as well as a reassessment of patients in the postoperative period, is essential.

This study has several limitations. First, our predictive model does not necessarily include all the predictive variables associated with in-hospital mortality and may have needed to be measured more. For instance, we were not able to access the operation records; therefore, operative details still need to be obtained. Pharmaceutical or anesthesiologic methods and other measures might be relevant to an increase in the chance of different patient outcomes. Moreover, complications of surgical techniques may cause postoperative complications or directly influence mortality. As a result, the AUROC of the prediction models did not exceed as high as we expected. Second, although surgery type and indication for surgery were included in the analyses, we did not consider the diagnosis to predict in-hospital mortality. As a result, the prediction capacity may range depending on groups with different diagnoses. Accordingly, the significance of each variable in the in-hospital mortality prediction is not ensured for the diagnostic groups with this model.

Additionally, the patients enrolled in this Japanese study were skinny, with an average BMI of 21.3 ± 4.2 kg/m2. The association between in-hospital mortality and outcomes of emergency colorectal surgery might be different in obese patients, as some studies demonstrated that severe obesity contributes to in-hospital mortality [35, 36].

As for the clinical implications, this study focused on risk stratification. The study findings can be utilized to manage patients who need emergency colorectal surgery more effectively regarding the material, human, and time-course resources. And also, they can provide the patients and the family members with their prognosis more precisely than before as a part of informed consent prior to surgery. In terms of research connotations, further research is necessary to examine whether patient outcomes can be intervened by improvement in mortality. On the other hand, Machine-learning analyses are capable of the inclusion of nonlinear interactions with predictors, which cannot be addressed with conventional methods such as logistic regression. Therefore, they can be a satisfactory option for dealing with various kinds of data regarding accurate prognostic models and clinical decision support.

# CONCLUSION

In this study, we generated a model that predicts in-hospital mortality after emergency colorectal surgery with high predictive performance using machine-learning analyses with 46 clinical variables, including baseline characteristics on admission. This machine-learning model can be used to evaluate the in-hospital mortality risk of patients who undergo emergency colorectal surgery.

# Abbreviations

AUPRC: area under the precision–recall curve

AUROC: area under the receiver operating characteristic curve

BMI: body mass index

BUN: blood urea nitrogen

GBDT: gradient-boosting decision trees

ICD-10: International Classification Disease 10th revision

LDH: lactate dehydrogenase

MLP: multilayer perceptrons

COPD: chronic obstructive pulmonary disease

POSSUM: Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity

SHAP: Shapley additive explanations

# Declarations

Ethics approval and consent to participate

The study was approved by the Tokushukai Group Joint Ethics Committee and the Research Promotion Center at Tokyo Women’s Medical University in accordance with the tenets of the Declaration of Helsinki.

Informed consent

The requirement for informed consent from the study subjects was waived by the Tokushukai Group Joint Ethics Committee due to the retrospective study design.

Competing interests

The authors declare that they have no competing interests.

Study methods

All methods were performed in accordance with the relevant guidelines and regulations.

Availability of data and materials

The data that support the findings of this study are available from the Tokushukai Medical Database. But restrictions are applied to the availability of the data which were used under license for the current study and are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the Tokushukai Medical Database. Katsunori Miyake (kmiyake17@gmail.com) is the correspondence of the data management, who should be contacted if someone wants to request the data from this study.

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Author's contributions

Shota Akabane, Katunori Miyake, and Masao Iwagami had full access to all the data in the study and take responsibility for the integrity and accuracy of the data. Shota Akabane drafted the manuscript. Shota Akabane, Katunori Miyake, Masao Iwagami, Kazunari Tanabe, and Toshio Takagi contributed to the concept and the design and the interpretation of the results as well as improved the manuscript.

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# Table

Table 1 is available in the Supplementary Files section.

# Figures

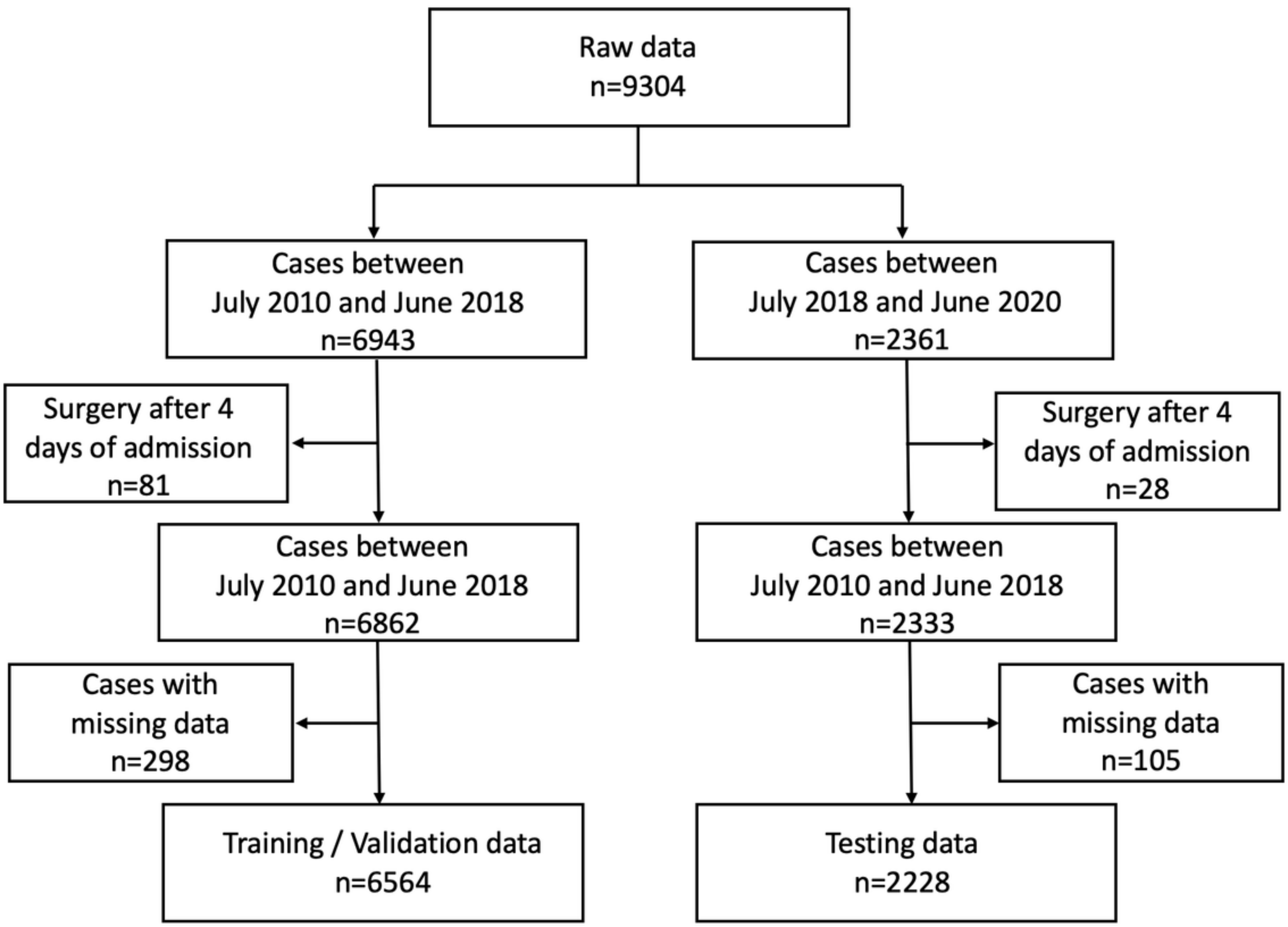
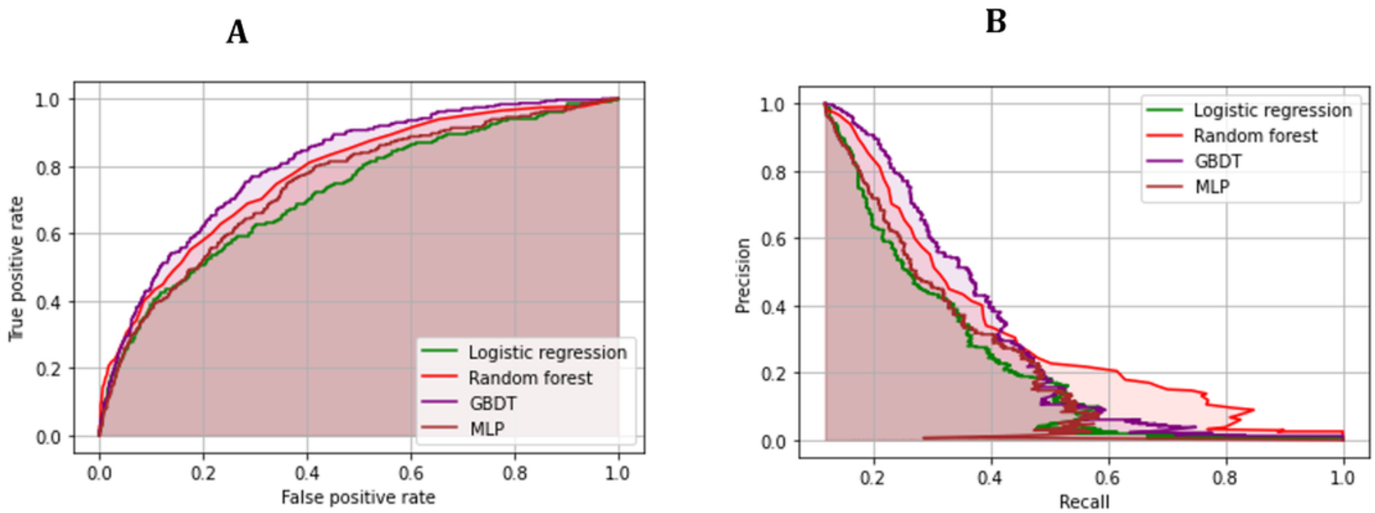



**Figure 1**

Schema of selection of the study participants and data processing.




| | AUROC (95%CI) |
|---|---|
| Logistic regression | 0.742 (0.718-0.770) |
| Random forest | 0.782 (0.754-0.817) |
| GBDT | 0.814 (0.784-0.843) |
| MLP | 0.768 (0.724-0.799) |

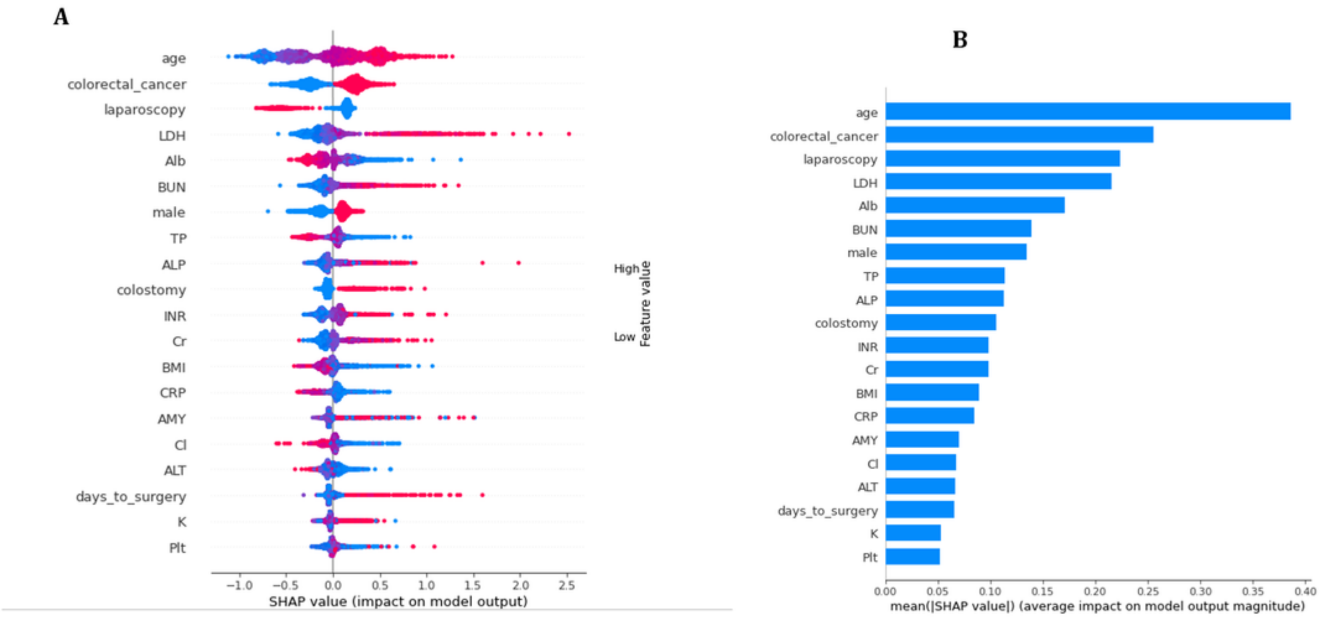
| | AUPRC (95%CI) |
|---|---|
| Logistic regression | 0.325 (0.299-0.354) |
| Random forest | 0.396 (0.368-0.428) |
| GBDT | 0.406 (0.371-0.433) |
| MLP | 0.339 (0.304-0.361) |

## Figure 2

The receiver operating characteristics curve and the area under the receiver operating characteristic (AUROC) curve of the models.

(A) The receiver operating characteristics curve and the area under the receiver operating characteristic (AUROC) curve of the models are shown. The results of the prediction using all testing data are described. The AUROC is demonstrated with a 95% confidence interval.

(B) The precision-recall curve and the area under the precision-recall (AUPRC) curve of the models are shown. The results of the prediction using all testing data are described. AUPRC is demonstrated with a 95% confidence interval.




### Figure 3

The Shapley addictive explanations (SHAP) values of the top 20 variables according to the result of the gradient-boosting trees.

(A) The bar graph demonstrates the mean total value of the SHAP value for each variable in order of the average absolute value of the SHAP value.

(B) The distribution of the SHAP value was also calculated with the testing dataset. Each plot indicates one prediction result in the testing dataset. The color of plots shows variable values as shown in color scale bars. In the figure, a positive SHAP value in the red plot contributes to in-hospital mortality. A negative SHAP value, which appears as the blue plot, implies the opposite.

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.pdf
- Suppl1.png
- Suppl2.png