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Research article

# Machine learning algorithm for predicting 30-day mortality in patients receiving rapid response system activation: A retrospective nationwide cohort study

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ABSTRACT

This study investigated the accuracy of a machine learning algorithm for predicting mortality in patients receiving rapid response system (RRS) activation. This retrospective cohort study used data from the In-Hospital Emergency Registry in Japan, which collects nationwide data on patients receiving RRS activation. The missing values in the dataset were replaced using multiple imputations (mode imputation, BayseRidge sklearn. linear model, and K-nearest neighbor model), and the enrolled patients were randomly assigned to the training and test cohorts. We established prediction models for 30-day mortality using the following four types of machine learning classifiers: Light Gradient Boosting Machine (LightGBM), eXtreme Gradient Boosting, random forest, and neural network. Fifty-two variables (patient characteristics, details of RRS activation, reasons for RRS initiation, and hospital capacity) were used to construct the prediction algorithm. The primary outcome was the accuracy of the prediction model for 30-day mortality. Overall, the data from 4,997 patients across 34 hospitals were analyzed. The machine learning algorithms using LightGBM demonstrated the highest predictive value for 30-day mortality (area under the receiver operating characteristic curve, 0.860 [95 % confidence interval, 0.825–0.895]). The SHapley Additive exPlanations summary plot indicated that hospital capacity, site of incidence, code status, and abnormal vital signs within 24 h were important variables in the prediction model for 30-day mortality.

*Abbreviations:* RRS, rapid response system; ICU, intensive care unit; GBM, Gradient Boosting Machine; XGBoost, eXtreme Gradient Boosting; GCS, Glasgow coma scale; $SpO_2$, percutaneous oxygen saturation; NEWS, National Early Warning Score; ROC, receiver operating characteristics; AUC, area under the curve; CI, confidence interval; SHAP, SHapley Additive exPlanations; DNAR, do not attempt resuscitation.

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## 1. Introduction

Worldwide implementation of the rapid response system (RRS) has promoted early identification of and prompt intervention for clinically deteriorating patients, thereby reducing the rate of adverse events and improving outcomes [1]. Clinical decisions following RRS activation should be based on risk stratification, patient background, and the quality of end-of-life care to optimize the efferent functions of the RRS [2–5]. Therefore, accurate mortality prediction models are expected to provide healthcare providers with reliable justifications for selecting appropriate candidates for further interventions and influencing clinical policies, including withholding or withdrawing therapeutic interventions.

With the development of artificial intelligence, machine learning algorithms allow the prediction of both clinical deterioration in hospitalized patients and clinical outcomes in patients following in-hospital cardiac arrest with more accuracy than before [6–9]. A previous study reported a machine learning model for predicting mortality in patients receiving RRS activation using registry data from the United States [10]. However, the model had unsatisfactory accuracy, with an area under the receiver operating characteristic curve (AUC) of 0.78, indicating the need for a more accurate prediction model.

The code status and comorbidities, which were not included in the construction of the previous machine learning algorithm [10], may potentially refine the performance of the prediction model. Our previous studies also demonstrated that timing, location, and facility characteristics were associated with outcome severity in patients receiving RRS activation [11,12]. Therefore, these findings indicate that using patient demographics, including code status and comorbidities, detailed information on RRS activation, and hospital characteristics could improve the accuracy of the prediction model. However, reports on machine learning algorithms that use these variables are rare.

We hypothesized that machine learning algorithms using a wide range of variables could predict mortality in patients receiving RRS activation with higher accuracy and identify important variables for the prediction model. Therefore, this study evaluated the accuracy of a machine-learning model for predicting 30-day mortality using data from an online registry of patients receiving RRS activation in Japan.

## 2. Materials and methods

### 2.1. Participants and study design

This retrospective cohort study used a Japanese nationwide online registry of patients receiving RRS activation, specifically the In-Hospital Emergency Registry (IHER-J) [12–16]. IHER-J, which is supported by the Japanese Society of Intensive Care Medicine and the Japanese Society for Emergency Medicine, is registered in the

University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR) (UMIN000012045, registered on October 16, 2013). All patients registered in the IHER-J who received RRS activation in 35 hospitals between April 2014 and March 2018, including inpatients, outpatients, and individuals within hospital facilities were enrolled in this study. The exclusion criteria were data registration from hospitals without an intensive care unit (ICU) and missing 30-day mortality data.

This study's protocol was reviewed and approved by the Ethics Committees of all 35 participating institutions in Japan (Institutional Review Board number: 2498) at the St. Marianna University School of Medicine, Japan, which is the representative of the IHER-J. The requirement for written informed consent was waived by the Institutional Review Board in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan.

### 2.2. Data collection and definition

Fifty-two input variables (Supplemental Table 1) were collected from the data registry. These variables included 1) baseline patient characteristics (age, sex, code status, department, existing comorbidity [malignancy, postoperative, sepsis, obstetric disease, and congenital heart disease], cardiac arrest, vital signs [body temperature, systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, percutaneous oxygen saturation ($SpO_2$), and Glasgow coma scale (GCS)], abnormal vital signs within 24 h, and repeated activation); 2) details of RRS activation (month of RRS activation, weekend or holiday, time of day, period of RRS activation-arrival, period of RRS activation-end, activator [physician, nurse, and others], site of incidence [general ward, high care unit, outpatient department, emergency room, examination/treatment room, and public space]); 3) reasons for RRS activation (desaturation, altered mental status, staff concern, hypotension, tachypnea, dyspnea, tachycardia, bradycardia, bradypnea, airway obstruction, cyanosis, seizure, inability to contact the attending physician, anaphylaxis, decreased urine output, uncontrollable pain, agitation, trauma, nausea, suicide attempt, or other reasons) and the number of reasons for RRS activation; and 4) hospital capacity, defined as the number of hospital beds for inpatients. Abnormal vital signs were defined as heart rate of $\geq$130 or $<$40 beats/min, respiratory rate of $\geq$28 or $<$8 times/min, systolic blood pressure of $<$90 mmHg, $SpO_2$ of $<$90 %, and altered mental status.

#### 2.2.1. Imputation of missing values

The missing values in the single dataset were replaced using the following multiple imputations: mode imputation for code status; BayseRidge sklearn. linear model for numerical data including age, respiratory rate, heart rate, blood pressure, and GCS; and K-nearest neighbor model for other numerical parameters, including $SpO_2$, body temperature, period of RRS activation-arrival, and period of RRS activation-end.

### 2.3. Statistical analyses

Four types of classifiers (Light Gradient Boosting Machine (LightGBM), eXtreme Gradient Boosting (XGBoost), random forest, and neural network) were used to develop machine learning algorithms for predicting 30-day mortality. Logistic regression analysis with the National Early Warning Score (NEWS) was compared with the four machine learning models as a control. After imputing missing values, the dataset was randomly assigned into training (75 %) and test (25 %) cohorts using scikit-learn train_test_split in accordance with the common method of dividing machine learning data [17]. In the training cohort, four-fold cross-validation was used to conduct hyperparameter optimization and determine the algorithm with the highest predictive performance for each model. After developing the machine learning algorithms using the training cohort, the established algorithms were applied to the test cohort. We evaluated the importance of the features in the machine learning model based on the SHapley Additive exPlanations (SHAP) value. The SHAP values of the established prediction algorithm were calculated using 20 features (hospital capacity, site of incidence, code status, abnormal vital signs within 24 h, systolic blood pressure, $SpO_2$, heart rate, department, age, GCS, malignancy, diastolic blood pressure, respiratory rate, month of RRS activation, verbal response in the GCS, RRS activation-end period, motor response in the GCS, time of day, sex, and activator) (Fig. 1).

Data are expressed as median (interquartile range) for continuous variables and absolute numbers and percentages for categorical variables. The performance of the model was evaluated using the AUC, sensitivity, accuracy, and specificity. Statistical significance was set at $P < 0.05$. All statistical analyses were conducted using Python 3.9.16 packages to construct the machine learning models on a computer (central processing unit; Intel (R) Xeon (R) CPU @ 2.20 GHz).

## 3. Results

### 3.1. Patient characteristics

Of the 6,784 RRS events in the registry, patients from hospitals without an ICU (n = 900) and those with missing mortality data (n = 887) were excluded. The entire cohort of 4,997 patients was randomly assigned into the training [3,747 patients (75.0 %)] and test [1,250 patients (25.0 %)] cohorts (Fig. 2). The 30-day mortality of the entire cohort was 14.8 %. Furthermore, the baseline characteristics, details of RRS activation, and reasons for RRS activation were comparable between the two cohorts (Tables 1 and 2, Supplemental Table 2).

### 3.2. Prediction of 30-day mortality in patients receiving RRS activation

The prediction algorithm for 30-day mortality using LightGBM showed the highest predictive value in the test cohort, with an AUC of 0.860 (95 % confidence interval [CI], 0.825–0.895) (Fig. 3, Table 3). Additionally, the AUC of the logistic regression analysis using the NEWS was 0.627 (95 % CI, 0.581–0.673).

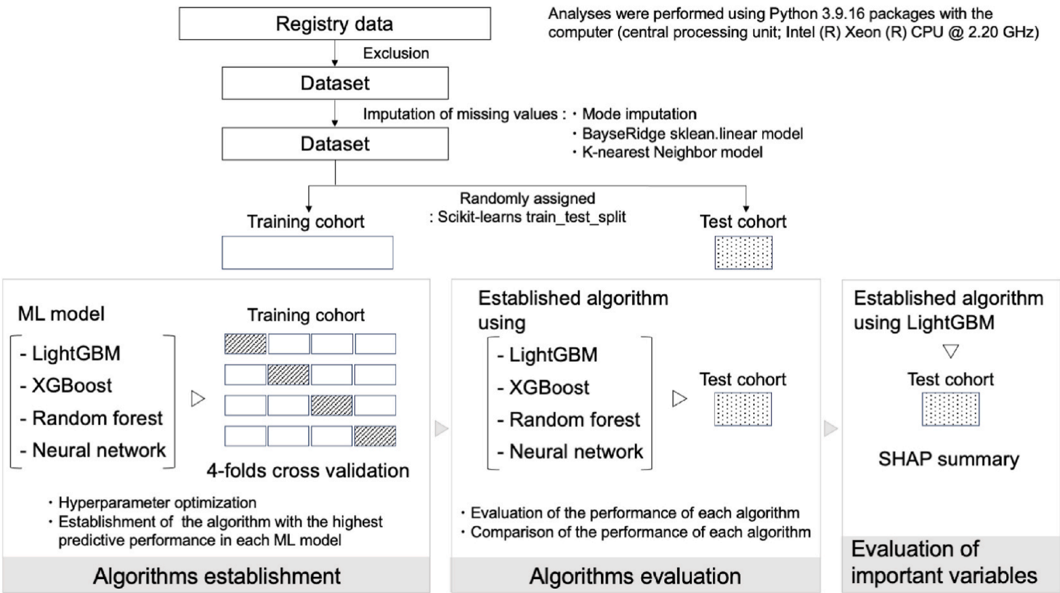


**Fig. 1.** Flowchart of the analysis process.
ML, machine learning; GBM: Gradient Boosting Machine, XGBoost, eXtreme Gradient Boosting, SHAP: SHapley Additive exPlanations.

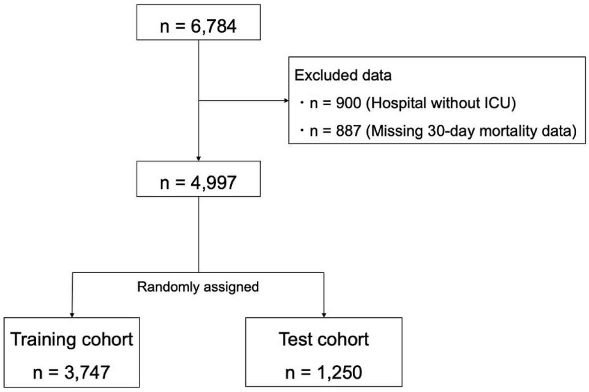


**Fig. 2.** Flow diagram of participant selection
ICU: intensive care unit.

**Table 1**
Baseline characteristics and outcome of the patients.

| | Training cohort (n = 3747) | Test cohort (n = 1250) |
|---|---|---|
| Demographic data | | |
| Age, years | 72 (60–80) | 72 (59–80) |
| Male, *n* (%) | 2259 (60.3) | 707 (56.6) |
| Code status, *n* (%) | | |
| DNAR | 297 (7.7) | 105 (7.0) |
| Partial DNAR | 119 (3.0) | 34 (3.4) |
| Full code | 2684 (73.7) | 921 (72.3) |
| Department, *n* (%) | | |
| Medical | 1850 (49.4) | 665 (53.2) |
| Surgical | 1220 (32.6) | 381 (30.5) |
| Others | 662 (17.7) | 200 (16.0) |
| Existing comorbidity, *n* (%) | | |
| Malignancy | 826 (22.0) | 282 (22.6) |
| Postoperative | 494 (13.2) | 152 (12.2) |
| Sepsis | 334 (8.9) | 126 (10.1) |
| Obstetric diseases | 78 (2.1) | 22 (1.8) |
| Congenital heart diseases | 22 (0.6) | 11 (0.9) |
| Vital signs | | |
| Cardiac arrest | 232 (6.2) | 91 (7.3) |
| Body temperature (°C) | 37.0 (36.5–37.7) | 36.9 (36.5–37.6) |
| Systolic blood pressure (mmHg) | 113 (84–138) | 111 (84–138) |
| Diastolic blood pressure (mmHg) | 65 (49–80) | 65 (50–80) |
| Heart rate (beats/min) | 94 (71–119) | 91 (71–115) |
| Respiratory rate (times/min) | 23 (16–30) | 23 (16–30) |
| Saturation of percutaneous oxygen (%) | 95 (86–98) | 95 (97–98) |
| Glasgow coma scale | 13 (7–15) | 13 (7–15) |
| Abnormal vital signs within 24 h, *n* (%) | 1142 (30.5) | 390 (31.2) |
| Outcome | | |
| 30-day mortality, *n* (%) | 555 (14.8) | 185 (14.8) |

DNAR: do not attempt resuscitation.

### *3.3. Important prognostic variables*

Since the performance of the LightGBM model was superior to that of the other three machine learning models for predicting 30-day mortality, we used it to determine the importance of the variables. The SHAP summary plot showed that "hospital capacity," "site of incidence," "code status," and "abnormal vital signs within 24 h" were the most important predictors of 30-day mortality in patients receiving RRS activation, followed by "systolic blood pressure" and "heart rate." The association between the feature and SHAP values indicated a positive and negative impact on the predictors of 30-day mortality. The extent of the values is depicted as red (positive) and blue (negative) plots. "Hospital capacity" was the most important factor, although no unidirectional correlation was found between hospital capacity and 30-day mortality. Regarding the "site of incidence (as categorical variables: 1, general ward; 2, high care unit; 3, outpatient department; 4, emergency room; 5, examination/treatment room, and 6, public space/others)," the results showed that some groups with higher numbers in the classification tended to have a better prognosis than others. The results showed that some groups with higher numbers in "code status (as categorical variables: 1, do not attempt resuscitation (DNAR); 2, partial DNAR; and 3,

**Table 2**
Details of the rapid response system activation.

| | Training cohort (n = 3747) | Test cohort (n = 1250) |
|---|---|---|
| Weekend or holiday, *n* (%) | 832 (22.2) | 247 (19.8) |
| Time of day, *n* (%) | | |
| 9:00–16:59 | 2044 (54.6) | 676 (54.1) |
| 17:00–0:59 | 927 (24.7) | 307 (24.60) |
| 1:00–8:59 | 776 (20.7) | 267 (21.4) |
| Period of RRS activation-arrival, min | 5 (2–6) | 5 (3–7) |
| Period of RRS activation-end, min | 37 (22–64) | 37 (21–61) |
| Activator, *n* (%) | | |
| Physician | 850 (22.7) | 325 (26.0) |
| Nurse | 1790 (47.8) | 569 (45.5) |
| Others | 185 (4.9) | 50 (4.0) |
| Site of incidence, *n* (%) | | |
| General ward | 2431 (64.9) | 812 (65.0) |
| High care units | 376 (10.0) | 121 (9.7) |
| Outpatient department | 321 (8.6) | 103 (8.2) |
| Emergency room | 153 (4.1) | 50 (4.0) |
| Examination/treatment room | 318 (8.5) | 114 (9.1) |
| Public space/others | 148 (3.9) | 50 (4.0) |

RRS: rapid response system.

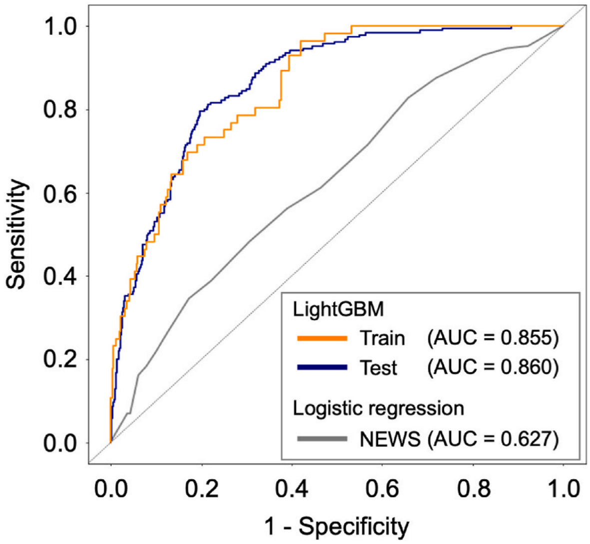


**Fig. 3.** Receiver operating characteristic curve of the prediction models for 30-day mortality in patients receiving RRS activation.
The receiver operating characteristic (ROC) curve and area under the curve for 30-day mortality in patients receiving rapid response system (RRS) activation were obtained using machine learning models (LightGBM) and logistic regression. NEWS: National Early Warning Score.

**Table 3**
Performance of predictive model algorithms for 30-day mortality in patients with rapid response system activation.

| Model | Training cohort | | Test cohort | | | | Time (s) |
|---|---|---|---|---|---|---|---|
| | AUC | Cross-validation | AUC (95 % CI) | Sensitivity | Accuracy | Specificity | |
| Machine learning | | | | | | | |
| LightGBM | 0.855 | 0.820 | 0.860 (0.825–0.895) | 0.714 | 0.810 | 0.826 | 19.8 |
| XGBoost | 0.816 | 0.784 | 0.842 (0.806–0.879) | 0.665 | 0.782 | 0.802 | 19.6 |
| Random forest | 1.000 | 0.809 | 0.838 (0.801–0.875) | 0.757 | 0.757 | 0.757 | 334.1 |
| Neural network | 0.792 | 0.727 | 0.815 (0.777–0.854) | 0.654 | 0.771 | 0.792 | 131.7 |
| Ensemble | NA | NA | 0.860 | 0.719 | 0.801 | 0.815 | 505.3 |
| Logistic regression | | | | | | | |
| NEWS | NA | NA | 0.627 (0.581–0.673) | NA | NA | NA | NA |

AUC, area under the receiver operating characteristic curve; CI, confidence interval; GBM: Gradient Boosting Machine; XGBoost, eXtreme Gradient Boosting; NEWS: National Early Warning Score; NA, not applicable.

full code)" tended to have a better prognosis than others. For "abnormal vital signs within 24 h (as categorical variables: 0, absence and 1, presence)," the results showed that some groups with a higher number in the classification tended to have a worse prognosis than others (Fig. 4).

## 4. Discussion

In this study, machine learning algorithms predicted 30-day mortality in patients receiving RRS activation with high accuracy using patient demographics, details of RRS activation, and hospital characteristics. Important variables for the prediction model included hospital capacity, site of incidence, code status, and abnormal vital signs within 24 h.

The accuracy of the machine learning models in predicting mortality in patients receiving RRS activation has been reported in two separate studies [10,18]. A previous study using the National Get with the Guidelines Medical Emergency Team registry, which is a large database of patients receiving RRS activation in the United States, reported that the AUC of the prediction model for in-hospital mortality among 282,710 hospitalized adult patients across 274 institutions was 0.78 [10]. In this study, systolic blood pressure, time since admission, and respiratory rate were reportedly the most important variables. Another study of 2,061 adult patients who were hospitalized after RRS activation at two Canadian tertiary care hospitals revealed that the prediction model for in-hospital mortality had an AUC of 0.77, with important predictors including age, platelet count, temperature, creatinine level, and neutrophil count [18]. The prognostic algorithms used in the present study demonstrated a higher predictive value for mortality in patients receiving RRS activation than those of previous studies. This high accuracy can be attributed to a wide range of variables, including patient demographics, details of RRS activation, and hospital characteristics. Furthermore, the population was expanded to include all clinically deteriorating patients, including inpatients, outpatients, and individuals within hospital facilities. Therefore, the higher predictive performance in this expanded population indicates that the algorithms used in the present study may be more useful in real-world situations than the previous ones.

The algorithm used in the present study identified hospital capacity, site of incidence, code status, and abnormal vital signs within 24 h as important variables, which may explain the high accuracy of these models. Although the characteristics of hospitalized patients vary according to hospital capacity, hospital capacity is correlated with the quality of patient care and treatment [19]. A previous study reported that facilities with more inpatients have a higher incidence of unexpected adverse events [12], possibly because of the higher severity status and complexity of patients [20]. Consistently, the present study showed that a larger facility size was associated with a higher 30-day mortality. Therefore, because hospital capacity is a non-modifiable factor, hospitals should establish RRSs that can cover the number of incidence and severity status of patients according to their hospital size.

Previous studies reported that the site of incidence is associated with the severity status of patients receiving RRS activation. These studies documented a high number of patients with severe deterioration in examination/treatment areas such as angiography and dialysis rooms [21–23] and a low number of patients with severe deterioration in public areas [11]. In the present study, the site of incidence was one of the most important variables. The cluster with low 30-day mortality observed in the SHAP values included clinically deteriorating patients in public spaces, which is consistent with the findings of previous studies. These results suggest that the site of incidence is an important predictor of mortality, and efficient allocation of medical resources according to the location should be provided to achieve a more effective RRS.

The code status was also identified as an important prognostic variable in the present study, which is expected since clinical outcomes change according to treatment limitations. Although RRS aims to improve the outcomes of deteriorating patients, end-of-life care has recently been recognized as an essential consideration in RRS [2–5]. The algorithm in the present study, which includes code status, is significant not only for predicting prognosis but also for reassigning code status after deterioration.

Previous studies have reported that abnormal vital signs and other physiological parameters are observed in many deteriorating patients before RRS activation [24,25] and delays in RRS activation are associated with poor outcomes [26,27]. Accordingly, we identified abnormal vital signs within 24 h as an important prognostic variable for 30-day mortality. Therefore, our findings support the importance of recognizing signs in deteriorating patients and intervening in the RRS afferent limb without delay.

Despite the strengths of this study, including the wide range of variables in patients receiving RRS activation and the use of large multicenter registry data from Japan, some limitations should be considered. First, this study was limited to Japan. Therefore, the predictive accuracy should be validated in an international study. Second, although we used a nationwide registry, the number of participating facilities was small. Consequently, further validation using data from a broad range of facilities is required. Finally, we did not consider the various RRS in each facility or RRS intervention. Additionally, the potential heterogeneity of the RRS interventions could have affected the results of this study. Therefore, further similar international multicenter studies involving several medical institutions are required to make the results of this study more meaningful.

## 5. Conclusions

Our study shows that machine learning algorithms accurately predicted 30-day mortality in patients receiving RRS activation using important variables, including hospital capacity, site of incidence, code status, and abnormal vital signs within 24 h. However, further validation of these results is required to improve the quality of the RRS.

**Trial registration:** This multicenter RRS epidemiological study, using an online registry, was registered in the UMIN-CTR (UMIN000012045, registered on October 16, 2013).

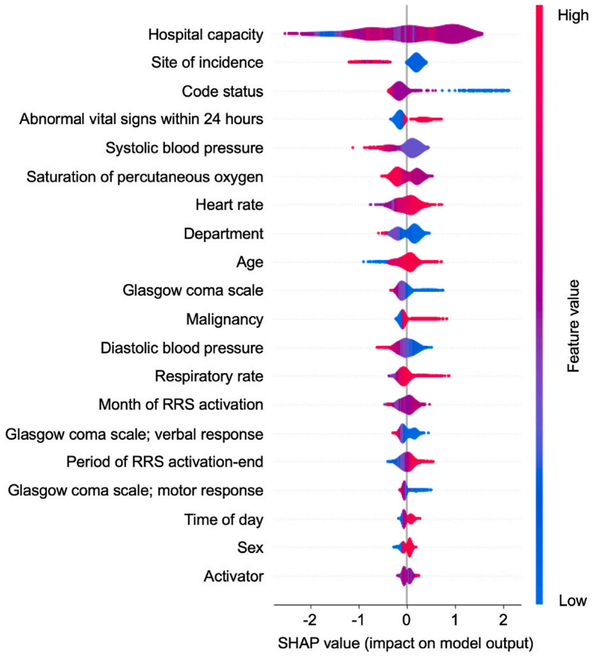


**Fig. 4.** SHAP values of the prediction model for predicting 30-day mortality in patients receiving RRS activation
The impacts of the 20 features on the model output for 30-day mortality in patients receiving RRS activation were expressed as SHAP values. The features are placed in descending order according to their importance. The association between the feature and SHAP values indicates a positive and negative impact on the predictors. The extent of this value is depicted in red (high) and blue (low). The categorical variables include site of incidence (1: general ward, 2: high care unit, 3: outpatient department, 4: emergency room, 5: examination/treatment room, and 6: public space/others); code status (1: do not attempt resuscitation [DNAR], 2: partial DNAR, and 3: full code); abnormal vital signs within 24 h (0: absence and 1: presence); department (1: medical, 2: surgical, and 3: others); malignancy (0: absence and 1: presence); time of day (1: 9:00–16:59, 2: 17:00–0:59, and 3: 1:00–8:59); sex (0: female and 1: male); and activator (1: physician, 2: nurse, and 3: others). RRS: rapid response system, SHAP: SHapley Additive exPlanations. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

## Ethics approval and consent to participate

The study protocol was reviewed and approved by the Ethics Committees of all 35 participating institutes in Japan (Institutional Review Board number: 2498) at St. Marianna University School of Medicine, Japan, which is the representative of the IHER-J. The Institutional Review Board waived the requirement for written informed consent in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. This multicenter RRS epidemiological study, using an online registry, was registered in the UMIN-CTR (UMIN000012045, registered on October 16, 2013).

## Consent for publication

Not applicable.

## Availability of data and materials

The datasets used and/or analyzed in the present study are available from the corresponding author upon reasonable request.

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## Data availability statement

Data will be made available on request.

## CRediT authorship contribution statement

**Takeo Kurita:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Takehiko Oami:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Yoko Tochigi:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Keisuke Tomita:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Takaki Naito:** Writing – review & editing, Data curation. **Kazuaki Atagi:** Writing – review & editing, Data curation. **Shigeki Fujitani:** Writing – review & editing, Data curation. **Taka-aki Nakada:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32655.

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