

Original Article

Novel score for predicting early emergency endovascular therapy in trauma care using logistic LASSO regression

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Aim: To support decision-making for early interventional radiology, this study aimed to derive and validate a novel and simple scoring system for predicting the necessity of interventional radiology therapies in trauma patients.

Methods: This retrospective study used data derived from the medical records of patients with severe traumatic injuries treated at a tertiary-level emergency institution. The score was derived from 168 patients treated between April 2015 and October 2016 and validated using data from 68 patients treated between November 2016 and July 2017. Logistic “least absolute shrinkage and selection operator (LASSO)” regression was used to select predictors. In order to compose the score, odds ratios derived from the logistic model were simplified to integer score coefficients. The score was evaluated using the area under the receiver operating characteristic curve. The best cut-off point for the score was determined using Youden’s index, and sensitivity and specificity were calculated.

Results: The derived score comprised three predictors (systolic blood pressure, positive findings in abdominal ultrasound assessment, and pelvic fracture) and ranged from 0 to 30. On validation, the area under the receiver operating characteristic curve for the score was 0.86 (95% confidence interval, 0.64–1.00). The sensitivity and specificity were 80% and 89%, respectively, with a cut-off point of 3.

Conclusion: This simple score, requiring variables obtainable immediately after hospital arrival, could aid in facilitating early interventional radiology team activation.

Key words: Decision-making, interventional radiology, LASSO regression, nonoperative management, trauma

INTRODUCTION

INTERVENTIONAL RADIOLOGY HAS become increasingly important for blunt trauma treatment.¹ Early interventional radiology team activation is crucial because increased door-to-angioembolization time is associated with poor prognoses.^{2–4} The rapid imaging capabilities of modern computed tomography enable safe, whole-body scanning for trauma patients, even those with hemodynamic instability, providing information for treatment planning.^{5,6} However,

the lack of specific indicators, other than computed tomography, for predicting the necessity of interventional radiology hinders early decision-making. Despite a strong recommendation to have 24-h capability to perform endovascular procedures within 60 min of the decision,⁷ not all trauma centers have the resources (e.g., in-house radiologists) to follow it. Therefore, we aimed to devise a simple score based on the clinical and imaging information obtainable immediately after hospital arrival, which would support decision-making regarding early interventional radiology team activation, even prior to computed tomography scanning.

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METHODS

Study design

THIS RETROSPECTIVE OBSERVATIONAL study utilized patient medical records from a single tertiary

emergency care center that treats severely injured patients. We created a simple score for predicting the necessity of interventional radiology therapies by selecting a minimum set of independent variables using a penalized regression model to avoid overfitting. Specifically, we used logistic “least absolute shrinkage and selection operator (LASSO)” regression.^{8,9}

Study settings

In the Japanese prehospital care system, the ambulance crew undertakes field triage at the scene according to a standardized protocol¹⁰; patients with severe and urgent conditions are directly transferred to tertiary care centers, bypassing the nearby hospitals. At the center where this study was carried out, trauma patients with severe hemodynamic instability are indicated for emergency surgery; decisions regarding whether surgery or interventional radiology procedures should be performed are made by emergency physicians, radiologists, and trauma surgeons. Interventional radiology therapies are carried out by the interventional radiologist using a gelatin sponge, coil, or N-butyl-2-cyanoacrylate as embolic material, depending on the patients’ conditions.

Study participants

Among the directly transferred patients, we selected those who were treated and hospitalized due to blunt trauma and underwent whole-body computed tomography ($n = 253$) between April 2015 and July 2017. Of these patients, we excluded those who underwent laparotomy ($n = 14$) because emergency laparotomy was decided based on highly unstable hemodynamics and such cases have a limited possibility of being managed nonoperatively. Data from 171 patients treated between April 2015 and October 2016 were considered for inclusion in the model derivation group. Three participants with missing data were excluded. Finally, a total of 168 patients were included in the group. Subsequently, data were derived from 68 patients treated between November 2016 and July 2017 for inclusion in the model validation group.

Analyses

First, we created a predictive score, the Interventional Radiology Activation Score for Trauma (IRAS), for activating the interventional radiology team based on a logistic LASSO regression analysis using the data of the model derivation group; the dependent variable was whether interventional radiology embolization procedures were carried out. LASSO regression modeling constrains the sum of the absolute

values of estimated coefficients.^{8,9} This method shrinks the coefficients toward zero to alleviate the problem of overfitting by narrowing the very wide range of predicted risks caused by overfitting. In a logistic regression model

$$\text{Logit}(Y) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \dots + \beta_k X_k,$$

the sum of the coefficients should be less than lambda (λ):

$$\sum_{i=1}^k |\beta_i| \leq \lambda.$$

The LASSO modeling would shrink coefficient estimates of some variables exactly to zero (noise variables) to be used for variable selection (signal variables are selected).^{8,9} The lambda was determined using a grid search with 10-fold cross-validation. A grid of lambda values covering the entire range was chosen to calculate the cross-validation error (misclassification) for each lambda value.¹¹ Then we chose the lambda that provided the most parsimonious model within one standard error of the optimum value, which gives the minimum misclassification error, because our purpose was to derive a simple prediction model. We undertook these procedures using the *cv.glmnet* function of R.¹¹

The initial model included the following independent variables that reflected the hemodynamic and hemorrhagic conditions obtainable immediately after hospital arrival (physiological assessment, laboratory tests, and images) and that were included in a score to predict the necessity of massive transfusion (Traumatic Bleeding Severity Score [TBSS]¹²): age; systolic blood pressure (sBP) on admission; heart rate; hemoglobin level; lactate level; pH; a number of regions with positive findings on Focused Assessment with Sonography for Trauma (FAST), as determined by a trauma team consisting of trauma surgeons and emergency physicians; and the AO pelvic fracture severity classification by X-ray radiography, which was interpreted by a radiologist retrospectively. Although the Glasgow Coma Scale (GCS) indicates trauma severity, it was excluded because it is modified when brain injuries exist. Impaired consciousness without head injury indicates the severity of patients’ hemodynamic instability, and surgery is usually the choice of treatment in our institution. The independent variables were categorized and coded, as shown in Table 1. The variables included in the TBSS exactly followed the categories in the TBSS¹²; the other variables followed the principle of categorization in the TBSS. The range from normal to slightly outside the normal range was defined as 0, and categories were then created from the “0” category onward, based on clinical significance with easily separable boundaries without fractions. For example, the pH has boundaries

Table 1. Classification and coding of the variables

Coded values [†]	sBP at hospital arrival (mmHg)	Number of positive findings of FAST (region)	Pelvic fracture classification by X-ray [‡]	Lactate concentration (mmol/L)	Age (years)	pH	Hemoglobin concentration (g/dl)	Heart rate (b.p.m.)
0	110+	0	No fracture	<2.5	<60	7.3 to <7.5	11.0+	<100
1	100 to <110	1	Type A	2.5 to <5.0	60+	7.5 + or 7.2 to <7.3	9.0 to <11.0	100 to <120
2	90 to <100	2	Type B	5.0 to <7.5		7.1 to <7.2	8.0 to <9.0	120 to <140
3	<90	3	Type C	7.5+		<7.1	<8.0	140+
4		4						
5		5						
6		6						

FAST, focused assessment with sonography for trauma; sBP, systolic blood pressure.

[†]Variables included in the Traumatic Bleeding Severity Score (TBSS) (sBP, FAST, pelvic fracture, lactate, and age) were in accordance with the categories in the TBSS¹²; for the other variables, the range from normal to slightly outside the normal range was defined as 0, and categories were then created based on clinical significance with easily separable boundaries. The pH has boundaries of 7.3, 7.2, and 7.1 for acidosis and 7.5 for alkalosis; the finer categorization for acidosis than alkalosis (7.5+) is because of the importance of acidosis in evaluating shock status. Hemoglobin concentration has boundaries of 11.0, 9.0, and 8.0 g/dl (the category “1” has a wider range because the hemoglobin concentration of 9.0–11.0 g/dl indicates slight anemia if not normal). The heart rate has boundaries of 100, 120, and 140 b.p.m. with a range of 20 b.p.m. because it can easily fluctuate.

[‡]Classification according to the AO Foundation: Type A; intact posterior arch, Type B; incomplete posterior arch disruption, Type C; pelvic ring fracture with complete posterior arch disruption.

of 7.3, 7.2, and 7.1 for acidosis, and 7.5 for alkalosis (the rough categorization for alkalosis is because of the importance of pH in evaluating shock status).

The cross-validation depends on the random division of the participants into 10 groups, generating different estimates for each trial. Therefore, to obtain stable estimates, we ran 100 cross-validations and reported the mean values. The variable selections depended on the minimization of the misclassification errors in the cross-validation; therefore, *P*-values or confidence intervals were not reported. The odds ratios in the derived model were then simplified to integer score coefficients maintaining the ratios.

Second, we applied the score to the data of the validation group, calculated the area under the receiver operating characteristic curve (AUC), and determined the sensitivity and specificity at the best cut-off point of the score using Youden's index. The index is the sum of sensitivity and specificity minus one, which indicates the diagnostic performance of the test at a given cut-off point, ranging from 0 (no diagnostic value) to 1 (perfect diagnostic performance). The maximum value of the index determines the best cut-off point.

For statistical analysis, we used R version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria); the

glmnet package for LASSO regression provided the cv.glmnet function.¹¹ With the sample size of the validation group, alpha of 0.05, and power of 0.8, the minimum detectable AUC (significantly different from 0.5) was 0.82.

RESULTS

IN THE MODEL derivation group ($n = 171$), the median age was 47 years, 72.5% were men, and the median Injury Severity Score was 25. Of them, 31 patients needed interventional radiology procedures; the median procedure time was 65 min (interquartile range [IQR], 12–140 min), and the median time from hospital arrival to completion of hemostasis by the interventional radiology was 220 min (IQR, 137–620 min). Receiving interventional radiology therapies was associated with lower sBP, hemoglobin, and pH and higher serum lactate, heart rate, FAST-positive regions, and pelvic fracture (Table 2). In the validation group, the median age was 49 years, 72.0% were men, and the median Injury Severity Score was 19; five patients needed interventional radiology procedures.

The logistic LASSO regression analysis revealed that sBP, FAST findings, and pelvic fracture classification were signal variables, with odds ratios of 1.42, 3.90, and 3.80

Table 2. Demographic and clinical characteristics of patients in the development phase

	Interventional radiology therapy		P-value
	Required (n = 31)	Not required (n = 140)	
Age (years), median (IQR) [†]	46 (33–69)	47 (33–66)	0.494
Sex (male), n (%) [‡]	16 (51.6%)	99 (70.7%)	0.008
Injury severity score, median, (IQR) [†]	37 (9–57)	20 (4–75)	<0.001
Mortality, n (%) [‡]	5 (16.1%)	6 (4.3%)	0.030
Unit of packed blood transfusion, mean (SD) [§]	32 (29)	5.0 (11)	<0.001
Glasgow Coma Scale, median (IQR) [†]	14 (13–15)	15 (14–15)	0.083
Systolic blood pressure (mmHg), median (IQR) [†]	124 (105–130)	137 (122–158)	<0.001
Heart rate (b.p.m.), median (IQR) [†]	88 (78–112)	82 (74–100)	0.064
Lactate level (mmol/L), median (IQR) [†]	3.14 (2.04–4.10)	2.19 (1.54–2.86)	0.006
Hemoglobin level (g/dl), median (IQR) [†]	13.0 (11.3–14.3)	13.9 (13.0–14.9)	0.013
pH, median (IQR) [†]	7.41 (7.39–7.43)	7.42(7.39–7.45)	0.388
FAST examination (case) [‡]	0 region: 19 1 region: 9 2 regions: 2 3 regions: 0 4 regions: 1	0 region: 128 1 region: 11 2 regions: 1	<0.001
Pelvic fracture/AO classification, (case) [‡]	No fracture: 9 Type A: 12 Type B: 9 Type C: 1	No fracture: 125 Type A: 8 Type B: 6 Type C: 1	<0.001
Interventional radiology procedure time (min), median (IQR)	65 (57–90)	–	

FAST, Focused Assessment with Sonography for Trauma; IQR, interquartile range; SD, standard deviation.

[†] Mann–Whitney *U*-test.

[‡] χ^2 -test.

[§] *t*-test.

(coefficient estimates of 0.35, 1.36, and 1.34), respectively, with lambda of 0.04 and misclassification proportion of 0.13 (Table 3). The odds ratios were simplified to integer score coefficients of 1, 3, and 3, respectively. The product of the coefficient and the code of the corresponding category is the score for each component. A total of three-component scores constitutes the IRAS, ranging from 0 to 30.

When the IRAS was applied to the validation group, the AUC was 0.86 (95% confidence interval, 0.64–1.00), and its sensitivity and specificity were 80.0% and 88.9%, respectively, with a cut-off point of 3 (Fig. 1). The presence of a pelvic fracture, positive FAST finding, or hypotensive state (sBP < 90 mmHg) would reach the cut-off.

DISCUSSION

THE IRAS IS quite simple, requiring only three variables obtainable immediately after admission, but it could facilitate early interventional radiology team activation before computed tomography imaging. Its introduction

could improve the management of trauma patients by reducing delayed interventional radiology procedures, which are associated with an increased risk of mortality among hemodynamically unstable trauma patients.^{2–4}

This study used a relatively new method of LASSO regression modeling, which can mitigate overfitting issues that are likely to occur in deriving predictive models, particularly when there are a large number of candidate predictors and a small number of events.^{8,9} Overfitted models tend to show poor predictive abilities. When variables could not be narrowed down based on hypotheses or review of published reports before the model derivation analyses, univariate screening procedures or step-wise methods were typically used. These methods required repeated analysis to find out the best combination of predictors causing unstable variable selection (i.e., small changes in the data or model selection procedures could cause different models). On the contrary, LASSO regression modeling has the ability to select variables without causing overfitting problems by shrinking the coefficients. Having a function to identify simple models, it

Table 3. Odds ratios from logistic regression analysis and score coefficients

	Values in LASSO, mean (SD) [†]	Odds ratio [‡]	Score coefficients [§]
Model coefficients			
sBP	0.35 (0.08)	1.42	1
FAST findings	1.36 (0.20)	3.90	3
Pelvic fracture	1.34 (0.10)	3.80	3
Lambda	0.04 (0.01)		
Misclassification error proportion (cross-validation error)	0.13 (0.01)		

FAST, Focused Assessment with Sonography for Trauma; LASSO, least absolute shrinkage and selection operator; sBP, systolic blood pressure; SD, standard deviation.

[†]Results of the LASSO logistic regression analysis among the model derivation group ($n = 168$), excluding three participants with missing values. Mean values (SD) of 100 cross-validations are indicated.

[‡]These odds ratios were divided by 1.42, the smallest ratio, to obtain a ratio of 1.00:2.75:2.68, which was then approximated to obtain integer score coefficients of 1, 3, and 3, respectively.

[§]The IRAS is calculated as follows:

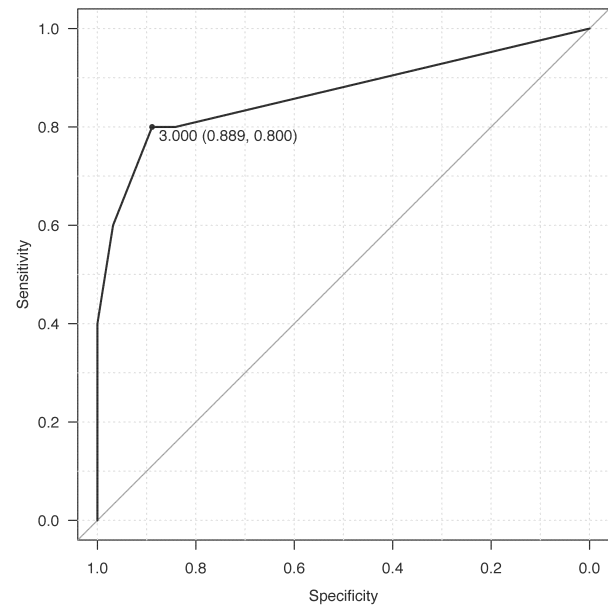
$$\text{IRAS} = \text{Code}_{\text{sBP}} \times 1 + \text{Code}_{\text{FAST}} \times 3 + \text{Code}_{\text{Pelvic}} \times 3$$

For example, the score for a patient with sBP of 80 mmHg ($\text{Code}_{\text{sBP}} = 3$), two regions of FAST positive ($\text{Code}_{\text{FAST}} = 2$), and no pelvic fracture ($\text{Code}_{\text{Pelvic}} = 0$) is:

$$\text{IRAS} = 3 \times 1 + 2 \times 3 + 0 \times 3 = 9$$

is a useful method when variable selection is required in model development.

The parameters used in this analysis were limited to those reflecting the patients' state and immediately obtainable after hospital arrival. Therefore, coagulation tests that require time to obtain test results were excluded. Additionally, despite the usefulness of the GCS in enhancing predictive abilities in various scores, the GCS was excluded from analysis for two reasons. First, it is not consistently included in scores. For example, it was excluded from a score for predicting massive blood transfusion for trauma patients.¹² Second, the GCS does not play an important role in determining the necessity of interventional radiology therapies in our institution, although it might influence the choice of embolization material. Unstable patients with poor consciousness go

**Fig. 1.** Receiver operating characteristic curve for the Interventional Radiology Activation Score for Trauma (IRAS) for predicting the necessity of interventional radiology therapies.

through emergency surgeries. Thus, our hypothetical independent variables did not include the GCS.

A key role of this score in real clinical settings is to show minimum standard in a very simple form, despite several tertiary-level medical institutions having their own protocol for activating the interventional radiology team. For example, the recently emerged hybrid emergency room system enables prompt computed tomography imaging, and rapid whole-body scanning provides accurate information for decision-making for surgery or interventional radiology therapies without FAST.^{5,6,13,14} However, it is not always feasible to maintain these systems in all medical institutions. Decision-making without computed tomography images is a norm, particularly in low- and middle-income countries with limited access to computed tomography imaging.^{15,16} In addition, the Eastern Association for the Surgery of Trauma or World Society of Emergency Surgery guidelines do not mention a specific scoring system for gathering the interventional radiology team.^{17,18} We believe that the IRAS has great significance in creating an objective criterion that is reproducible by each physician based on a common understanding, regardless of the size of the medical institution or the level of care. It is still meaningful to minimize treatment delays in facilities without a 24-h, in-house interventional radiologist.

Although this study focused on radiology team activation, the IRAS or its derivatives could be utilized to decide the

need for surgical interventions in initial care and the need for computed tomography scans at medical institutions with limited resources. Whereas trauma centers in high-income countries are usually staffed with in-house trauma surgeons and the trauma team is readily activated, many medical institutions worldwide remain poorly staffed (lacking surgeons or radiologists) and poorly equipped (lacking computed tomography scans).^{15,16} In such situations, tools, such as the IRAS, would aid in decision-making at an early stage without computed tomography images. For example, the IRAS with a higher cut-off point could be helpful in deciding the need for emergency laparotomy because patients with high hemodynamic instabilities and FAST-positive results, yielding a high score, would obviously require surgical interventions. Therefore, further studies on and modifications of the IRAS, in which different cut-off points or combinations of predictors (e.g., GCS) could be tested, would meet such needs.

The present study had several limitations. First, this study was based on retrospective data from a single center with a small sample size. Additional large-scale multicenter studies are required to further validate the accuracy of the IRAS and compare it to previous standards. Additionally, the current form of the IRAS, which requires pelvic radiography, cannot be used in prehospital settings; nonetheless, a minor modification from radiography to palpation to detect unstable pelvis can enable its use in prehospital settings. After hospital arrival, radiography can aid in identifying stable pelvic fracture undetected by palpation only.

CONCLUSIONS

THE IRAS COULD become a simple score used by any medical institution to enlist interventional radiology teams obtained before computed tomography imaging. Therefore, future prospective studies are required to validate our results by collecting data from various institutions.

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DISCLOSURE

APPROVAL OF THE research protocol with approval number and committee name: The study's protocol was approved by the ethics committee of Teikyo University School of Medicine.

Informed consent: Informed consent was waived due to the retrospective nature of this study.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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