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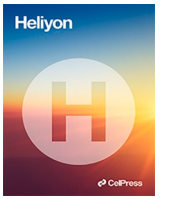

A clinical prediction model for non-operative management failure in patients with high-grade blunt splenic injury

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ABSTRACT

Background: Nonoperative management (NOM) is the standard treatment for hemodynamically stable blunt splenic injury (BSI). However, NOM failure is a significant source of morbidity and mortality. We developed a clinical risk scoring system for NOM failure in BSI.
Methods: Data from the Japanese Trauma Data Bank from 2008 to 2018 were analyzed. Eligible patients were restricted to those who underwent NOM with high-grade BSI (Organ Injury Scale ≥3). The primary outcome was a predictive score for NOM failure based on risk estimation.
Results: There were 1651 patients included in this analysis, among whom 110 (6.7%) patients had NOM failure. Multivariate analysis identified seven variables associated with failed NOM: systolic blood pressure, Glasgow coma scale, Injury Severity Score, other concomitant abdominal injury, pelvic injury, high-grade BSI, and angioembolization. An eight-point predictive score was developed with a cut-off of greater than 5 points (specificity, 98.2%; sensitivity, 25.5%) with an area under the curve of 0.81.
Conclusion: The clinical predictive score had good ability to predict NOM failure and may help surgeons to make better decisions for BSI.

1. Introduction

The spleen is one of the most commonly injured organs in abdominal trauma. Traditionally, splenectomy was performed for blunt splenic injury (BSI), and selective nonoperative management (NOM) was frequently conducted. NOM has several advantages such as being less invasive and allowing splenic salvage. NOM was established as the standard of care in hemodynamically stable patients in the 1990s [1]. A systematic review in 2011 reported that 68.4% of BSI patients were managed nonoperatively [2].

Initially, NOM was perceived as having a high failure rate among surgeons. However, over the last 20 years, the overall success rate for NOM has improved to over 90% [3]. Computed tomography (CT) scans have allowed better patient selection. However, NOM use has become so ubiquitous that there is concern for overuse, which could worsen the survival outcome. A multi-institutional study from the Eastern Association for the Surgery of Trauma (EAST) reported that all-cause mortality was significantly higher in patients with failed NOM than in those with successful NOM (16.5% vs. 4.2%) [4]. Thus, early identification of risk for NOM failure is important.

Many studies have reported that several factors, including a contrast blush, high-grade BSI, a high Injury Severity Score (ISS),

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advanced age, hemodynamical instability, and unconsciousness, were associated with NOM failure [3,5]. However, most of these factors are based primarily on retrospective and small cohort studies. Other risk factors including associated injury, comorbidities, and isolated BSI remain unknown. There is no prediction score to estimate the NOM failure rate in individual patients.

The goal of this study was to identify predictors of NOM failure and develop a risk scoring system for NOM failure using the database from a large, multicenter observational registry of trauma patients in Japan. A predictive score that enables identification of patients at high risk for NOM failure in patients with BSI would help surgeons to make better decisions and improve the survival outcome.

2. Methods

2.1. Study design, participants, and data collection

The Japan Trauma Databank (JTDB) research dataset from 2008 to 2018 was retrospectively reviewed. The JTDB is the largest nationwide trauma registry in which 280 major emergency medical centers participated across Japan in 2018. The content reproduced from the JTDB remains the full and exclusive copyrighted property of the Japan Trauma Care and Research (JTCR). Data collection was approved by the institutional review board at each participating center. The study was approved by the local ethics committee of Saiseikai Yokohamashi Tobu Hospital (No. 20220282). Our study population comprised patients who were 16 years of age or older who sustained a high grade blunt spleen injury (i.e., AAST-organ injury scale [OIS] grade three or greater) and were undergoing NOM. Patients were identified using the Abbreviated Injury System (AIS) coding system score (544214.3, 544224.3, 544226.4, and 544228.5). BSI grade assignment was based on the spleen AIS score [6]. Patients who were subjected to non-blunt trauma, died on arrival, died within 2 h after admission, had an AIS score of 6 for any other body region, or had missing data were excluded.

Patients were classified as either successful or failed NOM. Demographics and injury-specific factors were compared between the two groups. Demographic variables included age, sex, mechanism of injury, systolic blood pressure (SBP) obtained during the initial trauma work-up, comorbidity, BSI grade, Injury Severity Score (ISS), Glasgow Coma Scale (GCS), mechanism of injury, comorbidities, and concomitant injuries (AIS of head, chest, other abdominal, or pelvic fracture). CT scan, angiography, and therapeutic angioembolization (TAE) results for the abdomen were also obtained.

2.2. Interventions and outcomes

Emergency hemostasis procedures were identified from the records listed under the relevant JTDB section. NOM was defined as something reported other than only “celiotomy” that was checked in the initial emergency procedure-type field. Failed NOM was defined as the need for surgery (“celiotomy” reported in the emergency procedure-type field or “splenic surgery” reported in the surgery-type field) in patients with NOM within 48 h after admission. The 48-h timeframe was adopted based on the definition provided in JTDB’s input sheet, which categorizes non-initial emergency procedures as those occurring within 48 h. Patients with both “celiotomy” and “angioembolization” checked in the initial type of emergency procedure that was described were considered to have failed NOM based on a consensus among the study authors that it was unlikely that splenic artery embolization was performed after celiotomy.

2.3. Statistical analyses

Descriptive statistics were used to summarize baseline characteristics. Continuous data are presented as the median with interquartile range, and categorical data are presented as the count and percentage. Categorical associations were tested using Pearson’s chi-square test. Continuous variables were analyzed using a two-sample *t*-test if the data were normally distributed or a Mann–Whitney *U* test for continuous variables if the data were not normally distributed. To emphasize the clinical relevance, continuous variables were categorized or dichotomized.

For prediction analysis, all reliable variables associated with failed NOM were assessed by univariate analysis using logistic regression analysis. Variables significant ($p < 0.05$) in the univariate analysis were then entered into the multivariate analysis. Selection of significant covariates and confounders was performed to construct a multivariable model using backward stepwise elimination to identify variables independently associated with failed NOM. Using the remaining variables identified as significant in the multivariate analysis, we created a scoring system for predicting NOM failure events. Each predictor was assigned a weight of 1 or 2 points based on the calculation with a risk estimate [7]. Favoring simplicity, scores were stratified into three risk groups. High- and low-risk score thresholds were determined based on the probability of failed NOM using the risk score.

The risk score discrimination ability was assessed using the area under the receiver operating characteristic (ROC) curve. The prediction scoring model performance was internally validated across 1000 bootstrap resamples. The goodness-of-fit for the scores was evaluated using the Hosmer–Lemeshow test. The relationships between the observed and estimated probability using logistic regression were indicated for the calibration. The predictive score was evaluated as a diagnostic tool calculated sensitivity, specificity, and the positive and negative likelihood ratios. For the ROC curve comparison, improvement in the predictive ability of the models was evaluated by calculating the net reclassification index (NRI) and the integrated discrimination index (IDI) [8].

A value of $p < 0.05$ was considered statistically significant. The odds ratio (OR) was calculated with the corresponding 95% confidence interval (CI). All statistical analyses were performed using SPSS for Windows version 24.0 (IBM Corp., Armonk, NY, USA) and R version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Patient characteristics

Fig. 1 shows the flow of patient selection and excluded patients with their numbers and reasons for exclusion. Among 2434 patients with a BSI grade greater than II during this designated period, 593 (24.4%) patients underwent surgical management and 1841 (75.6%) patients underwent NOM. Finally, 1651 patients were included for this analysis, among whom 110 (6.7%) patients had failed NOM.

The patients' clinical characteristics are summarized in Table 1. Overall, most patients were men (73.0%), and their median age was 39 (23–60) years. The transfer rate from another hospital was 28.4%. For the BSI grade, patients had an OIS of III (73.2%), IV (23.8%), and V (3.0%). Compared with the successful NOM group, the failed NOM group had a significantly lower transfer rate, and higher rate of lower SBP, lower GCS, higher grade BSI, higher ISS, and other concomitant injuries.

3.2. Diagnostic image, therapeutic intervention, and outcomes

Table 2 presents the diagnosis imaging test, interventions, and outcomes. Most patients underwent a CT scan (94.2%) and angiography (69.0%). Among the patients with angiography, 69.8% of patients underwent TAE. The overall mortality was 6.1%. When compared with the successful NOM group, the failed NOM group had a longer hospital stay (26 days vs. 15 days, $p = 0.001$) and higher in-hospital mortality (20.0% vs. 5.1%, $p < 0.001$).

3.3. Predictors for NOM failure

On univariate analysis, SBP, GCS, ISS, concomitant injuries in other areas (head, chest, pelvis, and other abdominal injury), BSI grade, and isolated BSI were significantly associated with NOM failure (Supplemental Table 1). A multivariable analysis using backward stepwise logistic regression was performed, and the following seven variables were chosen as the predictive score for failed NOM: SBP, GCS, ISS, other abdominal injury, pelvic injury, high grade BSI, and TAE (Table 3).

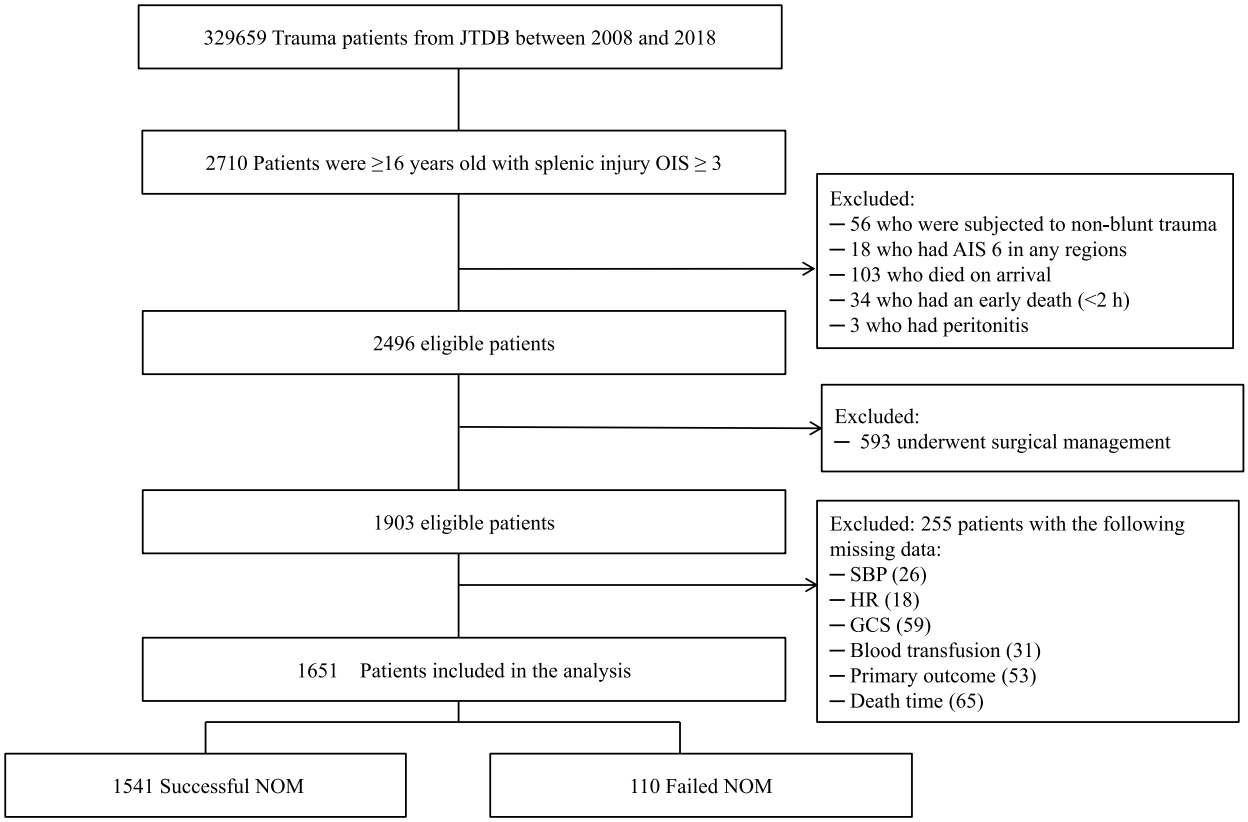

Fig. 1. Flowchart of patients with splenic injury.
JTDB, Japanese Trauma Data Bank; OIS, organ injury scale; AIS, abbreviated injury scale; SBP, systolic blood pressure; HR, heart rate; GCS, Glasgow Coma Scale.

Table 1
Demographics and injury characteristics in patients with blunt splenic injury who underwent NOM and the comparison between successful and failed NOM.

	Overall (n = 1651)	Successful NOM (n = 1541)	Failed NOM (n = 110)	*p* value
Age (years)	39 (23–60)	39 (22–60)	45 (28–64)	0.100
<40, n (%)	51.1 (844)	795 (51.6)	49 (44.5)	0.328
40–64, n (%)	470 (28.5)	436 (28.3)	34 (30.9)	
≥65, n (%)	337 (20.4)	310 (20.1)	27 (24.5)	
Male sex, n (%)	1205 (73.0)	1127 (73.1)	78 (70.9)	0.612
Transferred from another hospital, n (%)	463 (28.4)	442 (29.0)	21 (19.1)	0.028
Mechanism, n (%)				
Motorcycle crash	490 (29.7)	457 (29.7)	33 (30.0)	0.012
Fall	307 (18.6)	279 (18.1)	28 (25.5)	
Motor vehicle crash	288 (17.4)	270 (17.5)	18 (16.4)	
Bicycle accident	123 (7.5)	116 (7.5)	7 (6.4)	
Pedestrian accident	107 (6.5)	94 (6.1)	13 (11.8)	
Other	336 (20.4)	325 (21.1)	11 (10.0)	
Medical history, n (%)				
Respiratory disease	89 (5.4)	83 (5.4)	6 (5.5)	0.976
CKD	10 (0.6)	10 (0.6)	0 (0)	1
Liver cirrhosis	15 (0.9)	12 (0.8)	3 (2.7)	0.073
Hematologic disorders	15 (0.9)	14 (0.9)	1 (0.9)	1
SBP <90 mmHg, n (%)	287 (17.4)	244 (15.8)	43 (39.1)	<0.001
GCS <9, n (%)	141 (8.5)	115 (7.5)	26 (23.6)	<0.001
Grade of spleen injury, n (%)				
III	1208 (73.2)	1162 (75.4)	46 (41.8)	<0.001
IV	393 (23.8)	345 (22.4)	48 (43.6)	
V	50 (3.0)	34 (2.2)	16 (14.5)	
Isolated splenic injury	610 (36.9)	591 (38.4)	19 (17.3)	<0.001
ISS ≥25, n (%)	786 (47.6)	699 (45.4))	87 (79.1)	<0.001
Injured region AIS score, n (%)				
Head AIS ≥4	147 (8.9)	130 (8.4)	17 (15.5)	0.013
Chest AIS ≥4	484 (29.3)	433 (28.1)	51 (46.4)	<0.001
Pelvis AIS ≥4	107 (6.5)	79 (5.1)	28 (25.5)	<0.001
Other abdominal injury ≥3	152 (9.2)	126 (8.2)	26 (23.6)	<0.001

All data are expressed as the median (interquartile range) unless otherwise indicated.
NOM, nonoperative management; CKD, chronic kidney disease; SBP, systolic blood pressure; GCS, Glasgow coma scale; ISS, injury severity score; AIS, abbreviated injury scale; OIS, organ injury scale.

Table 2
Diagnostic tests, intervention, and outcomes for patients with blunt splenic injury who underwent NOM and the comparison between successful and failed NOM.

	Overall (n = 1651)	Successful NOM (n = 1541)	Failed NOM (n = 110)	*p* value
Radiological test and treatment, n (%)				
CT scan	1555 (94.2)	1450 (94.1)	105 (95.5)	0.556
Angiography	1140 (69.0)	1056 (68.5)	84 (76.4)	0.086
TAE (% of angiography)	796 (69.8)	726 (68.8)	70 (83.3)	0.005
Blood transfusion	725 (43.9)	624 (40.5)	101 (91.8)	<0.001
Hospital LOS, d	16 (9–29)	15 (9–28)	26 (9–60)	0.001
Mortality, n (%)	100 (6.1)	78 (5.1)	22 (20.0)	<0.001

All data are expressed as the median (interquartile range) unless otherwise indicated.
NOM, nonoperative management; CT, computed tomography; TAE, therapeutic angioembolization; LOS, length of stay.

3.4. Predictive score for NOM failure

Considering each adjusted OR (Table 3), TAE was assigned 2 points and the other variables were each assigned 1 point for the predictive factor, yielding a total predictive score of 0–8 points (Table 4). The area under curve (AUC) was 0.812 (95% CI, 0.769 to 0.855). Bootstrapping analysis revealed a mean overoptimism value of 0.0007 and a corrected AUC of 0.811 (95% CI, 0.768 to 0.854). Calibration was good as determined by the Hosmer–Lemeshow goodness-of-fit test ($p = 0.696$). The predictive score for failed NOM was stratified into low (0–2 points), medium (3–5 points), and high (6–8 points) (Supplemental Table 2). The observed and estimated probability of failed NOM by risk category are shown in Fig. 2A. At the cutoff point for high risk, the positive likelihood ratio was 14.0, and the positive predictive value was 50.0%, specificity was 98.2%, and sensitivity was 25.5%.

Table 3
Selected predictive variables for NOM failure from the multivariate logistic regression analysis.

	Risk points for NOM failure	Coefficient β	Adjusted OR (95% CI)	*p* value
SBP				
≥90 mmHg	0		1 [Reference]	
<90 mmHg	1	0.48	1.61 (1.01–2.57)	0.045
GCS				
≥10	0		1 [Reference]	
<9	1	0.86	2.36 (1.35–4.13)	0.003
ISS				
<25	0		1 [Reference]	
≥25	1	0.71	2.02 (1.19–3.44)	0.009
Other abdominal injury AIS				
<3	0		1 [Reference]	
≥3	1	0.84	2.31 (1.36–3.91)	0.002
Pelvis injury AIS				
<4	0		1 [Reference]	
≥4	1	1.05	2.87 (1.62–5.07)	<0.001
Splenic injury OIS				
<4	0		1 [Reference]	
≥4	1	1.05	2.86 (1.86–4.41)	<0.001
TAE				
No	0		1 [Reference]	
Yes	2	1.32	3.76 (2.21–6.38)	<0.001

NOM, non-operative management; OR, odds ratio, CI, confidence interval; SBP, systolic blood pressure; GCS, Glasgow coma scale; ISS, injury severity score; AIS, abbreviated injury scale; OIS, organ injury scale; TAE, therapeutic angioembolization.
The Hosmer–Lemeshow test was used to assess the goodness-of-fit for the model ($p = 0.990$).

Table 4
Predictive performance for NOM failure based on the number of risk factors.

Risk category	Risk score	Specificity[a] (%)	Sensitivity[a] (%)	Number of patients (%)	Probability of NOM failure (%)	
					Observed	Estimated
Low	0	0	100	337 (20.4)	0.9	0.6
	1	21.7	97.3	217 (13.1)	1.8	1.4
	2	35.5	93.6	414 (25.1)	2.9	2.9
Medium	3	61.6	82.7	322 (19.5)	4.5	6.2
	4	81.5	69.1	213 (12.9)	13.6	12.5
	5	93.4	42.7	92 (5.6)	20.7	23.6
High	6	98.2	25.5	46 (2.8)	52.2	40.2
	7	99.6	3.6	9 (0.5)	44.4	59.3
	8	100	0	1 (0.1)	0.0	76.0

NOM, non-operative management.
[a] The diagnostic analysis was calculated at the cut-off point for the risk score.

3.5. Predictive score without TAE variable for NOM failure

TAE was a strong predictor of failed NOM (incremental decrease OR, 3.79; 95%CI, 2.23 to 6.43), but indication and availability for TAE may vary widely depending on each hospital. We therefore developed a clinical prediction model without TAE.

The predictive ability and accuracy by score total are shown in Supplemental Table 3. A model without TAE with six variables from the risk score had an AUC of 0.782 (95% CI, 0.735 to 0.829). Bootstrapping analysis revealed a mean overoptimism value of 0.0001 and a corrected AUC of 0.782 (95% CI, 0.737 to 0.825). Calibration was good as determined by the Hosmer–Lemeshow goodness-of-fit test ($p = 0.652$). Thus, when the TAE variable was removed, the model resulted in an incremental C statistic decrease of 0.030 (95%CI, 0.026 to 0.034, $p = 0.024$). The NRI and IDI were −0.634 (95% CI, −0.784 to −0.485, $p < 0.001$) and −0.029 (95% CI, −0.042 to −0.016, $p < 0.001$), respectively. The ROC curves for SBP and ISS and these multivariate models to predict NOM failure are shown in Fig. 2B.

4. Discussion

NOM for BSI has many advantages, but NOM failure is a significant source of morbidity and mortality [4]. Therefore, surgeons need to carefully and quickly assess the feasibility of NOM success. The present study identified clinical and physiologic predictors for NOM failure and subsequently developed and internally validated a clinical prediction model that identifies the risk for NOM failure. The clinical predictors of NOM failure identified in this cohort of patients with severe BSI were low SBP, low GCS, high ISS, other concomitant abdominal injury and pelvic fracture, high-grade BSI (grades IV and V), and the need for TAE. These predictors were then

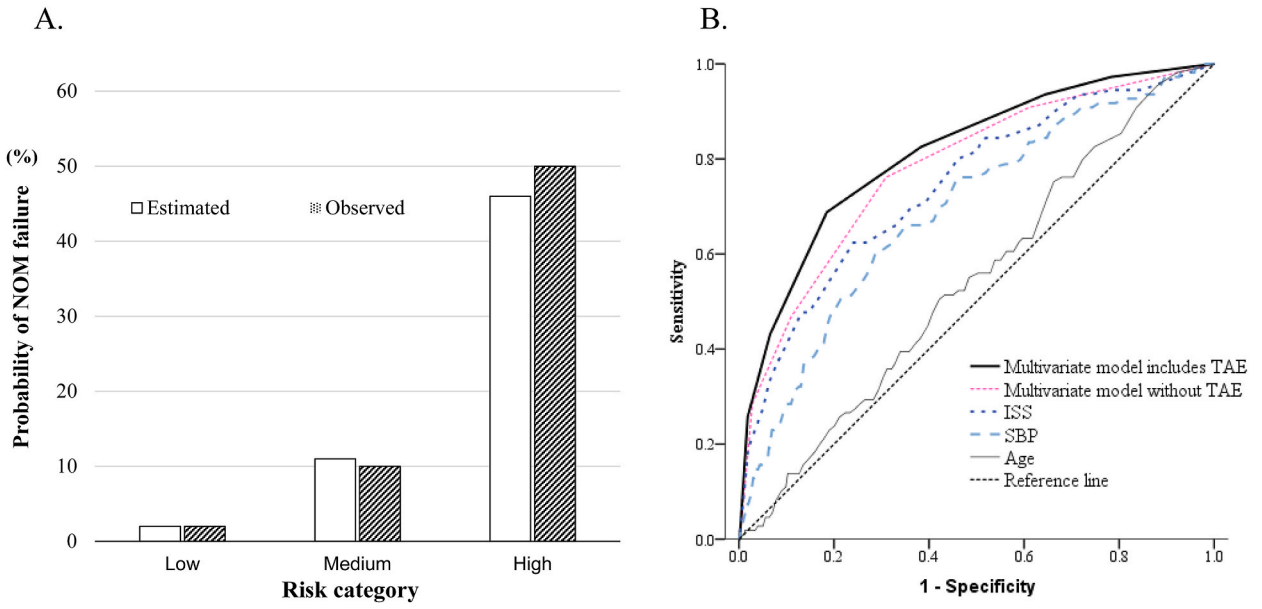

Fig. 2. A. The predicted and observed probability for NOM failure in each risk category. The predictions calibrate well with the observations. B. ROC curve analysis showing predictive performance for nonoperative management failure: a multivariate model includes TAE (AUC 0.812, 95% CI 0.769 to 0.855), multivariate model without TAE (AUC 0.782, 0.735 to 0.829), ISS (AUC 0.745, 0.695 to 0.796), and SBP (AUC 0.692, 0.640 to 0.744), age (AUC 0.547, 0.494 to 0.600).
ROC, receiver operating characteristic; TAE, therapeutic angioembolization; AUC, area under the curve; ISS, Injury Severity Score; CI, confidence interval.

incorporated into a simple clinical decision model with or without TAE, which can be easily calculated at the initial risk assessment for NOM failure in BSI. We found that patients with a high risk category had a 14-fold higher risk for NOM failure. The prediction model was also internally validated using a bootstrap validation technique for good classification performance. Although several studies have identified the risk factors for NOM failure in patients with BSI, no study has focused on predicting the failure rates. Additionally, a single factor cannot accurately predict NOM failure and indicate that laparotomy is required. This study may help optimize decision-making for better initial patient selection for NOM.

The primary outcome in this study was NOM failure defined as the need for celiotomy. However, there is no standard definition for NOM failure with BSI [3]. Some systematic reviews indicated that there was significant variability among previous studies regarding the definition of NOM failure, which makes these results difficult to interpret [3]. The definitions from previous studies can be approximately classified according to the presence or absence of angioembolization. We chose a definition that does not consider angioembolization as a surgical intervention because angioembolization is less invasive and can preserve the spleen and immunological function.

A previous systematic review in 2013 noted that the pooled NOM failure rate was 18.4% (95%CI, 11.5%–28.1%) [5]. The present study showed a relatively low NOM failure rate (6.7%). This may be because the data were collected in recent years. Radiologic tests and procedures may also contribute to better patient selection and decreasing NOM failure. Some centers that use angiography had decreased NOM failure rates [2]. In this study, over 90% of patients underwent CT scans, and nearly 70% of patients underwent angiography. CT scans can detect strong the failure factors including high-grade BSI, other concomitant injuries, and the need for angioembolization. Japanese trauma centers use a low threshold for CT scans and angiography [9]. Most Japanese trauma centers are equipped with high-speed CT scanners and angiography suites located closed to the trauma bay [10]. Japan has the largest number of CT scanners per person in the world [11]. The establishment of radiologic infrastructure may be essential for improving the safety of NOM in BSI patients. To begin with, it is difficult to diagnose BSI without a CT scan other than with surgical findings.

This study's findings were similar to well-known predictors of NOM failure (including lower admission SBP, lower GCS, higher ISS, higher AIS score in the abdomen/pelvis, and higher-grade BSI) [5,12]. High-grade BSI has more parenchymal and vascular disruption with bleeding, and lower SBP and GCS may reflect ongoing bleeding. Additionally, patients with massive trauma that is reflected by higher ISS or other concomitant injuries may be more likely to develop coagulopathy [13]. Among many previous reported predictors, a systematic review and the World Society of Emergency Surgery guideline have reported that advanced age, high ISS, and higher grade BSI are prognostic factors for NOM failure on the basis of strong evidence [5,14]. However, the present study did not show that advanced age was significantly associated with NOM failure. The result might be influenced because our cohort had older patients compared with previous studies. In recent years, there is a skeptical view about advanced age as the predictor [15]. Recent studies on algorithms from The Western Trauma Association do not place a high priority on advanced age for decision-making [3].

The most interesting, but unsurprising, finding is that patients who underwent TAE had higher NOM failure rates compared to

patients who did not undergo TAE. After adjusting for known confounders, TAE remained associated with NOM failure. Two meta-analyses reported that the introduction of angiography and embolization was significantly associated with decreasing NOM failure rates [2,16]. Although it is difficult to demonstrate the efficacy of angioembolization in randomized controlled trials, it is obvious that angioembolization can effectively control hemorrhage from angiographic findings. In this study, the higher NOM failure rates in patients who underwent TAE are most likely due to confounding by indication, which means that these patients need hemostasis and have unmeasured confounders. Thus, "angioembolization" should be interpreted as the "need for angioembolization" in this study. The Japanese guideline and several major guidelines recommend that TAE could be indicated if active extravasation of contrast was seen in the CT scan results [1,3,14,17]. Contrast extravasation is known to be an independent risk factor for NOM failure [14]. Currently, TAE can be applied easily in most trauma centers in Japan. Therefore, TAE may reflect the presence of contrast extravasation on CT scans. Unfortunately, the data set does not contain angiography and CT findings. Further research is needed to investigate the impact of extravasation on BSI management.

This study had several limitations. First, although this is a large study that used a nationwide trauma database, the data set is a "convenience sample" that was registered voluntarily rather than population-based. Additionally, this result may not be fully generalizable to global trauma centers because this study cohort had a high rate of patients who underwent angiography. Therefore, this retrospective study has both selection and information bias. Second, there is no precise information about NOM failure. Although the Japanese guideline which bear similarity to other guidelines for NOM indication is in widespread use in Japan, we do not know the actual indications for NOM and surgery in this study population [1,3,14,17]. Also, celiotomy could have been performed for other reason rather than ongoing bleeding from BSI. Third, the indications for angiography and angioembolization are not specified in the data set. There is great variation in the principle management for each radiographic intervention depending on the human and facility resources among hospitals. Finally, in this study, patients with celiotomy after TAE were considered to have NOM failure. However, some patients potentially underwent planned celiotomy after TAE overuse. For example, when performing TAE for a pelvic fracture, radiologists may try to take this opportunity to perform TAE for the spleen. The clinical dilemma about whether celiotomy or TAE should be used first in pelvic fracture and hemoperitoneum is common [18]. This may affect the result that pelvic fracture was associated with NOM failure in this study. Despite these limitations, we believe that this study provides a valuable score regarding NOM for BSI.

5. Conclusions

This study was the first to provide a predictive score for NOM failure in BSI patients. We identified seven independent predictors associated with NOM failure and provided additional evidence for several previously reported predictors. Additionally, we internally validated that this model had fair to good ability to predict NOM failure. This score may help physicians and surgeons to make a better decision at the initial assessment. These results should be further confirmed using a prospective and multi-institutional approach to assess the accuracy and determine the clinical utility.

Ethics approval and consent to participate

This study was approved by the institutional review board of Saiseikai Yokohamashi Tobu Hospital. Because of the anonymous and retrospective nature of the study, the need for informed consent was waived.

Consent for publication

Not applicable.

Author contribution statement

Shokei Matsumoto; Makoto Aoki: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.
Tomohiro Funabiki: Conceived and designed the experiments; Wrote the paper.
Masayuki Shimizu: Contributed analysis tools and data; Wrote the paper.

Data availability statement

Data included in article/supp. material/referenced in article.

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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20537.

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