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ORIGINAL ARTICLE

Emergency resuscitative thoracotomy in severe trauma: Analysis of the nation-wide registry data in Japan

Hiromu Okano[1,2] | Takero Terayama[3,4] | Hiroshi Okamoto[1] | Tsutomu Yamazaki[2]

[1]Department of Critical Care Medicine, St. Luke's International Hospital, Tokyo, Japan

[2]Department of Social Medical Sciences, Graduate School of Medicine, International University of Health and Welfare, Tokyo, Japan

[3]Department of Emergency, Self-Defense Forces Central Hospital, Tokyo, Japan

[4]Department of Traumatology and Critical Care Medicine, National Defense Medical College Hospital, Tokorozawa, Saitama, Japan

Correspondence
Hiromu Okano, Department of Critical Care Medicine, St. Luke's International Hospital, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan.
Email: okanohiromu0121@gmail.com

Abstract

Aim: Emergency resuscitative thoracotomy is a potentially lifesaving procedure for patients with cardiac pulmonary arrest and profound circulatory failure resulting from a severe injury. However, survival rate post-emergency resuscitative thoracotomy shows considerable variation, with many studies constrained by limited sample sizes and ambiguous criteria for inclusion. Herein, we assessed the outcomes of emergency resuscitative thoracotomy and identified predictors of futility using Japan Trauma Data Bank data.

Methods: Data of patients aged ≥18 years between 2004 and 2019 were analyzed. The primary outcome measure was survival at discharge. Descriptive statistics were used to compare the survivor and nonsurvivor groups. A multivariable logistic regression analysis was conducted to identify predictors of survival in patients undergoing emergency resuscitative thoracotomy while adjusting for confounding factors.

Results: Among patients who underwent emergency resuscitative thoracotomy, 684/5062 (13.5%) survived. Age <65 years (adjusted odds ratio, 1.351; 95% confidence interval, 1.130–1.615; $p < 0.001$), absence of cardiac pulmonary arrest on emergency department arrival (adjusted odds ratio, 1.694; 95% confidence interval, 1.280–2.243; $p < 0.01$), Injury Severity Score <16 (adjusted odds ratio, 2.195; 95% confidence interval, 1.611–2.992; $p < 0.01$), and penetrating injury (adjusted odds ratio, 1.834; 95% confidence interval, 1.384–2.431; $p < 0.01$) were identified as factors associated with survival at discharge.

Conclusion: The survival rate for emergency resuscitative thoracotomy in Japan stands at approximately 13.5%. Factors contributing to survival include younger age, absence of cardiopulmonary arrest at emergency department arrival, lack of severe trauma, and sustaining penetrating injuries.

KEYWORDS
cardiac arrest, database, Japan, resuscitation, thoracotomy

INTRODUCTION

Emergency resuscitative thoracotomy (ERT) is critical in severe trauma management, especially in cases involving cardiac pulmonary arrest (CPA) and catastrophic circulatory collapse resulting from major injuries.[1] ERT, which includes left anterolateral thoracotomy, pericardiotomy, aortic clamping, and open cardiac massage, targets critical issues such as cardiac tamponade, hemorrhage control, cerebral perfusion, and cardiac resuscitation. While ERT can be lifesaving, its effectiveness and survival rates fluctuate, as evidenced by rates ranging from 0% to 56.8%,[2] due to factors such as small study sizes, unclear inclusion criteria, and varied study quality, making comprehensive outcome assessment challenging.[3,4]

Regional variations in trauma types (penetrating versus blunt trauma) can also influence the effectiveness of

ERT. While North America and South Africa report relatively high success rates with ERT in penetrating trauma cases,[5–8] Europe, where blunt trauma is more common, reports different outcomes.[9] The distribution of trauma types in Japan differs from that in these regions, highlighting the need for region-specific data. Understanding how Japan's predominant trauma types affect ERT outcomes is crucial for tailoring effective treatment strategies for the Japanese population. Furthermore, the structure of Japan's healthcare system, such as the lack of established trauma centers, and the methodology of emergency medical service delivery, including differences in transportation distances, may differ from those in other regions, potentially influencing ERT outcomes. These findings indicate the need to understand how Japan's specific medical and emergency frameworks affect the success rates of such critical interventions, to describe the epidemiology of ERT in Japan, and to identify factors associated with survival.

Therefore, this study aimed to comprehensively assess ERT outcomes in Japan and explore the influence of regional trauma epidemiology on the effectiveness of ERT using Japan Trauma Data Bank (JTDB) data.

MATERIALS AND METHODS

Study design

This multicenter, retrospective, observational study analyzed JTDB data between 2004 and 2019. Our findings are described in accordance with Strengthening the Reporting of Observational Studies in the Epidemiology (STROBE) Statement for Observational Studies.[10]

The JDTB

The JTDB is a multicenter nation-wide trauma registry established in 2003 by the Japanese Association for the Surgery of Trauma and the Japanese Association for Acute Medicine to improve trauma care quality in Japan. It registers patients with trauma who are transported to the participating hospitals and have an Abbreviated Injury Scale (AIS) score of ≥3. The JTDB represents >250 participating hospitals and includes most of the high-level tertiary care centers.[11] In total, 92 information elements were registered in the JTDB, including age, sex, injury mechanism, transportation type, vital signs, AIS code for each injured site, Injury Severity Score (ISS), in-hospital procedures, and hospital outcomes.

Participants

We used the JTDB data released in 2021, which comprised information on trauma patients treated between January 1, 2004, and May 31, 2019. In this study, we included patients who had undergone ERT, excluding those aged <18 years.

Variables

The following data were collected: demographics (age and sex), year, prehospital and emergency department (ED) vital signs (including Glasgow Coma Scale), transport time, transport mode, ERT in the ED (including pericardiotomy, aortic clamping, and open cardiac massage), and in-hospital survival rates. Information on mechanism and body-region-specific severity of injuries was also recorded (AIS and ISS, which are anatomically based, consensus-derived, and globally accepted severity scoring systems).[12] In the JTDB, CPA is determined using vital signs obtained in the ED. Therefore, we defined CPA as systolic blood pressure and/or a pulse rate of 0.[13] The primary outcome was defined as survival at hospital discharge.

Statistical analysis

We dichotomized the patients into two categories according to survival status at hospital discharge: survivors and nonsurvivors. Descriptive statistics were compiled for both groups. Continuous variables are presented as medians and interquartile ranges, and categorical variables as frequencies and percentages. Next, we compared the two groups using the Mann–Whitney U test for continuous variables and the chi-square test or Fischer's exact test for categorical variables.

Factors associated with survival at discharge were identified through univariable logistic regression analysis, with results reported as odds ratios (OR) and 95% confidence intervals (CIs). Then, multivariable logistic regression analysis was used to identify factors independently associated with survival at discharge, with results reported as adjusted ORs (aORs) and 95% CIs. We selected a list of candidate predictors based on previous studies and their potential influence on the outcome[2,3,14,15]: trauma type, patient age, sex, heart rate upon ED arrival, systolic blood pressure in the ED, occurrence of CPA at ED arrival, and ISS. Fifty imputations were performed for missing values.[16] In subsequent subgroup analyses, we executed the same statistical approach distinctly for the blunt trauma subgroup and then for the penetrating trauma subgroup.

To assess the robustness of our results, we performed sensitivity analyses by computing E-values and their lower 95% CIs. E-values assess the likelihood of causation by measuring how strongly an unmeasured confounder would need to be linked to both exposure and outcome to suggest that the observed relationship is not causal.[17] For instance, an E-value of 2.0 implies that the ORs for the relationship of unmeasured confounders with both the exposure and outcome must be >2.0 to entirely negate the observed association between the exposure and outcome of interest.

All statistical analyses were performed using SPSS software version 29.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as a two-sided p-value <0.05.

RESULTS

Participant characteristics

Among the 33,8744 patients registered in the JTDB, 5062 were eligible for inclusion in the primary analysis (Figure 1). Among patients who underwent ERT, 684/5062 (13.5%) survived (Figure 1). The hospital arrival survival rate was 11.5% (392 /3423) for patients with CPA and 19.2% (274 /1430) for patients without CPA ($p < 0.01$).

ERT rates for adult severe trauma from 2004 to 2019 ranged at 1.46–2.02% (Figure 2). Table 1 shows participant characteristics in the prehospital setting for each group. Age ($p = 0.03$) and CPA upon contact with emergency medical services ($p < 0.01$) were significantly different between the survived and dead groups. Table 2 describes the characteristics of each group at ED arrival. Significant differences were observed in CPA rates ($p < 0.01$), vital signs ($p < 0.01$; temperature [$p = 0.038$]), and consciousness ($p < 0.01$). Table 1 also shows the demographic and injury profiles of both groups. Overall, 92.2% (4649/5062) patients experienced blunt trauma, while 6.2% (321/5062) had penetrating injuries. Significant differences were found in blunt ($p < 0.01$) and penetrating ($p < 0.01$) injury rates, ISS ($p < 0.01$), and ISS ≥16 ($p < 0.01$).

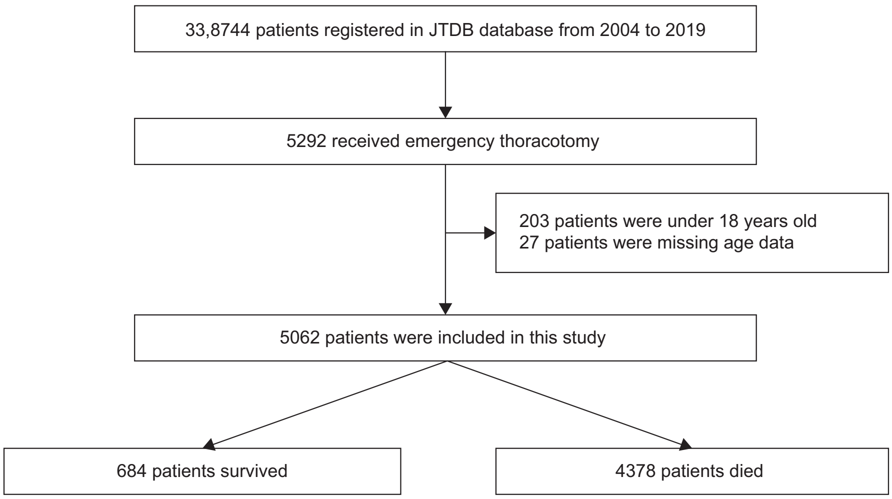

FIGURE 1 Patient selection and flow chart of the study. JTDB, Japan Trauma Data Bank.

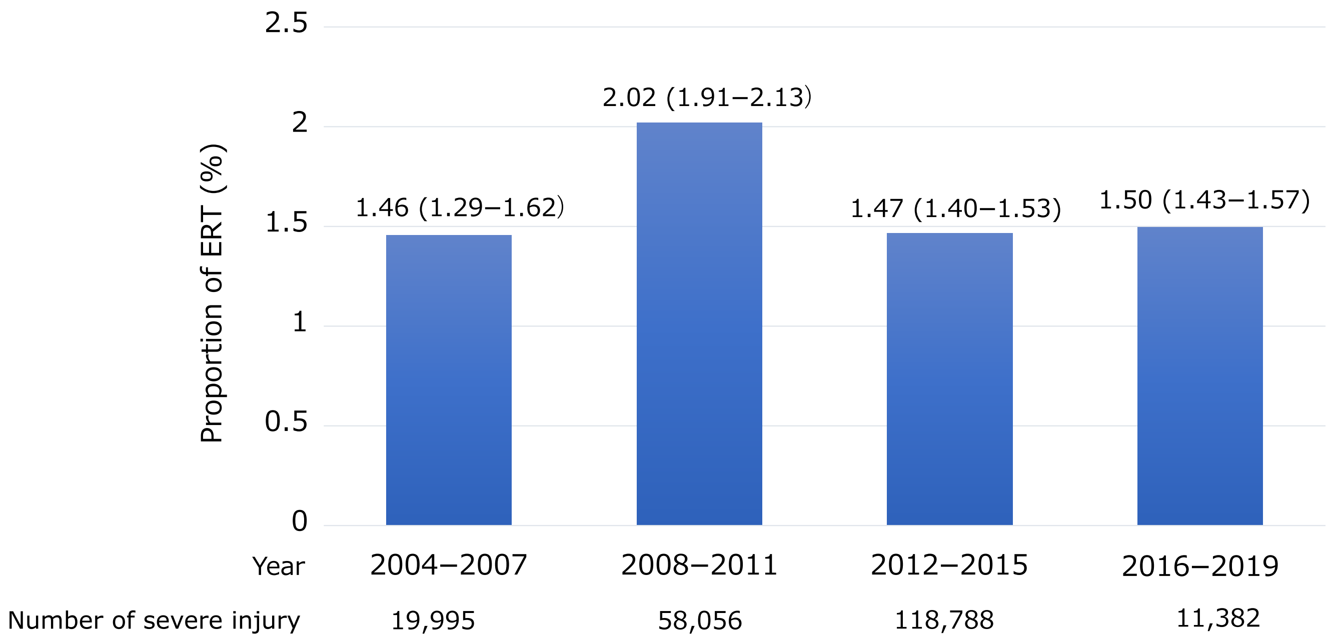

FIGURE 2 Number of severe injuries by year and percentage of ERTs performed. The data are presented as percentages with 95% CIs. The blue bars indicate the percentage of ERT. CI, confidence interval, ERT, Emergency resuscitative thoracotomy.

TABLE 1 Patient characteristics who received emergency resuscitative thoracotomy.

	Total (*n* = 5062)	Survivors (*n* = 684)	Nonsurvivors (*n* = 4378)	*p*-value
Age, years	55 (38–71)	51 (37–69)	56 (38–72)	0.03
18–64	3210 (63.4)	473 (69.2)	2737 (62.5)	<0.01
≥65	1852 (36.6)	211 (30.8)	1641 (37.5)	
Male, *n* (%)	3515 (69.4)	497 (72.6)	3018 (68.9)	0.049
Cause of trauma, *n* (%)				
Accident	3070 (60.6)	407 (59.5)	22,663 (60.8)	
Suicide	1270 (25.1)	174 (25.4)	1096 (25.0)	
Criminal	123 (2.4)	21 (3.1)	102 (2.3)	
Labor	279 (5.5)	41 (6.0)	238 (5.4)	
Other	10 (0.2)	2 (0.3)	8 (0.2)	
Unknown	272 (5.4)	33 (4.8)	239 (5.5)	
Time from EMS dispatch to ED arrival, min	11 (7–18)	12 (7–19)	11 (7–18)	0.151
Time from EMS contact to ED arrival, min	26 (19–37)	26 (19–37)	26 (19–38)	0.289
CPA on contact with EMS	1083 (21.4)	73 (10.6)	1010 (25.1)	<0.01
Injury mechanism (%)				
Blunt	4649 (92.2)	593 (86.7)	4056 (92.6)	<0.01
Penetrating	321 (6.2)	75 (11.0)	246 (5.6)	<0.01
Location of injury AIS				
Head	3 (3–5)	3 (3–5)	3 (3–5)	0.964
Face	2 (1–2)	2 (1–2)	2 (1–2)	0.88
Neck	3 (1–3)	3 (1–3)	3 (1–4)	0.758
Thorax	5 (4–5)	5 (4–6)	5 (4–5)	0.134
Abdomen and pelvic contents	3 (2.75–4)	3 (3–4)	4 (2–4)	0.259
Cervical spine	2 (2–3)	2 (2–3)	2 (2–3)	0.071
Upper extremity	2 (2–3)	2 (2–3)	2 (2–3)	0.267
Lower extremity	3 (3–4)	3 (3–4)	3 (3–4)	0.493
External	1 (1–1)	1 (1–1)	1 (1–1)	0.858
ISS	36 (25–57)	33 (25–50)	38 (25–57)	<0.01
ISS ≥16	4398 (86.9)	487 (71.2)	3911 (89.3)	<0.01

Note: For continuous variables, median and interquartile ranges (IQR) were determined, while frequencies and percentages were used for categorical variables.
Abbreviations: AIS, abbreviated injury scale; CPA, cardiopulmonary arrest, ED, emergency department; EMS, emergency medical services; ISS, injury severity score.
Injury mechanism (%).

Factors independently associated with survival

For multivariable logistic regression analysis, we used the following predetermined covariates: age <65 years, sex (male), occurrence of CPA in the ED, ISS, trauma type (penetrating), heart rate at ED arrival, and systolic blood pressure at ED arrival. Age <65 years (aOR, 1.351; 95% CI, 1.130–1.615; $p < 0.001$; E-value = 2.04), absence of CPA on ED arrival (aOR, 1.694; 95% CI, 1.280–2.243; $p < 0.001$; E-value = 2.78), ISS <16 (aOR, 2.195; 95% CI, 1.611–2.992; $p < 0.001$; E-value = 3.81), and penetrating injury (aOR, 1.834; 95% CI, 1.384–2.431; $p < 0.001$; E-value = 3.07) were identified as independent factors associated with survival (Table 3). The discriminative ability of each covariate for survival is presented in Table 4. The absence of CPA at ED arrival had a sensitivity of 0.411 (0.374–0.449), a specificity of 0.724 (0.710–0.737), and a positive predictive value of 0.192 (0.173–0.212). Considering the combination of age <65 years, absence of CPA at ED arrival, and penetrating injury, the sensitivity dropped to 0.063 (0.0492–0.0876), while the specificity increased to 0.993 (0.991–0.996) and the positive predictive value to 0.603 (0.501–0.732).

Subgroup analyses

Survival rates were 12.8% (593/4649) and 23.4% (75/321) in patients with blunt and penetrating trauma, respectively. In patients with blunt trauma, age <65 years (aOR, 1.303; 95% CI, 1.098–1.573; $p = 0.006$; E-value = 1.93), absence of CPA at ED arrival (aOR, 1.445; 95% CI, 1.062–1.965; $p = 0.019$; E-value = 2.25), and ISS <16 (aOR, 2.307; 95% CI, 1.639–3.246; $p < 0.001$; E-value = 4.04) were associated with survival (Table 5). Absence of CPA at ED arrival (aOR, 7.189; 95% CI,

TABLE 2 Vital signs at emergency department in patients who received emergency resuscitative thoracotomy.

	Total (n = 5062)	Survivors (n = 684)	Nonsurvivors (n = 4378)	p-value
CPA at ED	3423 (67.6)	392 (57.3)	3031 (69.2)	<0.01
Systolic blood pressure, mm Hg	0 (0–40)	0 (0–70)	0 (0–40)	<0.01
>90	505 (9.2)	106 (15.4)	399 (9.1)	
1–90	934 (18.4)	164 (24.2)	770 (17.6)	
=0	3350 (66.2)	386 (56.4)	2964 (67.7)	
Heart rate, beats/min	0 (0–78)	0 (0–104)	0 (0–70)	<0.01
=0	3098 (68.1)	347 (50.7)	2751 (62.8)	
Respiratory rate, breaths/min	0 (0–8)	0 (0–20)	0 (0–0)	<0.01
=0	3290 (65.0)	369 (53.9)	2921 (66.7)	
Glasgow Coma Scale on ED arrival, points	3 (3–3)	3 (3–6)	3 (3–3)	<0.01
≤8	4274 (84.4)	513 (75.0)	3761 (85.9)	<0.01
Temperature, °C	35.4 (34.4–36.1)	35.6 (34.6–36.2)	35.4 (34.4–36.1)	0.038

Note: For continuous variables, median and interquartile ranges (IQR) were determined, while frequencies and percentages were used for categorical variables.
CPA, cardiopulmonary arrest; ED, emergency department.

TABLE 3 Results of univariable and multivariable logistic regression analyses predicting survival at hospital discharge.

Survivors (n = 684)	OR	95% CI	aOR	95% CI	P-value	E-value†
Age <65	1.344	1.130–1.599	1.351	1.130–1.615	<0.01	2.04 (1.51)
Sex male	1.198	1.000–1.434	1.123	0.934–1.350	0.219	-
Without CPA on arrival at ED	1.795	1.548–2.169	1.694	1.280–2.243	<0.01	2.78 (1.88)
ISS <16	2.306	1.713–3.102	2.195	1.611–2.992	<0.01	3.81 (2.60)
Penetrating injury	2.067	1.573–2.716	1.834	1.384–2.431	<0.01	3.07 (2.11)
Systolic blood pressure at ED arrival ≥90 mm Hg	1.766	1.405–02.220	1.181	0.896–1.557	0.237	-
Heart rate at ED arrival ≥60 beats/min	1.684	1.401–2.024	1.055	0.791–1.407	0.714	-

Abbreviations: aOR: adjusted odds ratio; CI, confidence interval; CPA, cardiopulmonary arrest; ED, emergency department; EMS, emergency medical service; ISS, injury Severity Score; OR, odds ratio.
†E-value (and its lower 95% CI limit) indicates the strength of the association between an unmeasured confounder(s) and both the exposure and outcome required to fully explain the observed association.

2.980–17.343; $p < 0.01$; E-value = 13.86) was associated with survival in patients with penetrating trauma (Table 6).

DISCUSSION

To our knowledge, no previous study has described the epidemiology of ERT in Japan in such a large cohort. Our analysis using the JTDB data reveals a post-ERT survival rate of approximately 13.5%, with 11.5% for patients with CPA and 19.2% for those without CPA at ED arrival. Further, multivariable logistic regression analysis revealed age <65 years, CPA at ED arrival, ISS <16, and penetrating injury as factors associated with survival.

The trauma care system in Japan differs markedly from the centralized model used in the United States, resulting in varied approaches to trauma team formation across Japanese facilities. Research on ERT efficacy in Japan, as indicated by emergency centers with trauma units, has been limited. Matsumoto et al.[18] conducted a seminal study to delineate the epidemiology of ERT in Japan and analyzed ERT outcomes in prehospital and ED settings, revealing a survival rate of 3.2% (3/95). These findings indicate that differences in survival rate are attributable to factors such as ISS, the presence of prehospital thoracotomy, and blunt injury. Until recently, ERT data in Japan were scarce, with ambiguous epidemiological insights, whereas our study comprehensively clarified this epidemiology.

The proportion of blunt trauma affects the outcomes of ERT. In 2015, the Eastern Association for the Surgery of Trauma specified ERT indications for patients at ED,[5] based on a meta-analysis of 72 studies involving 10,238 patients with an overall survival rate of 8.6% (881/10,238), with 1.9% for blunt trauma (28/1449) and 13.8% for penetrating trauma (287/2072).[5] This guideline[5] primarily focused on ERT for blunt trauma, based on a U.S. study. In our study, the survival rate was lower for blunt trauma [12.8% (593/4649)] than for penetrating injury [23.4%

TABLE 4 Discriminative ability of each covariate for survival.

	Sensitivity	Specificity	PPV	NPV
Age <65	0.692 (0.656–0.725)	0.375 (0.364–0.389)	0.147 (0.135–0.159)	0.886 (0.872–0.900)
Without CPA on arrival at ED	0.411 (0.374–0.449)	0.724 (0.710–0.737)	0.192 (0.173–0.212)	0.885 (0.875–0.896)
ISS <16	0.118 (0.0924–0.145)	0.952 (0.945–0.959)	0.247 (0.198–0.301)	0.889 (0.800–0.898)
Penetrating injury	0.112 (0.0882–0.136)	0.943 (0.936–0.950)	0.234 (0.187–0.280)	0.873 (0.863–0.882)
Age <65 and without CPA on arrival at ED	0.279 (0.246–0.314)	0.845 (0.834–0.856)	0.223 (0.195–0.252)	0.881 (0.870–0.891)
Age <65, without CPA on arrival at ED, and penetrating injury	0.063 (0.0492–0.0876)	0.993 (0.991–0.996)	0.603 (0.501–0.732)	0.871 (0.862–0.881)

Abbreviations: CPA, cardiopulmonary arrest; ED, emergency department; ISS, injury Severity Score; NPV, negative predictive value; PPV, positive predictive value.

TABLE 5 Results of univariable and multivariable logistic regression analyses predicting mortality in blunt trauma patients at hospital discharge.

Survivors (n = 593)	OR	95% CI	aOR	95% CI	p-value	E-value[a]
Age <65	1.294	1.077–1.554	1.303	1.098–1.573	0.006	1.93 (1.43)
Sex male	1.202	0.991–1.457	1.130	0.928–1.376	0.223	-
Without CPA on arrival at ED	1.507	1.256–1.809	1.445	1.062–1.965	0.019	2.25 (1.32)
ISS <16	2.323	1.593–3.128	2.307	1.639–3.246	<0.01	4.04 (2.66)
Systolic blood pressure at ED presentation ≥90 mm Hg	1.503	1.168–1.934	1.140	0.843–1.543	0.394	
Heart rate at ED presentation ≥60 beats/min	1.458	1.191–1.783	1.054	0.765–1.451	0.749	

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CPA, cardiopulmonary arrest; ED, emergency department; EMS, emergency medical service; ISS, injury Severity Score; OR, odds ratio.

[a]E-value (and its lower 95% CI limit) indicates the strength of the association between an unmeasured confounder(s) and both the exposure and outcome required to fully explain the observed association.

TABLE 6 Results of univariable and multivariable logistic regression analyses predicting mortality in penetrating trauma patients at hospital discharge.

Survivors (n = 75)	OR	95% CI	aOR	95% CI	p-value	E-value[a]
Age <65	1.384	0.754–2.539	1.498	0.742–3.025	0.260	-
Sex male	1.138	0.637–2.034	1.190	0.606–2.336	0.613	-
Without CPA on arrival at ED	9.500	5.226–17.271	7.189	2.980–17.343	<0.01	13.86 (5.41)
ISS <16	1.971	1.020–3.807	1.970	0.885–4.386	0.097	
Systolic blood pressure at ED presentation ≥90 mm Hg	4.766	2.213–10.267	1.087	0.450–2.627	0.853	
Heart rate at ED presentation ≥60 beats/min	6.988	3.759–12.993	1.566	0.664–3.694	0.305	

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CPA, cardiopulmonary arrest; ED, emergency department; EMS, emergency medical service; ISS, injury Severity Score; OR, odds ratio.

[a]E-value (and its lower 95% CI limit) indicates the strength of the association between an unmeasured confounder(s) and both the exposure and outcome required to fully explain the observed association.

(75/321)]. Furthermore, a Japanese study by Suzuki et al.[19] involving 1377 patients with blunt trauma compared ERT with closed chest cardiac massage in patients with cardiac arrest and reported that ERT was associated with poorer outcomes. Yamamoto et al.[20] also used Japanese data to compare survival at discharge between patients who received ERT and those who did not; they used propensity scores and included adult patients with cardiac arrest who had approximately 90% blunt trauma on hospital arrival. Of the 1289 patients, 374 received ERT, and ERT was associated with lower survival at discharge in patients who received ERT versus those who did not. These findings indicate that the use of ERT in blunt trauma requires careful consideration.

Narvestad et al.'s[9] systematic review of eight European studies highlighted a high proportion of ERT in blunt trauma cases [51.3% (193/376)], with a survival rate of 25.4% (49/193). In contrast, our study found that 92.2% of ERTs were performed for blunt trauma, with a survival rate of 12.8%, indicating a higher frequency of ERTs for blunt trauma in Japan than in Europe. This difference in survival rates can be attributed to a higher percentage of CPA cases in our study [67.6%] than in Narvestad et al.'s study [39.6% (149/376)].

ERT can be effective for penetrating injuries. Previous studies[5,16] suggested its efficacy when vital signs were present upon arrival at trauma centers. Our data showed that the absence of CPA at ED arrival was associated with survival in penetrating trauma patients. These findings are consistent with those of previous research,[5,16] suggesting potential benefits of ERT for patients with penetrating trauma without CPA in Japan.

In our study, the survival rate was 60.3% for patients with age <65 years, absence of CPA at ED arrival, and penetrating trauma. This finding has important implications for decision-making regarding resuscitation, suggesting that physicians should consider ERT for younger patients without CPA at ED arrival and with penetrating trauma.

This study has some limitations. First, our study was retrospective, which may introduce unmeasured confounding factors, although our E-values support the robustness of our inferences. Second, the timing of ERT following CPA is critical[2]; however, our dataset lacked precise information on ERT timing following CPA. Third, while preceding guidelines[5] and other studies[2,5,19] suggest considering ERT for patients with signs of life upon ED arrival, our dataset did not capture these details, as the JTDB began collecting this information only since 2019. Fourth, our database-driven, multicenter cohort analysis may introduce discrepancies for ERT indications across various centers, questioning the direct applicability of ERT induction standards from other nations to Japan. Last, although each item had missing values, this limitation was overcome by multiple imputations.

CONCLUSION

This study revealed that the survival rate after ERT in Japan is approximately 13.5%, 11.5% for those with CPA, and 19.2% for those without CPA at ED arrival. Multivariable logistic regression analysis revealed that age <65 years, CPA at ED arrival, ISS <16, and penetrating injury were associated with survival.

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CONFLICT OF INTEREST STATEMENT
Authors declare no Conflict of Interests for this article.

DATA AVAILABILITY STATEMENT
An overview of the JTDB can be found at https://jtcr-jatec.org/traumabank/index.htm.

Detailed JTDB data supporting the results of this study are available from Japan Trauma Care and Research; however, the availability of these data is limited and not publicly available. They were used under a license for this study.

ETHICS STATEMENT
Approval of the research protocol: The protocol for this research project has been approved by suitably constituted Ethics Committees of the institutions, and it conforms to the provisions of the Declaration of Helsinki. Ethics Committee of the International University School of Health and Welfare Graduate School, Approval No. 23-Im-019, and Ethics Committee of the National Defense Medical College Hospital, Approval No. 4648.
Informed consent: We applied the opt-out method on an institutional website to obtain patient consent.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

ORCID
Hiromu Okano https://orcid.org/0000-0002-2116-0455

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