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Does early excision or skin grafting of severe burns improve prognosis? A retrospective cohort study

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ABSTRACT

The present study aimed to investigate the appropriate timing of excision or skin grafting of burn wounds in patients with severe burns. We retrospectively analyzed data from the Diagnosis Procedure Combination Database, a nationwide inpatient database in Japan. Patients with severe burns (burn index ≥10) who underwent excision or skin grafting within 7 days from September 2010 to March 2019 were included. We defined the early surgery group as patients who underwent excision or skin grafting within 2 days of admission and the delayed surgery group as those who underwent surgery within 3–7 days of admission. Propensity score matching was used to compare the in-hospital mortality between the two groups, yielding a cohort of 389 pairs. A total of 2362 eligible patients were categorized into the early surgery group (n = 626) and delayed surgery group (n = 1736). The overall in-hospital mortality was 19.6%. In-hospital mortality did not differ significantly between the early surgery (15.9%) and the delayed surgery groups (17.2%; $p = 0.70$). These results suggest that excision or skin grafting within 2 days of admission was not associated with improved in-hospital mortality compared with surgery thereafter for patients with severe burns.

1. Introduction

Burns are the fourth most common type of trauma worldwide, following traffic injuries, falls, and interpersonal violence [1,2]. In 2004, approximately 11 million people experienced burns requiring medical attention globally [3]. Since the 1970 s, advancements in the treatment of patients

Abbreviations: BMI, body mass index; ICD-10, International Classification of Diseases, 10th Revision; SMD, standardized mean differences; TBSA, total body surface area

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with severe burns have led to a significant decrease in mortality [4]; however, more than 300,000 people worldwide still die from burns each year. One of the major reasons for the improvement in the prognosis of severe burns may be early excision and skin grafting of the burn wound [5,6].

The leading cause of death in burn patients is multiple organ failure due to severe infection, which can be prevented by early necrosectomy and wound closure [7]. The early excision of burn wounds is widely recommended, and its pathophysiological advantages are increasingly well understood [8]. After Janzekovic et al. reported successful tangential burn wound excision with immediate grafting in 1970 [9], early burn wound excision has been reported to improve the prognosis of patients with severe burns [6,10,11]. Several guidelines for the initial management of burns [12–14] recommend early excision and grafting for the treatment of limited full-thickness burns. However, early excision of the burn wound and skin grafting are associated with deterioration of the general condition and complications associated with over-invasiveness [15,16]. Early excision of burn injuries greater than 30% of the total body surface area (TBSA) in adults has not been universally accepted [7].

We hypothesized that early excision or skin grafting would reduce mortality in patients with severe burns compared with delayed excision or skin grafting. The majority of previous observational and randomized studies defined early excision and skin grafting as those performed within 24–72 h of the injury [8,17,18]. Therefore, we defined early excision or skin grafting as those performed within 2 d of admission. The purpose of this study was to investigate whether early excision or skin grafting improves the prognosis of patients with severe burns compared with delayed excision or skin grafting, using a nationwide inpatient database in Japan.

2. Materials and methods

2.1. *Study design and data source*

For this retrospective cohort study, we used the Japanese Diagnosis Procedure Combination Database. Details of the database are described elsewhere [19]. Briefly, the database contains administrative claims data, clinical information, and discharge abstracts from more than 1200 acute-care hospitals nationwide and covers approximately 90% of all tertiary-care emergency hospitals in Japan. All 82 academic hospitals are obligated to provide information to this database, but participation by community hospitals is voluntary. The database also includes the following patient data: dates of admission and discharge, age, sex, diagnosis (primary diagnosis, comorbidities at admission, and post-admission complications) according to the International Classification of Diseases, 10th Revision (ICD-10) codes [20,21] and text in Japanese, whether transferred by ambulance, level of consciousness, and discharge status. Rather than TBSA, the database includes a burn index recorded at admission that reflects both the surface area and thickness of the burn and is calculated as follows [22,23]: burn index = full thickness of TBSA + 1/2 partial thickness of TBSA. The combination of age and burn index has been reported to be a good predictor of mortality [23]. In the present study, we defined patients with a burn index $\geq$ 10 at admission as those having severe burns [23,24]. The database is structured explicitly to differentiate comorbidities present before admission from post-admission complications. The dates of surgery, procedures performed, and drugs administered are also recorded. All clinical data for each patient are recorded at discharge by attending physicians.

This study was approved by the Institutional Review Board of the University of Tokyo. The need for informed consent was waived due to the use of anonymized data.

2.2. *Patient Selection*

We included all patients who were discharged between September 1, 2010, and March 31, 2019, who met the following criteria: patients (i) with a primary diagnosis of burn on admission (ICD-10 codes for burns are listed in Supplemental Table S1), (ii) with a burn index $\geq$ 10 at admission, and (iii) who underwent excision or skin grafting within 7 d of admission (Japanese procedure codes for excision or skin grafting are listed in Supplemental Table S2). The exclusion criteria were as follows: patients (i) who died within 7 d of admission (to avoid immortal time bias), (ii) with cardiac arrest on arrival, and (iii) with a second or subsequent admission for burns.

2.3. *Exposure and endpoint*

The exposure of interest was early surgery as compared with delayed surgery. The early surgery group was defined as patients who underwent skin excision or skin grafting within 2 d of admission. The delayed surgery group was defined as patients who underwent skin excision or skin grafting 3–7 d after admission. The primary outcome was in-hospital mortality, and the secondary outcomes were the length of hospital stay, duration of mechanical ventilation, and duration of catecholamine use. Catecholamines were defined as dopamine, dobutamine, adrenaline, or noradrenaline.

2.4. *Other variables*

Hospital volume was defined as the average number of patients with burns who underwent excision or skin grafting within 7 d of admission annually. Comorbidities on admission were extracted for each category of the Charlson Comorbidity Index using algorithms developed by Quan et al. [25]. The Charlson Comorbidity Index is widely used to measure case mixes and disease burdens. Complications after admission were defined using the ICD-10 procedure codes as listed in Supplemental Table S3. Five body mass index (BMI) categories were determined based on the World Health Organization classification. Patients without BMI data were categorized as missing. The level of consciousness on admission was evaluated using the Japan Coma Scale score, defined as follows: 0, alert consciousness; 1–3, awake without any stimuli; 10–30, aroused by some stimuli; and 100–300, coma. Intervention factors such as catecholamine use, blood transfusions, admission to the intensive care unit or high care unit, mechanical ventilation, and drug administration (immunoglobulin, antithrombin III, and haptoglobin) were determined to be present if they were administered within 2 d of admission.

2.5. Statistical Analysis

As in previous retrospective observational studies, we used propensity score methods to compare outcomes between groups with similar observed characteristics without specifying the relationship between confounders and outcomes [26,27]. We used propensity score matching to adjust for differences in baseline characteristics and the severity of the condition on admission between the early and delayed surgery groups. To estimate the probability of early surgery, a propensity score was calculated for each patient using a multivariable logistic regression model. All the baseline characteristics listed in Table 1 were included in the model as independent variables. After the propensity scores were estimated, all patients in the early surgery group were one-to-one matched with patients in the delayed surgery group based on nearest-neighbor matching without replacement. The caliper was set at 0.2 for the standard deviation of the propensity scores. The balance between the two groups was compared using standardized mean differences (SMD). An SMD of less than 0.1 was considered a negligible imbalance. The outcomes between the two groups were compared using Fisher's exact test for in-hospital mortality and the Mann–Whitney U test for the length of stay, duration of mechanical ventilation, and duration of catecholamine use. Kaplan–Meier survival curves were plotted for the early and delayed surgery groups and compared using the log-rank test.

We conducted subgroup analyses for in-hospital mortality according to all baseline characteristics, the burn index (10–30 at intervals of 5), and age (65–84 years divided into 5-year intervals and ≥85 years) using Breslow-Day tests. Statistical significance was set at $p < 0.05$. All analyses were conducted using SPSS version 22 (IBM Corp, Armonk, NY, US) and R version 3.1.3 (The R Foundation, Vienna, Austria).

3. Results

3.1. Patients

A total of 2362 patients were included in the study (Fig. 1), of which 626 underwent early surgery and 1736 underwent delayed surgery. Table 1 shows the patient characteristics before and after propensity score matching. After propensity score matching, the baseline patient characteristics were well-balanced between the two groups.

3.2. Endpoints

The overall in-hospital mortality was 19.6%. Table 2 presents the outcomes before and after propensity score matching. There was no significant difference in in-hospital mortality between the early and delayed surgery groups after propensity score matching (15.9% vs. 17.2%, respectively; $p = 0.700$).

Fig. 2 shows the Kaplan–Meier survival curves for the 30-day mortality rates of the two groups after propensity score matching. The 30-day mortality rate was not significantly different between the early and delayed surgery groups (log-rank test, $p = 0.487$).

Following propensity score matching, there were no significant differences in the length of stay (65.9 days vs. 64.2 days, $p = 0.731$), duration of mechanical ventilation (37.9 days vs. 33.3 days, $p = 0.316$), or duration of catecholamine use (33.6 days vs. 29.3 days, $p = 0.253$) between the early and delayed surgery groups, respectively.

3.3. Subgroup analysis

No significant interactions were observed in any of the subgroups. The results of subgroup analyses of the representative variables are shown in Table 3.

4. Discussion

The present study compared the outcomes of early and delayed excision or skin grafting in patients with severe burns. Early excision or skin grafting was not associated with improved prognosis in patients with severe burns with a burn index ≥ 10.

These results suggest that it may not be necessary to consider the timing of excision or skin grafting to improve the medium-term prognosis of patients. The favorable effects of early excision or skin grafting on fluid retention and infection prevention might have been counteracted by the complications associated with early surgery. Early excision or skin grafting in patients with severe burns may cause massive intraoperative bleeding and require blood transfusion [6,16,28]. It has been also reported that there is a risk of systemic deterioration and complications due to excessive invasion [18,27]. In the present study, early excision or skin grafting was not associated with a shorter duration of catecholamine use or mechanical ventilation. In addition, in the unmatched cohort, more patients in the early surgery group were administered catecholamine and blood transfusions within 2 d of admission than those in the delayed surgery group, which might have been due to early excision or skin grafting. While early excision of necrotic tissue from burn wounds may cause inflammation, skin grafts may protect against infections. These contradictory effects [29] might have been the reason that no significant difference in prognosis was observed between the two groups.

To avoid immortal time bias, 57 patients who died within 7 d of admission were excluded from the present study. This allowed us to evaluate the impact of infections in the subacute phase rather than those stemming from the poor acute phase conditions associated with severe burns. These 57 patients who died in the acute phase were most susceptible to circulatory disturbances during the burn-shock phase [15,16]. Previous reviews have not sufficiently assessed the medium- to long-term prognosis of burn patients without the influence of acute-phase conditions [6,12]. Our results suggest that in patients with severe burns who survive for

Table 1 – Baseline patient characteristics before and after propensity score matching.

Variables	Unmatched cohort			Propensity score-matched cohort		
	Delayed surgery (n = 1736)	Early surgery (n = 626)	SMD	Delayed surgery (n = 389)	Early surgery (n = 389)	SMD
Fiscal year, n (%)			0.12			0.09
2011	189 (10.9)	54 (8.6)		45 (11.6)	36 (9.3)	
2012	177 (10.2)	67 (10.7)		36 (9.3)	37 (9.5)	
2013	202 (11.6)	78 (12.5)		45 (11.6)	42 (10.8)	
2014	313 (18.0)	125 (20.0)		76 (19.5)	84 (21.6)	
2015	178 (10.3)	56 (8.9)		32 (8.2)	33 (8.5)	
2016	175 (10.1)	60 (9.6)		37 (9.5)	40 (10.3)	
2017	174 (10.0)	58 (9.3)		36 (9.3)	37 (9.5)	
2018	152 (8.8)	67 (10.7)		41 (10.5)	43 (11.1)	
2019	176 (10.1)	61 (9.7)		41 (10.5)	37 (9.5)	
Age, years, mean (SD)	62.9 (21.3)	59.7 (20.8)	0.15	59.75 (22.6)	59.2 (20.0)	0.02
BMI (kg/m^2), n (%)			0.09			0.09
< 18.5	258 (14.9)	94 (15.0)		61 (15.7)	56 (14.4)	
18.5–22.5	596 (34.3)	228 (36.4)		135 (34.7)	142 (36.5)	
22.5–24.9	361 (20.8)	132 (21.1)		69 (17.7)	75 (19.3)	
25.0–29.9	320 (18.4)	97 (15.5)		74 (19.0)	66 (17.0)	
≥ 30.0	87 (5.0)	37 (5.9)		20 (5.1)	23 (5.9)	
Missing	114 (6.6)	38 (6.1)		30 (7.7)	27 (6.9)	
Sex, female, n (%)	740 (42.6)	255 (40.7)	0.04	152 (39.1)	153 (39.3)	< 0.01
Burn index, mean (SD)	23.2 (14.8)	25.0 (17.4)	0.11	22.8 (15.6)	23.8 (16.6)	0.06
Inhalation injury, n (%)	300 (17.3)	97 (15.5)	0.05	54 (13.9)	54 (13.9)	< 0.01
Consciousness level, n (%)			0.05			0.06
Alert	1144 (65.9)	424 (67.7)		272 (69.9)	275 (70.7)	
Delirium	319 (18.4)	108 (17.3)		65 (16.7)	58 (14.9)	
Somnolence	93 (5.4)	29 (4.6)		19 (4.9)	19 (4.9)	
Coma	180 (10.4)	65 (10.4)		33 (8.5)	37 (9.5)	
Transferred by ambulance, n (%)	1305 (75.2)	384 (61.3)	0.30	232 (59.6)	231 (59.4)	< 0.01
Hospital volume, mean (SD)	19.5 (22.4)	21.0 (23.2)	0.07	21.6 (26.7)	21.2 (24.2)	0.02
Complications, n (%)						
Cardiovascular	130 (7.5)	65 (10.4)	0.10	35 (9.0)	37 (9.5)	0.02
Neurological	24 (1.4)	5 (0.8)	0.06	2 (0.5)	4 (1.0)	0.06
Hematological	50 (2.9)	27 (4.3)	0.08	12 (3.1)	12 (3.1)	< 0.01
Hepatic	1 (0.1)	1 (0.2)	0.03	0 (0)	0 (0)	< 0.01
Renal	50 (2.9)	18 (2.9)	< 0.01	9 (2.3)	8 (2.1)	0.02
Comorbidity, n(%)						
Cerebrovascular disease	50 (2.9)	12 (1.9)	0.06	8 (2.1)	9 (2.3)	0.02
Dementia	58 (3.3)	7 (1.1)	0.15	7 (1.8)	6 (1.5)	0.02
Chronic pulmonary disease	25 (1.4)	10 (1.6)	0.01	12 (3.1)	8 (2.1)	0.07
Rheumatic disease	7 (0.4)	3 (0.5)	0.01	3 (0.8)	2 (0.5)	0.03
Peptic ulcer	86 (5.0)	31 (5.0)	< 0.01	24 (6.2)	20 (5.1)	0.05
DM without complication	199 (11.5)	57 (9.1)	0.08	43 (11.1)	36 (9.3)	0.06
DM with complication	24 (1.4)	7 (1.1)	0.02	5 (1.3)	4 (1.0)	0.02
Hemiparaplegia	2 (0.1)	1 (0.2)	0.01	0 (0)	0 (0)	< 0.01
Renal	20 (1.2)	6 (1.0)	0.02	2 (0.5)	1 (0.3)	0.04
Malignancy	25 (1.4)	12 (1.9)	0.04	10 (2.6)	6 (1.5)	0.07
Metastatic disease	3 (0.2)	2 (0.3)	0.03	0 (0)	0 (0)	< 0.01
HIV-AIDS	0 (0)	0 (0)	< 0.01	0 (0)	0 (0)	< 0.01
Myocardial infarction	6 (0.3)	0 (0.0)	0.08	0 (0)	0 (0)	< 0.01
Congestive heart failure	38 (2.2)	20 (3.2)	0.06	11 (2.8)	11 (2.8)	< 0.01
Peripheral vascular disease	5 (0.3)	2 (0.3)	< 0.01	1 (0.3)	1 (0.3)	< 0.01
Liver disease	42 (2.4)	22 (3.5)	0.07	12 (3.1)	11 (2.8)	0.02
Catecholamine use, n (%)						
Dopamine	122 (7.0)	73 (11.7)	0.16	29 (7.5)	28 (7.2)	0.01
Dobutamine	51 (2.9)	23 (3.7)	0.04	16 (4.1)	10 (2.6)	0.09
Noradrenaline	230 (13.2)	153 (24.4)	0.29	74 (19.0)	71 (18.3)	0.02
Adrenaline	27 (1.6)	229 (36.6)	0.99	27 (6.9)	26 (6.7)	0.01
Vasopressin	8 (0.5)	8 (1.3)	0.09	4 (1.0)	4 (1.0)	< 0.01
Blood transfusion, n (%)						
Red blood cells	77 (4.4)	199 (31.8)	0.8	60 (15.4)	63 (16.2)	0.02
Platelet	15 (0.9)	51 (8.1)	0.36	10 (2.6)	14 (3.6)	0.06
Fresh frozen plasma	214 (12.3)	200 (31.9)	0.49	76 (19.5)	78 (20.1)	0.01

(continued on next page)

Table 1 – (continued)

Variables	Unmatched cohort			Propensity score-matched cohort		
	Delayed surgery (n = 1736)	Early surgery (n = 626)	SMD	Delayed surgery (n = 389)	Early surgery (n = 389)	SMD
Type of Unit, n (%)						
ICU	223 (12.9)	76 (12.1)	0.02	35 (9.0)	33 (8.5)	0.02
HCU	31 (1.8)	11 (1.8)	< 0.01	5 (1.3)	2 (0.5)	0.08
Interventions, n (%)						
Mechanical ventilation	635 (36.6)	245 (39.1)	0.05	108 (27.8)	123 (31.6)	0.08
Immunoglobulin	10 (0.6)	10 (1.6)	0.09	3 (0.8)	4 (1.0)	0.03
Angiotensin III	79 (4.6)	30 (4.8)	0.01	10 (2.6)	13 (3.3)	0.05
Haptoglobin	193 (11.1)	73 (11.7)	0.02	33 (8.5)	33 (8.5)	< 0.01

Abbreviations: SMD, standardized mean difference; SD, standard deviation; BMI, body mass index; ICU, intensive care unit; HCU, high care unit; DM, diabetes mellitus; HIV-AIDS, human immunodeficiency virus-acquired immunodeficiency syndrome. Data are presented as number (%) unless otherwise stated.

7 days, the timing of excision or skin grafting is not associated with medium-term prognosis.

According to the results of previous enrollment studies [30], the extent and depth of burn injury appear to be the discriminating factors between early and delayed excision. The database used in this study includes the burn index, which reflects the extent and depth of burn injury and has been reported to be a useful prognostic factor [23]. However, according to the characteristics of the patients included in this study (unmatched cohort in Table 1), there was no obvious difference in the burn index between the early and delayed excision groups, and the burn index did not affect the timing of surgery. In addition, there was no difference in the in-hospital mortality between the early and delayed surgery groups. Although we also conducted subgroup analyses, including more severe burn patients with burn indexes >20 and >30, none of the subgroups showed significant differences in the outcomes (Table 3). Based on these results, early excision or skin grafting may not be necessary for all patients with severe burns. Further research is warranted to identify those who would benefit from early surgery for severe burns.

4.1. *Strengths and limitations*

Several guidelines for the initial management of burns [23–26] recommend early wound excision and skin grafting. However, this recommendation is based on studies with small sample sizes of 50–100 patients [6]. The present study included a large number of patients with severe burns using a nationwide inpatient database in Japan. However, this study has several limitations. First, this was a retrospective study using an administrative database, which does not include clinical data such as laboratory tests, vital signs, Acute

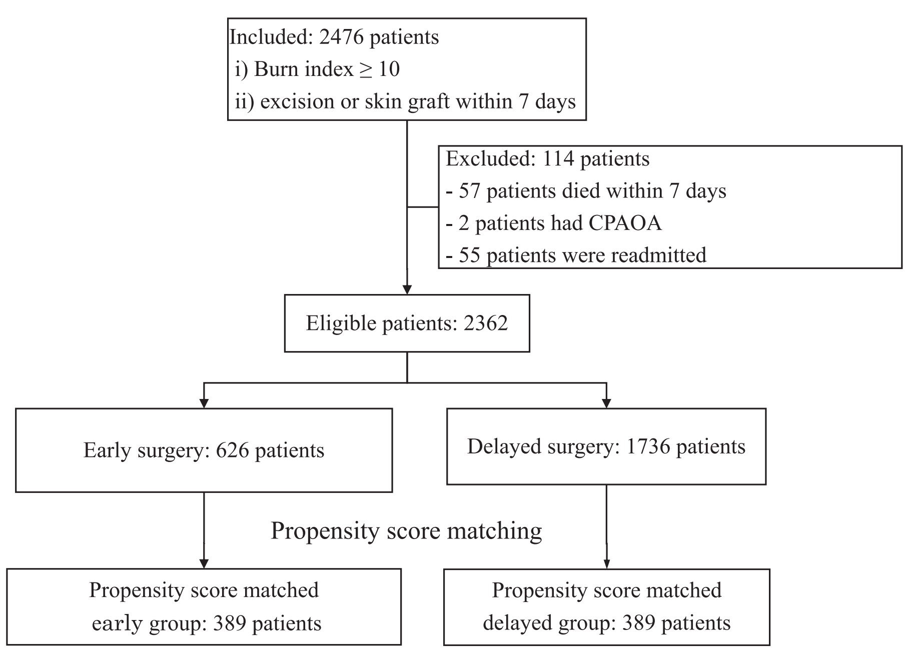

Fig. 1 – Flow chart of the patients included in the study. Abbreviations: CPAOA, cardiopulmonary arrest on arrival.

Table 2 – Outcomes before and after propensity score matching.

	Unmatched cohort			Propensity score-matched cohort		
	Delayed surgery (n = 1736)	Early surgery (n = 626)	*p* value	Delayed surgery (n = 389)	Early surgery (n = 389)	*p* value
In-hospital mortality, n (%)	340 (19.6)	123 (19.6)	1.000	67 (17.2)	62 (15.9)	0.700
Length of stay (days), mean (SD)	75.7 (81.3)	68.9 (93.4)	0.084	64.2 (54.4)	65.9 (81.0)	0.731
Duration of mechanical ventilation (days), mean (SD)	36.3 (42.1)	35.6 (43.0)	0.802	33.3 (32.1)	37.9 (51.2)	0.316
Duration of catecholamine use (days), mean (SD)	31.4 (39.7)	31.2 (33.9)	0.947	29.3 (28.3)	33.6 (37.4)	0.253

Abbreviations: SD, standard deviation.

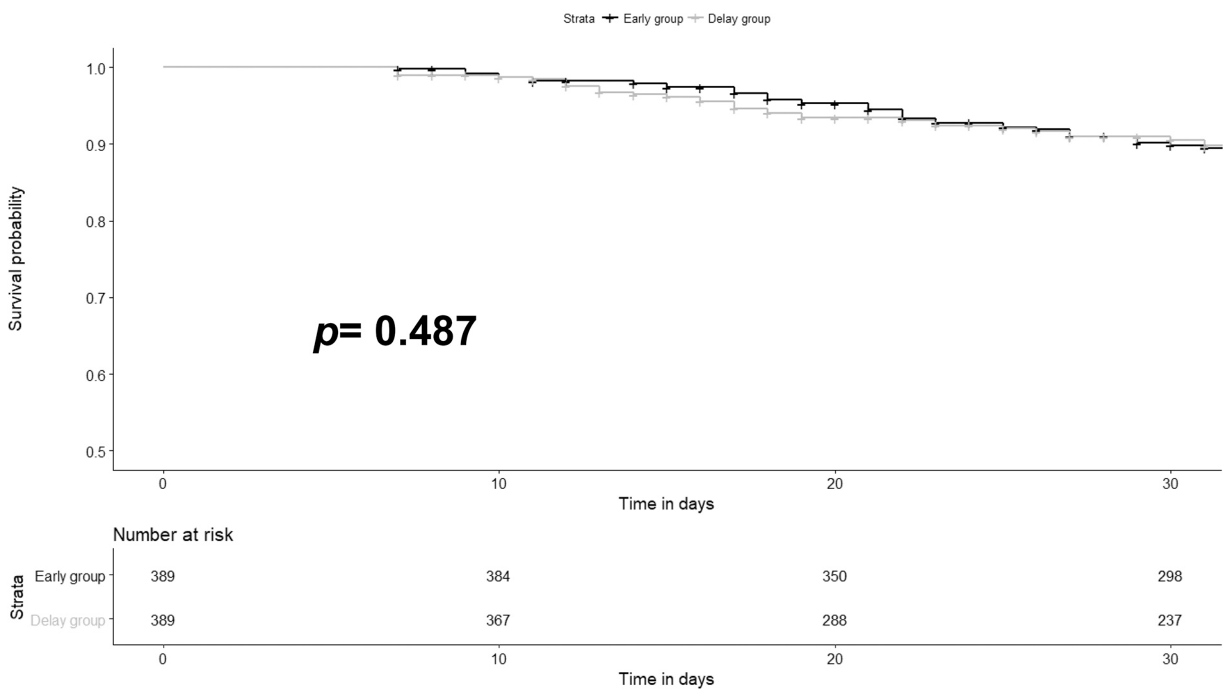

Fig. 2 – Kaplan–Meier survival curves for 30-day mortality after propensity score matching.

Table 3 – Results of the subgroup analyses of in-hospital mortality.

Variables	*p* for interaction In-hospital mortality
BMI	0.962
Burn index > 30	0.319
Burn index > 20	0.430
Inhalation injury	0.991
Mechanical ventilation within 2 d	0.130
Transferred by ambulance	0.313

Abbreviations: BMI, body mass index

Physiology and Chronic Health Evaluation scores, or Sequential Organ Failure Assessment scores. Although we adjusted for several potential confounding factors, such as the burn index, which is one of the most useful factors for assessing the prognosis of patients with severe burns [26,27], residual confounders might have biased the results. Second, information regarding the cause of the burn, type of wound surgery, or type of skin graft was not available in the database. Third, although we included patients who underwent excision or skin grafting within 7 d, we did not compare earlier surgeries performed within 1–2 d. Fourth, there was no information on clinical infection, laboratory data, or blood culture tests; therefore, the effects of early excision and skin grafting on infection were unclear.

5. Conclusions

Wound excision or skin grafting within 2 d of admission for patients with severe burns with a burn index ≥ 10 was not associated with in-hospital mortality, the length of stay, duration of mechanical ventilation, or duration of catecholamine use when compared with patients who underwent surgery within 7 d of admission. The results of this study suggest that it may not be necessary to consider the timing of excision or skin grafting to improve the medium-term prognosis, regardless of the burn index.

Statement of Ethics

This study was approved by the Institutional Review Board of the University of Tokyo (Tokyo, Japan). The requirement for patient consent was waived owing to the use of anonymized data.

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CRediT authorship contributions statement

KH, YS, HM, MN, MO, HO, KF, and HY designed and conducted the study. KH, YS, HM, MN, HO, and HY performed statistical analyses and drafted the manuscript. KO and HY supervised the writing of the manuscript. All authors contributed to the data interpretation, revised each draft for important intellectual content, and read and approved the final manuscript. The corresponding author (KH) attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted.

Declarations of interest

The authors declare that they have no competing interests.

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None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.burns.2023.01.013.

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