ORIGINAL ARTICLE

Effects of Delayed Wound Excision and Grafting in Severely Burned Children

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Hypothesis: Advances in burn treatment including early excision of the wound have increased survival in patients treated at specialized burn centers. We hypothesized that the patients with delayed wound excision and grafting would experience deleterious outcomes.

Methods: From 1995 to 1999, 157 children with acute burns covering 40% or more of total body surface area and having more than 10% of full-thickness burns were admitted to our institution within 2 weeks of injury. Among them, 86, 42, and 29 patients underwent first operation on days 0 to 2, days 3 to 6, and days 7 to 14 after burn, respectively. Outcomes observed were mortality, number of operative procedures, length of hospitalization, blood transfused, incidence of wound bacterial and fungal contamination, invasive wound infection, and sepsis.

Results: Demographic data for the groups showed no differences in sex or total body surface area burned. Mortality and number of operative procedures and blood transfusions were not different between groups. Hospitalizations were longer in the delayed groups, which was associated with a higher incidence of significant wound contamination ($P = .008$). Invasive wound infection also increased significantly with delay of excision ($P < .001$). An increased incidence of sepsis was seen in patients with delayed wound excision and grafting ($P = .04$).

Conclusions: Delays in excision were associated with longer hospitalization and delayed wound closure, as well as increased rates of invasive wound infection and sepsis. Our data indicate that early excision within 48 hours is optimal for pediatric patients with massive burns.

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THE BURN wound is considered to be a major source of inflammatory mediators, which play an important role in initiating and maintaining the postburn inflammatory response. The consequent acute-phase reaction, changes in vascular permeability, alteration in the coagulation system, impairment of gut function, hypermetabolic response, and immune depression are associated with the increased mortality and morbidity after severe burns.[1] A potential solution to avert these deleterious changes is to excise the wound before the response is maximized. Early burn wound excision and grafting, a surgical procedure performed to remove the burn wound eschar and cover the exposed wound with autograft, allograft skin, or artificial skin substitutes, is considered routine management in the treatment of the severely burned patients in most burn centers.[1-3] When compared with conservative wound treatment with serial debridement and delayed grafting, early wound excision and grafting was associated with decreased blood loss,[4] diminished wound infections,[5,6] and shortened hospital stay[7,8] in patients with medium or severe burns. However, its contribution to improved survival in extensive burns is debated.[4,7-9]

The most beneficial time point for early excision and grafting remains controversial. Past studies have described early excision to range from 24 hours to 7 days after burn.[4,8,10,11] Some studies questioned the safety and potential adverse effects of wound excision performed within 48 hours of injury. Issues discussed include the potential removal of otherwise viable tissue or, alternatively, incomplete excision of the burn wound during the early excision procedure because of inaccurate evaluation of the depth of the burn wound. These errors then could negatively influence the beneficial effect of performing early excision in severely burned patients.[12] To date, the impressive clinical advantage of the early excision has not allowed ethical conduct of a prospective controlled clinical trial to investigate the optimal time point for early wound excision and graft in massive burns. We are left with observational methods to determine the beneficial effects of early excision, and also to determine how early it should be done to derive the benefits.

Optimal operative and perioperative conditions are required to safely perform early total burn wound excision and grafting for the massive burn. This approach is therefore limited to burn centers. Thus, the time of the first surgical procedure will depend mostly on the time to burn center referral. This study reviews pediatric patients with burns greater than 40% of total body surface area (TBSA), referred to our burn center within 2 weeks after injury, and undergoing total burn wound excision within 48 hours of admission to our hospital. The intent of this study was to demonstrate different outcomes of relatively delayed wound excision and grafting compared with total burn wound excision and grafting within 48 hours after injury.

PATIENTS AND METHODS

One hundred fifty-seven children (aged from 1 month to 16 years) with acute burns greater than 40% of TBSA and third-degree burns greater than 10% of TBSA were admitted to Shriners Hospitals for Children at Galveston, Tex, between January 1, 1995, and December 31, 1999. The patients were excluded if the first wound excision grafting procedure was performed before admission, if the admission was later than 14 days after injury, if trauma such as fracture or visceral injury was present in addition to burn and inhalation injury, or if the patients underwent delayed resuscitation more than 24 hours after injury. Inhalation injury was identified by the presence of orofacial burns with the history of a closed-space injury, bronchoscopic evidence of soot and erythema, or blisters in the trachea or bronchus.

All patients received conservative wound care with topical antimicrobial agents during the period before admission to our institution. This included dressing with silver sulfadiazine cream applied once daily, and routine administration of systemic antibiotics according to the wound bacterial culture. Escharotomies were performed as needed before admission in patients with circumferential burns to the extremities or trunk at the referring hospital or en route to our hospital.

Patients were grouped into those admitted 0 to 2 days (within 48 hours), 3 to 6 days, and 7 to 14 days after injury. All patients originated from the southern United States, Mexico, or Central and South America. Total or near-total burn wound excision was performed within 24 hours of admission by tangential and/or fascial excision. The children were transported primarily by ground or air, accompanied by a physician, nurse, and respiratory therapist. All full-thickness burns were excised by 1 of 4 attending surgeons. Harvested autografts taken at 0.01 in (0.254 mm) with an electric dermatome (Padgett Instruments, Inc, Kansas City, Mo) or air dermatome (Zimmer, Inc, Warsaw, Ind) were meshed 4:1 with a mesher (Brennen Medical, Inc, St Paul, Minn), and were covered with 2:1 meshed cadaveric allograft (University of Texas Medical Branch Skin Bank, Galveston) for massive injuries. Some autografts were meshed 2:1 or 1:1 to maximize cosmetic outcomes where feasible. Meshed 2:1 cadaveric skin was used to cover all excised areas for which no autograft was available. Donor sites on the patients were covered with a sterile ointment dressing (Scarlet Red; Sherwood Services AG, St Louis, Mo). All remaining second-degree areas were covered with a mixture of half 1% silver sulfadiazine cream (Marion Merrill-Dow, Inc, Kansas City) and half 1% nystatin ointment (Pharmatek Laboratories, Inc, San Diego, Calif). All patients underwent bronchoscopic examination at the first operation to identify inhalation injury.

Patients were returned to the operating room every 5 to 10 days for further autografting after donor sites had healed. Broad-spectrum perioperative antibiotics were used in every case. In grafting, the hands were covered with sheet grafts or 1:1 mesh autograft without overlay. The face and neck were treated initially by application of a mixture of half 2% polymyxin B–bacitracin ointment (Burroughs Wellcome Co, Morris Plains, NJ) and half 1% nystatin ointment, then covered with sheet graft after separation of the eschar. Enteral nutrition was supplied to meet predicted requirements (1500 kcal/m^2 per day + 1500 kcal/m^2 burned per day). All patients with identifiable inhalation injury were treated with nebulized heparin sodium (100 units/kg per dose) and 20% acetylcysteine (Dey Laboratories, Inc, Napa, Calif).[13]

All patients were treated by means of presumptive standard protocols for nutritional support, infection control, and physiologic maintenance. Systemic antibiotics were routinely given perioperatively and once clinical evidence of infection and sepsis was apparent. Sepsis was defined after the patient met at least 4 of the following criteria: (1) body temperature greater than 38.5°C or less than 36.5°C; (2) respiratory rate greater than 30/min; (3) heart rate greater than 120 beats/min; (4) serum glucose level greater than 150 mg/dL (8.3 mmol/L); (5) thrombocytopenia with blood platelet count less than 100×10^3/μL; (6) white blood cell count greater than 15 000/μL or less than 5000/μL; (7) volume of nasogastric residual greater than 200 mL/h; (8) wound biopsy with bacterial counts equal to or greater than 10^5/g of tissue, and (9) confirmed evidence of pneumonia, urinary tract infection, or closed abscess. Wound infection was defined as wound culture with a quantitative bacterial count greater than 10^5/mL of tissue. Invasive wound infection was defined by the histologic finding of bacterial invasion into viable tissue.

Outcome measurements were mortality rate, amount of blood transfused, number of operations for wound closure, length of hospital stay, quantitative bacterial wound counts, invasive wound infection, incidence of sepsis, and complications such as adult respiratory distress syndrome and pneumonia during the hospital course. Pneumonia was diagnosed by fever and defined infiltrate on chest radiography. Adult respiratory distress syndrome was defined by a ratio of arterial oxygen pressure to fraction of inspired oxygen of less than 200, infiltrate in 5 lobes on chest radiography, and a pulmonary artery wedge pressure of 18 mm Hg or less (American-European Consensus Conference).[14]

Data are expressed as mean ± SEM, except when specifically mentioned. One-way analysis of variance followed by Tukey test for pairwise comparison and χ^2 or Fisher exact test were used where appropriate. Differences were considered significant at $P < .05$.

RESULTS

Demographic data are listed in **Table 1**. Total burn size, third-degree burn size, and incidence of inhalation injury were not significantly different between groups. Age, however, was significantly greater in patients admitted 3 to 6 days after injury. There were no significant differences in resuscitation time, heart rates, respiratory rates, and blood pressures among the groups in the initial stage of the burn injury.

Mortality is presented in **Table 2**. No significant differences were found between groups for overall mortality. Mortality rate of the patients with inhalation injury was increased in all groups, without differences between groups. The average postburn time of death in the day 0 to 2 group was 5.7±1.3 days, which was significantly earlier than that of the day 3 to 6 (34.5±1.5 days; $P<.001$) and day 7 to 14 (33.3±12.6 days; $P=.001$) groups (**Figure 1**). All patients who died in the day 3 to 6 and day 7 to 14 groups were diagnosed as having sepsis followed by multiple organ failure. Three of 13 patients died of sepsis in the early excision group. Other causes of death in the day 0 to 2 group were pulmonary complications (n=5), burn shock and renal failure (n=2), cerebral edema (n=2), and cardiac arrest (n=1).

Table 3 shows data for blood transfusion requirements during the first excision procedure (expressed as milliliters of blood transfused per squared centimeter excised), total blood requirement during hospitalization, the number of operative procedures, the length of hospital stay at our institution only (expressed as days per percentage of TBSA), and total length of hospital stay including the days before referral in survivors. No significant differences were found between groups for blood transfusions, number of operative procedures, and length of hospital stay at our institution. However, the total length of hospital stay in the day 7 to 14 group was significantly increased when compared with the day 0 to 2 group.

The incidence of significant wound bacterial or fungal contamination and invasive wound bacterial or fungal infection was 3 and 4 times increased in patients in the day 3 to 6 and day 7 to 14 groups, respectively, compared with the patients in the day 0 to 2 group (**Figure 2**). Similarly, the incidence of sepsis was increased in patients in both the day 3 to 6 and day 7 to 14 groups; however, the difference was not significant between these 2 groups (**Figure 3**).

No significant differences were found between groups for pulmonary complications, such as adult respiratory distress syndrome, pulmonary edema, and pneumonia (**Table 4**).

COMMENT

Early wound excision and grafting is considered the standard surgical approach in the management of severe burns, but the optimal time of early excision for severely burned children is still controversial. In this study, we reviewed data from 157 severely burned children with TBSA greater than 40% and third-degree

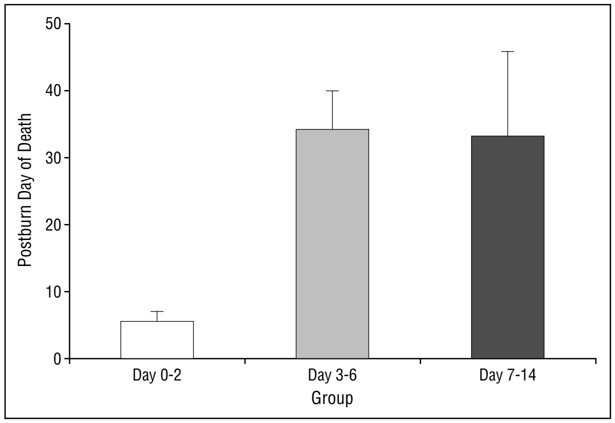

Figure 1. Postburn days of death. The average postburn time of the death in the day 0-2 group was significantly earlier than that of the day 3-6 ($P<.001$) and day 7-14 ($P=.001$) groups.

Table 1. Age, Sex, Burn Size, and Inhalation Injury in the Day 0-2, Day 3-6, and Day 7-14 Groups

	Day 0-2 Group (n = 86)	Day 3-6 Group (n = 42)	Day 7-14 Group (n = 29)
Sex, No. (%)			
Male	54 (62.8)	23 (54.8)	20 (69.0)
Female	32 (37.2)	19 (45.2)	9 (31.0)
Age, mean ± SD, y	5.4 ± 4.7	8.5 ± 5.0*	5.5 ± 3.7
Burn area, mean ± SD, % TBSA†	62.2 ± 17.5	60.3 ± 15.4	59.8 ± 16.6
Third-degree burn, mean ± SD, %	43.8 ± 30.2	40.0 ± 24.7	38.2 ± 26.2
Inhalation injury, No. (%)	44 (51.2)	19 (45.2)	10 (34.5)

*$P<.01$ vs day 0-2 and day 7-14 groups.
†TBSA indicates total body surface area.

Table 3. Comparison of Operative Data Between Groups*

	Day 0-2 Group (n = 73)	Day 3-6 Group (n = 38)	Day 7-14 Group (n = 26)
First BT†	0.45 ± 0.06	0.47 ± 0.04	0.42 ± 0.07
TBT†	1.83 ± 0.2	1.97 ± 0.3	1.67 ± 0.2
NOP	4.15 ± 0.2	4.42 ± 0.6	3.46 ± 0.3
HS‡	0.65 ± 0.03	0.65 ± 0.07	0.64 ± 0.05
THS‡	0.66 ± 0.03	0.71 ± 0.07	0.79 ± 0.06§

*Data are given as mean ± SEM. BT indicates blood transfusion; TBT, total blood transfusion; NOP, number of operative procedures; HS, hospitalized stay at our institution only; and THS, total length of hospital stay.
†In milliliters per squared centimeter of total body surface area.
‡Days per percentage of total body surface area.
§$P<.05$ between day 7-14 group and day 0-2 group.

Table 2. Comparison of Total Mortality in Patients With or Without Inhalation Injury

	Day 0-2 Group		Day 3-6 Group		Day 7-14 Group	
	No.	Death, No. (%)	No.	Death, No. (%)	No.	Death, No. (%)
Total	**86**	**13** (15.1)	**42**	**4** (9.5)	**29**	**3** (10.3)
Without inhalation injury	42	2 (4.8)	23	0	19	0
With inhalation injury	44	11 (25.0)*	19	4 (21.0)†	10	3 (30.0)†

*$P<.01$ between groups with and without inhalation injury.
†$P<.05$ between groups with and without inhalation injury (Fisher test).

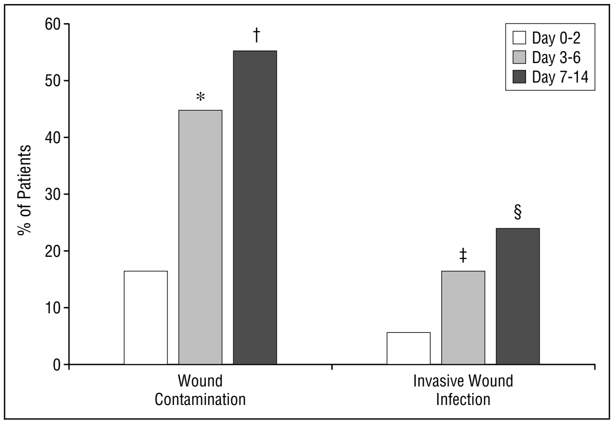

Figure 2. Percentage of patients with wound contamination or invasive wound infection. The incidence of significant wound bacterial or fungal contamination and invasive wound bacterial or fungal infection was significantly increased in patients in the day 3-6 and day 7-14 groups compared with the patients in the day 0-2 group (asterisk and double dagger, $P<.01$ and $P<.05$, respectively, between day 0-2 and day 3-6 groups; dagger and section mark, $P<.01$ and $P<.05$, respectively, between day 0-2 and day 7-14 groups).

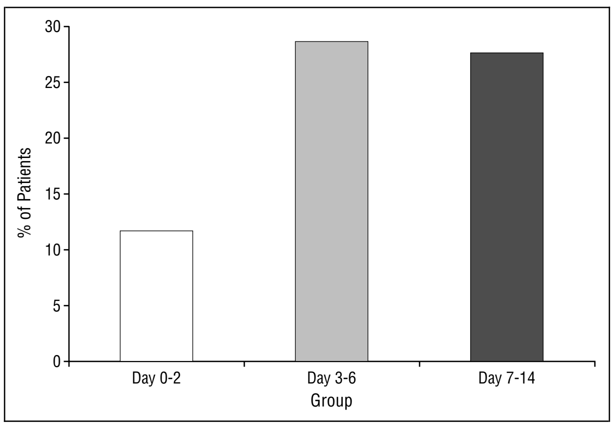

Figure 3. Percentage of patients with sepsis. The incidence of sepsis was significantly increased in patients in both the day 3-6 and day 7-14 groups compared with those in the day 0-2 group ($P<.05$). The difference was not significant between the day 3-6 and day 7-14 groups ($P=.05$).

burn greater than 10%, and compared outcomes for burned children who underwent first wound excision grafting within 48 hours, 3 to 6 days, and 7 to 14 days. The results showed that primary wound excision more than 48 hours after injury significantly increased the incidence of wound bacterial and fungal contamination, invasive wound infection, and sepsis compared with the patients who underwent early wound excision and grafting within 48 hours after injury. However, mortality, postburn pulmonary complications, the amount of blood transfused at the first operation and during the whole hospitalization, the number of operations for complete wound closure, and the length of hospitalization after referral were not different among these severely burned children. It was only with the addition of time spent at the referring hospital that differences between groups became apparent for total length of time to complete wound closure and discharge from any hospital. Nonetheless, total hospitalization time was significantly increased with increasing time to wound

Table 4. Postburn Pulmonary Complications*

Pulmonary Complication	No. (%) Day 0-2 Group	Day 3-6 Group	Day 7-14 Group
ARDS	7 (8.1)	8 (19.0)	3 (10.3)
Pneumonia	13 (15.1)	9 (21.4)	4 (13.8)
Pulmonary edema	33 (38.4)	18 (42.9)	12 (41.4)

*ARDS indicates adult respiratory distress syndrome. There were no significant differences between groups.

excision, arguing for a course of immediate excision (within 48 hours of injury) to improve this outcome.

Mortality and outcome after severe burns is influenced by several variables. In a previous study, our group identified increasing burn size and concomitant inhalation injury as 2 major factors in the prediction of the mortality in severely burned children.[15,16] In the current study, total mortality was not significantly different between patients undergoing total burn wound excision and grafting at an early time point within 48 hours, delayed to within 3 to 6 days, or later than 7 days after burn. Mortality was again significantly higher with presence of inhalation injury, suggesting that early wound excision and grafting within 48 hours does not specifically improve survival (as we expected) in severely burned pediatric patients concomitant with inhalation injury compared with relatively late wound excision.

In our patient population, no significant increase in postburn pulmonary complications, including adult respiratory distress syndrome, pulmonary edema, and pneumonia, was found by comparing different time points of excision and grafting. Immediate postburn wound excision had been shown in an animal study to increase pulmonary leukosequestration compared with the burn injury alone,[17] which is evidence that patients with very early excision might undergo an extra injury beyond the burn itself. In this study, we found that 5 patients (38.5% of the 13 who died) died of postoperative pulmonary complications, which may counter any benefits from immediate excision such that the 2 effects cancel each other, to result in no significant difference from relatively delayed excision in terms of pulmonary morbidity and mortality.

The average time of death in the day 0 to 2 group was within the first week (5.7±1.3 days), and that of the patients in the day 3 to 6 and day 7 to 14 groups was later than 4 weeks (34.5±5.5 and 33.3±12.6 days, respectively). This suggests that an early surgical approach within 48 hours could be an additional associated risk or, alternatively, that the patients in this group were influenced by the early insult of massive burn shock. However, patients in the day 3 to 6 and day 7 to 14 groups who were transferred to our hospital were those who survived beyond the initial period in those 2 groups. This might provide a potential source of bias favoring the later excision group to apparently decrease mortality in the day 3 to 6 and day 7 to 14 groups by excluding those who died before referral. Thus, in our opinion, the addition of these nonsurvivors to the analysis would likely have disclosed a benefit of excision within 48 hours. The amount of blood transfused during operations and throughout the hospitalization is determined by the amount required to maintain hemodynamic stability during the operation and prevent anemia. The blood requirement in the first operation of delayed wound excision is directly dependent on the blood loss at the wound and donor sites; however, in the early wound excision procedure, the amount of intravascular leakage into the interstitial space will be considered concomitantly. Our previous study showed that blood loss was significantly decreased in patients with TBSA greater than 30% when the first surgical procedure was performed within 24 hours of injury, compared with those who underwent the operation between 2 and 16 days, which was considered to be associated with the vessel constriction during the first 24 hours of burns.[4] We recently confirmed these results in a large study using regression techniques.[18] However, in this study, no significant difference in blood transfusion was found in the patients who had undergone relatively delayed wound excision compared with those with early wound excision. A potential explanation is that the power of this study was not sufficient to reach statistical significance. Refinement of excision techniques to minimize blood loss between the course of these studies could also explain the differences.

In this study, the surgical procedure was performed by using tangential or fascial excision to remove burn eschar. The wounds were then immediately covered with widely expanded meshed autograft overlaid with less expanded allograft, standard meshed autograft, or different kinds of biological or artificial skin substitutes. The removal of the burn eschar immediately by early wound excision and grafting potentially breaks the source of wound infection, and reestablishment of the skin barrier by wound coverage potentially improves burn-induced diminished immune response to prevent the further bacterial or fungal infection.[19-22] In this study, we definitively showed that delayed wound excision causes not only significantly more wound bacterial and fungal contamination, but also a higher incidence of invasive wound infection than that seen with early excision within 48 hours. Leaving devitalized tissue on the wound not only allowed increased bacterial and fungal colonization, but also induced increased bacterial and fungal invasion into subcutaneous viable tissue. This could be associated with impairment of the host immune defense system induced by the remaining burn wound, or facility of the induction of other routes of bacterial invasion, such as bacterial translocation.[23] The increased incidence of invasive bacterial and fungal infection into the viable tissue is likely to be the major cause of the increasing incidence of sepsis in the day 3 to 6 and day 7 to 14 groups. The patients in the day 3 to 6 group were 5 times more likely to develop significant wound infections and 2 times more likely to develop clinical sepsis, which suggests that the optimal time for early excision is within 48 hours of injury to avoid these complications. In this study, we used a definition of sepsis tailored specifically for burns.[24] Some cases were defined without a positive histologic finding of bacterial and fungal invasion into viable tissue or blood culture, but with such clinical criteria as the occurrence of hyperglycemia, thrombocytopenia, and enteric feeding intolerance. Bacteremia was detected only rarely. Thus, this clinical diagnosis of sepsis could be associated with the inflammatory mediator and endotoxin.[25,26] We did not measure metabolic variables in this study; however, according to a previous study by our group,[24] we suspect that patients in the delayed wound excision group are subject to much more hypermetabolism and catabolism than those with early wound excision. This might be, at least in part, associated with the higher incidence of sepsis and invasive wound infection in the delayed wound excision group. As we previously showed that sepsis was associated with increased hypermetabolism, this further argues for early excision to minimize metabolic complications after severe burn. All patients who died in the day 3 to 6 and day 7 to 14 groups were diagnosed as having sepsis followed by multiple organ failure; however, only 3 of 13 patients died of sepsis in the early excision group. This suggests that invasive bacterial and fungal wound infection and an increase in the risk of sepsis are major factors accounting for mortality in patients with delayed wound excision.

Although we did not show that increased incidence of significant wound contamination and sepsis directly influences mortality, length of hospitalization, blood transfusions, or the number of operative procedures to complete wound closure, we did find that the total length of hospital stay, including the days before referral, was significantly longer in the day 7 to 14 group than in the day 0 to 2 group. This implies that delayed wound excision only increased the time to complete wound closure, suggesting a benefit to the performance of immediate wound excision in massive burns.

From the present data, we conclude that, under the current management of extensive pediatric burns including sufficient resuscitation, early initiation of nutritional support, infection control, biological wound covering, and modulation of the hypermetabolic response, total or near-total burn wound excision within 48 hours after burns is feasible and beneficial in terms of length of hospitalization and the development of wound complications, but this may have no influence on survival. It should be emphasized that early referral to a burn center is of high priority. This allows early total burn wound excision and thus may reduce the risk of secondary infection.

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