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First aid is associated with improved outcomes in large body surface area burns

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ABSTRACT

Background: Animal studies indicate treating burn injuries with running water (first aid) for 20 min up to 3 h after burn reduces healing time and scarring. We have previously demonstrated the benefits of first aid in minor burn injuries with respect to a reduction in wound depth, faster healing, and decreased skin grafting utilisation. The purpose of this cohort study was to assess the effect of first aid on clinical outcomes in large body surface area burn injuries (≥20%).

Methods: Data was prospectively collected for patients with ≥20% TBSA burns from 2004– 2018. Multivariate regression analysis was used to determine the association of adequate first aid with 8 outcomes – mortality, total length of stay, total body surface area (TBSA), percentage/proportion of TBSA that was full thickness [PFTI], TBSA grafted, number of re-grafting sessions, intensive care admission, and intensive care length of stay. Adequate first aid was defined as the application of 20 min of cool, running tap water up to 3 h following the burn injury.

Findings: 390 patients were identified. Adequate first aid was received in 35.6% (139) of patients. There was a trend towards a reduction in mortality (OR 0.37; 95% CI 0.12–1.13; P = 0.08). Patients who received adequate first aid had a statistically significant 9.8% reduction in TBSA (95% CI −13.6% to −6.1%; P < 0.0001) as well as a 12% lower PTFI compared to patients who received inadequate first aid (95% CI −19% to −4%; P < 0.01). Whilst there was no significant effect of adequate first aid on the TBSA grafted (P = 0.37), adequate first aid was associated with a significantly less number of re-grafting sessions (95% CI −-0.29 to −0.08; P < 0.001).

Interpretation: Adequate first aid with 20 min of running water is associated with improved outcomes in large burn injuries. Significant benefits are seen in a reduction in TBSA, proportion of the burn wound that is full thickness, as well as decreased re-grafting. This has significant patient and health system benefits and adds to the body of evidence supporting 20 min of cooling in burns care.

1. Introduction

The progression of a burn injury is a process by which initially unburned tissue contiguous to the burn wound undergoes progressive necrosis after the actual insult has ceased. The Jackson Burn Wound Model showed the importance of this *zone of stasis*, the preservation of which, with proper treatment (including adequate first aid), is known to be critical in limiting the progression of burn depth and hence the subsequent

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morbidity and mortality [1]. Indeed, the conversion of a partial thickness burn wound that can heal spontaneously to a full thickness wound that benefits from excision and reconstruction, and results in permanent scarring or functionally-limiting contractures represents the most dramatic progression of the burn wound.

Cooling burn wounds with running water has been recognised as important for reducing progressive damage following a burn injury. Animal studies have demonstrated how the immediate application of cool, running water is associated with faster re-epithelialisation and reduced scarring [2–4]. Indeed, in a series of 4918 patients with up to 10% total body surface area (TBSA) burns, we demonstrated that adequate first aid in the form of cool, running tap water for 20 min (up to 3 h after the injury) was associated with benefits in wound-related outcomes including wound depth, healing time, and skin grafting utilisation [5]. The purpose of this study was to determine the effect of adequate first aid on clinical outcomes in severe burn (≥20% TBSA) injuries.

2. Methods

2.1. Setting and study population

The Burns Unit at Concord Repatriation General Hospital (CRGH) is one of two adult referral Burn Units in the state of New South Wales, Australia with a total population of over 7.5 million persons.

Admission to our Burns Unit is based on criteria established by the New South Wales Agency for Clinical Innovation Statewide Burn Injury Service. Indications for time critical retrieval include:

- Inhalational injury with cutaneous burns.
- Head and neck burns.
- Mid dermal, deep dermal or full thickness burns >20% total body surface area (TBSA) in adults.
- Burns with significant comorbidities.
- Deep circumferential burn to limbs or chest that compromises circulation or respiration.
- Significant electrical injuries.
- Significant chemical injuries.

Patients with significant TBSA burns and/or those who receive cardiovascular, respiratory or organ support are admitted to the intensive care unit.

2.2. Study design

This was a retrospective analysis of a cohort of patients using prospectively collected database data from the New South Wales Agency for Clinical Innovation Statewide Burn Injury Service. With institutional ethics approval (reference number 2008/11/113), data was collected prospectively between 2004 and 2018 for all adult patients above the age of 18 years with ≥20% TBSA burn injuries who were admitted to the Burns Unit, Concord Repatriation General Hospital (CRGH) in Sydney, Australia. The de-identified data was collected by trained nurses at our Burns Unit and then submitted to the New South Wales Agency for Clinical Innovation Statewide Burn Injury Service.

A total of 390 patients were identified from the database. Oral poisonings and inhalational injuries were excluded.

The following information was collected for each patient through database review:

- Patient demographics (age, gender).
- Burn mechanism.
- Smoking status.
- TBSA burned.
- Revised Baux score.
- Adequacy of first aid.
- Percentage of TBSA that was full thickness (PTFI).
- Total length of stay (tLOS).
- TBSA grafted.
- Number of re-grafting sessions.
- Need for intensive care unit (ICU) admission.
- Total length of intensive care unit admission (tLOSICU).
- Wound infection as defined by the American Burn Association consensus [6].

Adequate first aid was defined as application of a minimum of 20 min of cool, running tap water (between 8–25 °C) on to the burn wound within 3 h of the burn injury. First aid was administered either by the patient themselves, by first responders at the scene or by staff in referring hospitals.

Wound depth was assessed clinically and occurred after administration of first aid (if received). In our Unit, burn depth is assessed at the first presentation but may be amended as the burn wound evolves. Wound depth, for the purposes of this study, was not the depth recorded at initial assessment but rather the depth based on the trajectory of healing. Wound depth assessment was the same irrespective of whether the patient had received adequate first aid or not.

Overtly full thickness injuries in the setting of a ≥20% TBSA burn injury were generally treated with tangential burn wound excision within 72 h of the burn injury. Meshed autografting ensued if suitable donor sites were available. Alternatively, wounds were covered with a temporary skin substitute such as Biobrane™ until that time definitive wound reconstruction could occur. In instances where the majority of TBSA burned could demonstrate potential for spontaneous healing, wounds underwent debridement of blisters, removal of non-viable tissue, and scrubbing of surface contaminants followed by application of Biobrane™ in a manner similar to that described by Greenwood et al. [7]. Wound excision and skin grafting is recommended for wounds that do not show significant or satisfactory healing at 14 days after burn injury.

Throughout the period of 2004–2018, the same two burns surgeons in our Unit treated all the wounds in a consistent manner. Treatment protocols employed by our Unit are available online through our Statewide Burn Injury Service at https://www.aci.health.nsw.gov.au/networks/burn-injury.

2.3. Statistical analysis

Statistical analyses were performed using SAS software (SAS® Version 9.4, www.sas.com).

Baseline characteristics between the adequate first aid and inadequate first aid groups were compared using Pearson's chi-squared test for categorical variables (sex, burn mechanism, smoking status, mortality, ICU admission, and wound infection) and Wilcoxon rank sum tests for continuous variables (age, TBSA, Revised Baux score, PTFI, tLOS, TBSA grafted, number of re-grafting sessions, and tLOSICU).

A total of 8 distinct multivariate regression models were formed to assess relationships between those receiving adequate first aid (independent variable) and six dependent (outcome) variables, adjusting for appropriate potential confounders:

1. Mortality
2. TBSA
3. PTFI
4. tLOS
5. TBSA grafted
6. Number of re-grafting sessions
7. ICU admission
8. tLOSICU

Associations between adequate first aid and outcomes 4–8 were only conducted among patients that survived their burn injury.

Model 1 and 7 used logistic regression adjusting for burn mechanism, Revised Baux score, PTFI, and smoking status. Model 2 used Poisson regression (with an overdispersion parameter to better fit the model) adjusting for burn mechanism and age. Models 3–6 and 8 used Poisson regression (with an overdispersion parameter to better fit the model) adjusting for burn mechanism, Revised Baux score, PTFI, and smoking status.

Logistic regression models were assessed for goodness-of-fit using the method of Hosmer and Lemeshow [8].

From the logistic regression models, the Odds Ratio for the outcome (and 95% Confidence Interval) was determined. The least squares mean (change in outcome) and 95% Confidence Intervals were determined for all linear models. Statistical significance was defined as a P value <0.05 and all statistical tests were two-tailed.

3. Results

A total of 390 patients were identified. There were 306 males (78.5%) and 84 females (21.5%). The mean age at presentation was 41.8 ± 18.2 years (mean $\pm$ SD) with the mean TBSA $37.5\% \pm 19.1\%$ and mean PTFI $56\% \pm 40\%$.

The mean Revised Baux score was 90.1 ± 28.0. Overall mortality was 16.7% (65 patients) with the mean Revised Baux score in this group 124.5 ± 22.3. Of the 390 patients, 292 required intensive care admission with the mean tLOSICU 11.5 ± 14.4 days. The mean tLOS for patients who did not succumb to their burn injury was 40.8 ± 38.3 days.

The mean TBSA grafted amongst patients who did not succumb to their injury was $14.5 \pm 15.0\%$. Of the 325 patients who survived their burn injury, 70 patients (21.5%) underwent re-grafting with the mean number of re-grafting sessions 1.4 ± 0.7.

Adequate first aid, defined as cool, running tap water on the wound for at least 20 min and up to 3 h following the burn injury, was received in 139 patients (35.6%). First aid was inadequate in the remainder 251 patients (64.4%). A comparison of patients with adequate and inadequate first aid is provided in Table 1.

3.1. *Regression models*

Table 2 demonstrates the findings of multivariate regression analyses.

Patients who received adequate first aid had a trend towards a reduction in mortality (OR 0.37; 95% CI 0.12–1.13; $P = 0.08$). No statistically significant difference in tLOS was observed between those who received adequate and inadequate first aid (effect size −0.6 days; 95% CI -5.1 days – 3.8 days; $P = 0.78$).

Adequate first aid was associated with a statistically significant 9.8% reduction in TBSA (95% CI −13.6% to −6.1%; $P < 0.0001$). Regarding the percentage of the TBSA burn injury that was full thickness (PTFI), patients who received adequate first aid had a statistically significant 12% lower PTFI compared to patients who received inadequate first aid (95% CI −19% to −4%; $P < 0.01$). Whilst there was no significant effect of adequate first aid on the TBSA grafted ($P = 0.37$), adequate first aid was associated with a significantly less number of re-grafting sessions (effect size −0.19; 95% CI −0.29 to −0.08; $P < 0.001$).

There was no statistically significant effect of adequate first aid on need for ICU admission ($P = 0.39$) or tLOSICU ($P = 0.76$).

4. Discussion

This cohort study is the first to describe the effect of adequate, recommended cooling on a range of clinical outcomes in a large series of adult severely burn injured patients. Our results indicate that first aid is associated with a beneficial effect on clinical outcomes. Adequate first aid is not only associated with a significant reduction in TBSA and wound depth but also in the need for re-grafting. No significant relationship between adequate first aid and length of stay or ICU admission was observed but there was a trend towards a reduction in overall morality.

We have previously demonstrated, in a series of nearly 5000 patients with minor burn injuries, that adequate first aid has significant effects on wound-related clinical outcomes, namely a reduction in burn wound depth and healing time as well as a significant increase in the body surface area that does not undergo grafting (and therefore heals spontaneously)(5). We believe that the findings of this analysis of larger body surface area burn injuries represents an extension of our previous study. The combined effects of a reduction in overall TBSA and a decrease in the proportion of the total burn injury that is full thickness (and therefore an increase in the proportion that is partial thickness) reveals the importance of preservation of the zone of stasis by burn wound cooling. Indeed, it has been demonstrated that regression (or 'secondary deepening') of this zone of stasis often contributes to greater burn surface area and depth, which has multiple local and systemic

Table 1 – Comparison of patients with adequate and inadequate first aid.

Characteristic	Adequate first aid (n = 139; 35.6%)	Inadequate first aid (n = 251; 64.4%)	p-value[a]
Sex			0.04
Male	117 (84.2%)	189 (75.3%)	
Female	22 (15.8%)	62 (24.7%)	
Age (± SD; years)	40.0 ± 17.0	42.7 ± 18.9	0.30
TBSA (± SD; %)	31.5 ± 14.2	40.8 ± 20.6	<0.0001
Revised Baux score (± SD)	80.5 ± 25.2	95.4 ± 28.1	<0.0001
Smokers	3 (2.1%)	9 (3.6%)	0.42
Mechanism			0.02
Chemical	4 (2.9%)	3 (1.2%)	
Contact	0 (0.0%)	1 (0.4%)	
Electrical	0 (0.0%)	5 (2.0%)	
Explosion	26 (18.7%)	19 (7.6%)	
Flame	88 (63.3%)	188 (74.9%)	
Friction	0 (0.0%)	1 (0.4%)	
Other	0 (0.0%)	3 (1.2%)	
Radiant heat	2 (1.4%)	3 (1.3%)	
Scald	19 (13.7%)	28 (11.2%)	
PTFI (% of TBSA burned)	41.7 (37.4)	64.2 (38.4)	<0.0001
Mortality	7 (5.0%)	58 (23.1%)	<.0001
Length of stay[b] (± SD; days)	30.9 (27.0)	47.6 (43.1)	<.0001
TBSA grafted (± SD; % of body surface area burned)	11.9 (12.5)	16.4 (16.4)	0.06
Number of re-grafting sessions	0.2 (0.6)	0.3 (0.7)	0.39
ICU admission	84 (63.6%)	147 (76.2%)	0.01
ICU length of stay[b] (± SD; days)	5.2 (8.0)	10.0 (14.5)	<0.001

SD, standard deviation; TBSA, total body surface area; PTFI, percentage of TBSA that was full thickness injury; ICU, intensive care unit.
[a] Pearson's chi-squared for categorical variables and Wilcoxon rank sum for continuous variables.
[b] For patients who survived their burn injury.

consequences that increase morbidity [9]. Mechanisms that might underpin burn wound progression include inflammatory mediators, ischaemia, reactive oxygen species, and autophagy [10]. Cooling may target these very pathogenetic processes, with experimental evidence suggesting that it may improve cell survival by decreasing cellular energy requirements in this hypoxic environment [11] and blunt the local inflammatory response by inhibiting histamine release [12,13], decreasing bradykinin-mediated vasodilatation and vascular permeability, and decreasing activation of the arachidonic acid cascade [2].

The observation that cooling may retard burn wound progression is further supported by the finding that adequate first aid was associated with a lower use of re-grafting. The latter might suggest that patients who have inadequate cooling undergo further burn wound progression after early burn wound excision and autografting, and therefore undergo higher rates of re-grafting compared to wounds that have been adequately cooled and accurately excised. Although not specifically assessed in our study, the net effects of a reduction in overall TBSA, proportion of the total burn injury that is full thickness, and operative intervention are more rapid wound healing, decreased health care costs, less psychological trauma for the patient, and a reduction in scarring.

The results of this study and our previous analysis [5] represent the first form of clinical evidence for prior animal studies which have demonstrated a benefit from the application of 20 min of cool running water up to 3 h after burn [2,4,14].

Table 2 – Multivariate analyses of the association of adequate first aid with clinical outcomes.

Outcome	Effect size	95% Confidence Interval	p-value	Hosmer-Lemeshow test*
Mortality	OR 0.37	0.12 to 1.13	0.08	0.07
TBSA (%)	−9.8	−13.6 to −6.1	<0.0001	–
Percentage of TBSA that was full thickness injury (%)	−12	−19 to −4	<0.01	–
Total length of stay (days)	−0.6	−5.1 to 3.8	0.78	–
TBSA grafted (%)	−1.0	−3.3 to 1.2	0.37	–
Number of re-grafting sessions	−0.19	−0.29 to −0.08	<0.001	–
ICU admission	OR 0.77	0.42 to 1.40	0.39	0.99
Total length of ICU stay (days)	0.1	−0.6 to 0.8	0.76	–

OR, odds ratio; TBSA, total body surface area; ICU, intensive care unit.
* Hosmer-Lemeshow $P < 0.05$ indicates poor model fit, $P > 0.05$ indicates good model fit.

Only 3 contemporary studies have examined the effect of first aid on clinical outcomes in much smaller cohorts, and produced divergent results. One found that burns treated with first aid were less deep and underwent less skin grafting [15] while the other found a significant relationship between first aid and re-epithelialisation time in contact burn injuries only [16]. Wood et al. [17], in a more recent study, examined the effect of *any* duration of cooling after burn on indicators of burn severity (wound repair surgery, ICU admission, and length of hospital stay). The authors only identified a significant effect on wound repair surgery when first aid duration was 20–39 min (but not with any other intervals of less or more duration). Interestingly, a significant increase in probability for needing graft surgery was seen with first aid duration of 40 min or more. Moreover, the study did not detail the effect of first aid on other wound-related outcomes (depth, healing time, grafting requirements), and the authors observed similar inconsistent, non-linear associations between first aid duration and other burn severity indicators (e.g., a significant reduction in ICU admission for duration of 10–19 minutes but not other intervals), making their data difficult to interpret.

The present study has examined adequate, recommended first aid and its impact on outcomes in a large cohort of severe burn injuries and coupled with our previous results [5] provides a sound, clinical basis for prior experimental research. These findings have implications for the treatment of burn injuries worldwide. Cooling burn wounds with running water for 20 min (up to 3 h after burn) is a simple, inexpensive and widely available treatment for burn injuries. It should be promoted globally as a standard practice in the pre-hospital and hospital environment, as well as a fundamental public health education strategy. These studies also highlight the need for a clear, consistent, global first aid message, especially when first aid education is not consistent around the world [3,18], knowledge of recommended first aid treatment for burn injuries is inadequate amongst both the public [19] and health care workers [20], and when compliance with recommended first aid treatment in both the developed [16,21,22] and developing world [23–25] is poor.

While this study supports the beneficial effect of cooling burn wounds, there are certain limitations. The study size is modest in comparison to our previous study of nearly 5000 patients [5] but remains the largest in the literature with respect to large burn injuries (TBSA $\geq$ 20%). Additionally, severe burn injuries are complex and heterogenous, and treatment is individualized on the basis of patient factors, the burn wound, and sequelae of the burn injury. We were therefore unable to account for the impact of all aspects of clinical management (e.g., adequacy of fluid resuscitation, timing of wound excision, maintenance of normothermia, wound sepsis, dressing products etc). Furthermore, as burn wounds were not assessed prior to and after administration of first aid, there is no way to definitively and conclusively prove the effect of first aid on TBSA and reduction in PTFI. However, there are obvious ethical and logistic concerns in performing such a study.

There were other notable features regarding first aid identified in this study. Adequate first aid was received in 35.6% of patients in the present study which was more than 20% less than our previous study [5]. However, as far as we are aware, there are no studies in the literature that specifically examine the use of adequate first aid in the setting of large body surface area adult burn injuries. Indeed, the rates of adequate first aid receipt in the literature range from 7 to 39% [16,19,21,22,26] but these studies represent either a paediatric or minor burn injury cohort. The rate of adequate first aid receipt in the present study is probably explained by multiple factors including additional clinical priorities of the severe burn injury (e.g. intubation for inhalational injury or airway protection, rapid fluid resuscitation), lack of opportunity (e.g. no running water available at time of injury) or lack of education. At present, there is no evidence that cooling with running water contributes to hypothermia [27].

5. Conclusion

Preservation of the zone of stasis should be a priority in the initial management of severe burn injuries. This study demonstrates that first aid in the form of 20 min of cool, running water onto the burn wound (up to 3 h after burn) is associated with improved clinical outcomes in large burn ($\geq$20% TBSA) injuries. Benefits are seen in a reduction in TBSA, depth, and in re-grafting. This human cohort study adds to the clinical evidence supporting a clear, consistent first aid message. Current recommendations by organisations such as the Australian and New Zealand Burn Association supporting cooling of the burn wound for 20 min should be widely promoted on a global level.

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Ethics

Institutional ethics approval was obtained for the purposes of this study (reference number 2008/11/113).

Ethical review was by the New South Wales Population & Health Services Research Ethics Committee. This enabled use of all existing and prospectively collected data within the database of the New South Wales Agency for Clinical Innovation Statewide Burn Injury Service for research purposes.

Conflict of interest

None.

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