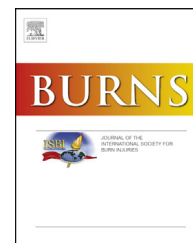


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First aid improves clinical outcomes in burn injuries: Evidence from a cohort study of 4918 patients

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ARTICLE INFO

Article history:

Accepted 13 September 2018

Keywords:

First aid

Cooling

Jackson burn wound model

Water

Burn wound

ABSTRACT

Background: Animal studies indicate treating burn injuries with running water (first aid) for 20min up to 3h post-burn reduces healing time and scarring. There is a lack of human data to support such a recommendation. The purpose of this cohort study was to assess the effect of first aid on clinical outcomes.

Methods: Data was prospectively collected for patients with <10% total body surface area (TBSA) burns from 2007–2012. Multivariate regression analysis was used to determine the association of adequate first aid with four outcomes — wound depth, requirement for skin grafting, healing time (in non-grafted patients), and TBSA not grafted (in grafted patients). Adequate first aid was defined as the application of 20min of cool, running tap water up to 3h following the burn injury.

Findings: 4918 patients were identified. Adequate first aid was received in 58.1% (2859) of patients. It was associated with a statistically significant reduction in burn wound depth (OR 1.39; 95% CI 1.24–1.55; $P < 0.001$) but was not associated with a reduction in TBSA ($P = 0.86$) or requirement for grafting ($P = 0.47$). In patients not requiring grafting, those who received adequate first aid were healed on average 10% (HR 1.10; 95% CI 1.03–1.18; $P < 0.01$) or 1.9 days faster (95% CI -2.9 to -0.9 ; $P < 0.001$). Adequate first aid in patients requiring grafting was associated with a 15% increase in TBSA that was not grafted (0.27%; 95% CI 0.01–0.52; $P = 0.04$). **Interpretation:** Adequate first aid with 20min of running water is associated with improved outcomes. Benefits are seen in a reduction in wound depth, faster healing, and decreased grafting requirements. This has significant patient and health system benefits, and calls for promotion of 20min of running water globally in burns care.

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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

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<https://doi.org/10.1016/j.burns.2018.09.024>

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the progression of burn depth and hence the subsequent morbidity and mortality [1]. Indeed, the conversion of a partial thickness burn wound that can heal spontaneously to a full thickness wound that requires debridement 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]. The current recommendation for first aid treatment of burns from the Australian and New Zealand Burn Association is to cool the burn wound with cool, running tap water for 20min, up to 3h after the injury has occurred [5]. There is, however, a lack of reported human data to support this, and there have been no randomised controlled human trials for both ethical and logistical reasons.

The purpose of this study was to determine the effect of adequate first aid on clinical outcomes in a large cohort of adult burn injured patients.

2. Methods

2.1. 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 2007 and 2012 for all adult patients above the age of 18 years with <10% total body surface area (TBSA) burn injuries who presented to the Burns Ambulatory Care Clinic at the Burns Unit, Concord Repatriation General Hospital 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 5035 patients were identified from the database. Patients whose first aid status was unknown were excluded (n=117) leaving a total of 4918 patients. Oral poisonings and inhalational injuries were excluded.

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

- patient demographics (age, gender)
- smoking status
- TBSA burned
- burn wound depth
- burn mechanism
- first aid adequacy
- received skin grafting
- TBSA grafted and not grafted (in patients requiring skin grafting)
- time to complete re-epithelialisation from date of burn (in patients not requiring skin grafting)
- number of outpatient visits (in patients not requiring skin grafting)

Burn depth was labelled superficial dermal, mid dermal or deep dermal/full thickness. The deepest part of the burn injury was the wound depth recorded for this study, as this was the area that would take the longest to heal.

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. The only exception to this is if it is an overtly full thickness burn injury in which case skin grafting follows if it is appropriately sized. In all other minor burn injuries, the wound is closely monitored in the first 7 days after the injury to determine the trajectory of healing potential. When healing is demonstrable and likely, these injuries are classified appropriately as superficial or mid dermal burn injuries. Those injuries that do not demonstrate a significant capacity to heal by 14 days from the date of the injury are considered deep dermal burns. Wound excision and skin grafting is recommended for injuries that do not show significant or satisfactory healing at 14–21 days post burn injury. Follow-up occurs until the burn wound has healed completely. 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 as defined above. Wound depth assessment was the same irrespective of whether the patient had received adequate first aid or not.

Adequate first aid was defined as the application of 20min of cool, running tap water up to 3h following the burn injury.

Throughout the period of 2007–2012, 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>.

2.2. 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, wound depth, smoking status, and grafting) and Wilcoxon rank sum tests for continuous variables (age, TBSA, time to re-epithelialisation, number of outpatient visits and TBSA not grafted).

A total of 6 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. Wound depth
2. TBSA
3. Underwent skin grafting
4. Time to re-epithelialization (for patients who did not undergo skin grafting)
5. Number of outpatient visits (for patients who did not undergo skin grafting)
6. TBSA not grafted (for patients who underwent skin grafting)

Associations between adequate first aid and time to re-epithelialisation as well as number of outpatient visits were only conducted among patients that did not undergo skin grafting as both these outcomes were altered by operative intervention. Separate analyses were conducted among patients who underwent grafting to examine the association between adequate first aid and the TBSA that was not grafted.

Model 1 used ordinal logistic regression (because wound depth was a categorical outcome with three groups of increasing severity) adjusting for burn mechanism. Model 3 used simple logistic regression, adjusting for age, smoking status, and wound depth. Models 2 and 6 used general linear regression, adjusting for burn mechanism, age, smoking status, and wound depth (and TBSA for model 6). Model 4 (assessing time to re-epithelialisation) was analysed by both Cox regression and general linear regression, adjusting for age, smoking, wound depth, and TBSA. Model 5 used Poisson regression adjusting for age, wound depth, and TBSA.

Covariates were all adjusted using multivariate logistic regression if the outcome was binary or multivariate linear regression if the outcome was a continuous variable.

From the logistic regression models (1 and 3), 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 linear models (2, 5, and 6). A hazard ratio (and 95% Confidence Interval) was determined for model 4.

Statistical significance was defined as a P value <0.05 and all statistical tests were two-tailed.

3. Results

A total of 4918 patients were identified. There were 2996 males (60.9%) and 1922 females (39.1%). The mean age at presentation was 38.2 ± 16.4 years (mean $\pm$ SD) and the mean TBSA was $1.9 \pm 2.1\%$. The distribution of burn mechanism is shown in Fig. 1.

Adequate first aid, defined as cool, running tap water on the wound for at least 20min and up to 3h following the burn injury, was received in 2859 patients (58.2%). There was inadequate first aid in the remainder 2059 patients (41.8%). A comparison of patients with adequate and inadequate first aid is provided in Table 1.

The deepest wound area recorded was superficial dermal in 1882 cases (38.2%), mid dermal in 2201 cases (44.8%), and deep dermal/full thickness in 835 cases (17.0%). The mean age of patients with superficial burn injuries (superficial dermal and mid dermal burns) and deep dermal/full thickness burns was 35.9 ± 15.2 years and 42.4 ± 18.4 years, respectively ($P < 0.001$).

There were 4343 patients (88.3%) that did not undergo skin grafting. The mean time to complete re-epithelialisation and number of outpatient visits in this cohort were 14.9 ± 17.3 days, and 3.5 ± 2.6 , respectively. Of these 4343 patients, 2587 patients (59.6%) received adequate first aid.

There were 575 patients (11.7%) that underwent skin grafting. Of these 575 patients, 272 patients (47.3%) received adequate first aid. The mean time to complete re-epithelialisation and mean number of outpatient visits were 31.9 ± 25.1 days, and 5.6 ± 4.0 , respectively. The mean TBSA requiring skin grafting (where this was known; 571 patients) was $2.2 \pm 1.6\%$ with the mean TBSA (where this was known; 568 patients) not grafted $0.8 \pm 1.6\%$.

3.1. Regression models

Table 2 demonstrates the findings of multivariate regression analyses.

Patients who received adequate first aid had a significant reduction in wound depth (Odds Ratio 1.39; 95% CI 1.24–1.55; $P < 0.001$). Those that received adequate first aid were 39% more likely to have a superficial dermal wound instead of a mid-dermal wound, and 39% more likely to have a mid-dermal instead of a deep dermal/full thickness wound ($P < 0.001$).

Fig. 2 demonstrates the predicted probabilities of wound depth for patients who received adequate and inadequate first aid organised by burn mechanism. A significantly higher probability of a superficial dermal wound was observed for all burn mechanisms in patients that received adequate first aid as compared to inadequate first aid (Fig. 2(a); $P < 0.001$). On the corollary, a significantly lower probability of a deep dermal/full thickness wound was observed for all burn mechanisms in patients that received adequate first aid as compared to inadequate first aid (Fig. 2(c); $P < 0.001$).

There was no statistically significant difference in TBSA between those who received adequate first aid and those who received inadequate first aid (effect size 0.01% TBSA; 95% CI -0.11 to $+0.13$; $P = 0.86$).

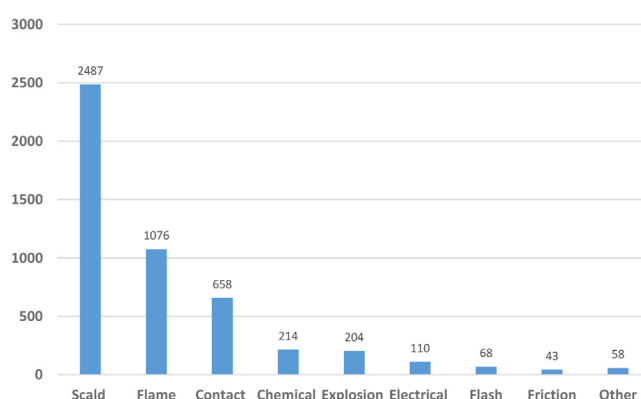


Fig. 1 – Mechanism of burn in 4918 outpatients treated between 2007 and 2012.

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

Characteristic	Adequate first aid (n=2859; 58.1%)	Inadequate first aid (n=2059; 41.9%)	p-Value ^a
Sex			0.78
Male	1737 (60.8%)	1259 (61.2%)	
Female	1122 (39.2%)	800 (38.8%)	
Age	37.0±15.1	40.0±17.9	<0.001
TBSA	1.9±2.1	1.8±2.0	0.23
Deepest wound			<0.001
Superficial	1158 (40.5%)	724 (25.3%)	
Mid-dermal	1351 (47.3%)	850 (29.7%)	
Deep-dermal or full thickness	350 (12.2%)	485 (17.0%)	
Smokers	434 (15.2%)	231 (11.2%)	<0.001
Mechanism			<0.001
Scald	1546 (54.1%)	941 (45.7%)	
Flame	685 (24.0%)	391 (19.0%)	
Contact	316 (11.0%)	342 (16.6%)	
Chemical	86 (3.0%)	128 (6.2%)	
Explosion	130 (4.5%)	74 (3.6%)	
Electrical	54 (1.9%)	56 (2.7%)	
Radiant	7 (0.2%)	61 (3.0%)	
Friction	10 (0.4%)	33 (1.6%)	
Other	25 (0.9%)	33 (1.6%)	
Underwent grafting	251 (8.8%)	324 (15.7%)	<0.001
Did not undergo grafting	2608 (91.2%)	1735 (84.3%)	
Time to re-epithelialization (among non-grafted patients)	12.7±12.0	16.2±21.0	<0.001
Number of outpatient visits (among non-grafted patients)	3.2±2.2	3.5±2.8	0.25
TBSA grafted (among patients who underwent skin grafts)	2.2±1.6	2.2±1.6	0.86
TBSA not grafted (among patients who underwent skin grafts)	1.0±1.8	0.6±1.3	<0.001

^a Pearson's chi-squared for categorical variables and Wilcoxon rank sum for continuous variables.

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

Outcome	Effect size	95% Confidence interval	p-Value
Reduction in wound depth ^a	OR 1.39	1.24–1.55	<0.001
TBSA	0.01	–0.11 to 0.13	0.86
Requirement for skin grafting	OR 0.91	0.70–1.18	0.47
Time to re-epithelialisation (among non-grafted patients)	HR 1.10 ^b	1.03–1.18	<0.01
	–1.9 ^c	–2.9 to –0.9	<0.001
Number of outpatient visits (among non-grafted patients)	–0.04	–0.17 to 0.09	0.58
TBSA not grafted (among patients who underwent skin grafts)	0.27	0.01–0.52	0.04

OR, odds ratio; TBSA, total body surface area; HR, hazard ratio.

^a Ordinal logistic regression with wound depth stratified hierarchically from superficial dermal to mid dermal to deep dermal/full thickness. Reduction in depth indicates probability that depth of the wound with adequate first aid was one level less deep (superficial dermal instead of mid dermal, and mid dermal instead of deep dermal/full thickness).

^b Cox regression result.

^c General linear regression result.

While adequate first aid slightly lowered the risk of grafting by 9% (Odds Ratio 0.91; 95% CI 0.70–1.18), this difference was not statistically significant ($P=0.47$).

In patients that did not receive skin grafting, time to re-epithelialisation, with general linear regression, was significantly shorter among those who received adequate first aid, occurring on average 1.9 days faster (effect size –1.9 days; 95% CI –2.9 to –0.9; $P<0.001$). Using Cox regression, time to re-epithelialisation with adequate first aid was 10% shorter (Hazard Ratio 1.10; 95% CI 1.03–1.18; $P<0.01$).

There was no significant difference in the total number of outpatient visits required between the adequate and

inadequate first aid groups (effect size –0.04 visits; 95% CI –0.04 to 0.03; $P=0.68$).

In patients that underwent skin grafting, adequate first aid was associated with a 15.0% increase in the TBSA not grafted (effect size 0.27% TBSA, 95% CI 0.01–0.52; $P=0.04$).

4. Discussion

This human cohort study is the first to describe the magnitude of the effect of first aid on wound-related clinical outcomes in a large series of adult burn injured patients. Our results indicate that first

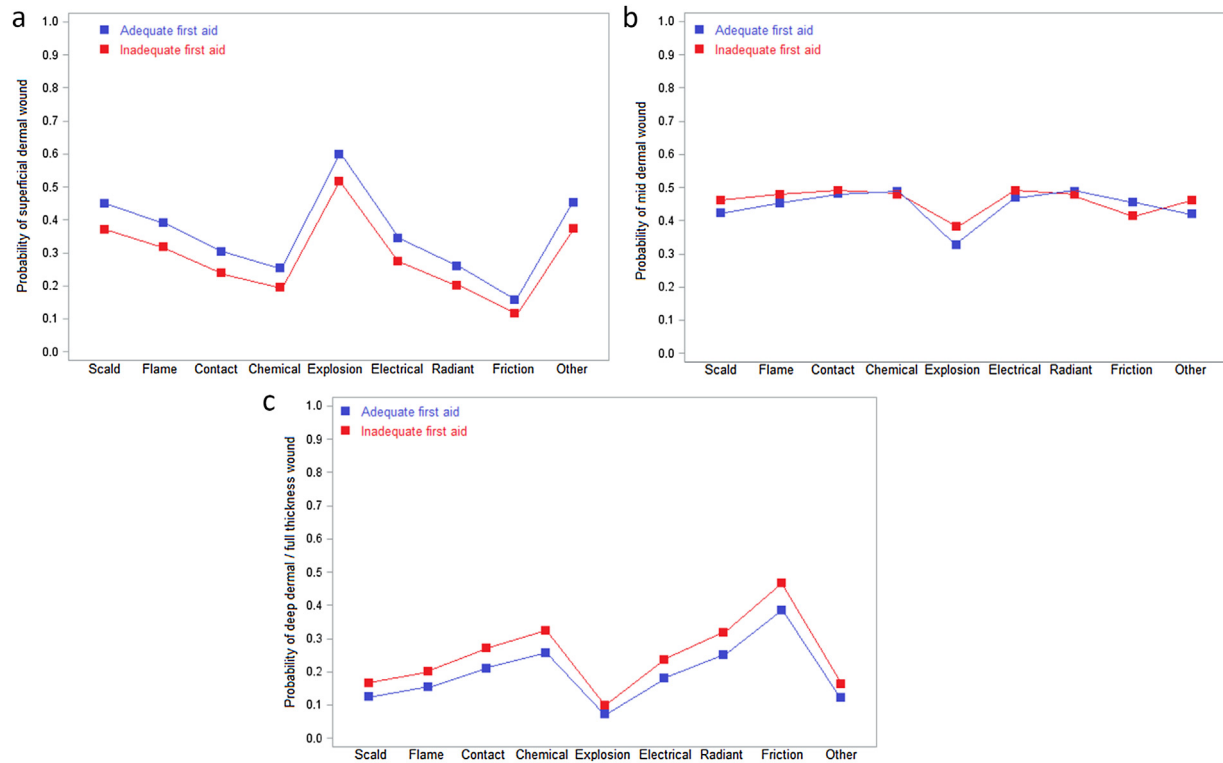


Fig. 2 – Predicted probabilities of wound depth for patients who received adequate and inadequate first aid organised by burn mechanism. (a) Superficial dermal wounds; (b) Mid dermal wounds; (c) Deep dermal/full thickness wounds.

aid is associated with a beneficial effect on clinical outcomes. Adequate first aid is not only associated with a reduction in burn wound depth but also in healing time. Whilst it did not affect the requirement for skin grafting, adequate first aid in patients that ultimately undergo skin grafting is associated with a significant increase in the body surface area (BSA) that does not require grafting (and therefore heals spontaneously).

The beneficial effects of adequate cooling on wound depth and healing time (but not the requirement for skin grafting) suggest that adequate first aid can affect burn wound progression in superficial and mid dermal injuries but cannot alter a deep dermal (or deeper) injury. The thermal injury required to produce a deep burn wound may lead to irreversible cell death which is refractory to the effects of cooling. In patients that underwent skin grafting, the benefit of cooling lies in its ability to increase the BSA that is a superficial injury and therefore is not grafted. The beneficial effects of faster healing and less grafting requirements will translate to decreased health care costs, less psychological trauma for the patient, and a reduction in scarring.

A number of mechanisms may be responsible for the positive effects of first aid. Cooling may improve cell survival by decreasing cellular energy requirements in this hypoxic environment, as localised hypothermia has been shown to lead to a decrease in metabolic rate [6]. First aid may also alleviate the inflammatory response in the burn injured wound. Studies have shown that cooling inhibits histamine release in thermally damaged tissues [7,8], decreases bradykinin-mediated vasodilatation and vascular permeability, and may even decrease activation of the arachidonic acid cascade [2].

Our findings 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 post-burn [4,9,10]. 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 [11] while the other found a significant relationship between first aid and re-epithelialisation time in contact burn injuries only [12]. Wood et al. [13], in a more recent study, examined the effect of any duration of cooling post-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 (eg, a significant reduction in ICU admission for duration of 10–19 min but other intervals), making their data difficult to interpret.

The present study has examined adequate, recommended first aid and its impact on wound-relevant outcomes in a very large cohort of outpatients where the impact of additional medical priorities of burn injuries (eg, inhalational injury, shock, hypothermia, septicemia etc.) have been controlled for. This provides a sound, clinical basis for prior experimental

research. The effect of first aid on severe burn injuries (e.g., >20% TBSA) will require further study but we believe that clinically beneficial associations demonstrated in our cohort can be extrapolated to these injuries.

Our findings have implications for the treatment of burn injuries worldwide. Cooling burn wounds with running water for 20min (up to 3h post-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 in all community, schooling and workplace burn-injury minimisation campaigns. This large human cohort study highlights the need for a clear, consistent, global first aid message, especially when first aid education is not consistent around the world [3,14], knowledge of recommended first aid treatment for burn injuries is inadequate amongst both the public [15] and health care workers [16], and that compliance with recommended first aid treatment in both the developed [12,17,18] and developing world [19–21] is poor.

While this study strongly supports the beneficial effect of cooling burn wounds, there are certain limitations. We were unable to account for the effects of additional treatments (e.g., dressing products) on clinical endpoints. However, as nearly 5000 patients were included in this study, any such effect is almost certainly negligible. 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 clinical outcomes. However, there are obvious ethical and logistic concerns in performing such a study. We believe again that the sheer magnitude of patients in this study allows for valid inferences to be made regarding adequate first aid.

There were other notable features regarding first aid identified in this study. Adequate first aid was received by equal proportions of patients with superficial and mid dermal injuries (62%) yet by only 42% in patients with deeper burn injuries, suggesting that adequate first aid is predominantly applied to superficial burn wounds that are more sensate and painful compared with deeper burns where sensation is blunted or no longer intact. Patients with superficial burn injuries (superficial dermal and mid dermal burns) were also significantly younger compared to those with deeper injuries (mean difference 6.5 years; $P < 0.001$), perhaps suggesting that first aid knowledge is higher among younger people. Overall, however, adequate first was received in 58% of patients. Interestingly, this finding is significantly higher than that reported in previous studies which range from 7 to 39% [12,15,17,18,22]. The higher proportion of patients receiving adequate first aid in our study may reflect a more contemporary time frame compared with previous reports. Nevertheless, as an absolute figure, 58% represents a suboptimal rate of burn wound cooling. The cause for this is likely to be multifactorial and may include seeking medical attention more than 3h post-burn, lack of opportunity (e.g. no running water available at time of injury) or lack of education about optimal duration of cooling. Indeed, a survey of 7320 respondents in our geographical region revealed that fewer than 10% were aware of the optimal time (20min) for cooling a burn injury [15]. This is further compounded by inaccurate and inconsistent burn first aid recommendations that the public

have access to [14] and poor knowledge of recommended first aid treatment amongst referring clinicians [16]. These very same factors probably also account for the observed higher rate of inadequate first aid received in our cohort of chemical burn injuries, for which burns clinicians encourage a longer duration of first aid.

5. Conclusion

Limiting progression of tissue necrosis should be the goal in the initial management of burn injuries. This study demonstrates that first aid in the form of 20min of cool, running water onto the burn wound (up to 3h post-burn) is associated with significantly improved clinical outcomes in burn injuries. The benefits of first aid are in a reduction in burn wound depth, faster healing and decreased skin grafting requirements. This large human cohort study highlights the need for 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 20min should be widely promoted on a global level.

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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare that there is no source of financial or other support, or any financial or professional relationships which may pose a competing interest.

Acknowledgements

We wish to thank Anne Darton and the New South Wales Agency for Clinical Innovation Statewide Burn Injury Service Data Registry for their assistance with data acquisition.

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