Long-term Effects of Pediatric Burns on the Circulatory System

Janine M. Duke, PhD[a], Sean M. Randall, BSc (Hons)[b], Mark W. Fear, PhD[a], James H. Boyd, BSc(Hons)[b], Suzanne Rea, MB, BCh, PhD[a,c], Fiona M. Wood, MBBS[a,c]

abstract

BACKGROUND: The systemic responses to burns (in particular, elevated levels of catecholamines and stress hormones) have been shown to have an impact on cardiac function for at least 3 years in children with burns. However, it is not clear if these changes lead to long-term effects on the heart. The aim of this study was to assess whether pediatric burn injury is associated with increased long-term hospital use for circulatory diseases.

METHODS: A population-based longitudinal study was undertaken using linked hospital and death data from Western Australia for children younger than 15 years when hospitalized for a first burn injury (n = 10 436) in 1980–2012 and a frequency matched noninjury comparison cohort, randomly selected from Western Australia's birth registrations (n = 40 819). Crude admission rates and cumulative length of stay for circulatory diseases were calculated. Negative binomial and Cox proportional hazards regression modeling were used to generate incidence rate ratios and hazard ratios, respectively.

RESULTS: After adjustment for demographic factors and preexisting health status, the burn cohort had 1.33 (incidence rate ratio) times (95% confidence interval [CI]: 1.08–1.64) as many circulatory system hospitalizations, 2.26 times the number of days in hospital with a diagnosis of a circulatory disease (2.26, 95% CI: 1.06–4.81), and were at a higher risk of incident admissions (hazard ratio 1.22, 95% CI: 1.03–1.46), compared with the uninjured cohort.

CONCLUSIONS: Children who sustain burn injury experience elevated hospital admission rates and increased length of hospital stay for diseases of the circulatory system for a prolonged period of time after burn discharge.

[a]*Burn Injury Research Unit, School of Surgery, University of Western Australia, Perth, Australia;* [b]*Centre for Data Linkage, Curtin University, Perth, Australia; and* [c]*Burns Service of Western Australia, Royal Perth Hospital and Princess Margaret Hospital, Perth, Australia*

Dr Duke conceived the study design, participated in data analysis and interpretation, and drafted and revised the manuscript; Ms Wood and Dr Rea conceived the study design, provided interpretation of the data, and critically reviewed the manuscript; Dr Fear provided data interpretation and critically reviewed the manuscript; Mr Boyd and Mr Randall provided analytical advice and support and data interpretation and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2015-1945

DOI: 10.1542/peds.2015-1945

Accepted for publication Aug 3, 2015

Address correspondence to Janine M. Duke, PhD, Burn Injury Research Unit, School of Surgery, Faculty of Medicine, Dentistry and Health Sciences, The University of Western Australia, M318 35 Stirling Highway, Crawley, 6009, Western Australia, Australia. E-mail: janine.duke@uwa.edu.au

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

WHAT'S KNOWN ON THIS SUBJECT: Systemic responses occur after burn injury that lead to widespread changes to the body, including the heart. Elevated levels of catecholamines and stress hormones have been found up to 3 years after severe burns. Little is known about the longer-term effects.

WHAT THIS STUDY ADDS: Children with burns had 1.3 times as many admissions and 2.3 times the number of days in hospital for circulatory diseases compared with uninjured children. Children with minor burns had an increased risk of incident admissions for circulatory diseases.

Metabolic changes and systemic inflammatory responses occur after burn injury[1] that can lead to widespread changes in multiple organ systems of the body, including the heart and circulatory system. These responses may occur after both minor and moderate burn injuries.[2–5] Research of severe pediatric burns has demonstrated profound changes to resting energy expenditure, body composition, metabolic markers and cardiac function for up to three years post-burn demonstrating significant and prolonged sequelae attributed in part to the hypermetabolic response.[6] However, even nonsevere burns have been demonstrated to have profound systemic effects in both animal models and humans, altering bone composition, bone marrow mobilization, and cutaneous innervation, with many changes persisting in the long term.[2,5,7,8] These changes have been postulated to be mediated by the acute inflammatory response.[9]

Understanding the long-term health effects of burns is of particular importance to young children, who have the highest incidence of burn injuries[10] and the longest time to be affected by any secondary pathology subsequent to burn injury. To date, limited data have been available to examine the long-term health effects of pediatric burns beyond 3 years postburn. "Whole-of-population"–linked health administrative data provide a cost-effective means to examine long-term morbidity in terms of the number of hospital admissions and length of stay for specific disease classifications.[11,12]

Recent analysis of population-based health administrative data identified increased long-term mortality after both severe and minor burn injury in children.[13] Given the potential of burn injury to have longer-term impacts on the heart and circulatory system, the aim of this study was to use population-based linked health data to assess whether children who are hospitalized for a burn injury when younger than 15 years of age have increased longer-term hospital use for circulatory diseases, after adjustment for demographic factors and preexisting comorbidities.

METHODS

This study forms part of the Western Australian Population-based Burn Injury Project, a population-based retrospective cohort study using linked health administrative data provided from the Western Australian Data Linkage System (WADLS). The WADLS is a validated record linkage system that routinely links administrative health data for Western Australia using probabilistic record linkage methods[14] where quality audits of linkages have estimated false-positive matches (mismatches) of $<0.3\%$.[15] Quality and accuracy audits of the core data sets are also undertaken routinely.[16] The project was approved by the Human Research Ethics Committees of the University of Western Australia and the Western Australian Department of Health.

A deidentified extraction of all linked hospital morbidity (Hospital Morbidity Data System) records for all children younger than 15 years when admitted to the hospital with a first (index) burn injury in Western Australia, for the period January 1, 1980, to June 30, 2012, was undertaken by the WADLS. The index burn injury was defined as the first hospital admission in a patient record set with a burn injury as the principal and/or additional diagnosis using the *International Classification of Diseases*, *Ninth Revision, Clinical Modification* (ICD-9-CM) codes 940–949 and *Tenth Revision, Australian Modification* (ICD-10-AM) codes T20–T31. A population-based comparison cohort was randomly selected from the Western Australian Birth Registrations; any person with an injury hospitalization during the study period was excluded from the population-based noninjury cohort. The resultant uninjured comparison cohort was frequency-matched on birth year (4:1) and gender of the burn injury cases for each year from 1980–2012.

Hospital and death data were linked to each cohort (burn, noninjury) for the period 1980–2012. Hospital admissions data included principal and additional diagnoses, external cause of injury, age and gender, Aboriginal status, index admission and separation dates, mode of separation, burn injury characteristics (total burns surface area percent [TBSA%], burn depth, site), geographic location (census collectors district, postcode). Indices of social disadvantage (Socioeconomic Indices for Areas[17]) and remoteness (Accessibility Remoteness Index of Australia[18]) were supplied for the burn and uninjured cohorts. Mortality data included the date and cause of death. Admissions for diseases of the circulatory system were identified and classified using principal diagnosis data (ICD-9 390–459; ICD-10 I00–I99, G45).

Age was categorized into 3 groups (0–4, 5–9, 10–14 years), with Aboriginal status classified by identification of Aboriginal or Torres Strait Islander status on any record. TBSA% was classified by *ICD* supplementary codes (ICD-9 948; ICD-10 T31) and categorized into 3 groups: minor burns (TBSA $<20\%$), severe burns (TBSA $\geq 20\%$), and unspecified TBSA%. Comorbidity was assessed using the Charlson Comorbidity Index (CCI)[19] using principal and additional diagnosis fields in the hospital morbidity data with a 5-year look-back period.[20] The derived CCI score was used to classify comorbidity at baseline (0 CCI = 0; 1 CCI > 0). Indices of social disadvantage were partitioned into quintiles from the most to the least disadvantaged. A record of an existing congenital anomaly was identified using principal and additional diagnosis data (ICD-9 740–759; ICD-10 Q00–G99). The geographic remoteness index was used to classify geographic disadvantage and physical distance from services by 5 remoteness categories: major cities, inner regional, outer regional, remote, and very remote.

The total number of years a person was at risk (person-years) was estimated from the final discharge date for the burn cases. This date was used for the respective frequency matched noninjury controls. Categorical and nonparametric continuous variables were compared by using χ^2 and Kruskal-Wallis tests, respectively. A P value ≤.05 was considered indicative of statistical significance.

The total number of circulatory disease admissions after burn injury discharge and the cumulative length of stay for circulatory disease diagnoses were used as outcome measures. The hospitalization of the index injury was not included in these outcomes or the analyses undertaken on the total burns and uninjured cohorts. Crude yearly admission rates were calculated for these variables. Adjusted IRRs were calculated using negative binomial regression. Demographic (gender, Aboriginality, age group [0–4, 5–9, 10–14 years], social disadvantage, remoteness of place of residence, year of admission) and health status variables (any comorbidity at baseline, previous history of cardiovascular disease, congenital anomaly) were included as covariates in the models.

Survival analyses using the Kaplan-Meier method and Cox proportional hazards models were performed to assess admission rates for first time hospital use for circulatory diseases postburn discharge. Survival analyses models were adjusted for demographic and health covariates (as listed earlier). The proportional hazard assumption for the burn-injured versus noninjured children was tested using scaled and unscaled Schoenfeld residuals and by adding a group-by-time interaction term.[21] If preliminary results revealed nonproportionality, adjusted hazard ratios (HRs) were modeled for each year after burn discharge and for time periods guided by Aalen's linear hazard models and plots.[22]

Attributable risk percentages were calculated as the adjusted rate ratio (incident rate ratio [IRR], HR) minus 1, divided by the adjusted rate ratio (IRR, HR), multiplied by 100.[23] Attributable risk percentage was used to estimate the proportion of long-term hospital use and incident admissions for diseases of the circulatory system, where burn injury was a component cause.[24–26]

Statistical analyses were performed by using Stata version 12 (StataCorp LP, College Station, TX).

RESULTS

Cohort Characteristics

There were 10 436 children younger than 15 years of age hospitalized for a first (index) burn injury (burn injury cohort) in the study period and 40 819 children in the noninjured cohort. The median age for both cohorts was 2 years (interquartile range: 1–7); there was a slightly lower proportion of children in burn injury cohort in the 5-year age group 0 to 4 years and a higher proportion in the 10- to 14-year age group when compared with the noninjury comparison group. Overall, the burn cohort had significantly higher

TABLE 1 Baseline Demographic and Preexisting Health Status Factors for Children <15 y of Age at First Burn Injury Hospitalization and Frequency Matched Noninjury Cohort, Western Australia, 1980–2012.

Characteristics	No Injury, *n* (%)	Burn Injury, *n* (%)	*P*
Total	40 819	10 436	
Demographic			
Male	25 020 (61.3)	6462 (61.9)	.263
Age group (y)			
0–4	27 061 (66.3)	6800 (65.2)	.039
5–9	6966 (17.1)	1797 (17.2)	
10–14	6792 (16.6)	1839 (17.6)	
Aboriginal			
Yes	1974 (4.8)	2056 (19.7)	<.001
Social disadvantage quintiles[a]			
Quintile 1 (most disadvantaged)	5197 (12.8)	2370 (22.9)	<.001
Quintile 2	10 371 (25.5)	3405 (33.0)	
Quintile 3	7360 (18.1)	2058 (19.9)	
Quintile 4	6880 (16.9)	1268 (12.3)	
Quintile 5 (least disadvantaged)	10 790 (26.6)	1230 (11.9)	
Remoteness[b]			
Major city	27 284 (67.4)	5454 (52.6)	<.001
Inner regional	4267 (10.6)	1069 (10.3)	
Outer regional	4691 (11.6)	1649 (15.9)	
Remote	2640 (6.5)	1207 (11.6)	
Very remote	1610 (4.0)	984 (9.5)	
Health status			
Any comorbidity (CCI ≥ 1)[c]	492 (1.2)	236 (2.3)	<.001
Previous admission for disease of circulatory system[d]	127 (0.3)	51 (0.5)	.007
Record congenital anomaly	1226 (3.0)	432 (4.1)	<.001

[a] Socioeconomic Indices for Areas socioeconomic disadvantage quintiles; 1% missing values for burn and 0.5% for uninjured.

[b] Accessibility Remoteness Index of Australia remoteness classification; 0.71% missing values for burn and 0.8% for uninjured.

[c] Comorbidity based on derived CCI using 5-y look back.

[d] Principal diagnosis record of hospitalization for disease of circulatory disease (ICD-9 390–459; ICD-10 I00–I99, G45) using 5-year look-back period

proportions of Aboriginal children and children who lived in areas outside the major cities and from socially disadvantaged areas compared with the noninjury comparison cohort. Although the proportions of those with any comorbidity and record of a congenital anomaly were low, these were higher for the burn injury cohort (Table 1).

For children with burn injury, 46.4% had minor burns (<20% TBSA), 1.3% had severe burns (≥20% TBSA), and TBSA was unspecified for 52.4%. Full-thickness burns were sustained by 8.4%, 45.6% had partial thickness burns, 13.9% had erythema burns, and burn depth was unspecified for 35.2%; records had combinations of burn injury anatomic sites and burn depth. Burn sites included 20.0% to head and neck; 28.0% to trunk; 39.6% to upper limbs/hands; 33.5% to lower limbs/feet; 3.4% to eyes; 1.0%, respectively, to respiratory tract and other internal organs; 6.1% multiple regions; and for 3%, the site was unspecified.

TABLE 2: Classification (%) of Post–Burn Discharge Admissions for Primary Diagnosis Circulatory System Diseases for Children Younger Than 15 Years When Hospitalized for Burn Injury, Western Australia, 1980–2012

	ICD-9	ICD-10	Percentage % (*n*)	
			No Injury	Burn
Circulatory diseases (combined)	390–459	I00–I99, G45	100 (714)	100 (314)
Acute rheumatic fever	390–392	I00–I02	2.4 (17)	8.3 (26)
Chronic rheumatic heart diseases	393–398	I05–I09	2.0 (14)	1.6 (5)
Hypertensive diseases	401–405	I10–I15	2.1 (15)	3.5 (11)
Ischemic heart diseases	410–414	I20–I25	1.5 (11)	11.5 (36)
Pulmonary heart disease and diseases of pulmonary circulation system	415–417	I26–I28	3.6 (26)	2.2 (7)
Other forms of heart disease	420–429	I30–I52	19.7 (141)	22.6 (71)
Heart failure			3.4 (24)	5.1 (16)
Acute pericarditis			0.6 (4)	1.6 (5)
Cardiomyopathy			0.3 (2)	1.6 (5)
Paroxysmal tachycardia			4.9 (35)	4.1 (13)
Atrial fibrillation			1.5 (11)	4.8 (15)
Other cardiac arrhythmias			2.1 (15)	1.9 (6)
Other			7.0 (50)	3.5 (11)
Cerebrovascular diseases	430–438	I60–I69, G45	5.2 (37)	1.9 (6)
Diseases of arteries, arterioles and capillaries	440–449	I70–I79	3.5 (25)	1.6 (5)
Diseases veins, lymphatic vessels	451–457	I80–I89	59.2 (423)	44.2 (139)
Phlebitis and thrombophlebitis			1.1 (8)	3.5 (11)
Embolism/thrombosis of other veins			1.0 (7)	3.8 (12)
Varicose veins of lower extremities			4.9 (35)	4.1 (13)
Haemorrhoids			32.9 (235)	14.6 (46)
Varicose veins of other sites			7.8 (56)	6.1 (19)
Nonspecific lymphadenitis			10.1 (72)	11.1 (35)
Other			1.4 (10)	1.0 (3)
Other and unspecified disorders of the circulatory system	458–459	I95–I99	0.7 (5)	2.5 (8)

Admissions for Circulatory System Diseases: Counts and Cumulative Length of Stay

There were 314 hospital admissions with a primary diagnosis of a circulatory system disease after burn injury discharge (total burn cohort). The burn cohort spent a total of 1300 days in hospital for diseases of the circulatory system. Counts for individual subcategories can be found in Table 2.

Unadjusted incidence rates for circulatory system admissions and length of stay using the total burn and uninjured cohorts are shown in Fig 1. These graphs show little difference between the burn cohort and controls in terms of number of admissions and time spent in hospital.

After adjustment for demographic factors and preexisting health status, the burn cohort had 1.33 times (IRR 1.33, 95% CI: 1.08–1.64) as many circulatory system admissions to hospital, and 2.26 times the number of days in hospital with a diagnosis of a circulatory system disease (IRR 2.26, 95% CI: 1.06–4.81) over the 33-year period than the comparison cohort. This equated to an excess of 25% of admissions (n = 78) and 56% of days (n = 728 days) of hospitalization for diseases of the circulatory system experienced by the total burn cohort compared with the uninjured cohort.

Incidence: Survival Analyses

Survival analyses were performed on the pediatric burn (n = 10 042) and uninjured (n = 39 398) cohorts excluding those who had a record of circulatory system hospitalization and/or congenital anomaly during the 5-year period before the start of the study. There were 210 (2.1%) and 563 (1.4%) incident admissions for the burn and uninjured cohorts, respectively. The Kaplan-Meier survival plot (unadjusted) showed reduced survival (Fig 2). Log rank tests for equality of survivor functions showed higher observed than expected counts of first time admissions for circulatory diseases for minor burns and burns of unspecified TBSA% and for male and female burn survivors (Table 3). Multivariate Cox regression modeling did not reveal evidence of nonproportionality. After adjustment for confounders, the burn injury cohort was found to be at higher risk of incident or first time hospitalization for diseases of the circulatory system after burn discharge (HR 1.22, 95% CI: 1.03–1.46).

Among members of the burn cohort, 30.4% (3172) had a record of nonburn injury admission (pre- or postburn). Multivariate Cox regression modeling was then

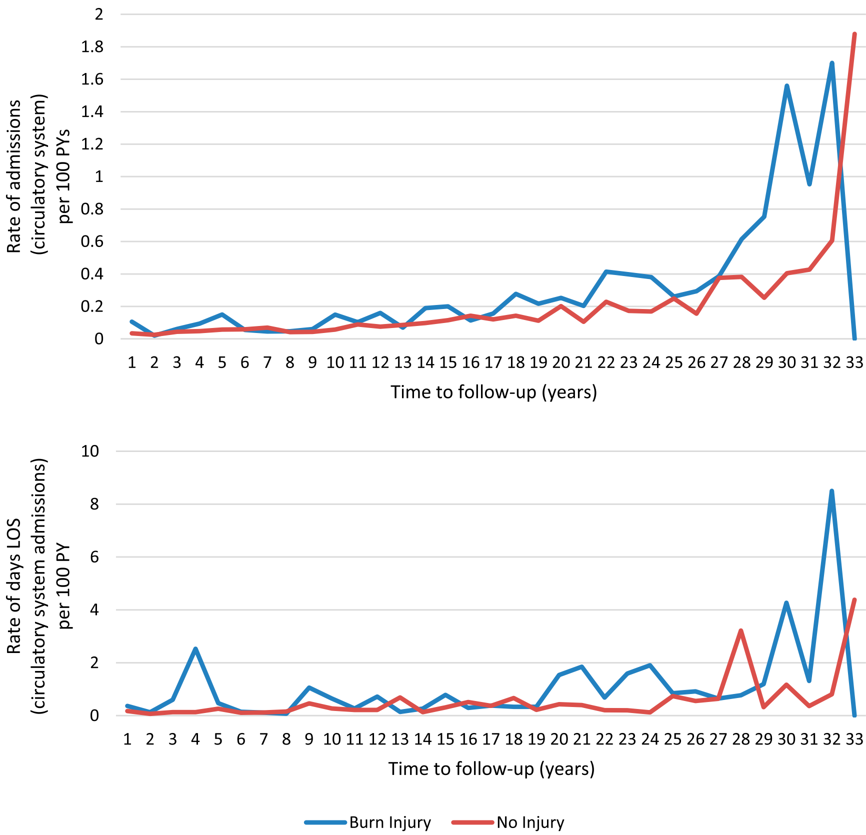

FIGURE 1

Unadjusted rates of hospital admissions and cumulative length of stay (LOS; per 100 person years [PYs]) for diseases of the circulatory system among children younger than 15 years of age with burn injury versus no injury.

repeated excluding those in the pediatric burn cohort who had a record of a nonburn injury admission. Preliminary results revealed nonproportionality, and adjusted pooled estimates were generated for specific time periods. A significant elevation of incident admissions (HR 2.32, 95% CI: 1.14–4.75) was found for the period 12.5 to 15 years after burn discharge compared with the uninjured cohort, equating to 56.9% of first-time admissions for circulatory diseases during this period being attributed to burn injury. Elevated admission rates were observed for the first 6 years (HR 1.44, 95% CI: 0.89–2.25) and from 17 to 21 years postdischarge (HR 1.58, 95% CI: 0.92–2.72); however, these results were not statistically significant.

Gender-specific analyses identified nonproportionality in modeling of male data. Boys in the burn cohort were found to have significantly greater incident admissions during the periods 12.5 to 15 years (HR 2.62, 95% CI: 1.17–5.87) and from 17.5 to 21 years after burn discharge (HR 1.89, 95% CI: 1.02–3.52) compared with uninjured boys. No difference in incident admissions over the study period was found for girls with burns compared with uninjured girls (HR 0.97, 95% CI: 0.69–1.37).

Minor burns were associated with significantly elevated incident admissions over the study period (HR 1.63, 95% CI: 1.11–2.38) compared with the uninjured, equating to 39% of first-time circulatory disease admissions over the study period attributed to the burn injury. Significant results were not found for severe burns (HR 1.37, 95% CI: 0.19–9.78) or burns of unspecified TBSA (HR 0.89, 95% CI: 0.68–1.15).

DISCUSSION

This study quantifies the long-term hospital use for circulatory diseases by pediatric burn injury patients in Western Australia from 1980 to 2012 after controlling for sociodemographic factors and preexisting comorbidities. Children under 15 who sustained a burn injury severe enough to require hospitalization experienced greater hospital use in terms of both admissions and the length of hospital stay for circulatory diseases, when compared with a gender and age frequency-matched uninjured cohort. The burn cohort also experienced a low but statistically significantly greater rate of incident or first-time hospitalizations for circulatory diseases over the 33-year study period, also suggesting longer-lasting effects of burn injury.

The observed numbers of admissions for circulatory diseases did not support subcohort analysis by disease subgroups with statistical power. Ischemic heart disease and other forms of heart disease, including cardiomyopathy and heart failure, accounted for 34% and 21% of circulatory disease admissions for the burn and uninjured cohorts, respectively. Diseases of the veins and lymphatic vessels were the most common primary diagnoses for circulatory disease admissions for both the burn and uninjured cohorts.

It has been found that catecholamines and stress hormones such as cortisol remain elevated up to 36 months postburn in children with severe burns, with heart rates increasing immediately after burn and remaining significantly high for a 3-year postburn study follow-up.[6] This study supports these findings and suggests that these long-term changes do become detrimental with time and, in the population studied, lead to increased hospitalization.

Increased 10-year health service use after injury in adults has been reported.[27] Consequently, additional

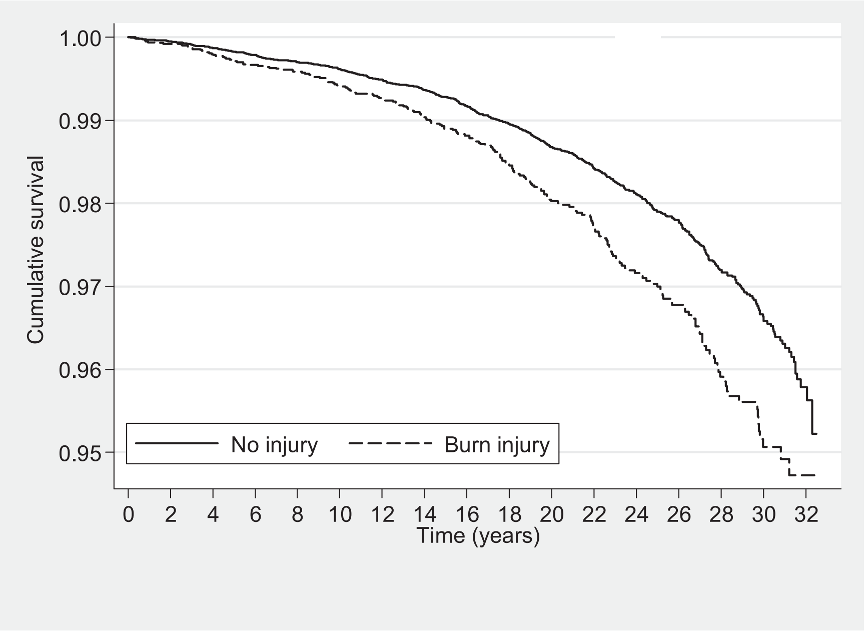

FIGURE 2
Kaplan-Meier estimates of the survivor function for first admission for diseases of the circulatory system for children younger than 15 years of age, burn injury versus no injury. Kaplan-Meier plots for data excluding those with previous admissions for circulatory system disease or congenital anomaly (or both).

survival analyses were performed on data excluding persons in the burn cohort with a record of a primary diagnosis nonburn injury admission, thereby excluding any potentially additive trauma-related systemic effects. Although metabolic alterations after severe burn are similar to any major trauma, it has been reported that severe burns are characterized by a hypermetabolic response that is more severe and sustained.[28] After adjustment for confounders, several periods of elevated admissions over the study period were identified. For the period 12.5 to 15 years post–burn injury discharge, the burn cohort had more than double the admission rates for circulatory diseases when compared with the uninjured cohort. The survival analyses revealed no significant differences between girls with burns and those with no injury. However, the male members of then burn cohort had admission rates almost 3 times greater than boys in the uninjured cohort for the 12.5- to 15-year post–burn discharge period, and almost double the rates for the period 17.5 to 21 years post–burn discharge.

TABLE 3 Log-rank Tests to Assess Equality of Survivor Functions for Incident Admissions for Circulatory Disease Between Children Younger Than 15 Years of Age at First Burn Injury Hospitalization Compared With the Uninjured Cohort

	Observed Events	Expected Events	*P*
Burn (total) vs no injury			
No injury	563	612.86	<.001
Burns	210	160.14	
Burn (by TBSA) vs no injury			
No injury	563	612.86	<.001
Minor burns (<20% TBSA)	45	25.59	
Severe burns (20%+ TBSA)	1	1.17	
Burns, TBSA unspecified	164	133.38	
Burn and no injury by gender			
No injury, male	356	374.62	<.001
No injury, female	207	238.18	
Burns, male	134	100.20	
Burns, female	76	60.00	

Analyses performed on data that excluded persons with previous admission for diseases of the circulatory system and/or record of congenital anomaly.

After adjustment for confounders, minor burns were associated with significantly higher admission rates over the entire study period, whereas no significant difference was found for burns of unspecified TBSA and severe burns. Although previous research identified a need for prolonged treatment of severely burned patients,[6] the findings of increased admissions for circulatory diseases after minor burns suggests that children with minor burns may also have prolonged treatment needs or require primary care monitoring. Other long-term sequelae of minor burns have been reported, including bone loss and increased long-term mortality associated with pediatric minor burns.[8,13] Despite the absence of a hypermetabolic response, minor burns elicit a substantial acute inflammatory response.[9] It may be that this response in part mediates the profound long-term changes observed after minor burn injuries.[8] Although the incidence rate of admissions was elevated after severe burns, the lack of a significant association may be related to the small numbers of patients with severe burns in this patient cohort, the classification of TBSA used (<20% and ≥20%), and, potentially, that survivors of severe burns in this study represent a healthier patient subcohort. Patients with severe burns have treatments to mitigate the initial systemic inflammatory and endocrine responses and hypermetabolism and are more likely to have scar-related readmissions and high levels of ongoing care.[29,30] Hospitalizations for diseases typically represent the more serious cases. It is possible that treatment and monitoring after severe burns may lead to earlier diagnosis and better management of secondary pathologies, with reduced need for hospitalization for a more serious presentation of the condition.

Study Strengths and Limitations

Single-center studies of pathophysiology of pediatric severe burns (no control)[31] and with a 3-year follow-up of (with control)[6] have been reported. Although longer-term effects on health service use of adults hospitalized for injury (all cause) using population-based linked data has been reported, the representation of burn patients was small.[24] The current population-based project provides an opportunity to examine the long-term health effects among pediatric burn patients, with extensive follow-up and a noninjured comparison group. This study adjusted for comorbidity and indices of socioeconomic disadvantage and geographic access to services. Socioeconomic status provides a proxy measure of lifestyle risk factors associated with poorer health outcomes.[32,33] Use of linked health data reduces issues associated with selection and losses to follow-up. This study represented the more serious burns and disease admissions, and the results may underestimate postburn impact on circulatory diseases experienced in the community.

Incomplete TBSA% coding data and small numbers of children with severe burns in this study limited the full understanding of burn severity on long-term hospital use. *ICD* coding changes during the study period may have introduced a misclassification bias with the overall effect of underestimating the observed measures of risk. It is anticipated that these findings are generalizable to other populations with similar health care systems and demographic characteristics.

CONCLUSIONS

These population-based results provide preliminary data to support that children who sustain burns severe enough to be hospitalized experience increased long-term hospitalizations for circulatory diseases compared with uninjured children. After healing of the burn injury wound, it may be prudent for burn patients to have regular health assessments with their primary care physician. Future research that better describes the cardiac health of patients, both before and after the burn, will provide a clearer clinical picture of the effects of burns and assist in identifying subsets of patients at greatest risk.

ACKNOWLEDGMENTS

We thank the staff of the Health Information Linkage Branch for access to the Western Australian Data Linkage System and for their assistance in obtaining the data, the WA Health Data Custodians for access to the core health datasets and the Western Australian Department of Health.

ABBREVIATIONS

CI: confidence interval
CCI: Charlson Comorbidity Index
HR: hazard ratio
ICD: *International Classification of Disease*
IRR: incident rate ratio
TBSA: total burn surface area
WADLS: Western Australian Data Linkage System

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This study was supported by a Raine Medical Research Foundation Priming grant to Dr Duke. Dr Duke is supported by Woodside corporate sponsorship via the Fiona Wood Foundation. Dr Fear is supported by Chevron Australia via the Fiona Wood Foundation.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Jeschke MG, Chinkes DL, Finnerty CC, et al. Pathophysiologic response to severe burn injury. *Ann Surg*. 2008;248(3):387–401
2. Anderson JR, Zorbas JS, Phillips JK, et al. Systemic decreases in cutaneous innervation after burn injury. *J Invest Dermatol*. 2010;130(7):1948–1951
3. Borue X, Lee S, Grove J, et al. Bone marrow-derived cells contribute to epithelial engraftment during wound healing. *Am J Pathol*. 2004;165(5):1767–1772
4. Horgan PG, Mannick JA, Dubravec DB, Rodrick ML. Effect of low dose recombinant interleukin 2 plus indomethacin on mortality after sepsis in a murine burn model. *Br J Surg*. 1990;77(4):401–404
5. Rea S, Giles NL, Webb S, et al. Bone marrow-derived cells in the healing burn wound—more than just inflammation. *Burns*. 2009;35(3):356–364
6. Jeschke MG, Gauglitz GG, Kulp GA, et al. Long-term persistance of the pathophysiologic response to severe burn injury. *PLoS One*. 2011;6(7):e21245
7. Morellini NM, Fear MW, Rea S, West AK, Wood FM, Dunlop SA. Burn injury has a systemic effect on reinnervation of skin and restoration of nociceptive function. *Wound Repair Regen*. 2012;20(3):367–377
8. O'Halloran E, Kular J, Xu J, Wood F, Fear M. Non-severe burn injury leads to depletion of bone volume that can be ameliorated by inhibiting TNF-α. *Burns*. 2015;41(3):558–564

9. Valvis SM, Waithman J, Wood FM, Fear MW, Fear VS. *The immune response to skin trauma is dependent on the etiology of injury in a mouse model of burn and excision*. J Investigat Dermatol. 2015;135(8):2119–2128
10. Duke J, Wood F, Semmens J, et al. A study of burn hospitalizations for children younger than 5 years of age: 1983–2008. *Pediatrics*. 2011;127(4). Available at: www.pediatrics.org/cgi/content/full/127/4/e971
11. Gardner C, Rankin JM, Geelhoed E, et al. Evaluation of long-term clinical and health service outcomes following coronary artery revascularisation in Western Australia (WACARP): a population-based cohort study protocol. *BMJ Open*. 2014;4(10):e006337
12. Hendrie D, Miller TR. Assessing the burden of injuries: competing measures. *Inj Control Saf Promot*. 2004;11(3):193–199
13. Duke JM, Rea S, Boyd JH, Randall SM, Wood FM. Mortality after burn injury in children: a 33-year population-based study. *Pediatrics*. 2015;135(4). Available at: www.pediatrics.org/cgi/content/full/135/4/e903
14. Holman CDJ, Bass AJ, Rouse IL, Hobbs MST. Population-based linkage of health records in Western Australia: development of a health services research linked database. *Aust N Z J Public Health*. 1999;23(5):453–459
15. Rosman D, Garfield C, Fuller S, Stoney A, Owen T, Gawthorne G. Measuring data and link quality in a dynamic multi-set linkage system. Paper presented at Symposium on Health Data Linkage: Its Value for Australian Health Policy Development and Policy Relevant Research Proceedings; March 20–21, 2002; Sydney, Australia
16. Department of Health Western Australia. *Clinical Information Audit Program—Hospital Activity Report*. Perth, Australia: Department of Health Western Australia; 2009
17. Trewin D. *Socio-economic Indexes for Areas (Information Paper, Census of Population and Housing)*. Canberra, Australia: Australian Bureau of Statistics; 2003
18. Glover J, Tennant S. *Remote areas statistical geography in Australia: Notes on the Accessibility/Remoteness Index for Australia (ARIA+ version)* (Working Papers Series No. 9). Adelaide, Australia: Public Health Information Development Unit, The University of Adelaide; 2003
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383
20. Preen DB, Holman CDAJ, Spilsbury K, Semmens JB, Brameld KJ. Length of comorbidity lookback period affected regression model performance of administrative health data. *J Clin Epidemiol*. 2006;59(9):940–946
21. Hosmer DW, Lemeshow S. *Applied Survival Analysis: Regression Modeling of Time to Event Data*. New York, NY: Wiley; 1999
22. Hosmer DW, Royston P. Using Aalen's linear hazards model to investigate time-varying effects in the proportional hazards regression model. *Stata J*. 2002;2(4):331–350
23. Gordis L. *Epidemiology*. 2nd ed. Philadelphia, PA: W.B. Saunders; 2000
24. Cameron CM, Purdie DM, Kliewer EV, McClure RJ. Long-term mortality following trauma: 10 year follow-up in a population-based sample of injured adults. *J Trauma*. 2005;59(3):639–646
25. Duke JM, Boyd JH, Rea S, Randall S, Wood FM. Long-term mortality among older adults with burn injury: a population-based study in Australia. *Bull World Health Organ*. 2015;93:400–406
26. Orton E, Kendrick D, West J, Tata LJ. Persistence of health inequalities in childhood injury in the UK: a population-based cohort study of children under 5. *PLoS One*. 2014;9(10):e111631
27. Cameron CM, Purdie DM, Kliewer EV, McClure RJ. Ten-year health service use outcomes in a population-based cohort of 21,000 injured adults: the Manitoba injury outcome study. *Bull World Health Organ*. 2006;84(10):802–810
28. Pereira CT, Murphy KD, Herndon DN. Altering metabolism. *J Burn Care Rehabil*. 2005;26(3):194–199
29. Armour AD, Billmire DA. Pediatric thermal injury: acute care and reconstruction update. *Plast Reconstr Surg*. 2009;124(suppl 1):117e–127e
30. Prasad JK, Bowden ML, Thomson PD. A review of the reconstructive surgery needs of 3167 survivors of burn injury. *Burns*. 1991;17(4):302–305
31. Sheridan RL, Hinson MI, Liang MH, et al. Long-term outcome of children surviving massive burns. *JAMA*. 2000;283(1):69–73
32. Bentley R, Kavanagh AM, Subramanian SV, Turrell G. Area disadvantage, individual socio-economic position, and premature cancer mortality in Australia 1998 to 2000: a multilevel analysis. *Cancer Causes Control*. 2008;19(2):183–193
33. Mishra G, Ball K, Patterson A, Brown W, Hodge A, Dobson A. Socio-demographic inequalities in the diets of mid-aged Australian women. *Eur J Clin Nutr*. 2005;59(2):185–195

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Long-term Effects of Pediatric Burns on the Circulatory System

Janine M. Duke, Sean M. Randall, Mark W. Fear, James H. Boyd, Suzanne Rea and Fiona M. Wood

Pediatrics 2015;136;e1323
DOI: 10.1542/peds.2015-1945 originally published online October 12, 2015;