Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/burns

Burns and long-term infectious disease morbidity: A population-based study

Janine M. Duke [a,*], *Sean M. Randall* [b], *Fiona M. Wood* [a,c], *James H. Boyd* [b], *Mark W. Fear* [a]

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

ARTICLE INFO

Article history:
Received 6 September 2016
Received in revised form
19 October 2016
Accepted 24 October 2016
Available online xxx

Keywords:
Burns
Infections
Long-term health
Population-based
Cohort

ABSTRACT

Background: There is a growing volume of data that indicates that serious injury suppresses immune function, predisposing individuals to infectious complications. With recent evidence showing long-term immune dysfunction after less severe burn, this study aimed to investigate post-burn infectious disease morbidity and assess if burn patients have increased long-term hospital use for infectious diseases.

Methods: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia for all persons hospitalised for a first burn (n=30,997) in 1980–2012. A frequency matched non-injury comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll (n=123,399). Direct standardisation was used to assess temporal trends in infectious disease admissions. Crude annual admission rates and length of stay for infectious diseases were calculated. Multivariate negative binomial and Cox proportional hazards regression modeling were used to generate adjusted incidence rate ratios (IRR) and hazard ratios (HR), respectively.

Results: After adjustment for demographic factors and pre-existing health status, the burn cohort had twice (IRR, 95% confidence interval (CI): 2.04, 1.98–2.22) as many admissions and 3.5 times the number of days in hospital (IRR, 95%CI: 3.46, 3.05–3.92) than the uninjured cohort for infectious diseases. Higher rates of infectious disease admissions were found for severe (IRR, 95%CI: 2.37, 1.89–2.97) and minor burns (IRR, 95%CI: 2.22, 2.11–2.33). Burns were associated with significantly increased incident admissions: 0–30 days (HR, 95%CI: 5.18, 4.15–6.48); 30 days–1 year (HR, 95%CI: 1.69, 1.53–1.87); 1–10 years (HR, 95%CI: 1.40:1.33–1.47); >10 years (HR, 95%CI: 1.16, 1.08–1.24). Respiratory, skin and soft tissue and gastrointestinal infections were the most common. The burn cohort had a 1.75 (95%CI: 1.37–2.25) times greater rate of mortality caused by infectious diseases during the 5-year period after discharge than the uninjured cohort.

Conclusions: These findings suggest that burn has long-lasting effects on the immune system and its function. The increase in infectious disease in three different epithelial tissues in the burn cohort suggests there may be common underlying pathophysiology. Further research to

* *Corresponding author at*: M318 35 Stirling Highway, Crawley 6009, Perth, Western Australia, Australia.
E-mail addresses: janine.duke@uwa.edu.au (J.M. Duke), Sean.Randall@curtin.edu.au (S.M. Randall), Fiona.Wood@health.wa.gov.au (F.M. Wood), j.boyd@curtin.edu.au (J.H. Boyd), mark@fionawoodfoundation.com (M.W. Fear).
http://dx.doi.org/10.1016/j.burns.2016.10.020

Please cite this article in press as: J.M. Duke, et al., Burns and long-term infectious disease morbidity: A population-based study, Burns (2016), http://dx.doi.org/10.1016/j.burns.2016.10.020

understand the underlying mechanisms are required to inform clinical interventions to mitigate infectious disease after burn and improve patient outcomes.

1. Background

There is a growing volume of data that indicates that serious injuries suppress immune function, predisposing individuals who sustain such injuries to infectious complications [1–4]. The immune response after severe injury is complex and encompasses both innate and adaptive immunity [5,6]. After an injury to the skin, a range of pathways are activated in an effort to restore tissue integrity and homeostasis, including the coagulation cascade, inflammation and the adaptive immune system [7,8]. Post-burn there is an increased risk of blood stream infections and sepsis-related mortality [9,10] and these outcomes are largely due to the disturbances in the skin, including changes in microflora [11]. Other problems related to burn include a persistent innate pro-inflammatory response or systemic inflammatory response syndrome [12], dendritic cell suppression and loss of adaptive immunity T-cell responses [3,13]. The elevation in morbidity and mortality in the acute post-burn phase is further complicated by compensatory anti-inflammatory responses [3,14].

While recent animal-based research indicates long-term immune dysfunction after non severe burn [15], to date the effect of severe and less severe burn on the long-term function of the immune system has not been comprehensively investigated. Initial investigations of long-term morbidity after burn using population-based data have identified increased post-burn circulatory morbidity, after both minor and severe burns [16], suggesting a substantial acute inflammatory response [15], as well as increased incidence of some types of cancers [17,18], suggesting long-term effects of burns on the immune system.

Population-based linked administrative health data provide valuable opportunities to assess long-term health outcomes and morbidity in terms of diseases sufficiently serious to require admission [19]. This study used whole-of-population data from the Western Australian Population-based burn Project (WAPBIP) to assess post-burn infectious disease admissions. To examine the potential for long-term immune dysfunction after burns, the data were analyzed to assess if a cohort of burn patients had greater long-term infectious disease morbidity and mortality when compared to an uninjured cohort, after adjustment for socio-demographic and pre-existing health factors.

2. Methods

The WAPBIP is a retrospective longitudinal project that supports multiple investigations of long-term health, trends and costs of burns. Detailed information on the Western Australian Data Linkage System [20,21], cohort selection, data extraction and standard methods applied, has been previously published [16,22–24]. This study used data of 30,997 individuals hospitalised for an incident burn (burn cohort) in Western Australia during the period 1 January 1980 to 30 June 2012 and an (~4:1) age and gender frequency matched cohort of 123,399 individuals with no record of injury admission (uninjured cohort). This study had human research ethics committee approvals from the Western Australian Department of Health and the University of Western Australia.

The linked hospital and death data provided information on the following variables included in the analyses: International Classification of Diseases (ICD9-CM and ICD10AM) coded diagnosis, causes of injury, age and gender, indigenous status, admission and discharge dates, burn features (total burns surface area percent (TBSA%), depth, site), residential postcode and date and cause of death. TBSA% was classified as minor (TBSA $<$ 20%), severe burns (TBSA $\geq$ 20%) or burns of unspecified TBSA%. The Charlson comorbidity index (CCI) [25] was used to classify pre-existing comorbidity (0 CCI=0; 1 CCI$>$0) using hospital records [26]. Quintiles of social disadvantage (Socio-economic Indices for Areas (SEIFA) [28]) and geographic remoteness and access to services (Accessibility Remoteness Index of Australia (ARIA+) [29]), derived from the national census data, were assigned to each member of both cohorts. ICD9-CM codes were mapped to ICD10-AM [27].

An infectious disease admission was defined as an episode of care with a principal diagnosis belonging to the ICD code set of major infectious diseases developed by Baker et al. [30]. Refer to Appendix A in Supplementary material, for the ICD-based infectious disease code set used in this study. The Baker et al. [30] code set builds on a coding system established by the United States of America Centers for Disease Control and Prevention [31,32] and incorporates ICD9-CM and ICD10-AM codes.

Univariate analyses were conducted using chi square and Kruskal–Wallis tests with 5% level of significance. The total number of years of person risk (person-years) was estimated from the final discharge date for the index or first burn admission; this date was used for the corresponding frequency matched uninjured controls. The number of annual admissions (total) and summed length of hospital stay (LOS) for infectious diseases identified during the study period were used as outcome measures.

To assess trends over time, rates of hospitalisations for infectious diseases (total) for the burn and uninjured cohorts were standardised to the age structure of the Australian population at the 2001 national census [33]. Admission rates, total and by decade of study entry (1980–1989; 1990–1999; and 2000–2012), were age-standardised and classified by major infectious disease category (e.g. lower respiratory, skin and soft tissue, enteric etc.).

Multivariate negative binomial regression analyses were used to assess the link between burn and infectious disease admissions. Multivariate Cox proportional hazards regression was used to assess the effects of burns on first time (incident) admissions and long-term mortality for infectious diseases.

Please cite this article in press as: J.M. Duke, et al., Burns and long-term infectious disease morbidity: A population-based study, Burns (2016), http://dx.doi.org/10.1016/j.burns.2016.10.020