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Diabetes mellitus after injury in burn and non-burned patients: A population based retrospective cohort study

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

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

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ABSTRACT

Objective: To compare hospitalisations for diabetes mellitus (DM) after injury experienced by burn patients, non-burn trauma patients and people with no record of injury admission, adjusting for socio-demographic, health and injury factors.
Methods: Linked hospital and death data for a burn patient cohort (n=30,997) in Western Australia during the period 1980–2012 and two age and gender frequency matched comparison cohorts: non-burn trauma patients (n=28,647); non-injured people (n=123,399). The number of DM admissions and length of stay were used as outcome measures. Multivariate negative binomial regression was used to derive adjusted incidence rate ratios and 95% confidence intervals (IRR, 95%CI) for overall post-injury DM admission rates. Multivariate Cox regression models and hazard ratios (HR) were used to examine time to first DM admission and incident admission rates after injury discharge.
Results: The burn cohort (IRR, 95%: 2.21, 1.80–2.72) and other non-burn trauma cohort (IRR, 95% CI: 1.63, 1.24–2.14) experienced significantly higher post-discharge admission rates for DM than non-injured people. Compared with the non-burn trauma cohort, the burn cohort experienced a higher rate of post-discharge DM admissions (IRR, 95%CI: 1.40, 1.07–1.84). First-time DM admissions were significantly higher during first 5-years after-injury for the burn cohort compared with the non-burn trauma cohort (HR, 95%CI: 2.00, 1.31–3.05) and non-injured cohort (HR, 95%CI: 1.96, 1.46–2.64); no difference was found >5 years (burn vs. non-burn trauma: HR, 95%CI: 0.88, 0.70–1.12; burn vs non-injured: 95%CI: 1.08 0.82–1.41). No significant difference was found when comparing the non-burn trauma and non-injured cohorts (0–5 years: HR, 95%CI: 1.03, 0.71–1.48; >5years: HR. 95%CI: 1.11, 0.93–1.33).
Conclusions: Burn and non-burn trauma patients experienced elevated rates of DM admissions after injury compared to the non-injured cohort over the duration of the study. While burn patients were at increased risk of incident DM admissions during the first 5-years after the injury this was not the case for non-burn trauma patients. Sub-group analyses showed elevated risk in both adult and pediatric patients in the burn and non-burn trauma. Detailed clinical data are required to help understand the underlying pathogenic pathways

* *Corresponding author at*: Burn Injury Research Unit, Faculty of Health and Medical Sciences, The University of Western Australia, M318 35 Stirling Highway, Crawley, 6009, Western Australia, Australia.
E-mail address: janine.duke@uwa.edu.au (J.M. Duke).
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triggered by burn and non-burn trauma. This study identified treatment needs for patients after burn and non-burn trauma for a prolonged period after discharge.

1. Introduction

It is now accepted that hyperglycaemia, glucose intolerance and insulin resistance occur after many acute illnesses, surgery and injuries, including burns, and in patients with no prior history of Type 2 diabetes [1–7]. The patterns and severity of these responses differ between types of trauma and sepsis [8,9]. Burns trigger profound stress responses and hypermetabolism that can persist for many years, whereas for other trauma and sepsis, the severity and length of these responses are reported to be of less magnitude [10–13].

Our previous research found that burn patients had significantly higher hospital admission rates for diabetes mellitus for a prolonged period after the injury when compared with uninjured people [14], providing evidence that burns have longer term effects on blood glucose and insulin regulation after wound healing. This study also identified the first five years after burn discharge as a critical period with significantly elevated incident admissions for diabetes mellitus observed during this time.

The persistence of effects and underlying pathophysiological pathways after burns and other trauma are complex and not fully understood. The objective of this study was to build on our previous population-based burns research and compare post-injury diabetes mellitus (DM) morbidity experienced by burns patients with other non-burn trauma patients and uninjured people.

2. Methods

This project was approved by the Human Research Ethics Committees of the Western Australian Department of Health and the University of Western Australia, and is a sub study of the Western Australian Population-based Burn Injury Project [14].

This study analysed linked hospital (Hospital Morbidity Data System) and death register data of 30,997 people hospitalised with a first burn in Western Australia during the period 1980–2012 and two comparison cohorts (i) non-burn trauma patients (n=28,647); and (ii) non-injured (n=123,399) people. The non-burn trauma cohort was age and gender frequency-matched from the same Statistical Local Area (SLA) as the index burn case (~1:1) for each year. This non-burn trauma cohort excluded those with burns; effects of foreign bodies entering through orifices; injuries to nerves and spinal cord; poisoning; toxic effects of nonmedical substances (e.g. alcohol); and complications of surgical and medical care. The non-injury control cohort included individuals randomly selected from the birth registrations and electoral roll and did not have a record of injury admission during the study period. This cohort was frequency-matched on age, gender from the same SLA as the index burn case (~4:1).

De-identified data were supplied by the Western Australian Data Linkage System (WADLS) [15] and included demographic factors (age, gender, indigenous status and geographic location) and indices of social disadvantage (Socio-economic Indices for Areas (SEIFA) [16]) and remoteness (Accessibility Remoteness Index of Australia (ARIA+) [17]). International Classification of Diseases and Health Related Problems (ICD) codes were used to classify injury characteristics for the burn and other trauma cohorts. A measure of comorbidity was derived using the Charlson Comorbidity hospital records with a 5-year look back period [18,19]. Burn severity (total body surface area percent; TBSA %) was classified: minor $<20\%$; severe $\geq 20\%$. An injury severity score was derived using the International Classification for Injury Severity Score (ICISS) [20] based on survival probabilities for each recorded injury; for multiple injuries the ICISS score represented the product of respective injury survival probabilities. ICISS was classified using standard cut-offs: minor ICISS ≥ 0.99; moderate ICISS > 0.941 and < 0.99; and, severe ICISS ≤ 0.941 [21,22]. Mortality data were used to identify deaths at index admission and during study period after discharge.

The total number of years a person was at risk (person-years) was estimated from the final discharge date for the burn cases to time of death or study end. This date was used for the respective frequency matched non-burn trauma and non-injury cohorts. Categorical variables were compared using the $\chi 2$ tests with level of significance 5%.

Admissions for DM were identified using ICD codes in the principal diagnosis field (ICD10 E10–E14; ICD9 codes mapped to ICD10) and the number of DM admissions and length of stay (LOS) were used as outcome measures. Crude yearly admission rates were calculated for these variables. The index injury admission was not included in these outcomes. Multivariate negative binomial regression was used to derive incidence rate ratios (IRR) and 95% confidence intervals (CI) adjusting for demographic factors (gender, indigenous, age group, place of residence), social disadvantage, year of admission, and health status variables (comorbidity at baseline, previous DM admission) and injury severity. Sub cohort analyses were undertaken for gender, age ($<$18 years; 18–39 years; 40–59 years; $\geq$60 years) and two selected ICD classified injury subgroups, closed fractures and open wounds, to assess potential differences in patterns of DM related to injury to the skin.

Multivariate Cox proportional hazards models were used to assess time to and rate of first post-injury (incident) DM admission. Follow up was from time of index injury discharge to first DM admission, death or study end, which ever occurred first. Survival analyses models were adjusted for demographic and health and injury covariates (as listed above). The proportional hazard assumption was tested [23]. Survival analyses performed on excluding those with a prior record of DM admission as well as those with a record of injury admission after study start, to minimise potential confounding by additional injury-related systemic effects. Statistical