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Burn injury and multiple sclerosis: A retrospective case-control study

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ABSTRACT

Objectives: The purpose of this study was to determine whether having a previous diagnosis of multiple sclerosis (MS) changed acute care needs in burn-injured patients.
Methods: This was a retrospective case-control study that included adult (aged ≥18 years) patients with an acute burn injury. Control patients were matched with eleven patients with a history of MS at a 4:1 ratio. Outcomes included fluid resuscitation volumes, temperature, heart rate, mean arterial pressure, in-hospital complications, and hospital length of stay (LOS).
Results: There were fifty-five patients included and of those, eleven had a documented history of MS. Fluid resuscitation volumes, temperature, heart rate, and mean arterial pressure were similar between groups during the resuscitation period ($p > 0.05$). LOS was similar between both groups (12, IQR: 2–17 vs. median 16, IQR: 12–21; $p = 0.090$). However, when normalized to % TBSA burn, patients with MS had a significantly higher median LOS/% TBSA burned (1.2, IQR: 0.7–2.0 vs. 2.1, IQR: 1.1–7.1; $p = 0.031$).
Conclusions: Patients with concurrent burn injuries and MS have a significantly longer LOS/% TBSA burn suggesting that more time is required to heal their wounds. Surprisingly, there were no other significant differences in the after the burn acute phase between these two cohorts.

1. Introduction

In 2016, 486,000 burn injuries occurred in the United States [1]. Over time, advances in fluid resuscitation, nutrition management, pulmonary care, wound care and infection control have led to improved survival outcomes for patients with burn injuries [2,3]. Despite these advances in critical care, the consequences of and subsequent management for burn injuries in patients with MS continues to be under investigated and poorly understood.

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With an increasing global incidence, MS is the most common autoimmune disease of the central nervous system (CNS) currently affecting over 2.5 million people [4]. MS primarily affects young adults and is characterized by multifocal neurologic inflammation, demyelination, gliosis and neuronal cell loss within the CNS. A prospective study interested in trauma injuries reported that patients with MS had a higher incidence of minor burns compared to controls [5]. However, a meta-analysis of observational studies in MS patients trauma cases showed that there was no association between burn incidence at any age and/or diagnosis of MS [6]. While having MS does not appear to contribute to a higher incidence of severe burns, once patients are admitted to an ICU, they are at higher risk for mortality both in the ICU and at one year after admission [7,8]. MS is associated with an immunocompromised state, couple with the special precautions and treatment strategies specific to burn care, this population is at an amplified risk for infections. Consequently, deaths in patients with MS who acquire burn injuries are likely related to infections, particularly of the respiratory tract, and/or septic shock [9–11].

Demyelinating plaques in patients with MS can damage the descending fibres of the spinal cord reducing the capacity for autonomic nervous system (ANS) regulation [12,13]. Attenuated ANS capacity can present within a range of severities, from whole-body multi-organ dysfunction to localized single system disruptions, where the cardiovascular system is commonly affected [14–16]. Cardiovascular dysfunction can involve changes in orthostatic blood pressure, heart rate response, vagal efference and sympathetic vasomotor activity [17]. Additionally, during the acute phase of burn injury there is significant loss of plasma fluid volume as result of capillary permeability, increased cardiac output and compensatory cardiac rate and peripheral vascular resistance [18]. This burn-related cardiac stress has been shown to persist for at least 2 years after injury [19]. The combination of MS-related ANS dysfunction and cardiodynamic derangements after burn complicated the specific fluid resuscitation delivery for burn patients with MS. Accordingly, this study focused on burn-injured patients and examining differences between patients with a known history of MS compared to controls.

Documented scenarios at our burn centre describe MS-related motor impairments that have restricted patients from removing burning clothing from themselves or slowed them from getting up after spilling scalding water on themselves. We recognized the challenging nature of critical care for these individuals, namely with resuscitation, and hypothesized that there is a dysregulation of the immune system that contributes to worse patient outcomes. In this matched, case-control study, we investigated the acute care outcomes of patients with burn injuries and concurrent MS. We focused our analysis on the resuscitation stage of acute burn injury critical care. Patients admitted to a single burn centre were analysed to determine differences in the acute period, LOS and mortality rates between individuals with MS and controls.

2. Material and methods

2.1. Study design

Inclusion criteria for this study consisted of admission to an adult burn centre between May 2006 and May 2016 for management of an acute burn injury. Propensity scoring was used to match control patients with patients that had a previous diagnosis of MS at a 4:1 ratio. Matching was based on age (±5 years), % TBSA burned (±5%) and presence of inhalation injury. Stage of MS, time since diagnosis, and prescribed medication (disease-modifying and relapse-managing) were noted from patient charts. Clinical variables including, fluid intake (mL), urine output (mL), heart rate (beats per minute), mean arterial pressure (mmHg), blood pressure (mmHg), and core body temperature (°C) were recorded during the first 96 h after burn injury. The study protocol was approved by our institutional research ethics board.

2.2. Statistical analysis

The data are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Statistical analyses included the Student's t-test, Mann–Whitney U and Fisher's exact test where appropriate. All tests were 2-tailed and a p value of <0.05 was considered statistically significant. Analyses were performed using SPSS Statistics version 20.0 (IBM Corp., Armonk, NY).

3. Results

Between May 2006 and May 2016, 1643 burn patients were admitted to our provincial burn centre. During the study period, eleven patients had a previous diagnosis of MS. Of these eleven patients, nine were diagnosed with relapsing-remitting MS, one was diagnosed with primary-progressive MS and one had progressed to secondary-progressive MS. Control patients were matched at a 4:1 ratio with MS patients with burn injuries. Table 1 summarizes the demographic and injury characteristics of patients based on MS diagnosis. There were no significant differences in age or gender between the two groups (Table 1). Median % TBSA burned (8, IQR: 4–12 vs. 8, IQR: 3–14; $p=0.983$) was also not significantly different. However, patients in the MS group had a significantly higher median 3rd degree % TBSA burn (0, IQR: 0–4 vs. 5, IQR: 1–12; $p=0.013$). LOS was similar in both groups (12, IQR: 2–17 vs. median 16, IQR: 12–21; $p=0.090$). But, when LOS was normalized per % TBSA burn, MS patients had a significantly higher median LOS/% TBSA burn (1.2, IQR: 0.7–2.0 vs. 2.1, IQR: 1.1–7.1; $p=0.031$). There were no significant differences in complications such as, bacteremia, sepsis, pneumonia or acute renal failure ($p>0.05$; Table 1). While fluid volumes were relatively higher in the MS group during the first 96 h after burn injury, there were no significant differences in fluid intake or output ($p>0.05$; Fig. 1). Heart rate, mean arterial pressure, and blood pressure were also similar between groups during the first 96 h after burn ($p>0.05$; Fig. 2). Temperature was lower in patients diagnosed with MS and was significantly lower during day one after burn ($p=0.037$; Fig. 2).

4. Discussion

MS is the one of the most prevalent neurological conditions afflicting young people. There are only a limited number of

Table 1 – Demographics and outcomes of patients by presence of MS diagnosis.

Characteristic	Controls	MS	*p*
No. of patients	44	11	
Demographics			
Age, years, mean ± SD[a]	53 ± 10	53 ± 11	0.917
Male, no. (%)[b]	24 (55%)	5 (46%)	0.739
Injury characteristics			
Etiology, no. (%)			
Flame[b]	27 (61%)	6 (55%)	0.739
Scald[b]	14 (32%)	4 (36%)	1.000
Chemical[b]	2 (5%)	0	1.000
Contact[b]	1 (2%)	1 (9%)	0.363
Inhalation injury, no. (%)	0	0	–
TBSA, %, median (IQR)[b]	8 (4–12)	8 (3–14)	0.983
3rd degree TBSA, %, median (IQR)[c]	0 (0–4)	5 (1–12)	0.013
Outcomes			
Bacteremia, no. (%)[b]	5 (11%)	1 (9%)	1.000
Sepsis, no. (%)[b]	3 (7%)	1 (9%)	1.000
Pneumonia, no. (%)[b]	5 (11%)	0	0.571
Renal failure, no. (%)[b]	0	1 (9%)	0.200
Ventilated, no. (%)[b]	8 (18%)	1 (9%)	0.669
LOS, days, median (IQR)[c,b]	12 (2–17)	16 (12–21)	0.090
LOS/TBSA, days/%, mean ± SD[a,d]	1.2 (0.7–2.0)	2.1 (1.1–7.1)	0.031
Non-survivor, no. (%)[b]	0	1 (9%)	0.200

LOS, length of stay; MS, multiple sclerosis; TBSA, total body surface area. Numbers may not add to 100 due to rounding.
[a] Compared with Student's t-test.
[b] Compared with Fisher's exact test.
[c] Compared with Mann–Whitney U test.
[d] Analysis restricted to patients alive until discharge.

studies to date which have evaluated prognosis, clinical care or predisposing factors of burn injuries within the MS population. At our centre, patients with MS associate the cause of their burn injuries with motor impairment and neurological symptoms underlying MS. Despite the likelihood that MS patients are at an increased risk of burn injury, this area of research remains largely overlooked. Our MS cohort demographic was reflective of the typical MS population, having a higher prevalence in women and an average age of 53 years old [16].

The majority of the analyzed clinical markers during the acute resuscitation phase of burn care were not significantly different between the MS cohort and the control group. Despite their lack of statistical significance, notable findings in this study should prompt further investigation.

Most importantly, the fluid delivery for the MS population were higher compared to the control group. This is potentially related to the well-established cardiac and autonomic dysfunction observations in MS patients precipitating a weaker response to fluid resuscitation [14,15,17,20]. Prior studies have recognized a correlation between the severity of autonomic dysfunction and the degree of disease progression [16]. However, our data collection method limited our capacity to document the progression of disease. In addition, the duration since MS diagnosis varied within our population, ranging from a few years to a few decades. Last, the small number of patients with MS admitted to our burn center made it impractical to adjust for these factors.

In the MS cohort, LOS normalized to % TBSA burned was significantly higher compared to the control group. Previous studies have indeed demonstrated that patients with MS admitted for general ICU cases are at higher risk of infection and have an increased one-year mortality rate [7]. This suggests that the burden of burn injury may be increased with a history of MS. These patients may be more prone to complications and require higher levels of care ultimately, prolonging their LOS. While the incidence of in-hospital complications was similar both groups, the longer LOS contributing to a greater LOS/%TBSA is likely an indication of more time to heal wounds in the MS group. Wound healing is a complex series of cascading events that requires both immune and skin cell interaction to achieve healing. In individuals with MS, we hypothesized that they have an impaired wound recovery and therefore require longer to heal.

Temperature hypersensitivity in the MS population is a well-established observation [21–24]. Namely, Uhthoff's

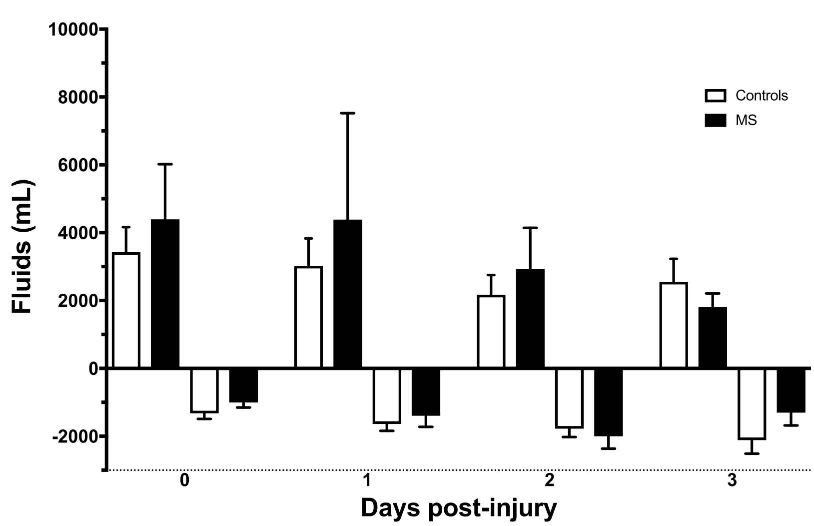

Fig. 1 – Fluid intake and output during the first four days after burn injury. Error bars indicate SEM.

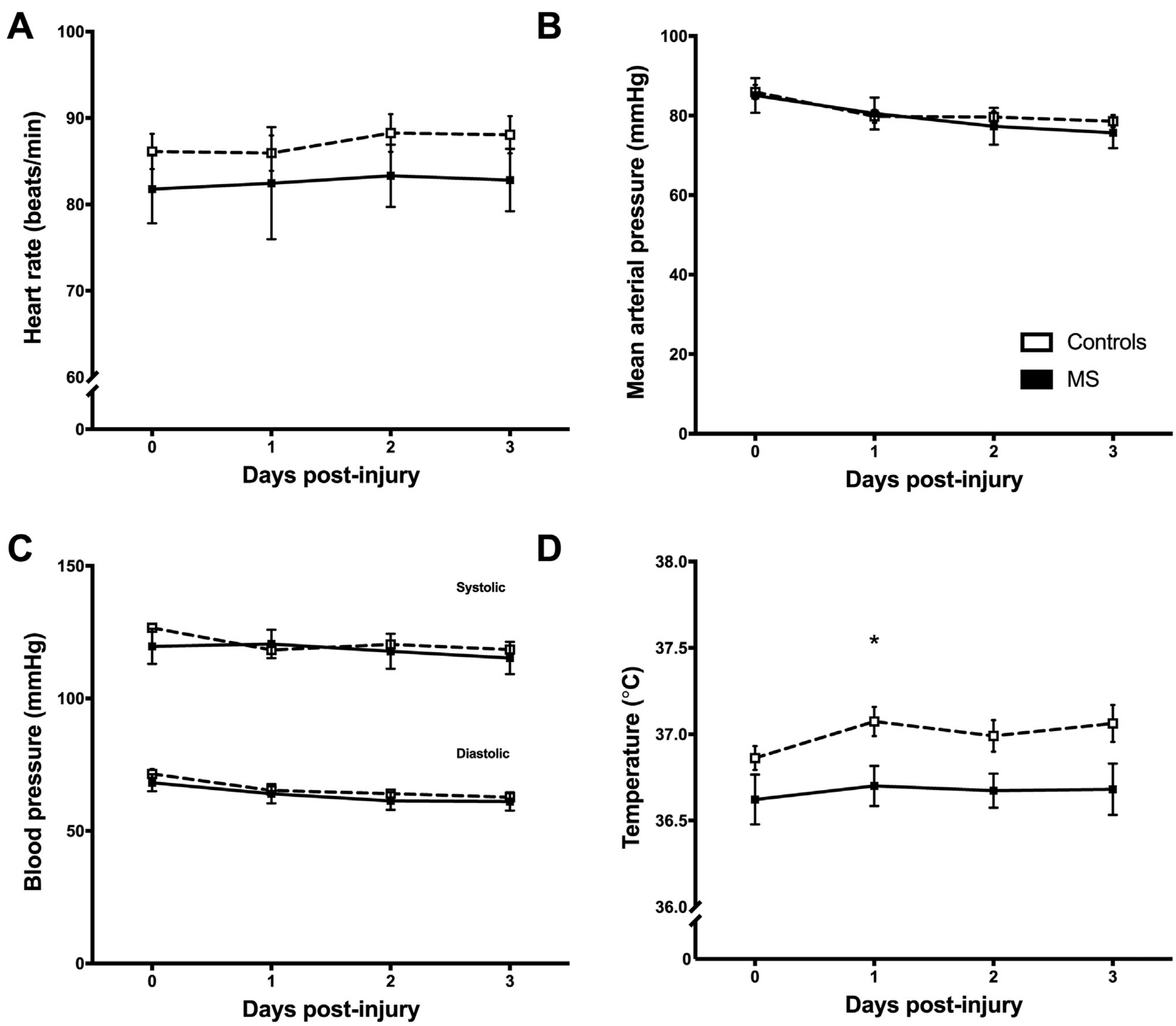

Fig. 2 – Mean heart rate (A), mean arterial pressure (B), blood pressure (systolic/diastolic) (C), and temperature (D). Error bars indicate SEM. $^{*}p<0.05$.

phenomenon is characterized by heat triggered or exacerbated new neurological symptoms and is reported in 60–80% of individuals with MS [22]. Heat acts to exacerbate hindered action potential firing, a result of demyelination fundamental to MS. Inevitably, MS as well as heat-exacerbated MS is correlated with fatigue and is a predictor of falls. However, heat sensitivity has been largely disregarded in many studies [22,24]. This characteristic likely puts patients with MS patients at an increased risk of acquiring a burn injury as well as exacerbates their neurological dysfunction in burn injury settings. However, no studies have evaluated autonomic dysfunction triggered by heat in the context of a burn injury. Further investigation is needed to fully understand the unique needs of patients who present with both burn injury and MS.

With advances in burn care such as fluid resuscitation, nutrition management, pulmonary care, wound care and infection control, burn-associated mortality has declined [4]. While much progress has been made, little is understood about the unique demographic background of burn patients with MS. The autonomic system plays a significant role in initiating an appropriate stress response is after burn injuries. It is well-understood that this demyelinating, autoimmune disease of the CNS is associated with cardiovascular and other autonomic dysfunctions which may potentially complicate trauma management [17]. The higher incidence of ICU comorbidities and greater one-year ICU mortality rate in the MS population suggests that this patient demographic will receive a greater level of care to achieve successful outcomes. Our study found that hospital LOS was prolonged for MS burn patients compared to otherwise healthy burn patients when % TBSA burned was controlled for. However, the other clinical parameters, including the number of complications and resuscitation volumes, were not significantly different between the two groups in our study. Future studies should investigate larger sample sizes to better understand the capabilities of MS patients to tolerate burn injuries. It is interesting to note that patients with MS in our study had a longer LOS, but only when accounting for % TBSA burn In a general ICU study, patients with MS had a longer LOS after ICU admission than the matched population [25]. Therefore, the LOS may be attributable to the % TBSA burn as well as MS. Prolonged hospitalization within a burn centre results in increased colonization of *Enterobacteriaceae*, *Pseudomonas* spp., and *Staphylococcus aureus* [26] and is directly proportional to the risk of acquiring multidrug resistant gram-negative bacteria [27]. This is highly problematic in patients with MS who are often prescribed immunomodulary and immunosuppressive treatments [28] because thermal injuries induce a state of immunosuppression that can further increase patients' of infections.

This study has several limitations. Due to a small sample size, the study may have been underpowered to detect differences in complications or adjust for disease progression and type. Additionally, the analysis did not account for potential interactions between measures. As a retrospective study at a single centre, there is potential for bias. However, to mitigate the impact, we performed a matched-analysis and did not undertake subgroup analyses. Lastly, our burn centre cares for patients from a large geographical area.

In summary, this retrospective case-control study describes factors contributing to the outcomes of burn-injured patients previously diagnosed with MS. When normalized to burn size, patients with MS have a longer hospital LOS, implying impaired or delayed wound healing. Increased efforts to prevent burn injury in these patients is paramount. Future studies should aim to investigate whether MS condition severity modulates the inflammatory and immune acute response after burn.

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Competing interests

All authors have completed the ICMJE uniform disclosure and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Author contributions

MRM, SR, WF, and MGJ conceived the project and conducted study design. MRM, WF, and SR acquired study data. MRM, SR, and MGJ performed analysis and interpretation of data. All authors were involved in drafting the article, revising it critically for content and all authors approved the final version.

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