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## Fatigue Following Burn Injury: A Burn Model System National Database Study

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### Abstract

Fatigue is a commonly reported but not well-documented symptom following burn injury. This study's objective was to determine the frequency and severity of fatigue over time and to identify

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predictors of fatigue in the adult burn population. Data from the Burn Model System National Database (April 1997 to January 2006) were analyzed. Individuals over 18 years of age who were alive at discharge were included. The vitality subscale of the Short-Form 36 Item Health Survey was examined at preinjury and discharge and at 6, 12, and 24 months postinjury. Mean and number of low vitality scores were calculated at each time interval. Descriptive statistics were generated for demographic and medical data. Cross-sectional regression models analyzed predictors of vitality at 6, 12, and 24 months postinjury. The study included 945 subjects. The population was 72.5% male and had a mean age of 40.6 years and mean burn size of 17.4%. Fatigue symptoms were present in a majority of the population (74.6%) and were most commonly reported at discharge. Although fewer burn survivors reported fatigue symptoms at each subsequent follow-up ( $P < .001$ ), approximately one-half (49%) of the population continued to report fatigue symptoms at 24 months postinjury. Larger burn size was the only variable that was significant or approaching significance at all follow-up time points ( $P < .0167$ ). Fatigue symptoms are common after burns and many burn survivors continue to report symptoms at 2 years postinjury. Burn survivors did not return to preinjury fatigue levels, highlighting the importance of understanding and monitoring fatigue.

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After burn injuries, many individuals experience a variety of long-term physical, psychological, and social challenges. Both patients and clinicians are increasingly identifying fatigue as a significant issue following burn injury; however, it remains loosely defined. Fatigue may be physical, psychological, or mental. In a general sense, it has been described as a subjective feeling of tiredness, weakness, or lack of energy.<sup>1</sup> It is associated with a wide range of medical conditions, including fibromyalgia,<sup>2</sup> multiple sclerosis,<sup>3,4</sup> traumatic brain injury,<sup>5</sup> and cancer,<sup>6</sup> among others. In many cases, it may severely limit physical activities and increase risk of disability.<sup>7,8</sup> Fatigue has been shown to have a significant impact on well-being and quality of life both during and after recovery; however, it remains “under-recognized, under-assessed, and under-treated.”<sup>1</sup>

There are several reasons why burn survivors may experience fatigue symptoms. Major burns result in a pathophysiological stress response, which in turn leads to a hypermetabolic state that reflects an increase in whole-body oxygen consumption above the normal range.<sup>9</sup> Burn-induced hypermetabolism is associated with poor clinical outcomes and has been shown to persist long-term in large injuries,<sup>10</sup> possibly contributing to fatigue for years postinjury. Additionally, muscle wasting can delay healing and greatly contribute to the long-term morbidity of burn survivors.<sup>9</sup> This may result in postinjury weakness that can make activities of daily living challenging. In burns involving more than 30% total body surface area (TBSA), muscle wasting can persist for several years postinjury.<sup>9</sup> Similarly, physical and functional impairments following burn injury may cause regular activities to be more tiresome and contribute to higher fatigue levels.<sup>11</sup> Depression and anxiety following burn injury may also lead to reductions in physical functioning and higher levels of fatigue.<sup>12</sup> There are many non-burn-specific causes of posthospitalization fatigue, including deconditioning and general weakness following prolonged hospitalization and bed rest, infection, hypotension, insomnia, viruses, immune system issues, inflammation, and arthritis.

A burn survivor must overcome multiple physical and psychological barriers in order to return to regular daily activities. In the authors' experience, fatigue is a commonly reported symptom following burn injury; however, it is rarely included in outcomes studies and is not well documented in the literature. Fatigue is strongly associated with poorer health-related quality of life and greater work-related disability, and the risk of developing moderate to severe fatigue following burn injury has been found to increase with burn size.<sup>13</sup> Women and people living in rural and remote areas have been found to be at greater risk of developing moderate-to-severe fatigue.<sup>13</sup> Fatigue has been shown to persist as long as 17 years postinjury<sup>14</sup>; however, no previous studies have examined the progression of fatigue beyond a 1-year follow-up. As fatigue symptoms can contribute to depression, social isolation, inability to care for oneself and others, and inability to work, fatigue can have a serious impact on long-term quality of life and impair a burn survivor's ability to achieve preinjury levels of satisfaction.

The extent to which fatigue is a barrier in burn recovery has not been extensively examined. Studies to date have been limited by small sample size, non-North American burn populations, and short follow-up windows. The objective of this study was to determine the frequency and severity of fatigue symptoms, as well as changes in the severity of fatigue over time, in the adult burn population. Additionally, predictors of fatigue at each follow-up time point will be determined.

## METHODS

### Data Source

Data from the prospectively collected Burn Model System (BMS) National Database between April 1997 and January 2006 were analyzed. Six burn centers in the United States have contributed to this database over the lifespan of the project (1993 to current).<sup>15</sup> Individuals over 18 years of age who were alive at the time of acute care discharge were included. For this time period, the BMS National Database included data on survivors who met the American Burn Association criteria for a severely burned person, namely those with 1 or more of the following:

- Deep second- and third-degree burns greater than 10% TBSA in patients over 50 years of age.
- Deep second- and third-degree burns greater than 20% TBSA.
- Deep second- and third-degree burns with serious threat of functional or cosmetic threat that involve face, hands, feet, genitalia, perineum, or major joints.
- Third-degree burns greater than 5% TBSA.
- Deep electrical burns including lightning injury.
- Burn injury with inhalation injury.
- Circumferential burns of the extremity or chest.

Modifications were made to the inclusion criteria over time. Details of the BMS National Database inclusion criteria, data collection process, and data collection sites can be found at <http://burndata.washington.edu/>.

### Variables

Demographic (age, race, gender, marital status, and employment status) and medical (burn etiology, burn size, acute care length of stay, drug abuse, alcohol abuse, psychiatric treatment, and preexisting physical disability) variables were collected through self-report or medical records at discharge. Drug and alcohol abuse were evaluated using the CAGE questionnaire.<sup>16</sup>

### Outcome

The vitality subscale of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), which was administered by BMS centers between April 1997 and January 2006, was used to determine fatigue symptoms. A lower vitality score indicates greater fatigue. The subscale has been used in cancer,<sup>17</sup> head injury,<sup>18</sup> and fibromyalgia<sup>19</sup> populations to assess fatigue levels. It includes 4 questions that are scored on a 1–5 scale, where 1 is “All of the time” and 5 is “None of the time.” Two of the 4 questions were reverse coded. Vitality scores were examined at preinjury (collected at discharge, with a preinjury recall period) and discharge, as well as at 6, 12, and 24 months postinjury.

### Data Analysis

Descriptive statistics were generated for demographic and medical data. Responses to the items of the vitality scale questions were transformed to a *t*-score with a mean of 50 and SD of 10 based on a U.S. population.<sup>20</sup> Fatigue was defined as a score less than 50. Mean vitality scores and the percentage of the population reporting fatigue were calculated at each time interval. Wilcoxon signed rank-sum tests were conducted to compare vitality scores preinjury and at 24 months postinjury, as well as at discharge and at 24 months postinjury. Multivariate linear regression models were utilized to identify demographic and clinical predictors of fatigue at 6, 12, and 24 months postinjury. Due to concerns about multiple testing, a Bonferroni correction to the alpha level of 0.05 was used, resulting in a *P* value of <.0167 for statistical significance.

A secondary analysis was conducted to evaluate relationships between vitality scores and employment status and between vitality scores and mental health scores at 6, 12, and 24 months postinjury. The SF-36 mental health score has been used to measure depression in several other injury populations.<sup>21,22</sup>

## RESULTS

### Population Characteristics

The study included 945 subjects who reported vitality score data at discharge. The population was 72.5% male, had a mean age of  $40.6 \pm 14.6$  years, and a mean burn size of  $17.4 \pm 15.7\%$  TBSA (Table 1). Fire/flame was the most common burn etiology (58.1%). Of

the 945 participants, 71% (n = 672) were working at the time of injury, 47% (n = 441) were single, and 68% (n = 2409) were white and non-Hispanic.

### **Vitality Score**

The mean vitality score before injury was  $55.9 \pm 10.9$ . The mean vitality score was lowest at discharge ( $43.1 \pm 10.9$ ) and improved at each subsequent time period ( $P < .001$ ). The highest mean vitality score postinjury was exhibited at 24 months ( $49.6 \pm 11.5$ ); however, the vitality scale score at 24 months did not return to the preinjury level ( $P < .001$ ).

Fatigue symptoms were most commonly reported at discharge and seen in a majority of the population (vitality score < 50: 74.6%). Although fewer burn survivors reported fatigue symptoms at each subsequent follow-up (Figure 1), approximately one-half (49%) of the population continued to report fatigue symptoms at 24 months postinjury.

### **Regression Analysis**

Larger burn size (6, 12 months), older age (6 months), female sex (12 months), electrical injury (24 months), and other burn etiology (6, 12 months) were strongly correlated with greater fatigue ( $P < .0167$ ; Table 2). Larger burn size at 24 months was approaching significance ( $P = .018$ ).

### **Secondary Analysis**

Unemployment was associated with greater fatigue at all 3 follow-up time points ( $P < .0167$ ). Mental health scores were correlated with vitality scores at all 3 follow-up time points ( $r = 0.7479$  at 6 months;  $r = 0.7140$  at 12 months;  $r = 0.7647$  at 24 months).

## **DISCUSSION**

Little attention has been given to fatigue symptoms following burn injury, and fatigue is unlikely to be prioritized by burn care clinicians. This is the second study to examine fatigue after burn injury.<sup>13</sup> In addition to confirming the prevalence of postinjury fatigue among adult burn survivors, this study evaluates fatigue at 2 years postinjury, examines a North American population, and identifies predictors of fatigue at 3 follow-up time points. Together, these 2 studies offer a greater understanding of an important but not well-documented symptom.

Fatigue is common following burn injury, and a majority of burn survivors continue to report symptoms at 24 months postinjury. Symptoms seem to gradually subside over time; however, burn survivors did not return to preinjury baseline levels. The causes of fatigue are not well understood; however, the high prevalence of fatigue long-term, as well as the detrimental impact these symptoms can have on work, family, and social activities, indicates that this is a persistent issue that must be addressed in order to improve quality of life for burn survivors.

In the present study, burn size was positively associated with the severity of fatigue symptoms at 6 and 12 months postinjury. This result is unsurprising, and existing literature offers several explanations, including hypermetabolism, deconditioning, muscle wasting,

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and other burn sequelae.<sup>9,14</sup> Previous studies demonstrating persistent muscle weakness and lower levels of aerobic fitness among adult burn survivors further support these explanations.<sup>23,24</sup> Electrical injury was also associated with greater fatigue at 24 months postinjury, indicating that the nature of electrical injuries has a greater impact on long-term fatigue than fire/flame injuries. This is consistent with previous research showing that individuals with electrical burns are more likely to experience complications such as amputations.<sup>25</sup> Female gender was also associated with greater fatigue at 12 months postinjury. This reflects findings related to chronic fatigue in the general population,<sup>26</sup> as well as a previous study using the BMS database that showed women experience greater depression following burn injury.<sup>27</sup>

Though treatment options for chronic fatigue symptoms are limited, addressing the potential underlying causes may help improve long-term outcomes. Psychological distress is common after a traumatic event, and it may be linked to greater postinjury fatigue.<sup>12</sup> More specifically, depression is a well-known long-term problem following burn injury that may contribute to the development of fatigue symptoms.<sup>28,29</sup> In the present study, burn survivors with greater fatigue had lower mental health scores at all follow-up time points, further suggesting a relationship between fatigue and depression following burn injury. Psychological issues, as well as physical sequelae such as pain and itch, may also interfere with sleep. Sleep dissatisfaction has been found to be associated, in a dose-dependent fashion, with increasing burn size, as well as with many quality of life measures, including pain, itch, physical function, social interactions, family concerns, and work reintegration.<sup>30</sup> Moreover, up to 61% of burn survivors report sleep dissatisfaction 1 year postinjury.<sup>31</sup> Thus, poor sleep quality following burn injury is common, and it is likely that problems with sleep decrease a survivor's overall energy and increase levels of fatigue. Addressing sleep concerns, as well as psychological distress, at long-term burn care follow-up may help alleviate lasting fatigue.

Exercise may also improve persistent fatigue symptoms after burn injury. Burn survivors have been shown to have impaired muscle strength years following injury.<sup>32</sup> Burn-induced muscle wasting is a hallmark of severe burn trauma, and reduced muscle mass has been shown to persist years following injury.<sup>9</sup> Thus, exercise is a key component of rehabilitation. Exercise helps restore muscle mass and cardiovascular fitness following prolonged hospitalization,<sup>33</sup> and better overall fitness can make daily tasks less challenging. However, one challenge to intensive rehabilitation following burn injury is thermoregulation. Compared with unburned skin, burned skin does not allow for the release of heat. It is expected that burn survivors' internal temperature will increase, more than that of someone without a burn, during exercise. Several recent studies have shown that exercise following injury is safe, though burn survivors do experience a moderate increase in temperature and heart rate compared with the non-burned controls.<sup>34,35</sup>

Additionally, management of the pathophysiological stress response to burn injury may aid the treatment of fatigue. Oxandrolone, an anabolic steroid, has been shown to increase muscle protein synthesis and weight gain and is associated with decreased hospital stays in severe burns.<sup>36</sup> It is a safe and effective treatment for hypermetabolism and thus may help attenuate fatigue symptoms. Skeletal muscle protein damage resulting from mitochondrial

hypermetabolism might represent a new target for interventions aimed at treating and preventing muscle wasting and hypermetabolism.<sup>37</sup> Proper nutrition also plays an important role in combating muscle wasting and hypermetabolism<sup>9</sup> and should be taken into account when treating chronic fatigue. Despite past research efforts, further investigation is needed to better understand the pathophysiology of long-term fatigue symptoms after burn injury and to evaluate the impact of these and other potential interventions. It is possible that mechanistic information for the cause of postburn fatigue could be obtained by examining burn-induced metabolism-related transcriptome changes within energy production genes and mitochondria.<sup>38,39</sup>

Postburn injury fatigue can have many far-reaching implications on community reintegration, including employment. Energy is an important factor in returning to work after burn injury, and long-term fatigue symptoms pose a large barrier to work productivity in all populations. Workers with fatigue are significantly more likely to miss work than workers without fatigue.<sup>40</sup> One study estimated that U.S. workers with fatigue cost employers over \$100 billion annually in lost productive time when compared with workers without fatigue.<sup>41</sup> Fatigue is a highly prevalent issue for burn survivors, and unemployment was associated with fatigue at all 3 follow-up time points examined in this study. Consistent with this finding, the authors have found that patients often cite fatigue as a primary reason for not returning to preinjury jobs. This is particularly important, given that burn survivors who are not working appear to have more pain and lower quality of life compared with those who are working.<sup>42</sup> Additional research is needed to further explore the relationship between fatigue and employment and other community reintegration outcomes following burn injury.

### **Study Limitations**

Several limitations to this study must be noted. The preinjury data are collected at the time of acute care discharge, allowing for the possibility of recall bias. Although the vitality score is used in other studies to assess fatigue, there are other, newer measures that are specifically designed to assess fatigue. Additionally, the data were collected between 1997 and 2006 and thus may not reflect the most current state of fatigue after burn injury. Nonetheless, given the paucity of literature on the topic and the size of the multicenter database, this is an important first step in establishing fatigue as a common symptom complex after burns.

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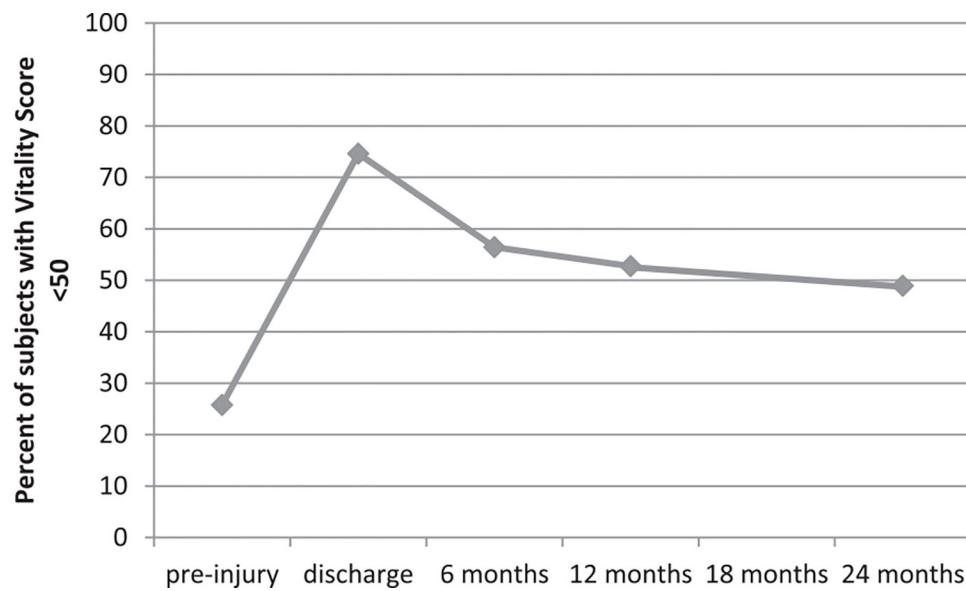
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**Figure 1.**

Frequency of fatigue over time. Responses to the items of the SF-36 vitality scale questions were transformed to a  $t$ -score with a mean of 50 and SD of 10 based on a U.S. population. Fatigue was defined as a score less than 50, and the percentage of subjects with low vitality scores was calculated at preinjury (collected at discharge) and discharge, as well as at 6, 12, and 24 months postinjury. SF, Short Form.

**Table 1.**

Demographic and medical characteristics of study population at discharge

Variable	Total (N = 945)
Age, mean (SD)	40.6 (14.6)
Male gender, n (%)	685 (72.5)
Race/ethnicity, n (%)	
White, non-Hispanic	632 (66.9)
Black, non-Hispanic	178 (18.9)
Hispanic	93 (9.8)
Asian	11 (1.2)
Native American	8 (0.9)
Multiracial	4 (0.4)
Pacific Islander	3 (0.3)
Other	3 (0.3)
Employment status, n (%)	
Working	672 (71.1)
Not working	195 (20.6)
Homemaker	7 (0.7)
Volunteer	2 (0.2)
Retired	66 (7.0)
Marital status at the time of burn, n (%)	
Single	441 (46.7)
Married	387 (41.0)
Partner/significant other	45 (4.8)
Etiology of injury, n (%)	
Fire/flame	549 (58.1)
Scald	108 (11.4)
Contact with hot object	39 (4.1)
Grease	81 (8.6)
Electricity	55 (5.8)
Other burn	86 (9.1)
TBSA burned, mean (SD)	17.4 (15.7)
Length of hospital stay, mean (SD)	23.1 (20.1)
Inhalation injury, n (%)	102 (10.8)
Drug abuse, n (%)	87 (9.2)
Alcohol abuse, n (%)	97 (10.3)
Psychiatric treatment, n (%)	402 (11.2)
Preexisting physical disability, n (%)	398 (11.1)

**Table 2.**

Linear regression analysis results examining predictors of the SF-36 vitality scores at 6, 12, and 24 months after injury

Variables	6 mo		12 mo		24 mo	
	$\beta$	P	$\beta$	P	$\beta$	P
Age	-.138*	.008*	-.122	.020	-.074	.232
Female gender	-.060	.240	-.154*	.004*	-.0141	.018
Race/ethnicity, compared with white						
Black, non-Hispanic	-.110	.026	-.058	.253	-.089	.122
Other	.001	.987	-.041	.419	0.016	.780
Working at the time of injury	.061	.277	0.032	.566	0.075	.263
Married	.015	.772	0.036	.493	0.013	.825
TBSA burned	-.179*	.005*	-.174*	.011*	-.0181	.018
Etiology, compared with fire/flame						
Scald	-.098	.058	-.111	.033	-.042	.482
Grease	.002	.974	-.019	.720	0.013	.833
Electricity	-.083	.107	-.119	.029	-.153*	.012*
Other	-.154*	.003*	-.158*	.003*	-.060	.325
Length of hospital stay	.065	.299	0.017	.790	0.095	.199
Inhalation injury	.012	.817	-.059	.256	0.029	.627
Drug abuse	-.063	.206	-.046	.378	0.034	.600
Alcohol abuse	-.080	.115	-.054	.298	-.049	.425
Psychiatric treatment	-.099	.048	-.084	.109	-.114	.068
Preexisting physical disability	-.038	.493	-.112	.038	-.019	.763

SF, Short Form.

\* Indicates significance ( $P < .0167$ ).