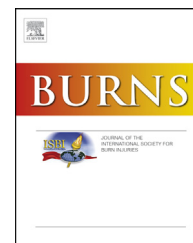


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Increased risk for stroke in burn patients: A population-based one-year follow-up study

Shiu-Dong Chung^{a,b}, Chin-Shyan Chen^c, Heng-Ching Lin^b,
Jiunn-Horng Kang^{d,e,*}

^a Division of Urology, Department of Surgery, Far Eastern Memorial Hospital, Ban Ciao, Taipei, Taiwan

^b Sleep Research Center, Taipei Medical University Hospital, Taipei, Taiwan

^c Department of Economics, National Taipei University, Taipei, Taiwan

^d Department of Physical Medicine and Rehabilitation, Taipei Medical University Hospital, Taipei, Taiwan

^e Department of Physical Medicine and Rehabilitation, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

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ABSTRACT

Introduction: The study aimed to explore the frequency and risk of stroke following hospitalization for burn through the analysis of a population-based dataset in Taiwan.

Methods: We identified 692 hospitalized subjects who had received a diagnosis of burn. We randomly selected 2768 comparison subjects to match the study subjects by sex and age group. We individually tracked each subject for one year identifying all those who received a diagnosis of stroke during that period. Cox proportional hazards regressions were performed to calculate the longitudinal hazard of stroke between the two cohorts.

Results: We found that the incidence rate of stroke during the one-year follow-up period was 6.65 (95% CI: 4.92–8.79) per 100 person-years and 2.75 (95% CI: 2.18–3.42) per 100 person-years for study cohort and comparison cohort, respectively. After adjusting for urbanization level, monthly income, geographic region, hypertension, diabetes, coronary heart disease, heart failure, atrial fibrillation, hyperlipidemia, and chronic kidney disease, and censoring the cases that died from non-stroke causes, the hazard ratio (HR) for stroke during the one-year follow-up period for study cohort was 2.52 (95% CI = 1.73–3.68, $P < 0.001$) that of comparison subjects. We further analyzed the HR of stroke according to the extent of burned body surface area (<10%, 10–29%, and >29%). We found that there was no significant difference in the risk of stroke during the one-year follow-up period among these three groups of subjects.

Conclusions: We found that burn victims were at higher risk for subsequent stroke that matched comparison subjects during one-year follow-up.

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1. Introduction

Burns are common injuries which can be associated with significant mortality and morbidity [1,2]. Burns can be

complicated with electrolyte imbalances, shock, infection, multiple organ dysfunction syndrome, and respiratory failure. Burn victims may also suffer from a variety of central nervous system complications, such as metabolic and infectious encephalopathies, and cerebral vascular diseases [3,4].

* Corresponding author at: Department of Physical Medicine and Rehabilitation, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan. Tel.: +886 27361661; fax: +886 27361661.

E-mail address: jhk@tmu.edu.tw (J.-H. Kang).

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Stroke has been reported in some case reports among patients suffering from burns [5]. However, the epidemiological data regarding this association is still very scanty. In an early study performed by Winkelmann et al., it was reported that ischemic stroke was evident from the autopsy examinations of 18% of burn victims [4]. The authors proposed that septic emboli, disseminated intravascular coagulation (DIC), shock, and cardiac arrhythmia may be underlying causes of stroke in burn patients. However, their study cannot be generalized to the overall population of burn victims as they only included the more severe burn patients who expired during treatment. Furthermore, the results of that study may be outdated as the clinical management of burn patients has improved over the past 20 years. More recently, Cho et al. reported that the incidence rate of stroke among the burn patients in a single-hospital study was about 0.07%, concluding that stroke is a rare complication following a burn event [6]. However, while previous studies have noted incidence data among burn victims, the risk for stroke when compared with the general population is still unknown.

In the present study, we aimed to explore the epidemiological profile of stroke occurrence following burn events among hospitalized subjects. The longitudinal risk for stroke occurrence was analyzed from a retrospective cohort study using a population-based dataset.

2. Methods

2.1. Database

The data used to perform the analyses conducted in this study were retrieved from the “Longitudinal Health Insurance Database (LHID2000)”. The LHID2000 consists of all the original medical claims for 1,000,000 enrollees under the Taiwan National Health Insurance (NHI) program, and was created and publicly released to researchers in Taiwan by the Taiwan National Health Research Institute. The included 1,000,000 enrollees of the LHID2000 were randomly selected from all the enrollees listed in the 2000 Registry of Beneficiaries ($n = 23.72$ million) under the NHI program. The Taiwan National Health Research Institute has validated the representativeness of the LHID2000 relative to the whole population of NHI enrollees in terms of gender distribution. The release of the LHID2000 allows researchers in Taiwan to follow-up on all the medical service utilizations for these 1,000,000 enrollees starting with the initiation of the NHI program in March 1995. Many prior studies have demonstrated the high validity of the LHID2000 [7,8] and hundreds of papers employing the LHID2000 have been published in internationally peer-reviewed journals.

This study was exempt from full review by the Institutional Review Board of Taipei Medical University because the LHID2000 consists of de-identified secondary data released to the public for research purposes.

2.2. Study sample

This investigation was designed as a retrospective cohort study. As for the selection of the study cohort, we first

identified 788 subjects ≥ 40 years and who had received their first principal diagnosis of burn (ICD-9-CM codes 941–949) during hospitalizations between 1 January 2001 and 31 December 2008. In this study, we only selected subjects ≥ 40 years since the incidence rate of stroke was low among subjects less than 40 years. We assigned the date of their first hospitalizations for receiving the burn diagnosis as index date. We further excluded subjects who had a history of stroke (ICD-9-CM codes 430–438) prior to index date ($n = 96$). However, the NHI program was inaugurated in 1995, so the dataset used in the present study only allowed us to trace medical utilization prior to 1995. Therefore, we could not rule out the possibility that the selected study subjects may have had a stroke event prior to 1995. Ultimately, there were 692 burn subjects included in the study cohort.

We likewise retrieved subjects for the comparison cohort from the LHID2000. We first identified all subjects ≥ 40 years who had been hospitalized with a principal diagnosis of acute appendicitis (ICD-9-CM codes 540, 540.0, 540.1 or 540.9) and received an appendectomy (ICD-OP code 47.0) between 1 January 2001 and 31 December 2008. The reason for the selection of appendectomy subjects as the comparison cohort was that subjects undergoing appendectomies were relatively indistinguishable from the general population. In addition, this allowed us to adjust for the possible effect of hospitalization on the development of stroke. We randomly selected 2768 comparison subjects (4 comparison subjects per study subject) matched with the study subjects on sex, age group (40–49, 50–59, 60–69, and >69), and index year. We assigned the date of their first hospitalization for appendectomy as their index date. We further assured that none of the selected comparison subjects had received a diagnosis of burn since the beginning of the NH or a diagnosis of stroke prior to the index date. We individually tracked each subject in this study ($n = 3460$) for one year following their index date and identified each subject that received a subsequent principal diagnosis of stroke (ICD-9-CM codes 430–438) during that follow-up period.

2.3. Statistical analysis

We used the SAS statistical package (SAS System for Windows, Version 8.2, Cary, NC, USA) to conduct the statistical analyses performed in this study. We also used the Kaplan–Meier method and log-rank test to examine the differences in one-year stroke-free survival rates between the study and comparison cohort. Additionally, we used Cox proportional hazards regression (stratified by sex, age group, and index year) to compute the one-year risk of subsequent stroke following a diagnosis of burn. In this study, we found that the proportional hazards assumption was satisfied as the survival curves for both strata (subjects in the study cohort and comparison cohort) had hazard functions that were proportional over time. This study also took co-morbidities into consideration in the regression model. The co-morbidities selected for adjustment in this study included hypertension, diabetes, coronary heart disease (CHD), heart failure, atrial fibrillation, hyperlipidemia, and chronic kidney disease (CKD) (Appendix A). These co-morbidities have all been reported to be risk factors for stroke. In this study, we only considered these co-morbidities if they occurred in an inpatient setting, or

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