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Increased diabetes risk and interaction with social and medical events in patients upon stroke: Two nationwide studies

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ABSTRACT

Background & aims: The relationship between stroke and diabetes is not completely understood. This study evaluated diabetes risk and post-diabetes adverse events in patients with stroke.
Methods: We identified 10,255 adults, newly diagnosed with stroke from 2000 to 2005, using the Taiwan's National Health Insurance Research Database. A comparison cohort of 41,020 adults without stroke was randomly selected from the same dataset, frequency matched by age and sex. Diabetes events from 2000 to 2013 were ascertained from medical claims. Adjusted hazard ratios (HRs) and 95% CIs were calculated for diabetes associated with stroke. A nested cohort study of 33,437 patients with inpatient care for diabetes between 2008 and 2013 was conducted to calculate the adjusted odds ratios (ORs) and 95% CIs for adverse events after diabetes, in patients with and without stroke.
Results: During 489,561 person-years of follow-up, there were 10,742 newly diagnosed diabetes cases. The incidence of diabetes for people with and without stroke was 43.9 and 17.8 per 1000 person-years, respectively ($p < 0.0001$). Compared to that for people without stroke, the adjusted HR for diabetes was 2.69 (95% CI 2.56–2.82) for stroke patients. The ORs of post-diabetes pneumonia, urinary tract infection, and mortality associated with stroke were 1.35 (95% CI 1.17–1.55), 1.52 (95% CI 1.36–1.70), and 1.71 (95% CI 1.27–2.29), respectively.
Conclusions: We provide evidence that the consequences of stroke are not limited to the neurological defect, but evoke diabetes and a plethora of associated medical, psychological and social impacts the physician must be strongly aware of if evaluating and treating stroke patients.

1. Introduction

Diabetes is a chronic disease with worldwide prevalence estimated to affect 366 million people by 2030 [1]. In the United States, 9.3% of the population has diabetes and the total estimated cost of diagnosed diabetes in 2012 was $245 billion [2]. Hypertension, dyslipidemia, physical inactivity, smoking, and alcohol use are important risk factors of diabetes, and it is known that stroke is one

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of the comorbidities for diabetic patients [3].

Stroke, which has an overall prevalence estimated at 2.8% in the United States, is projected to have a 20.5% increase in prevalence from 2012 to 2030 [4]. Complications of stroke include recurrent stroke, epileptic seizure, urinary and chest infections, falls, pressure sores, deep venous thrombosis, pulmonary embolism, pain and depression [5]. Post-stroke hyperglycemia is a common phenomenon due to an acute stress response, even in non-diabetic patients [6]. Impaired glucose metabolism or pre-diabetes may also present in non-diabetic patients with newly diagnosed stroke and progress to diabetes. However, the risk of diabetes in stroke patients is not completely understood because previous studies have several limitations, such as focusing on the specific subtype of stroke [7–12], cross-sectional study designs [10–14], inadequate control for confounding factors [7,9,10,12,13,15–18], and small sample sizes [7–14,16–19]. Using Taiwan's National Health Insurance Research Database, this study evaluated diabetes risk and post-diabetes adverse events in patients with stroke.

2. Materials and methods

2.1. Study design

We used Taiwan's National Health Insurance Research Database to perform the two current studies. The data source and details of this national database have been described in our previous reports [20–22]. Using the representative sample of one million people from the Taiwan's National Health Insurance Research Database, we conducted a retrospective cohort study (Study I) of 10,255 patients with newly diagnosed stroke (defined as people who visited emergency care or were hospitalized with a physician's first-time diagnosis of stroke since 1996, which was the beginning of insurance claims in Taiwan's National Health Insurance Research Database). With frequency matching by age and sex (case-control ratio = 1:4), 41,020 patients without stroke history were also identified as a non-exposure cohort with the same index date. These two cohorts aged ≥20 years were established between January 1, 2000, and December 31, 2005, and then followed up until December 31, 2013. The events of newly diagnosed diabetes were considered as outcomes during the follow-up period. The inclusion criteria of stroke and diabetes were based on our previous studies [20–22]. People who had the first-time visit of emergency care or inpatient care with physician's primary diagnosis of stroke were defined as stroke patients. Event of diabetes was defined as people had first-time visit of medical care with physician's primary diagnosis of diabetes during. We calculated person-years during the follow-up period for each participant until the diagnosis of diabetes or until being censored because of death, withdrawal from the insurance system, or loss to follow-up. The non-stroke group included the remaining people who did not experience stroke throughout follow-up. The purpose of Study I was to investigate the diabetes risk in stroke patients.

We also identified a diabetes cohort from Taiwan's National Health Insurance Research Database. This nested cohort study (Study II) consisted of 33437 patients with first-time inpatient care for diabetes from 2008 to 2013, and 11.5% (n = 3855) of them had a history of stroke. We compared the outcomes, including pneumonia, urinary tract infection, admission to intensive care, length of hospital stay, medical expenditure, and mortality for a 30-day period after first-ever diabetes admission between diabetic patients with and without a history of stroke. The purpose of Study II was to investigate the impact of stroke history on the outcomes of diabetes.

2.2. Ethical approval

Insurance reimbursement claims from Taiwan's National Health Insurance Research Database were used in this study. To protect personal privacy, the electronic database was decoded and patient identifications were scrambled to prevent further academic access for research [20–22]. Our study was approved by the Institutional Review Boards of Taipei Medical University (TMU-JIRB-201705065; TMU-JIRB-201705063) and E-DA Hospital (EDA-JIRB-2017005; EDA-JIRB-2017004; EDA-JIRB-EMRP105144).

2.3. Measures and definition

The following selection criteria and definitions were based on our previous studies [20–22]. Low-income status was defined as patients qualifying for a waiver of medical copayment, verified by the Taiwan Bureau of National Health Insurance. The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) was used to define coexisting medical conditions and complications, including stroke (ICD-9-CM 430-438), diabetes (ICD-9-CM 250), hypertension (ICD-9-CM 401-405), mental disorders

Table 1
Sociodemographic factors, coexisting medical conditions and diabetes in people with and without stroke.

	Non-stroke (N = 41020)		Stroke (N = 10255)		*p*
	n	(%)	n	(%)	
Age, years					
20-29	656	(1.6)	164	(1.6)	
30-39	1376	(3.4)	344	(3.4)	
40-49	3532	(8.6)	883	(8.6)	
50-59	6172	(15.1)	1543	(15.1)	
60-69	10112	(24.7)	2528	(24.7)	
70-79	13012	(31.7)	3253	(31.7)	
≥80	6160	(15.0)	1540	(15.0)	
Sex					
Female	17096	(41.7)	4274	(41.7)	
Male	23924	(58.3)	5981	(58.3)	
Low income	1299	(3.2)	735	(7.2)	<0.0001
Coexisting medical conditions					
Hypertension	14836	(36.2)	6425	(62.7)	<0.0001
Mental disorders	9513	(23.2)	4066	(39.7)	<0.0001
Ischemic heart disease	7732	(18.9)	3384	(33.0)	<0.0001
COPD	9908	(24.2)	3435	(33.5)	<0.0001
Heart failure	2094	(5.1)	1102	(10.8)	<0.0001
Hyperlipidemia	3755	(9.2)	898	(8.8)	0.2102
Liver cirrhosis	2057	(5.0)	534	(5.2)	0.4258
Alcohol-related illness	1007	(2.5)	511	(5.0)	<0.0001
Atrial fibrillation	516	(1.3)	329	(3.2)	<0.0001
Renal dialysis	389	(1.0)	288	(2.8)	<0.0001
Smoking cessation	629	(1.5)	131	(1.3)	0.0550
Number of medical conditions					<0.0001
0	15490	(37.8)	1475	(14.4)	
1	10258	(25.0)	2602	(25.4)	
2	7689	(18.7)	2551	(24.9)	
3	4606	(11.2)	1872	(18.3)	
≥4	2977	(7.3)	1755	(17.1)	
Medication use					<0.0001
Types of medication					
Aspirin	9852	(24.0)	7395	(72.1)	<0.0001
Anti-platelet agents	1579	(3.9)	1636	(16.0)	<0.0001
Coumadin	530	(1.3)	889	(8.7)	<0.0001
Enoxaparin	206	(0.5)	599	(5.8)	<0.0001
Heparin	2109	(5.1)	1408	(13.7)	<0.0001
Statin	5006	(12.2)	2227	(21.7)	<0.0001
Anti-hypertension	9544	(23.3)	4439	(43.3)	<0.0001

COPD, chronic obstructive pulmonary disease.
Anti-hypertension included ACEI, angiotension II, beta-blocker, CCB, and diuretics.