Adverse outcomes after surgery in patients with previous stroke

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List of abbreviations

CI, confidence interval

RR, rate ratio

ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification

ICU, intensive care unit

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Abstract

Background: Limited information is available on the association between a medical history of stroke and postoperative outcomes. This study aimed to investigate the outcomes after non-neurological surgeries in patients with previous stroke.

Methods: Using Taiwan's National Health Insurance Research Database, a nationwide cohort study was conducted consisting of patients who underwent non-neurological surgeries 2008 to 2010 with a medical history of stroke within the 24-month period prior to surgery. Patients who underwent non-neurological surgeries without previous stroke were selected as controls by the propensity score-matched pair method. The 30-day postoperative complications and in-hospital mortality were compared between the groups of patients.

Results: There were 1 426 795 adults who underwent major inpatient non-neurological surgeries and 45 420 of them had previous stroke. Patients that underwent surgeries with previous stroke had increased risk of postoperative pneumonia, septicemia, acute renal failure, acute myocardial infarction, pulmonary embolism, and 30-day in-hospital mortality, adjusted rate ratio (RR) 1.79 (95 per cent confidence interval (c.i.) 1.61 to 1.99). Compared with controls, patients with previous stroke due to intracerebral hemorrhage, RR 3.41 (2.97 to 3.91) and who were treated in an intensive care unit intensive care, RR 2.55 (2.24 to 2.90), or received neurosurgery, RR 2.49 (2.12 to 2.92) had an increased 30-day in-hospital mortality. Postoperative mortality also increased with preoperative stroke related comorbidities, and a

medical history of stroke within 1-6 months prior to surgery, RR 3.31 (2.91 to 3.75).

Conclusions: Patients with previous stroke had a higher risk for postoperative adverse outcome with a 30-day in-hospital mortality nearly twofold that of patients without previous stroke.

Introduction

Although the incidence of stroke has been declining¹, stroke remains the worldwide leading cause of acquired disability and death in adults²⁻⁴. Risk factors, prevention strategies and genetic biomarkers for stroke have been studied extensively³. Rehabilitation, such as physical therapy, may prevent sequelae after stroke and improve functional status⁵. However, patients with previous stroke still suffer from the common sequelae and complications such as dementia, depression, pneumonia, urinary tract infection, decubitus ulcer, hip fracture, traumatic brain injury, epilepsy, dysphagia and constipation⁵⁻⁸. Thus, the acute care services for patients with previous stroke have been documented with higher complication and mortality rates^{6,7,9}.

Studies investigating postoperative adverse events in patients with previous stroke have been limited by small sample sizes¹⁰⁻¹², single type of surgical procedure¹⁰⁻¹⁶, lack of control group¹⁰⁻¹⁹, without matching¹⁰⁻¹⁹, inadequate adjustment for potential confounding effects^{10,14} and reporting single outcome^{10-12,15}.

By the use of Taiwan's National Health Insurance Research Database, a population-based, cohort study was conducted to investigate the full spectrum of postoperative adverse outcomes and analyze the impact of disease severity for patients with previous stroke that received non-neurological major surgeries.

Methods

Source of data

The reimbursement claims data from Taiwan's National Health Insurance were used in this study. More than 99 per cent of the 22.6 million Taiwan residents are enrolled in this system.

Taiwan's National Health Research Institutes established a National Health Insurance Research Database recording all in- and outpatient medical services of beneficiaries, including patient demographics, primary and secondary diagnoses of diseases, procedures, prescriptions and medical expenditures^{5,20-25}. The accuracy of major diagnosis codes in the National Health Insurance Research Database was validated in the previous study²⁶.

Ethical approval

Insurance reimbursement claims from Taiwan's National Health Insurance Research Database are maintained by the National Health Research Institutes and are available for public access. To protect personal privacy, the electronic database was de-identified with patient identifications scrambled for further public access for research. According to National Health Research Institutes regulations, informed consent is not required due to decoded and scrambled patient identification. However, this study was evaluated and approved by Taiwan's National Health Research Institutes. This study was conducted in accordance with the Helsinki Declaration.

Study design

From the medical claims of National Health Insurance Research Database, this study identified adults aged 20 years and above who underwent major inpatient non-neurological surgeries from 2008 to 2010. Patients underwent non-neurological surgeries defined as surgeries requiring general, epidural or spinal anesthesia and hospitalization for more than one day and who had a history of stroke within the 24-month period prior to surgery were included in the study. The criteria for identifying patients with a medical history of stroke were defined in the previous studies^{5,20,21}.

This study used propensity score matched-pair method to select control patients without previous stroke. The propensity score was estimated using a logistic regression model including covariates generally considered to be associated with adverse events after surgery. The selected matching factors were based the previous surgical studies²²⁻²⁵.

Definitions

The information of operation in teaching hospital and low-income status was identified according to Bureau of National Health Insurance regulations. Low income was defined as patients qualified for waived medical copayment as certified by the Bureau of National Health Insurance. The age of study population was defined when the index surgery occurred.

According to the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM), stroke was defined as ICD-9-CM 430-438 in this study. Coexisting medical conditions that were considered (Suppl.Table 1) included hypertension, diabetes, mental

disorders, chronic obstructive pulmonary diseases, ischemic heart disease, hyperlipidemia, and liver cirrhosis (ICD-9-CM 571.2 and 571.5) that were diagnosed within the 24-month period prior to surgery. Renal dialysis was also identified as a coexisting medical condition in this study.

Acute myocardial infarction, acute renal failure, deep wound infection, pneumonia, postoperative bleeding, pulmonary embolism, and septicemia, were identified as major postoperative complications occurring within the 30-day period after the index surgeries; patients who were diagnosed with these conditions during the 24-month prior to surgery were excluded from analysis. Medical resource utilization such as length of hospitalization, admission to intensive care unit (ICU) within 30 days after the index surgery and in-hospital medical expenditures were analyzed. The lengths of stay and in-hospital medical expenditures of patients underwent surgeries with and without previous stroke were categorized by dividing into quartiles. Patients who underwent surgeries within the highest quartile of length of stay or in-hospital medical expenditures among the total number of patients were defined as the individuals having increased length of stay or elevated medical expenditures.

To explore the correlation between the severity of stroke and postoperative adverse outcomes, the type of treatment for stroke, the utilization of medical resources and medical expenditures were considered for further analysis. Stroke-related comorbidities such as traumatic brain injury, dementia, pneumonia and decubitus ulcer were also identified as

clinical indicators of stroke severity⁶⁻⁸.

Statistical analysis

To reduce confounding influence of covariates, a propensity score was used to match age, sex, low-income status, coexisting medical conditions, operation in teaching hospital or not, types of surgery and anesthesia between patients with and without previous stroke. The chi-square tests were used to examine the difference of parameters between patients underwent surgeries with and without previous stroke.

Adjusted rate ratios (RR) with 95 per cent confidence interval (c.i.) for 30-day postoperative complications, in-hospital mortality, prolonged length of stay, ICU stay and elevated medical expenditure between patients underwent surgeries with or without stroke were analyzed with multivariable Poisson regression by including age, sex, low-income status, operation in teaching hospital or not, preoperative coexisting medical conditions and types of surgery and anesthesia. To assess the impact of stroke severity on 30-day postoperative in-hospital mortality, multivariable Poisson regression was used to control the potential confounders; stroke-related neurosurgery, stroke within 1-6 months preoperatively, ICU stay, medical expenditure, traumatic brain injury, dementia, pneumonia and decubitus ulcer. Differences between groups were considered significant if two-sided *P* value was smaller than 0.05. Statistical analysis was performed with SAS, software version 9.1 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Among 1 426 795 patients underwent major non-neurological surgeries, 45 420 of them had previous stroke. There were significant differences between patients underwent surgeries with and without previous stroke (Table 1).

After propensity score-matching (Table 2), there were no significant differences between patients underwent surgeries with and without previous stroke in terms of socio demographic variables, operation in teaching hospital, type of surgery, types of anesthesia, and medical conditions.

Before propensity score-matching (Table 3), previous stroke was associated with postoperative pneumonia, septicemia, acute renal failure, acute myocardial infarction, pulmonary embolism any complications, prolonged hospital stay, ICU stay, increased medical expenditure and 30-day in-hospital mortality. After propensity-score matching and multivariable adjusting, patients with previous stroke had higher risk of postoperative 30-day in-hospital mortality, RR 1.79, prolonged hospital stay, RR 1.40, ICU stay, RR 1.24, and increased medical expenditure, RR 1.19 as well as postoperative complications including pneumonia, septicemia, acute renal failure, acute myocardial infarction, and pulmonary embolism (Table 3). Compared with control patients (Table 4), patients with stroke within 1-6 months prior to surgery had an increased 30-day postoperative in-hospital mortality (RR 3.31). Furthermore, patients with previous stroke and with low income had an increased 30-day

postoperative in-hospital mortality compared with patients without previous stroke.

Several indicators of stroke severity were associated with 30-day in-hospital mortality, including: stroke due to intracerebral hemorrhage, ICU treatment for stroke, stroke related neurosurgery, and high stroke-related medical expenditure. Preoperative stroke-related comorbidities increased postoperative mortality including traumatic brain injury (RR 2.01), dementia (RR 2.10), pneumonia (RR 2.16) and decubitus ulcer (RR 2.35).

Discussion

Stroke *per se* has been identified as one of the major risk factors for postoperative mortality and complications. The results of the present study, which was designed with propensity score-matching and adjusted by multivariable regression models, validated the increased rates of surgical adverse events in patients with a medical history of stroke prior to surgery. The risk of postoperative mortality for patients in the propensity score-matched cohort was lower than in the non-matched cohort. This means that the risk of postoperative mortality would be overestimated if propensity score-matching had not been used, even if multivariable regression analysis had been performed to control for confounders. The matched study design with propensity score should therefore be considered for outcomes studies²⁷⁻²⁹.

The postoperative incidence of pneumonia, sepsis and acute renal failure increased remarkably in patients with previous stroke, as were myocardial infarction and pulmonary embolism, albeit to a lesser extent.

The present study considered stroke-related characteristics, treatments and complications as the clinical indicators for the severity of stroke, and dementia, traumatic brain injury, pneumonia and decubitus ulcer were highly correlated with postoperative adverse outcomes in patients with previous stroke⁶⁻⁸. Stroke within 1-6 months prior to surgery was associated with a more than threefold increased 30-day postoperative in-hospital mortality. Patients with a medical history of hemorrhagic stroke, ICU stay, neurosurgery for stroke and patients within

the highest quartile of preoperative medical expenditure before surgery had an increased 30-day mortality rate. These findings show a severity-dependent association between stroke and postoperative in-hospital mortality.

Stroke is a manifestation of vascular disease that may attribute to more complications and subsequent mortality after surgery. There are, however, several other possible reasons for worse outcomes in patients with a medical history of stroke, including limited physical function, reduced pain sensitivity and mental dysfunction; the two latter may delay diagnosis and treatment of complications²⁵. Overdosing or under dosing related to interactions between analgesics, anesthetics and patients' regular medications may occur^{25,30}. Socioeconomic factors such as lack of family support and geographic challenges might hinder some patients from seeking medical services, and this may affect quality of care.

Several limitations in the present study are acknowledged. First, the database lacked detailed socio demographic variables and lifestyle information as well as records of physical and biomedical examinations. Second, this study used ICD codes used by most physicians for stroke diagnosis. Stroke-related clinical risk scores and information on lesion characteristics were not available for analysis of stroke severity. Third, patients diagnosed with stroke before the 24-month period prior to surgery could have been included in the control group and conversely, patients with minor symptoms of stroke without emergency treatment or hospitalization may potentially be missing in case group of patients. Finally, although the

accuracy of major diagnosis codes in the National Health Insurance Research Database has been studied²⁶, the validity of comorbidity and complications determined by using reimbursement codes needs to be verified.

In the context of the limitations of the study, the results of the present investigation show that patients with stroke in the 24 month period prior to surgery have a higher incidence postoperative complications and 30-day mortality.

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Suppl. Table 1 Definition of coexisting medical conditions and postoperative complications

Medical conditions	ICD-9-CM	Complications	ICD-9-CM
COPD	490-496	Acute myocardial infarction	410
Diabetes	250	Acute renal failure	584
Hyperlipidemia	272.9	Deep wound infection	958.3
Hypertension	401-405	Postoperative bleeding	998.0, 998.1, 998.2
Ischemic heart disease	410-414	Pulmonary embolism	415
Liver cirrhosis	571.2, 571.5	Pneumonia	480-486
Mental disorders	290-319	Septicemia	038, 998.5
Renal dialysis*	D8, D9		
Stroke	430-438		

*Defined by administration code.

COPD, chronic obstructive pulmonary disease; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification.

Table 1 Characteristics of the cohort of patients with and without stroke in the 24 month period prior to surgery.

	No stroke n=1381375		Stroke n=45420		<i>P</i>
Sex	n	(%)	n	(%)	<0.001
Female	785615	(56.9)	18480	(40.7)	
Male	595760	(43.1)	26940	(59.3)	
Age, years					<0.001
20-29	218284	(15.8)	591	(1.3)	
30-39	296777	(21.5)	1022	(2.3)	
40-49	264382	(19.1)	2602	(5.7)	
50-59	248939	(18.0)	6457	(14.2)	
60-69	166512	(12.1)	9333	(20.6)	
≥70	186481	(13.5)	25415	(56.0)	
Operation in teaching hospital	1174886	(85.0)	41068	(90.4)	<0.001
Low income status*	27810	(2.0)	1542	(3.4)	<0.001
Type of surgery					<0.001
Skin	55583	(4.0)	2585	(5.7)	
Breast	34755	(2.5)	376	(0.8)	
Musculoskeletal	393643	(28.5)	17199	(37.9)	
Respiratory	74484	(5.4)	2954	(6.5)	
Cardiovascular	30940	(2.2)	4021	(8.9)	
Digestive	289747	(21.0)	9600	(21.1)	
Kidney, ureter, bladder	108759	(7.9)	4970	(10.9)	
Delivery, CS, abortion	178778	(12.9)	157	(0.4)	
Eye	14761	(1.1)	634	(1.4)	
Others	199925	(14.5)	2924	(6.4)	
Types of anesthesia					<0.001
General	895034	(64.8)	30842	(67.9)	
Epidural or spinal	486341	(35.2)	14578	(32.1)	
Coexisting medical conditions					
Hypertension	227733	(16.5)	20156	(44.4)	<0.001
Diabetes	119808	(8.7)	12999	(28.6)	<0.001
Mental disorders	174339	(12.6)	11521	(25.4)	<0.001
COPD	132181	(9.6)	9413	(20.7)	<0.001
Ischemic heart disease	58576	(4.2)	7223	(15.9)	<0.001
Hyperlipidemia	71250	(5.2)	2947	(6.5)	<0.001

Renal dialysis	15394	(1.1)	1927	(4.2)	<0.001
Liver cirrhosis	36868	(2.7)	1552	(3.4)	<0.001

COPD; chronic obstructive pulmonary disease, CS; caesarian section.

*Defined as patients qualified for waived medical copayment as certified by the Bureau of National Health Insurance.

Table 2 Characteristics of propensity score-matched patients with and without previous stroke

	No stroke n=45420		Stroke n=45420		<i>P</i>
Sex	n	(%)	n	(%)	1.000
Female	18480	(40.7)	18480	(40.7)	
Male	26940	(59.3)	26940	(59.3)	
Age, years					1.000
20-29	591	(1.3)	591	(1.3)	
30-39	1022	(2.3)	1022	(2.3)	
40-49	2602	(5.7)	2602	(5.7)	
50-59	6457	(14.2)	6457	(14.2)	
60-69	9333	(20.6)	9333	(20.6)	
≥70	25415	(56.0)	25415	(56.0)	
Operation in teaching hospital	41068	(90.4)	41068	(90.4)	1.000
Low income status*	1542	(3.4)	1542	(3.4)	1.000
Type of surgery					1.000
Skin	2585	(5.7)	2585	(5.7)	
Breast	376	(0.8)	376	(0.8)	
Musculoskeletal	17199	(37.9)	17199	(37.9)	
Respiratory	2954	(6.5)	2954	(6.5)	
Cardiovascular	4021	(8.9)	4021	(8.9)	
Digestive	9600	(21.1)	9600	(21.1)	
Kidney, ureter, bladder	4970	(10.9)	4970	(10.9)	
Delivery, CS, abortion	157	(0.4)	157	(0.4)	
Eye	634	(1.4)	634	(1.4)	
Others	2924	(6.4)	2924	(6.4)	
Types of anesthesia					1.000
General	30842	(67.9)	30842	(67.9)	
Epidural or spinal	14578	(32.1)	14578	(32.1)	
Coexisting medical conditions					
Hypertension	20156	(44.4)	20156	(44.4)	1.000
Diabetes	12999	(28.6)	12999	(28.6)	1.000
Mental disorders	11521	(25.4)	11521	(25.4)	1.000
COPD	9413	(20.7)	9413	(20.7)	1.000
Ischemic heart disease	7223	(15.9)	7223	(15.9)	1.000
Hyperlipidemia	2947	(6.5)	2947	(6.5)	1.000
Renal dialysis	1927	(4.2)	1927	(4.2)	1.000

Liver cirrhosis	1552	(3.4)	1552	(3.4)	1.000
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COPD, chronic obstructive pulmonary disease, CS; caesarian section.

*Defined as patients qualified for waived medical copayment as certified by the Bureau of National Health Insurance.

Table 3 Postoperative adverse events for patients with preoperative stroke before and after using propensity-score matching methods

	No stroke		Stroke		Adjusted*
	n	(%)	n	(%)	RR (95% c.i.)
Before propensity-score matching					
Postoperative complications					
Pneumonia	15442	(1.1)	2365	(5.2)	1.86 (1.77-1.94)
Septicemia	46793	(3.4)	5096	(11.2)	2.14 (2.08-2.21)
Acute renal failure	7223	(0.5)	1434	(3.2)	2.18 (2.05-2.31)
Acute myocardial infarction	2521	(0.2)	487	(1.1)	1.47 (1.33-1.63)
Deep wound infection	7434	(0.5)	282	(0.6)	1.04 (0.92-1.18)
Pulmonary embolism	792	(0.1)	85	(0.2)	1.53 (1.21-1.93)
Postoperative bleeding	7575	(0.6)	358	(0.8)	1.05 (0.94-1.17)
Any of the above	77815	(5.6)	8218	(18.1)	1.90 (1.85-1.94)
30-day postoperative mortality	5205	(0.4)	956	(2.1)	2.41 (2.24-2.59)
Prolonged LOS†	260747	(18.9)	16911	(37.2)	1.49 (1.46-1.52)
ICU stay	312251	(22.6)	26240	(57.8)	1.77 (1.75-1.79)
Increased medical expenditure†	268671	(19.5)	16328	(36.0)	1.19 (1.17-1.21)
After propensity-score matching					
Postoperative complications					
Pneumonia	1223	(2.7)	2365	(5.2)	1.93 (1.80-2.07)
Septicemia	2785	(6.1)	5096	(11.2)	1.83 (1.75-1.92)
Acute renal failure	841	(1.9)	1434	(3.2)	1.71 (1.57-1.86)
Acute myocardial infarction	372	(0.8)	487	(1.1)	1.31 (1.14-1.50)
Deep wound infection	285	(0.6)	282	(0.6)	0.99 (0.84-1.16)
Pulmonary embolism	50	(0.1)	85	(0.2)	1.70 (1.20-2.41)
Postoperative bleeding	361	(0.8)	358	(0.8)	0.99 (0.86-1.15)
Any of the above	4896	(10.8)	8218	(18.1)	1.68 (1.62-1.74)
30-day postoperative mortality	538	(1.2)	956	(2.1)	1.79 (1.61-1.99)
Prolonged LOS†	7242	(15.9)	10141	(22.3)	1.40 (1.36-1.44)
ICU stay	15473	(34.1)	19114	(42.1)	1.24 (1.21-1.26)
Increased medical expenditure†	8308	(18.3)	9860	(21.7)	1.19 (1.15-1.22)

ICU, intensive care unit; LOS, length of stay; c.i., confidence interval; RR, rate ratio.

*Adjusted for age, sex, teaching hospital, low income, urbanization, coexisting medical conditions, type of surgery and type of anesthesia.

†Categorized into quartiles. Surgical patients who had the highest quartile of length of stay or in-hospital medical expenditures were defined as the individuals having

increased length of stay or elevated medical expenditures.

Table 4 Adjusted rate ratio and 95 per cent confidence intervals of 30-day mortality associated with stroke-related treatment, characteristics and comorbidities prior to surgery

Preoperative characteristics for stroke	n	Deaths	Mortality, %	30-day mortality
				RR (95% c.i.)*
Time period for stroke diagnosis				
No stroke	45420	538	1.2	1.00 (reference)
Stroke within 13-24 months preoperatively	28348	424	1.5	1.25 (1.10-1.42)
Stroke within 7-12 months preoperatively	6494	96	1.5	1.25 (1.00-1.55)
Stroke within 1-6 months preoperatively	10578	436	4.1	3.31 (2.91-3.75)
Low income status†				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke without low income	43878	913	2.1	1.77 (1.59-1.97)
Patients with stroke with low income	1542	43	2.8	2.30 (1.68-3.15)
Type of stroke				
No stroke	45420	538	1.2	1.00 (reference)
Ischemic stroke	24561	414	1.7	1.42 (1.25-1.61)
Other unclassified stroke	11862	185	1.6	1.36 (1.15-1.61)
Hemorrhagic stroke	8997	357	4.0	3.41 (2.97-3.91)
Preoperative ICU stay				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke without ICU stay	32243	541	1.7	1.45 (1.29-1.64)
Patients with stroke with ICU stay	13177	415	3.2	2.55 (2.24-2.90)
Stroke related neurosurgery				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and without neurosurgery	39378	743	1.9	1.61 (1.44-1.80)
Patients with stroke and with neurosurgery	6042	213	3.5	2.49 (2.12-2.92)
Stroke-related medical expenditure				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and very low income	9086	134	1.5	1.31 (1.08-1.59)
Patients with stroke and low income	9083	146	1.6	1.39 (1.16-1.67)
Patients with stroke and moderate income	9083	145	1.6	1.36 (1.13-1.63)
Patients with stroke and high income	9084	239	2.6	2.19 (1.88-2.55)
Patients with stroke and very high income	9084	292	3.2	2.35 (2.04-2.71)
Preoperative TBI				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and without TBI	36836	745	2.0	1.68 (1.51-1.88)

Patients with stroke and with TBI	8584	211	2.5	2.01 (1.72-2.36)
Preoperative dementia				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and without dementia	38429	780	2.0	1.68 (1.51-1.88)
Patients with stroke and with dementia	6991	176	2.5	2.10 (1.75-2.51)
Preoperative pneumonia				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and without pneumonia	32069	565	1.8	1.54 (1.37-1.74)
Patients with stroke and with pneumonia	13351	391	2.9	2.16 (1.89-2.46)
Preoperative decubitus ulcer				
No stroke	45420	538	1.2	1.00 (reference)
Patients with stroke and without decubitus ulcer	41932	849	2.0	1.69 (1.52-1.88)
Patients with stroke and with decubitus ulcer	3488	107	3.1	2.35 (1.91-2.91)

ICU, intensive care unit; RR, rate ratio; c.i., confidence interval; TBI, traumatic brain injury.

*Adjusted for age, sex, teaching hospital, low income, urbanization, coexisting medical conditions, type of surgery and anesthesia.

†Defined as patients qualified for waived medical copayment as certified by the Bureau of National Health Insurance.