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SHORT COMMUNICATION

DETECTION OF CEREBRAL MICROHEMORRHAGES BY SUSCEPTIBILITY-WEIGHTED IMAGING IN STROKE PATIENTS MAY INFLUENCE HOSPITAL LENGTH OF STAY

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Abstract

Hospital length of stay contributes substantially to stroke inpatient direct cost. Existing cost models do not incorporate cerebral microhemorrhage (CMH), a marker of microangiopathy, prevalent in stroke and hypertensive patients. We investigated whether CMH detected by Susceptibility-Weighted Imaging (SWI) technique, is predictive of hospital length of stay amongst adult stroke patients. A case-control study was nested within the SWI study cohort at the Department of Radiology, Loma Linda University Medical Center (LLUMC). Stroke diagnosis was based on ICD/9 430–438 or ICD/10 I60–I69. Cases were stroke patients presenting with CMH, as detected on SWI; controls were stroke patients not presenting with CMH, as detected on SWI. Covariates included age, sex, history of smoking, alcohol use and hypertension, medications taken for hypertension prior to admission or stroke incident, cardiovascular disease, use of low dose aspirin for cardiovascular disease prophylaxis, history of diabetes mellitus, clotting abnormalities and family history of stroke. The median length of stay (LOS) was 7 and 10 days amongst the controls and cases respectively. After the fourth day of admission, patients with CMH stayed significantly shorter in hospital. The study suggests that CMH as detected by SWI could be a significant predictor of hospital length of stay models for stroke inpatients.

Keywords: “cerebral microhemorrhage”, “stroke”, “hospital length of stay”

Introduction

Cerebral microhemorrhages (CMH) are focal microscopic deposits of hemosiderin in the brain tissue (Blitstein & Tung, 2007). These may form due to rupture of small cerebral blood vessels and leakage of blood into the brain tissue. Microglia then sequester iron from leaked erythrocytes into hemosiderin , to mark the hemorrhagic sites. CMH are often smaller than 5 mm in diameter and occur more frequently in the deep brain structures, usually the thalamus, brain stem, basal ganglia, cerebellum (Fazekas *et al, 1999;* Koennecke, 2006).

Stroke is an acute neurological injury in which blood supply to a part of the brain is interrupted. This may occur either as a blockage of an artery within the brain leading to ischemia in the dependent parts (ischemic stroke) or sudden rapture of an artery releasing blood that then compress brain parts (hemorrhagic stroke). Most stroke events are ischemic. In a recent report 88% of all strokes were ischemic, 9% due to intracerebral hemorrhage, and 3% were due to subarachnoid hemorrhage (American Heart Association 2006). Stroke is the third leading cause of death in the United States, after cardiovascular diseases and neoplasia associated besides significant disability (such as paralysis and speech difficulties) and emotional problems (Heron *et al., 2009*; Neyer *et al., 2005*). It presents substantial cost, often with long hospitalization and rehabilitation time.

CMH has been found in stroke patients (Tsushima *et al., 2002*; Roob et al., 1999; Roob *et al., 2000*; Jeerakathil et al., 2004; Naka, *et al., 2006;* Boulanger et al., 2006; Fan *et al., 2004*; Jeong et al., 2004). It is common in elderly patients, with preponderant diagnosis of hypertension and, particularly high systolic blood pressure and stroke. But in cohorts without stroke CMH is common in elderly male patients with hypertension and history of smoking.

The standard method for detection of CMH is computed tomography (CT) and magnetic resonance (MR) imaging, especially gradient echo technique (Blitstein & Tung, 2007). Susceptibility-Weighted Imaging (SWI) has recently been introduced and offers greater sensitivity in CMH detection than conventional imaging techniques (Nandigam *et al., 2009*).

Anticoagulants and antithrombotic drugs are useful in the management and prevention of stroke (Mohr *et al., 2001*; Coull et al., 2002; Go, 2004). The pro-hemorrhagic effects of these medications may predispose to vascular pathology, CMH and subsequent (recurrence of) stroke. Careful evaluation of patients to individually balance the anti-ischemic and pro-hemorrhagic effects of these drugs is recommended to preclude post-stroke event complications that may increase hospital length of stay (McCarron & McVerry, 2009; Saxena *et al., 2007*).

Direct cost of stroke hospitalization is found to be largely determined by length of stay (Jorgensen et al., 1997; Mamoli et al., 1999; Porsdal & Boysen, 1999). Understanding the significant determinants of LOS and their dynamics may inform the hospitalization cost-control strategies. CMH may serve as a reliable component for patient evaluation, especially in identifying patients with fragile vascular integrity and prognosticate on length of stay. Available models have not tested CMH in such an evaluation (Diringer et al., 1999; Svendsen et al., 2009; Chang et al., 2002; Ingeman et al., 2011). We investigated if CMH on SWI predicts stroke patients' hospital length of stay.

Materials and Methods

Study design

This study is a nested case-control study within the retrospective SWI cohort study database. The SWI cohort is a database with records of patients referred to the Department of Radiology, LLUMC since 2001.

Study population

The study population comprised stroke patients admitted at Loma Linda University Medical Center and who had their cases referred to the Radiology Department for susceptibility-weighted imaging (SWI). We searched the patients' charts for key words related to stroke and then reviewed their cerebral micro-hemorrhage status based on SWI.

Subjects were first-time stroke cases admitted and imaged at LLUMC Department of Radiology between January 2001 and December 2007. Subjects were matched on age, sex and type of stroke. A case was stroke patient presenting with CMH as detected by SWI technique. Control was stroke patient not presenting with CMH as detected by SWI technique. Stroke was defined and classified by ICD/9 430–438 or ICD/10 I60–I69. Cases were 1:1 matched to controls by sex, age (+/-5yrs) and type of stroke. The study was IRB approved.

Sample size

Keeping 80% power and 95% confidence a minimum sample size of 25 cases was sufficient to detect a minimum of 2 days (or 28%) difference in length of stay per week. We got 38 cases from the hospital records. These were matched to controls by age at 1:1 ratio.

Data collection

Every patient's discharge summary chart was reviewed and subjects with ICD/9 430–438 or ICD/10 I60–I69 diagnosis of stroke enrolled into the study. Stroke type was ascertained either as hemorrhagic or ischemic and a trained radiologist ascertained the CMH status of the subjects from axial SWI images of the brain. Subjects were assigned to either cases or control by CMH status. Data on subject length of stay and total charges were abstracted as well as subject demographics including age and gender.

Inclusion and exclusion criteria

Patients were eligible for inclusion if admitted at LLUMC between January 2001 and December 2007 with incident stroke diagnosis (ICD/9 430–438 or ICD/10 I60–I69). Only those referred to the Department of Radiology, LLUMC MR imaging by SWI technique were included in the study. Subjects were at least 45 years old with no mortality at discharge and non-traumatic cerebral hemorrhage.

Variables

The dependent variable was Hospital Length of Stay (LOS) in days, counted from the day of admission to the day of discharge. The main effect was the presence of cerebral microhemorrhage (CMH) visualized in axial images of the brain on SWI. Other variables were history of smoking, alcohol use and hypertension, medications taken for hypertension prior to admission or stroke incident, cardiovascular disease, use of low dose aspirin for cardiovascular disease prophylaxis, history of diabetes mellitus, clotting abnormalities and family history of stroke, sex and race. The participants were matched by age.

Statistical Methods

Conditional logistic regression was used to model the relationship between CMH and hospital length of stay. Data was analyzed in SAS 9.2

Table 1 Characteristics of the study participants

	Cases	Controls
No. of Patients	38	38
Women	19	19
Men	19	19
Patient age		
Mean	71.8	73.9
Median	72	77
Minimum	55	51
Maximum	90	89
Stroke Type		
Ischemic	17	17
He,morrhagic	21	21
Length of stay		
Mean	14	13
Median	10	7
Range	1-95	1-49
Race		
White (non-Hispanic)	68	
White (Hispanic)	5	
African American	3	
Others	2	

Results

Table 1 shows the patient distribution by sex, age, stroke type and length of stay. Half the study subjects (19) were women, distributed evenly within the case-control groups. Age ranged between 51 and 90 years. The age between the cases and controls was

Table 2 Covariates and their association with *LOS*

	Cases	Controls	χ^2 *p-value*
Alcohol			
Yes	7	8	0.1873
No	31	30	
Smoking			
Yes	12	12	0.8071
No	26	25	
Family History of Stroke			
Yes	8	9	0.7831
No	30	29	
Aspirin			
Yes	13	15	0.6344
No	25	23	
Hypertension Medications			
Yes	22	21	0.8170
No	16	17	
Anti-Clotting Medications			
Yes	10	10	1.0
No	28	28	
History of CVD			
Yes	15	11	0.4686
No	23	27	
History of Diabetes			
Yes	13	17	0.4818
No	25	21	

71.8 and 73.9 years respectively. Similarly, the median age was 72 and 77. There were 21 hemorrhagic and 17 ischemic stroke patients in each group. The mean LOS was 14 and 13 days while the median LOS was 7 and 10 days amongst the cases and controls respectively. There were 68 whites (non-Hispanic), five Hispanics or Latino, three Black or African American and two individuals of other races in the study.

Table 3 Association of LOS and CMH

	β	SE_{β}	p	**OR**	**95%CI**	
					L	**U**
CMH	-0.23	1.09	0.039	0.105	0.012	0.888
Aspirin (low dose)	-0.84	0.70	0.23	0.434	0.110	1.709
Hypertension meds	0.46	0.57	0.42	1.586	0.520	4.835
Clotting	-0.30	0.77	0.70	0.745	0.163	3.397
CVD	0.90	0.60	0.13	2.471	0.761	8.023
Diabetes	-0.90	0.65	0.15	0.393	0.111	1.395
Family hist., stroke	-0.69	0.78	0.38	0.505	0.109	2.321
Smoking	0.42	0.62	0.50	1.520	0.450	5.141

Table 2 shows association of LOS to the other variables. The following were not associated with LOS: history of alcohol intake, smoking, prophylactic low dose aspirin intake, use of hypertensive medications and anti-clotting medicines with. Neither was family history of stroke, history of cardiovascular disease nor diabetes.

Table 3 shows odds ratios for the variables from logistic regression. CMH was the only variable significantly associated with length of stay (Odds Ratio 0.105; 95% CI 0.012-0.888).

Discussion

Previous models of stroke and inpatient LOS have included medical complications (Saxena *et al., 2007*) age, race, hospital type and location (Russell *et al., 2006*; Shelby *et al., 2001*). Significance of CMH has not been tested. But CMH has been associated with stroke (Kato *et al., 2002*; Naka *et al., 2006*) and is thought to significantly influence stroke management (McCarron & McVerry, 2009). We show that models of stroke hospital length of stay models ought to consider presence of CMH from SWI as an important predictor. In this study, it is likely that the presence of CMH significantly contributed to days of in-patient stay beyond 4 days. We suggest that CMH as detected by SWI is a significant predictor of hospital length of stay greater than 4 days. Detection of CMH could inform clinical management resulting in shorter stays in patients that stayed in hospital longer than 4 days. Patients staying longer than 4 days are often severe cases where delicate management and prolonged observation are necessary. The shorter LOS may mean better utilization of hospital resources and lower costs of hospitalization (Jorgensen *et al., 1997*; Mamoli et al., 1999; Porsdal & Boysen, 1999).

We had of 38 case events which limited the ability to control for numerous likely confounders. The study subjects were also mainly of one race, lacking the requisite heterogeneity of the general community. Further study with adequate power to fit multivariable models is recommended. A prospective and larger multi-center study envisaged that should correct for multiple covariates and further test this hypothesis. The study would incorporate community hospitals and improve participant heterogeneity.

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