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Less favorable neurological recovery after acute stroke in patients with hypercholesterolemia

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ABSTRACT

Objectives: We aimed to investigate the effect of hypercholesterolemia on recovery after acute ischemic stroke.
Methods: Data of 3048 patients admitted for acute ischemic stroke from January to December 2009 were collected from the Stroke Registry in the Chang Gung Healthcare System. Baseline characteristics of patients with and without hypercholesterolemia were compared. The association of hypercholesterolemia with neurological severity and recovery was analyzed using multivariate logistic regression. The patients were then divided on the basis of age for subgroup analysis.
Results: The number of patients with and without a history of hypercholesterolemia was 474 (15.6%) and 2574 (84.4%), respectively. Univariate analysis showed that patients with hypercholesterolemia had a lower National Institutes of Health Stroke Scale (NIHSS) score on admission ($p = 0.004$). However, during hospitalization, these patients displayed less improvement in their NIHSS score ($p = 0.002$). These results remained significant in multivariate logistic regression analysis ($p < 0.001$ and $p = 0.002$, respectively). Subgroup analysis showed a similar association for hypercholesterolemia in both younger (age < 70) and older (age ≥ 70) age groups.
Conclusions: Acute ischemic stroke in patients with hypercholesterolemia was correlated with reduced severity on admission and less favorable recovery during hospitalization, regardless of age.

1. Introduction

Hypercholesterolemia is a risk factor of cardiovascular disease. Its role in myocardial infarction has been well established [1–3]. In addition to coronary artery diseases, systemic atherosclerotic disease, including intimal and medial thickness of the common carotid artery, has been proven to be associated with cholesterol level [4]. Stroke risk increases with the progression of carotid artery stenosis [5,6]. A direct link between hypercholesterolemia and stroke risk most likely exists, although there is less supportive evidence [7,8]. Cholesterol-lowering agents have become a standard agent in treatment to prevent further cerebrovascular events after ischemic stroke [9].

Despite evidence of the development of atherosclerosis and cardiovascular diseases in people with hypercholesterolemia, hypercholesterolemia has been associated with a better outcome after ischemic stroke [10–14]. However, most of these studies were unable to explain the mechanisms underlying this phenomenon. These studies focused on the initial severity and long-term mortality after ischemic stroke with hypercholesterolemia. The association between hypercholesterolemia and the neurological change after an acute ischemic stroke in hospitalized patients has not been well studied. In addition, the effect of hypercholesterolemia on cardiovascular disease varies between different age groups [15–18]. The effect of cerebral infarction on neurological change may also vary with age.

The aim of this observational study was to investigate the association between hypercholesterolemia and neurological change after an acute ischemic stroke in hospitalized patients via a review of data for 2009 from the Stroke Registry in the Chang Gung Healthcare System (SRICHS). The patients were then further divided into younger (age < 70) and older (age ≥ 70) age groups to observe any potential differential effects [17,18].

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2. Patients and methods

2.1. SRICHS

Patient data were obtained from the SRICHS. There are 4 hospital branches in the Chang Gung healthcare system, which are located in Keelung, Linkou, Chiayi, and Kaohsiung. SRICHS, an electronic chart-based system, was formally launched on March 1, 2007. To establish the registry system, consensus conferences attended by the staff from the 4 hospital branches were held first on December 2, 2006 and then quarterly thereafter. The data for the cases corresponding to the International Classification of Diseases, Ninth Revision codes 430–437 were prospectively entered into the SRICHS upon patient admission. The physicians simultaneously performed data entry and electronic chart writing. Patients exited from the SRICHS if their diagnoses changed during admission. To improve the registry system and data quality, monthly conferences attended by the staff from the neurology and computer departments were held in Linkou. An auto-audit system was created to ensure the accuracy of data entry and to prevent manual negligence. An auto-download mechanism was used to transfer any existing data from the hospital computer system to the registry system to prevent typing errors.

2.2. Case selection and data collection

In total, 3843 patients with acute ischemic stroke were recorded in the SRICHS in 2009. We included 3048 patients who initially underwent computed tomography (CT) or magnetic resonance imaging (MRI) of the brain at the emergency room and had completed a survey at the neurology department. We collected data including patient demographics, vascular risk factors, imaging findings, National Institutes of Health Stroke Scale (NIHSS) scores, modified Rankin scale (mRS) scores, length of ward stay, infection events, and acute ward mortality. Patients with an incomplete evaluation at the emergency room or neurological ward were excluded due to an uncertain diagnosis of acute stroke. This study was approved by the Keelung Chang Gung Memorial Hospital Human Studies Institutional Review Board.

Ischemic stroke was defined as a new onset of neurological deficit when brain CT or MRI either showed a compatible lesion or was normal without evidence of other causes that might explain the neurological deficits. Diagnosis, mRS scores, and NIHSS scores were recorded on admission and on discharge by trained neurologists. Determination of stroke etiology was on the basis of the Trial of ORG 10172 in the Acute Stroke Treatment (TOAST) stroke criteria classification system [19]. Hypercholesterolemia was defined as a cholesterol level of ≥200 mg/dL or low density lipoprotein (LDL) level of ≥130 mg/dL on admission. Because the serum cholesterol level decreased soon after an acute stroke [20–24], patients with a history of cholesterol level ≥200 mg/dL or LDL level ≥130 mg/dL within 1 year before stroke onset were also included. Severe neurological deficits were defined as an NIHSS score ≥6. A neurological change during hospitalization was defined as the difference in the NIHSS score between the time of admission and discharge (ΔNIHSS = NIHSS score on admission − NIHSS score on discharge). A reduction in NIHSS score between admission and discharge was defined as a favorable neurological recovery (ΔNIHSS > 0).

A patient was said to have hypertension if the patient was diagnosed with hypertension prior to admission or if a blood pressure ≥ 160/95 mmHg was detected on 2 separate occasions during the acute stage of admission. A patient was said to have diabetes mellitus (DM) if the patient had known DM or if the fasting glucose level was ≥126 mg/dL and/or random glucose level was ≥200 mg/dL. A history of previous stroke or transient ischemic attack (TIA) was obtained from patient information or medical records. Atrial fibrillation (Af) was diagnosed when observed on a standard 12-lead electrocardiogram. Coronary artery disease (CAD) was defined by past incidences of acute myocardial infarction or angina pectoris. Previous infarcts on brain CT or MRI were verified by a report from the radiologist. An infection was defined as a fever that was treated with antibiotics during admission.

2.3. Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 12.0 for Windows. Chi-squared tests were performed for categorical variables including gender, risk factors, previous infarcts on a brain CT/MRI, TOAST classification, infection events, and mortality. Continuous variables, including age and length of ward stay, were expressed as mean ± standard deviation and analyzed using an independent sample *t*-test. The NIHSS score and ΔNIHSS were also expressed as mean ± standard deviation and analyzed using the Wilcoxon signed-ranked and Mann–Whitney tests. Multivariate logistic regression analysis was performed to identify factors associated with severe neurological deficits and favorable recovery. All the factors were analyzed as independent variables using a forward stepwise program. In addition to the baseline variables, changes in the NIHSS scores from admission to discharge varied according to the length of admission. The value was also statistically subject to ceiling and floor effects. Thus, 2 different models were used to assess the neurological changes during admission. In model 1, only the baseline factors were included. In model 2, the length of admission and initial score of NIHSS were taken into account. A p value < 0.05 was considered significant.

3. Results

The study sample consisted of 3048 patients between 17 and 100 years of age (mean = 67.8 ± 12.6 years). Among these patients, 1908 patients were men (62.6%) and 1140 patients were women (37.4%). The total number of patients with and without hypercholesterolemia was 474 (15.6%) and 2574 (84.4%), respectively. The baseline characteristics are shown in Table 1. Patients with hypercholesterolemia often had other vascular risk factors including hypertension ($p < 0.001$), DM ($p < 0.001$), previous stroke ($p < 0.001$), previous TIA ($p = 0.004$), and CAD ($p < 0.001$). A brain CT/MRI often revealed previous infarcts ($p < 0.001$).

Univariate analysis indicated that patients with hypercholesterolemia had less severe neurological deficits upon admission ($p = 0.004$) and less favorable neurological recovery during hospitalization ($p = 0.002$). Similarly, multivariate logistic regression analysis, which was adjusted for baseline confounding factors, revealed fewer severe neurological deficits upon admission ($p < 0.001$) and less favorable recovery during hospitalization ($p = 0.002$) in hypercholesterolemic patients. These data are presented in Table 2. Factors associated with poor neurological recovery during admission in model 1 and 2 are shown in Table 3. Hypercholesterolemia ($p = 0.002$ and $p = 0.005$, respectively) was a significant factor in both model 1 and 2. Other significant factors included male gender, Af, and NIHSS score upon admission.

In subgroup analysis, the number of patients who were ≥70 and <70 years were 1501 (49.2%) and 1547 (50.8%), respectively. Multivariate logistic regression analysis, which was adjusted for baseline confounders, showed that compared to patients without hypercholesterolemia, hypercholesterolemic patients had significantly fewer severe neurological deficits on admission and lesser favorable neurological recovery during admission in both younger and older age groups. These data are shown in Table 4.