Association between Left Ventricular Dysfunction and Functional Outcomes at Three Months in Acute Ischemic Stroke

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Background: Left ventricular dysfunction (LVD) was associated with stroke occurrence and mortality. However, few studies have published the impact of LVD on functional stroke outcomes in the acute stroke period. *Methods:* We enrolled 1554 patients who were admitted to Dong-A University Hospital between January 2011 and November 2014. To determine the functional outcomes, the modified Rankin Scale (mRS) score at 3 months after stroke was used. The severity of LVD was defined depending on ejection fraction (EF): (1) severe (EF ≤ 40%); (2) mild (40% < EF < 55%); and (3) normal (EF ≥ 55%). EF was measured using transthoracic two-dimensional echocardiography. The distribution of mRS scores at 3 months after stroke was presented using LVD. Multivariable analysis was performed to predict poor functional outcomes. *Results:* Of the 1554 patients, 1417 had normal LV function, 87 had mild LVD, and 50 had severe LVD. Patients with LVD were older and had a high incidence of diabetes mellitus, atrial fibrillation, coronary artery disease, and severe stroke symptoms. With respect to treatment, patients with LVD received more thrombolysis and more anticoagulation medication after stroke. Stroke-related disability at discharge and at 3 months was significantly associated with LVD. In the multivariable analyses, old age, diabetes mellitus, high initial National Institutes of Health Stroke Scale score, stroke mechanism, and LVD were independent predictors of poor functional outcomes at 3 months. *Conclusions:* LVD is associated with poor functional outcomes after acute ischemic stroke.
Key Words: Left ventricular dysfunction—cerebral infarction—functional outcome—heart failure.

Introduction

Heart disease is an important factor of ischemic stroke. Atrial fibrillation (AF) is the main cause of cardioembolic stroke, followed by left ventricular dysfunction (LVD). In the SAVE (Survival and Ventricular Enlargement) study, an 18% increase in the risk of stroke was noted for every 5% reduction in ejection fraction (EF).[1] In another study in patients with low EF, a 58% increase in thromboembolic events was noted for a 10% decrease in EF in women, but this was observed not for men.[2] The NOMAS (Northern Manhattan Study) found that a decreased EF was associated with the occurrence of ischemic stroke, but the risk of stroke was not related to the severity of EF reduction.[3]

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The low EF might be associated with stroke functional outcome. According to Milionis, patients with low EF were associated with high stroke severity at admission or poor disability outcome and high mortality.[4] A study on U.S. hospital stroke patients showed that stroke patients with a low EF had 2 times higher in-hospital mortality rate than the patients with preserved EF.[5]

LVD increases the left ventricular end diastolic volume that promotes blood stasis and then increases the chance of thrombus formation and the risk of cardioembolic stroke. Additionally, LVD in stroke patients causes a hypoperfusion state.[6] Although autoregulation prevents a reduction in cerebral flow, some studies have shown that a low EF is correlated with decreased cerebrovascular reactivity[7] and decreased global cerebral blood flow.[8]

LVD impacts on the functional outcome in acute cerebral infarction, and a small number of studies have published the effect of prior LVD on disability in stroke patients during the acute period. The aim of this study was to investigate the impact of LVD on acute ischemic stroke and its associated factors.

Methods

Study Subjects

This study retrospectively enrolled a consecutive series of ischemic stroke patients who had been admitted to the stroke center, Dong-A University Hospital, between January 2011 and November 2014. We selected patients who were hospitalized within 7 days after symptom onset and had relevant ischemic lesions on computed tomography or magnetic resonance imaging (MRI). Patients were excluded from the study if they had no echocardiography recording or no outcome data at 3 months. Patients who required dependence for their activities of daily lining (modified Rankin Scale [mRS] score 3 or over) before stroke were excluded.

Medical history, clinical profiles and risk factors for stroke, acute management of stroke, discharge treatment, and laboratory finding are available in the prospective stroke registry database or supplemented by reviewing electronic medical records. Baseline stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) by neurologists and the initial stroke mechanism was classified by the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria.[9] TOAST classification denotes 5 major classes: large artery atherosclerosis (LAA), small vessel occlusion (SVO), cardioembolism (CE), other determined cause (OD), and undetermined cause (UD). The stroke mechanism was classified by a stroke neurologist during hospitalization and was determined using MRI-based diagnostic algorithm for acute ischemic stroke subtype classification (MAGIC).[10] For univariate and multivariate analyses, we combined OD with UD in the TOAST criteria because of the small sample size for OD. The definition of disease or risk factors, data management, and querying depends on the Clinical Research Center for Stroke-Fifth Division (CRCS-5) registry rules.[11] The study was approved by the institutional review board.

Outcome

For assessing the functional outcome, the mRS score was used. The scale consists of 7 grades, from 0 to 6. A score of 0 indicates no symptom; 5 indicates severe disability; and 6 indicates death. A trained nurse took the mRS scores at discharge and contacted stroke patient for telephone interviews at 3 months after stroke. We decided the primary outcome as mRS at 3 months after stroke.

Echocardiographic Finding

Transthoracic two-dimensional echocardiography was performed during hospitalization. EF is the proportion of left ventricular volume emptied during ventricular systole and is a reliable echocardiographic measure of left ventricular systolic function. The definition of reduced EF varied with the guidelines of left ventricular EF ≤ 35%, ≤40%, or ≤50%. Generally, EF under 40% was considered as heart failure (HF), and EF between 50 and 55 was regarded as gray area or borderline normal. So, we selected 2 criteria, EF ≤ 40 and EF ≥ 55%.[12,13] The LVD was defined according to EF: (1) severe (EF ≤ 40%); (2) mild (40% < EF < 55%); and (3) normal (EF ≥ 55%).

Statistical Analysis

Categorical variables in patients with demographic and risk factors were expressed as absolute values (percentages) and those between groups were compared using chi-square tests. Continuous variables were presented as means and standard deviation or median (interquartile range) and were compared using one-way ANOVA (analysis of variance) test or Kruskal–Wallis test.

The associations of clinical variables and the LVD with functional outcome were assessed using logistic regression analyses. For the logistic regression analysis, we dichotomized outcome variables into independence (good outcome, mRS score 0-2) or dependence/death (poor outcome, mRS score 3-6). All demographic factors and variables in risk factors with P values of <.1 in the bivariate analysis were selected for the adjustment in the multivariable analysis. Discharge medications were not chosen as an adjusting covariate because those might be affected by the functional state. We performed a multiple regression model in the sequence. Model 1 was adjusted by demographic factors and LVD; model 2 was adjusted by demographic factors, risk factors, and LVD; model 3 was adjusted by demographic factors, risk factors, the other factors, and LVD. The results of the multivariable analysis were summarized as odds ratios (OR) and 95% confidence intervals (CI). All statistical analyses were