JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2017

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2017.02.015

Left Ventricular Geometry Determines Prognosis and Reverse J-Shaped Relation Between Blood Pressure and Mortality in Ischemic Stroke Patients

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ABSTRACT

OBJECTIVES This study sought to investigate the prognostic significance of left ventricular (LV) mass and geometry in ischemic stroke survivors, as well as the LV geometry-specific differences in the blood pressure–mortality relationship.

BACKGROUND LV mass and geometry are well-known prognostic factors in various populations; however, there are no data on their role in ischemic stroke patients.

METHODS We prospectively recruited 2,328 consecutive patients admitted with acute ischemic stroke to our institute between 2002 and 2010. Of these, 2,069 patients were analyzed in whom echocardiographic data were available to assess LV mass and geometry.

RESULTS All-cause mortality was significantly greater in patients with concentric hypertrophy (adjusted hazard ratio [HR]: 1.417; 95% confidence interval [CI]: 1.045 to 1.920) and concentric remodeling (HR: 1.540; 95% CI: 1.115 to 2.127) but nonsignificantly in those with eccentric hypertrophy (HR: 1.388; 95% CI: 0.996 to 1.935) compared with normal geometry in multivariate analyses. Relative wall thickness was a significant predictor of all-cause mortality (HR: 1.149 per 0.1-U increase in relative wall thickness; 95% CI: 1.021 to 1.307), whereas LV mass index was not (HR: 1.003 per 1 g/m^2 increase in LV mass index; 95% CI: 0.999 to 1.007). Similar results were observed with cardiovascular mortality. In multivariable fractional polynomials, patients with altered LV geometry showed reverse J-curve relationships between acute-phase systolic blood pressure and all-cause or cardiovascular mortality, with the highest risks in the lower extremes, whereas those with normal geometry did not.

CONCLUSIONS Echocardiographic assessment of LV geometry provided independent and additive prognostic information in ischemic stroke patients. A reverse J-shaped relation of mortality with blood pressure was found in patients with abnormal LV geometry. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

Stroke is a highly prevalent disease and the second-leading cause of mortality in the world (1). Ischemic stroke is the most common type of stroke and has a substantial case fatality rate (1,2). For this reason, various attempts have been made to enhance clinical outcomes after ischemic stroke, including the identification of potential prognosticators such as the National Institutes of Health Stroke

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Manuscript received October 21, 2016; revised manuscript received January 30, 2017, accepted February 7, 2017.

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

BP = blood pressure

CBF = cerebral blood flow

LV = left ventricular

LVMi = left ventricular mass index

NIHSS = National Institutes of Health Stroke Scale

RWT = relative wall thickness

Scale (NIHSS) (3). Indeed, recent studies showed a temporal trend of a decrease in both stroke incidence and mortality along with improvements in the control of risk factors, in particular hypertension (4). However, the mortality rates were still unacceptably high after incident ischemic strokes (533 of 929; 57.4%) (4), which suggests the need for better risk stratification and tailored treatment to further improve clinical outcomes.

In the diagnostic work-up of ischemic stroke patients, transthoracic echocardiography is widely performed to determine the presence of cardioembolic sources (5). Given that echocardiography provides useful prognostic information in various diseases (6,7), it can also be used as a practical tool to stratify patients with ischemic stroke according to risk. Specifically, one study demonstrated that the risk of developing stroke was associated with left ventricular (LV) mass and geometry measured by echocardiography (8). In spite of these previous reports, there are no data on the prognostic value of LV geometry for the prediction of long-term outcomes in patients after acute ischemic stroke, except for lacunar stroke (9).

Among risk factors for ischemic stroke, high blood pressure (BP) is a major contributor, not only to its development but also to poor outcomes after acute ischemic stroke (10,11). Conversely, there have been concerns about whether ischemic stroke patients with BP below certain cutoff values, even within normal range, are associated with grave prognosis (12). In particular, among patients with underperfused but still viable brain tissue (i.e., penumbra), any fall in BP can increase the infarct area by reducing the survival of penumbra, subsequently resulting in stroke progression. In this regard, pressure-dependent cerebral blood flow (CBF) for penumbra has been suggested as a plausible mechanism for a U- or J-shaped curve, with higher mortality rates at low BP and at very high BP in ischemic stroke patients (13,14). Furthermore, the threshold of low BP that leads to a reduced cerebral perfusion can be different depending on the severity and duration of the underlying hypertension (15,16). Given that adverse cardiac remodeling reflects myocardial response to pressure overload integrated over time, including hypertension (17), it can be speculated that patients with different LV geometric patterns could have different BP cutoff values for impaired cerebral perfusion and potentially poor clinical outcomes after ischemic stroke than those with concentric forms of remodeling.

In this study, we investigated the prognostic value of LV mass and geometry in predicting mortality after acute ischemic stroke. We also hypothesized that the adverse influence of low BP on mortality would be more prominent in stroke patients with altered LV geometry than in those with a normal geometry.

METHODS

STUDY DESIGN AND PARTICIPANTS. The design of the registry has been described elsewhere (18). Briefly, this prospective registry was designed to include consecutive patients with acute ischemic stroke (i.e., <7 days from stroke onset). Only patients with available echocardiographic recordings were eligible for this study. Exclusion criteria were diagnoses of intracerebral hemorrhage, subarachnoid hemorrhage, or in-hospital stroke. Among 2,328 patients recruited from October 2002 to September 2010, the final sample size was 2,069 for this study, because individuals were further excluded for the following reasons: poor echocardiographic image (n = 174), insufficient anthropometric data (n = 47), significant valvular heart disease (n = 36), and hypertrophic cardiomyopathy (n = 2). The institutional review board of the Seoul National University Hospital approved the study protocol (H-1009-062-332), and written informed consent was obtained from all participants or from the next of kin when it was not possible to obtain the patient's agreement.

DATA COLLECTION. We recorded baseline demographic, clinical, and laboratory data for all patients. We defined acute post-stroke BP as the first BP measured in the emergency department or other area (19).

Ischemic stroke subtype was assessed by stroke physicians on the basis of clinical and radiological data and classified into 5 categories according to TOAST (Trial of Org 10172 in Acute Stroke Treatment) (20): 1) large-artery atherosclerosis; 2) small-artery occlusion; 3) cardioembolism; 4) stroke of other origin; and 5) stroke of undetermined origin. In addition to 5 original subtypes, transient ischemic attack was included in the analysis, which was defined as an episode of focal neurological deficit that resolved within 24 h and was attributed to focal cerebral ischemia. The initial neurological severity was estimated with the NIHSS score at admission (21). Body surface area was calculated by the DuBois and DuBois formula. Brain magnetic resonance imaging was obtained with a 1.5-T or 3.0-T system and was performed according to a standard protocol (22). Significant carotid artery stenosis was defined as luminal diameter narrowing ≥50% in the internal carotid artery. Body mass index was calculated as measured body weight divided by