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Left ventricular hypertrophy assessed by electrocardiogram is associated with more severe stroke and with higher in-hospital mortality in patients with acute ischemic stroke

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ABSTRACT

Background and aims: Left ventricular hypertrophy (LVH), assessed by electrocardiogram (ECG), is associated with increased risk for stroke. However, few studies that evaluated whether ECG-detected LVH predicts ischemic stroke severity and outcome. We aimed to evaluate these associations.
Methods: We prospectively studied 922 patients consecutively admitted with acute ischemic stroke (age 79.6 ± 6.9 years). Stroke severity was assessed at admission with the National Institutes of Health Stroke Scale (NIHSS). Severe stroke was defined as NIHSS≥5. LVH was evaluated with the Sokolow-Lyon index and the Cornell voltage-duration product criteria in an ECG obtained at admission. The outcome was assessed with dependency at discharge (modified Rankin scale 2–5) and in-hospital mortality.
Results: Independent predictors of severe stroke were age (relative risk (RR) per year 1.07, 95% confidence interval (CI) 1.03–1.11, $p<0.001$), female gender (RR 0.36, 95% CI 0.17–0.76, $p<0.01$), atrial fibrillation (RR 2.07, 95% CI 1.30–3.29, $p<0.005$), chronic kidney disease (RR 2.38, 95% CI 1.04–5.44, $p<0.05$), heart rate (RR per 1/min 1.02, 95% CI 1.01–1.04, $p<0.005$), glucose levels (RR 1.012, 95% CI 1.006–1.018, $p<0.001$), high-density lipoprotein cholesterol levels (RR 0.976, 95% CI 0.960–0.993, $p<0.005$) and LVH defined according to the Cornell voltage-duration product criteria (RR 2.08, 95% CI 1.12–3.86, $p<0.05$). Independent predictors of dependency at discharge were age (RR per year 1.08, 95% CI 1.03–1.13, $p<0.001$), past smoking (RR versus no smoking 0.42, 95% 0.19–0.89, $p<0.05$), history of ischemic stroke (RR 2.13, 95% CI 1.23–3.71, $p<0.01$) and NIHSS at admission (RR 1.48, 95% CI 1.35–1.63, $p<0.001$). Independent predictors of in-hospital mortality were glucose levels (RR 1.014, 95% CI 1.003–1.025, $p<0.05$), NIHSS at admission (RR 1.29, 95% CI 1.19–1.41, $p<0.001$) and LVH according to the Cornell voltage-duration product criteria (RR 4.95, 95% CI 1.09–22.37, $p<0.05$).
Conclusions: LVH according to the Cornell voltage-duration product criteria appears to be associated with more severe stroke and with higher in-hospital mortality in patients with acute ischemic stroke.

1. Introduction

Ischemic stroke is a leading cause of death and long-term disability worldwide [1–3]. However, the severity and outcome of acute ischemic stroke vary widely [4,5]. In order to optimize stroke management, alleviating stroke severity and improving the outcome of these patients, there is a pressing need to identify readily available markers that accurately predict the severity and outcome of stroke [6,7].

Left ventricular hypertrophy (LVH), assessed by electrocardiogram (ECG), is a readily available marker of target-organ damage and has been associated with increased risk for stroke in several prospective studies in the general population [8–12]. Moreover, LVH detected with ECG predicts recurrent cardiovascular events in patients with a recent minor ischemic stroke [13,14]. Despite these associations and the wide availability and limited cost of assessing LVH with ECG, there are no studies that evaluated whether ECG-

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detected LVH predicts stroke severity at presentation and the functional outcome of Caucasian patients with acute ischemic stroke. In a recent report, LVH on ECG did not predict death or disability at 1 month after acute stroke in patients from Nigeria and Ghana [15].

The aim of the present study was to evaluate the predictive value of LVH assessed by ECG in patients admitted with acute ischemic stroke.

2. Materials and methods

We prospectively studied all patients with acute ischemic stroke, admitted in our Department between September 2010 and March 2016 (n = 922; 42.2% males, age 79.6 ± 6.9 years).

At admission, demographic data and history of cardiovascular risk factors and concomitant cardiovascular disease (CVD) were recorded and a clinical examination was performed. The severity of stroke was assessed at admission with the National Institutes of Health Stroke Scale (NIHSS). Severe stroke was defined as NIHSS ≥5.

Routine laboratory investigations were performed after overnight fasting at the first day after admission. Low-density lipoprotein cholesterol levels were calculated using Friedewald's formula [16]. Glomerular filtration rate (GFR) was estimated with the Chronic Kidney Disease Epidemiology Collaboration equation [17]. Chronic kidney disease (CKD) was defined as GFR < 60 ml/min/1.73 m^2 [17].

All patients underwent brain computed tomography (CT) at admission and a second brain CT was performed if clinically indicated.

Left ventricular hypertrophy was evaluated with the Sokolow-Lyon index (S in V_1 + R in V_5 or V_6 (whichever is larger) ≥ 35 mm) and the age, gender and body mass index-adjusted Cornell voltage-duration product criteria (using thresholds specific for gender and the presence of hypertension and obesity) in an ECG obtained at admission [18,19].

The outcome was assessed with dependency rates at discharge and with in-hospital mortality. Dependency was defined as modified Rankin scale at discharge between 2 and 5.

All data were analyzed with the statistical package SPSS (version 17.0; SPSS, Chicago, IL, USA). Data are presented as percentages for categorical variables and as mean and standard deviation for continuous variables. Differences in categorical and continuous variables between groups were assessed with the chi-square test and the independent samples *t*-test, respectively. Binary logistic regression analysis was used to identify independent predictors of severe stroke at admission, dependency at discharge and in-hospital mortality. Age, gender, body mass index (BMI), systolic and diastolic blood pressure (BP), serum glucose levels, HbA_{1c}, GFR and variables that differed between patients with and without the outcome of interest (i.e. between patients with severe stroke and those without severe stroke, between patients who were dependent at discharge and those who were independent at discharge, and between patients who died during hospitalization and those who were discharged) with a significance level of $p<0.1$ were included in the models.

3. Results

Patients' characteristics at admission are shown in Table 1. LVH according to the Sokolow-Lyon index was present in 27 patients (2.9% of the study population) whereas LVH according to the Cornell voltage-duration product criteria was present in 200 patients (21.7% of the study population; Table 1). When either criterion was used, LVH was present in 218 patients (23.6% of the study population; Table 1). Patients with LVH defined according to the Sokolow-Lyon index did not differ in any clinical parameter from patients without LVH. Patients with LVH according to the Cornell voltage-duration product criteria were older than patients without LVH and were also more frequently female and had higher BMI and lower prevalence of hypertension and smoking than the latter.

At admission, 55.2% of patients had severe stroke. Patients with severe stroke had higher prevalence of LVH defined according to the Cornell voltage-duration product criteria than patients without severe stroke (27.1 and 16.2%, respectively; $p<0.005$). In contrast, the prevalence of LVH defined according to the Sokolow-Lyon index did not differ between the 2 groups ((2.7 and 3.1%, respectively; $p = 1.000$). However, the Sokolow-Lyon index was lower in patients with severe stroke than in those without severe stroke (15.3 ± 8.2 *vs.* 16.6 ± 8.2 mm, respectively; $p<0.05$). In contrast, the Cornell voltage-duration product did not differ between the 2 groups (949 ± 265 *vs.* 905 ± 263 mV*msec, respectively; $p = 0.057$). Parameters associated with severe stroke in univariate and multivariate analysis are shown in Table 2. In binary logistic regression analysis, independent predictors of severe stroke were age, female gender, CKD, heart rate, serum glucose and high-density lipoprotein cholesterol (HDL-C) levels and LVH defined according to the Cornell voltage-duration product criteria. The sensitivity, specificity, positive and negative predictive values of LVH according to the Cornell voltage-duration product criteria for predicting severe stroke were 27.1, 16.2, 66.7 and 49.0%, respectively.

At discharge, 60.8% of patients were dependent. Patients who were dependent at discharge had higher prevalence of LVH defined according to the Cornell voltage-duration product criteria than patients who were independent at discharge (25.4 and 17.1%, respectively; $p<0.05$). In contrast, the prevalence of LVH defined according to the Sokolow-Lyon index did not differ between the 2 groups (2.6 and 3.7%, respectively; $p = 0.544$). The Sokolow-Lyon index was lower in patients who were dependent at discharge than in those who were independent (15.2 ± 8.1 *vs.* 16.5 ± 8.9 mm, respectively; $p<0.05$). In contrast, the Cornell voltage-duration product was higher in the former (950 ± 265 *vs.* 898 ± 255 mm, respectively; $p<0.05$). Parameters associated with dependency at discharge in univariate and multivariate analysis are shown in Table 3. In binary logistic regression analysis, independent predictors of dependency at discharge were age, past smoking, history of ischemic stroke and NIHSS at admission. The sensitivity, specificity, positive and negative predictive values of LVH according to the Cornell voltage-duration product criteria for predicting dependency at discharge were 25.4, 17.2, 68.7 and 42.6%, respectively.

During hospitalization, 9.4% of patients died. The prevalence of LVH defined according to the Sokolow-Lyon index did not differ between patients who died and those who were discharged (2.3 and 2.9%, respectively; $p = 1.000$). The prevalence of LVH defined according to the Cornell voltage-duration product criteria also did not differ between the 2 groups (29.9 and 21.0%, respectively; $p = 0.260$). The Sokolow-Lyon index also did not differ between patients who died and those who were discharged (14.4 ± 8.3 and 15.8 ± 8.4 mm, respectively; $p = 0.183$). The Cornell voltage-duration product also did not differ between the 2 groups (953 ± 300 and 926 ± 261 mV*msec, respectively; $p = 0.520$). Parameters associated with in-hospital mortality in univariate and multivariate analysis are shown in Table 4. In binary logistic regression analysis, independent predictors of in-hospital mortality were serum glucose levels, NIHSS at admission and LVH according to the Cornell voltage-duration product criteria. The sensitivity, specificity, positive and negative predictive values of LVH according to the Cornell voltage-duration product criteria for predicting in-hospital mortality were 29.5, 21.0, 10.3 and 93.2%, respectively.

The value of ECG-detected LVH for predicting severe stroke, dependency at discharge and in-hospital mortality was similar in hypertensive patients (n = 750) and in patients at the lower age