High Morning and Bedtime Home Blood Pressures Strongly Predict for Post-Stroke Cognitive Impairment

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Background: Hypertension may be the most modifiable risk factor for post-stroke cognitive impairment (PSCI). We investigated how home blood pressure (HBP) can predict PSCI as well as stroke recurrence. *Methods:* We studied 249 consecutive patients with noncardioembolic minor ischemic stroke including single lacunar infarct (sLI), multiple lacunae (mLI), and atherothrombotic infarction, which were tracked at our outpatient clinic. HBP was measured in the early morning (m-HBP) and just before going to bed (b-HBP). HBP categories based on systolic blood pressure were created as follows: HB1, both m-HBP and b-HBP less than 135 (mmHg); HB2, m-HBP less than or equal to135 and b-HBP less than 135; HB3, m-HBP less than 135 and b-HBP less than or equal to 135; HB4, both m-HBP and b-HBP less than or equal to 135. After 4.1 years of tracking, the patients were divided into 4 groups: Group 1, good outcome (n = 188); Group 2, the development of silent infarcts (n = 16); Group 3, the development of PSCI (n = 33); and Group 4, stroke recurrence (n = 15). *Results:* HB2 and HB4 (versus HB1) (hazard ratio [HR]: 6.5, $P = .0068$ and HR: 9.5, $P = .0008$, respectively) and mLI (versus sLI) (HR: 4.0, $P = .021$) were independently associated with Group 2. HB3 and HB4 (HR: 4.2, $P = .037$; HR: 5.4, $P < .0001$) and mLI (HR: 6.4, $P < .0001$) were significantly associated with Group 3. HB4 (HR: 8.1, $P = .0002$) and mLI (HR: 10.2, $P = .0003$) were significantly associated with Group 4. Clinic blood pressure (BP) was not significantly associated with any adverse groups. *Conclusions:* High HBP and mLI were strongly associated with PSCI as well as stroke recurrence. BP should be monitored based on HBP, especially bedtime HBP, for the prevention of PSCI. **Key Words:** Home blood pressure—bedtime blood pressure—post-stroke cognitive impairment—multiple lacunae.

Introduction

Hypertension is the strongest risk factor for stroke and for subcortical small-vessel disease. Hypertension is also a major risk factor for vascular cognitive impairment.[1,2] Hypertension may be the most modifiable risk factor for the secondary prevention of stroke and for post-stroke cognitive impairment. While 2 large secondary prevention studies of stroke patients showed a reduced risk of cognitive impairment associated with the use of antihypertensive treatments,[3,4] 2 other randomized controlled trials did not show reduced risk of post-stroke cognitive impairment associated with antihypertensive treatments.[5,6] The role of blood pressure (BP) and its various components and times of measurement has yet to be fully investigated in post-stroke cognitive impairment.

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Home blood pressure (HBP) measurement has been established as a better predictor of cardiovascular risk than conventional BP measurements.[7,8] Moreover, a recent study in Japan demonstrated that the HBP values were more strongly associated with cognitive decline than conventional BP values.[9] HBP measurements are more reproducible and more suggestive of target organ damage than conventional BP measurements.

We conducted this HBP study to better elucidate the relationship between BP and stroke recurrence and post-stroke cognitive impairment using 2 different HBP measurements consisting of morning HBP and bedtime HBP.

Subjects and Methods

Subjects

We studied 249 consecutive patients with noncardioembolic minor ischemic strokes or transient ischemic attack (TIA). HBPs were studied during outpatient follow-up. Patients were selected from 1021 consecutive ischemic stroke and TIA patients who entered our hospital from January 2006 to December 2008. The following patients were excluded: 320 patients with potential cardiac and any other source of embolism, and 239 disabled patients who scored more than 5 points on the National Institutes of Health Stroke Scale (NIHSS). Twenty-two patients died. From the remaining patients, 146 with cognitive impairment were also excluded. We performed Mini-Mental State Examination (MMSE) for all patients and cognitive impairment was defined as MMSE less than 24 points. Forty-five patients could not continue to visit our outpatient clinic. Consequently, 249 patients with minor stroke defined as less than or equal to 5 points of NIHSS and TIAs were followed up in the outpatient clinic. All of the patients consented to participate in this study.

HBP Measurement

All patients recorded their HBPs measured in the early morning (m-HBP) and just before going to bed (b-HBP)[8] using an electric device based on the cuff-oscillometric principle. Patients were asked to measure their own BPs twice in the sitting position within after 2 minutes of rest and to record the measurements. The morning measurements were made within the hour after waking, after micturition, and before breakfast. The bedtime measurements were made just before going to bed more than 30 minutes after bathing. Two measurements of HBP were averaged. Patients continuously recorded their HBP measurements more than 3 months. The value and variability of HBP of 7 successive days 3 months after index stroke, during a period in which each patient's BP seemed to be stable, were calculated as the average and within-participant standard deviation (SD) of the measurements. The coefficient of variation was calculated for the different HBP measurements. The goals of BP control were determined based on clinic BP as follows: systolic blood pressures (SBPs) were controlled below the level of 140 mmHg in patients who were 80 years old or younger and 150 mmHg in patients who were 80-89 years old, and diastolic blood pressures (DBPs) were controlled below the level of 90 mmHg in all age groups. Clinic BP was averaged in 2 measurements by a semiautomatic BP measuring device in the outpatient clinic. Clinic BP values for 3 successive clinic visits were used for calculating the mean value of clinic BP.

Stroke Subtype

Stroke subtyping was based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.[10] Patients with small-vessel occlusion were further classified into 2 categories: single lacunar infarct (sLI) and multiple lacunae (mLI) in whom asymptomatic lacunar infarcts may have coexisted with sLI. Atherothrombotic infarction (ATB) was defined as infarcts caused by either significant (>50%) stenosis or occlusion of a major intracranial brain artery or branch cortical artery, presumably due to atherosclerosis.

Conventional Risk Factors and Kidney Function

Hypertension was defined as previous or present use of antihypertensive agents or an SBP less than or equal to 140 mmHg and/or a DBP less than or equal to 90 mmHg, measured in a sitting position on at least 2 different occasions 2 weeks after ictus without administration of antihypertensive agents. Diabetes mellitus was defined as previous or present use of an antidiabetic medication or hemoglobin A1c less than or equal to 6.5%. Dyslipidemia was defined as previous or present use of lipid-lowering agents or a fasting total cholesterol level less than or equal to 240 mg/dL and/or a fasting low-density lipoprotein cholesterol greater than 160 mg/dL. Cigarette smoking was defined as regular smoking at the time of stroke.

As kidney dysfunction is established to be associated with cognitive impairment, we estimated kidney function. The estimated glomerular filtration rate (eGFR) was calculated from the serum creatinine (Cr) value and age using the abbreviated Modification of Diet in Renal Disease equation modified by the Japanese coefficient[11] as follows: $\text{eGFR}\ (\text{mL/min/1.73 m}^2) = .741 \times 175 \times \text{age}^{-.203} \times \text{Cr}\ (\text{mg/dL})^{-1.154}$ (if female, $\times .742$). Then, kidney function was categorized based on eGFR as follows: GF1, eGFR >60 (mL/min/1.73 m^2); GF2, 30-60; GF3, <30.

Image Diagnosis

All patients underwent magnetic resonance imaging (MRI)/magnetic resonance angiography, color-coded Duplex sonography, and a 12-lead electrocardiogram. Extracranial