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## Research Article

# Lipid Profiles and Postprandial Glucose Status of Hypertensive Individuals with Stroke in Indonesia

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## Abstract

**Background and Objective:** Stroke is the second leading cause of death worldwide. Stroke caused 23.48% of all deaths in Indonesia, a country with the highest prevalence of stroke in the world. The main risk factor for stroke is hypertension. In Indonesia, hypertension is the most prevalent non-communicable disease (25.8%). The objective of this study was to determine lipid profile and postprandial (PPG) status among hypertensive people with stroke in Indonesia. **Materials and Methods:** In this study cross-sectional study design was used and obtained data from secondary data of Riskesdas 2013. The number of respondents was 8,511. Data was analyzed using Cochran's and Mantel-Haenzel test. **Results:** Prevalence of stroke cases in people with hypertension was 9%. Most of stroke respondents have high T-cholesterol, LDL-C, triglyceride and PPG. Factors related to stroke are: age, LDL-C level (PR = 1.21; 95% CI = 1.026-1.431) and PPG levels (PR = 1.28; 95% CI = 1.102-1.1492). After adjusting for gender and age, PPG was associated with stroke prevalence in hypertensive people in Indonesia. **Conclusion:** Prevalence of high LDL-C and PPG levels in hypertensive people with stroke is high. Those related to stroke incident among hypertensive people. It needs an educational effort to the stroke group to control LDL-C levels for prevention of recurrent stroke and other impacts.

**Key words:** Stroke, T-Cholesterol, LDL-C, HDL-C, triglyceride, postprandial glucose

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**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Stroke is a medical condition of concern both in Indonesia and globally, it is the second leading cause of death worldwide, causing 11.3% of all deaths<sup>1</sup>. In 2011, it was reported that 30.7 million individuals globally had previously experienced a stroke, 12.6 million individuals had moderate to severe disability as a result of stroke<sup>2</sup>. The burden of stroke globally is estimated to increase from 38-61 million disability-adjusted life years (DALYs) from 1990-2020. Additionally, stroke has been the single largest cause of disability in the United Kingdom (UK)<sup>3</sup>. In the United States (US), stroke and coronary heart disease (CHD) related health service costs were the most expensive, reaching more than 320.1 billion US dollars (USD) in 2013<sup>1</sup>.

Riset Kesehatan Dasar (Riskesdas), the Indonesian Basic Health Survey conducted by Ministry of Health Indonesia, reported that the incidence of stroke was 8.3/1000 population in 2007. This incidence increased to 12.1/1000 population in 2013<sup>4,5</sup>. Additionally, the incidence of mortality due to stroke also reached 200.16/100,000 population in 2013 in Indonesia. Stroke was the leading cause of death in Indonesia based on World Health Organization (WHO) data in 2015, with the number of deaths reaching 328,525 or 23.48% of all deaths in Indonesia. Moreover, Indonesia has the highest burden of strokes in the world<sup>6</sup>, thus increasing the risk of a large number of individuals living with poor health and quality of life<sup>7</sup>. According to Jaminan Kesehatan Nasional (JKN, National Health Insurance) data, stroke is the most costly medical condition to treat in Indonesian hospitals with total costs of treatment and care reaching 115.35 million USD<sup>8</sup>.

Hypertension is a major risk factor of stroke. Hypertension increased the risk of stroke 3.89 (99% confidence interval [CI] = 3.33-4.54) times when compared to the risk in non-hypertensive individuals<sup>9</sup>. Hypertension is also the most prevalent non-communicable disease in Indonesia with a prevalence of 25.8%<sup>5</sup>.

The relationship between lipid profiles and the postprandial glucose (PPG) status with stroke are well known. The risk of stroke increases 3.75 (95% CI 1.83-7.7) fold for higher total cholesterol<sup>10</sup>, 2.29 (95% CI 1.1-4.8) fold for higher low-density lipoprotein cholesterol (LDL-C)<sup>10</sup>, 0.52 (95% CI 0.28-0.96) fold for lower high-density lipoprotein cholesterol (HDL-C)<sup>10</sup>, 0.97 (95% CI 0.956-0.978) fold for higher triglyceride<sup>11</sup> and 2.71 (95% CI 1.24-5.91) fold for higher PPG<sup>12</sup>. Lipid profile<sup>13</sup> and PPG<sup>14</sup> status also play a pivotal role in prevention of recurrent stroke. However, there is lack of

information about the lipid profiles and PPG status in hypertensive individuals, who experienced stroke. Riskesdas 2013<sup>15</sup> was the latest survey conducted by Ministry of Health, Indonesia. This survey collected comprehensive health data, nevertheless lipid profiles and PPG levels in hypertensive individuals with stroke in Indonesia have not yet been reported on. The aim of this study was to determine the prevalence of stroke in hypertensive individuals in Indonesia and to report on their lipid profiles and PPG status based on the data from the Riskesdas, 2013.

## MATERIALS AND METHODS

**Design and sample research:** This cross-sectional study used secondary survey data from Riskesdas 2013<sup>15</sup>. This survey was the latest Riskesdas done and provide current condition describe health status and its determinants. This survey also provide comprehensive secondary health data and describe current condition of lipid profiles and PPG status that associated with hypertensive people with stroke in Indonesia. Subjects included were hypertensive respondents of Riskesdas 2013, subjects with incomplete data were excluded. Detailed information about the methods employed for the completion of Riskesdas 2013<sup>15</sup>, in addition to the data collected using this survey has been described in previous reports<sup>5,15</sup>.

**Data collection:** Riskesdas 2013<sup>15</sup> was a community-based survey covering all regions of Indonesia. Riskesdas collected baseline data and health indicators that represented a national, provincial and district/city description. Riskesdas is intended to be implemented every 3 years and the latest survey was conducted in 2013. This was a cross-sectional study with respondents from 33 provinces and 497 districts/cities in Indonesia, with a total of 1,027,763 respondents. This study was approved by the Ethics Committee, the National Institute of Health Research and Development (NIHRD), Ministry of Health, Indonesia in 2013. Respondents with hypertension were defined by having: Blood pressure  $\geq 140$  mm Hg (systolic pressure) and/or  $\geq 90$  mm Hg (diastolic pressure),<sup>16</sup> who were diagnosed with hypertension by a health professional, or prescribed antihypertensive medication. Stroke was determined by asking respondents whether or not they had been diagnosed as having a stroke by a health professional (doctor or nurse) in the past or were suddenly showing symptoms of a stroke. Symptoms, as assessed in Riskesdas 2013<sup>15</sup> included: experiencing paralysis on one side of the body, tingling or numbness on one side of the body, mouth droops without eye

muscle paralysis, slurred speech and difficulty in speaking and/or understanding conversation<sup>5</sup>. Factors that were analyzed were limited to age and biomedical parameters such as total cholesterol, LDL-C, HDL-C, triglyceride and PPG levels. Total cholesterol, LDL-C, HDL-C and triglyceride levels were measured using an auto analyzer TRX 7010<sup>®</sup> and PPG was measured using an Accu-Chek Performa<sup>®</sup>.

Age was categorized as young (<45 years), middle aged (45-65 years) and elderly (>65 years). Total cholesterol, LDL-C, HDL-C and triglyceride levels were determined based on the dyslipidemia guidelines according to the Per kumpulan Endokrinologi Indonesia (PERKENI, The Indonesia Society of Endocrinology)<sup>17</sup>. PPG levels were determined according to the Ministry of Health, Indonesia monitoring guidelines on the risk factors for non-communicable diseases<sup>18</sup>. High risk total cholesterol, LDL-C, HDL-C and triglyceride levels were defined as a concentration  $\geq 190$  mg dL<sup>-1</sup>, a concentration  $\geq 110$  mg dL<sup>-1</sup>, a concentration <40 mg dL<sup>-1</sup> for men and <45 mg dL<sup>-1</sup> for women and a concentration  $\geq 150$  mg dL<sup>-1</sup>. Abnormal PPG levels were defined as a concentration  $\geq 180$  mg dL<sup>-1</sup>.

**Statistical analysis:** Characteristics of respondents were presented as frequencies and proportions. Here explored lipid profiles and PPG levels that were related to the prevalence of stroke adjusted for age and gender in hypertension patients using Cochran's and Mantel-Haenszel analysis. p-values <0.05 were considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 13.0 for Windows, IBM SPSS Inc., Chicago, IL).

## RESULTS

In total, 8,511 respondents were included in the study of which 767 (9.0%) had stroke. The majority of the respondents were female (65.5%), aged 45-55 years (51.1%), had high risk total cholesterol (57.3%) and LDL-C (75.5%) and normal HDL-C (70%), triglyceride levels (71.8%) and PPG levels (77.9%). The clinical and demographic characteristics of respondents are presented in Table 1.

Out of seven variables assessed, the bivariate analysis found three related variables: Age, LDL-C levels and PPG levels (Table 2). The prevalence of stroke was more common in women (9.2%) than in men (8.6%), however, this difference was not statistically significant ( $p = 0.347$ ).

Overall, 10.5, 10 and 6.7% of the prevalence of stroke occurred among those aged >65, 45-65 and <45 years, respectively. Current study found that there was a significant

Table 1: Characteristics of the subjects included in the analysis

| Characteristics  | Frequency (n) | Proportion (%) |
|--|---------------|----------------|
| <b>Gender</b>  |               |                |
| Male   | 2,933         | 34.5           |
| Female   | 5,578         | 65.5           |
| <b>Age group</b>   |               |                |
| <45 years  | 1,386         | 16.3           |
| 45-65 years  | 4,345         | 51.1           |
| >65 years  | 2,780         | 32.7           |
| <b>T-Cholesterol levels</b>  |               |                |
| $\geq 190$ mg dL   | 4,873         | 57.3           |
| <190 mg dL <sup>-1</sup>   | 3,638         | 42.7           |
| <b>LDL-C levels</b>  |               |                |
| $\geq 100$ mg dL <sup>-1</sup>   | 6,426         | 75.5           |
| < 100 mg dL <sup>-1</sup>  | 2,085         | 24.5           |
| <b>HDL-C levels</b>  |               |                |
| At risk (M < 40 mg dL <sup>-1</sup> ; F < 45 mg dL <sup>-1</sup> )           | 2,556         | 30.0           |
| No risk (M $\geq 40$ mg dL <sup>-1</sup> ; F $\geq 45$ mg dL <sup>-1</sup> ) | 5,955         | 70.0           |
| <b>Triglyceride levels</b>   |               |                |
| $\geq 150$ mg dL <sup>-1</sup>   | 2,397         | 28.2           |
| <150 mg dL <sup>-1</sup>   | 6,114         | 71.8           |
| <b>PPG levels</b>  |               |                |
| $\geq 180$ mg dL   | 1,885         | 22.1           |
| <180 mg dL <sup>-1</sup>   | 6,626         | 77.9           |
| <b>Stroke</b>  |               |                |
| Yes  | 767           | 9              |
| No   | 7744          | 91             |

LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol

relationship between age and stroke prevalence in hypertensive individuals in Indonesia in all age groups when compared to reference group (<45 years). Respondents aged >65 and 45-65 years were at 1.57 and 1.48 times the risk of stroke when compared to respondents aged <45 years, respectively.

The prevalence of stroke was found to be higher in the high risk total cholesterol group (9.5%) compared to the no risk group (8.4%). However, there was no significant association between total cholesterol levels and the prevalence of stroke in hypertensive individuals in Indonesia ( $p = 0.087$ ,  $\alpha = 0.05$ ).

A significantly higher prevalence of stroke prevalence was found in the high risk LDL-C group (9.4%) compared to the no risk group (7.2%). ( $p = 0.025$ ,  $\alpha = 0.05$ ). Respondents in the high risk LDL-C group were 1.21 times more likely to have a stroke than respondents, who were in the no risk LDL-C group. The prevalence of stroke was higher in the no risk HDL-C group (9.2%) than in the high risk HDL-C group (8.6%), however this difference was not significant ( $p = 0.465$ ,  $\alpha = 0.05$ ). The prevalence of stroke was higher in the high risk triglyceride group (9.8%) than the no risk triglyceride group (8.7%), however, this difference was not significant ( $p = 0.120$ ,  $\alpha = 0.05$ ). Finally, the prevalence of stroke was significantly higher in the abnormal PPG group (10.9%) when compared to

Table 2: Relationship between parameters and stroke among respondents with hypertension

| Parameter  | Stroke (n = 747) |      | Stroke (n = 7744) |      | p-value | PR   | 95% CI       |
|--|------------------|------|-------------------|------|---------|------|--------------|
|  | No.              | %    | No.               | %    |         |      |              |
| <b>Gender</b>  |                  |      |                   |      |         |      |              |
| Male   | 252              | 8.6  | 2,681             | 91.4 | 0.347   | 0.93 | 0.806-1.075  |
| Female   | 515              | 9.2  | 5,063             | 90.8 |         |      |              |
| <b>Age group</b>   |                  |      |                   |      |         |      |              |
| >65 years  | 146              | 10.5 | 1,240             | 89.5 | 0.0001  | 1.57 | 1.274-1.925  |
| 45-65 years  | 434              | 10.0 | 3,911             | 10.0 | 0.0001  | 1.48 | 1.259-1.751  |
| <45 years  | 187              | 6.7  | 2,593             | 93.3 |         |      |              |
| <b>T-Cholesterol levels</b>                                      |                  |      |                   |      |         |      |              |
| ≥190 (mg dL <sup>-1</sup> )                                      | 462              | 9.5  | 4,411             | 90.5 | 0.087   | 1.13 | 0.985-1.298  |
| < 190 (mg dL <sup>-1</sup> )                                     | 305              | 8.4  | 3,333             | 91.6 |         |      |              |
| <b>LDL-C levels</b>  |                  |      |                   |      |         |      |              |
| ≥100 (mg dL <sup>-1</sup> )                                      | 605              | 9.4  | 5,821             | 90.6 | 0.025   | 1.21 | 1.026-1.431  |
| <100 (mg dL <sup>-1</sup> )                                      | 162              | 7.8  | 1,923             | 92.2 |         |      |              |
| <b>HDL-C levels</b>  |                  |      |                   |      |         |      |              |
| At Risk (M <40 mg dL <sup>-1</sup> ; F <45 mg dL <sup>-1</sup> ) | 221              | 8.6  | 2,335             | 91.4 | 0.465   | 0.94 | 0.812-1.095  |
| No Risk (M ≥40 mg dL <sup>-1</sup> ; F ≥45 mg dL <sup>-1</sup> ) | 546              | 9.2  | 5,409             | 90.8 |         |      |              |
| <b>Triglyceride levels</b>                                       |                  |      |                   |      |         |      |              |
| ≥150 (mg dL <sup>-1</sup> )                                      | 235              | 9.8  | 2,162             | 90.2 | 0.12    | 1.13 | 0.974-1.304  |
| <150 (mg dL <sup>-1</sup> )                                      | 532              | 8.7  | 5,582             | 91.3 |         |      |              |
| <b>PPG levels</b>  |                  |      |                   |      |         |      |              |
| ≥180 (mg dL <sup>-1</sup> )                                      | 205              | 10.9 | 1,680             | 89.1 | 0.002   | 1.28 | 1.102-1.1492 |
| <180 (mg dL <sup>-1</sup> )                                      | 562              | 8.5  | 6,064             | 91.5 |         |      |              |

Table 3: Comparison of prevalence ratio

| Parameters    | Model 1*PR (95% CI)     | Model 2** PR (95% CI)  | Model 3*** PR (95% CI) | Model 4**** PR (95% CI) |
|---------------|-------------------------|------------------------|------------------------|-------------------------|
| T-Cholesterol | 1.13<br>(0.985-1.298)   | 1.14<br>(0.976-1.325)  | 1.10<br>(0.941-1.277)  | 1.09<br>(0.937-1.277)   |
| LDL-C         | 1.30*<br>(1.054-1.597)  | 1.23*<br>(1.024-1.473) | 1.20<br>(0.996-1.433)  | 1.20<br>(0.997-1.439)   |
| HDL-C         | 0.94<br>(0.812-1.095)   | 0.94<br>(0.798-1.108)  | 0.98<br>(0.830-1.153)  | 0.99<br>(0.840-1.168)   |
| Triglyceride  | 1.13<br>(0.974-1.304)   | 1.15<br>(0.976-1.349)  | 1.12<br>(0.954-1.319)  | 1.16<br>(0.981-1.359)   |
| PPG           | 1.28*<br>(1.102-1.1492) | 1.31*<br>(1.107-1.552) | 1.25*<br>(1.057-1.483) | 1.24*<br>(1.043-1.464)  |

\*Significant p value at <0.05, \* Model 1: Crude prevalence ratio, \*\*Model 2: Prevalence ratio after adjusted by gender, \*\*\* Model 3: Prevalence ratio after adjusted by age, \*\*\*\* Model 4 : Prevalence ratio after adjusted by gender and age

the normal group (8.5%) (p = 0.002, α = 0.05). Respondents with abnormal PPG levels had 1.28 times the risk of stroke than respondents, who had normal PPG levels.

The comparisons of the prevalence ratios in each model is shown in Table 3. Before adjusting for other variables, LDL-C and PPG were significantly related to stroke prevalence among individuals with hypertension in Indonesia (Model 1). Similarly, after adjustment for gender, LDL-C and PPG were significantly related to stroke incident among hypertensive individuals in Indonesia (Model 2). However, the prevalence ratio (PR) for LDL-C increased from 1.21-1.23, while from PPG it increased from 1.28-1.31. After adjustment for age in Model 3, only PPG was significantly related to stroke prevalence among individuals with hypertension in Indonesia leading to a reduction in the PR from 1.28 (Model 1) -1.25 (Model 3).

Similarly, after adjustment for age and gender, only PPG was significantly related to the prevalence of stroke among individuals with hypertension in Indonesia leading to a reduction in the PR from 1.28 (Model 1)-1.24 (Model 4).

## DISCUSSION

In this study found that 9% of individuals in Indonesia with hypertension included in this study experienced stroke. This prevalence rate is lower than that previously reported from a study conducted in Nigeria<sup>19</sup>. Here determined that age, LDL-C levels and PPG status were significantly associated with the occurrence of stroke among hypertensive individuals in Indonesia. However, there was no association between the prevalence of stroke and gender, total cholesterol, HDL-C and

triglyceride levels. Previous report<sup>19</sup> on lipid profiles and PPG status among hypertensive individuals with stroke are limited. A Nigerian study<sup>19</sup> showed that modifiable factors related to stroke occurrence included higher maximum and minimum blood pressure in preceding 3 months, higher fasting plasma glucose levels, large amounts of alcohol consumption, less physical activity and increased carotid intima medial thickness (CIMT).

In this study found a significant relationship between age and the prevalence of stroke in hypertensive individuals in Indonesia, the risk of stroke increases with increasing age. The majority of the cases of stroke were identified among those aged >65 years (10.5%), while among those <45 years it was much lower (6.7%). Generally, stroke occurs due to aging. Naturally, the blood vessels will become more rigid as a result of plaque buildup<sup>20</sup>. In young adults, increased risk of infarction and vascular risk factors in developing countries are associated with behaviors such as increased smoking and urbanization<sup>21</sup>. Although the relationship between age and stroke incident has been well documented, this study adds to the existing body of evidence on the association between age and stroke, particularly among hypertensive individuals in Indonesia.

In this study found a significant relationship between LDL-C levels and the prevalence of stroke. Respondents, who had LDL-C levels >100 mg dL<sup>-1</sup> had 1.30 times the risk of experiencing stroke than respondents with LDL-C levels <100 mg dL<sup>-1</sup>. However, after adjustment for age and gender, LDL-C levels were not significantly related to the occurrence of stroke.

The association between LDL-C levels and coronary heart disease has previously been proven. However, the relationship between LDL-C levels and the prevalence of stroke is controversial. The findings of this study were in line with those of a study performed in Kerala, India<sup>10</sup> which reported that respondents with a cholesterol level >200 mg dL<sup>-1</sup> were 2.29 times more likely to have a stroke than those with normal cholesterol levels ( $p = 0.009$ , 99% CI:1.27-4.15). Likewise, a study conducted in the Neurology Department of Sina Hospital, Iran<sup>11</sup> also revealed similar findings, LDL-C levels were a predictor of hemorrhagic stroke. Increased cholesterol and LDL-C levels were associated with a higher risk of ischemic stroke. Investigators concluded that LDL-C was a risk factor in both ischemic and hemorrhagic stroke<sup>11</sup>. The LDL-C levels were also associated with mortality after long-term stroke but was not a prognostic factor<sup>22</sup>. The relationship between LDL-C levels and stroke was different in an Indonesian cohort study<sup>12</sup> in the common population and in a Nigerian-African study<sup>19</sup> in a hypertensive population. These differences may be due to

differences in the number of respondents, control of other confounding factors, or limitations in the data.

In this study found a significant relationship between PPG levels and the prevalence of stroke in hypertensive individuals in Indonesia. Respondents with abnormal PPG levels had 1.28 times the risk of experiencing stroke than respondents with normal PPG levels. However, after adjusted for age and gender, PPG was a significant variable related to stroke incident, decreasing the PR from 1.28 (Model 1)-1.24 (Model 4).

Research on the relationship between PPG levels and the occurrence of stroke is limited both in the general and hypertension populations. Most previous studies<sup>12,19</sup> have included fasting blood Glucose (FBG) levels as a research variable. A cohort study in Indonesia<sup>12</sup> showed a significant association between PPG levels and stroke incidence in the general population, however, after controlling for other potentially confounding variables, PPG was not the dominant variable causing stroke<sup>12</sup>. However the study in Nigeria (2013)<sup>19</sup> used FBG levels in order to determine the relationship between FBG and stroke incidence in patients with hypertension. The investigators found a significant relationship between FBG and the incidence of stroke in patients with hypertension. However, when other potentially confounding variables were controlled for, FBG levels were not the dominant variable causing stroke in hypertensive patients.<sup>19</sup> The San Luigi diabetes study showed that PPG was a strong cardiovascular predictor of FBG in individuals with type 2 diabetes mellitus, particularly in women.<sup>23</sup> High PPG levels or postprandial hyperglycemia are characterized by hyperglycemic spikes that cause endothelial dysfunction, inflammatory reactions and oxidative stress, which can lead to the development of atherosclerosis and the occurrence of cardiovascular events. Research has shown that postprandial hyperglycemia may predispose individuals to the development of atherosclerosis and cardiovascular events<sup>24</sup>.

This study showed a significant association between PPG levels and stroke incidence in hypertensive patients in Indonesia. Findings of this study might be different from those observed in the Nigerian study<sup>19</sup> because this study included more respondents and collected more robust data. Patients with hypertension, who had abnormal PPG levels had 1.28 times the risk of stroke when compared to those with normal PPG levels. After controlling for age, this risk decreased from 1.28-1.25 times the risk. Nonetheless, this study provides new insights as to stroke among hypertensive patients, that there is a significant relationship between PPG levels and the incidence of stroke in hypertensive individuals, especially in Indonesia.

This study was subject to several limitations. As this was a cross-sectional study, exposures and effects were measured in the same time period, thus, it is unknown exactly which events occurred first (i.e., whether respondents had hypertension, stroke, or high-risk LDL-C levels first). Additionally, we were unable to explain the LDL-C status before the data collection. However, from Table 2 it can be observed that 9.4% of stroke patients still had high risk LDL-C levels ( $\geq 100$  mg dL<sup>-1</sup>). These findings suggest that LDL-C levels were poorly controlled in the stroke group. Future studies are needed to explain the role of PPG levels on the increased risk of stroke.

### CONCLUSION

The majority of hypertensive individuals with stroke have high LDL-C and PPG levels. There was a significant relationship between age and LDL-C and PPG levels and the prevalence of stroke in hypertensive individuals in Indonesia. After adjustment for gender and age, PPG levels were significantly associated with prevalence of stroke among hypertensive patients. Education should be provided to those, who have experienced a stroke in the past in order to provide them with mechanisms to control LDL-C and PPG levels for the prevention of recurrent stroke.

### SIGNIFICANCE STATEMENTS

This study investigated the LDL-C and PPG levels related to hypertensive individuals with stroke. This study help the researchers to uncover the critical area risk factors of stroke, especially lipid profiles and PPG levels in individuals with hypertension that many researchers have not been able to explore in past. Current study found that LDL-C and PPG were the main risk factors of stroke in hypertensive individuals, thus interventions should target these high risk populations.

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