Interankle Systolic Blood Pressure Difference Is a Marker of Prevalent Stroke in Chinese Adults: A Cross-Sectional Study

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This cross-sectional study carried out from November 2014 to December 2014 aimed to determine whether the interankle systolic blood pressure (SBP) difference is an independent marker of prevalent stroke. Simultaneous four-limb blood pressure measurements (oscillometric devices) and calculated SBP difference between the lower limbs were collected from 1485 participants aged 35 years and older. Questionnaires about traditional stroke risk factors were completed. Interankle SBP difference ≥7 mm Hg was independently associated with a history of stroke after adjusting for traditional stroke risk factors (odds ratio, 1.64; 95% confidence interval, 1.53–3.59; *P*=.0123). Net reclassification improvement analysis showed that adding the interankle SBP difference to traditional risk factors improved the predictive ability for stroke risk by 18.5% (*P*<.001). In conclusion, an interankle SBP difference ≥7 mm Hg could be an independent marker of stroke history in Chinese adults. It could offer an extra benefit in identifying individuals with risk of stroke beyond conventional clinical features. *J Clin Hypertens (Greenwich).* 2017;19:58–66. © 2016 Wiley Periodicals, Inc.

Stroke is the leading cause of death and disability in China and imposes a significant economic burden.[1] The traditional risk factors only explain a small proportion of the clinical events, and stroke remains unexplained in many patients. Thus, it is necessary to identify new and better risk factors or markers of stroke in order to improve primary prevention.

The role of hypertension in the risk of cardiovascular diseases is well-known,[2,3] but the use of crude measurements of blood pressure (BP) is limited,[4] and new technologies are seeking to use more refined BP-derived data to improve the prediction of the risk of cardiovascular events.[5–7] The interankle systolic BP (SBP) difference is an index derived from four-limb BP measurements.[5] In recent years, the interankle SBP difference was proposed to be useful for the prediction of cardiovascular events.[5] Calculation of the interankle SBP difference may provide additional information for identifying patients with peripheral vascular disease and left ventricular hypertrophy.[8] The interankle SBP difference has been associated with rapid renal progression and progression to renal endpoints in patients with stage 3 to 5 chronic kidney disease.[9] Although the interankle SBP difference has been found to predict the risk of overall cardiovascular events,[10,11] few studies have evaluated the association between interankle SBP difference and stroke, and the threshold of interankle SBP difference associated with a significant risk of stroke in the general population remains undefined. The use of interankle SBP difference could help identify patients who are at risk for stroke but do not have the traditional risk factors of stroke.

Therefore, the aim of the present study was to evaluate the association between the interankle SBP difference and a history of stroke in Chinese adults using data from a large epidemiological survey of hypertension in China.

METHODS

Study Design

This was a cross-sectional study conducted using data from the China Hypertension Survey from two Shuangcheng Manchu towns. Shuangcheng is located in the Heilongjiang province in northeast China. The China Hypertension Survey was a large-scale epidemiological survey supported by the Chinese Ministry of Science and Technology.[12] It was carried out from November 2014 to December 2014 to evaluate cardiovascular diseases and risk factors among adults 35 years and older. The patients were selected using a simple random sampling method.[12] The ethics committee of the First Affiliated Hospital of Harbin Medical University approved the study protocol. All participants provided written informed consent.

Study Population

A total of 1591 patients were enrolled (participation rate of 80%). We excluded 106 patients because four-

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limb BP measurement was not performed (n=34), no blood test was performed (n=17), or some epidemiological data were missing (n=55). Thus, the number of participants included in the present analysis was 1485.

Study Protocol and Evaluation Criteria

In the China Hypertension Survey, each participant underwent physical examination and was administered a standardized questionnaire by a trained interviewer blinded to all patient data. The questionnaire included data on age, sex, smoking status (past or present smoker, number of cigarettes smoked daily, and smoking years), alcohol intake (past or present alcohol consumption, amount of daily alcohol intake, and drinking years), family history of stroke, and personal history of stroke, hypertension, and diabetes. In this study, as per the original study design, smoker was defined as having smoked every day for more than 1 year and alcohol drinking was defined as having at least one drink every day.

After the patient had been resting ≥5 minutes in the sitting position, an experienced physician measured right-arm BP three consecutive times using a validated Omron HBP-1300 oscillometric BP monitor (Omron, Kyoto, Japan). The Omron HBP-1300 was found to comply with the Association for the Advancement of Medical Instrumentation standards and British Hypertension Society protocol requirements.[13]

Hypertension was defined as a sitting SBP (average of three readings) of ≥140 mm Hg or diastolic BP (DBP) ≥90 mm Hg or the use of antihypertensive drugs. An SBP ≥140 mm Hg was defined as high SBP.

Ankle BP and ankle-brachial index (ABI) were measured using two Watch BP Office ankle-brachial index devices (Microlife, Widnau, Switzerland), which use an oscillometric technique that has been validated.[14,15] Trained technicians and physicians placed the pressure cuffs on both arms and both ankles and performed the measurements after the patient had been resting for approximately 10 minutes in the supine position. The ankle cuff was placed on the leg, making sure that the edge of the cuff was approximately 2 to 3 cm above the ankle and that the artery mark was on the posterior tibial artery. The device simultaneously and automatically measured BP three times at 1-minute intervals. Interankle SBP difference was calculated as the average and absolute systolic values of the difference between the right and left ankle BP.

Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters squared). A normal BMI was defined as <24 kg/m^2.[16]

Venous blood samples were drawn after an overnight fast for the measurement of blood glucose, serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels. Impaired fasting blood glucose (FBG) and dyslipidemia were defined according to guidelines.[17,18] Diabetes mellitus was defined as an FBG ≥7.0 mmol/L, prior diagnosis of diabetes mellitus, or the use of antidiabetic agents.[17]

Stroke was diagnosed by a neurologist in a hospital at or above the county levels based on the self-reported history of stroke and cranial computed tomography or magnetic resonance imaging. Nonfatal ischemic stroke, hemorrhagic stroke, and transient ischemic attack (TIA) were all included. Of the 136 patients with stroke, 107 (78.7%) had ischemic stroke, six (4.4%) had hemorrhagic stroke, and 23 (16.9%) had TIA.

Statistical Analysis

Data distribution was examined using the Smirnov-Kolmogorov test. Continuous variables are expressed as mean±standard deviation and were analyzed using the Student *t* test or analysis of variance with the Tukey's post hoc test. Nonnormally distributed data (TG, FBG, interarm BP difference, and interankle BP difference) are presented as median (interquartile range [IQR]) and were analyzed using the Mann-Whitney or the Kruskal-Wallis test, as appropriate. Categorical variables are presented as proportions and were analyzed using the chi-square test. The receiver operating characteristic (ROC) curves for interankle SBP difference and ABI were plotted using stroke as the dependent factor; the area under the curve (AUC) was used to compare the different methods. Logistic regression analysis was performed to assess the association between interankle SBP differences and a history of stroke. Adjustments were made for age, sex, ethnicity, family history of stroke, BMI, smoking status, alcohol use, SBP or hypertension, and levels of TC, LDL-C, HDL, TG, and FBG. The incremental value of the interankle SBP difference was also tested by comparing the AUC of the ROC curve. ROC_{AUC} was estimated using a regression model that included age, family history of stroke, and hypertension as categorical variables, and using a model that included age, family history of stroke, hypertension, and interankle SBP differences (dichotomized using the 7-mm Hg cutoff value determined by ROC analysis) ≥7 mm Hg as a categorized variable. In both models, the history of stroke (with vs without) was the dependent variable. The net reclassification improvement (NRI) for participants when adding the categorized interankle SBP difference (dichotomized using the cutoff value determined by ROC analysis) to age, family history of stroke, and SBP model for predicting a history of stroke was calculated. The NRI was analyzed using the *Z* test.[19,20] SAS 9.13 (SAS Institute, Cary, NC) and R (R Development Core Team) were used for database management and statistical analysis. Two-sided *P* values <.05 were considered statistically significant.

RESULTS

The 1485 participants (740 men, 49.8%) were aged 54.8±11.5 years, among whom 136 (9.2%) had stroke, 621 (41.8%) had hypertension, and 111 (7.5%) had diabetes mellitus. Of the study participants diagnosed with stroke, six (4.4%) had hemorrhagic stroke

(including two with subarachnoid hemorrhage), 107 (78.7%) had ischemic stroke, and 23 (16.9%) had TIA. Manchu ethnicity accounted for 50.2% of the population. The median interankle SBP difference was 5.7 mm Hg (IQR, 2.3–11.7 mm Hg) (Table S1). There was no difference in interarm and interankle SBP differences between stroke patients with normal limbs and those with hemiplegic limbs (*P*=.87 and *P*=.68, respectively) (Table S2).

The characteristics of the participants according to stroke history are shown in Table I. Compared with patients without stroke, those with stroke were older (*P*<.0001) and had higher SBP (*P*<.0001), DBP (*P*<.0001), interankle SBP (*P*=.0024), FBG (*P*=.0040), TC (*P*=.0012), and LDL-C (*P*<.0001) values and lower HDL-C (*P*=.0127) values. In addition, participants with stroke had a higher frequency of hypertension (*P*<.0001) and use of antihypertensive drugs (*P*<.0001).

Figure 1 shows that the prevalence of stroke tended to increase with the increase of tertiles/quartiles/quintiles of the distribution of the interankle SBP difference (Fisher's exact test; *P*=.0055, *P*=.0024, and *P*=.0011, respectively).

The ROC_{AUC} was estimated for the optimal cutoff value of the interankle SBP difference for the prediction of stroke (Figure S1). Comparison of the ROC_{AUC} for various interankle SBP difference cutoff values (6, 7, 8, 9, and 10 mm Hg) revealed that an interankle SBP difference of 7 mm Hg was probably a good candidate (0.5906 [95% confidence interval (CI), 0.55–0.63]); the curves for 7 and 8 mm Hg were nearly identical, but the 95% CI was narrower for 7 mm Hg. Therefore, the cutoff value of 7 mm Hg was selected for the subsequent analyses.

Previous studies showed that ABI <0.9 could be used for the prediction of stroke.[5,15,21–23] Therefore, an interankle SBP difference of 7 mm Hg was compared with ABI <0.9. The ROC_{AUC} shown in Figure S2 indicate that an interankle SBP difference ≥7 mm Hg was superior to ABI <0.9 in the diagnosis of stroke, which is a common accepted predictor of stroke (*P*=.0071).

Multivariate analyses were performed to determine the value of interankle SBP difference using two models: since SBP and hypertension were covariant, model 1 (Figure 2a) included hypertension, while model 2 (Figure 2b) included SBP. After adjusting for the traditional risk factors of stroke (age, sex, ethnicity, family history of stroke, BMI, smoking, alcohol, hypertension or SBP, and levels of TC, LDL-C, HDL-C, TG, and FBG), multiple logistic regression analysis showed that an interankle SBP difference ≥7 was independently associated with a history of stroke (model 1: odds ratio [OR] =1.64 [95% CI, 1.11–2.40], *P*<.01; model 2: OR=1.73

TABLE I. Stroke-Stratified Characteristics of the Participants

Variable	History of Stroke (n=1349)	No History of Stroke (n=136)	*P* Value
Age, mean±SD, y	53.8±11.3	64.4±9.1	<.0001
Manchu ethnicity, No. (%)	672 (50.0)	76 (55.2)	.2294
BMI, mean±SD, kg/m^2	24.7±3.7	24.5±4.6	.5995
Family history of stroke, No. (%)	296 (22.0)	37 (27.2)	.8934
Hypertension, No. (%)	524 (38.7)	97 (71.3)	<.0001
Use of antihypertensive drugs, No. (%)	204 (15.1)	61 (44.9)	<.0001
Diabetes mellitus, No. (%)	97 (7.2)	14 (10.3)	.1896
SBP on higher arm side, mean±SD, mm Hg	131.7±19.5	147.5±23.3	<.0001
DBP on higher arm side, mean±SD, mm Hg	80.7±10.2	85.8±11.4	<.0001
Interarm SBP, mm Hg			
SBP, median (IQR)	3.0 (1.3–5.7)	3.7 (1.6–5.7)	.2433
ΔSBP ≥15 mm Hg, No. (%)	26 (1.9)	7 (5.2)	.0152
ΔSBP ≥10 mm Hg, No. (%)	104 (7.7)	15 (11.0)	.1741
Interankle SBP, mm Hg			
SBP, median (IQR)	5.3 (2.3–11.3)	8.7 (3.3–14.0)	.0024
ΔSBP ≥15 mm Hg, No. (%)	225 (16.7)	29 (21.3)	.1704
ΔSBP ≥10 mm Hg, No. (%)	402 (29.8)	58 (42.7)	.0020
ABI, mean±SD	1.18±0.1	1.13±0.13	.0004
ABI <0.9, No. (%)	17 (1.3)	9 (6.6)	<.0001
FBG, median (IQR), mmol/L	5.2 (4.9–5.6)	5.3 (5.0–5.9)	.0040
TC, mean±SD, mmol/L	4.89±0.96	5.19±1.04	.0012
HDL-C, mean±SD, mmol/L	1.48±0.35	1.41±0.32	.0127
LDL-C, mean±SD, mmol/L	2.83±0.81	3.14±0.81	<.0001
TG, mean±SD, mmol/L	1.29±0.87	1.43±0.82	.0649

Abbreviations: ABI, ankle-brachial index; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides; Δ, difference.

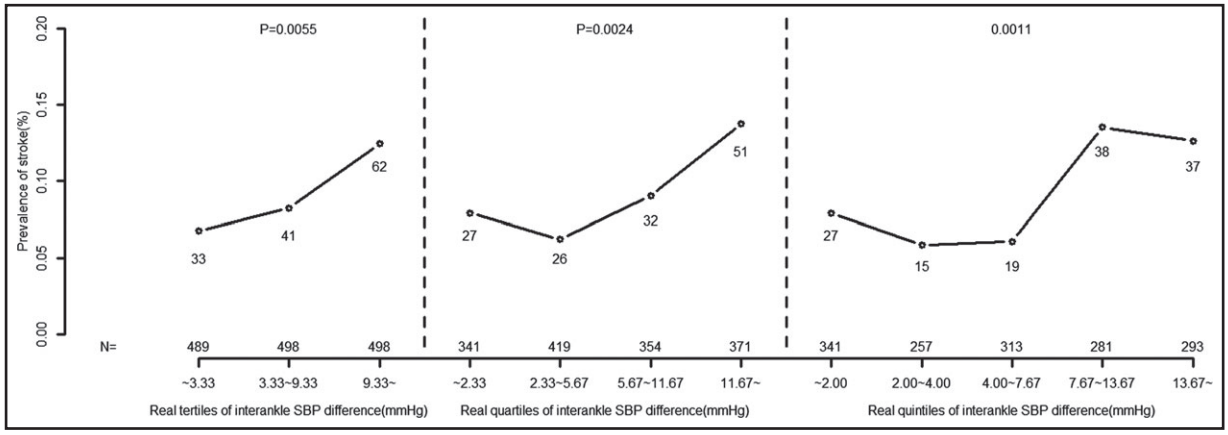

FIGURE 1. Prevalence of stroke stratified according to tertiles/quartiles/quintiles of the distribution of interankle systolic blood pressure (SBP) difference.

[95% CI, 1.18–2.53], *P*<.01). In addition, age, hypertension or SBP, and family history of stroke were independently associated with stroke (*P*<.001, *P*<.001/*P*=.0104, *P*=.0066/*P*=.0032, for models 1/2, respectively) (Figure 2).

The prevalence of the ≥7-mm Hg interankle SBP difference was 43.1%. The differences between participants with and without an interankle SBP difference ≥7 mm Hg are presented in Table II. Compared with patients with an interankle SBP difference <7 mm Hg, those with an interankle SBP difference ≥7 mm Hg were found to be older (*P*<.0001) and to have higher values of BMI (*P*<.0001), SBP (*P*<.0001), DBP (*P*=.0003), TC (*P*=.0053), and LDL-C (*P*=.0032). In addition, participants with an interankle SBP difference ≥7 mm Hg had a higher prevalence of stroke (*P*<.0001), hypertension (*P*<.0001), and use of antihypertensive drugs (*P*<.0001).

We assessed discrimination and reclassification to evaluate the contribution of an interankle BP difference ≥7 mm Hg to the prediction of stroke risk. The incremental value of the interankle BP difference ≥7 mm Hg is shown in Figure 3. The ROC_{AUC} was 0.7786 (95% CI, 0.74–0.81) for the model incorporating the independent risk factors alone and 0.7926 (95% CI, 0.76–0.83) when both independent risk factors and interankle BP difference ≥7 mm Hg were included (DeLong method,[24] *P*=.0073). When including the interankle SBP difference in the ROC analysis, the result of ROC_{AUC} was 1.4% higher than the ROC_{AUC} of the curve without interankle SBP difference. These two curves include only risk factors for stroke; protective factors were not included.

NRI analyses were undertaken to further establish whether the addition of an interankle SBP difference ≥7 mm Hg to the factors independently associated with stroke (identified in the logistic regression analysis) would improve the prediction of stroke prevalence. The results of this analysis are presented in Table III. When the interankle SBP difference (≥7 vs <7 mm Hg) was used in addition to the other variables, 27.9% of participants with stroke were correctly reclassified to a higher risk category, and none were incorrectly reclassified to a lower risk category. Similarly, when the interankle SBP difference was used, 9.5% of participants without stroke were incorrectly moved up to a higher risk category. These reclassification rates gave an estimated NRI of 18.5% (95% CI, 10.8–26.2; *P*<.001). Thus, the addition of interankle SBP difference ≥7 mm Hg may improve the prediction of stroke history by the combination of independent risk factors (age, family history of stroke, and SBP).

DISCUSSION

The aim of the present study was to evaluate the association between a history of stroke and interankle SBP difference obtained from simultaneous four-limb BP measurements. The major finding was that an interankle BP difference ≥7 mmHg was an independent marker of stroke history in Chinese adults. In addition, a new model integrating interankle SBP difference ≥7 mm Hg with traditional risk factors of stroke had a higher predictive accuracy for history of stroke and allowed the reclassification of participants with stroke from a lower to higher pretest likelihood of stroke.

To our knowledge, this study is the first population-based cross-sectional observational study of the association between interankle SBP difference and stroke. Some studies have demonstrated that the ankle SBP difference is a useful BP index. Increased ankle BP difference is a marker of arterial stiffness or subclinical atherosclerosis and an independent risk marker for future dementia and cardiovascular morbidity and mortality.[5–7,25] An interankle SBP difference ≥15 mm Hg may provide additional information for identifying patients with peripheral vascular disease and increased left ventricular mass index. An interankle SBP difference ≥10 mm Hg may predict elderly death.[5] Various cutoff values were used and have been

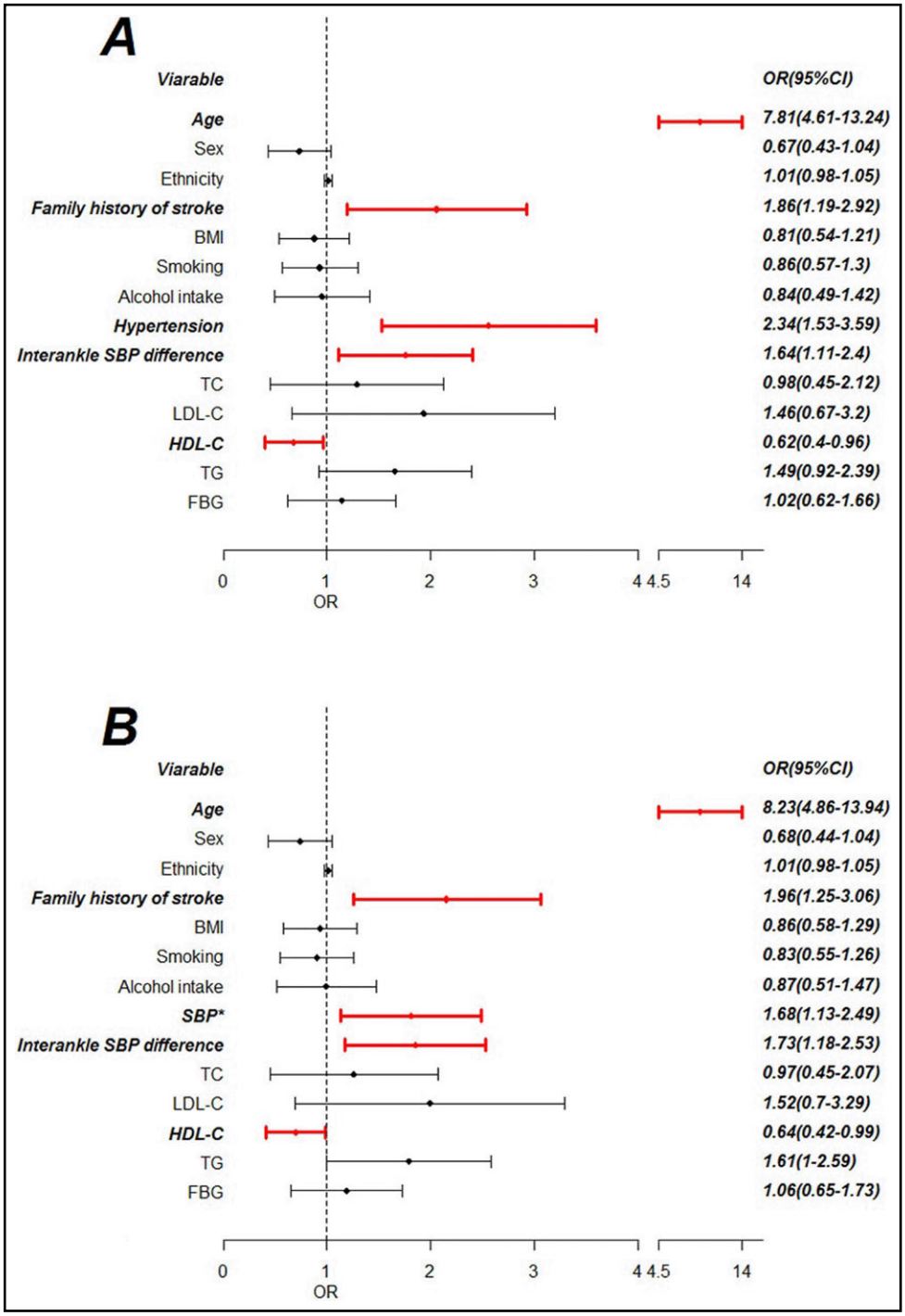

FIGURE 2. Multivariate logistic regression analysis of interankle systolic blood pressure (SBP) difference ≥7 mm Hg and other factors associated with the prevalence of stroke. The variables included in both models were sex (0, female; 1, male), age (0, 35–55 years; 1, >55 years), ethnicity (0, Han; 1, Manchu), smoking (1, smoking every day for more than 1 year; 0, otherwise), alcohol intake (1, once at least every day; 0, otherwise), body mass index (BMI) (0, <24 kg/m^2; 1, ≥24 kg/m^2), interankle SBP difference (0, <7 mm Hg; 1, ≥7 mm Hg), triglycerides (TG) (1, ≥5.21 mmol/L; 0, otherwise), total cholesterol (TC) (1,≥1.7 mmol/L; 0, otherwise), low-density lipoprotein cholesterol (LDL-C) (1, l≥3.3 mmol/L; 0, otherwise), high-density lipoprotein cholesterol (HDL-C) (0, <0.9 mmol/L; 1, otherwise), fasting blood glucose (FBG) (1, ≥6.0 mmol/L; 0, otherwise). (a) Adjusted covariables with P<.05 in the univariate analysis and other well-documented risk factors for stroke (smoking status, alcohol intake, and family history of stroke) were introduced into the multiple logistic regression model. Hypertension (1, SBP ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive drugs; 0, otherwise) was included in this model. (b) Adjusted covariables with SBP instead of hypertension were introduced into the multiple logistic regression models. SBP (1, ≥140 mm Hg; 0, otherwise) was included in this model.

TABLE II. Comparison of Baseline Characteristics According to Interankle SBP Difference ≥7 or <7 mm Hg

Variable	All (N=1485)	<7 mm Hg (n=845)	≥7 mm Hg (n=640)	*P* Value
Age, mean±SD, y	54.8±11.5	54.0±11.1	55.8±11.9	.0029
Manchu ethnicity, No. (%)	746 (50.2)	417 (49.4)	329 (51.4)	.4324
BMI, mean±SD, kg/m^2	24.7±3.7	24.5±3.5	24.9±3.9	.0472
Use of antihypertensive drugs, No. (%)	265 (17.9)	123 (14. 6)	142 (22.2)	<.0001
Stroke, No. (%)	136 (9.2)	55 (6.5)	81 (12.7)	<.0001
Hypertension, No. (%)	621 (41.8)	298 (35.3)	323 (50.5)	<.0001
Family history of stroke, No. (%)	333 (22.4)	177 (21.0)	156 (24.4)	.1167
Diabetes mellitus, No. (%)	208 (14.0)	107 (12.7)	101 (15. 8)	.0864
SBP on higher arm side, mean±SD, mm Hg	133.1±20.4	130.2±18.8	137.0±21.8	<.0001
DBP on higher arm side, mean±SD, mm Hg	81.2±10.5	80.3±10.3	82.3±10.5	.0003
SBP on higher ankle side, mean±SD, mm Hg	162.6±24.2	157.2±23.1	169.8±23.7	<.0001
DBP on higher ankle side, mean±SD, mm Hg	80.0±10.8	79.0±10.9	81.4±10.5	<.0001
Interankle SBP, median (IQR), mm Hg	5.7 (2.3–12)	2.7 (1.3–4.7)	13.2 (9.3–19.7)	<.0001
FBG, median (IQR), mmol/L	5.2 (4.89–5.66)	5.2 (4.87–5.60)	5.21 (4.90–5.74)	.0540
TC, mean±SD, mmol/L	4.92±0.97	4.86±0.96	5.00±0.98	.0053
HDL-C, mean±SD, mmol/L	1.48±0.35	1.49±0.36	1.46±0.34	.176
LDL-C, mean±SD, mmol/L	2.86±0.82	2.80±0.79	2.93±0.85	.0032
TG, mean±SD, mmol/L	1.30±0.86	1.27±0.87	1.35±0.86	.0633

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides.

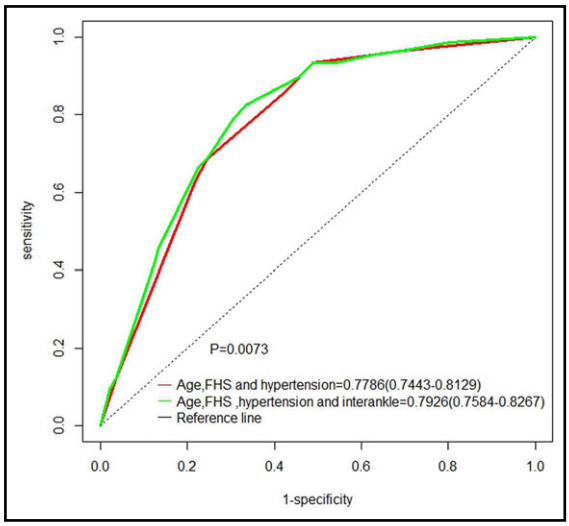

FIGURE 3. Incremental prognostic value of an interankle systolic blood pressure (SBP) difference ≥7 mm Hg for stroke. The red line represents the area under the receiver operating characteristic (ROC_{AUC}) curve estimated for a regression model with independent risk factors for stroke (age, family history of stroke [FHS], and hypertension), and the green line represents ROC_{AUC} estimated for a model consisting of the same factors plus interankle SBP difference ≥7 mm Hg as a categorical variable, both in relation to a dichotomous outcome of history of stroke (with vs without).

suggested by different studies of different populations[5,21]; thus, there is no consensus on the threshold value for elevated interankle SBP difference. One reason is that different dysfunctional cardiovascular statuses probably have different threshold values of interankle SBP difference. Another reason is variations in study population such as hemodialysis patients or community population.[21,26] It is necessary to confirm whether different values of interankle SBP difference may have different clinical significance. The present study strongly suggests that an interankle SBP difference cutoff value of ≥7 mm Hg was superior to ABI <0.9 for history of stroke.

The prevalence of interankle SBP difference ≥7 mm Hg was 43.1% in Chinese adults aged 35 years and older, with no significant difference between women and men (43.2% vs 43.1%). In the present study, 59.6% of participants with an interankle SBP difference ≥7 mm Hg had a history of stroke. Participants with an interankle SBP difference ≥7 mm Hg had a significantly higher prevalence of stroke history than those with an interankle SBP difference <7 mm Hg (59.6% vs 41.4%). Using multivariable analysis adjusted for other traditional confounding factors, we confirmed that an interankle SBP difference ≥7 mm Hg was an independent marker for a history of stroke in Chinese adults. In addition, traditional stroke risk factors such as age, family history of stroke, and hypertension or SBP remained significantly associated with history of stroke even after including elevated interankle SBP difference in the model.

A recent study showed that interankle SBP difference remained an independent marker for overall and cardiovascular mortality after further adjustment for atherosclerosis.[21] Hence, it may be hypothesized that some mechanisms other than atherosclerosis may be responsible for the association between interankle SBP

TABLE III. NRI by Adding Interankle SBP Difference to the Risk Factors Independently Associated With Stroke

	Reclassified Predicted Risk (With IΔSBP)		Reclassified, %		
Predicted risk (without IΔSBP)	<20%	≥20%	Increased risk	Decreased risk	Net correctly Reclassified
With stroke (n=136)					
<20%	84	38	27.9%	0%	27.9%
≥20%	0	14	(38)	(0)	
Without stroke (n=1349)					
<20%	1182	128	9.5%	0%	9.5%
≥20%	0	39	(128)	(0)	
NRI (95% CI)	18.5 (10.8–26.2), *P*<.001				

Abbreviations: CI, confidence interval; IΔSBP, interankle systolic blood pressure (SBP) difference; NRI, net reclassification improvement. The risk factors independently associated with stroke were age, family history of stroke, and SBP.

difference and adverse outcomes.[8] Current clinical evaluations of stroke risk such as BP, lipid levels, FBG levels, and even ankle-brachial BP index provide limited insight into relevant abnormal mechanisms for a particular patient.[22] We may acquire a better understanding of the mechanism of stroke after thoroughly studying the underlying pathophysiology of elevated interankle SBP difference. Nevertheless, additional studies are still necessary to examine the value and reliability of interankle SBP difference since there is a possibility that pressure may be modified by muscle atrophy or muscle stiffening in the leg affected by stroke. In the present study, there was no difference between stroke with normal limbs and stroke with hemiplegic limbs, but the sample size was small. In patients with hemiplegic stroke, it has been suggested that BP should be measured in the unaffected arm,[27] but this is controversial since some studies reported higher[28,29] or lower[30,31] BP in the affected arm.

The estimation of cardiovascular risk is a key element of current primary prevention strategies, despite its limited accuracy. An important observation of the present study is that the addition of an interankle SBP difference ≥7 mm Hg to the traditional risk factors for stroke (age, family history of stroke, and hypertension or SBP) had a higher predictive accuracy for stroke and improved the prediction of stroke history. An interankle SBP difference ≥7 mm Hg tended to appropriately reclassify the participants with stroke from a lower to higher risk strata. Our findings suggest that the currently used risk assessment tools underestimate the prevalence of stroke. However, the above finding warrants further confirmation.

During the past 40 years, global stroke incidence rates have fallen by 42% in developed countries but have increased by >100% in undeveloped and developing countries.[32] A high incidence and low mortality will result in high prevalence. In China, most of the epidemiological studies on cerebrovascular diseases revealed geographic variations. For instance, the highest incidence was found in Northeast China (441–486/100,000), while the lowest incidence was found in Southern China (81–136/100,000).[33,34] A study carried out between January 2012 and August 2013 using a representative sample of people aged 35 years and older from rural areas of the Liaoning Province (Northeast China) showed that the prevalence of stroke was 8.9% and that about 18% of the hypertensive patients had a history of stroke.[35] These findings are in agreement with our results. The present study was performed in the rural area of the Heilongjiang Province (Northeast China), where the winter is very cold and where the residents have several specific life habits including a high-salt and high-fat diet and low level of physical activity. Heilongjiang is a Chinese province with a high prevalence of hypertension (about 28.9%). Hypertension is a major independent risk factor for stroke, which may explain, at least in part, the high prevalence of stroke in Heilongjiang Province. Another possible reason for the high prevalence of stroke history is that the present study included patients with TIA.

STUDY LIMITATIONS

The present study is not without limitations. First, this study focused on SBP rather than DBP. In hypertension, SBP is more often increased than DBP.[6,11,25] Therefore, using DBP could lead to some underestimation. Second, because of the cross-sectional design, FBG was measured only once and the risk of underestimating the prevalence of diabetes had to be considered. Hence, diabetes mellitus was excluded from the multivariate logistic regression analyses. In addition, a cross-sectional study cannot be used to determine causality. Third, a survival selection bias may have influenced our observations and conclusions since we analyzed only patients who were still alive after their stroke. Fourth, the history of stroke was based on self-reported data, which may lead to underestimation of the real prevalence of stroke, especially for TIA without imaging features. Finally, a number of genetic variations are known to be associated with hypertension such as CaMK4,[36] PlA2,[37,38] and GRKs,[39] but these

polymorphisms were not assessed in the present study. It is our intention to follow up with the participants of this cohort and explore whether the interankle SBP difference can predict the incidence of stroke. Nonetheless, large-scale prospective studies are needed to confirm and extend these findings.

CONCLUSIONS

An interankle SBP difference ≥7 mm Hg could be an independent marker of stoke history in Chinese adults. The addition of interankle SBP difference ≥7 mm Hg to the traditional risk factors of stroke may improve the prediction of stroke.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Sex-stratified baseline characteristics of the study population

Table S2. Comparison of interarm and interankle SBP differences between stroke patients with normal limbs and hemiplegic limbs

Figure S1. Receiver operating characteristic curve analysis to determine the optimal cutoff value of interankle systolic blood pressure (SBP) difference for the prediction of stroke.

Figure S2. Receiver operating characteristic curve analysis to compare interankle systolic blood pressure (SBP) difference in the diagnosis of stroke to make the comparison fair. ABI indicates ankle-brachial index.