Blood Pressure, Carotid Flow Pulsatility, and the Risk of Stroke
A Community-Based Study

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Background and Purpose—High blood pressure is a major cause of cardiovascular events, and carotid flow pulsatility may be associated with cardiovascular events. However, the combined effect of blood pressure and flow pulsatility on the development of stroke remains unclear. Therefore, we investigated the combined influence of central blood pressure and pulsatility index (PI) on the incidence of stroke.

Methods—Baseline data from 2033 adults (≥30 years) without stroke history in the Cardiovascular Disease Risk Factor Two-Township Study were linked to incident stroke. Common carotid flow PI was calculated by peak systolic velocity, end-diastolic velocity, and mean vessel velocity, which were measured in the common carotid artery. Hazard ratios for the risk of total stroke resulting from high central systolic blood pressure (CSBP) and high PI were calculated with Cox proportional hazard models.

Results—Over a median follow-up of 9.81 years, 132 people incurred stroke events. The incidence rates of stroke were 1.3, 6.4, and 13.2 per 1000 person-years for tertile groups of CSBP (*P* for trend<0.05) and 4.3, 7.0, and 9.4 per 1000 person-years for tertile groups of PI (*P* for trend<0.05). Compared with the first tertile of CSBP, hazard ratios were 4.88 (95% confidence interval, 2.29–10.43) for the second tertile and 10.42 (5.05–21.53) for the third tertile. Hazard ratios of PI were 2.18 (1.39–3.42; third tertile) and 1.64 (1.02–2.63; second tertile) compared with the first tertile. The individuals with a high CSBP and high PI had a 13-fold higher stroke risk compared with those with low CSBP and low PI (13.2; 1.75–99.71) after adjusting for age, sex, and traditional cardiovascular risk.

Conclusions—CSBP and common carotid PI jointly and independently predicted future stroke. Carotid flow pulsatility may play an important role in the development of stroke. (***Stroke***. 2016;47:2262-2268. DOI: 10.1161/STROKEAHA.116.013207.)

Key Words: adult ■ blood pressure ■ prospective studies ■ risk factors ■ stroke

Although there has been a significantly decreased trend of stroke mortality over the past few decades,[1] stroke is still one of the leading causes of death in East Asian[2] and the United States.[1] Stroke occurrence is increasing because of the growing proportion of the aged population worldwide.[1] Elevated blood pressure is one of the major and modifiable risk factors for stroke onset.[2] Recent studies[3–5] have reported that central blood pressure is more effective than brachial pressure for predicting cardiovascular events. The Strong Heart Study[3] revealed that central pressure is more strongly related to vascular outcome than brachial pressure among disease-free individuals. Moreover, an unselected geriatric population[4] in Italy demonstrated the superior prognostic use of central compared with brachial blood pressure. Furthermore, a community-based and prospective study[5] with ethnic Chinese

observed that central systolic blood pressure (CSBP) is more valuable than peripheral blood pressure for predicting cardiovascular mortality.

Flow velocity, obtained by Doppler sonography, has been demonstrated to have prognostic value.[6] Low carotid flow end-diastolic velocity (EDV) is associated with an increased risk of stroke[6] and significantly increases the prediction of cardiovascular events.[7] The carotid flow pulsatility, calculated from the difference between peak systolic velocity (PSV) and EDV divided by the mean flow velocity, reflects the transmission of pulsatile energy into the cerebral microcirculation. High pulsatile flow may cause brain microbleeds and lacunar infarcts.[8] Most studies have investigated the association between carotid flow pulsatility and cerebrovascular disease in a cross-sectional design[9] or in high-risk groups.[10,11] Few studies have

investigated the carotid flow pulsatility and stroke occurrence in the general population.

Therefore, we aimed to investigate the relationship between carotid flow pulsatility and stroke occurrence and further investigated the effect of combined carotid flow pulsatility and CSBP for stroke risk in a prospective study with the general population.

Methods

Study Population

The CVDFACTS (Cardiovascular Disease Risk Factors Two-Township Study) is a community-based follow-up study focusing on risk factor evaluation and cardiovascular disease development in Taiwan. From 1991 to 1993, all residents >3 years old who were listed in the household registries of 5 villages in Zhudong Township and another 5 villages in Puzi Township were invited to participate in the baseline examination. A total of 5146 residents aged 30 years and older participated in the cycle-3 examination (1994–1996), in which biochemical data were collected; 3146 of these individuals also participated in the cycle-4 examination (1997–1999), in which carotid artery ultrasonographic measurements were performed. All participants were covered by Taiwan's National Health Insurance Program.

Sampling and data collection were as described elsewhere.[12] Of these study subjects, 30 subjects had stroke history and 1083 subjects had missing flow (mL/min) information; we therefore did not incorporate these individuals. Thus, a total of 2,033 subjects constituted the present study population. Those subjects without and with flow (mL/min) information had no difference in age (55.7 versus 55.9 years; P=0.72) and central systolic blood (115.1 versus 115.9 mm Hg; P=0.21), but those without flow information had significant and slightly higher central diastolic blood pressure (73.6 versus 70.5 mm Hg; P<0.001) and slightly lower PSV (66.8 versus 71.5 cm/s; P<0.001) and EDV (18.6 versus 21.4 cm/s; P<0.001). All participants gave informed consent at baseline and at follow-up.

Measurement and Definition of Variables

Central blood pressure was obtained with a SphygmoCor device (AtCor Medical, Sydney, Australia) using radial arterial pressure waveforms and a validated generalized transfer function, according to the manufacturer's instructions.[13] Hypertension was defined as peripheral systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg at a seating position and after 5 minutes resting or using antihypertensive agents. Studies reported that vessel flow velocity was influenced by hypertensive medicine, propranolol[14]; we therefore used the electric medicine recorders to identify the exposure of antihypertensive drugs, including angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, α-blocker, β-blocker, calcium-channel blocker, and diuretics. Diabetes mellitus was defined as fasting glucose >126 mg/dL or using antiglucose medicine. Family history of cardiovascular disease was according to the self-reported questionnaire of parents' history of heart disease or stroke. Alcohol drinking and smoking habits were collected by structural questionnaire and face-to-face interview.

Quantitative Ultrasonography

Phased-arrayed ultrasonography was performed during the cycle-4 examination using a color-coded and duplex Doppler ultrasonographic system (SONOs 1000; Hewlett-Packard) with a transducer frequency of 7.5 MHz and color Doppler frequency of 5.4 MHz. The assessments were performed with the participants in the supine position, with the head turned and the neck immobile. All ultrasonic readings were evaluated and appraised by a technician who had no knowledge of the patient profiles. A standardized protocol, modified from Howard et al,[15] was used for B-mode image analysis.

Color-coded duplex ultrasound was used to determine the thickness of the intima-media complex. The artery was continuously imaged by pushing the transducer slowly along the course of the vessel in all segments. For plaque identification in all segments, vessel diameter and plaque thickness in both far and near walls were plotted and recorded; the value was the average of 2 measurements. In all subjects, the measurements of intima-media thickness (IMT) were made within a 1-cm-long smooth, plaque-free portion of the far wall of the common carotid artery (CCA) in the longitudinal plane, proximal to the carotid bulb. Near-and far-wall IMT was measured at 2 points on each side of the CCA. The IMT was defined as the distance between the intima-blood interface and the adventitia-media junction in the diastolic cardiac cycle. Plaque was defined as a localized wall thickening at least twice the thickness of the adjacent IMT. For each measurement, the image was frozen and a single measurement was made with electronic calipers. The image was then unfrozen, the IMT was relocated, and another measurement was made. The magnification of the ultrasound image was used to improve the accuracy of caliper placement if necessary. In the case of an unusually continuous plaque along the whole 1-cm length, the IMT in the least-affected portion was chosen. The 2 measurements on each side were averaged; the subject's IMT was defined as the larger of the 2 averaged measurements. The correlation coefficient between repeated measurements was 0.872 in the right CCA and 0.871 in the left CCA (n=43).

For Doppler spectral analysis, PSV and EDV were measured by continuous-wave Doppler examination in the internal carotid artery proximity and distally, as well as in the CCA 2 to 4 cm proximal to the bifurcation. For all participants, the scan head was applied longitudinally for at least 3 cardiac cycles for blood flow velocity measurements. Because of the consequence of initial forward flow, the highest velocity during systole was identified as the PSV, and the lowest velocity during diastole was used as the EDV. The highest value of the minimum of 3 measurements was recorded. Pulsatility index (PI) was as the difference between PSV and EDV divided by mean flow velocity.

Ascertainment of Stroke

To identify individuals who had a stroke event during the follow-up period, we used either the death registry database or the *International Classification of Diseases*, Ninth edition, codes 430 to 438 (cerebrovascular disease). For each of these subjects, we generated a time-sequenced electronic medical record by medical claim data and death, and we defined stroke occurrence and onset. Finally, we identified the occurrence of ischemic stroke using the *International Classification of Diseases* codes and the prescription of ischemic stroke drugs.

Statistical Methods

We used survival analysis to evaluate the associations of central blood pressure and blood flow with stroke. Survival time was calculated from the date of ultrasound/central blood pressure measurement to the onset of stroke, date of death, or the end of follow-up. The Kaplan–Meier method was used to estimate survival curves, and the log-rank test was used to examine the equality among survival curves. The Cox proportional hazard model was used to estimate the hazard ratio and 95% confidence interval. All statistics were calculated using SAS version 9.3 software.

Results

Incidence of Stroke Events and Mortality

There were 132 stroke events with 5 stroke deaths (72 men and 60 women) among the 2033 participants (who were ≥30 years old on enrollment) from 1997 to 2007 (median, 9.81 years; Table 1). Of them (n=132), the subtypes of stroke were 82.5% for ischemic (n=109), 13.6% for hemorrhagic (n=18), and 3.1% for subarachnoid hemorrhage (n=5). The incidence of stroke was 6.86 per 1000 person-years (PYs). Men had a higher risk of stroke than women (8.41 versus 5.63 per 1000 PYs; P=0.0232).

Characteristics of Subjects With Higher Carotid Flow Pulsatility

Subjects were classified into tertile groups by PI. The adults with higher carotid flow pulsatility had significantly higher

Table 1.   Characteristics of Study Individuals

Baseline Variables	Nonstroke (n=1901; 93.51%)		Stroke (n=132; 6.49%)		*P* Value
Age, y	55.2	12.0	66.2	8.6	<0.0001
Men, n (%)	844	44.4	72	54.6	0.0235
Waist circumference, cm	80.3	9.2	84.6	9.7	<0.0001
Body mass index, kg/m²	24.6	3.3	25.5	3.3	0.0019
Total cholesterol, mg/dL	194.2	40.7	198.0	39.7	0.3334
HDL cholesterol, mg/dL	48.4	15.7	46.0	29.2	0.1440
LDL cholesterol, mg/dL	120.9	37.7	128.1	37.4	0.0543
Triglycerides, mg/dL	127.4	90.2	139.1	73.4	0.1157
Fasting glucose, mg/dL	101.4	26.4	108.5	35.1	0.0083
Peripheral SBP, mm Hg	125.3	19.2	141.6	19.5	<0.0001
Peripheral DBP, mm Hg	68.2	10.9	73.3	11.2	<0.0001
Central SBP, mm Hg	114.9	18.5	130.2	19.3	<0.0001
Central DBP, mm Hg	70.2	11.0	75.4	11.5	<0.0001
Pressure pulsatility index	0.53	0.13	0.59	0.15	<0.0001
Peak systolic velocity, cm/s	71.9	15.7	67.4	14.0	0.0016
End-diastolic velocity, cm/s	21.6	6.1	17.6	5.0	<0.0001
Velocity pulsatility index	1.5	0.4	1.6	0.4	<0.0001
Intima-media thickness, mm	0.55	0.16	0.64	0.18	<0.0001
Hypertension, %	29.7		62.1		<0.0001
Diabetes mellitus, %	6.94		19.70		<0.0001
Alcohol drinking, %	9.89		6.82		0.2487
Smoking, %	19.36		24.24		0.1723
Family history for CVD, %*	11.15		17.42		0.0293
Hypertension medicine, %					
ACEI or ARB	3.89		6.82		0.1087†
α-blocker	1.05		3.79		0.0198†
β-blocker	4.10		8.33		0.0428†
Calcium-channel blocker	6.84		15.91		<0.0001†
Diuretics	2.58		5.30		0.0889†

ACEI indicates angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blockers; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and SBP, systolic blood pressure.

*CVD included heart disease and stroke.

†Fisher exact test.

peripheral and central systolic but not diastolic blood pressure in comparison with adults with low pulsatility. Those adults with higher carotid pulsatility were older age, larger waist circumference, higher fasting glucose, lower high-density lipoprotein cholesterol, and higher proportion of angiotensin-converting enzyme inhibitors or angiotensin receptor blocker and calcium-channel blocker (Table 2).

Association of Carotid Flow and Stroke
Carotid flow pulsatility was positively associated with the development of stroke. The incidence of stroke in subjects in the lowest, middle, and highest tertile groups of pulsatility was 4.3, 7.0, and 9.4 per 1000 PYs, respectively (*P* for trend<0.001; Table 3). As compared with the lowest tertile

group of pulsatility, the hazard ratio of stroke was 1.64 (95% confidence interval, 1.02–2.63) for the middle group and 2.18 (1.39–3.42) for the highest group of carotid flow pulsatility.

The risk of stroke was also dramatically increased by CSBP. The stroke incidence rate was only 1.3 per 1000 PYs for those with CSBP of <106 (mm Hg; the lowest tertile), then increased to 6.4 per 1000 PYs for CSBP in the middle tertile (106–122 mm Hg), and reached 13.2 per 1000 PYs for those with a CSBP of >122 (mm Hg; the highest tertile). Compared with the lowest CSBP tertile, the hazard ratio of stroke was 4.88 (95% confidence interval, 2.29–10.43) for the middle group and was 10.42 (95% confidence interval, 5.05–21.53) for the highest tertile.

Table 2.   Characteristics of Study Population, Stratified by Carotid Flow Pulsatility

	Pulsatility Index			
	<1.32 (n=682; 33.11%)	1.32–1.60 (n=673; 33.59%)	>1.60 (n=678; 33.30%)	P Value
Age, y	54.5±10.9	56.6±11.8*	56.5±13.4*	0.0021
Men, n (%)	159 (23.3)	293 (43.54)*	464 (68.44%)	<0.0001
Waist circumference, cm	78.5±8.9	80.3±9.3*	83.1±9.2	<0.0001
Body mass index, kg/m^2	24.6±3.3	24.5±3.4	24.7±3.2	0.1355
Total cholesterol, mg/dL	196.2±40.4	193.2±43.2	193.8±38.1	0.4319
HDL cholesterol, mg/dL	50.0±15.8	49.1±20.0	45.8±14.1	<0.0001
LDL cholesterol, mg/dL	121.5±38.2	121.0±39.4	121.6±35.6	0.9640
Triglycerides, mg/dL	125.3±85.8	125.0±88.5	133.9±93.1	0.1702
Fasting glucose, mg/dL	100.7±25.0	100.7±26.6	104.1±29.3	0.0573
Peripheral SBP, mm Hg	123.3±18.6	127.0±20.2*	129.3±20.0*	<0.0001
Peripheral DBP, mm Hg	68.1±11.1	69.2±11.3	68.2±10.5	0.1038
Central SBP, mm Hg	114.2±18.1	116.9±19.7*	116.7±18.9*	0.0121
Central DBP, mm Hg	70.1±11.3	71.3±11.5	70.2±10.6	0.0963
Pressure pulsatility index	0.52±0.12	0.53±0.12	0.54±0.14	0.0075
Peak systolic velocity, cm/s	66.8±13.0	70.4±14.4*	77.6±17.4	<0.0001
End-diastolic velocity, cm/s	24.4±6.3	21.1±5.1*	18.4±5.3	<0.0001
Velocity pulsatility index	1.15±0.13	1.44±0.08*	1.90±0.29	<0.0001
Intima-media thickness, mm	0.53±0.16	0.56±0.16*	0.58±0.17	<0.0001
Hypertension, %	29.47	38.34	41.45	<0.0001
Diabetes mellitus, %	5.87	6.69	10.77	0.0015
Alcohol drinking, %	7.48	8.17	13.42	0.0003
Smoking, %	13.34	18.42	27.29	<0.0001
Family history for CVD,%*	10.85	12.04	11.80	0.7770
Hypertension medicine, %				
ACEI or ARB	2.64	4.31	5.31*	0.0424
α-blocker	0.73	1.19	1.77	0.2206
β-blocker	3.37	5.50	4.28	0.1588
Calcium-channel blocker	5.43	8.02	8.85*	0.0425
Diuretics	2.79	2.53	2.95	0.8912

ACEI indicates angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blockers; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and SBP, systolic blood pressure.

*P<0.05 when compared with the reference group with the lowest pulsatility index of carotid velocity.

†P<0.05 when compared with the reference group with a pulsatility index of carotid velocity between 1.32 and 1.60.

We further evaluated the combined effect of the CSBP and carotid flow pulsatility for stroke risk. We found a significant joint effect of CSBP and carotid flow pulsatility for stroke risk. The subjects with the lowest CSBP (<106 mm Hg) and lowest PI (<1.32) had the lowest stroke incidence (0.84 per 1000 PYs), and the subjects with the highest CSBP (>122 mm Hg) and the highest PI (>1.60) had the highest stroke incidence (19.77 per 1000 PYs) (Figure; Table 4). Furthermore, the trend of the effect was significant and consistent in the 3 groups when stratified by CSBP. This association remains significant in the multivariate model when controlling for traditional confounders (Table 4).

Discussion

Main Findings

This study demonstrated a significant relationship between common carotid flow pulsatility and stroke incidence among the general population in a community-based cohort. Most previous studies of patients with stroke investigated the association between flow pulsatility and cerebral disease.[10] No study has investigated the combined effect of CSBP and flow pulsatility for stroke. Our study revealed that CSBP and flow pulsatility independently predicted stroke occurrence, and the relationships of central blood pressure and flow pulsatility

Table 3. Incidence of Stroke by Central Blood Pressure and Carotid Velocity Pulsatility

	n	PYs	Events	Incidence	Crude Hazard Ratio (95% CI)
Central systolic blood pressure					
T1 (<106)	651	6370	8	1.3	Reference
T2 (106–122)	685	6489	40	6.4	4.88 (2.29–10.43)
T3 (>122)	697	6370	84	13.2	10.42 (5.05–21.53)
Carotid flow pulsatility index					
T1 (<1.32)	682	6539	28	4.3	Reference
T2 (1.32–1.60)	673	6392	45	7.0	1.64 (1.02–2.63)
T3 (>1.60)	678	6299	59	9.4	2.18 (1.39–3.42)

Pulsatility index = ([peak systolic velocity] − [end-diastolic velocity])/mean velocity. CI indicates confidence interval; and PYs, person-years.

were significantly observed. Even in the low CSBP group, the relationship remains noteworthy.

Central Blood Pressure Versus Stroke

Central pressure is better related to future cardiovascular events than is brachial pressure.[16] In the Strong Heart Study, central pressure was more strongly related to future cardiovascular events than brachial pressure in disease-free individuals.[3] Moreover, the Dicomano Study in Italy[4] and a community-based study in Taiwan[5] both observed a stronger association between central blood pressure and cardiovascular mortality than between peripheral blood pressure and cardiovascular mortality. Furthermore, a meta-analysis[17] reported that central blood pressure independently predicts cardiovascular events. Further study[18] indicated that central blood pressure is significantly associated with the presence of silent cerebral lacunar infarcts in an apparent general population. Our study also indicated that CSBP had a stronger correlation than peripheral blood pressure with stroke in a community-based population.

Flow Velocity Versus Stroke

Lower carotid flow velocity is associated with an increased risk of stroke and heart disease.[6,7,19] A cross-sectional case-controlled study showed that lower flow velocity (PSV and EDV) and higher resistive index are associated with an increased risk of ischemic stroke.[19] A prospective study further demonstrated that low EDV combined with higher IMT can predict the risk of ischemic stroke onset,[6] and recent results showed that EDV improves the prediction of cardiovascular disease.[7] Carotid flow velocity is a potential marker of intracranial resistance.[19] Moreover, a clinical trial[20] indicated that higher EDV could be a marker of reperfusion therapies for patients with proximal arterial occlusion. The above-mentioned studies indicate that flow velocity is not only a predictor of the risk of cardiovascular disease but also an index for treatment monitoring.

Pulsatility Versus Stroke

Previous studies investigating the association between carotid flow pulsatility and cardiovascular disease were of a cross-sectional design[9] or in high-risk populations, and results remain controversial. A cross-sectional study[9] of Australian women reported that the carotid flow PI is not independently associated with ischemic heart disease. The PI of middle cerebral arteries is correlated with intracranial carotid artery calcification[10] in consecutive patients with acute ischemic stroke or transient ischemic stroke. Moreover, the PI may be associated with particular types of stroke.

Among Japanese patients with stroke,[11] the carotid flow PI is a useful parameter for discriminating among ischemic stroke types. Moreover, a study[21] of stroke survivors reported that patients with lacunar stroke have significantly higher common carotid flow pulsatility than those with large-artery atherosclerosis or cryptogenic stroke. Few studies have investigated the association between the carotid flow PI and stroke in the general population. Our study, using a prospective design, demonstrated that the carotid flow PI significantly predicted the onset of stroke, independent of central blood pressure and other cardiovascular risk factors, in the general population.

Animal studies reported that antihypertensive agents influence the blood flow velocity in vessels[14] and were associated with development of atherosclerosis.[22,23] Propranolol, methyldopa, and clonidine decreased and hydralazine increased the mean blood velocity.[14] Our study demonstrated that angiotensin-converting enzyme inhibitors/angiotensin receptor blocker and calcium-channel blocker were positively
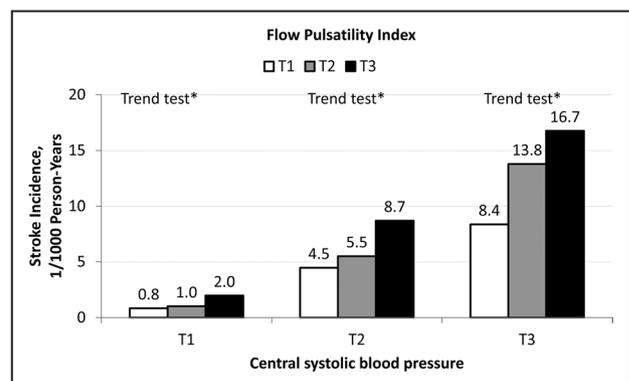

Figure. The stroke incidence in the combined group by tertiles of pulsatility index and tertiles of central systolic blood pressure. *Indicates *P*<0.05.

Table 4. Combined Association of Central Blood Pressure and Pulsatility Index for Stroke in the Multivariate Model

Central Systolic Blood Pressure, mm Hg	Carotid Flow Pulsatility Index	n	PYs	Events	Incidence	Crude Analysis	Model 1	Model 2	Model 3
T1 (<106)	T1 (<1.32)	243	2387	2	0.84	Reference	Reference	Reference	Reference
	T2 (1.32–1.60)	200	1963	2	1.02	1.21 (0.17–8.61)	2.56 (0.23–28.34)	2.54 (0.23–28.21)	2.50 (0.03–27.7)
	T3 (>1.60)	208	2020	4	1.98	2.36 (0.43–12.89)	4.92 (0.55–44.35)	4.89 (0.54–44.09)	4.92 (0.55–44.37)
T2 (106–122)	T1 (<1.32)	235	2241	10	4.46	5.31 (1.16–24.19)	5.79 (0.71–47.20)	5.76 (0.71–46.98)	5.72 (0.70–46.72)
	T2 (1.32–1.60)	228	2180	12	5.50	6.54 (1.46–29.19))	5.90 (0.73–47.50)	5.85 (0.73–47.13)	5.70 (0.71–45.92)
	T3 (>1.60)	222	2068	18	8.70	10.29 (2.39–44.34)	12.29 (1.61–93.96)	12.17 (1.59–93.17)	12.14 (1.59–92.93)
T3 (>122)	T1 (<1.32)	204	1911	16	8.37	9.95 (2.89–43.27)	8.52 (1.10–66.15)	8.43 (1.08–65.60)	8.25 (1.06–64.20)
	T2 (1.32–1.60)	245	2249	31	13.78	16.28 (3.90–68.01)	13.31 (1.78–99.56)	13.17 (1.76–98.66)	12.80 (1.71–95.91)
	T3 (>1.60)	248	2211	37	16.74	19.77 (4.77–81.98)	14.03 (1.87–105.5)	13.79 (1.83–104.17)	13.20 (1.75–99.71)

Multivariate model controlled baseline age (y), sex (men vs women), waist circumference (cm), fasting sugar (mg/dL), HDL cholesterol (mg/dL), total cholesterol (mg/dL), triglycerides (mg/dL), smoking habits, and drinking habits. Model 2 controlled for those covariates in model 1 and intima-media thickness. Model 3 controlled for those covariates in model 2 and antihypertensive agents and family history of cardiovascular disease. PYs indicates person-years.

associated with PI, but α-blocker, β-blocker, and diuretics were not. Moreover, the significant association between CSBP, pulsatility, and stroke incidence remains in the multivariate model with adjusting for traditional risk factors and antihypertensive agents.

Blood Pressure and Pulsatility Versus Stroke

A study by O'Rourke and Safar[8] suggested that brain microbleeds, white-matter hyperintensities, and lacunar infarcts are caused by the damaging forces of high pulsatile pressure and flow in cerebral micro vessels. Few prospective studies have investigated the combined effect of central blood pressure and flow pulsatility on the risk of stroke. In 1 such study, patients with lacunar stroke had higher common carotid flow pulsatility and central blood pressure than ischemic stroke with carotid pulsatility or with cryptogenic stroke.[21] This study suggests that increasing the transmission of pressure and flow pulsatility into the cerebral arterioles may contribute to the pathogenesis of lacunar stroke. Our study further supported this speculation that the combined effect of CSBP and flow pulsatility predicted stroke.

Carotid flow pulsatility was associated with risk factors for cardiovascular disease in our study. Higher flow pulsatility may indicate the incipient changes in arterial wall properties. Young obese subjects have a higher mean carotid PI than age-matched healthy controls.[24] Furthermore, among patients with acute ischemic stroke, the transcranial Doppler PI is significantly correlated with central aortic pressure, especially pulse pressure.[25] It has been suggested that arteries with high pulsatility are associated with stiffened arteries.[26] Our study also revealed that the carotid flow PI was positively associated with blood pressure, which was in line with findings of previous studies.[26,27] Additional studies have also demonstrated that intracranial pulsatility is positively associated with intracranial pressure and negatively associated with cerebral perfusion pressure.[26] Therefore, flow pulsatility may be mechanically involved in the occurrence of stroke events.

Limitations

We did not measure the artery stiffness in this population, so we did not control for the influence of artery stiffness on the association between carotid pulsatility and stroke. However, the central blood pressure has been highly associated with carotid–femoral pulse wave velocity. Although all ultrasonic readings were evaluated and appraised by an experienced technician, reproducibility data were not retained. Nonetheless, there was a significant association between the carotid flow PI and the occurrence of stroke. Another limitation is that we did not have any echocardiographic information, so we could not control for potential confounders related to cardiac function and structures. However, the study population consisted of subjects without known heart disease. In addition, this study was performed in Asian participants only; the findings should be confirmed in other ethnic groups.

Conclusions

CSBP and carotid flow PI jointly and independently predicted future incident stroke. Carotid flow pulsatility could be one of the causes of the development of stroke.

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