nature publishing group

Reference Values for the Arterial Pulse Wave in Chinese

Yan Li[1], Jan A. Staessen[2], L.H. Li[1], Q.F. Huang[1], Lu Lu[1] and J.G. Wang[1]

BACKGROUND
Pulse wave analysis using the SphygmoCor system allows the estimation of central pulse pressure (PP) and peripheral and central augmentation indexes (AIxs). We studied the limits of normality of these measurements in Chinese.

METHODS
We computed limits of normality as the 95% confidence boundaries from regression models relating the arterial indexes to age.

RESULTS
The reference population included 924 subjects (50.7% men, mean age 40.7 years) without overt cardiovascular disease. Men, compared to women, had higher peripheral (43.3 vs. 41.7 mm Hg; $P = 0.01$) and central (32.9 vs. 30.9 mm Hg; $P < 0.0001$) PPs, but lower peripheral (69.0 vs. 74.2%; $P < 0.0001$) and central (16.6 vs. 21.0%; $P < 0.0001$) AIxs. All arterial measurements showed a curvilinear relation with age. Both before and after adjustment for confounding factors, peripheral and central PPs increased less ($P \leq 0.01$) with age in men than in women, whereas the relation of peripheral and central AIxs with age was similar ($P \geq 0.13$) in both sexes. In 40-year-old Chinese, approximate thresholds for peripheral and central PPs, peripheral and central AIxs were 58 mm Hg, 48 mm Hg, 105% and 45%, respectively. Considering the age range from 20 to 60 years, thresholds varied within ~5 mm Hg, ~10 mm Hg, ~20%, and ~15% of the aforementioned thresholds for peripheral and central PPs, peripheral and central AIxs, respectively.

CONCLUSIONS
Pending further validation in prospective studies, our present study provides preliminary diagnostic thresholds for PP and AIxs in Chinese.

Am J Hypertens 2008; **21**:668-673 © 2008 American Journal of Hypertension, Ltd.

Over the past decades, O'Rourke and other investigators[1–4] developed a simple and reproducible method to assess various indexes of arterial function.[5,6] A validated algorithm permits transformation of the peripheral arterial to the central aortic waveform.[7–9] Analysis of the shape and timing of these waveforms allows measurement of central pulse pressure (PP) and central and peripheral augmentation indexes (AIxs). Recent studies established a strong and independent association of peripheral and central PPs and AIxs with cardiovascular events.[10–13] Assessment of these indexes will improve cardiovascular risk stratifications. Although the association between these arterial stiffness indexes and cardiovascular risk is probably continuous without a threshold at which the risk suddenly increases, clinicians need reference values to separate normal from abnormally elevated values to make clinical decisions.

Anthropometric characteristics, such as sex, age and body height, impact on the timing of the forward and reflected pulse waves and are therefore important determinants of AIxs.[14] Similarly, cardiovascular risk factors also influence the functional and structural properties of large arteries. Compared to western and African populations, Chinese, especially those living in rural areas, have a shorter stature, are less obese, and have lower cholesterol levels.[15–16] Because of these ethnic differences between populations, the recently proposed reference frames for central PP and AIxs in whites[17] and blacks[18] might not be applicable to Chinese. We therefore determined diagnostic thresholds for the aforementioned measurements of arterial function in a Chinese population without cardiovascular disease.

METHODS

Study population. In the framework of our ongoing Chinese study on genes in hypertension,[15,16] from 2003 through 2005, we recruited participants from 14 villages in the JingNing County, a rural area ~500 km south of Shanghai. The Ethics Committee of Ruijin Hospital and Shanghai Jiaotong University School of Medicine approved the study. We invited all villagers with a minimum age of 12 years to take part in this study. Of 2,059 eligible subjects, 1,486 gave informed written consent. The participation rate was therefore 72.2%. At the time of writing of this report, 1,438 participants had their pulse wave recorded.

We administered a standardized questionnaire to obtain information on each subject's medical history, smoking and drinking habits, and use of medications. Fasting venous blood

[1]Centre for Epidemiological Studies and Clinical Trials, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China; [2]The Studies Coordinating Centre, Division of Hypertension and Cardiovascular Rehabilitation, Department of Cardiovascular Diseases, University of Leuven, Leuven, Belgium. Correspondence: Ji-Guang Wang (jiguangwang@netscape.net)

Received 30 October 2007; first decision 29 November 2007; accepted 1 March 2008; advance online publication 10 April 2008. doi:10.1038/ajh.2008.151

was collected to measure the concentration of total cholesterol, blood glucose, and serum creatinine. Brachial (peripheral) blood pressure was the average of five consecutive readings measured by the mercury sphygmomanometer after the subjects had rested for at least 5 min at the sitting position. Hypertension was defined as a blood pressure of at least 140 mm Hg systolic or 90 mm Hg diastolic or the use of antihypertensive drugs. Using <25 kg/m^2, 25–30 kg/m^2 and ≥30 kg/m^2 as thresholds, we classified subjects into those with normal weight, overweight, and obesity. Diabetes mellitus was defined as a blood glucose concentration of at least 126 mg/dl fasting (96.1% of the study sample) or 200 mg/dl random (3.9%), or the use of antidiabetic drugs.[19] To generate a healthy adult population sample, we excluded 33 adolescents (age <18 years) and 481 participants because of hypertension (n = 349), diabetes (n = 9), obesity (n = 8), hypercholesterolemia (serum total cholesterol ≥240 mg/dl; n = 72), renal dysfunction (serum creatinine ≥2 mg/dl; n = 2), or self reported thyroid disease (n = 4), or because they had previous or concomitant cardiovascular diseases, such as coronary heart disease, heart failure, stroke, transient ischemic attack, or intermittent claudication (n = 37). The reference sample therefore included 924 subjects.

Arterial measurements. To ensure steady state, we performed the arterial measurements in a quiet room of a temporarily established examination center at each village. To avoid the circadian variation of pulse waveforms, one trained physician (Y.L.) performed all arterial measurements in the morning after subjects had rested for 15 min in the supine position. Subjects were asked to refrain from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for at least 2 h before the examination. During an 8-s period, she recorded the radial arterial waveform at the dominant arm by applanation tonometry. We used a high-fidelity SPC-301 micromanometer (Millar Instruments, Houston, TX) interfaced with a laptop computer running the SphygmoCor software, version 7.1 (AtCor Medical, West Ryde, New South Wales, Australia). Recordings were discarded when the systolic or diastolic variability of consecutive waveforms exceeded 5% or when the amplitude of the pulse wave signal was <80 mV. We calibrated the pulse wave by measuring the brachial blood pressure immediately before the SphygmoCor recordings, using the validated[20] OMRON 705CP oscillometric sphygmomanometer (Omron, Kyoto, Japan).

From the radial signal, the SphygmoCor software calculates the aortic pulse wave by means of a validated and population-based generalized transfer function.[7–9] The peripheral (radial) AIx was the ratio of the second to the first peak of the pressure wave expressed in percentage. The central (aortic) AIx was the difference between the second and first systolic peaks given as a percentage of the aortic PP. Peripheral and central PPs were defined as the difference between systolic and diastolic blood pressures derived from the brachial blood pressure measured at the subjects' homes and from the aortic pulse wave, respectively. By repeat examination of 16 subjects at a mean time interval of 1 h, we computed the coefficient of variation as the ratio of the mean difference between the two repeat measurements to the s.d. of the within-subject differences multiplied by 100.[21] The intra-observer coefficients of variability were 9.2 and 6.7% for the central and peripheral AIxs, respectively.

Statistical analysis. For database management and statistical analysis, we used SAS software, version 9.1 (SAS Institute, Cary, NC). The central tendency and the spread of the data are reported as the mean ± s.d. We evaluated departure from normality by Shapiro–Wilk's W statistic[22] and by the coefficient of skewness, i.e., the third moment about the mean divided by the cube of the standard deviation. We applied the normal distribution to determine the significance of the coefficient of skewness. We compared means, medians, and proportions by a large sample z-test, Wilcoxon's test, and the χ^2-statistic, respectively.

Our statistical methods also included single and multiple linear regressions. After stratification for sex, we standardized the arterial measurements to a pulse rate of 75 beats per min, which was approximately the mean in our Chinese reference populations. We applied the formula $A_s = A_o - b\,(PR_o - 75)$, where A_s is the standardized arterial measurements, A_o is the observed arterial measurements, b is the regression coefficient relating A_o to pulse rate, and PR_o is the observed pulse rate in each individual. To evaluate possible sex differences in the age dependency of the arterial measurements, we tested whether the interaction terms of sex with age and age squared significantly increased the explained variance after adjustment for confounding factors. We computed the limits of normality from the upper 95% confidence boundary of the prediction interval for individual values from regression models, relating the arterial indexes to the linear and squared terms of age. We rounded these limits to the closest integer value.

RESULTS

Characteristics of the participants

Our reference sample of 924 subjects included 456 women (49.4%). Age ranged from 18 to 83 years. Compared to women (P < 0.0001), men were on average 4.0 years older, had higher stature and body weight, higher serum total cholesterol, and higher levels of blood glucose and serum creatinine (**Table 1**). Among the 456 women, 70 (15.4%) reported natural or surgical menopause, and 15 (3.2%) reported the use of oral contraceptives.

Distribution of the arterial measurements

In all subjects, the distributions of peripheral and central PPs and peripheral AIx departed from normality and were positively skewed (P < 0.001). The coefficients of skewness were 0.46, 2.25, and 0.29, respectively. Central AIx was normally distributed (P = 1.0) with coefficients of skewness amounting to −0.40. **Figure 1** shows the distributions of these arterial measurements in our reference population. In all subjects, peripheral and central PPs averaged 42.5 mm Hg (95% confidence interval (CI), 41.9–43.1 mm Hg) and 31.9 mm Hg (CI, 31.2–32.5 mm Hg), respectively. Peripheral and central AIxs averaged 71.6% (CI, 70.2–72.9%) and 18.7% (CI, 17.8–19.7%), respectively (**Table 1**).

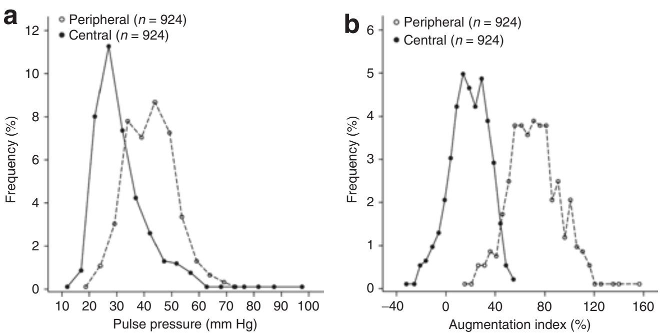

Figure 1 | The distribution of the peripheral and central pulse pressures (**a**) and the peripheral and central augmentation indexes (**b**) in 924 Chinese subjects.

Table 1 | Characteristics of the participants by sex

Characteristic	Men ($n = 468$)	Women ($n = 456$)	*P*
Anthropometric measurements			
Age (years)	42.7 ± 13.2	38.7 ± 11.6	<0.0001
Height (cm)	162.6 ± 6.5	153.0 ± 5.8	<0.0001
Weight (kg)	57.6 ± 7.5	51.8 ± 7.5	<0.0001
Body mass index (kg/m^2)	21.8 ± 2.3	22.1 ± 2.7	0.04
Lifestyle factors			
Current smoking, *n* (%)	316 (67.5)	0	<0.0001
Alcohol intake ≥ 5 g/week, *n* (%)	352 (75.2)	119 (26.1)	<0.0001
Biochemical measurements			
Total cholesterol (mg/dl)	180 ± 29	176 ± 29	0.02
Blood glucose (mg/dl)	77 ± 13	79 ± 10	0.003
Serum creatinine (mg/dl)	1.2 ± 0.2	1.0 ± 0.1	<0.0001
Peripheral arterial measurements			
Systolic pressure (mm Hg)	115.7 ± 10.9	112.1 ± 12.0	<0.0001
Diastolic pressure (mm Hg)	72.4 ± 8.4	70.4 ± 8.7	0.0004
Pulse pressure (mm Hg)	43.3 ± 9.2	41.7 ± 9.4	0.01
Augmentation index (%)	69.0 ± 21.1	74.2 ± 20.0	0.0001
Heart rate (beats per min)	71.8 ± 10.9	74.6 ± 10.3	<0.0001
Central arterial measurements			
Systolic pressure (mm Hg)	110.0 ± 16.7	105.6 ± 16.6	<0.0001
Diastolic pressure (mm Hg)	77.2 ± 9.3	74.7 ± 9.1	<0.0001
Pulse pressure (mm Hg)	32.9 ± 10.4	30.9 ± 10.1	0.003
Augmentation index (%)	16.6 ± 15.6	21.0 ± 14.4	<0.0001

Values are mean ± s.d. or numbers (%).

Arterial measurements in relation to sex and age

Tables 2 and 3 provide detailed statistics for peripheral and central PPs and for peripheral and central systolic AIxs by sex and age. Before 40 years of age, men had higher peripheral (42.8 vs. 39.9 mm Hg; $P = 0.0001$) and central (29.6 vs. 27.0 mm Hg; $P < 0.0001$) PPs than women. However, after 40 years, men and women had similar peripheral (43.8 vs. 44.7 mm Hg; $P = 0.35$) and central (36.3 vs. 37.1 mm Hg; $P = 0.50$) PPs. Across the whole age range, men had lower peripheral and central AIxs than women (Table 1). After adjustment for age, body height, mean blood pressure, pulse rate, current smoking and alcohol intake, the gender difference in peripheral (mean 5.24%; 95% CI 2.59–7.90%; $P = 0.0001$) and central (6.63%; 3.51–9.76%; $P < 0.0001$) AIxs remained statistically significant.

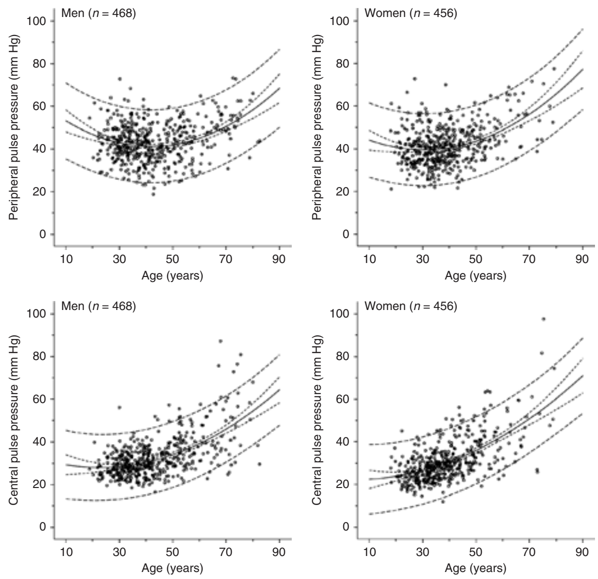

Figure 2 | Relations of the peripheral (top) and central (bottom) pulse pressures with age in men (left) and women (right). Each panel displays the regression line (solid) with 95% confidence intervals for the predictions of mean (short-dotted lines) and individual values (long-dotted lines).

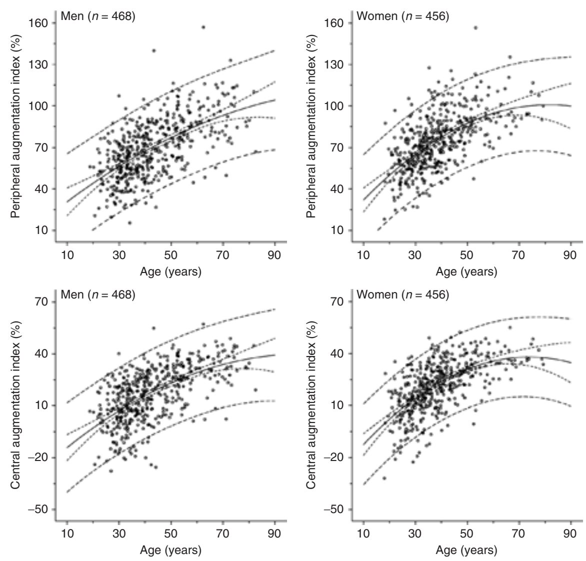

Figure 3 | Relations of the peripheral (top) and central (bottom) augmentation indexes with age in men (left) and women (right). Each panel displays the regression line (solid) with 95% confidence intervals for the predictions of mean (short-dotted lines) and individual values (long-dotted lines).

In both men and women, peripheral and central PPs (Figure 2) and peripheral and central AIxs (Figure 3) showed a curvilinear relation with age. After adjustment for body height, mean blood pressure, pulse rate, current smoking and alcohol intake, the partial regression coefficients relating the arterial measurements to age differed between men and women for the peripheral (age, −1.04 vs. −0.80; age squared, 0.012 vs. 0.011; $P < 0.0001$) and central (age, −0.48 vs. −0.38; age squared, 0.0089 vs. 0.0093; $P = 0.017$) PPs, but not for the peripheral (age, 1.41 vs. 1.78; age squared, −0.0063 vs. −0.012; $P = 0.21$) and central (age, 1.25 vs. 1.58; age squared, −0.0068 vs. −0.011; $P = 0.13$) AIxs.

Proposal for diagnostic thresholds

To determine diagnostic thresholds, we rounded the upper 95% confidence boundary of the prediction interval for individual

Table 2 | Peripheral and central pulse pressures by sex and age

	Men					Women				
Age group	<30	30–39	40–49	≥50	All	<30	30–39	40–49	≥50	All
Number	71	167	101	129	468	109	174	102	71	456
Peripheral (mm Hg)										
Mean	43.8	42.4	40.3	46.6	43.3	40.7	39.4	41.3	49.6	41.7
s.d.	8.0	8.9	8.3	9.7	9.2	9.3	8.0	8.0	10.5	9.4
P5	30.4	28.8	26.8	29.2	28.8	28.0	26.4	28.4	35.2	28.0
P10	34.8	30.8	30.4	33.2	31.6	31.2	29.6	31.2	36.8	31.2
P50	43.2	41.6	39.6	47.2	43.2	38.8	38.6	41.4	46.8	40.8
P90	56.0	54.0	51.6	58.0	55.6	54.0	49.6	51.6	65.2	54.0
P95	58.0	56.4	53.2	62.4	58.0	56.8	53.2	54.0	68.8	58.8
Central (mm Hg)										
Mean	29.6	29.6	31.0	40.4	32.9	25.2	28.2	32.2	42.8	30.9
s.d.	12.2	5.4	7.0	12.4	10.4	5.9	6.1	8.3	14.2	10.1
P5	21.8	21.2	21.9	25.8	21.9	17.6	20.3	23.2	23.9	19.3
P10	22.7	22.3	22.6	28.5	23.2	18.7	21.0	24.4	26.9	20.9
P50	27.1	28.9	30.4	38.4	30.5	24.1	28.2	30.5	40.9	28.8
P90	35.4	37.3	38.4	57.6	42.8	33.2	35.3	46.4	59.5	44.6
P95	38.4	38.8	42.2	62.9	51.6	37.1	40.0	49.9	63.8	50.5

P5, P10, P90, and P95 indicate percentile values.

Table 3 | Peripheral and central augmentation indexes by sex and age

	Men					Women				
Age	<30	30–39	40–49	≥50	All	<30	30–39	40–49	≥50	All
Number	71	167	101	129	468	109	174	102	71	456
Peripheral (%)										
Mean	53.4	61.0	70.6	86.6	69.0	59.4	70.9	82.3	93.5	74.2
s.d.	16.8	15.7	18.7	18.5	21.1	16.3	16.9	16.1	16.7	20.0
P5	27.2	37.9	44.3	55.4	37.9	34.0	44.3	58.3	70.9	43.5
P10	31.7	39.4	48.2	62.9	43.8	41.4	52.3	61.1	77.0	50.8
P50	52.9	59.7	70.3	85.1	68.0	58.2	69.6	81.8	90.9	73.9
P90	74.4	81.2	90.3	110.1	97.4	82.3	92.2	102.3	113.5	100.9
P95	80.2	87.3	96.9	114.5	105.4	87.5	104.8	108.7	120.6	108.4
Central (%)										
Mean	4.77	10.6	18.2	29.5	16.6	9.35	19.1	27.4	34.1	21.0
s.d.	14.0	12.8	14.2	10.8	15.6	13.6	12.2	10.5	9.5	14.4
P5	−19.7	−14.4	−2.42	8.22	−11.26	−14.5	−3.9	10.4	17.1	−4.59
P10	−15.0	−7.02	−0.05	13.5	−3.05	−8.96	5.7	14.0	24.1	1.68
P50	5.28	10.2	20.6	31.0	18.1	10.1	19.5	28.0	34.6	21.9
P90	21.2	26.4	33.1	42.3	36.2	27.2	34.0	40.0	45.8	38.8
P95	26.6	30.2	36.2	44.8	40.0	33.3	38.2	44.1	46.8	42.4

P5, P10, P90, and P95 indicate percentile values.

Table 4 | Proposed thresholds for men and women with and without standardization for heart rate

	Age (years)	Proposed thresholds by age 20	30	40	50	60
Without standardization for heart rate						
Peripheral pulse pressure (mm Hg)	Men	64	60	58	59	62
	Women	58	56	57	60	66
Central pulse pressure (mm Hg)	Men	47	46	48	51	57
	Women	40	42	46	52	58
Peripheral augmentation index (%)	Men	78	90	101	110	119
	Women	82	97	109	119	126
Central augmentation index (%)	Men	22	32	40	48	54
	Women	25	37	46	53	58
Standardized to 75 beats per min						
Peripheral pulse pressure (mm Hg)	Men	64	60	58	59	62
	Women	58	57	57	60	66
Central pulse pressure (mm Hg)	Men	46	46	48	51	56
	Women	40	42	46	51	58
Peripheral augmentation index (%)	Men	77	89	100	109	118
	Women	83	97	109	118	125
Central augmentation index (%)	Men	21	31	39	47	53
	Women	26	37	46	53	57

The diagnostic thresholds (rounded) are based on the upper 95th prediction band of the curvilinear relations between the vascular measurements and age. The reference sample included 468 men and 456 women.

values from the regression models, relating the arterial measurements to the linear and squared terms of age (**Figures 2** and **3**). **Table 4** lists these thresholds per decade of age for men and women separately, with and without standardization to a pulse rate of 75 beats per min. Thresholds with and without standardization were nearly similar.

With standardization to a pulse rate of 75 beats per min, in 40-year-old Chinese, approximate thresholds of normality for the peripheral and central PPs were 58 mm Hg and 48 mm Hg and those for the peripheral and central AIxs were 105 and 45%, respectively. Considering the age range from 20 to 60 years (**Table 4**), thresholds varied within ~5 mm Hg, ~10 mm Hg, ~20%, and ~15% of the aforementioned rounded thresholds at 40 years for the peripheral and central PPs and for the peripheral and central AIxs, respectively.

DISCUSSION

We studied the distributional characteristics and the limits of normality of various measures of arterial pulse wave in relation to age in Chinese men and women. Before 40 years of age, men compared to women had higher peripheral and central PPs. However, after 40 years, peripheral and central PPs were similar between men and women. The increase of PP with age was steeper in women than in men. Men had lower peripheral and central AIxs than women across the whole age range. The regression slopes of AIxs with age were similar between men and women. The proposed diagnostic thresholds reflect these sex- and age-specific trends.

The arterial pressure wave consists of a forward component generated by the heart and reflected waves returning to the heart from peripheral sites. In young subjects with elastic arteries, the reflected waves coincide with diastole and raise diastolic pressure. In old subjects with stiff arteries, the reflected waves move faster, reach the central arteries during systole and cause an augmentation of systolic pressure and PP, whereas diastolic pressure decreases.[23] Central AIx is calculated as a percentage of augmentation pressure divided by PP, and can be used as an indirect measure of arterial stiffness. Pulse wave velocity, the distance of reflection points to the heart, blood pressure levels, and heart rate are the main determinants of AIxs. The gender difference in AIxs in our study might be attributed to the differences between men and women in age, body height, blood pressure levels, and heart rate.

A previous report on reference values for the SphygmoCor device included 534 Europeans without cardiovascular disease (57.3% women; mean age 34.9 years), recruited in the European Project on Genes in Hypertension.[17] Consistent with our findings, European men had higher peripheral and central PPs than women before 40 years of age, while after 40 years, men and women had similar PPs. In this European study, the proposed thresholds of the arterial measurements with age approximated to 60 mm Hg for the peripheral PP, 40 mm Hg for the central PP, 90% for the peripheral AIx, and 30% for the central AIx.[17] We noticed that across the age range in both men and women, the proposed limits for normality in Chinese were ~8 mm Hg higher for the central PP, and about 10% higher for the peripheral and central AIxs than in Europeans. Our Chinese participants were on average 5.3 years older than the Europeans. Moreover, we hypothesize that the smaller body height (mean, 158 cm vs. 170 cm) of Chinese subjects is probably the main determinant of the ethnic differences in the proposed thresholds of normality.

In a smaller sample of 185 South Africans of black ancestry without hypertension, diabetes or previous or concomitant cardiovascular disease (58.4% women; mean age 33.5 years), the peripheral and central PP and the peripheral and central AIxs increased with age, but the quadratic term of age did not significantly improve this relation.[18] The upper 95% confidence boundary of this relation at age 30 years were ~70 mm Hg for the peripheral PP, 50 mm Hg for the central PP, 100% for the peripheral AIx, and 40% for the central AIx. These thresholds needed adjustment by ~2.5 mm Hg, 4.0 mm Hg, 10%, and 6% for each decade that age differed from 30 years.[18] In this black population, body height averaged 162 cm and pulse rate 63 per min.[18] The proposed thresholds were higher than the estimates in our Chinese subjects and Europeans.[17] Random variability due to the small sample size or more selective recruitment with a lower participation rate might explain the higher thresholds in the South African sample.

In our study, we found that both PPs and AIxs showed a curvilinear relation with age. However, with age, PPs increased more in the elderly, whereas AIxs increased more in the young subjects. These observations were consistent with the results in

Europeans[24] and in the Framingham study.[25] In 4,001 healthy individuals recruited in the Anglo-Cardiff Collaborative Trial, McEniery and colleagues reported that central AIx showed a curvilinear relationship with age, and increased more with age in younger than older individuals.[24] The continuous increase of systolic pressure with age and the leveling off or even decrease of diastolic pressure starting at 55 years of age might explain the greater increase of PP in the elderly than the young subjects. The steeper increase in PP (denominator for the computation of AIx) in older subjects might result in the less increase or even decrease of AIx in the elderly. Indeed, Fantin and colleagues found in 458 white subjects that AIx increased with age up to 55 years but plateaued thereafter, whereas augmentation pressure continued to increase in the elderly.[26]

To our knowledge, our study is the first describing measures of arterial stiffness and wave reflections on an epidemiologic scale in a Chinese population. However, it has to be interpreted within the context of its limitations. We used analysis of the radial pulse wave to assess the central PP and the central AIx. Such an approach may introduce some errors in the estimation of central blood pressures by using a radial-to-aorta transfer function with calibration on brachial instead of radial blood pressures.[27] However, these calibration errors do not affect the computation of AIx.[28] We did not exclude smokers from our reference sample. Smoking may increase the stiffness of large arteries and wave reflection, but we asked our subjects to refrain from smoking for at least 2 h before the examination. Although in the present analysis the difference in arterial measurements between male smokers and non-smokers was not statistically significant ($P > 0.08$), the influence of smoking cannot be ruled out. Finally, the normal reference group was defined by traditional risk factors, other than outcome data or invasive arterial imaging. The criteria for identifying a normal reference group might be incomplete. The ultimate definition of normality should depend on the multivariate-adjusted relation between cardiovascular outcome and the risk factor under study. The thresholds we proposed need to be tested further in prospective studies and other Chinese populations.

Acknowledgments: The JingNing study would not have been possible without the voluntary collaboration of the participants and the support of the local public health authorities. The National Natural Science Foundation of China (grant 30571607), the Shanghai Commissions of Science and Technology (grants 03JC14058 and 05ZR14100 and the "Rising Star" program (06QA14043)) and Education (grant 07ZZ32 and the "Dawn" program), and the European Union (InGenious HyperCare, grant LSHM-CT-2006-037093) supported this research.

Disclosure: The authors declared no conflict of interest.

1. Karamanoglu M, O'Rourke MF, Avolio AP, Kelly PJ. An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. *Eur Heart J* 1993; 14:160–167.
2. Kelly RP, Hayward C, Ganis J, Daley J, Avolio A, O'Rourke MF. Noninvasive registration of the arterial pressure pulse wave form using high-fidelity applanation tonometry. *J Vasc Med Biol* 1989; 1:142–149.
3. O'Rourke MF. Influence of ventricular ejection on the relationship between central aortic and brachial pressure pulse in man. *Cardiovasc Res* 1970; 4:291–300.
4. O'Rourke MF, Gallagher DE. Pulse wave analysis. *J Hypertens* 1996; 14(Suppl): S147–S157.
5. Filipovsky J, Svobodová V, Pecen L. Reproducibility of radial pulse wave analysis in healthy subjects. *J Hypertens* 2000; 18:1033–1040.
6. Wilkinson IB, Fuchs SA, Jansen IM, Spratt JC, Murray GD, Cockcroft JR, Webb DJ. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. *J Hypertens* 1998; 16:2079–2084.
7. Chen CH, Ting CT, Nussbacher A, Nevo E, Kass DA, Pak P, Wang SP, Chang MS, Yin FC. Validation of carotid artery tonometry as a means of estimating augmentation index of ascending aortic pressure. *Hypertension* 1996; 27:168–175.
8. Chen CH, Nevo E, Fetics B, Pak PH, Yin FC, Maughan WL, Kass DA. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. *Circulation* 1997; 95:1827–1836.
9. Pauca AL, O'Rourke MF, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. *Hypertension* 2001; 38:932–937.
10. Blacher J, Staessen JA, Girerd X, Gasowski J, Thijs L, Liu L, Wang JG, Fagard RH, Safar ME. Pulse pressure, not mean pressure, determines cardiovascular risk in older hypertensive patients. *Arch Intern Med* 2000; 160:1085–1089.
11. Safar ME, Blacher J, Pannier B, Guerin AP, Marchais SJ, Guyonvarc'h PM, London GM. Central pulse pressure and mortality in end-stage renal disease. *Hypertension* 2002; 39:735–738.
12. Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, Eber B. Arterial stiffness, wave reflection and the risk of coronary artery disease. *Circulation* 2004; 109: 184 –189.
13. Agabiti-Rosei E, Mancia G, O'Rourke MF, Roman MJ, Safar ME, Smulyan H, Wang JG, Wilkinson IB, Williams B, Vlachopoulos C. Central blood pressure measurements and antihypertensive therapy: a consensus document. *Hypertension* 2007; 50:154–160.
14. Wilkinson IB, Mohammad NH, Tyrrell S, Hall IR, Webb DJ, Paul VE, Levy T, Cockcroft JR. Heart rate dependency of pulse pressure amplification and arterial stiffness. *Am J Hypertens* 2002; 15:24–30.
15. Li Y, Staessen JA, Li LH, Gao PJ, Thijs L, Brand E, Brand-Herrmann SM, Zhu DL, Wang JG. Blood pressure and urinary sodium excretion in relation to the A-1984G adrenomedullin polymorphism in a Chinese population. *Kidney Int* 2006; 69:1153–1158.
16. Li Y, Wang JG, Dolan E, Gao PJ, Guo HF, Nawrot T, Stanton AV, Zhu DL, O'Brien E, Staessen JA. Ambulatory arterial stiffness index derived from 24-hour ambulatory blood pressure monitoring. *Hypertension* 2006; 47:359–364.
17. Wojciechowska W, Staessen JA, Nawrot T, Cwynar M, Sleidlerová J, Stolarz K, Gasowski J, Tichá M, Richart T, Thijs L, Grodzicki T, Kawecka-Jaszcz K, Filipovský J; European Project on Genes in Hypertension (EPOGH) Investigators. Reference values in white Europeans for the arterial pulse wave recorded by means of the ShygmoCor device. *Hypertens Res* 2006; 29:475–483.
18. Shiburi CP, Staessen JA, Maseko M, Wojciechowska W, Thijs L, Van Bortel LM, Woodiwiss AJ, Norton GR. Reference values for SphygmoCor measurements in South Africans of African ancestry. *Am J Hypertens* 2006; 19:40–46.
19. American Diabetes Association. Screening for type 2 diabetes. *Diabetes Care* 1999; 22(Suppl 1):S20–S23.
20. O'Brien E, Mee F, Atkins N, Thomas M. Evaluation of three devices for self-measurement of blood pressure according to the revised British Hypertension Society Protocol: the Omron HEM-705 CP, Philips HP5332 and Nissei DS-175. *Blood Press Monit* 1996; 1:55–62.
21. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1:307–310.
22. Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). *Biometrika* 1965; 52:591–611.
23. Nichols WW, O'Rourke MF. Contours of pressure and flow waves in arteries. In *McDonalds Blood Flow in Arteries. Theoretical, Experimental and Clinical Principles*. Hodder Arnold: London, United Kingdom, 2005, pp 165–191.
24. McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR; ACCT Investigators. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). *J Am Coll Cardiol* 2005; 46:1753–1760.
25. Mitchell GF, Parise H, Benjamin EJ, Larson MG, Keyes MJ, Vita JA, Vasan RS, Levy D. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. *Hypertension* 2004; 43:1239–1245.
26. Fantin F, Mattocks A, Bulpitt CJ, Banya W, Rajkumar C. Is augmentation index a good measure of vascular stiffness in the elderly? *Age Ageing* 2007; 36:43–48.
27. Van Bortel LM, Balkestein EJ, van der Heijden-Spek JJ, Vanmolkot FH, Staessen JA, Kragten JA, Vredeveld JW, Safar ME, Struijker Boudier HA, Hoeks AP. Non-invasive assessment of local arterial pulse pressure: comparison of applanation tonometry and echo-tracking. *J Hypertens* 2001; 19:1037–1044.
28. Papaioannou TG, Lekakis JP, Karatzis EN, Papamichael CM, Stamatelopoulos KS, Protogerou AD, Mavrikakis M, Stefanadis C. Transmission of calibration errors (input) by generalized transfer functions to the aortic pressures (output) at different hemodynamic states. *Int J Cardiol* 2006; 110:46–52.