

Are published characteristics of the ambulatory blood pressure generalizable to rural Chinese? The JingNing population study

Yan Li^{a,b}, Ji-Guang Wang^{a,b}, Pingjin Gao^a, Huifeng Guo^a, Tim Nawrot^b, Guliang Wang^a, Yuesheng Qian^a, Jan A Staessen^b and Dingliang Zhu^a

Objective We investigated the ambulatory blood pressure (BP) in rural Chinese and compared its characteristics with those reported in other population-based studies.

Methods We enrolled inhabitants from six villages of the JingNing County, China. We recorded the ambulatory BP using 90207 SpaceLabs monitors. Trained physicians measured the conventional BP at the participants' homes. Hypertension was defined as a conventional BP of $\geq 140/\geq 90$ mmHg or a condition requiring the intake of antihypertensive drugs. Using MEDLINE, we searched for population-based studies on ambulatory BP monitoring.

Results The 356 participants (12–86 years) included 192 (53.9%) women and 117 (32.9%) hypertensive patients. In all participants, systolic/diastolic BP averaged 129/80 mmHg at home. The ambulatory BP means were 121/77 mmHg over 24 h, 126/81 mmHg during daytime (0800 to 1800 h) and 112/70 mmHg during night-time (2200 to 0400 h). The awake and asleep BPs averaged 126/82 and 112/70 mmHg, respectively. Using previously published definitions of daytime (1000 to 2000 h) and night-time (midnight to 0600 h) instead of those given above, inflated the BP differences with the awake and asleep BPs from 0.4/0.2 to 1.2/1.0 mmHg and from 0.3/0 to 1.4/1.6 mmHg, respectively. Compared with daytime values, conventional BP was 2.7/3.1 mmHg lower in normotensive individuals, but 14.9/1.3 mmHg higher in hypertensive patients. In our normotensive individuals, the whole-day and night-time diastolic BPs were from 1 to 4 mmHg and from 3 to 7 mmHg higher than in five other population studies in Caucasians or Japanese, whereas night-time BP in our

participants was 9/5 mmHg lower than in Chinese living in Taiwan.

Conclusions We demonstrated significant differences in the characteristics of the ambulatory blood pressure across Asian and Caucasian populations. To what extent different activity patterns and genetic and environmental factors explain this context-dependency remains to be clarified. *Blood Press Monit* 10:125–134 © 2005 Lippincott Williams & Wilkins.

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^aCentre for Epidemiological Studies and Clinical Trials, Ruijin Hospital, Shanghai Institute of Hypertension, Shanghai Second Medical University, Shanghai, China and ^bStudiecoördinatiecentrum, Hypertensie en Cardiovasculaire Revalidatie Eenheid, Departement Moleculair en Cardiovasculair Onderzoek, Katholieke Universiteit Leuven, Leuven, Belgium.

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Correspondence to Dingliang Zhu, Ruijin Hospital, Shanghai Institute of Hypertension, Ruijin 2nd Road 197, 200025 Shanghai, China. Tel: +86 21 6437 0045 ext 610901; fax: +86 21 5465 4498; e-mail: f97075@guomai.sh.cn

Requests for reprints to Jan A Staessen, MD, PhD, Studiecoördinatiecentrum, Laboratorium Hypertensie, Campus Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium. Tel: +32 16 34 7104; fax: +32 16 34 7106; e-mail: jan.staessen@med.kuleuven.ac.be

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Introduction

Ambulatory blood pressure monitoring is increasingly used in clinical practice [1,2]. Current guidelines and consensus documents propose various operational thresholds for the clinical use of ambulatory blood pressure monitoring [3,4]. Initially, these thresholds were based on large-scale epidemiological studies in well-defined professional groups [5,6], in normotensive [7] and hypertensive individuals [8,9] and in the population at large [10–17]. Subsequently, they have been validated in prospective outcome studies in hypertensive patients [18–24] and in the longitudinal Ohasama study in Japan [25].

Until now, most published studies on operational thresholds for ambulatory blood pressure monitoring involved individuals recruited in industrialized countries [10,12,15,17] or from urban environments [6,11]. To the best of our knowledge, few studies have been performed in remotely living rural Chinese [14]. We therefore investigated in a random population sample to what extent previously published characteristics of the ambulatory blood pressure can be extrapolated to a rural population living in a remote rural mountainous area approximately 500 km south of Shanghai.

Methods

Study population

In the framework of an ongoing Chinese study on genes involved in hypertension, we visited all homes in six villages randomly selected from the JingNing County, in which approximately 90% of the inhabitants are She Chinese, and the remainder belong to the Han ethnicity. The literacy rate among adults is 65.5% and life expectancy at birth is 74.7 years. We invited family members to take part in our study, if at least two offspring with a minimum age of 12 years and one parent were available for examination. Of 839 eligible individuals, 509 (61.7%) participated. At the time of writing of this report, 366 individuals had their ambulatory blood pressure measured. The Ethics Committees of Ruijin Hospital and the Shanghai Second Medical University approved the study protocol. All participants gave informed written consent.

We excluded four individuals from analysis because their conventional blood pressure measured at home was unavailable and six individuals because their ambulatory recordings did not meet our pre-specified quality criteria [8,12,16], namely more than 20 h of recording and more than 10 and five readings for the computation of the daytime and night-time means, respectively. Thus, the number of participants included in the present analysis was 356.

Ambulatory blood pressure measurement

At the first contact with each participant, the observers ascertained that there was no clinically significant difference in the blood pressure readings obtained at the left and right arm. After a 5 min rest in the sitting position, the blood pressure was measured on both arms, always starting with the non-dominant arm. The interval between these two readings had to be less than 1 min. If systolic and diastolic blood pressure were within 10 mmHg at either side, all blood pressure readings were obtained using the non-dominant arm. In the other individuals, the arm giving the highest blood pressure readings was chosen for all blood pressure measurements.

We programmed oscillometric SpaceLabs 90207 monitors (SpaceLabs Inc., Redmond, Washington, USA) [26] to obtain blood pressure measurements with an interval of 20 min from 0800 until 2200 h and every 45 min from 2200 to 0800 h. The calibration of these devices was checked monthly against a mercury column.

If the ambulatory recordings were longer than 24 h, only the first 24 h were used for analysis. Intra-individual means of the ambulatory measurements were weighted by the time interval between successive readings [27]. Considering the pattern of daily activities of the study participants (90% farmers), we defined daytime and

night-time as the intervals ranging from 0800 to 1800 h and from 2200 to 0400 h, respectively. These fixed clock-time intervals [12,27] eliminate the transition periods in the morning and evening during which the blood pressure rapidly changes in most individuals. On monitoring days, the participants kept a diary, in which they noted the time of going to bed in the evening and getting up in the morning and from which we determined the awake and asleep periods of the day.

Auscultatory blood pressure readings

Five physicians repeatedly visited the participants at their homes. By means of mercury sphygmomanometer, they measured the participants' blood pressure five times consecutively on at least two occasions 3 to 4 weeks apart after the participants had rested for 5 min in the sitting position. Systolic and diastolic (phase V) pressures were determined to the nearest 2 mmHg according to the recommendations of the European Society of Hypertension [3]. As the arm circumference of all participants was less than 32 cm, we only used standard cuffs, which had an inflatable bladder with a length of 22 cm and a width of 12 cm. For analysis, we averaged the five readings of the first home visit, because in most epidemiological studies blood pressure is only measured at one occasion. During the home visits, the physicians administered a standardized questionnaire to inquire into each participant's smoking habits, alcohol consumption and intake of medications.

In agreement with current guidelines [3], hypertension and normotension were defined on the basis of conventional sphygmomanometry. Hypertension was present, if the conventional blood pressure was equal to or exceeded 140 mmHg systolic or 90 mmHg diastolic, or if the individuals were on antihypertensive medication irrespective of their blood pressure.

The physicians involved in blood pressure measurement received special training. They only qualified as observer, if all their blood pressure readings ($n = 20$) from a video film featuring a falling mercury column with Korotkoff sounds (Blood Pressure Measurement, British Medical Journal, BMA House, London, UK) were within 5 mmHg of the reference standard.

Comparison with other epidemiological studies

To compare our present finding with other large-scale epidemiological studies, we performed an electronic search of the literature using MEDLINE and the key words 'ambulatory blood pressure monitoring' and 'population'. We did not restrict our search by language. We considered studies for inclusion in our comparative analyses, if they had an overall sample size of at least 300, and if they included separate statistics for normotensive participants.

Statistical methods

Database management and statistical analyses were performed with SAS software, version 8.1. (The SAS Institute Inc., Cary, North Carolina, USA). Departure from normality was evaluated by Shapiro–Wilk's statistic [28] and skewness by the computation of the coefficient of skewness, namely the third moment about the mean divided by the cube of the standard deviation [29]. The normal distribution was used to determine the significance of the coefficient of skewness [29].

Our statistical methods included Student's *t*-test, the standard normal z -test for the comparison of large samples, the chi-squared statistic, and simple and multiple linear regression [30]. We performed multivariate analysis of variance to test the null hypothesis of no differences between the parameters of regression equations [30]. Between-group comparisons of correlation coefficients were done by means of Fisher's z -transformation [31].

Results

Characteristics of the participants

Men ($n = 164$) and women ($n = 192$) had similar age (mean \pm SD, 46 ± 16 years; range, 12–86). In men, mean values for the anthropometric measurements were 57.2 ± 10.0 kg for body weight, 22.0 ± 3.0 kg/m² for body-mass index, and 24.3 ± 2.3 cm for upper arm circumference; in women, these averages were 53.0 ± 8.8 kg, 23.1 ± 3.1 kg/m², and 23.9 ± 2.5 cm, respectively.

Of the 356 participants, 96 (27.0%; all men) were smokers and 163 (45.8%; 120 men and 43 women) reported regular alcohol intake. Among smokers, median tobacco use was 19 cigarettes per day (range, 2–40). Among drinkers, median alcohol consumption was 46 g/day (range, 3–200). Of the study participants, 268 (75%) individuals consumed tea on a daily basis, but nobody reported drinking coffee. Three (0.8%) participants had diabetes mellitus, because their fasting glucose exceeded 7 mmol/l. No participants were on antidiabetic drug treatment. Only one woman reported taking the contraceptive pill.

Ambulatory blood pressure measurement

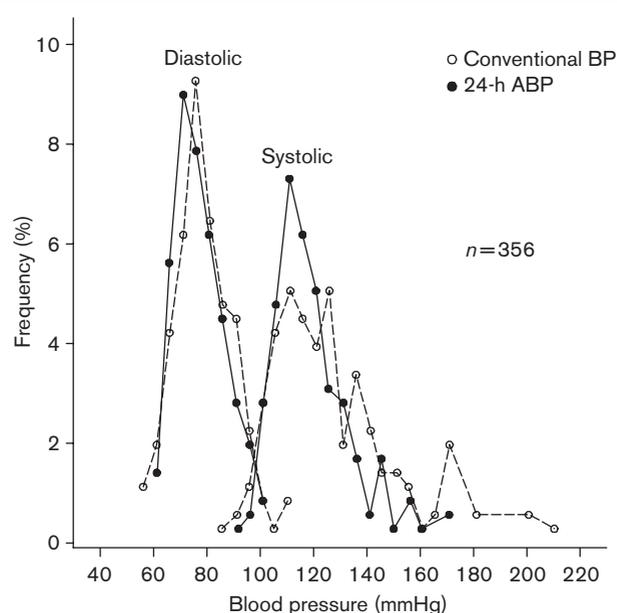
The days on which the ambulatory blood pressure recordings took place were similarly distributed among men and women (18.8% of the recordings were performed on Mondays, 18.8% on Tuesdays, 11.5% on Wednesdays, 14.0% on Thursdays, 9.9% on Fridays, 9.8% on Saturdays and 17.4% on Sundays).

In all 356 participants, the distributions of the 24-h systolic and diastolic blood pressure departed from normality ($P < 0.001$; Fig. 1) and were positively skewed ($P < 0.001$); the coefficients of skewness were 1.03 and

0.66, respectively. The 24-h ambulatory blood pressure averaged 121.0 mmHg [95% confidence interval (95% CI), 119.3–122.6] systolic and 77.0 mmHg (95% CI, 76.0–78.1) diastolic. The daytime blood pressure averaged 125.8 mmHg (95% CI, 124.2–127.4) systolic and 81.4 mmHg (95% CI, 80.4–82.4) diastolic. The night-time averages were 112.3 mmHg (95% CI, 110.4–114.1) and 70.0 mmHg (95% CI, 68.8–71.2), respectively. Additional statistics for the ambulatory blood pressure are presented by gender and age (≤ 39 , 40–59, and ≥ 60 years) in Table 1. The average blood pressure values and corresponding 95% CI for any hour during the day are shown in Figure 2 for men and Figure 3 for women. Mean values in beats per min for the 24-h, daytime and night-time pulse rate were 72.4 (95% CI, 54.8–88.9), 79.3 (95% CI, 58.9–99.7) and 62.1 (95% CI, 45.6–78.6), respectively.

As shown in Table 2, among the 343 participants, who had completed a diary, the awake blood pressure averaged 126.1 mmHg (95% CI, 124.4–127.7) systolic and 81.5 mmHg (95% CI, 80.5–82.6) diastolic, while the averages during sleep were 112.3 mmHg (95% CI, 110.5–114.1) and 69.6 mmHg (95% CI, 68.5–70.8), respectively. Irrespective of hypertension status, the means determined according to the diary method were within 0.5 mmHg of those computed from fixed clock-time intervals. In exploratory analyses, we also defined daytime and night-time as in our previous publications [12,32,33]

Fig. 1



The distribution of the systolic (right) and diastolic (left) blood pressures in 356 individuals drawn at random from a rural Chinese population. Dots denote the 24-h ambulatory blood pressure (24-h ABP) and circles the conventional blood pressure measured at home (Conventional BP).

Table 1 Systolic/diastolic pressures in 356 participants randomly selected from the JingNing population

	Men				Women				Both sexes
	≤ 39 years	40–59 years	≥ 60 years	All men	≤ 39 years	40–59 years	≥ 60 years	All women	
Number	74	50	40	164	88	65	39	192	356
Conventional ^a									
Mean	121/78	131/83	141/80	129/80	115/76	135/82	151/83	129/79	129/80
SD	18/12	20/11	25/11	22/11	17/12	24/12	27/12	26/13	24/12
P ₅	98/60	105/65	110/66	102/64	92/59	102/60	103/63	96/60	100/61
P ₅₀	118/77	126/83	136/78	125/79	112/75	132/80	145/83	122/78	124/78
P ₉₀	138/95	162/94	173/95	159/95	138/92	171/96	189/98	170/95	165/95
P ₉₅	151/102	171/105	191/99	171/102	153/95	174/100	199/105	178/100	177/101
Daytime									
Mean	123/80	130/86	131/82	127/82	117/78	128/84	138/83	125/81	126/81
SD	12/10	14/8	16/9	14/10	11/9	15/9	19/11	17/10	16/10
P ₅	106/65	109/73	111/69	109/68	100/67	108/68	104/69	104/68	105/68
P ₅₀	121/78	128/86	125/82	124/81	115/75	124/82	135/81	121/79	122/80
P ₉₀	137/91	144/96	152/95	144/94	133/89	152/95	162/100	152/95	147/95
P ₉₅	144/98	157/99	159/97	154/98	138/97	156/98	167/104	159/100	157/99
Night-time									
Mean	107/66	114/74	123/75	113/71	101/64	114/73	131/75	112/69	112/70
SD	12/11	17/10	16/10	16/11	11/9	17/11	22/13	19/12	18/11
P ₅	88/50	94/61	100/59	94/56	87/52	95/58	94/55	89/55	90/55
P ₅₀	106/65	109/74	120/76	109/69	98/62	111/72	130/73	107/67	109/68
P ₉₀	118/79	129/83	148/89	134/84	115/75	139/89	153/91	140/86	138/85
P ₉₅	123/86	136/94	150/91	147/90	122/82	144/91	179/105	150/90	147/90
Whole day									
Mean	117/75	125/82	127/79	122/78	111/72	123/79	135/80	120/76	121/77
SD	11/10	15/8	15/8	14/9	11/9	15/9	18/11	17/10	16/10
P ₅	102/63	106/68	107/67	105/65	97/62	106/66	106/64	101/64	102/64
P ₅₀	116/72	121/81	126/77	119/77	109/71	118/78	137/77	115/75	117/76
P ₉₀	129/86	139/91	145/91	137/90	125/83	146/93	159/97	146/92	143/92
P ₉₅	134/94	145/93	156/93	145/93	128/92	150/95	169/100	154/96	154/95

Daytime ranges from 0800 to 1800 h and night-time from 2200 to 0400 h.

^aAverage of five consecutive readings obtained by conventional sphygmomanometry at participant's home.

as the intervals ranging from 10:00 to 20:00 h and from midnight to 06:00 h, respectively. Applying these definitions, increased the differences between the awake and daytime blood pressures to 1.2 mmHg (95% CI, 0.8–1.5; $P < 0.001$) systolic and 1.0 mmHg (95% CI, 0.8–1.2; $P < 0.001$) diastolic and those between the asleep and night-time blood pressures to 1.4 mmHg (95% CI, 0.9–1.8; $P < 0.001$) and 1.6 mmHg (95% CI, 1.3–1.9; $P < 0.001$), respectively.

A total of 117 (32.9%) participants were hypertensive, because their conventional blood pressure measured in the absence of treatment reached diagnostic thresholds ($n = 67$; 57.3%) or because they were on treatment with antihypertensive drugs ($n = 50$; 42.7%). When only the 239 normotensive individuals were considered in the analysis, the 24-h blood pressure averaged 113.6 mmHg (95% CI, 112.4–114.7) systolic and 73.1 mmHg (95% CI, 72.2–74.0) diastolic. The daytime blood pressure in the normotensive individuals was 118.6 mmHg (95% CI, 117.4–119.8) systolic and 77.6 mmHg (95% CI, 76.6–78.5) diastolic, whereas the blood pressures at night were 104.7 mmHg (95% CI, 103.3–106.1) and 65.5 mmHg (95% CI, 64.5–66.6), respectively. Additional statistics for the ambulatory blood pressure measurements in normotensive individuals are presented in Table 3.

Conventional compared with daytime blood pressure

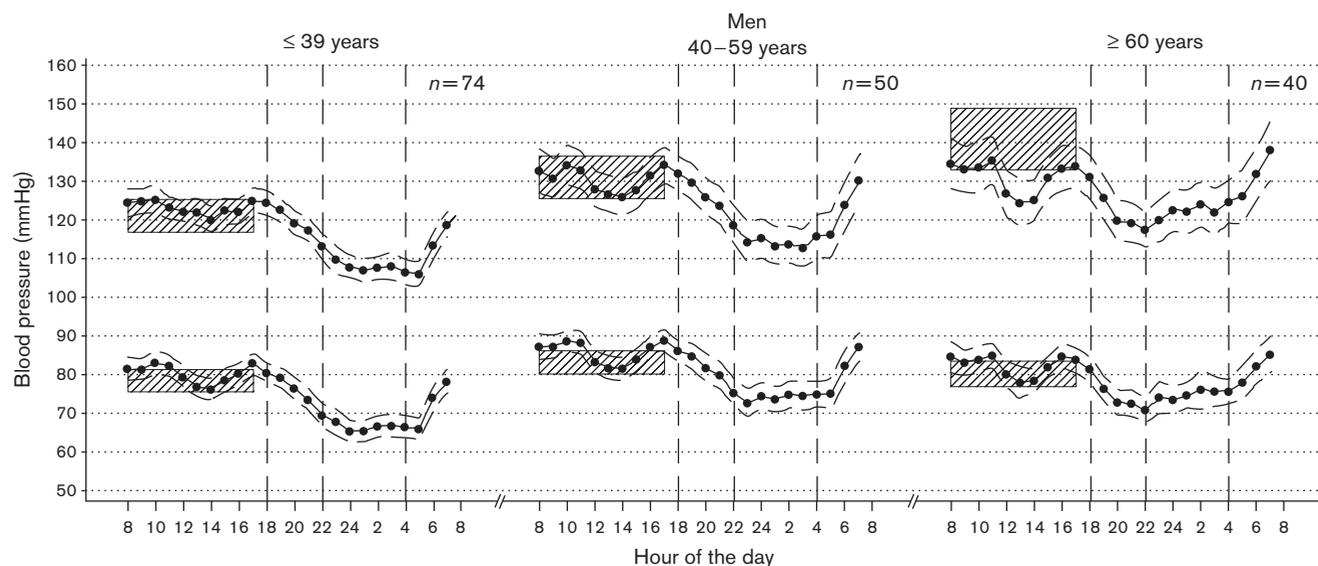
We obtained 3560 blood pressure readings at the participants' homes (five per participant). In terms of digit preference, 16.2% of the readings ended in 0, 20.3% in 2, 19.7% in 4, 21.1% in 6 and 22.7% in 8.

In the total study sample ($n = 356$), the conventional blood pressure averaged 128.9 mmHg (95% CI, 126.4–131.4) systolic and 79.7 mmHg (95% CI, 78.5–81.0) diastolic (Table 1). In the 239 normotensive individuals (Table 3), the conventional blood pressure averaged 115.9 mmHg (95% CI, 114.5–117.4) systolic and 74.4 mmHg (95% CI, 73.4–75.5) diastolic. In 117 hypertensive patients, these values were 155.4 mmHg (95% CI, 151.7–159.1) and 90.5 mmHg (95% CI, 88.5–92.5), respectively. Differences between the conventional and daytime blood pressures according to the absence or presence of hypertension and treatment status are presented in Table 4. At home, the conventionally measured pulse rate averaged 72.2 beats per min (95% CI, 54.6–89.8).

Age as blood pressure determinant

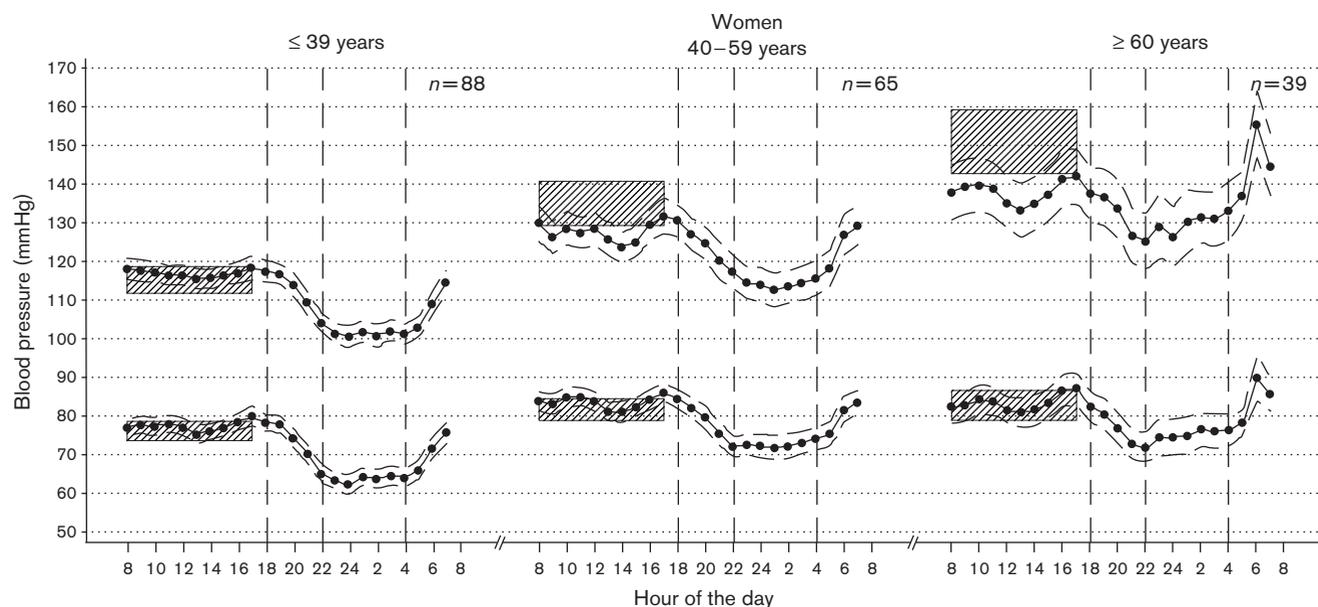
For the conventional as well as the 24-h ambulatory blood pressure, the relation with age was linear for systolic pressure and curvilinear for diastolic pressure. A

Fig. 2



Ambulatory systolic and diastolic blood pressures in men of three age categories. The hourly means with 95% confidence interval are presented. The shaded bands indicate the 95% confidence interval for the conventional blood pressure measured at home (average of five readings in the sitting position).

Fig. 3



Ambulatory systolic and diastolic blood pressures in women in three age categories. For further details see Fig. 2.

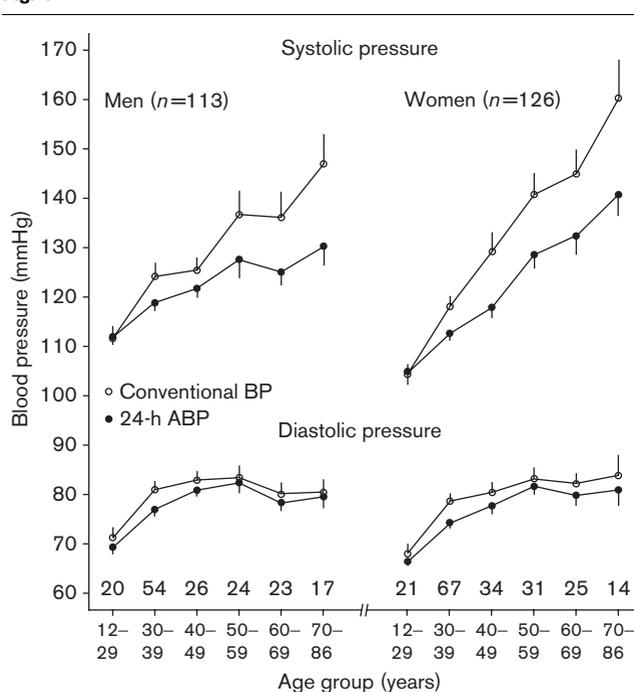
regression model including both the linear and squared terms of age was therefore only required for diastolic blood pressure. Multivariate analyses to compare the parameters of the regression equations demonstrated that in men and in women alike the conventional

systolic pressure increased steeper ($P < 0.001$) with age than the daytime systolic pressure, whereas for the diastolic pressure the relations with age were similar ($P > 0.47$) for the two types of measurement (Fig. 4).

Table 2 Differences between ambulatory blood pressure means determined according to diary or fixed clock-time intervals

	All participants with diary (n=343)			Normotensive individuals with diary (n=232)		
	Mean \pm SD (mmHg)	Difference ^a (mmHg)	P	Mean \pm SD (mmHg)	Difference ^a (mmHg)	P
Wakefulness						
Awake						
Systolic	126.1 \pm 15.7	0.36 (0.11–0.61)	0.004	118.9 \pm 9.4	0.20 (–0.07 to 0.47)	0.14
Diastolic	81.5 \pm 9.8	0.17 (–0.00 to 0.34)	0.06	77.8 \pm 7.2	0.18 (–0.02 to 0.37)	0.08
Asleep						
Systolic	112.3 \pm 16.9	0.35 (–0.01 to 0.70)	0.05	105.1 \pm 10.1	0.33 (–0.05 to 0.71)	0.09
Diastolic	69.6 \pm 10.8	–0.10 (–0.37 to 0.17)	0.47	65.5 \pm 8.0	0.02 (–0.29 to 0.33)	0.91

^aMean differences (95% confidence interval) were calculated by subtracting daytime (0800 to 1800 h) from awake blood pressure and night-time (2200 to 0400 h) from asleep blood pressure.

Fig. 4

The conventionally measured blood pressure (average of five readings at home, open symbols) and the 24-h ambulatory blood pressure (closed symbols) by age in men and women. Values are means \pm SEM.

Comparison with other population studies

Our electronic search identified nine other large-scale epidemiological studies on ambulatory blood pressure monitoring [6,10–17]. The sample size of these studies ranged from 352 to 1855. To compare our present data with those previously published, we excluded one British [15] and two Danish studies [13,17], because the reports did not include separate statistics for normotensive individuals. Among the six remaining studies [6,10–12,14,16], The conventional blood pressure was measured either at an examination center [6,10,14] or at the participants' homes [11,12,16]. Mean age ranged from 33 to 54 years.

Among normotensive individuals aged 20 years or more, the diastolic blood pressure as measured by ambulatory

monitoring during night-time and the whole day was consistently higher among Chinese recruited in JingNing and Taiwan than in all other countries; the mean differences in night-time diastolic blood pressure ranged from 3 to 11 mmHg (Table 5). Furthermore, the night-time systolic blood pressure was 8 to 10 mmHg higher in Chinese living in Taiwan than in all other populations, including our JingNing individuals. With regard to daytime and conventional blood pressures, no consistent pattern emerged in the between-population comparisons (Table 5).

Discussion

In the present study, we recorded the ambulatory blood pressure in Chinese randomly recruited from the population of a remote rural area. To investigate to what extent previously published characteristics of ambulatory blood pressure measurements can be extrapolated, we compared our JingNing results with those of other population surveys [6,10–12,14,16]. The key finding of our research was that whereas ambulatory blood pressure means by and large were of the same order of magnitude across populations, one should not take the generalizability of epidemiological observations on ambulatory blood pressure monitoring for granted. Indeed, the application of fixed clock-time intervals to determine the daytime and night-time ambulatory blood pressures must account for the lifestyle of the population under study. Moreover, in our JingNing individuals, diastolic blood pressure during the whole day and at night was from 1 to 4 mmHg and from 3 to 7 mmHg higher than in all other population studies [6,10–12,16] with the exception of one survey in Taiwan [14].

The awake or out-of-bed and asleep or in-bed blood pressures are usually considered to be the best standard to analyze ambulatory blood pressure recordings in terms of human diurnal activity [34]. However, they add to the complexity of the analysis and errors may occur in the notation of the exact times of individuals going to bed and getting up. Daytime and night-time ambulatory blood pressure means computed from fixed clock-time intervals can reasonably approach the awake and asleep blood pressures. However, wide fixed

Table 3 Systolic/diastolic pressures (mmHg) in 239 normotensive individuals

	Men				Women				Both sexes
	≤ 39 years	40–59 years	≥ 60 years	All men	≤ 39 years	40–59 years	≥ 60 years	All women	
Number	63	31	19	113	76	39	11	126	239
Conventional									
Mean	116/75	120/79	122/74	118/76	110/73	120/75	121/73	114/73	116/74
SD	11/8	10/8	9/5	11/8	11/9	12/9	13/9	12/9	12/8
P ₅	98/60	105/63	105/64	101/62	91/58	100/56	96/61	94/59	96/59
P ₅₀	115/75	120/80	123/76	118/76	110/74	120/75	126/73	114/74	116/75
P ₉₀	130/86	134/88	134/80	132/86	124/84	136/87	134/85	131/86	132/86
P ₉₅	137/88	135/89	138/81	137/88	130/88	138/89	134/89	135/88	136/88
Daytime									
Mean	120/77	124/83	123/78	122/79	114/75	119/79	116/76	116/76	119/78
SD	9/7	9/7	10/8	9/8	8/6	9/8	13/8	9/7	9/7
P ₅	106/65	108/72	111/68	107/68	99/66	105/66	98/60	100/66	104/67
P ₅₀	119/77	125/82	122/77	122/78	113/74	120/81	118/75	116/76	119/77
P ₉₀	131/88	134/92	141/91	134/89	123/83	130/91	134/86	127/85	131/88
P ₉₅	136/89	138/93	143/97	138/92	127/85	136/93	139/90	130/89	136/91
Night-time									
Mean	105/64	108/71	116/70	108/67	99/62	106/69	112/68	102/64	105/66
SD	8/8	9/7	14/9	11/9	8/6	11/9	14/7	10/8	11/8
P ₅	88/50	94/61	93/59	92/54	86/52	92/55	86/55	87/54	88/53
P ₅₀	105/63	108/72	112/69	107/65	97/61	103/67	109/69	101/63	103/64
P ₉₀	114/76	121/79	141/83	121/78	109/70	121/85	130/76	119/75	119/77
P ₉₅	117/78	126/82	150/89	126/81	113/75	125/86	131/79	122/79	125/81
Whole day									
Mean	115/72	119/79	120/74	117/74	108/70	115/75	115/72	111/72	114/73
SD	8/7	8/6	10/7	8/7	7/5	9/7	11/7	9/7	9/7
P ₅	102/63	103/68	105/63	103/64	96/62	102/64	101/62	99/63	100/63
P ₅₀	114/71	120/79	115/73	116/73	108/70	114/76	112/72	110/71	113/72
P ₉₀	124/82	129/88	135/85	128/84	117/77	129/86	129/81	123/80	126/82
P ₉₅	128/84	130/90	137/91	130/88	120/79	129/91	137/85	127/84	129/86

Normotension was defined as a systolic pressure <140 mmHg and a diastolic pressure <90 mmHg on conventional blood pressure measurement at home (average of five readings in the sitting position). Daytime ranged from 0800 to 1800 h and night-time from 2200 to 0400 h.

Table 4 Differences between the conventional and daytime blood pressures according to hypertension and treatment status

	<i>n</i>	Difference in systolic blood pressure ^a	Difference in diastolic blood pressure ^a
Normotensive subjects	239	-2.7 (-4.0 to -1.4)	-3.1 (-4.1 to -2.2)
Hypertensive patients	117	14.9 (11.5–18.3) ^b	1.3 (-0.4 to 3.0) ^b
Untreated	67	15.9 (12.2–19.6) ^b	1.7 (-0.2 to 3.5) ^b
Treated	50	13.6 (7.2–20.0) ^b	0.8 (-2.3 to 4.0) ^b

^aValues are mean differences (conventional minus daytime blood pressure) with 95% confidence interval.

^b*P*<0.01, compared to normotensive individuals.

clock-time methods, which embrace the whole day (24 h) always include variable portions of the actual awake and asleep periods and therefore introduce inaccuracy in the analysis. In contrast, narrow fixed clock-time intervals substantially reduce this error and yield daytime and night-time blood pressures means, which approximate to the average awake and asleep values [35,36]. In the present study, we confirmed this concept. Indeed, irrespective of hypertension status, the means computed from short fixed clock-time intervals were within 0.5 mmHg of those determined by the diary method. Although small, some of these differences attained statistical significance, because of the relatively large number of individuals enrolled in our study. In our previous publications [12,32,33], daytime and night-time were defined as the intervals ranging from 1000 to 2000 h and from midnight to 0600 h, respectively. However, this definition clearly deviated from the diurnal activity

pattern of our JingNing population. Had we not accounted for the difference in lifestyle, by applying the previously published intervals [12,32,33], we would have inflated the differences between the blood pressure means determined by the diary method as compared with those computed from short fixed clock-time intervals. We therefore re-defined daytime and night-time as intervals ranging from 0800 to 1800 h and from 2200 to 0400 h, respectively.

In our study, compared with the daytime means, the conventional blood pressure measured at home by physicians was 2.7/3.1 mmHg lower in 239 normotensive individuals, but 14.9/1.3 mmHg higher in 117 hypertensive patients. Thus, in line with previous publications [12,21,32], including the International Database on Ambulatory Blood Pressure Monitoring [37], our study confirmed that normotensive individuals usually have a

Table 5 The conventional (CBP) and ambulatory blood pressures (ABP) in normotensive participants enrolled in seven population studies

Study	BPS	EPOGH ^a	AIB	PAMELA	OHASAMA	Taiwan	JingNing
Setting	rural	rural/urban	urban	urban	rural	rural/urban	rural
Normotensive subjects	729	931	777	1225	335	720	231
Mean age (range, years)	50 (20–87)	35 (20–74)	45 (25–51)	46 (25–64)	54 (≥ 20)	51 (≥ 30)	42 (20–81)
Women (%)	53%	58%	52%	51%	68%	49%	53%
CBP							
Mean	118/74	118/75	115 ^{BE} /73 ^E	115 ^{BE} /72 ^{BE}	121 ^{BEAP} /70 ^{BEAP}	119 ^{EAP} /74 ^{PO}	116 ^{OT} /75 ^{PO}
SD	10/8	11/8	11/8	13/9	12/10	11/8	12/8
P ₉₅	136/86	135/87	132/85	138/87	–	–	136/88
24-h ABP							
Mean	115/70	116/70	116/71 ^{BE}	115/72 ^{BEA}	116/69 ^{AP}	116/73 ^{BEAPO}	114 ^{EA} /73 ^{BEAPO}
SD	8/6	9/6	9/6	8/6	10/7	10/7	9/7
P ₉₅	129/80	131/81	130/82	128/82	139/81	–	129/86
Daytime							
Mean	121/75	122/76	122/77 ^{BE}	120 ^{EA} /77 ^{BE}	121/72 ^{BEAP}	118 ^{BEAPO} /75 ^{APO}	119 ^{BEA} /78 ^{BEOT}
SD	9/7	10/7	10/7	9/7	11/7	10/7	10/7
P ₉₅	137/88	139/87	137/88	134/88	–	–	136/91
Night-time							
Mean	104/60	105/61 ^B	104/59 ^E	105 ^{BA} /63 ^{BEA}	106 ^{BA} /61 ^{AP}	114 ^{BEAPO} /71 ^{BEAPO}	105 ^T /66 ^{BEAPOT}
SD	9/7	10/7	9/7	9/7	11/7	11/7	11/8
P ₉₅	121/72	122/74	120/71	121/74	–	–	125/81

Acronyms and references: BPS, Belgian population study [12]; EPOGH, European Project on Genes of Hypertension [16]; AIB, Allied Irish Bank Study [6]; PAMELA, Pressioni Arteriose Monitorate E Loro Associazioni, Monza, Italy [11]; OHASAMA, survey conducted in Ohasama, Iwate Prefecture, 100 km north of Sendai, Japan [10]; Taiwan, study conducted on the Taiwan and Kinmen (Quemoy) islands [14].

^aThe participants were randomly recruited from the population of Bucharest (Romania; $n=189$), Cracow (Poland; $n=194$), Mirano (Italy; $n=212$), Pilzen and Prague (Czech Republic; $n=223$), and Novosibirsk (Russia; $n=212$). P -values for the between-population differences were adjusted for multiple comparisons by Bonferroni's method. B, $P \leq 0.05$ vs BPS; E, $P \leq 0.05$ versus EPOGH; A, $P \leq 0.05$ versus AIB; P, $P \leq 0.05$ versus PAMELA; O, $P \leq 0.05$ versus OHASAMA; and T, $P \leq 0.05$ versus Taiwan.

higher daytime ambulatory than conventional blood pressure, whereas hypertensive patients, confronted with a doctor, often experience a white-coat effect and therefore have the higher levels on conventional measurement [38]. In keeping with other population studies [12,32], we also confirmed that in Chinese age is a much stronger determinant of the conventional than the ambulatory systolic pressure.

Why the 24-h and night-time diastolic blood pressures were higher in Chinese individuals recruited in JingNing and Taiwan [14] compared with Caucasians [6,11,12,16] and Japanese [10] remains to be elucidated. We do not believe that these findings just arose from random variability, because they were consistent across two independent studies in Chinese. Our study does not allow us to clarify to what extent genetic determinants, lifestyle, environmental factors, or a combination thereof underlie the higher diastolic blood pressure in Chinese. However, according to current hemodynamic concepts, diastolic and mean blood pressure reflect peripheral arterial resistance, whereas systolic blood pressure behaves as a dynamic index of the coupling between left ventricular ejection and the distensibility of the large arteries [39]. Several lines of evidence suggest that Asians compared with Caucasians have lower renin activity and are more susceptible to a volume-dependent type of hypertension [40]. If these assumptions apply, sodium homeostasis in Chinese might be more dependent on pressure natriuresis, which in turn might explain the

higher night-time diastolic blood pressure. Interestingly, several investigators noticed that Blacks, an ethnic group also characterized by low renin activity, also have higher night-time blood pressure than White individuals [41,42]. Whatever the underlying mechanism, the present findings raise the issue of the generalizability of the distributional characteristics of the ambulatory blood pressure across population.

The present study has to be interpreted within the context of its limitations. It is an ongoing project. According to epidemiological standards, our present report is based on a relatively small sample size. Our findings might not be applicable to the majority of Chinese who belong to the Han ethnicity. On the other hand, we applied a validated protocol of phenotyping and we maintained a strict quality control program [16]. For blood pressure measurement, we strictly adhered to the recommendations of European Society of Hypertension [3]. For ambulatory monitoring, we used validated and calibrated SpaceLabs recorders [43].

In conclusion, we demonstrated significant differences in the characteristics of the ambulatory blood pressure across Asian and Caucasian populations. However, to what extent different activity patterns and genetic and environmental factors explain this context-dependency remains to be clarified. If confirmed, our observations suggest that statistical parameters of ambulatory blood pressure measurements should be internally validated

within ethnicities and populations. Moreover, working definitions of normality derived from the distribution of the ambulatory blood pressure in normotensive individuals always need further validation in terms of cardiovascular complications.

Contributors

P.G. and J.A.S. raised funding. D.Z. organized and supervised the study in China. J.-G.W. and Y.L. coordinated the acquisition of the data, and together with J.A.S. constructed the database, performed the statistical analysis and wrote the first draft of the manuscript. All named authors critically revised the manuscript for important intellectual content, took part in the interpretation of the results and prepared the final version of the manuscript.

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