Ambulatory Blood Pressure Monitoring in Uygur Centenarians

Medet Jumabay, MD; Yukio Ozawa, MD; Hiroshi Kawamura, MD*;
Satoshi Saito, MD; Yoichi Izumi, MD; Hiromi Mitsubayashi, MD*;
Yuji Kasamaki, MD; Tomohiro Nakayama, MD; Masum Mahumut, MD**;
Zuheng Cheng, MD**; Shezhen Wang, MD**; Katsuo Kanmatsuse, MD

Cross-sectional surveillance was carried out in long-lived Uygur in China to investigate blood pressure (BP) and pulse rate (PR) variation in centenarians. The study group comprised 33 centenarians (age ≥ 100 years), 103 longevous subjects (age 90–99 years) and 100 elderly (age 65–70 years) subjects. Office BP was measured, and 24-h noninvasive ambulatory blood pressure monitoring (ABPM) was performed. The office BP was higher and hypertension occurred more frequently in the centenarians than in either the longevous or elderly subjects. Mean 24-h systolic and diastolic BP was higher in the centenarians than in the other 2 groups. However, mean 24-h PR did not differ between them. Day–night differences in systolic BP decreased, and the non-dipper-type BP pattern was common in the centenarians (79.1% vs 68% and 63.6% in longevous and elderly subjects, respectively). Circadian BP was characterized by 3 peaks in longevous subjects and multiple peaks in centenarians. Morning rising and nocturnal dipping of BP were observed in both longevous and elderly subjects. In conclusion, BP in longevous and elderly Uygur was characterized by circadian rhythmicity, but the nocturnal fall in BP was not seen in centenarians. Differences in day–night BP and circadian rhythmicity may decrease with advancing age, especially in centenarians. (*Circ J* 2002; 66: 75–79)

Key Words: Ambulatory blood pressure monitoring; Centenarians; Circadian rhythm; Elderly; Longevity

It has been shown that the humans living to a very old age have a genetic tendency toward moderate and balanced blood pressure (BP).^{1,2} The Uygurs in Xinjiang are a naturally longevous population, surviving to a very old age without any medical treatment or services. There have been studies showing that the Uygur people do live to an older age than other people in the Xinjiang Uygur Autonomous Region of China,^{3,4} but these reports have not provided information on the blood pressure (BP) variations, such as the day–night BP differences and the circadian rhythm, in the Uygur centenarians.

Noninvasive 24-h ambulatory blood pressure monitoring (ABPM) devices are now commercially available and are often used to overcome the ‘white-coat’ effect and identify white-coat hypertension when studying the circadian rhythm of BP. A person’s ambulatory BP measured during daily life can provide more meaningful information than can recordings of BP taken in the physician’s office, and interesting information is provided when this method is used for persons of different ethnicities. Therefore we used ABPM in our study of office and ambulatory BP, pulse rate (PR), prevalence of hypertension, difference between day- and night-time BP and PR, and circadian BP and PR rhythms in

centenarian, longevous, and elderly Uygurs.

Methods

Study Population

Two hundred and thirty-six clinically healthy subjects were recruited from Uygur residences by randomized, parallel-design sampling in Hotan, Xinjiang Uygur Autonomous Region, People’s Republic of China during July and August 2000. All subjects gave their informed consent to participate. Subjects were divided into 3 groups according to age: a centenarian group (33 subjects, age ≥ 100 years), a longevous group (103 subjects, age 90–99 years) and an elderly group (100 subjects, age 65–70 years). Elderly and longevous subjects were engaged in physical labor, despite advancing age, but the centenarians only managed their daily physical activities. We confirmed the age of subjects through resident registration forms, and marital, family and personal histories conveyed in the local language. The office BP examination was undertaken at the local hospital. All subjects resided in a dormitory of the health-care center of the village for the 3 days of this investigation. Twenty-four-hour ABPM was conducted in each subject’s place of residence and they were asked to maintain their normal schedule of activity and regular rest. A diary of their activities was recorded during the BP monitoring. All subjects were served their usual meals at 07.00, 11.30, and 19.00 h. Subjects underwent other physical examinations after the ABPM ceased. None of the subjects had previously received antihypertensive agents.

Office BP and 24-h BP/PR Monitoring

The office BP was determined at the beginning of the

(Received June 15, 2001; revised manuscript received October 5, 2001; accepted October 17, 2001)

2nd Department of Medicine, Itabashi Hospital, Nihon University School of Medicine and *Department of Medicine, Nippon Dental University, School of Dentistry at Tokyo, Tokyo, Japan, and **Department of Internal Medicine, First affiliated Hospital, Xinjiang Medical University, Urumqi, China

Mailing address: Professor Yukio Ozawa, MD, Nihon University School of Medicine, 30-1 Oyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan

Table 1 General Physiologic Characteristics of Uygur Subjects

	Elderly (n=100)	Longevous (n=103)	Centenarian (n=33)
M/F	66/34	66/37	25/8
Age (years)			
Men	68±2.0	95±6	104±5
Women	67±2.0	93±3	104±3
BL (cm)			
Men	160±5.7	158±8.7	154±12
Women	149±4.7	146±6.3	148±6.9
BW (kg)			
Men	55±5.8	52±7.8	53±6.6
Women	46±6.7	40±5.2	40±5.6
BMI (kg/m ²)			
Men	21±1.9	21±3.3	22±6.1
Women	21±2.8	19±2.0	18±1.9

BL, body length; BW, body weight; BMI, body mass index. Values are mean±SD.

Table 2 Blood Pressure and Pulse Rate in Uygur Subjects

	Elderly	Longevous	Centenarian
Office			
SBP	127±20	128±22	134±23**
DBP	73±12	76±13	80±14**
PR	83±11	85±12	82±15
24-h ABPM			
SBP	124±16	125±18	131±24**
DBP	71±7	71±8	73±12*
PR	77±7	78±8	76±11
Daytime			
SBP	126±17	126±17	132±22**
DBP	72±7	72±8	74±11*
PR	80±9	81±8	79±11
Nighttime			
SBP	117±18	120±21	129±29**
DBP	68±7	69±10	71±14*
PR	71±12	72±11	71±13

SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); PR, pulse rate (beats/min); ABPM, ambulatory blood pressure monitoring. * $p<0.05$, ** $p<0.001$ (differences between centenarians and other groups). Values are mean±SD.

study as the mean of the 3 readings at intervals of 5 min by the Korotkoff cuff method. Subjects rested for 5 min in a seated position in the patient examination room of the local hospital before BP was measured. For this study, subjects were classified as having hypertension when systolic BP (SBP) was above 140 mmHg and/or diastolic BP (DBP) was above 90 mmHg.

The 24-h ABPM was carried out with the TM-2421 device (A&D Co Ltd, Tokyo, Japan) by the Korotkoff method. The monitor was programmed to obtain BP and PR measurements every 30 min, and its accuracy was determined against values obtained with a mercury sphygmomanometer by the Korotkoff cuff technique (ie, standard ambulatory cuff, mounted on the left arm; subjects were asked to hold the arm still and to keep it from moving during cuff deflation and during the actual measurement). BP and PR were recorded for 26 h because the data collected during the initial 2 h were discarded to avoid any novelty effect. Daytime BP was calculated between 05.00 and 20.30 h, excluding daytime naps. Nighttime BP was calculated between 23.00 and 04.00 h excluding periods of awakening during sleep. Abnormal TM-2421 values were excluded based on the following criteria: (1) SBP lower than 50 mmHg and/or DBP lower than 40 mmHg with no similar preceding or subsequent value; (2) SBP greater than 250 mmHg and/or DBP greater than 140 mmHg with no

similar preceding or subsequent value; (3) SBP and/or DBP measuring skipped more than 2 h. Height and weight were measured with the subject in light clothing before the 24-h ABPM, and body mass index (BMI) was calculated.

Statistical Analysis

Data are expressed as means ± SD. All statistical calculations were performed with the Statistical Analysis System (SAS Institute Inc, Cary, NC, USA) computer program. Group comparisons were made by analysis of variance (ANOVA) followed by the multiple comparison tests. A p value <0.05 was considered statistically significant.

Results

Physiologic Characteristics

The subjects' physiologic characteristics are summarized in Table 1. There were more men than women in all 3 groups. Body length (BL), body weight (BW) and BMI did not differ significantly between the groups. Temperature and humidity did not differ during testing of all subjects.

Office and Ambulatory BP, PR, and Prevalence of Hypertension

The office and 24-h ambulatory measurements are shown in Table 2. Office and 24-h SBP and DBP values were

higher in centenarian subjects than in longevous and elderly subjects. Office and mean 24-h PR values were similar between all groups. Daytime and nighttime SBP and DBP were higher in centenarians than in either longevous or elderly subjects ($p<0.001$). However, the daytime and nighttime SBP and DBP values were similar between the longevous and elderly subjects. Mean daytime SBP, DBP and PR were greater than the mean nighttime values in longevous and elderly subjects ($p<0.001$). However, in centenarians, SBP did not differ significantly between day and night.

Hypertension occurred more frequently in the centenarians than in either longevous or elderly subjects ($p<0.001$). The ratio of hypertension was 39% in centenarians, 23% in longevous subjects and 16% in elderly subjects, by office measurement, respectively. The ratio of daytime hypertension was 15% in the elderly subjects, 14% in the longevous subjects, and 42% in the centenarians when mean daytime SBP was above 135 mmHg and/or mean daytime DBP was above 85 mmHg. The ratio of nighttime hypertension was 28% in the elderly subjects, 25% in the longevous subjects and 52% in the centenarians when mean nighttime SBP was above 125 mmHg and/or mean nighttime DBP was above 75 mmHg.

Day–Night Differences in BP and PR

The magnitude of day–night differences in DBP and PR did not differ significantly between the groups, as shown in Fig 1. However, the day–night difference in SBP was less in centenarians than in the other 2 groups. The day–night difference in SBP was also less in longevous subjects compared with the elderly subjects. The magnitude of the day–night differences of SBP increased in the elderly subjects compared with centenarians.

A dipper-type change (a decrease in nighttime BP when mean nighttime SBP was decreased more than 10% below the mean daytime SBP) was observed in 36% of the elderly subjects, 32% of the longevous subjects, and in 21% of the centenarians. The centenarians showed a higher nighttime BP and fewer dipper patterns than were observed in the other 2 groups.

Circadian Patterns

Two peaks, one in the morning and the other in the after-

Fig 1. Day–night blood pressure (BP) differences in the 3 groups were calculated as mean daytime value–mean nighttime value. SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate; * $p<0.05$; ** $p<0.001$, differences between groups. Comparison was analysis of variance (ANOVA) followed by the multiple comparison tests.

noon, and one dip during the night, as shown in Fig 2, characterized the circadian SBP in elderly subjects. In the longevous subjects, however, SBP demonstrated a 3 peaks variation during the day, the first and last peaks of which were similar to those observed in the elderly subjects, but with an additional peak at noon that differed significantly from the elderly subjects' pattern ($p<0.001$). In the centenarians, SBP showed multiple peaks, and the overall pattern tended to be flat (Fig 2). There was no morning surge, and the SBP was greater significantly both day and night

Fig 2. Circadian variation in systolic blood pressure (per group), which was obtained every 30 min in each subject from 00.00 to 23.30 h. * $p<0.01$, differences between centenarian and other groups, compared by GML procedure (SAS).

Fig 3. Circadian variation in diastolic blood pressure (per group), which was obtained every 30 min in each subject from 00.00 to 23.30 h. * $p<0.01$, centenarian vs longevous and elderly subjects, compared by GML procedure (SAS).

Fig 4. Circadian variation in pulse rate (per group), which was obtained every 30 min in each subject from 00.00 to 23.30 h. * $p<0.01$, centenarian vs longevity and elderly subjects, compared by GML procedure (SAS).

compared with the other subjects. DBP variation was similar between the longevous and elderly subjects, characterized by a 2-peaks and 1-dip pattern. The circadian DBP pattern showed multiple peaks in the centenarians (Fig 3).

Circadian PR showed a similar pattern in all subjects (Fig 4), although the PR in the centenarians rose more slowly in the morning than in the longevous and elderly subjects.

In summary, office and ambulatory BP, as well as the prevalence of hypertension, were higher in the centenarians than in either the longevous or elderly subjects. The magnitude of the day–night differences in SBP was smaller in centenarians and they had fewer dipper patterns. A pattern of multiple peaks in centenarians and 3-peaks in the longevous subjects characterized the circadian variation in BP.

Discussion

Centenarians and Hypertension

Many factors affect life span. The Uygurs in Xinjiang, China, are particularly long-lived; for example, in Hotan, one of the densely populated areas of Uygurs, the proportion of centenarians in the population is 18.9/100,000.³ The number of men in our study was greater than the number of women, indicating that Uygur men are longer lived than the women, and the male/female ratio we obtained was consistent with that reported from a previous population study in Xinjiang.⁴ Lifestyle is likely one factor that influences the life expectancy of the Uygurs. According to a previous investigation, a Uygur man has a high probability of marrying, has minimal mental stress, and engages in physical labor despite advancing age. The Uygur have a lower BMI and eat many more fruits and vegetables than other racial groups in Xinjiang.

The prevalence of hypertension in China differs according to ethnicity, but averages 13.58% in the general population and 32–49% in the elderly (age ≥ 65 years).^{5,6} In Xinjiang, the Uygur have been shown to have a lower prevalence of hypertension than the Han or Kazakh people,^{7–9} and in the present study, the elderly Uygur subjects were less hypertensive compared with the general elderly Chinese population. The longevous Uygur subjects were also less hypertensive, so it seems that those who are less hypertensive have an advantage in terms of life expectancy.

The study of ABPM in relation to longevity has received comparatively little attention, although some studies have reported a drop in 24-h BP in women and a rise in men from the eighth to the ninth decade of life.^{10,11} In the present study, the office and 24-h BP levels did not change between the ages of 65 and 99 years, but increased, together with the incidence of hypertension, in the centenarians. It is well known that BP increases with advancing age and that hypertension threatens life expectancy and is related to cardiovascular morbidity and mortality.¹² Therefore, prevention of hypertension may play an important role in longevity.

Day–Night Differences

In the present study, the same day–night definition was used for all subjects and daytime naps and awake-time during sleep were not factored into the calculation of day–night BP differences, which were thus based on actual waking and sleeping times. It has been shown that a reduced day–night BP difference and increased daytime BP variability is associated with a high incidence of hypertensive cardiovascular disorders,¹³ but it is unclear whether

the reduced day–night BP difference is the cause or the consequence of the organ damage. There are various causes of a decrease in the difference between day- and night-time BP. One study showed that nocturnal falls in SBP decline with advancing age in the very elderly, especially females, mainly because of a higher nighttime BP.¹⁴ In the present study, the day–night difference in SBP was less in the longevous subjects than in the elderly subjects, and was much less in the centenarians compared with the longevous subjects. However, the day–night differences in DBP and PR were similar between all groups. The magnitude of the day–night difference in SBP, rather than that in DBP or PR, may be associated with advancing age, and may decrease with advancing age, especially in centenarians.

Although BP rises during the daytime and falls at night in healthy individuals, there are many conditions in which BP does not show the usual nocturnal decrease. The familiar diurnal BP pattern includes a pre-awakening rise that occurs at relatively fixed heart rates and reducing this pressure rise is thought to reduce the incidence of stroke and myocardial infarctions that occurs in the early morning.¹⁵ In the present study subjects, the centenarians showed fewer dipper patterns. No morning rise in BP was seen and they had a higher nighttime BP than the longevous or elderly subjects. The present study confirms a reduction in the fall in SBP, mainly because of a higher nighttime SBP with advancing age.

Circadian Rhythm

BP and PR demonstrated circadian rhythmicities, as shown by a nocturnal fall and a morning rise, in the longevous and elderly subjects, confirming that BP preserves its circadian rhythm despite very old age¹ and implying that humans can live to a very old age, depending on their BP status. The BP profile varied during the daytime, however, as shown by the 3-peaks pattern in the longevous subjects and the 2-peaks pattern in the elderly subjects. The elderly Uygur subjects demonstrated a 1-dip–2-peaks pattern of BP, which was similar to the general circadian pattern of BP. However, the new finding from this study is the 1-dip–3-peaks pattern in the longevous Uygurs and the flattened pattern in the centenarians. ABPM was conducted on all subjects in the same environment and according to the same schedule, and the activity recorder showed that there was no difference in the daily activities between the elderly and longevous subjects. Therefore the additional peak, which appears around noon in the longevous subjects, does not appear to be associated with their activity. The daytime SBP is a strong predictor of early carotid atherosclerosis, and a decrease in baroreceptor sensitivity would increase BP variability.^{16–19} Because the arterial baroreceptor reflex function declines with advancing age, the BP variation seen in the longevous Uygur subjects may be associated with atherosclerosis or other factors, an aspect that requires further study.

The loss of the circadian pattern of BP in the Uygur centenarians is related to activity, sleeping quality, arteriosclerosis and other factors. Most of the centenarians were drowsy during the day and had a lower level of activity, compared with the longevous or elderly subjects. Unfortunately we did not assess sleeping quality, but there was no difference in the disturbance of sleep related to the need to urinate during the night between the centenarians according to their ABPM diary notes. Another reason for the flattened pattern of circadian BP in centenarians may be

the extent of arteriosclerosis, and the function of the central nervous system and the response to sympathetic stimulation may be also related.

We also found a diminished morning PR in the centenarians, although the time of awakening in the morning and the level of activity was similar among the groups. Blunting of the circadian rhythm of heart rate can express either a lower than normal ability of the heart rate to accelerate in response to sympathetic stimulation or a lower than normal ability of heart rate to decelerate in response to vagal stimulation, or both.²⁰ The diminished morning PR in centenarians may be an indicator of aging. These changes in nocturnal BP and morning PR have been associated with increased rate of cardiovascular disorders although the cause–effect relation remains unclear. Further studies are required to determine the risk of cardiovascular disease in centenarians and the vascular changes that occur with aging.

In conclusion, Uygur centenarians demonstrated high BP, especially during the night. The difference in day–night SBP declined at a very old age and may be an indicator of longevity. Circadian rhythms of BP may decrease with advancing age.

Acknowledgments

This study was supported by a Nihon University Presidents Grant for Specified Interdisciplinary Research.

References

1. Cugini P, Leone G, Lucia P, Sepe FA, Pelosio A, Caparrelli T, et al. Compodimele study, blood pressure and heart rate in clinically healthy elderly subjects. *Chronobiol Int* 1994; **11**: 381–392.
2. Cugini P, Sepe F, Leone G, Pelosio A, Zannella FP, Fonzo DF, et al. Lower 24-h blood pressure regimen in subjects with a familial genealogy of longevity. *Clin Ter* 1998; **149**: 419–423.
3. Zhang SR, Xu CR. Statistical analysis of centenarians in Xinjiang. *Xinjiang Med* 1987; **17**: 213–215.
4. Wang XY, Masum M, Li CS, Xi JJ. Investigation of 213 centenarian people in Hotan, Xinjiang. *Xinjiang Med* 1986; **16**: 127–133.
5. Zhang L, Li Y. 24 hr Ambulatory blood pressure in elderly. *J China Circ* 1984; **29**: 218–260.
6. He J, Klag MJ, Wu Z. Stroke in the People's Republic of China: Geographic variations in incidence and risk factors. *Stroke* 1995; **26**: 2222–2227.
7. Zhang JY, He BX, Li CS, Masum M. Hypertension study of 567 subjects of Uygur elderly in Xinjiang. *Xinjiang Med* 1987; **17**: 193–197.
8. Mu YM, Ozawa Y, Wang SZ, Cheng ZH, Kawamura H, Yang CR, et al. Ultrasonographic study of carotid artery structural changes with natural longevity. *Jpn Circ J* 2000; **64**: 243–248.
9. Kawamura H, Jumabay M, Mitsubayashi H, Izumi Y, Soma M, Ozawa Y, et al. 24-hour blood pressure in Uygur, Kazakh and Han elderly subjects in China. *Hypertens Res* 2000; **23**: 177–185.
10. Imai Y, Magai K, Sakuma M, Sakuma H, Nakatsuka H, Satoh H, et al. Ambulatory blood pressure of adults in Ohasama, Japan. *Hypertension* 1993; **22**: 900–912.
11. Lee DR, Swift CG, Jackson SH. 24h blood pressure monitoring in healthy elderly people. *Age Aging* 1995; **24**: 91–95.
12. Trenkwalder P, Ruland D, Stender M, Gebhard J, Trenkwalder C, Lydtin H, et al. Prevalence, awareness, treatment and control of hypertension in a population over the age of 65 years: Results from the Starnberg Study on Epidemiology of Parkinsonism and Hypertension in the Elderly (STEPHY). *J Hypertens* 1994; **12**: 709–716.
13. Palatini P, Penzo M, Racioppa A, Zugno E, Guzzardi G, Anacletio M, et al. Clinical relevance of nighttime blood pressure and of daytime blood pressure variability. *Arch Intern Med* 1992; **152**: 1855–1860.
14. Fotherby MD, Potter JF. Twenty-four-hour ambulatory blood pressure in old and very old subjects. *J Hypertens* 1995; **13**: 1742–1746.
15. Purcell HJ, Gibbs JSR, Coats AJS, Fox KM. Ambulatory blood pressure monitoring and circadian variation of cardiovascular disease: Clinical and research applications. *Int J Cardiol* 1992; **36**: 135–149.
16. Sander D, Kukla K, Klingelhofer J, Winbeck K, Conrad B. Relationship between circadian blood pressure patterns and progression of early carotid atherosclerosis a 3 year follow-up study. *Circulation* 2000; **102**: 1536–1541.
17. Tochikubo O, Kawano Y, Miyajima E, Ishikawa T, Ishii M. Hemodynamic factors regulating blood pressure during sleep in patients with mild essential hypertension. *Jpn Circ J* 1997; **61**: 25–37.
18. Harrington F, Murray A, Ford GA. Relationship of baroreflex sensitivity and blood pressure in an older population. *J Hypertens* 2000; **18**: 1629–1633.
19. Manica G, Di Rienzo M, Parati G. Ambulatory blood pressure monitoring use in research and clinical practice. *Hypertension* 1993; **21**: 500–524.
20. Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Telera MP, Pede S, et al. Adverse prognostic value of a blunted circadian rhythm of heart rate in essential hypertension. *J Hypertens* 1998; **16**: 1335–1343.