

Published in final edited form as:

Biomed Pharmacother. 2005 October ; 59(Suppl 1): S54–S57.

Effect of aging on blood pressure in Leh, Ladakh, a high-altitude (3524 m) community, by comparison with a Japanese town

K. Otsuka^{a,*}, T. Norboo^b, Y. Otsuka^a, H. Higuchi^a, M. Hayajiri^c, C. Narushima^a, Y. Sato^d, T. Tsugoshi^e, S. Murakami^f, T. Wada^g, M. Ishine^g, K. Okumiya^h, K. Matsubayashiⁱ, S. Yano^j, T. Chogyal^b, D. Angchuk^b, K. Ichihara^k, G. Cornélissen^l, and F. Halberg^l

^aDepartment of Medicine, Medical Center East, Division of Neurocardiology and Chronoecology, Tokyo Women's Medical University, Nishiogu 2-1-10, Arakawa, Tokyo 116-8567, Japan

^bLadakh Heart Foundation, Ladakh, India

^cGraduate School of Agriculture, Hokkaido University, Sapporo, Japan

^dMedical Institute of Bioregulation, Kyushu University, Beppu, Japan

^eNagai Clinic, Misato, Saitama, Japan

^fOsaka Medical College, Takatsuki, Japan

^gDepartment of Field Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan

^hResearch Institute for Humanity and Nature, Kyoto, Japan

ⁱCenter for Southeast Asian Studies, Kyoto University, Kyoto, Japan

^jHokkaido Institute of Public Health, Sapporo, Japan

^kDivision of Clinical Laboratory Sciences, Faculty of Health Sciences, School of Medicine, Yamaguchi University. Ube, Japan

^lHalberg Chronobiology Center, University of Minnesota, Minneapolis, MN, USA

Abstract

The effect of aging on blood pressure (BP) and heart rate (HR) was investigated in a cross-sectional study in the high-altitude community of Leh, Ladakh (altitude: 3524 m) and a Japanese community in U town, Hokkaido (altitude: 25 m). BP and HR were obtained in a sitting position from 332 subjects 13–81 years of age in Ladakh, and from 216 Japanese citizens, 24–79 years of age. Measurements were taken after a 2-min rest, using a semi-automated BP device (UA-767 PC, A&D Co. LTD, Tokyo). High-altitude people showed higher diastolic BP and HR values than lowland people (83.2 vs. 76.9 mmHg and 78.6 vs. 69.2 bpm, $P < 0.001$), but no difference in systolic BP. Highland people also showed a steeper BP increase with age than the lowland people (systolic BP: 0.7476 vs. 0.3179 mmHg/year, $P < 0.0005$; diastolic BP: 0.3196 vs. 0.0750 mmHg/year, $P < 0.001$). This chronoecologic investigation in Ladakh examined the circulation as a physiological system at high-altitude. Our data indicate the need for a more comprehensive cardiovascular assessment for a better diagnosis and a more fruitful treatment. Longitudinal observations of effects of socio-ecologic factors on the cardiovascular system should help prevent strokes and other cardiovascular events, especially at high altitude.

Keywords

Aging; Blood pressure; High-altitude community; Comprehensive cardiovascular assessment

1. Introduction

Although physiological adaptation to high-altitude has been studied in resident populations of the Andes, Tibet, Nepal, North America and Europe, much less is known about high-altitude natives of India. Ladakh is one of the most remote regions of India, located with the Karakoram to the northwest, the Himalayas in the southwest, and the Trans-Himalayas at its core. There lies a sparsely populated area of Indian Himalaya at 3-4500 m altitude, consisting mainly of arid desert. We examined the effect of aging on blood pressure (BP) and heart rate (HR) in a high-altitude community of Ladakh (Leh, altitude: 3524 m). Results were compared with similar data obtained in a Japanese community in Hokkaido (U town, altitude: 25 m).

2. Subjects and methods

We measured the BP and HR of 332 subjects, 13-81 years of age (mean \pm S.D.: 50.0 \pm 14.8 years) living in Leh, Ladakh. In August 2004, a medical check of neurocardiovascular function was carried out. For comparison, we studied 216 citizens of U town in Hokkaido, 24-79 years of age (mean \pm S.D.: 56.8 \pm 11.3 years), where a medical check was performed in July 2004. BP, HR, and body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) were measured for all participants. BP and HR were measured in a sitting position after a 2-min rest, using a semi-automated BP device (UA-767 PC, A&D Co., LTD, Tokyo, Japan).

Linear regressions of BP and HR with age examined any changes as a function of aging in each population. Regression coefficients were compared by Student t-test between the two populations in order to assess any effect of altitude. Analyses were done with the Statistical Software for Windows (Stat-Flex Ver.5.0, Artec, Osaka, <http://www.statflex.net>). Statistical significance reached a value of $P < 0.05$.

3. Results

As shown in Table 1, Ladakhi people at an altitude of 3524 m had a higher diastolic BP and a higher HR than Japanese people at an altitude of 25 m (DBP: 83.2 vs. 76.9 mmHg, $t = 6.625$, $P < 0.001$; HR: 78.6 vs. 69.2 bpm, $t = 8.998$, $P < 0.001$). No difference in systolic BP was found between the two populations. As compared to the Japanese subjects, Ladakhis were younger (50.0 vs. 56.8 years, $t = 5.800$, $P < 0.001$) and leaner (BMI = 23.5 vs. 24.5 kg/m², $t = 3.428$, $P < 0.001$).

Both relations between BP and age and between BP and BMI are shown in Table 2. Ladakhi people at 3524 m show a steeper increase in BP with age than Japanese people (systolic BP: 0.7476 vs. 0.3179 mmHg/year, $t = 3.642$, $P < 0.0005$; diastolic BP: 0.3196 vs. 0.0750 mmHg/year, $t = 3.410$, $P < 0.001$), Fig. 1. No difference in HR was found between the two populations. As shown in Table 2, there was no statistically significant difference in the regression slope of BP or HR with BMI between the two populations.

4. Discussion

The main result of the present study is that high-altitude people showed a steeper increase in BP with age than low-altitude people. Several reasons may account for the difference. First, at higher altitude, atmospheric oxygen is lower; hypoxemia stimulates sympathetic nerve activity,

which is associated with an increase in BP and HR [1]. Second, it has been reported that carotid bodies from the Karakorams (including Ladakh) are heavier and larger, presumably related to the hypobaric hypoxia of the mountain environment. Such histological characteristics of the carotid bodies may alter the cardiovascular coordination in Ladakh people [2]. Third, Ladakh is one of the most remote regions of India, and lies embedded in the mountains of the Karakoram in the north-west, the Himalayas in the south-west, and the Trans-Himalayas at its core. Ladakh is a cold desert and its environmental temperature drops as low as -45°C in winter, whereas in summer, the temperature reaches up to 27°C , a factor that will also stimulate sympathetic activity and increase BP. Fourth, it has been reported that salt intake in Ladakh people is larger than in Japanese. A report [3] lists urinary sodium values (in $\text{nmol}/24\text{ h}$) of 209.1 and 198.2 for males and females in Ladakh, as compared to 191.0 and 145.6 for males and female in Osaka. This difference may result in an exaggerated increase in systolic and diastolic BP with age, as well as with a higher diastolic BP at rest, compared to Japanese people [3]. Fifth, angiotensin-converting-enzyme gene I/D polymorphism is reportedly associated with high-altitude disorders as well as with differences in physical performance [4-6]. It is also speculated that this polymorphism may be related to the larger increase in BP with age observed herein. Sixth, it has been reported that in Ladakh, silicosis is widespread among older people exposed to environmental dust. This may result in advanced fibrotic lung disease associated with disability [7-10]. Saiyed et al. [9] reported that environmental dust was associated with the severity of dust storms and the use of chimneys in the kitchens. Seventh, medical services are only now developing in Ladakh, and citizens do not have sufficient access to medicines. Eighth, poverty in Ladakh is such that delivery of electric power is insufficient. Lastly, Leh, the capital of Ladakh, was once the central meeting-point for trade caravans from Central Asia and the plains of India. The main religion is Tibetan Buddhism and many monks practice it in its original form. Cultural differences between Ladakh and Japan may also contribute to the differences in the effect of aging on BP.

Obesity is a risk factor for a number of chronic diseases. Herein, we found a difference in BMI between Ladakh and Japan. Whereas Ladakhi people are leaner, there was no statistically significant difference in the change in BP with BMI between the two populations, suggesting that BMI may not be the reason for an increase in BP in the Ladakhi people.

In conclusion, this investigation focused on the chronoecology of Ladakh, as it may affect the circulation as a physiological system at high altitude, by comparison with the chronoecology of U town in Japan. The main result of this study is a higher diastolic BP and a larger increase in BP with age in people living at high altitude in a cold desert area, as compared to Japanese people living at low altitude. Our data indicate the need for a comprehensive cardiovascular assessment to achieve a better diagnosis for a more fruitful treatment. Specifically, the effect of different environmental factors such as the weather, inside and outside temperatures, sunshine duration, geomagnetic latitude and geographical altitude, of lifestyle features such as body weight, salt intake, fruit and vegetable intake, alcohol consumption, smoking, physical activity and duration of sleep, as well as of depression and QOL scores (healthiness, mood, family relationship, financial satisfaction, life satisfaction and sense of happiness), and of neurobehavioral functions needs to be assessed together with BP changes, including circadian (24-h), circasemiseptan (3.5-day) and circaseptan (7-day) characteristics such as amplitudes (swinging), day-night ratios (dipping), morning surge and complexity of BP variability. Observations should be repeated longitudinally to assess the effect of these socio-ecologic factors on the cardiovascular system, as a step toward the prevention of stroke and the decline in cognitive function of the elderly, notably in a high-altitude community such as Leh, Ladakh.

Acknowledgements

This study was supported by Fukuda Foundation for Medical (Grant in 2004 for the study on association between arterial stiffness and cognitive impairment in community-dwelling subjects over 70 years-old).

References

- [1]. Norboo T, Saiyed HN, Angchuk PT, Tsering P, Angchuk ST, Phuntsog ST, et al. Mini review of high-altitude health problems in Ladakh. *Biomed Pharmacoth* 2004;58:220–225.
- [2]. Khan Q, Heath D, Smith P, Norboo T. The histology of the carotid bodies in highlanders from Ladakh. *Int J Biometeorol* 1988;32:254–259. [PubMed: 3235211]
- [3]. Centre-specific results by age and sex. *J Human Hypertens* 1989;5:331–407. Appendix Tables
- [4]. Qadar Pasha MA, Khan AP, Kumar R, Grover SK, Ram RB, Norboo T, et al. Angiotensin-converting-enzyme insertion allele in relation to high-altitude adaptation. *Ann Human Genetics* 2001;65:531–536. [PubMed: 11851983]
- [5]. Kumar R, Qadar Pasha MA, Khan AP, Gupta V, Grover SK, Norboo T, et al. Association of high-altitude systemic hypertension with the deletion allele-of the angiotensin-converting enzyme (ACE) gene. *Int J Biometeorol* 2003;48:10–14. [PubMed: 12743791]
- [6]. Ahsan A, Charu R, Pasha MA, Charu R, Afrin F, Ahsan A, et al. eNOS allelic variants at the same locus associate with HAPE and adaptation. *Thorax* 2004;59:1000–1002. [PubMed: 15516480]
- [7]. Norboo T, Yahya M, Bruce NG, Heady JA, Ball KP. Domestic pollution and respiratory illness in a Himalayan village. *Int J Epidemiol* 1991;20:749–757. [PubMed: 1955261]
- [8]. Norboo T, Angchuk PT, Yahya M, Kamat SR, Pooley FD, Corrin B, et al. Silicosis in a Himalayan village population: role of environmental dust. *Thorax* 1991;46:341–343. [PubMed: 2068689]
- [9]. Saiyed HN, Sharma YK, Sadhu HG, Norboo T, Patel PD, Venkaiah K, et al. Non-occupational pneumoconiosis at high-altitude villages in central Ladakh. *Br J Industrial Med* 1991;48:825–829.
- [10]. Wood S, Norboo T, Lilly M, Yoneda K, Eldridge M. Cardiopulmonary function in high-altitude residents of Ladakh. *High-Altitude Med Biol* 2003;4:445–454.

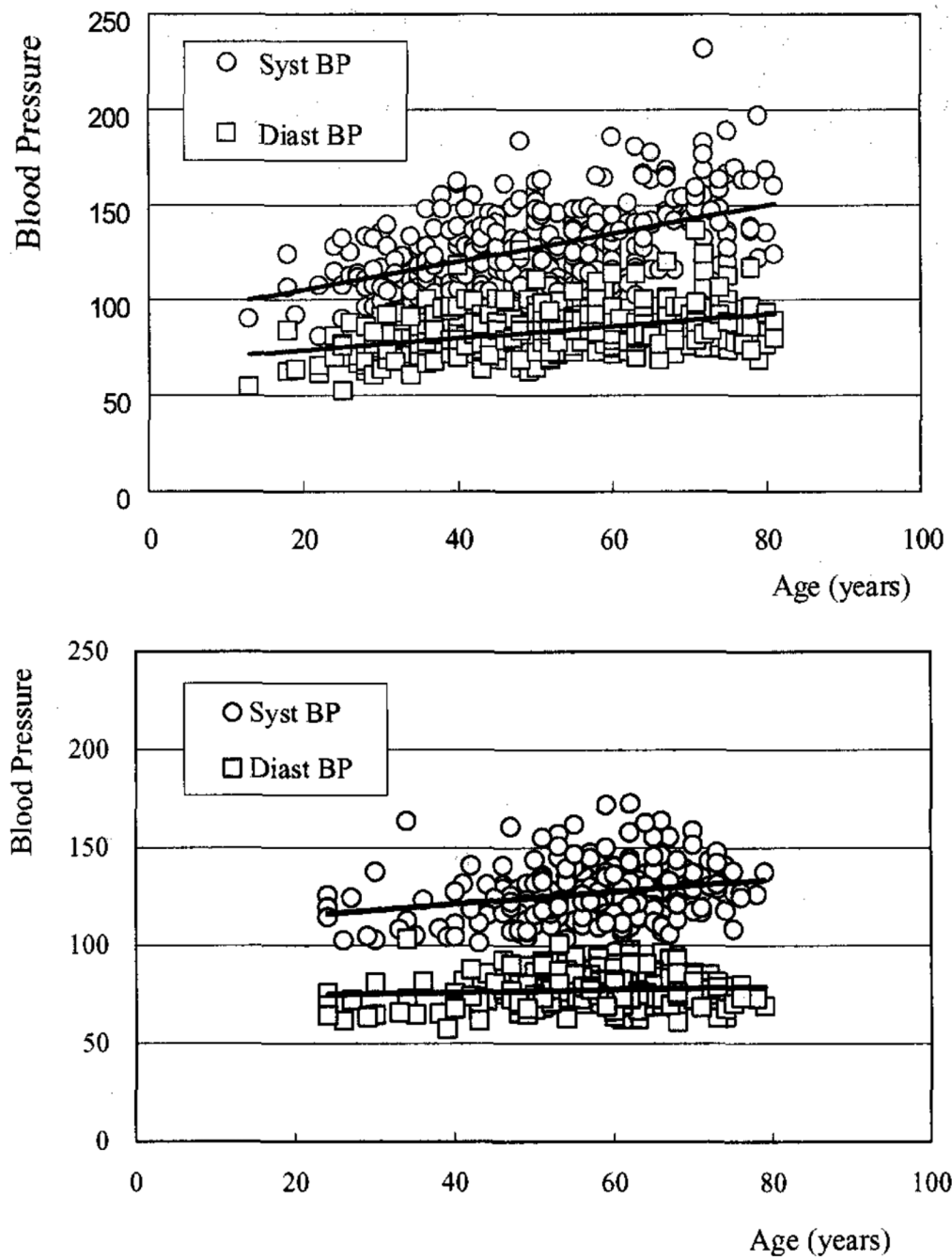


Figure 1.

Comparison of slopes of regression lines between BP and age in highland (Leh, Ladakh, altitude 3524 m, top) and lowland (U town, Hokkaido, altitude 25 m, bottom) citizens. In this cross-sectional study, the increase in BP with age is steeper among highland than lowland residents (systolic BP: 0.7476 vs. 0.3179 mmHg/year, $t = 3.642$, $P < 0.0005$; diastolic BP: 0.3196 vs. 0.0750 mmHg/year, $t = 3.410$, $P < 0.001$).

Table 1
Comparison of BP, HR and BMI between subjects in Japan and Ladakh

	Japan (U town) <i>n</i> = 216			Ladakh (Leh) <i>n</i> = 332			Student <i>t</i>	<i>P</i> -value		
	Mean	S.D.	Min	max	Mean	SD			min	max
Age (years)	56.8	11.3	24	79	50.0	14.8	13	81	5.800	<0.0001
SBP (mmHg)	126.0	14.7	95	172	127.7	21.0	81	232	-1.027	N.S.
DBP (mmHg)	76.9	8.4	57	103	83.2	12.0	52	136	-6.625	<0.0001
HR (bpm)	69.2	7.2	48	92	78.6	14.1	47	122	-8.998	<0.0001
BMI (kg/m ²)	24.5	2.9	17.5	34.7	23.5	3.8	15.7	41.7	3.428	<0.0001

DBP: Systolic BP; DBP: Diastolic BP; HR: Heart Rate; BMI: Body Mass Index

Table 2

Comparison of the slope of BP and HR changes with age between Japan and Ladakh from cross-sectional surveys

	Japan	Ladakh	Student t	P-value
SBP vs. age	0.3179	0.7476	-3.6420	<0.0005
DBP vs. age	0.0750	0.3196	-3.4100	<0.001
HR vs. age	-0.1915	-0.1485	-0.5174	N.S.
BMI vs. age	0.0370	0.0306	0.2648	N.S.
SBP vs. BMI	0.0672	0.0593	0.4556	N.S.
DBP vs. BMI	0.8463	0.7401	0.3656	N.S.
HR vs. BMI	0.0849	-0.1019	0.5628	N.S.

SBP: Systolic BP; DBP: Diastolic BP; HR: Heart Rate; BMI: Body Mass Index.