Low nocturnal blood pressure is associated with reduced cerebral blood flow in the cohort “Men born in 1914”

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F Reinprecht, J Axelsson, A Siennicki-Lantz, S Elmståhl. Low nocturnal blood pressure is associated with reduced cerebral blood flow in the cohort “Men born in 1914”. *Int J Angiol* 2008;17(2):71-77.

BACKGROUND: “Men born in 1914” is a population-based cohort study of the epidemiology of cardiovascular and cerebral disease. Little is known about how diurnal variation in blood pressure (BP) levels influence cerebral perfusion in very elderly populations.

OBJECTIVES: To study the association between systolic (SBP) and diastolic BP (DBP) levels, during the day and at night, expressed through 24 h ambulatory BP monitoring (ABPM) and regional cerebral blood flow (rCBF) disturbances.

METHODS: A cross-sectional study from a population-based cohort of 108 men 81 years of age (born in 1914) was performed in an outpatient university clinic. Cerebral blood flow measurements using ^{99m}Tc-hexamethylpropyleneamine oxime single photon emission computed tomography and 24 h ABPM were performed. Eleven men were excluded due to incomplete ABPM data.

RESULTS: Mean DBP at night for each tertile was correlated to rCBF for the medial temporal right (P=0.012) and left (P=0.039) regions. Also, DBP during the day was correlated to the medial temporal right region (P=0.025). When analyses were stratified for DBP during the day, subjects with high DBP during the day (greater than 70 mmHg) showed a stronger association between low medial temporal right rCBF and low mean DBP at night (r=0.32, P=0.009) compared with subjects who had a lower daytime DBP. A corresponding positive correlation was noted for the medial temporal left region and daytime SBP, whereas a negative correlation was noted for frontal left region blood flow and SBP at night.

CONCLUSIONS: A significant association was seen between low BP levels, especially at night, and rCBF in subjects with otherwise normal daytime DBP that may indicate a risk for nocturnal cerebral ischemia.

Key Words: Blood pressure monitoring; Cerebral autoregulation; Cohort study; Nocturnal blood pressure, Regional cerebral blood flow

It is well established that regional cerebral blood flow (rCBF) mirrors brain metabolic activity (1) and provides information about the functional level of the cerebral cortex. In healthy subjects, the maintenance of constant rCBF (cerebral autoregulation) occurs within a wide range of arterial blood pressures (BPs). Cerebral blood flow (CBF) is generally autoregulated to a mean arterial BP (MABP) of between 70 mmHg and 140 mmHg (2). Beyond these limits, autoregulation is unable to compensate for the pressure changes.

In patients with orthostatic hypotension, the autoregulation range may be shifted downwards, so that lower arterial pressures may be tolerated without symptoms. However, in elderly patients, cerebral autoregulation failure may contribute to the development of clinical signs of cerebral ischemia (3). These findings imply that such patients may be at particular risk for brain damage from even minor decreases in BP (4). Cerebral hypoperfusion due to systemic arterial blood hypotension as a cause of brain damage is a disputed issue. However, some studies confirm earlier observations that certain types of brain damage, especially in the white matter, may develop due to hypotensive episodes, and are often associated with cardiovascular disorders such as cardiac arrhythmia (5,6).

Normal aging is associated with the degeneration of specific neural systems; functional imaging data generally show impairment in global CBF with age. These findings suggest that

advancing age has a differential effect on cerebral perfusion, affecting certain areas in the frontal, parietal, temporal and occipital lobes on different brain levels (7). Brain atrophy, white matter changes and silent infarctions, frequently detected in the elderly by computed tomography (CT) and magnetic resonance imaging, are correlated with vascular risk factors and cognitive decline (8).

There is still no evidence that explains how the presence of vascular disease affects brain function in elderly patients without dementia. So far, to our knowledge, few studies have investigated the distribution of white matter changes in elderly patients and their possible relationship with systemic BP, expressed as rCBF (9,10). It is still unknown how the diurnal variation in BP levels, calculated from individually defined day and night times, are correlated with rCBF changes in the very elderly population. Subjects with lower BP levels at night may have impaired autoregulation and may be at risk for developing cerebral hypoperfusion.

A previous longitudinal cohort study (11) on atherosclerosis, the prospective “Men born in 1914” cohort, previously examined at 68 years of age, was re-examined at 81 years of age. The aims of the present study are to investigate the association between both diastolic (DBP) and systolic BP (SBP) levels, during the day and at night, expressed through 24 h ambulatory BP monitoring (ABPM), and CBF disturbances, expressed as rCBF in a cohort of men born in 1914.

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METHODS

Population

The "Men born in 1914" study (11) is a prospective population study that has been in progress since 1968 – the men were first examined at age 54. The cohort includes all men born in even months of 1914 and residing in Malmö, Sweden. Five hundred of 560 men participated in a health examination between 1982 and 1983, which also included measurements of carotid blood flow, circulation in the leg, lipid analysis, smoking habits and alcohol consumption.

Between 1995 and 1996, at the most recent follow-up of the cohort, 281 men were still alive and were invited to participate. Of these, 186 men (66%) agreed to take part in the new investigation. The previous examinations were repeated on this occasion. One man filled in the questionnaire but declined to take part in the clinical investigation; this individual was excluded because of incomplete data. A description of the background data of the 185 subjects in the recent cohort of the study, and the follow-up between 1982 and 1996 was made previously (11,12). During the following year, subjects were contacted and asked to participate in rCBF examination and ABPM; 108 men performed both. Eleven men were excluded due to incomplete ABPM data. They showed a deficit of data for up to 6 h accumulated during the day, more than 3 h accumulated at night (22:00 to 06:00), more than 3 h of consecutive deficit during the day or at least 2 h of consecutive deficit at night. Finally, data from 97 subjects were analyzed.

Questionnaire and health examination

A letter of invitation was sent out in January 1995 to the 281 survivors who had previously participated in the study. The 186 men who agreed to participate were sent a written questionnaire to fill in at home. The first part of the questionnaire included sociodemographic variables (marital status, education and social class). Marital status was dichotomized into two groups: unmarried or noncohabitant, and married or cohabitant. Education was classified into four categories: four to six years, seven to nine years, 10 to 13 years and more than 14 years education. Categorization of social class was based on data about former professions, working tasks and positions. Social class III included 'blue-collar' workers and social class II included low and medium level 'white-collar' workers. Social class I included subjects in leading positions – professionals with university degrees and owners of business enterprises with employees (13,14).

The second part of the questionnaire included questions on prescribed medications, tobacco consumption, alcohol intake in the past month, physical activity, health status and history of previous ischemic heart disease. Ischemic heart disease was indicated if the proband fulfilled the diagnostic criteria for angina pectoris according to the Rose Questionnaire (15), if the patient was hospitalized for myocardial infarction (MI), or both. The men were categorized into three groups according to their smoking habits: nonsmokers (those who had never smoked regularly, or had smoked less than 1 g of tobacco per day for less than one year), ex-smokers (previous smokers who had stopped at least one month before the investigation) and current smokers (those who smoked at least 1 g of tobacco per day, or had given up smoking less than one month before the investigation). Physical activity was classified as follows: low physical activity (mostly sedentary activities such as reading and watching television), moderate physical activity (over 4 h

per week of walking, cycling, light gardening) and high physical activity (more than 3 h per week of swimming, running, heavy gardening) (16).

The medical examination included BP measurement. Upper arm SBP and DBP were measured sphygmomanometrically, with the subject supine after 15 min of rest, using a calibrated mercury manometer and a standard rubber cuff 12 cm × 35 cm. Three pressures were recorded to the nearest 5 mmHg and the mean was calculated from the assessments. Hypertension was defined as brachial SBP and DBP 160 mmHg or greater and 90 mmHg or greater, respectively, or medication for hypertension (17). All examinations were performed without changing hypertension treatments. Diabetes mellitus was defined as a fasting blood glucose level greater than 7 mmol/L or medication for diabetes mellitus (18).

Data on mortality and cause of death were obtained from the Mortality Register at the Swedish National Bureau of Statistics (19). Causes of death were coded in accordance with the *International Statistical Classification of Diseases, Injuries, and Causes of Death, Eighth Revision* (20). Information on incident stroke between 1982 and 1995 among nonparticipants was retrieved from medical records using the Stroke Registry database at the hospital. Stroke was defined according to the *International Statistical Classification of Diseases, Injuries, and Causes of Death, Ninth Revision* (21).

rCBF measurement

rCBF was measured with single photon emission CT (SPECT). The radiopharmaceutical used for estimating perfusion was ^{99m}Tc-hexamethylpropyleneamine oxime (Ceretec, GE Healthcare) (22,23). Measurement was obtained 1 h after intravenous injection of 800 MBq of this substance.

The subjects were placed prone on the gamma camera couch, and each subject's head was fixed using a vacuum cushion. Examination was performed under resting conditions, in normal lighting and background noise. A triple-headed gamma camera system (MultiSPECT, Siemens, USA) was used with fan beam low energy collimators. The acquisition was performed in 360° (rotation, 64 views, 20 s/view, in a 128 × 128 matrix and a zoom factor of 1.23). A 15% energy window was centred over the 140 kV peak. Image processing included reconstruction of 10 transaxial slices, 1 cm thick, from 1 cm below the orbitomeatal line and upward. Regions of interest (ROIs) were delineated in each slice through the use of a standardized set of free-dimensional regions. The ROIs were positioned and scaled to the recorded SPECT slices based on the external borders of each slice. They included the cerebellum, occipital area, and in each hemisphere, the cortex of the frontal orbital, lateral and medial regions, parietal superior and inferior regions, and the temporal medial and lateral regions. The measured value in each ROI was quantified as a percentage of the mean cerebellar concentration of the 800 MBq radiopharmaceutical presented above.

ABPM

Monitoring ambulatory BP requires a mercury sphygmomanometer. In the present case, a Micro AM Recorder, Model KI5600 (Kontron Instruments, France) was used (24). The accuracy of the KI5600 was confirmed by simultaneous measurements with a standard mercury sphygmomanometer; ambulatory readings were accepted if they were within 10 mmHg of the standard method. Intervals were programmed

TABLE 1

Prevalence (%) of various vascular risk and lifestyle factors for the 81-year-old men in the lowest tertile versus the other two tertiles of mean diastolic (DBP) and systolic blood pressure (SBP) at night

Data	DBP, night					SBP, night				
	Lowest tertile		Other tertiles		P	Lowest tertile		Other tertiles		P
	n	%	n	%		n	%	n	%	
Hypertension	32	13	65	32	0.036	32	22	65	28	0.538
Antihypertensive drug treatment	31	36	65	42	0.658	31	45	65	37	0.506
Diabetes mellitus	32	16	65	5	0.064	32	13	65	6	0.285
Smoking habits	32		65		0.235	32		65		0.148
Nonsmoker		22		28			19		29	
Former smoker		69		57			72		55	
Current smoker		9		15			12		15	
Alcohol consumption	31		65		0.741	31		65		0.391
Yes		87		83			90		81	
Abstainer		13		17			10		19	
Physical activity										
Moderate	32	84	65	83	0.871	32	84	65	83	0.871
Ankle-brachial index <0.90	32	22	64	28	0.511	31	26	65	26	0.971
Angina pectoris	32	31	65	15	0.069	32	25	65	19	0.454
Myocardial infarction	32	34	65	11	0.005	32	34	65	11	0.005
Stroke	32	6	65	8	0.796	32	6	65	8	0.796
Civil status	32		65		0.673	32		65		0.572
Unmarried or noncohabitant		19		22			22		18	
Married or cohabitant		81		79			78		80	
Education	32		65		0.477	32		65		0.845
4–6 years		13		9			13		9	
7–9 years		69		72			69		72	
10–13 years		9		15			16		12	
>14 years		9		3			3		6	
Social class	32		65		0.692	32		65		0.340
I		13		14			22		12	
II		44		37			41		37	
III		44		49			38		51	

Limits for the lowest tertile: DBP<61 mmHg, SBP<115 mmHg

in the following way: three readings per hour at 20 min intervals during the day (from 06:20 to 21:40) and at 60 min intervals at night (from 22:00 to 06:00). The Research Department at Malmö University Hospital fitted the monitors to the subjects. Physical activity was advised against only if it would interfere with obtaining accurate readings. Because of the need to monitor the subjects for 24 h, the data had to be collected in their own private environment.

Measures of cognitive functions

The Mini Mental State Examination (MMSE) (25) was added and a battery of cognitive tests were excluded from the analyses of the present study at follow-up.

Statistical analyses

A mean value of DBP at night was calculated and divided into tertiles. The lowest tertile was compared with the other two tertiles, and the mean rCBF was tested using the Mann-Whitney U test. Spearman correlation coefficients were used to describe the relationship between CBF in different regions, and mean DBP and SBP at night.

RESULTS

The description of prevalence of vascular risk and lifestyle factors, at 81 years of age, in relation to the lowest tertile of mean SBP and DBP at night, is given in Table 1. Higher proportions of MI and angina pectoris ($P=0.005$ and $P=0.069$, respectively) were noted among subjects in the lowest tertile of DBP at night. A higher proportion of MI was also noted among subjects with SBP at night in the lowest tertile, compared with the other tertiles ($P=0.005$).

Mean DBP and SBP during the day were 76 ± 10 mmHg and 131 ± 12 mmHg, respectively. Mean DBP and SBP during the night were 68 ± 11 mmHg and 121 ± 13 mmHg, respectively. Mean levels of DBP and SBP, by tertile, at night and during the day are presented in Table 2. Similar mean values of rCBF in the low and high DBP and SBP tertiles were noted in different cerebral regions. However, rCBF for the medial right and left temporal lobes, areas involved in memory functions, correlated to mean DBP and SBP at night (Table 3). Similar findings were also noted for daytime DBP and SBP.

Of the 34 subjects with low DBP at night (less than 61 mmHg), 11 subjects (32%) had a daytime DBP greater than

TABLE 2

Mean night-time diastolic (DBP) and systolic blood pressure (SBP) by tertiles, and regional cerebral blood flow (rCBF) in men 81 years of age

CBF region or mean blood pressure	DBP, night			SBP, night		
	Low, n=32 <61 mmHg	Medium, n=33 61–70 mmHg	High, n=32 >70 mmHg	Low, n=32 <115 mmHg	Medium, n=31 115–125 mmHg	High, n=34 >125 mmHg
Mean DBP night, mmHg	56.9±3.2	65.8±2.9	79.9±7.9	59.2±5.8	67.5±6.8	75.4±11.4
Mean DBP day, mmHg	66.8±6.5	74.4±5.8	85.4±8.6	69.4±8.5	74.7±7.2	82.0±10.9
Mean SBP night, mmHg	111.1±10.0	120.5±9.8	130.9±9.9	106.7±5.43	120.8±3.4	134.2±7.3
Mean SBP day, mmHg	123.0±9.9	130.0±11.2	138.6±10.5	120.0±7.9	129.4±6.9	141.6±9.9
Frontal lobe, right	81.8±5.3	81.4±6.3	80.4±5.4	82.2±6.5	80.6±5.6	80.7±4.9
Frontal lobe, left	81.5±5.5	80.8±5.8	80.1±5.0	81.9±6.2	80.4±5.4	80.0±4.7
Temporal lobe, right medial	79.5±5.1	79.8±5.2	81.6±4.0	80.0±6.4	79.9±3.8	80.9±4.1
Temporal lobe, right lateral	79.5±5.3	79.0±5.4	80.2±4.4	79.9±6.8	79.4±3.6	79.2±4.3
Temporal lobe, left medial	79.4±4.7	79.5±4.7	80.7±3.7	79.7±6.1	79.6±3.2	80.3±3.5
Temporal lobe, left lateral	79.3±5.2	78.5±4.8	79.3±4.6	79.3±6.3	79.3±3.9	78.4±4.1
Parietal lobe, right	81.7±6.0	81.2±5.7	82.3±5.8	81.9±6.9	81.3±5.2	81.9±5.2
Parietal lobe, left	81.3±5.8	80.6±6.4	81.0±6.0	81.5±6.7	80.8±5.8	80.4±5.7
Occipital lobe	89.3±5.8	88.4±6.9	90.7±6.8	89.3±7.1	89.1±6.1	89.7±6.7

The CBF values express the percentage ± SD of regional gamma ray uptake in relation to uptake in the cerebellum. DBP and SBP are expressed as mean ± SD

TABLE 3

Spearman rank correlation coefficients (r_s) between cerebral blood flow (CBF) by region, and mean diastolic (DBP) and systolic blood pressure (SBP) both at night and during the day

CBF region	DBP night		DBP day		SBP night		SBP day	
	r_s	P	r_s	P	r_s	P	r_s	P
Frontal lobe								
Right	−0.21	0.034	−0.11	0.255	−0.11	0.257	−0.06	0.569
Left	−0.24	0.015	−0.11	0.298	−0.22	0.031	−0.15	0.146
Temporal lobe								
Right medial	0.250	0.012	0.22	0.025	0.19	0.053	0.20	0.045
Right lateral	0.09	0.381	0.07	0.511	0.04	0.686	0.09	0.390
Left medial	0.21	0.039	0.18	0.072	0.20	0.045	0.23	0.023
Left lateral	0.05	0.657	−0.09	0.394	0.01	0.937	−0.01	0.914
Parietal lobe								
Right	0.09	0.354	0.02	0.829	0.12	0.243	0.06	0.543
Left	−0.03	0.752	−0.10	0.301	−0.03	0.782	−0.07	0.477
Occipital lobe	0.10	0.340	0.05	0.606	0.09	0.371	0.07	0.472

70 mmHg (Table 4). Thus, measuring daytime BP only would not identify the patients with low DBP at night. Associations between rCBF and DBP at night for subjects stratified for DBP during the day are given in Table 5. Among subjects with a daytime DBP greater than 70 mmHg, a stronger association was noted between the right temporal medial region and mean DBP at night ($r=0.32$, $P=0.009$) (Figure 1) compared with subjects with lower daytime DBP. No association was noted between subjects with low daytime DBP and rCBF regions. Thus, measurement of daytime DBP only will not discriminate between possible associations between (low) DBP at night and low CBF in temporal regions. Levels of rCBF among the

65 subjects with high daytime DBP (greater than 70 mmHg) were significantly lower in the right and left temporal medial regions among those with low DBP at night (DBP less than 61 mmHg; $n=11$) compared with those in the other tertiles (DBP greater than 61 mmHg; $n=54$), 77.6 mmHg versus 80.4 mmHg, $P=0.04$, and 77.2 mmHg versus 79.8 mmHg; $P=0.05$, for those with low DBP at night and those in the other tertiles, respectively. No significant difference of rCBF, in relation to DBP at night, was noted in the subgroup with low DBP during the day.

The mean ($\pm$ SD) MMSE score was 28.4 ± 1.7 (range 18 to 30); three subjects had a MMSE score below 25. Analysis after

TABLE 4

Cross-tabulation of 108 men, who underwent 24 h ambulatory blood pressure monitoring at the age of 81, sorted by tertiles for mean diastolic blood pressure (DBP) during the day (rows) and at night (columns)

DBP, day	DBP, night			Total
	Low (<61 mmHg)	Medium ($61-70$ mmHg)	High (>70 mmHg)	
Lowest tertile (<71 mmHg)	23 (63.9)	11 (30.6)	2 (5.6)	36 (100)
Two highest tertiles	11 (15.3)	28 (38.9)	33 (45.8)	72 (100)
Total	34 (31.5)	39 (36.1)	35 (32.4)	108 (100)

Results presented as n (%)

exclusion of these three subjects showed the same pattern with significant correlation between the medial temporal region and DBP night by tertiles (data not shown).

Ninety-seven of the 185 subjects completed all measurements. Analysis of the 88 dropouts revealed no significant differences among the listed lifestyle characteristics and vascular risk factors given in Table 1, compared with the participants, except for marital status. A higher proportion of participants were married compared with nonparticipants (79% versus 65%).

DISCUSSION

The present cohort study demonstrates an association between BP levels and rCBF, especially at night. No previous studies have examined variation of BP at night as a risk factor for ischemic cerebral circulation in elderly patients.

Mean levels of BP at night were calculated and showed a relation to rCBF. It is possible that transient drops in low BP levels may not have been captured, because BP was only measured hourly at night, and the circadian variability may have been underestimated (4,26). However, low BP levels at night could be a more important indicator of cerebral ischemia than episodic changes of BP. Such findings indicate that continuous BP recording is of special value for studying the relation between cerebral function and BP variations.

Normal BP has a diurnal variation, with the lowest levels occurring at night. Some of the participants, who had missing data for more than a total of 6 h accumulated during the daytime, more than 3 h accumulated at night, more than 3 h consecutive during the daytime or at least 2 h consecutive at night, were excluded. To our knowledge, in previous studies, MABP during the day and night were calculated, but the participants with missing data were not excluded (26,27). The chosen limits for missing data during recording were arbitrary, but if more participants had been included, the mean calculated levels during the night may have been falsely high. Incomplete registration of BP at night may reduce assessment of circadian variability. In the present study, 32% of participants had complete registration, and 34% and 26%, respectively, had missing data from one and two registrations. The remaining 8% had missing data from more than two registrations. Mean SBP and DBP at night did not differ between these groups, nor did the variability expressed as SD between groups. A lower mean BP level at night among those

TABLE 5

Spearman rank correlation coefficients (r_s) between diastolic blood pressure (DBP) at night and cerebral blood flow (CBF) in different regions stratified for DBP during the day (low versus middle and high tertiles)

CBF region	Daytime DBP <70 mmHg (low tertile, n=32)		Daytime DBP >70 mmHg (other tertiles, n=65)	
	DBP, night, r_s	P	DBP, night, r_s	P
Frontal lobe				
Right	0.03	0.874	-0.12	0.329
Left	-0.04	0.833	-0.05	0.686
Temporal lobe				
Right medial	-0.06	0.728	0.32	0.009
Right lateral	-0.13	0.487	0.23	0.061
Left medial	-0.12	0.513	0.28	0.022
Left lateral	-0.10	0.624	0.19	0.125
Parietal lobe				
Right	0.13	0.470	0.08	0.505
Left	0.11	0.555	0.04	0.732
Occipital lobe	-0.03	0.869	0.13	0.296

Figure 1 Positive association between low mean diastolic blood pressure (DBP) at night and low cerebral blood flow in the medial temporal right region in subjects with DBP greater than 70 mmHg during the day, but no association for subjects with low DBP (less than 70 mmHg) during the day. CBF Cerebral blood flow; NS Not significant

with complete assessments would have been expected if incomplete registration was associated with a systematic bias.

The rCBF method is sensitive in detecting cerebral changes related to stroke and dementia (9,28,29). Furthermore, the SPECT method has shown high correlation with the CBF ratio as estimated with positron emission tomography (7,10). Cerebral atrophy results in a compensatory increase of the cerebral ventricle system that can introduce false low rCBF estimations in regions close to the ventricles. However, the regions were chosen according to previous studies using both rCBF and CT (8,30). Another limitation of the method is the appearance of artifacts from head movements during examination. In the present study, examinations were performed at rest condition using a vacuum cushion to minimize this kind of error.

If multiple small ROIs are used for statistical analyses, the risk of false positive results will increase due to the multiple comparisons phenomenon. Therefore, the number of ROIs was limited in the present study to reduce Type I error, using large lobular ROIs. The consequence of using large ROIs is that minor vascular changes go undetected.

We have shown, in our study, that nocturnal BP levels influence cerebral circulation and are correlated with rCBF patterns in elderly men. The analysis of correlation between rCBF and mean DBP at night, by tertiles, showed significant correlation of DBP with the temporal right and left medial regions. Also, daytime DBP was correlated to the temporal right medial region. These regions are especially vulnerable to ischemic damage.

So far, there are few published studies investigating the functional brain changes in age-associated memory impairment or mild cognitive impairment with SPECT or positron emission tomography. Studies of brain-damaged patients with selective memory impairment have convincingly demonstrated that some forms of long-term memory depend on the integrity of the medial temporal lobe (30-32). The medial temporal lobe system consists of the hippocampal formation, including the adjacent, anatomically related parahippocampal gyrus and entorhinal cortex. The medial temporal lobe has widespread reciprocal connections, with an associative neocortex as well as subcortical structures. Abnormalities in these brain structures are related to vascular diseases and cardiovascular risk factors, and can be seen as a clinical syndrome of intellectual decline produced by ischemic, hypoxic brain lesions.

It is well known that hypertension predisposes for different types of both intra- and extracerebral arterial lesions, which may cause cerebrovascular damage (11,33-35).

Other mechanisms have been discussed and may be of importance in the development of cerebrovascular insufficiency, ie, those in which the CBF is inadequate for the metabolic needs of brain tissue. Several conditions, such as heart disorders and hypotension, may lead to hypoperfusive lesions in vulnerable parts of the brain. Cerebral perfusion is directly related to cardiac output, and cardiac abnormalities may therefore lead to cerebral hypoperfusion. Cardiac infarction in elderly patients, heart rhythm disorders and stenosis of the carotid artery have been pointed out as important risk factors (6).

This is in accordance with the higher frequency of MI among men with low DBP at night in the present study. The mean SBP was 131 mmHg, and one-third had an SBP below 115 mmHg at night. However, the association between cerebral perfusion and cardiac output remained similar.

The association of nocturnal and postprandial hypotension and the presence of lacunes in the elderly were also observed

(7,29). A J-shaped curve between BP and stroke morbidity was reported (27).

Low BP and orthostatic hypotension are common findings in patients with dementia, especially in the late stage, who also present with reduced levels of rCBF (9). However, when the men with suspected cognitive decline, defined as having an MMSE score below 25, were excluded, the association remained the same.

The association between low rCBF in vulnerable areas, such as the temporal regions, and low DBP at night was noted among subjects with high DBP during the day (greater than 70 mmHg) indicates the usefulness of ABPM for identifying possible risk groups. A clinical finding is that one-third of the subjects with low DBP at night had normal or high daytime DBP levels; these could only be identified through 24 h ABPM. A surprising finding was the lack of association between rCBF and DBP at night among subjects with low daytime DBP. One explanation may be that this group has fewer vascular risk factors, such as hypertension, and less MI and angina pectoris that could hypothetically affect cerebral autoregulation.

Previous studies in patients with hypertension have reported that nondipping of BP during the night is a risk for cerebrovascular disease, in contrast with the present study (36). Consistent variations in BP occur as a result of diurnal rhythm, with the highest pressures in the morning and the lowest during sleep (37). BP in some patients with essential hypertension is known to remain elevated throughout the night. These patients, whose 24 h BP does not follow the normal diurnal pattern and remains high at night, are likely to suffer more cerebrovascular complications, as well as other atherosclerotic cardiovascular diseases, than those patients whose BP decreases at night. An explanation for this finding could be that the MABPs among those men were within normal levels. However, the prevalence of cardiovascular disease was more prominent in the group with low DBP at night; this may indicate disturbed autoregulation.

The association between low BP, especially at night, and lower rCBF may be explained by insufficient cerebral autoregulation. This may lead to an extensive reduction of cerebral perfusion and subsequent ischemic damage (2,38). Autoregulation of rCBF is effective over a wide range of arterial BPs, but has a lower, as well as an upper, pressure limit. Under normal conditions, these limits are MABPs of between approximately 70 mmHg and 140 mmHg (39).

In the present study, the mean DBP level at night for the lowest tertile was 56 mmHg. Interpretation of the present study's results is limited to men, but we have no reason to believe that autoregulation differs between sexes. Furthermore, selection bias seems unlikely, because participants and nonparticipants had no differences in lifestyle factors and sociodemographic characteristics.

CONCLUSION

The noted association between rCBF and low BP, especially at night, may indicate an increased risk for nocturnal cerebral ischemia. Further longitudinal studies are needed to analyze cognitive function and the possible risk for cognitive decline in relation to low BP at night.

FUNDING SOURCES: Swedish Research Council (K2004-27X-15016-01A) and the Faculty of Medicine at Lund University.

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