Influence of Age, Hypertension or Myocardial Infarction on Cardiovascular Responses to Changes in Body Position

A population-based study in 30-, 50- and 60-year-old men

BY

ANNA HOFSTEN

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ABSTRACT

Hofsten, A. 2000. Influence of age, hypertension or previous myocardial infarction on cardiovascular responses to changes in body position. A population-based study in 30-, 50- and 60-year-old men. 39 pp. Uppsala ISBN 91-506-1433-9.

An age-related attenuation of the normal increase in diastolic blood pressure and heart rate upon standing has previously been observed in man. Whether this is due to aging as such or is a consequence of a higher prevalence of cardiovascular disease in older compared to younger subjects is unclear. This population-based study addresses this question and presents the blood pressure and heart rate responses to sudden changes in body position in representative groups of men aged 30 (n=50), 50 (n=44) and 60 (n=69) years, as well as in 60-year-old men with hypertension (n=75) or previous myocardial infarction (n=39) and in a control group (n=41) free from these diseases.

Blood pressure and heart rate were measured during three seven-minute periods (supine-standing-supine), using an unbiased non-invasive method. Whereas there was an initial decrease in systolic blood pressure upon standing in men aged 50 and 60 years, an increase was seen in the 30-year-olds. The diastolic blood pressure increased in all age groups, but less in the older compared to the younger men. In all age groups, the change in systolic blood pressure upon standing was transient, while the changes in the diastolic blood pressure lasted during the entire observation period. The heart rate increased to a similar extent upon standing in all age groups. After resuming the supine position, both blood pressure and heart rate returned to the levels initially recorded. The cardiovascular responses were both qualitatively and quantitatively similar in all three groups of 60-year-old men (with or without hypertension or previous myocardial infarction).

In conclusion, this population-based study confirmed previous observations of an age-related attenuation of the blood pressure response to change in body position. However, 60-year-old men with hypertension or previous myocardial infarction had blood pressure responses similar to those of men of the same age and free from these diseases. This indicates that the attenuated response in older compared to younger subjects is not explained by the higher prevalence of these cardiovascular diseases in the elderly, but appears to be the result of normal aging.

Key words: Age factors, blood pressure, epidemiology, hypertension, myocardial infarction, posture.

Anna Hofsten, Department of Public Health and Caring Sciences, Uppsala Science Park, SE-751 85 Uppsala, Sweden

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ORIGINAL PAPERS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

I. Hofsten A, Elmfeldt D, Svärdsudd K. Age-related differences in blood pressure and heart rate responses to changes in body position: Results from a study with serial measurements in the supine and standing positions in 30-, 50- and 60-year-old men. Blood Press 1999; 8: 220-6.

II. Hofsten A, Elmfeldt D, Svärdsudd K. Does hypertension or a previous myocar-dial infarction influence the blood pressure and heart rate responses to changes in body position? – Results from a study with serial measurements in the supine and standing positions in 60-year-old men. Blood Press 2000 (in press).

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INTRODUCTION

The ability of man to adapt to a rapid change in body position from supine to standing without fainting is critically dependent on the ability to maintain mean arterial pressure and cerebral blood flow within rather narrow ranges. It has been reported that this haemodynamic adaptation is attenuated with increasing age [1-3] and cardiovascular disease [4-7]. Whether this is due to aging as such, or is a consequence of a higher prevalence of cardiovascular disease in older compared to younger subjects is unclear.

Cardiovascular responses to changes in body position

The purpose of the circulatory system is to provide sufficient perfusion to all cells in order to ensure adequate transport of nutrients, oxygen, heat, hormones and waste products to and from the tissues. This is a closed system in which the blood is pumped by the heart. The blood pressure within the system is dependent on the output of the pump, cardiac output, and the resistance to flow in the vascular system, the total peripheral resistance. This relationship is expressed by the formula: arterial blood pressure = cardiac output x total peripheral resistance.

By means of a number of regulatory mechanisms, the blood pressure is normally kept within a physiologically acceptable range. The cardiac output is modulated by intrinsic mechanisms as well as by sympathetic and parasympathetic nerve activity and circulating catecholamines (adrenaline), and can increase 5-6-fold during exercise. The total peripheral resistance represents the sum of resistances in the vascular beds of the different organs and tissues, and changes with the degree of vasodilatation or vasoconstriction. The vascular resistance is mainly determined by the intrinsic activity of the smooth muscle cells of the arterial resistance vessels and is modulated by a number of local factors (such as oxygen, carbon dioxide, histamine and endothelial nitric oxide, NO), circulating factors (such as angiotensin II, kinins and adrenaline) and the autonomic nervous system. Both the cardiac output and the total peripheral resistance is regulated by the vasomotor centre in the brain stem, which integrates information received from the higher nervous centres and from the circulatory baroreceptors [8]. A schematic representation of the nervous control of the circulation is given in Figure 1.

To maintain circulatory stability when standing up, a complex of physiological mechanisms is required. About 10% of the total blood volume is almost immediately relocated by peripheral pooling from the thorax to the dependent regions, i.e. the lower parts of the body, and thus temporarily denied to the heart for pumping purposes. However, the heart must pump blood against a higher pressure to provide adequate blood flow to the head. In young healthy adults the stroke volume falls 30-40% upon standing while the heart rate only increases 20-25%. Since the increase in heart rate cannot fully compensate for the fall in stroke volume, there is a 15-20% decline in cardiac output upon standing.

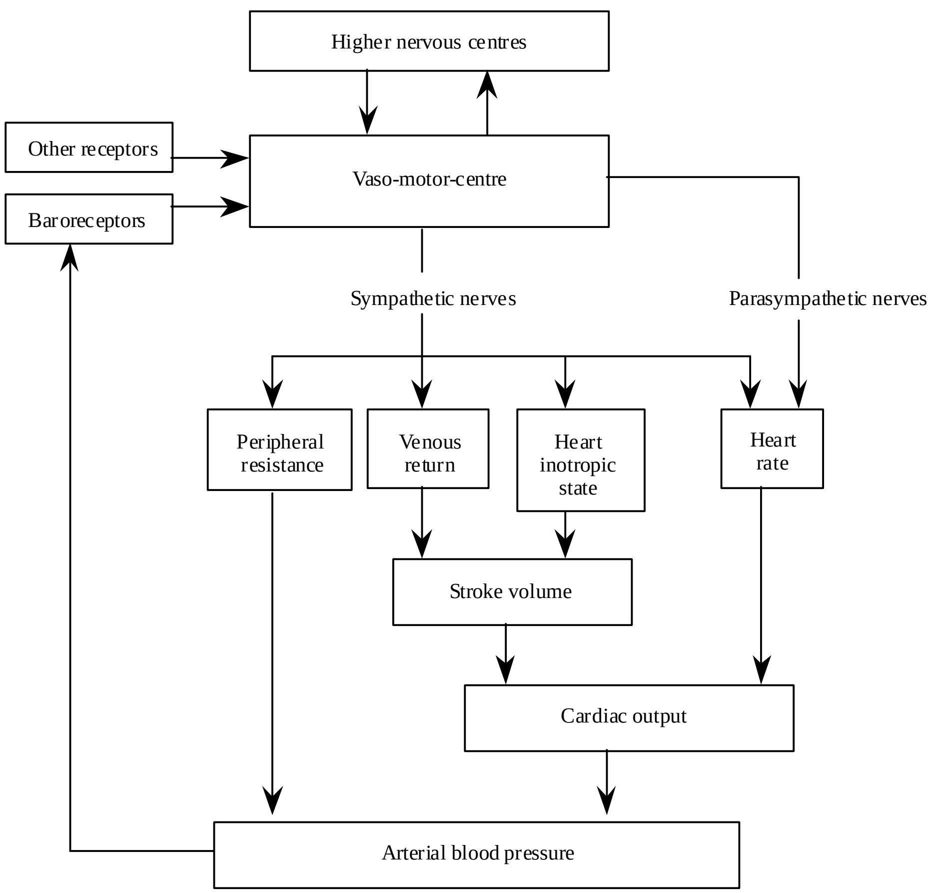


FIGURE 1 - Nervous circulatory control.

The immediate blood pressure reduction upon standing due to pooling of blood and decreased cardiac output activates baroreflexes which lead to stimulation of sympathetic and withdrawal of parasympathetic nerve activity. As a result, myocardial contractility and heart rate increase and vascular smooth muscle cells in the arterial and venous beds contract, leading to a relatively well maintained cardiac output and increased peripheral resistance. The venous return to the heart, and the stroke volume, are supported by venous constriction, caused partly by the sympathetic nerve activation and partly by contraction of the skeletal muscles in the lower extremities upon standing. This effect of contracting skeletal muscle on the venous return is sometimes referred to as “the muscle pump” or “the second heart”. By means of all these mechanisms, the central arterial pressure is rather well maintained and the blood flow to key organs and tissues is not seriously compromised upon standing [9].

The most important baroreceptors in the blood pressure regulation are situated just above the bifurcation of the carotid artery and in the walls of the aortic arch. These baroreceptors are stretch receptors and respond to a temporary fall or rise in blood pressure, i.e. they will adapt their firing pattern to the prevailing level of mean blood pressure and only temporarily oppose a change in mean blood pressure. Other baroreceptors, the cardio-pulmonary receptors, are located in the pulmonary vessels and in both atria of the heart, and are particularly sensitive to blood volume changes. However, their role in the regulation of vascular resistance during orthostatic stress is not clear [8-11].

The sensitivity of the baroreflex can be assessed in humans by intravenous administration of drugs which rapidly increase or decrease the blood pressure, or by direct mechanical manipulation of the baroreceptors using a neck chamber in which the pressure can be raised or lowered. The baroreceptor sensitivity is quantified as the change in heart rate (or RR-interval in the electrocardiogram, ECG) in relation to the change in pressure [8,9,11].

The baroreflexes are of great importance in the immediate control of blood pressure, whereas hormonal systems (such as the renin-angiotensin-aldosterone system and the anti-diuretic hormones) play an important role in the longterm control via the renal regulation of salt and water homeostasis. These different systems interact with each other in a complex fashion to keep blood pressure within normal limits in the supine and standing position, during rest and exercise, and in various environments [8,12].

Does the postural cardiovascular responses change with age, hypertension or coronary heart disease?

The cardiovascular adaptation to standing up has been reported to become attenuated with increasing age [1-3], resulting in an increased risk of orthostatic hypotension in the elderly [13,14]. There are also several reports of higher prevalence of orthostatic hypotension, possibly due to an impaired sympathetic response in patients with hypertension [4,5,15]. When the baroreflex sensitivity was tested with vasoactive drug injection or the neck chamber technique, it was reported that the carotid baroreflex of hypertensive subjects differed in various important ways from that of normotensives. In normotensives the pressor response that followed a reduction in carotid baroreceptor activity was greater than the depressor response that followed an increase in carotid baroreceptor activity, whereas in hypertensives the reverse was the case. Thus, while in normotensives the carotid baroreflex was more effective in protecting against hypotension, in hypertensives the antihypertensive function of the reflex was favoured, which might exaggerate postural hypotension among the hypertensive patients [7,16]. Other reports of an attenuated baroreflex in hypertensive patients are also available [17-19]. Patients with other diseases associated with atherosclerosis and stiffening of arterial vessels, such as coronary heart disease, have also been reported to have an impaired tolerance to changes in body position, i.e. an increased risk of orthostatic hypotension [11,14,20,21].

The Study of Men Born in 1913 – an asset in cardiovascular research

In 1963 the Study of Men Born in 1913 was initiated in Gothenburg, Sweden, by Tibblin [22]. Gothenburg is an industrial, maritime and commercial city situated on the west coast of Sweden with approximately 450 000 inhabitants at the time of the start of the investigation. The study is essentially an epidemiological investigation of the natural history of cardiovascular disease and associated risk factors, and it has both a cross-sectional and a longitudinal (prospective) approach.

The study received its name because the original study population (n=855) consisted of a randomly sampled third of all men born in 1913 and living in Gothenburg at the time. Focusing on representative subjects of the same age (initially 50 years) and sex (male) from the total population, the moderate number of participants was sufficient to yield enough cases of different cardiovascular diseases in different stages to ensure new and valuable population-based scientific information.

The original cohort from 1963 has been followed and re-examined roughly every five years until today. A number of social, physical, physiological and laboratory variables have been recorded during the years, together with information on morbidity and mortality.

New cohorts of 50-year-old men born in 1923, 1933 and 1943 have subsequently been studied in a similar way, as have the sons of the men born in 1913 and the sons' mothers [23,24]. A Section of Preventive Cardiology has been established, and registers of myocardial infarction and stroke events, a primary preventive trial and a population study of women have all been inspired by the Study of Men Born in 1913. More than twenty dissertations and more than 300 scientific articles have been published during the years by a number of researchers affiliated to the Section of Preventive Cardiology. The two investigations on which this study is based were also performed as part of the Study of Men Born in 1913.

AIMS OF THE STUDY

The aims of the study were to assess and compare the blood pressure and heart rate responses to changes in body position from supine to standing, and back to supine

- in groups of men aged 30, 50 and 60 years (Paper I);
- in groups of 60-year-old men with hypertension or a previous myocardial infarction, and in a control group without these diseases (Paper II).

STUDY POPULATIONS

During the time period February 1973 to June 1974, representative samples of men from three age groups, 60, 50 and 30 years old, were examined according to the original Study of Men Born in 1913 cardiovascular risk factor concept. In addition, all 60-year-old men in Gothenburg with previous myocardial infarction were identified and invited to take part in the risk factor examination [23].

The participants in the two present investigations (Papers I and II) were invited to this special blood pressure examination during the time period November 1973 to May 1974. They were sampled among the men attending the cardiovascular risk factor study with the aim of including a relatively large number of subjects in all subgroups. The number of participants in the six subgroups of Papers I and II, and the interrelations between the groups, are shown in Figure 2.

	30-year-olds	50-year-olds	60-year-olds	MI-60-year olds	HT-60-year olds	**Subgroups Paper II**
CV-risk-factor study (7-month period)	128	108	350	45	105	
Control	48	40	41	-	-	41
HT	2	4	21	-	54	75
MI - hospitalised	-	-	6	33	-	39
MI - not hospitalised			1			
Subgroups Paper I	50	44	69			

CV = cardiovascular MI = mycardial infarction HT = hypertension

FIGURE 2 - Number of participants in the different subgroups studied in Papers I and II, and the interrelations between the groups.

Paper I subgroups

The **60-year-old men** were randomly sampled from the population register in Gothenburg for the cardiovascular risk factor study based on day of birth (dates divisible by three, i.e. the 3rd, 6th, 9th, 12th etc etc day of each month) [25]. Depending on the availability of the blood pressure equipment used, 69 men were examined in the blood pressure study. They were sampled for the blood pressure study based on four days of birth (the 3rd, 15th, 21st and 27th day of each month).

The **50-year-old men** were randomly sampled from the population register in Gothenburg for the cardiovascular risk factor study based on day of birth (the 3rd, 15th and 27th day of each month) [23]. Depending on the availability of the blood pressure equipment used, 44 of these men were examined in the blood pressure study. They were sampled for the blood pressure study based on two days of birth (the 3rd and 27th day of each month).

The **30-year-old men** were sons of the 60-year-olds in the cardiovascular risk factor study. All sons aged approximately 30 were invited to the cardiovascular risk factor study and their mean age was 30.8 years (range 28-37 years) [23]. Depending on the availability of the blood pressure equipment used, 50 men were examined in the blood pressure study. They were sampled for the blood pressure study based on even dates of birth.

Paper II subgroups

The **hypertension group** consisted of 60-year-old men from the cardiovascular risk factor study. They were 71% of the 60-year-old hypertensive men in the cardiovascular risk factor study during this period. The criterion for hypertension was either a sitting systolic blood pressure >175 mmHg and/or a sitting diastolic blood pressure >115 mmHg at the screening examination (22/75) or previously diagnosed hypertension based on the responses to a questionnaire (53/75). Depending on the availability of the blood pressure equipment used, 75 men were examined in the blood pressure study. According to the questionnaire, 34 (46%) of these men were treated with antihyper-tensive drugs at the time of examination. Their hypertension was "uncomplicated", i.e. subjects with a history of major cardiovascular complications, such as myocardial infarction or stroke, were not included.

The **myocardial infarction group** consisted of 60-year-old men who had previously suffered myocardial infarction. They were 49% of those identified by scrutinising all hospital registers in Gothenburg for admission to hospital of patients born in 1913 with a diagnosis of acute myocardial infarction [23]. Depending on the availability of the blood pressure equipment used, 39 men were examined in the blood pressure study. Approximately half of the patients had suffered their myocardial infarction within three years before the investigation. No subject had had a stroke.

The **control group** consisted of 60-year-old men sampled from the cardiovascular risk factor study based on day of birth (the 3^{rd}, 15^{th}, 21^{st} and 27^{th} day of each month) and being free from hypertension or previous myocardial infarction or stroke. Fortyone men were examined.

METHODS

All examinations were done by the same two physicians, before noon, in the same quiet room at Sahlgrenska University Hospital, Gothenburg. The subjects had fasted over-night and had not smoked or drunk coffee before the examination.

The blood pressure measurements were taken in the right arm using an automatically inflated and deflated standard cuff, 12 x 23 cm (Boucke Brecht, Tübingen), and with a heart sound microphone (Siemens Elema, Stockholm), which was placed over the brachial artery. Cuff pressure, Korotkoff sounds and an ECG were simultaneously recorded on a Mingograph 82 (Siemens Elema). Blood pressure was calculated from the recordings on electrocardiographic paper and determined to the nearest 1 mm Hg. Diastolic blood pressure was recorded as phase V, i.e. when the Korotkoff sounds disappeared. Cuff inflation was rapid and deflation lasted for approximately half a minute. Heart rate was assessed from the tracings of the Korotkoff sounds over a period of approximately 15 seconds. This technique of blood pressure measurement has been standard for many years in the Non-invasive Laboratory at Sahlgrenska University Hospital and has previously been described [26,27]. The device was checked and calibrated daily.

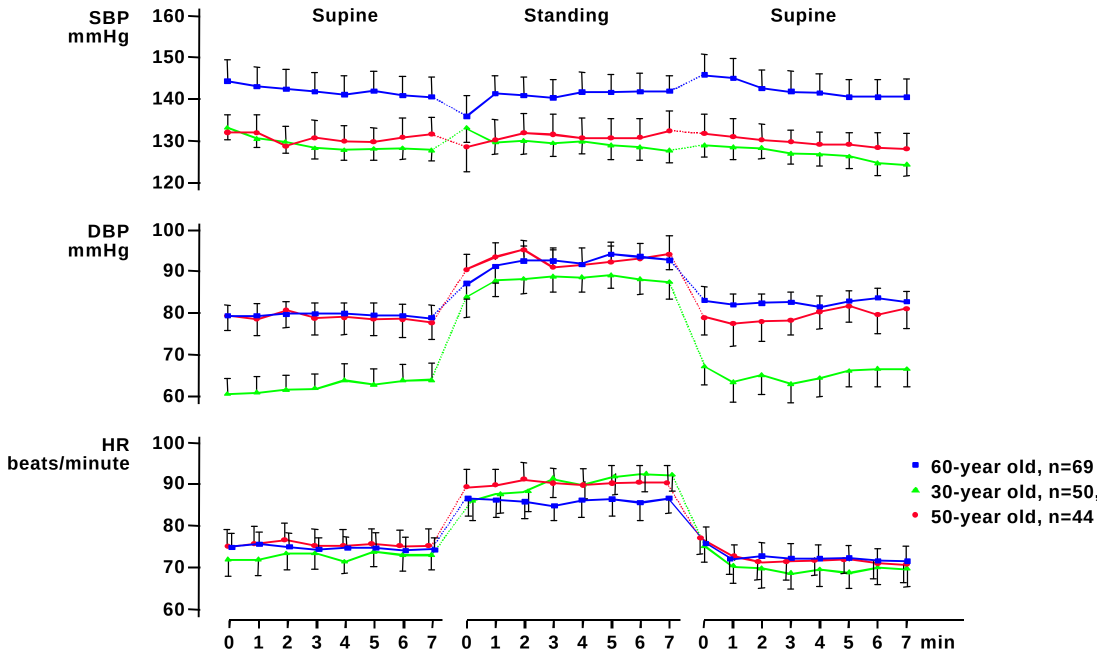
The subjects were first resting supine for approximately five minutes while the blood pressure measuring device was applied and checked. Measurements were then taken at the start (0 minutes) and every minute for seven minutes in the supine position, then immediately and every minute for seven minutes in the standing position, and finally immediately and every minute for seven minutes after the subject had resumed the supine position.

Statistical methods

The data were computerised and analysed using the Statistical Analysis System (SAS) and JMP program packages [28]. Standard methods were used to calculate means, standard deviations (SD) and 95% confidence intervals (CI). Parametric methods were used in all statistical analyses. However, a few variables were skewed (Shapiro-Wilk´s test $W<0.95$) and in these instances the results were also analysed using non-parametric methods. Similar results were obtained with parametric and non-parametric methods (Wilcoxon Signed Rank /Kruskal-Wallis Test of Rank Sums).

For the calculation of changes in blood pressure and heart rate upon changes in body position, the mean of the last two measurements in the previous period (6th and 7th min) was used as baseline and compared with the first measurement (0 min) in the following period. Means of blood pressure readings and heart rates were first calculated for each individual. Based on these individual means, the group means were computed. Within-group changes of blood pressure and heart rate in response to changes in body position were analysed using the paired t-test. Differences in levels and changes of blood pressure and heart rate between any of the three groups studied in Papers I and II, respectively, were analysed using analysis of variance (ANOVA). When the ANOVA produced a statistically significant result the pair-wise comparisons were made using the unpaired t-test. A p-value <0.05 was considered statistically significant.

FIGURE 3 - Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) in the supine and standing positions in men of different ages. Means and 95% confidence intervals are also given.



RESULTS

Paper I – Postural responses in 30-, 50- and 60-year-old men

Characteristics of the participants

The mean height, body weight and body mass index, as well as the prevalence of hypertension, diabetes mellitus and previous myocardial infarction or stroke for the subgroups in Paper I are presented in Table I. The 30-year-old men were taller than the 50- and 60-year-old men while the mean body weights were similar in the three age groups. Hypertension was most common in the 60-year-old men. The diagnoses were based on the subjects' answers to a questionnaire and in the case of myocardial infarc-tion confirmed from hospital records.

TABLE I - Means and standard deviations for height, body weight and body mass index and prevalence of hypertension, myocardial infarction, stroke and diabetes mellitus by age group.

	30-year-olds n=50	50-year-olds n=44	60-year-olds n=69
Height (cm)	182 ± 6.6	174 ± 5.6	175 ± 5.7
Body weight (kg)	79 ± 11.1	76 ± 12.0	79 ± 12.1
BMI[a] (kg/m^2)	24 ± 2.6	25 ± 3.4	26 ± 3.5
Hypertension (%)	4	9	23
treated (%)	2	0	19
untreated (%)	2	9	4
Myocardial infarction (%)	0	0	9
Stroke (%)	0	0	0
Diabetes mellitus (%)	0	2	6

[a] BMI = body mass index

Blood pressure

The mean (with 95% CI) systolic and diastolic blood pressures in men aged 30, 50 and 60 during the investigation are shown in Figure 3. In each of the periods,

TABLE II - Estimated mean change in blood pressure and heart rate upon standing up from the supine position in men of different ages and estimated mean differences in change between the age groups. The 95% confidence intervals (CI) for the true means and p-values are also given.

	Within group changes			Between groups differences			
	30-year-olds n=50	50-year-olds n=44	60-year-olds n=69	p-value ANOVA	30 vs 50	30 vs 60	50 vs 60
SBP							
mmHg	5.9	-1.1	-4.7	<0.0001	7.0	10.7	3.6
95% CI	2.9;8.9	-3.9;1.6	-7.1;-2.3		3.0;11.1	6.8;14.5	-0.1;7.4
p-value[1)]	<0.001	>0.20	<0.001		<0.001	<0.0001	=0.06
per cent	4.6	- 0.8	-3.3				
DBP							
mmHg	19.7	12.3	7.9	<0.0001	7.5	11.8	4.4
95% CI	16.4;23.1	9.8;14.7	5.8;10.0		3.2;11.7	8.1;15.5	1.1;7.6
p-value[1)]	<0.0001	<0.0001	<0.0001		<0.001	<0.0001	<0.01
per cent	30.7	15.8	10.0				
Heart rate							
bpm	12.6	14.1	12.2	>0.20	-1.5	0.3	1.8
95% CI	9.8;15.4	11.6;16.5	10.5;14.0		-5.2;2.2	-2.8;3.5	-1.1;4.7
p-value[1)]	<0.0001	<0.0001	<0.0001		-	-	-
per cent	17.3	18.8	16.5				

[1)] t-test SBP= systolic blood pressure DBP=diastolic blood pressure bpm=beats per minute

with the subjects supine and standing and again supine, both the systolic and diastolic blood pressures stabilised after a few minutes. Although the differences in blood pressure levels between the groups were not formally tested, the blood pressure seemed lowest in the 30-year-old men and highest in those aged 60.

The mean changes (with 95% CI and p-values) in blood pressure levels upon standing up within each age group and the mean differences in changes between the groups are presented in Table II. The immediate blood pressure response to standing in 50- and 60-year-old subjects was a slight decrease in the systolic blood pressure and a marked increase in the diastolic blood pressure. In those aged 30, there was a moderate increase in the systolic blood pressure and a marked increase in the diastolic blood pressure. The responses in both systolic and diastolic blood pressures in the

TABLE III - Estimated mean change in blood pressure and heart rate upon lying down from the standing position in men of different ages and estimated mean differences in change between the age groups. The 95% confidence intervals (CI) for the true means and p-values are also given.

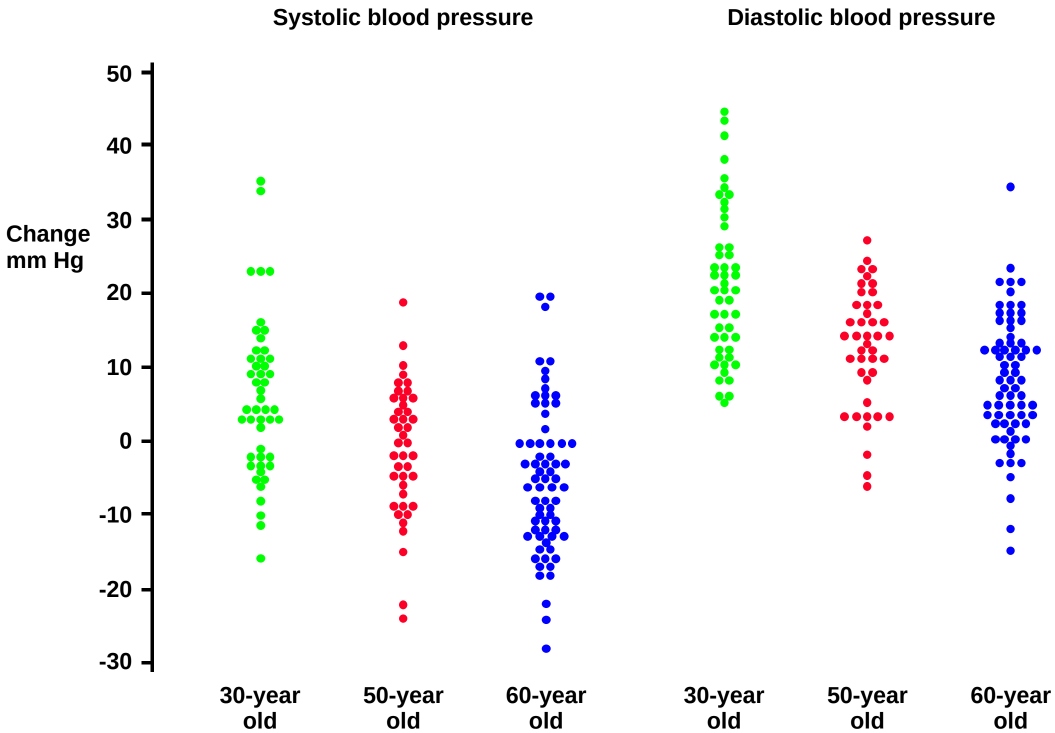
	Within group changes			Between groups differences			
	30-year-olds n=50	50-year-olds n=44	60-year-olds n=69	p-value ANOVA	30 vs 50	30 vs 60	50 vs 60
SBP							
mmHg	1.2	0.4	3.7	=0.14	0.8	-2.5	-3.2
95% CI	-0.9;3.3	-3.0;4.0	1.6;5.8		3.2;4.7	-5.5;0.6	-7.0;1.9
p-value[1)]	>0.20	>0.20	<0.001		-	-	-
per cent	0.9	0.3	2.6				
DBP							
mmHg	-20.0	-14.5	-9.4	<0.0001	-5.6	-10.6	-5.0
95% CI	-23.4;-16.4	-16.7;-12.2	-11.4;-7.5		-10.0;-1.1	-14.4;-6.7	-8.0;-2.0
p-value[1)]	<0.0001	<0.0001	<0.0001		=0.01	<0.001	<0.01
per cent	- 22.9	-15.6	-10.2				
Heart rate							
bpm	-16.9	-13.0	-10.2	<0.001	- 4.0	- 6.7	- 2.8
95% CI	-19.7;-14.2	-15.5;-10.5	-12.2;-8.1		-7.6;-0.2	-10.0;-3.4	-6.0;0.4
p-value[1)]	<0.0001	<0.0001	<0.0001		=0.04	<0.0001	=0.09
per cent	-18.4	-14.4	-11.9				

[1)] t-test SBP= systolic blood pressure DBP=diastolic blood pressure bpm=beats per minute

30-year-olds were significantly different from the responses in the 50- and 60-year-old men. In all age groups, the immediate change in systolic blood pressure after standing up was transient, and the pressure returned within one minute to the level observed in the preceding supine position (Figure 3). The diastolic blood pressure, however, was slightly further increased during the first one or two minutes in the standing position, then stabilised on a higher level than in the supine position.

Individual changes in systolic and diastolic blood pressure immediately upon standing are shown in Figure 4. Only a few subjects had a decrease in systolic blood pressure of more than 20 mmHg and/or a decrease in diastolic blood pressure of more than 10 mmHg upon standing. None of the subjects reported hypotensive symptoms, such as dizziness, during the investigation.

FIGURE 4 - Individual changes in the systolic and diastolic blood pressure upon standing up from the supine position in men of different ages.



Mean changes in blood pressure upon lying down within each age group, and the mean differences in changes between the groups, are shown in Table III. The mean decrease in diastolic blood pressure in the 30-year-old men was significantly greater than that in both the 50- and 60-year-olds.

Heart rate

The supine heart rates were similar in the 50- and 60-year-old men, but appeared slightly lower in those aged 30 (Figure 3). Heart rate increased immediately upon standing, with no difference between the age groups (Table II). In men aged 30 years, the rapid initial increase in heart rate was followed by a slight further increase during the seven minutes of standing. After resuming the supine position, the subjects' heart rate rapidly returned to the level observed in the first period with a significantly larger decrease for 30-year-old men than in the older subjects (Table III).

Paper II – Postural responses in men with hypertension or a previous myocardial infarction and in a control group

Characteristics of the participants

The mean height, body weight, body mass index, prevalence of hypertension and previous myocardial infarction and diabetes mellitus as well as information on treatment with cardiovascular medication for the subgroups in Paper II are presented in Table IV. Although no subject in the control group had suffered myocardial infarction or had hypertension, four men were treated with cardiovascular drugs (diuretics, beta-blockers or digitalis) for other reasons. The definition of hypertension was defined as described above i.e., either a sitting systolic blood pressure >175 mmHg and/or a sitting diastolic blood pressure >115 mmHg at the screening examination or an indication in the questionnaire of previously diagnosed hypertension.

Blood pressure

The mean (with 95% CI) systolic and diastolic blood pressure in the groups of men with hypertension or previous myocardial infarction, and in the control group are plotted in Figure 5. The mean systolic blood pressure and diastolic blood pressure

FIGURE 5 - Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) in the supine and standing positions in 60-year-old men with hypertension, previous myocardial infarction and in a control group. Means and 95% confidence intervals are also given.

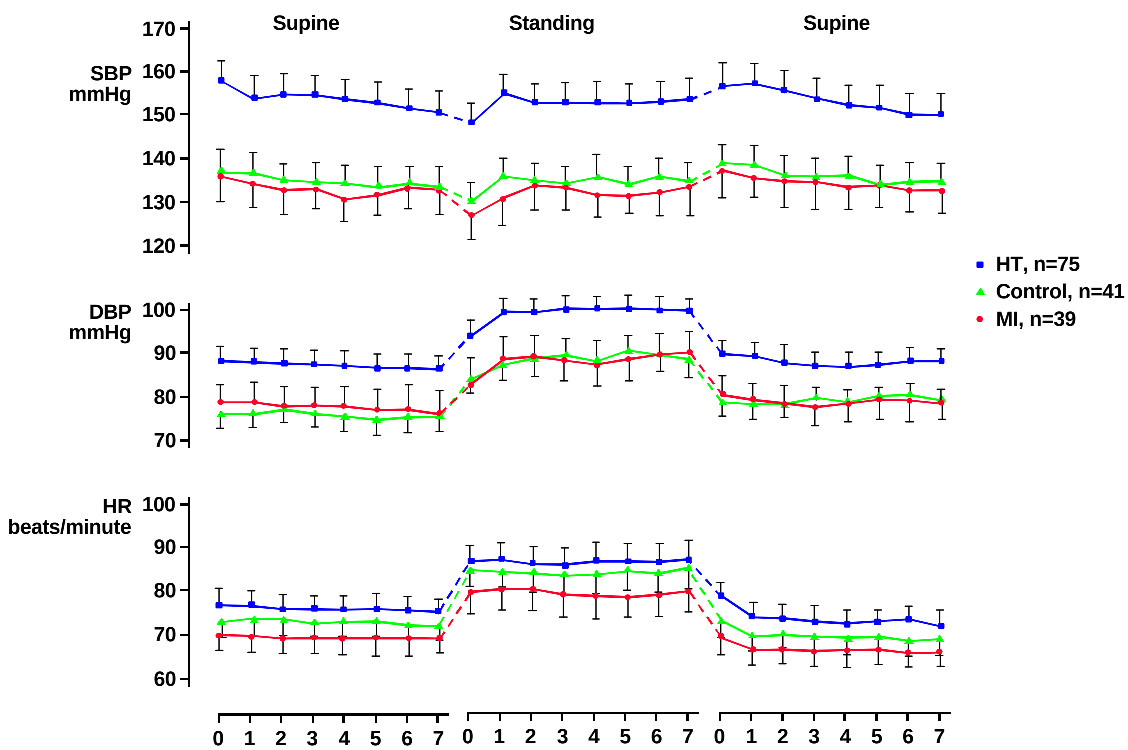


TABLE IV - Characteristics of 60-year-old men with hypertension or previous myocardial infarction, and in a control group.

	Control	Myocardial infarction	Hypertension
	n=41	n=39	n=75
Height (cm, mean ± SD)	175±4.9	175±7.5	174±6.2
Body weight (kg, mean ± SD)	79±9.8	77±11.5	81±11.8
BMI (kg/m^2, mean ± SD)	26±3.2	25±3.4	27±3.1
Myocardial infarction (%)	-	100	-
Diabetes mellitus (%)	5	3	8
Hypertension (%)	-	26	100
Medication			
diuretics (%)	2	26	31
beta-blockers (%)	5	33	20
digitalis (%)	5	31	8
nitroglycerine (%)	-	31	1
other CV drugs (%)	-	8	15
any of the above (%)	10	67	51
none of the above (%)	90	33	49

CV = cardiovascular

during the first seven-minute supine period were significantly higher in the hypertension group than in the control group or the myocardial infarction group, in spite of a large proportion (46%) of the hypertensives being treated. The differences in blood pressure between the hypertension group and the other groups were generally maintained during standing, and also when the supine position was resumed, although the absolute levels of blood pressure changed with the body position.

The responses in blood pressure to standing up from the supine position within each of the three groups, and the differences in response between groups, are recorded in Table V. There was an initial slight, but significant, decrease in systolic blood pressure in the control group and the myocardial infarction group and an even less marked, non-significant, decrease in the hypertension group upon standing, but no significant differ-ences between the groups. The diastolic blood pressure was significantly increased in all groups upon standing, with no differences between the groups.

The individual changes in systolic blood pressure and diastolic blood pressure immediately upon standing and after one minute are shown in Figure 6. In the hypertension and the control groups, only a few subjects (5% or less) had marked reductions in blood pressure (i.e. systolic blood pressure >20 mmHg or diastolic

FIGURE 6 - Individual changes in the systolic and diastolic blood pressure upon standing up from the supine position in 60-year-old men with hypertension, previous myocardial infarction and in a control group.

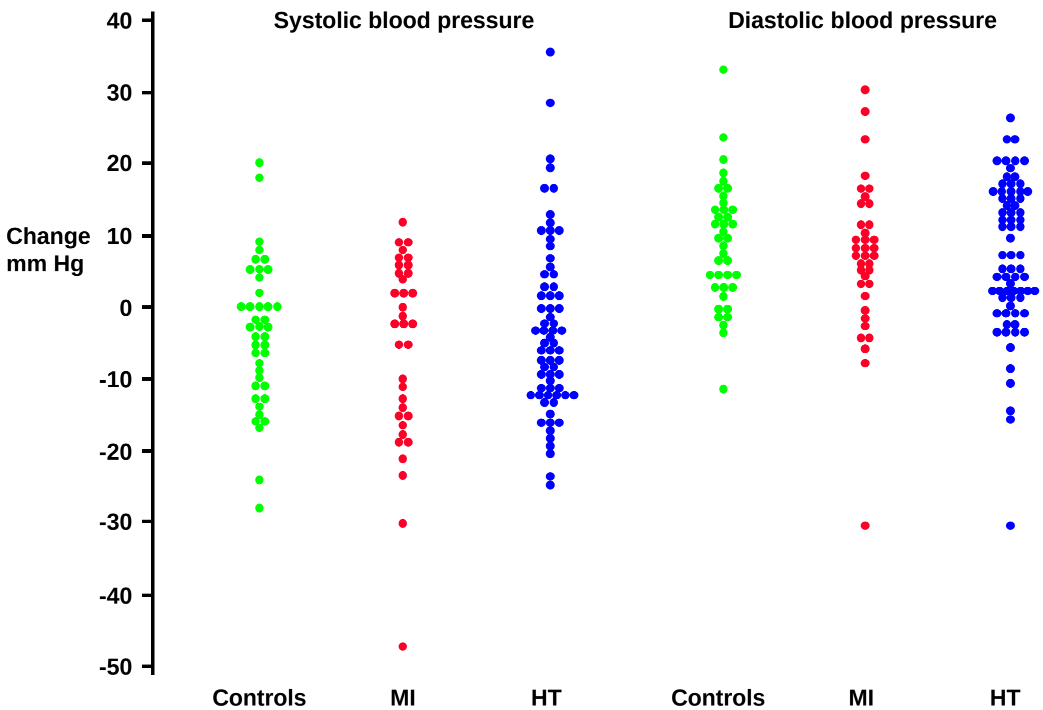


TABLE V - Estimated mean change in blood pressure and heart rate upon standing up from the supine position in 60-year-old men with hypertension or previous myocardial infarction and in a control group, and estimated mean differences in change between the groups.

	Within group changes			Between groups differences			
	Control n=41	MI n=39	HT n=75	p-value ANOVA	Control vs MI	Control vs HT	MI vs HT
SBP							
mmHg	-3.8	-6.2	-2.7	>0.20	2.4	-1.1	-3.5
95% CI	-6.9;-0.7	-10.5;-1.9	-5.6;0.2		-2.7;7.6	-5.5;3.4	-8.5;1.5
p-value	=0.02	=0.01	=0.07		-	-	-
per cent	-2.6	- 4.5	- 1.7				
DBP							
mmHg	8.6	7.6	7.7	>0.20	1.0	0.9	-0.4
95% CI	6.1;11.1	4.1;11.2	5.2;10.1		-3.2;5.2	-2.8;4.6	-4.2;4.2
p-value	<0.0001	<0.0001	<0.0001		-	-	-
per cent	12.3	13.0	9.8				
Heart rate							
bpm	12.6	10.5	12.1	>0.20	2.2	0.6	-1.6
95% CI	10.7;14.6	8.3;12.7	10.2;13.9		-0.7;5.0	-2.3;3.4	-4.6;1.4
p-value	<0.0001	<0.0001	<0.0001		-	-	-
per cent	18.1	15.3	16.6				

SBP=systolic blood pressure DBP=diastolic blood pressure bpm=beats per minute
MI=myocardial infarction HT=hypertension

blood pressure >10 mmHg) upon standing. However, an immediate reduction of >20 mm Hg systolic was noted in four subjects (11%) in the myocardial infarction group. None of these four subjects had marked reductions in both systolic and diastolic blood pressure. The number of subjects with this magnitude of reduction in blood pressure did not increase during the prolonged standing (up to seven minutes). No hypotensive symptoms, such as dizziness, were reported during the investigation.

After resuming the supine position, the subjects' blood pressures returned to a level similar to that observed in the first supine period (Figure 5). The within-group changes and the differences between groups are presented in Table VI. In all groups, a slight increase in systolic blood pressure was seen (significant in the hypertension group only), whereas there was a significant decrease in diastolic blood pressure to the

TABLE VI - Estimated mean change in blood pressure and heart rate upon lying down from the standing position in 60-year-old men with hypertension or previous myocardial infarction and in a control group, and estimated mean differences in change between the groups.

	Within group changes			Between groups differences			
	Control n=41	MI n=39	HT n=75	p-value ANOVA	Control vs MI	Control vs HT	MI vs HT
SBP							
mmHg	2.7	4.1	3.2	>0.20	-1.4	-0.5	0.9
95% CI	-0.02;5.4	-0.6;8.7	0.8;5.5		-6.7;3.9	-4.2;3.2	-3.7;5.5
p-value	=0.05	=0.09	=0.01		-	-	-
per cent	2.1	3.5	2.3				
DBP							
mmHg	-10.1	-9.6	-9.4	>0.20	0.4	-0.7	-0.3
95% CI	-12.7;-7.4	-13.0;-6.2	-11.3;-7.4		-4.7;3.8	-4.0;2.6	-3.9;5.5
p-value	<0.0001	<0.0001	<0.0001		-	-	-
per cent	-10.8	-9.8	-9.2				
Heart rate							
bpm	-11.6	-10.2	-8.7	=0.17	-1.3	-2.9	-1.6
95% CI	-13.9;-9.2	-12.6;-7.9	-10.6;-6.8		-4.6;2.0	-6.0;0.2	-4.7;1.6
p-value	<0.0001	<0.0001	<0.0001		-	-	-
per cent	-13.1	-12.8	-9.4				

SBP=systolic blood pressure DBP=diastolic blood pressure bpm=beats per minute
MI=myocardial infarction HT=hypertension

level of the previous supine period. There were no significant differences between the groups in their responses to lying down from the standing position.

Heart rate

The mean heart rate showed the same pattern but on slightly different levels in the three groups (Figure 5). There was an increase in heart rate in all groups upon standing up, which was maintained during prolonged standing, and a similar decrease upon laying down (Tables V and VI). There were no significant differences between the groups with respect to changes in heart rate upon standing up or lying down.

Influence of cardiovascular drug treatment

Many patients with a previous myocardial infarction or hypertension were treated with cardiovascular drugs (Table IV). The possible influence of treatment with a beta-blocker or other cardiovascular drugs on supine blood pressure and heart rate levels, and the responses to standing up, is presented in Table VII. Subjects with cardiovascular drugs had similar blood pressure levels and responses as un-treated. The supine heart rates and the heart rate responses to standing up were, however, numerically lower in subjects receiving beta-blocker treatment. The supine heart rate was actually significantly lower in the beta-blocker-treated patients than in the untreated patients with myocardial infarction (mean difference: 17.3 beats/min, 95% CI 8.3-26.4, $p<0.001$). The supine heart rate levels were similar in the untreated hypertensive and myocardial infarction patients however.

TABLE VII - Estimated mean blood pressure and heart rate during seven minutes in the supine position, as well as estimated mean change in blood pressure and heart rate upon standing up, in 60-year-old patients with hypertension or previous myocardial infarction by cardiovascular drug treatment. The 95% confidence intervals (CI) for the true means are also given.

	Hypertension				Myocardial infarction			
	ANOVA between groups	no CV drugs n=36	beta-blockers n=15	other CV drugs n=23	ANOVA between groups	no CV drugs n=13	beta-blockers n=13	other CV drugs n=13
SBP (mmHg)	>0.20	153.9	155.3	151.8	>0.20	129.8	134.9	132.8
95% CI		148.0;159.9	143.1;167.6	142.6;161.0		122.4;137.2	123.3;146.5	124.7;140.9
DBP (mmHg)	>0.20	87.1	84.9	88.1	>0.20	74.6	78.3	78.3
95% CI		82.5;91.7	76.8;92.5	84.4;91.8		64.7;84.6	68.9;87.6	73.3;83.2
Heart rate (bpm)	=0.10	76.8	68.5	77.3	<0.0001	76.0	58.7	72.3
95% CI		71.8;81.9	62.7;74.3	71.6;83.0		67.2;84.8	54.7;62.6	69.0;75.6
SBP change (mmHg)	=0.07	0.9	-4.3	-6.6	>0.20	-1.8	-9.6	-7.6
95% CI		-3.8;5.6	-10.5;1.9	-11.3;-1.8		-7.8;4.2	-19.9;0.8	-14.8;-0.5
DBP change (mmHg)	=0.16	10.0	5.9	4.9	>0.20	6.0	10.0	7.1
95% CI		6.1;13.8	1.2;10.6	0.4;9.4		-2.3;14.3	4.1;15.9	1.8;12.3
Heart rate change (bpm)	=0.06	13.7	7.7	11.9	>0.20	11.5	9.3	10.7
95% CI		11.2;16.2	3.2;12.2	8.2;15.5		6.8;16.2	4.3;14.2	8.0;13.3

SBP=systolic blood pressure DBP=diastolic blood pressure bpm=beats per minute CV=cardiovascular

DISCUSSION

In this study of men aged 30, 50 and 60, an age-related attenuation in the blood pressure responses to changes in body position was found (Paper I). The blood pressure responses were, however, similar in 60-year-old men with hypertension, or previous myocardial infarction and men without these diseases (Paper II). Thus, the attenuated blood pressure responses in older compared to younger subjects are not likely to be explained by the higher prevalence of hypertension or coronary heart disease in the elderly but appear to be the result of normal ageing.

Representativeness of the participants

The study population in Paper I can be regarded as representative of urban Swedish men aged 30, 50 and 60 at the time of the investigation. The 50- and 60-year olds in the cardiovascular risk factor study were randomly sampled from the total population in Gothenburg and therefore certainly representative [23,25]. The assumption that the 50- and 60-year olds sampled for the present study were also representative is supported by similar prevalence rates for hypertension, myocardial infarction and diabetes mellitus in the studied subjects and in the entire cardiovascular risk factor study [23,25,29]. The 30-year-olds were all sons of the 60-year-old men, and thus not a random sample, and not all exactly 30 years old. However, it has been shown that there were no significant differences between these 30-year-old sons and another population sample of 30-year-old men in Gothenburg, with respect to blood pressure, serum cholesterol, smoking habits and physical activity [23].

The study population in Paper II is likely to be representative of 60-year-old urban Swedish men with hypertension or a previous myocardial infarction at the time of the investigation. The risk of systematic bias in the sampling of men for the blood pressure investigation is minor since the only basis for the sampling was the wish to include a relatively large number of subjects in each subgroup and the capacity of the special equipment used. The 60-year-old men in the control group were certainly representative for the reasons discussed above.

No special analysis of the non-participants in this investigation was done but according to other studies within the project Study of Men Born in 1913 the vast majority of the invited men (81% of the 60-year-olds and 75% of the 50-year-olds) participated in the investigations 1973 [30].

All studies should be seen in their own temporal and cultural context. Although the study was performed several years ago, there is little reason to believe that the main results in Paper I would differ considerably from what would be found in 30-, 50- and 60-year-old men of today. Indeed, similar age-related results on postural blood pressure and heart responses have been reported in more recent investigations [1-3]. It is possible that definitions of hypertension or myocardial infarction other than those used in the present study would have influenced the results in Paper II. For example, an attenuation of the postural responses might have been detected if patients with more pronounced hypertension with target organ damage (e.g. cardiovascular hypertrophy, coronary heart disease and stroke) had been studied. Information on the size of the myocardial infarction suffered by the patients in this group, or whether the infarction was complicated by heart failure was not available. However, most of these patients did not use diuretics or digitalis (23/39), which indicates that heart failure was not a common complication. It is conceivable that a larger proportion of patients with heart failure would have resulted in an abnormal orthostatic response in the myocardial infarction group since heart failure is often accompanied by impaired cardiovascular reflexes [11,16]. However, an increased tolerance to changes in body position among patients with congestive heart failure, due to an increased blood volume, has also been reported [21,31]. It is important though, to study and compare the cardiovascular responses to changes in body position among patients representative of the total population as in the present study, i.e. with all degrees of hypertension or myocardial infarction.

It is likely that the present results are valid not only for urban Swedish men aged 30, 50 and 60, but also for men of this age in similar countries. Whether the same results would have been obtained in women or in very old subjects can obviously not be concluded from this study.

Measurements

In all studies dealing with blood pressure, especially changes in blood pressure, the technique of measurement is important since it determines the precision of the assessment. The best precision is achieved with the direct method using an intra-arterial catheter connected to a pressure transducer. For obvious reasons, this method cannot be applied on a large scale and indirect methods of measuring blood pressure have therefore been developed. The most widely used non-invasive technique is the auscultatory method, in which the Korotkoff sounds phase I and V are taken as the systolic and diastolic blood pressures, respectively. Although a well accepted method, it is largely dependent on the observer, in particular on his or her technique and biases. In order to avoid most of these drawbacks, a method of indirect assessment of blood pressure in which the Korotkoff sounds are determined with a microphone over the brachial artery and displayed together with the cuff pressure was used in the present study [26,27]. Obviously, this technique does not permit the assessment of very rapid, beat-to-beat, changes of blood pressure. Therefore, the immediate measurements (0 minutes) in the present study were actually performed after some 15 seconds. At the time when this study was performed, there was no non-invasive technique available for the assessment of the very rapid changes in blood pressure, such as the Finapres® [32, 33]. In this study, the subjects were standing rather than tilted head-up since standing up is a more physiological way of testing the normal circulatory response to a change in body position. It should be emphasised that the present study was entirely clinically oriented, using simple methods to assess the ability to adapt blood pressure and heart rate to sudden postural changes.

Statistical considerations

To avoid the problem of mass-significance, statistical tests were generally performed when necessary to fulfill the aims of the study. For example, only the immediate blood pressure and heart rate responses to changes in position were tested, while descriptive statistics, e.g. graphs, were used for other results. Means may hide important inter-individual variation. To give the reader complete information on the blood pressure responses to standing up, Figures 4 and 6 provide the individual data.

Parametric methods were used in all statistical analyses, and 95% CI are given to provide full information on the “precision” of the estimated mean differences. In the comparisons between groups, an ANOVA was first made, and only if it was significant were pair-wise t-tests performed. This is a recommended procedure for studies with no more than three groups [34]. Some of the subgroup analyses (none in Table II, one in Table III, two in Tables III and IV) were skewed. Since the non-parametric tests gave the same results as the parametric tests in these few situations, all figures in the tables were given as parametric means and 95% CI, to make it possible to compare the results.

Table VII is actually not related to the original aims of the study, but illustrates the possible influence of cardiovascular drug treatment on the blood pressure and heart rate responses to changes in body position. Although the groups in Table VII were rather small and several (19/36) of the results were skewed, parametric means and CI were given in this table, as the results were similar using non-parametric and parametric tests, and to make it comparable with the other tables.

The influence of the regression towards the mean must always be considered when groups with extreme values are selected and studied. In the group of men with high blood pressure at screening and in whom hypertension was not previously known (n=22), the blood pressure was considerably lower during the investigation than at screening. This decrease in blood pressure was much greater than that observed in the groups of men with previously known hypertension (n=53), or previous myocardial infarction or in men free from these diseases. This observation can partly be explained by regression towards the mean.

Age-related attenuated postural response

Age-related differences in blood pressure responses to standing up, qualitatively similar to those observed in Paper I, have previously been reported [1-3]. In studies including subjects over 65 years of age, decreased systolic blood pressure and almost unchanged diastolic blood pressure have been reported [14,31,35]. The increase in diastolic blood pressure upon standing observed in the present study was greater than that reported in most other investigations [2,14,37]. A possible explanation is that the microphone used in our study is more accurate in determining the phase V of the Korotkoff sounds than a human observer. In the present study there was a marked and similar increase in heart rate upon standing in all age groups. In other studies, however, an age-related attenuation of the heart rate response to standing up has been reported in subjects over the age of 60 [1,2,38].

The age-related differences in the blood pressure and heart rate responses to changes in body position are usually considered to be a result of an impaired baroreflex mechanism in the elderly [2,19]. This may be due to malfunction at one or several levels in the reflex. For example, the baroreceptors may not be influenced by blood pressure changes due to stiffening of the aging arterial wall, or the neuronal activity in the reflex arch may be damaged, or the end-organs (heart and vessels) may not respond adequately to changes in the sympathetic or parasympathetic discharge [8,39,40].

The decrease in systolic blood pressure upon standing, particularly in elderly subjects, is partly due to decreased venous return and stroke volume as a result of pooling of blood in the dependent parts of the body [12]. The immediate increase in systolic blood pressure upon lying down observed in the 60-year-old men in the present study may be explained as a consequence of rapid return of an important amount of pooled blood resulting from an impaired buffering capacity of the baroreflexes.

The normal, very rapid, baroreflex-mediated compensatory response in blood pressure and heart rate to standing up was best illustrated in the 30-year-old men. The initial blood pressure decrease, which triggers the reflex activity, was already gone when the first measurement was taken after some 15 seconds. Indeed, an “overshoot”, which was most obvious for the systolic blood pressure was observed. Such an “overshoot” in young people has previously been described by others [8,33].

Postural response in patients with hypertension or previous myocardial infarction as compared to a control group

In Paper II no significant differences in blood pressure or heart rate responses to changes in body position were observed between the groups of men with hypertension or a previous myocardial infarction and the control group. Most other studies in this area have been carried out in subjects over 60 years old and have focused on the prevalence of orthostatic hypotension. Increased orthostatic hypotension and an attenuated blood pressure response to postural changes in patients with hypertension [4-6,11,42,43] or a previous myocardial infarction has been reported [14,21]. However, as in the present study, other investigators have not found such differences in the response between subjects with and without cardiovascular diseases [20,31,32,36].

Investigation of the baroreflex sensitivity, in contrast to our more clinically oriented study, makes it possible to study the baroreflex in more detail. Several investigators have reported decreased baroreflex sensitivity in hypertensive subjects [6,7,17,19]. Less bradycardia evoked by a rise in blood pressure has been observed in hypertensive patients compared to normal subjects, but no difference in the extent of tachycardia during a fall in blood pressure seems to exist. It is more likely that this difference results from an impairment of vagal excitation in hypertension than from impaired sympathetic inhibition [8,11,18].

Some subjects with hypertension or previous myocardial infarction and some in the control group did not take any cardiovascular drug, while others did. Because of the relatively small groups in this subanalysis, firm conclusions cannot be drawn. Nevertheless, some indications of possible effects of drug treatment on the results may be found. In agreement with other studies, no differences between the groups were seen [43,44], except for an effect of the beta-blockers on heart rate in the myocardial infarction group. Interestingly, the supine heart rate levels were almost the same in the untreated hypertensive group and the untreated myocardial infarction group. This indicates that the heart rate difference observed between the total groups is mainly due to a lower heart rate as a result of treatment with beta-blockers in the myocardial infarction group and not to the disease.

CONCLUSIONS

Based on this study of 30-, 50- and 60-year-old men, the following conclusions can be drawn:

- Previous observations of an age-related attenuation in blood pressure response to change in body position were confirmed.

- Blood pressure and heart rate were rapidly stabilised upon standing up. Thus, there should be no general need to observe subjects for more than a couple of minutes upon standing, unless orthostatic hypotension is suspected in a specific individual.

- Sixty-year-old men with hypertension or previous myocardial infarction had blood pressure and heart rate responses to standing up and lying down which were similar to the responses in a control group of men of the same age and free from these diseases.

- The attenuated response in older compared to younger men was not explained by the higher prevalence of cardiovascular disease in the elderly, but appears to be the result of normal aging.

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