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Findings in a Health Survey of Middle-aged Subjects in Uppsala 1981–82

Risk factors for diabetes mellitus and cardiovascular disease

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ABSTRACT

In a health survey in 1981-82 in the city of Uppsala 819 subjects (443 females and 376 males), 47-54 years old, were examined. A 75 g oral glucose tolerance test OGTT was performed in each subject, and fasting and 2-h venous whole blood glucose values were determined. The 2-h value was somewhat higher in females, 4.7 $mmol \cdot l^{-1}$, than in males, 4.4 $mmol \cdot l^{-1}$ ($p < 0.01$). Known or probable manifest diabetes was present in 1.9 % of all subjects. Glucose values within the limits for WHO criteria of glucose intolerance were found in another 7.1 % of all subjects after one OGTT. The rates were similar in both sexes. A history of diabetes in first-degree relatives was noted in 13.2 % of all subjects.

According to a questionnaire, 1.1 % of all subjects had had hospital care for myocardial infarction, 4.7 % had angina pectoris and 2.4 % had intermittent claudication. The rate of subjects on antihypertensive treatment or with untreated high blood pressure $\geq$ 170/105 mm Hg was 11.2 %; of these only 1.8 % had untreated high blood pressure. Of the treated subjects, the treatment was adequate in 82.9 %. Obesity, defined as relative body mass index $\geq$ 120 %, was found in 34.0 % of all subjects, more frequently in females than in males. The rate of smokers was 28.5 %.

A comparison was made with the results of a similar health survey of about 2 300 middle-aged men in Uppsala in 1970-73. The prevalence of angina pectoris was higher among the men of the present survey than among those of the 1970-73 survey, which may at least partly be due to differences in methodology. Relative body weight was higher, and fewer men were regularly active during leisure for at least 2-3 h per week in the present study. The rates of hypertension were similar, but fewer men had untreated high blood pressure and more men were on antihypertensive treatment in the present study. There was a lower frequency of smokers in this study.

INTRODUCTION

Manifest diabetes is a well-known risk factor for atherosclerotic cardiovascular disease. Glucose intolerance /GI/ or impaired glucose tolerance, verified by a glucose tolerance test, is a risk factor for the development of manifest diabetes. According to several studies, 20-60 % of GI subjects per ten years will develop manifest diabetes (5,17,20,24,25,28). The association between GI per se and atherosclerotic coronary artery disease has been found in several follow-up studies, e.g. by Whitehall, Bedford and Lund (6,15,16,26), although this could not be verified in the prospective studies of the International Collaborative Group (30). An increased frequency of GI has been found in patients with manifest atherosclerotic disease of coronary, peripheral and cerebral arteries in several investigations (18,23,32).

Other known risk factors for cardiovascular disease are hypertension, smoking and hyperlipemia. Further suggested risk factors are heredity for such disease and physical inactivity.

The aim of the present study was to detect and characterize the presence of diabetes, GI, cardiovascular disease, hypertension, obesity, smoking habits and physical activity in middle-aged females and males in the city of Uppsala, and to compare the results with those obtained in a similar health survey of middle-aged men in Uppsala ten years earlier (11). This comparison was made for the purpose of detecting any changes in risk factor patterns during the last decade among similarly aged males living in the same city.

MATERIAL AND METHODS

The background study population for the health survey consisted of all 47-54-years-old males and females born in 1927-1934 and resident in the northern (Gamla Uppsala) and the eastern (Vaksala) Parishes of the city of Uppsala, - 1 858 males and 2 084 females. 1 170 subjects, 549 males /M/ and 621 females /F/ were selected consecutively according to their national registration number from the register of the County Council of Uppsala and invited to attend a health survey.

The health examination was performed by the author and registered nurses between April 1981 and June 1982 at a primary care unit in Bangårdsgatan, Uppsala, in association with the Department of Internal Medicine of the University Hospital of Uppsala.The subjects were invited by letter, one invitation was sent.

A self-administered questionnaire was used to obtain the relevant family and medical history. Questions concerning angina pectoris and intermittent claudication were those proposed by Rose & Blackburn (27). These questions and also others concerning cardiovascular disease, exercise, smoking habits and heredity were the same as those used in a study of the Health Profile in Skaraborg County (8) and in primary preventive studies in Gothenburg (36, 37). Subjects under medical control and treatment were classified according to their diseases (Table 5). Marital status was obtained from the register of the County Council. Division into social classes was based on interview reports and was performed according to the system of the National Central Bureau of Statistics (2).

The oral glucose tolerance test (OGTT) was carried out in the morning after 10 h of fasting. The subjects took their ordinary diet during the week prior to the test. Water was permitted during fasting. No physical training, smoking or intake of vitamin C, hypnotics or analgesic agents were allowed from the evening prior to the test. Subjects with fever were called back later. The subjects remained seated during the test. A load of 75 g of anhydrous glucose in 300 ml of water was drunk over a period of 5 min, with zero time as the start of drinking.

Venous blood samples were drawn into tubes containing sodium fluoride at the start of and 2 h after the glucose challenge, for measurement of glucose in whole blood by a glucose oxidase method (Yellow Spring Instrument Model 23 AM). Diagnostic values for a 75 g OGTT are given in Table 1 (35).

Table 1. Diagnostic glucose values for a 75 g OGTT under standard conditions, using a specific enzymatic glucose assay.
From: WHO Expert Committee On Diabetes Mellitus: Second Report. Technical Report Series 646:p 10, 1980

	Glucose concentration $mmol \cdot l^{-1}$
	venous whole blood
DIABETES MELLITUS	
Fasting	≥ 7.0
and/or 2 h after glucose load	≥ 10.0
GLUCOSE INTOLERANCE	
Fasting	< 7.0
and 2 h after glucose load	$7.0 - < 10.0$

The blood pressure was measured in the sitting position after the OGTT, in all subjects by the author. Mercury manometers were used, and the cuff had a rubber bladder 12.5 cm wide and 35 cm long. Systolic and diastolic blood pressures /BP/ were read to the nearest 5 mm Hg mark. Diastolic BP was recorded as the disappearance of the Korotkoff sound (phase 5).

The height (without shoes) was measured to the nearest whole centimeter. The weight (with clothing but without shoes) was measured to the nearest whole kilogram and an assumed clothing weight of 1 kg was substracted. Body mass index /BMI/ was calculated as weight/height^2($kg \cdot m^{-2}$). Relative BMI as proposed by the Society of Actuaries (21) and West (34) was calculated, since this concept is considered to allow a comparison between sexes. From an ideal BMI, 20.6 in females and 22.1 in males, the per cent relative BMI can be calculated. Obesity was defined as a value of $\geq$ 120 %. Relative body weight according to the tables of Lindberg (19) was also calculated for comparison with weight data from the Uppsala study ten years earlier.

Statistical methods

Student's t-test was used for comparison of mean values. The chi-square $(X)^2$ test with Yates' correction was employed for comparing proportions. Pearson's coefficient was used for correlations between fasting glucose and log. 2-h glucose values. The 2-h glucose values were transformed logarithmically, since they were skewed to the right (4).

RESULTS WITH COMMENTS

I. Characteristics of participants

The subjects sampled for this study are presented in Table 2.
Out of 1 170 persons invited to attend the survey, 819 participated, 443 females and 376 males. The participation rate was 70 % (71 % of F; 69 % of M). Only eight of the participants were foreign citizens. Ninety-eight per cent of all participants had lived in Uppsala for more than 5 years. Six females and four males, who had been known to have diabetes mellitus prior to this survey, did not answer a questionnaire and did not undergo OGTT. One female and one male in whom diabetes was detected during the survey did not answer a questionnaire. So that these patients should not influence the results unduly, they were not included in calculations of glucose correlations, (see Table 7).

The marital statuses of the 807 participants who answered the questionnaire (436 F; 371 M) are shown in Table 3.

The proportions of unmarried, divorced and widowed females among the participants were a little higher than the corresponding figures in males.

Table 2. Participants of the study out of 1 170 invited males and females, 47-54 years old, in the city of Uppsala in 1981-82

Born	Called for examination			Participants					
	F n	M n	A n	F n	% of called	M n	% of called	All n	% of called
1927-34	621	549	1170	443	71	376	69	819	70

Table 3. Marital status of participants 47-54 years old.

	Females		Males		All	
	n	% of females	n	% of males	n	% of all
Married	320	73.4**	307	82.7	627	77.7
Unmarried	34	7.8	18	4.9	52	6.4
Divorced	63	14.4	42	11.3	105	13.0
Widows/ widowers	19	4.4*	4	1.1	23	2.9
All	436		371		807	100.0

*$p < 0.05$ **$p < 0.01$; females compared with males.

Occupational data and the social classification are given in Table 4. Gainfully employed subjects constituted 93.2 % of all participants. Of all participants in the health survey 45.7 % were workers, 25.7 % of them were salaried employees with fewer than three years of education and 20.4 % were salaried employees with more than three years of education. The percentages of females and males in the different classes are given in Table 4.

All diseases under medical control and treatment were recorded (see Table 5). Of all participants, 24.4 % were receiving regular medical attendance (28.4 % of F; 19.7 % of M).

Table 4. Social classification of 807 females and males, 47-54 years old, based on the questionnaire and interview, according to the system of the Central Bureau of Statistics.

Social classification	Females		Males		All	
	n	% of females	n	% of males	n	% of all
Workers, <2 yrs' education	187	43.3***	102	27.5	289	35.8
Workers, >2 yrs' education	14	3.2***	66	17.8	80	9.9
Salaried employees, <2 yrs' education	78	17.7***	30	8.1	108	13.4
Salaried employees, 2-3 yrs' education	41	9.4**	58	15.6	99	12.3
Salaried employees, 3-5 yrs' education	60	13.6	62	16.7	122	15.1
Salaried employees, >5 yrs' education, including university education	9	2.0***	34	9.2	43	5.3
Farmers and employers	4	0.9	7	1.9	11	1.4
Summary of gainfully employed subjects (whole or part of day)	393	89.2***	359	96.8	752	93.2
Subjects at home	30	6.8***	0	0.0	30	3.7
Unemployed subjects	1	0.2	1	0.3	2	0.2
Pensioners	9	2.1	8	2.1	17	2.2
Students	3	0.7	3	0.8	6	0.7
All subjects	436	100.0	371	100.0	807	100.0

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$; females compared with males

Table 5. Classification of 126 females and 74 males under medical control and treatment according to their diseases.

Classification	Number of subjects	
	Females	Males
Infectious diseases	1	0
Endocrine disorders	21	1
Diseases of the blood	3	3
Mental disorders	3	2
Diseases of the nervous system	6	4
Diseases of the cardiovascular system	44	28
Diseases of the respiratory tract	6	6
Diseases of the digestive tract	8	7
Diseases of the urinary tract	2	6
Diseases of the genital tract	24	1
Diseases of the ears and eyes	0	4
Diseases of muscles, bones and joints	6	6
Diseases of the skin	2	6

Comments

In the present study no attempt was made to persuade the individual to participate by a second invitation, since one aim of the study was to identify and select subjects with GI for a preventive feasibility trial with the aim of normalizing the blood glucose values. This, and the fact that most of the invited subjects had been called to a general health examination organized by the County Council about one year before, may explain why the participation rate was 70 % in this study, compared to 83 % in a similar study (11). This previous study, henceforth referred to as the 1970-73 study, comprised about 2 300 fifty-year-old men resident in the city of Uppsala, who were invited twice.

Concerning marital status, the proportions of married men and widowers in our study, 82.7 % and 1.1 % respectively, were similar to those in the 1970-73 study, 84 % and 1 %. The proportion of unmarried men in our study, 4.9 %, was lower than that in the 1970-73 study, 10 % ($p < 0.01$). The proportion of divorced men in our study, 11.3 %, was higher than in the previous study, 5 % ($p < 0.001$).

As seen by the data concerning marital status, occupation and social classification, the sample of this study was representative of a Swedish urban population, although the number of salaried employees with more than three years of education in this university city might be a little higher than in other Swedish cities.

The proportion of male subjects suffering from diseases in our study, i.e. of those receiving regular medical attendance, 19.7 % of all males, was higher than the rate of men found to have a previous disease in the 1970-73 study, 11 %. This may be partly explained by the fact that our classification of disease was broader; thus, in the previous study the term "disease" comprised only previous disease that had led to a disability pension, inability to work for more than six months immediately prior to the study, or disease requiring long-term medication. Social classification according to occupation was not performed in the 1970-73 study.

Although the participation rate and the marital status of the males in the present study (Tables 2 and 3) were not quite identical to those in the 1970-73 study (see above), the two studies were in many ways performed in a similar manner, allowing valid comparisons.

II. Glucose tolerance tests

The results from a 75 g OGTT in each subject provide a picture of venous whole blood glucose values in the health examinees. Fig. 1 shows the distribution of fasting glucose values and Fig. 2 the distribution of 2-h values. In Table 6a and 6b the fasting and 2-h values are subdivided into percentiles, given in arithmetic and logarithmic values. The fasting glucose values were normally distributed, with a mean value of 4.4 $mmol \cdot l^{-1}$ for all subjects. The 2-h values were slightly skewed to the right, as seen in Fig. 2 and Table 6a, and they became normally distributed after logarithmic transformation (Table 6b). The mean 2-h glucose value was 4.5 $mmol \cdot l^{-1}$ in all subjects, i.e. the glucose values had returned to the fasting level after 2 h. Females, however, on the average, showed a slightly slower return to the baseline level than males ($p < 0.01$).

The correlations between fasting and 2-h glucose values were significant (Table 7). They were of mediumgrade in all subjects ($r = 0.41$, $p < 0.001$) and in subjects with glucose values within GI limits ($r = 0.47$, $p < 0.001$), and were of lower grade in subjects with glucose values within normal limits ($r = 0.27$, $p < 0.001$).

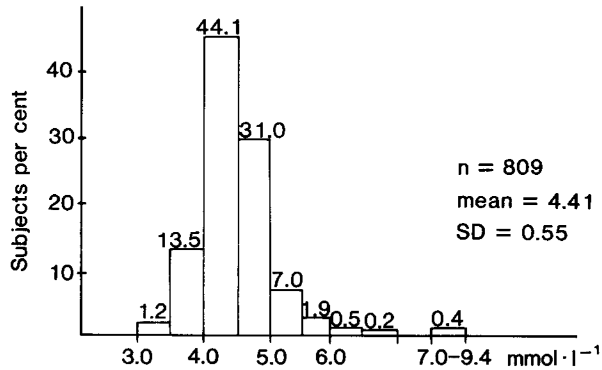

Fig. 1. Distribution of venous whole blood glucose levels at fasting in all 809 subjects.

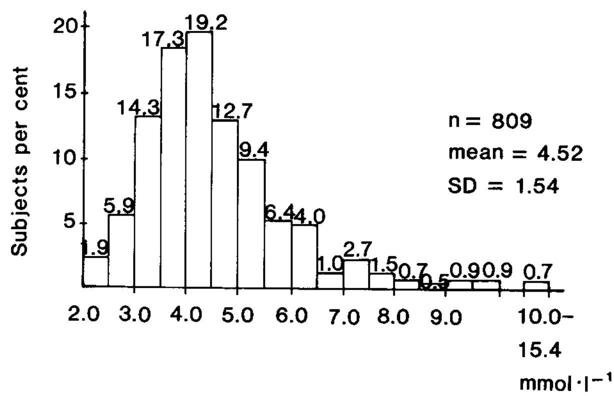

Fig. 2. Distribution of venous whole blood glucose levels at 2-h during OGTT in all 809 subjects.

Table 6a. Venous whole blood glucose levels in 809 subjects 47-54 years old, on fasting and at the 2-h interval during one 75 g OGTT. Mean, standard deviation and percentiles.

Group Hours	Sample size	Mean $mmol \cdot l^{-1}$	Stand. devi-ation	Percentiles $mmol \cdot l^{-1}$									
				10th	20th	30th	40th	50th	60th	70th	80th	90th	95th
Females													
0-h	437	4.39	0.55	3.8	4.0	4.1	4.2	4.3	4.4	4.6	4.7	5.0	5.4
2-h	437	4.65	1.55	3.1	3.5	3.8	4.1	4.3	4.7	5.1	5.6	6.4	7.5
Males													
0-h	372	4.43	0.55	3.9	4.0	4.2	4.3	4.4	4.5	4.6	4.7	4.9	5.2
2-h	372	4.39	1.52	2.9	3.2	3.6	3.9	4.1	4.4	4.7	5.1	6.1	7.3
All subjects													
0-h	809	4.41	0.55	3.8	4.0	4.1	4.2	4.3	4.5	4.6	4.7	5.0	5.3
2-h	809	4.52	1.54	3.0	3.4	3.7	4.0	4.2	4.5	4.9	5.4	6.3	7.5

Table 6b, Venous whole blood glucose values in 809 subjects 47-54 years old, on fasting and at the 2-h interval during the same OGTT as above. Percentiles in logarithmic values.

Group Hours	Sample size	Percentiles $mmol \cdot l^{-1}$									
		10th	20th	30th	40th	50th	60th	70th	80th	90th	95th
All subjects											
0-h	809	0.580	0.602	0.613	0.627	0.633	0.649	0.666	0.672	0.699	0.724
2-h	809	0.477	0.529	0.565	0.597	0.632	0.652	0.689	0.732	0.799	0.875

The outcome of one screening 75 g OGTT is shown in Table 8. Prior to the OGTT studies 1.3 % of all subjects were known to have manifest diabetes and were not tested. A further 0.6 % of all subjects had 2-h glucose values $\geq$ 10.0 $mmol \cdot l^{-1}$, thus above the limit for manifest diabetes according to WHO criteria. The GI criteria were met by 7.1 % of all subjects (7.4 % of F; 6.6 % of M); thus they had fasting blood glucose values < 7.0 $mmol \cdot l^{-1}$ and 2-h values of 7.0-<10.0 $mmol \cdot l^{-1}$.

Table 7. Pearson s correlation coefficients between fasting glucose and log 2-h glucose values in 807 subjects, 47-54 years old, at a 75 g OGTT in a health survey. Subjects with glucose values above diabetic limits are excluded.

Group	Females	Males	All
Subjects with normal glucose tolerance	0.31*** (n=400)	0.23*** (n=345)	0.27*** (n=745)
Subjects with glucose values within GI limits	0.39* (n=36)	0.57** (n=26)	0.47*** (n=62)
All subjects (normal + within GI limits)	0.46*** (n=436)	0.36*** (n=371)	0.41*** (n=807)

Significance levels: * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 8. Venous whole blood glucose levels in 819 subjects, 47-54 years old, on fasting and at 2-h during a 75 g OGTT. NIDDM = non-insulin-dependent diabetes mellitus.

Fasting glucose level Subsequent 2-h level ($mmol \cdot l^{-1}$)	Females n	Males n	All n	Per cent of all subjects %
Fasting level <7.0	436	371	807	98.5
2-h level <7.0	400	345	745	91.0
2-h level 7.0 - <10.0	33	25	58	7.1
2-h level ≥ 10.0	3	1	4	0.4
Fasting level ≥ 7.0	1	1	2	0.2
2-h level < 7.0	0	0	0	0.0
2-h level 7.0 - < 10.0	0	0	0	0.0
2-h level ≥ 10.0	1	1	2	0.2
All fasting levels	437	372	809	98.7
NIDDM, fasting level not known, not challenged by OGTT, NIDDM according to previous history	6	4	10	1.3
All subjects	443	376	819	100.0

Comments

The proportion of males in the present study who had glucose values within the limits of GI and manifest diabetes according to WHO criteria at one 75 g OGTT, 8.2 %, cannot be directly compared with the results of the glucose tolerance test in the 1970-73 study, since 0.5 $g \cdot kg^{-1}$ intravenous glucose tolerance tests (IVGTT) were used in the latter. In the 1970-73 study, among the males a K value of < 0.9 was found in 9.7 %, of < 1.0 in 13.6 % and of < 1.1 in 19.2 %. OGTT might be more sensitive than IVGTT in detecting GI, and moreover, comparison between the two tests is difficult.

Correlations between fasting and post-load 2-h parameters were calculated in order to study the comparability between the two values if used for screening. Fairly good comparability was found for all subjects and for the GI group.

The distribution of blood glucose values is given as percentiles in addition to graphs, since this is nowadays a useful means of comparison between distributions in different studies.

III. Aspects of family history of diabetes and cardiovascular disease

The percentages of patients with first-degree relatives with diabetes are given in Table 9. It was found that females knew of more relatives with diabetes than males.

Table 10 gives the history of cardiovascular disease in the parents. Myocardial infarction was significantly more often reported for the fathers than for the mothers of all participants, while the rate of hypertension was higher in the mothers.

Table 9. Proportions of subjects with first-degree relatives with diabetes mellitus, among 807 males and females 47-54 years old.

	Subjects					
	fem n	% of females	males n	% of males	all n	% of all
One first-degree relative with diabetes	69	15.8***	26	7.0	95	11.8
Insulin treatment	17		9		26	
Diet and/or oral agent	47		15		62	
Treatment not known	5		2		7	
Two or more first-degree relatives with diabetes	8	1.8	3	0.8	11	1.4
Insulin treatment	3		1		4	
Diet and/or oral agent	5		2		7	
Treatment not known	0		0		0	

Significance level: *** $p < 0.001$; females compared with males.

Table 10. Presence of cardiovascular disease in parents of 807 middle-aged subjects.

	Father		Mother	
	n	% of all fathers	n	% of all mothers
Myocardial infarction	160	19.8***	75	9.3
Cerebrovascular disease	106	13.1	119	14.7
Hypertension	95	11.8***	237	29.4

*** $p < 0.001$; fathers compared with mothers

Twenty-six per cent of all participants (28.4 % of F; 24.0 % of M) had one or two parents with myocardial infarction, 25.4 % (25.9 % of F; 24.8 % of M) had parents with cerebrovascular disease and 36.3 % (41.5 % of F; 30.2 % of M) had parents with hypertension.

Comments

The numbers concerning heredity are minimum numbers, since they are based only on the participants' knowledge of the presence of disease in their parents. The proportion of one or more first-degree relatives with diabetes in the present study reported by males, 7.8 %, was lower than in the study of 1970-73, 14.7 % ($p < 0.001$), while the proportion reported by all subjects in the present study, 13.2 % ($p > 0.05$) was similar to that in the previous study.

The percentages of cardiovascular disease among the parents of participants (Table 10) were similar in the two studies.

IV. Cardiovascular morbidity

Hospital care for previous myocardial infarction was reported by 1.1 % of all subjects (0 of F; 2.4 % of M). Heart weakness, heart enlargement or other unspecified heart disease was reported by 2.2 % of all subjects (1.4 % of F; 3.2 % of M).

Angina pectoris verified previously by a physician was reported by 1.0 % of all participants (0.9 % of F; 1.1 % of M). All of these and another 3.7 % of all subjects (3.0 % of F; 4.6 % of M) reported pain in the chest on effort, disappearing within 10 min when slowing down or stopping, and diagnosed as angina pectoris on the basis of the questionnaire.

Hospital care for cerebrovascular disease was reported by one female and by no males. Intermittent claudication verified by a physician was reported by 0.4 % of all subjects (0 of F; 0.8 % of M). All of them and another 2.0 % of all subjects (2.5 % of F; 1.3 % of M) reported pain in one or both calves when walking on flat ground or uphill, disappearing within 10 min when slowing down or stopping, and diagnosed as intermittent claudication on the basis of the questionnaire.

Comments

The rate of myocardial infarction in the present study, 2.4 % among males, was higher than the rate in the 1970-73 study, 0.6 %, but the figures were too small for a valid statistical analysis. The prevalence in 1970-73 was based on hospital records, whereas only interview data were used in the present survey. When non-participants and fatal cases were included in the 1970-73 study, the total figure for myocardial infarction was 1.0 %.

The proportion of males with angina pectoris diagnosed on the basis of the questionnaire in the present study, 5.7 % of all males, was higher than that in the 1970-73 study, 1.6 %, based on clinical examination ($p < 0.001$). A questionnaire as proposed by Rose was used in the present study, as it has been found to have a high specificity and sensitivity in comparison with the physician's diagnosis (12). However, the degree of validity of this questionnaire was lower in another recent study (9). The diagnosis of both angina and intermittent claudication in the study of 1970-73 was screened for by a questionnaire ad modum Collen (3) and was subsequently confirmed by examination by the investigator, and the examination excluded several of the subjects who had reported symptoms in the questionnaire. With use of the WHO questionnaire, the prevalence of angina in 50-year-old men in Gothenburg was 2.1 % (31) and in Copenhagen 4.4 % (7).

One female was found to have suffered from cerebrovascular disease in the present study, compared to two participants and two non-participants, according to hospital records, in the study of 1970-73.

The proportion of males with intermittent claudication in the present study, either verified by a physician or previously diagnosed on the basis of the questionnaire, 2.1 % of all males, was higher than that in the 1970-73 study, 0.1 %. These figures were too small to allow a valid statistical analysis. However, 4.5 % of the men in 1970-73 had answered affirmatively to the question concerning pain in the calves when walking, but none of these men were diagnosed as suffering from intermittent claudication when examined by the investigator. It should be noted that the among 55-year-old men in Malmö, the prevalence of this disease was found to be 1.1 % when venous occlusion plethysmography was used and 2.8 % when based on the WHO questionnaire (14).

Thus, it cannot be decided with certainty whether the higher rates of angina and intermittent claudication in the present study are explained by an increased proportion of these diseases in the present population or by different diagnostic methods.

V. Blood pressure

The distribution and the mean values of systolic and diastolic BP are presented in Fig. 3a and 3b for males and females. The distribution was somewhat skewed to the right. The mean of systolic and diastolic BP in all subjects were 133.0 ± 13.7 and 83.4 ± 7.0 mm Hg respectively. Both systolic and diastolic mean BP were similar in males and females.

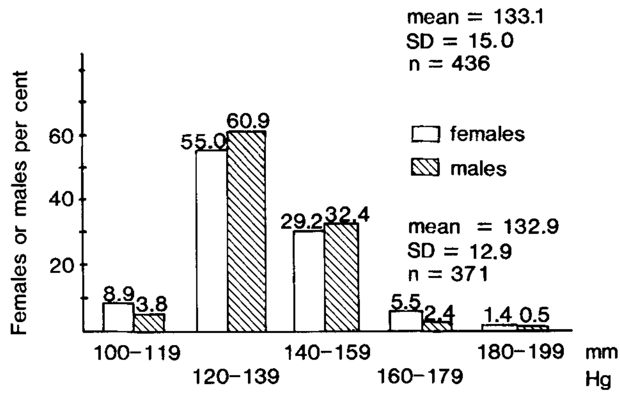

Fig. 3a. Distribution of sitting systolic blood pressure in 436 middle-aged women and 371 middle-aged men.

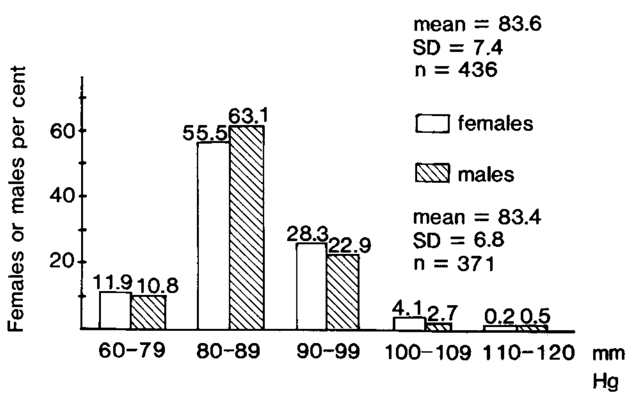

Fig. 3b. Distribution of sitting diastolic blood pressuree in 436 middle-aged women and 371 middle-aged men.

Subjects treated with antihypertensive agents constituted 9.4 % of all participants (11.0 % of F; 7.5 % of M). When BP < 170/105 mm Hg was considered as a measure of adequate treatment, it was found that 82.9 % of the treated subjects (85.4 % of treated F; 78.6 % of treated M) were being adequately treated. A BP < 160/100 mm Hg was found in 75.3 % of all treated subjects (79.3 % of treated F; 72.9 % of treated M). The prevalence of high BP was 11.2 % of all participants (12.8 % of F; 9.2 % of M), when defined as comprising all subjects receiving antihypertensive treatment independent of BP level and all untreated subjects with BP ≥ 170/105 mm Hg. The prevalence was 13.0 % (15.6 % of F; 10.0 % of M), when all treated subjects, independent of BP level, and all untreated subjects with BP ≥ 160/100 mm Hg were included. The prevalence, among males only, of men being treated independent of BP level and untreated men with diastolic BP ≥ 105 mm Hg was 8.3 % (calculated for comparison with the 1970-73 study).

Table 11 shows the antihypertensive agents that were used. Thiazides and/or beta-blocking agents were used as single drugs or in combination with each other by 81.6 % of all treated subjects (85.4 % of treated F; 75.0 % of treated M).

Table 11. Antihypertensive agents used by the 78 subjects receiving antihypertensive treatment in the study.

	Females		Males		All subjects	
	n	% of females	n	% of males	n	% of all
1. Thiazides, furosemide	12	25.0***	2	7.1	14	18.4
2. Beta-adrenergic blocking agents	18	37.5§	13	46.5	31	40.9
1. + 2.	11	22.9	6	21.4	17	22.4
3. Aldosterone antagonists	3	6.3	0	0.0	3	3.9
4. Hydralazine in combination with 1. and/or 2.	2	4.2	6	21.4	8	10.5
5. Bethanidine in combination with 1. + 2.	1	2.1	0	0.0	1	1.3
6. Others (Clonidine + nifedipine	1	2.1	1	3.6	2	2.6
All types of agents	48	100.0	28	100.0	78	100.0

§ not significant, *** $p < 0.001$, females compared with males in 1. and 2.

Comments

The rate of hypertension in men in the present study, defined as comprising all treated men and all untreated men with a diastolic BP $\geq$ 105 mm Hg, 8.3 %, was similar to the rate of hypertension in the study 1970-73, 7.5 % of middle-aged men ($p > 0.05$), defined in the same way. The mean systolic and diastolic BP in men in the present and earlier studies were similar, 133.2/83.4 and 133.2/83.7 mm Hg 1970-73, respectively. Only 0.8 % of the men in the present study, however, had untreated high BP $\geq$ 105 mm Hg, compared with 3.8 % of those in the 1970-73 study ($p < 0.01$). The proportions of men with untreated high BP $\geq$ 160/100 mm Hg were 2.5 % in the present study and 9.5 % in the previous one ($p < 0.001$). Not only was the rate of untreated high BP lower, but the proportion of men receiving antihypertensive treatment was higher in the present study, 7.5 %, compared with 3.7 % in the previous survey ($p < 0.01$).

More men were being adequately treated in the present study than in 1970-73. Of the treated men in the present study, 78.6 % had a BP < 170/105 mm Hg as a measure of adequate treatment and 72.9 % had a high BP < 160/100 mm Hg, compared with 55 % of the treated men in the study 1970-73 with a diastolic BP < 105 mm Hg ($p < 0.001$).

Diuretics were being used by 7.1 % of the treated men and by 18.4 % of all treated subjects in the present study, compared with 19.5 % of the treated men in the study of 1970-73 ($p > 0.05$). Diuretics as single drugs or in combination with different antihypertensive agents were being used by 39.2 % of the treated men and by 47.4 % of all treated subjects in the present study, as against 61 % of the men in 1970-73 ($p > 0.05$). Beta-blocking agents as a single drug was used by 46.5 % of the treated men and by 40.9 % of all subjects in the present study, compared with 16 % of the treated men in the previous study ($p < 0.01$). Beta-blocking agents as a single drug or in combination with different antihypertensive agents were being used by 89.3 % of the treated men and by 73.7 % of all treated subjects in the present study, compared with 38 % of the men in 1970-73 ($p<0.001$). Thus, more men were taking beta-blocking agents and fewer men were using diuretics in the present study.

Concerning sex differences in our study, it should be noted that the proportion of treated subjects and untreated subjects with BP $\geq$ 160/100 mm Hg was higher in females than in males ($p < 0.05$). More females than males were being treated with diuretics ($p < 0.001$).

Smoking habits

Smokers of all kinds constituted 28.5 % of all subjects (26.5 % of F; 31.0 % of M). The proportion of ex-smokers among all subjects was 22.9 % (15.8 % of F; 31.3 % of M). Thus, 48.6 % of all participants (57.7 % of F; 37.7 % of M) had never smoked. The smoking habits of the 235 smokers are presented in Table 12. Heavy cigarette smokers, smoking more than 24 cigarettes per day, constituted 5.7 % of all cigarette smokers (2.6 % of F; 9.4 % of M). Those smoking 15-24 cigarettes per day constituted 32.4 % of all cigarette smokers (27.2 % of F; 38.5 % of M).

Table 12. Smoking habits in 235 smokers 47-54 years old.

Smoking habit category	fem. n	% of females	males n	% of males	all n	% of all
Cigarettes only	114	99.1***	96	83.5	210	91.3
1-4 cig/day	9	7.8	13	11.3	22	9.6
5-14 "	71	61.7***	37	32.2	108	47.0
15-24 "	31	27.0	37	32.2	68	29.5
> 24 "	3	2.6	9	7.8	12	5.2
Pipe only	0	0***	17	14.8	17	7.4
½ packet/week			16	13.9	16	7.0
½-2 "			0	0	0	0
> 2			1	0.9	1	0.4
Cigars only	1	0.9	2	1.7	3	1.3
1 cigar/day	1		1	0.85	2	0.9
2-3 "						
4-5 "						
> 5 "			1	0.85	1	0.4
All smokers	115	100.0	115	100.0	230	100.0

*** $p < 0.001$, females compared with males

Comments

Fewer men were smokers in the present study, 31.0 %, than in the 1970-73 study, 51 % ($p < 0.001$). There was a higher proportion of male ex-smokers in the present study, 31.3 %, than in the previous one, 23.2 % ($p < 0.001$). Cigarette smokers constituted 83.5 % of all male smokers in the present study, compared with 69 % in the previous study, ($p > 0.05$). The corresponding figures for pipe smokers were 14.8 % and 22 % ($p > 0.05$), and for cigar smokers 1.7 % and 6.3 % ($p > 0.05$), respectively. The proportion of heavy cigarette smokers among cigarette smoking men in the present study (more than 24 cigarettes per day), 9.4 %, was lower than previously (more than 20 cigarettes per day), 17.8 %. Only 38.5 % of cigarette smoking men now smoked 15-24 cigarettes per day compared to 61.4 % of the men previously smoking 11-20 cigarettes per day. Thus, fewer middle-aged men were smoking in Uppsala now compared with ten years earlier.

As expected concerning sex differences in the present study, more men than women were smokers ($p < 0.05$). One woman smoked a pipe.

VII. Body mass index and relative body weight

The distribution and mean values of BMI in females and males are presented in Fig. 4a and 4b. The distributions are somewhat skewed to the right, with BMI mean value of 24.8 and median value of 23.2 $kg \cdot m^{-2}$ respectively in females, mean value of 25.3 and median value of 23.1 $kg \cdot m^{-2}$ respectively in males. Relative BMI values, calculated from an ideal BMI of 20.6 in females and 22.1 $kg \cdot m^{-2}$ in males, are noted in the Figures. The mean relative BMI value in all subjects was 117.8±17.1 %. This mean value was higher in females, 120.4± 19.1 %, than in males, 114.6±13.6 % ($p < 0.01$). Obesity, defined here as relative BMI $\geq$ 120 %, was found in 40.9 % of the females and in 27.5 % of the males ($p < 0.001$). In all subjects the rate of relative BMI $\geq$ 120 % was 34.0 %.

The relative body weight was also calculated for males only according to the tables of Lindberg (19), for comparison with the 1970-73 study. The mean value for males was 110.9 $\pm$ 13.8 %.

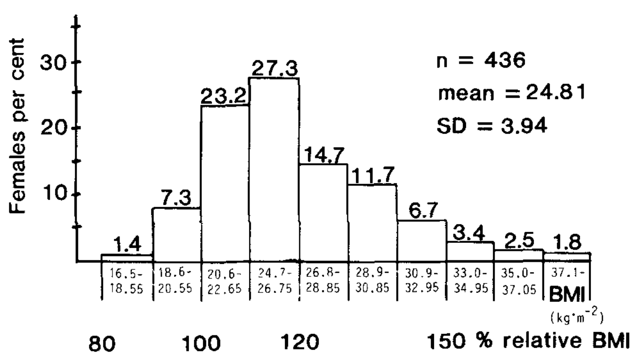

Fig. 4a. Distribution of body mass index (BMI) and relative BMI in females 47-54 years old.

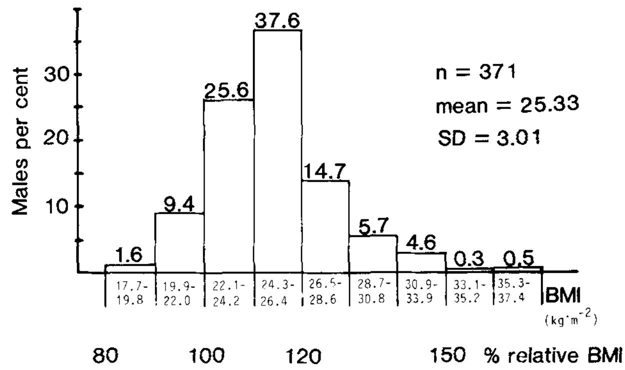

Fig. 4b. Distribution of BMI and relative BMI in males 47-54 years old.

Comments

The mean relative body weight estimated according to Lindberg's tables in the present study, 110.9 %, was about 2 % higher than the mean value for middle-aged men in the 1970-73 study, 109 % ($p < 0.01$). Thus, the middle-aged men in the present study were somewhat more obese than those in 1970-73, and in this study the women were more obese than men.

VIII. Physical activity at work and during leisure

The history of physical activity obtained from the questionnaires is given in Table 13a and 13b. Concerning activity at work, it is seen that only 1.1 % of the females had heavy manual work, compared with 5.7 % of the males ($p < 0.01$). Concerning activity during leisure-time, regular physical training for at least 2-3 h per week was reported by 7.8 % of the females and by 24.5 % of the males ($p < 0.001$).

Comments

The questions concerning physical activity in the present study were similar and comparable to those in the 1970-73 study. E.g students and workers at home were registered in physical job activity group I. Sedentary work was less common in the present than in the previous study. This was reported by 28.8 % and 35.5 %, respectively, of all gainfully employed men ($p < 0.001$). The rate of heavy manual work was lower in the present than in the previous study, 5.7 % and 15.5 % respectively ($p < 0.001$).

Table 13 a. Classification of physical activity at work in 752 subjects 47-54 years old.

Occupational physical activity	Females n	% of females	Males n	% of males	All n	% of all
Predominantly sedentary	146	33.5	107	28.8	253	31.4
Predominantly standing and walking, no heavy lifting	183	42.0	161	43.4	344	42.6
The same + lifting and walking upstairs	102	23.4	82	22.1	184	22.8
Heavy manual work	5	1.1**	21	5.7	26	3.2
	436	100.0	371	100.0	807	100.0

Significance level: ** $p < 0.01$, females compared with males

Table 13b. Classification of physical activity during leisure-time in 807 subjects 47-54 years old.

Leisure time physical activity	Females n	% of females	Males n	% of males	All n	% of all
Inactive	40	9.2	48	12.9	88	10.9
Some activity (walking or cycling)	362	83.0***	232	62.6	594	73.6
Regular physical training at least 2-3 hours/week	33	7.6***	86	23.2	119	14.8
Regular hard physical training	1	0.2	5	1.3	6	0.7
	436	100.0	371	100.0	807	100.0

Significance level: *** $p < 0.001$, females compared with males.

The rate of inactivity during leisure-time was similar in the present and the 1970-73 study, with figures of 12.9 % and 14.7 % respectively ($p > 0.05$). The proportion of men carrying out at least 2-3 h of regular physical training, however, was lower in the present study, 24.5 %, than in the previous study, 48.9 % ($p < 0.001$). Regular hard physical training was reported by only 1.3 % of the men in our study and by 5 % in the 1970-73 study ($p < 0.001$).

IX. Concluding remarks

One of the purposes of this study was to detect subjects with GI and invite them to participate in a preventive feasibility trial, since GI is a risk factor for the development of manifest diabetes and might be a risk factor for cardiovascular disease. It was found that OGTT can be performed without difficulty in a small laboratory at an outpatient clinic or primary care unit, provided that adequate equipment for exact measurement of blood glucose is available. OGTT was performed according to the WHO recommendation with measurement of blood glucose on fasting and a 2-h intervals for screening purposes. It should be remembered that at least one additional abnormal blood glucose value is needed to confirm a clinical diagnosis of manifest diabetes in the absence of symptoms or of GI, e.g. a pathological 1-h value during the first test or an elevated fasting or 2-h value during a subsequent OGTT (35). All subjects with pathological glucose values in the present study were therefore invited to undergo a subsequent OGTT, as reported elsewhere (1).

The rate of manifest diabetes found in the present study was 1.9 %. In the 1970-73 study it was 0.9 %. The rate in the rural municipality of Tierp, 70 km north of Uppsala, was recently reported to be 3.0 % in females and 3.3 % in males, 45-64 years old (10), compared with 2.3 % in females and 1.6 % in males in the present study. The rates in Tierp were based on recording of medical visits and prescriptions of antidiabetic agents in the municipality, and the population was older than in our study. The rate of diabetes in our study is a minimum rate, since diabetic patients under regular medical control may have been inclined not to participate.

The present study comprised both men and women. It was found that females exhibited a significantly higher mean 2-h blood glucose concentration than males during OGTT, while the rates of manifest diabetes and GI based on a screening OGTT, 2.3 % and 7.4 % in females, 1.6 % and 6.6 % in males, respectively, were not significantly different. No female reported hospital care for myocardial infarction, as against 2.4 % of males, and the rates of angina and intermittent claudication were somewhat lower in females, although the sex differences were not significant. The mean BP was similar in the two sexes, while the prevalence of subjects receiving antihypertensive treatment and of those with an untreated BP $\geq$ 160/100 mm Hg was significantly higher among females, 15.6 %, than among males, 10.0 %. Females were significantly more obese than males, as expressed by a 6 % higher mean relative BMI. Nearly half of the females passed the limit of obesity, defined as a relative BMI $\geq$ 120 %, compared with one-fourth of the males. Females also carried out significantly less regular activity during leisure than males; 7.8 % of the females were assigned to the two more active groups, as against 24.5 % of the males.

In comparison with the middle-aged men in Uppsala ten years earlier, it was found that the proportion of men within limits of diabetes and GI in the present study, 8.2 % of the males, was similar to the rate of a K value < 0.9 at IVGTT in the 1970-73 study, 9.7 %. The prevalence of angina pectoris was significantly higher among males in the present study. It is not clear, however, whether the difference is due to a change in the true frequencies in the populations or to the use of different methods of diagnosis in the two studies. The proportions of males with myocardial infarction and intermittent claudication were also higher in the present study, but the numbers were too small to allow a valid statistical analysis. Though the mean BP and the rate of hypertension in males in the two studies were similar, the proportion of males receiving antihypertensive treatment was significantly higher and the proportion of males with untreated high BP significantly lower in the present study. This is probably a reflection of the increased activities for detection and treatment of hypertension in Uppsala during the last ten years including the extensive general health examination organized by the County Council (13).

The two samples of middle-aged men in Uppsala, in 1970-73 and now 1980-81, may be compared with two cohorts of 50-year-old men in Gothenburg, men born in 1913 studied in 1963, and men born in 1923 studied in 1973 (33). The two Gothenburg cohorts were followed up for 7 years concerning the incidence of non-fatal myocardial infarction and death from myocardial infarction or ischemic heart disease (see Table 14). Concerning the initial presence of cardiovascular risk factors, there were no significant differences in mean blood pressure in Gothenburg, as in Uppsala, but the mean values were higher in Gothenburg. The rate of treated hypertensive subjects was higher in the second sample in Gothenburg, as was seen in Uppsala. It seemed as if most hypertensive subjects in Gothenburg were still being treated with diuretics in 1973, as in the 1970-73 study in Uppsala, while beta-blockers were the major agent in Uppsala ten years later. This illustrates the increased detection of hypertension during the last 10-20 years and a change in the choice of antihypertensive agents during the last years. The rate of smokers was still unchanged in Gothenburg in 1973, whereas it was lowered in Uppsala in 1980-81. Concerning body weight, the increased body mass index in the second sample in Gothenburg was in line with the finding of an increased relative weight in the second sample in Uppsala. In spite of the increased body mass index in Gothenburg in 1973, there were no significant differences concerning blood lipids between the Gothenburg samples.

When the two cohorts in Gothenburg were followed up for 7 years, it was found that the incidence of total IHD was higher in the second cohort. Risk factors were studied for men in whom IHD did and did not develop during the follow-up. In addition to higher blood pressure, a higher frequency of smoking

Table 14. Two cohorts of 50-year-old men in Gothenburg (men born in 1913 and 1923) and the two studies of approximately 50-year-old men in Uppsala - a comparison.

	1970-73 study in Uppsala		1980-81 study in Uppsala	Men born in 1913 (1963)		Men born in 1923 (1973)
Systolic BP, mm Hg, mean±SD	133.2 ±18.1	-NS-	133.2 ±12.8	138.3 ±20.9	-NS-	137.4 ±22.1
Diastolic BP, mm Hg, mean±SD	83.7 ±11.2	-NS-	83.4 ± 6.8	91.6 ±13.2	-NS-	91.6 ±14.2
Rate of treated hypertensives, %	3.7	-**-	7.5	1.6	-***-	6.6
Antihypertensive agents (thiazides, beta-blocking agents), %	61 % thiaz. 38 % b-bl.	-NS- -***-	39 % thiaz. 89 % beta-bl.	Most treated with diuretics		Most treated with diuretics
Rate of smokers, %	51	-***-	32	56	-NS-	51
Serum cholesterol, $mmol \cdot l^{-1}$, mean±SD	-		-	6.42 ±1.12	-NS-	6.46 ±1.34
Serum triglycerides, $mmol \cdot l^{-1}$, mean±SD	-		-	1.26 ±0.82	-NS-	1.30 ±0.77
Body mass index, $kg \cdot m^{-2}$, in Gothenburg; relative weight, %, in Uppsala - mean±SD	109 ±14	-**-	110.9 ±12 (25.3 $kg \cdot m^{-2}$)	24.8 ± 3.2	-**-	25.4 ±3.2
Incidence of total IHD (non-fatal MI or death from MI or IHD) during 7 years of follow-up	-		-	4.2	-*-	8.0

Significance levels concerning comparison of the Uppsala studies and the Gothenburg studies, respectively: * $p<0.05$, ** $p<0.01$, *** $p<0.001$, NS = not significant.
IHD = ischemic heart disease, MI = myocardial infarction

(not significant in 1973) and higher blood lipids in men with IHD, it was found that BMI emerged as a new risk factor in 1973. These results are corroborated by the findings of a higher body weight and a higher rate of angina pectoris in the second sample in Uppsala (although the difference concerning angina was uncertain because of differences in methods of diagnosis in the two Uppsala samples). It should be pointed out that GI as a cardiovascular risk factor was not studied in Gothenburg.

The examinees in the present study, representative of middle-aged subjects in a Swedish community, may be compared with 40-59-year-old subjects of some other international population studies. Thus the mean 2-h glucose value in venous whole blood in males, 4.4 $mmol \cdot l^{-1}$, was similar to the mean 2-h level in the Finnish Helsinki Policemen study of 1967, 4.6 $mmol \cdot l^{-1}$ venous whole blood (in males, using 75-90 g OGTT) (30). It was somewhat lower than the mean 2-h level in the French Paris Prospective study of 1967-72 - 4.9 $mmol \cdot l^{-1}$ after conversion to venous whole blood (in males, using a 75 g OGTT) (30). It was lower in all subjects in the present study, 4.5 $mmol \cdot l^{-1}$, than the mean 2-h level in HANES II, United States, 1976-80 - 5.7 $mmol \cdot l^{-1}$ after conversion to venous whole blood (in females and males, 75 g load) (29). Comparison with other studies using 50 or 100 g loads was not made here, since the size of the glucose load seems to be important, as different 2-h levels have been reported with use of 50 and 100 g loads in the same subjects (22).

The mean systolic and diastolic BP in the present study lay in the middle of the mean values of fifteen population studies of the International Collaborative Group (30) with systolic ranges of 124-143 mm Hg and diastolic ranges of 78-87 mm Hg. All these studies were carried out in middle-aged men in 1960-76. The mean BMI was similar to the mean values in Finland, Denmark and several other Western European countries, where the ranges were 24.7-25.6 $kg \cdot m^{-2}$; it was lower than in the United States, with a range of 25.7-27.1 $kg \cdot m^{-2}$ and higher than in Japan, where a mean value of 22.5 $kg \cdot m^{-2}$ has been reported compared with 25.3 $kg \cdot m^{-2}$ for males in the present study (30). The rate of male cigarette smokers in the present study, 26 % (pipe and cigar smokers excluded), was remarkably lower than in all fifteen international studies, where the ranges were 38-71 % (30), including only cigarette smokers.

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