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Comparison of Glucose Tolerance, Serum Insulin, Serum Lipids and Skinfold Thickness between 50- and 60-year-old Men

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ABSTRACT

Two apparently healthy male groups, one 60 (n = 67) and one 50 (n = 367) years of age were compared with respect to blood glucose, serum lipid and serum insulin concentration and intravenous glucose tolerance.

These groups were recruited from two health surveys performed on male populations of these ages in the municipality of Uppsala. The prevalence of diabetes mellitus in the two health survey populations were 4.5 % and 0.9 %, respectively. No significant differences in serum triglycerides, serum cholestrol and fasting serum insulin concentrations were found between the two age groups. Significantly higher k-values and higher early serum insulin response to i.v. glucose were found in the younger than in the older age group. The older age group was more obese, than the younger group. It is concluded that the prevalence of diabetes increases considerably in males between 50 and 60 years of age. In parallel, the prevalence of decreased glucose tolerance is increasing, which might partly be explained by increased body weight and partly by an impaired pancreatic β-cell function.

INTRODUCTION

Great interest has been focused on the increasing morbidity and mortality due to ischemic heart disease (IHD) and cerebrovascular disease (CVL) (15). These account for an increasingly high share of both hospital care and of deaths in the population of the Uppsala Hospital region. Thus, these two groups of diseases were responsible for 16 % of all days in hospital care in 1964 - 1968 (Socialstyrelsen, 1974) and this figure had increased to 18 % in 1973 (Socialstyrelsen, 1975). A similar trend was observed for mortality due to IHD, in the whole of Sweden (36). The increase was most pronounced for males aged 45 - 54 years.

On account of these tendencies, studies with the aim of estimating the prevalence of etiological risk factors for IHD in these age groups have been

afforded special interest (6, 14, 28, 37). The possibilities of changing the risk factor patterns by preventive actions have been given consideration (17, 31).

Two of the risk factors discussed for IHD and CVL are impaired glucose tolerance and elevated serum lipid levels. The question of how age influences these two parameters has been controversial (13, 18, 23). This study was therefore undertaken to investigate the prevalence of impaired glucose tolerance and increased serum lipid concentraions in two male populations of the critical ages between 50 and 60 years.

MATERIAL

All men born in 1915 and living in the city of Uppsala, Sweden, were invited to a health examination. The total population numbered 422 men. Of these 331 subjects (78.4 %) attended the examination which was carried out in the autumn of 1975 (34). Of the subjects participating in the screening, a random subsample of 67 (20.2 %) apparently healthy men was chosen for an intravenous glucose tolerance test (IVGTT), including serum (S-) insulin determinations. All these 67 subjects denied the presence of disease and were having no pharmaceutical or dietary treatment. The results from the investigation of these 67 subjects were compared with findings in a subsample of apparently healthy 50-year-old men (n = 367) born in 1924. The latter men had undergone a similar health screening examination in the same municipality (19) in the autumn of 1973.

METHODS

Medical history

A modified self-administered questionnaire (8) was used, in addition to a personal interview. Thus, information about medicines taken, dietary regimens, presence of disease and heredity for diabetes mellitus was obtained.

Anthropometric measurements

Height and weight in undershorts were measured. Relative body weight was calculated and expressed as an index. The reference for this relative body weight was obtained from the same anthropometric measurements of the population (n = 2322) of 50-year-old men born in 1920 - 1924 (19). The heights (x) and weights (y) of these subjects were subjected to a linear regression analysis ($y = 0.76 x - 56.0$). This equation of the regression line was used to determine each subject's ideal body weight. Actual divided by ideal body weight was the body weight index.

The skinfold thickness was measured (in mm), with the subject in the sitting position, at three sites of the body, beneath the angle of the right scapula, at the mid-point on the posterior aspect of the upper arm and on the abdominal wall to the right of the umbilicus. A Harpender caliper (12) was used. The measurements on the 60-year-old men were made by the same registered nurse as had performed the skinfold measurements in the 50-year-old men.

Serum lipids

Venous blood samples were taken in the fasting state in the morning for determinations of serum triglycerides (fS-Tg) (24) and serum cholesterol (fS--Chol) (25) concentrations. For comparison with the 50-year-old men, serum samples taken from the latter 2 years previously, frozen and stored in liquid nitrogen, were thawed and re-analysed for fS-Tg and fS-Chol concentrations. Regression and correlation analyses of these values as against the corresponding values for the 50-year-old men obtained at the original survey gave the following figures. For fS-Tg and fS-Chol the correlation coefficients were 0.96 and 0.82 and the equations of linear regression $y = 0.99\ x - 0.01$ and $y = 1.00\ x + 0.49$, respectively. All values are given in millimoles per liter (mmol/l). These equations were used for adjustment of the earlier values of fS-Tg and fS-Chol in 50-year-old men. In the statistical comparisons of fS-Tg and fS-Chol concentrations between 50- and 60-year-old men, both transformed and non-transformed values were used.

IVGTT and blood glucose

The IVGTT was performed in the fasting state. A glucose dose of 0.5 g/kg body weight was injected into the antecubital vein in 2.5 min. Samples for determinations of fasting blood (fB)-glucose (20) were taken immediately prior to the injection of B-glucose 6, 20, 30, 40, 50, and 60 min after. This part of the investigation was also carried out by the same registered nurse as assisted in the IVGTT investigations of 50-year-old men. The B-glucose values obtained at 20, 30, 40, and 50 min were used to calculate glucose tolerance, which was expressed as the k-value from the formula (21)

$$k = \frac{\text{half time of glucose disappearance}}{0.693}$$

The line of the elimination curve was calculated from the method of least squares by the experimental points on a lin (time) log (B-glucose concentration) scale.

S-insulin

S-insulin determinations in the 60-year-old men were done in duplicate using the Phadebas insulin test (Pharmacia, Uppsala, Sweden). In the same way as for fS-Tg and fS-Chol, serum samples from the 50-year-old men were re-analysed for insulin concentration. The correlation coefficient between the original values obtained at the IVGTT of the 50-year-old men and the values obtained at the re-analyses was 0.98. The regression equation was $y = 1.00\ x - 0.0001$.

Blood samples for S-insulin determination were taken prior to glucose injection (fS-insulin) and 4, 6, 8 and 60 min after. Both the fS-insulin value and the early serum insulin response (ER) were calculated. The ER value was the sum of the S-insulin concentrations at 4, 6, and 8 min divided by three. The serum insulin index was defined as the ratio between ER and fS-insulin (4). The late serum insulin response (LR) was defined as S-insulin concentration at 60 min.

Adipose tissue fat cell size

A needle biopsy was taken from subcutaneous adipose tissue to the right of the umbilicus, prior to the glucose injection. Adipose tissue fat cell size was determined by the method described by Sjöström (30).

Statistical analyses

Conventional statistical methods were used to calculate mean values and standard deviations. The significancies of the differences between the mean values were estimated by Student's t-test (two-tailed test). Comparisons of frequencies were made by the χ^2 (chi-square) test.

The subsamples of populations of 50- and 60-year-old men were divided into quintiles (Q_1 - Q_5).

RESULTS

Relative body weight and skinfold thickness

The relative body weight was higher ($p < 0.05$) in the 60-year-old than in the 50-year-old men. The distribution of adipose tissue seemed to differ between the two subsamples. Thus, the 60-year-old men had a significant ($p < 0.001$) greater skinfold thickness at the triceps site than the younger men. However, at the scapular site the 50-year-old men had a greater skinfold thickness ($p < 0.001$) than the older men. The mean values for abdominal skinfold thickness did not differ between the two age groups (Table I).

Table I. Mean values and standard deviations of body weight index, based on anthropometric finding of 50-year-old men in Uppsala, and skinfold thickness (mm) in 60-year-old men (60 yr, n = 67) and 50-year-old men (50 yr, n = 367).

Variable	$Q_1 - Q_5$ 60 yr	50 yr
Triceps	20.3 ± 9.7***	10.1 ± 4.2
Subscapular	11.3 ± 4.2***	16.6 ± 6.2
Umbilicus	19.5 ± 7.5	17.5 ± 9.6
Body weight index	1.00 ± 0.11*	0.97 ± 0.10

*) $p < 0.05$ compared to 50-year-old men
***) $p < 0.001$ compared to 50-year-old men

Serum lipids

The mean fS-Tg and fS-Chol concentrations for the 60- and 50-year-old population subsamples are given in Table II. For the latter group both the original values and the values adjusted by the procedure described under methods are presented. The adjustment did not appreciably affect the original values of fS-Tg, but did alter the fS-Chol values to some extent. The mean fS-Tg concentration in the older subsample was lower ($p > 0.05$) than that in the younger men. The mean fS-Chol concentrations of the two age groups did not differ significantly.

Glucose tolerance

The prevalence of known diabetes mellitus was 4.5 % among the total 331 60-year-old men (Table III) and at the health screening two further subjects with diabetes mellitus were detected. These two men had fB-glucose values of > 6.6 mmol/l. The prevalence of diabetes among the 50-year-old men was 0.9 % (19).

Table II. Mean values and standard deviations of S-triglycerides and S-cholesterol in 60-year-old men (60 yr, n = 67) and 50-year-old men (50 yr, n = 367).

Variable	$Q_1 - Q_5$ 60 yr	50 yr
Cholesterol (transformed)	-	6.52 ± 1.13
Cholesterol (non-transformed)	6.23 ± 1.18	6.03 ± 1.05
Triglycerides (transformed)	-	1.61 ± 1.08
Triglycerides (non-transformed)	1.51 ± 1.02	1.63 ± 1.09

The prevalence of reported heredity for diabetes mellitus is also shown in Table III. No significant differences were found between the two total populations with regard to the reported heredity for diabetes mellitus for sibs, parents and children. However, it was found that more subjects in both popula-

Table III. Comparisons of information obtained by interview and questionnaire between 50-year-old (n = 2,322) and 60-year-old men (n = 331).

Information	Subjects with positive replies: 50-year-old men, No of subjects	50-year-old men, Per cent	60-year-old men, No of subjects	60-year-old men, Per cent
Do you have diabetes ?	21	0.9 %	15	4.5 %
Does (Did) your father have diabetes ?	113	4.9 %	10	3.0 %
Does (Did) your mother have diabetes ?	203	8.7 %	31	9.4 %
Do (Did) any of your brother or sister have diabetes ?	84	3.6 %	16	4.8 %
Do (Did) your children have diabetes ?	16	0.7 %	5	1.5 %

tions reported diabetes in their mothers than in their fathers. This difference was significant ($p < 0.001$) for the older age group, but not for the younger men ($p > 0.05$).

When comparing the whole subsample the mean k-value of the younger men was higher ($p < 0.05$) than that of the older age group.

S-insulin

The mean fS-insulin did not differ significantly between the two age groups. The mean values in the younger men was 12.8 mU/l $\pm$ 7.5 (S.D.) and 12.9 $\pm$ 7.3 in the older men (see Table IV). The 50-year-old men had a significantly higher ($p < 0.05$) mean S-insulin ER than the 60-year-olds (Table IV).

Table IV. Mean values and standard deviations of serum insulin (mU/l) and K-values obtained at IVGTT in 60-year-old men (60 yr, n = 67) and 50-year-old men (50 yr, n = 367).

Variable	$Q_1 - Q_5$ 60 yr	50 yr
Basal insulin	12.9 $\pm$ 7.3	12.8 $\pm$ 7.5
Early response	55.4 $\pm$ 27.0*	64.6 $\pm$ 43.4
Insulin index	5.0 $\pm$ 2.8	5.6 $\pm$ 3.3
Late response	29.4 $\pm$ 18.4	28.7 $\pm$ 17.5
K-value	1.59 $\pm$ 0.48*	1.75 $\pm$ 1.50

*) $p < 0.05$ compared to 50-year-old men.

The mean insulin LR values in the two age groups did not differ. The mean serum insulin indices for the two age groups were not significantly different (Table IV).

In the 60-year-old men the k-values of IVGTT were significantly correlated to the ER values ($r = 0.49$, $p < 0.0005$) and to the serum insulin indices ($r = 0.35$, $p < 0.005$).

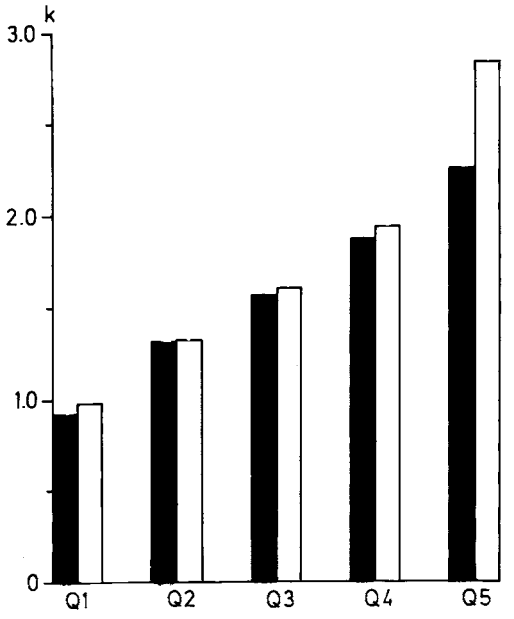

Fig. 1. Mean values for the k-values within the five quintiles (Q_1 - Q_5). Black bars represent 60-year-old men (n = 67) and white bars represent 50-year-old men (n = 367).

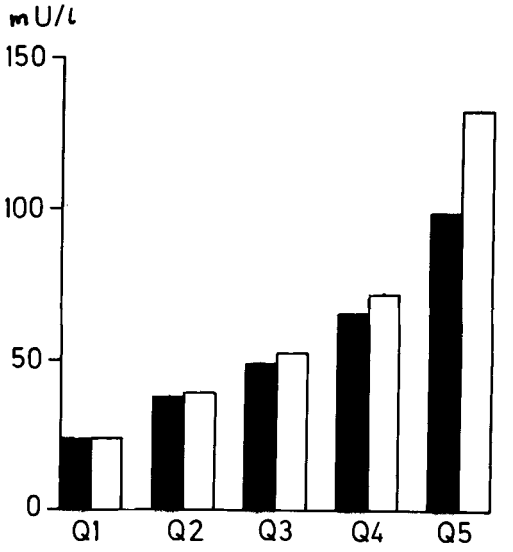

Fig. 2. Mean values of early serum insulin response (ER) within the five quintiles (Q_1 - Q_5). Black bars represent 60-year-old men (n = 67). White bars represent 50-year-old men (n = 367).

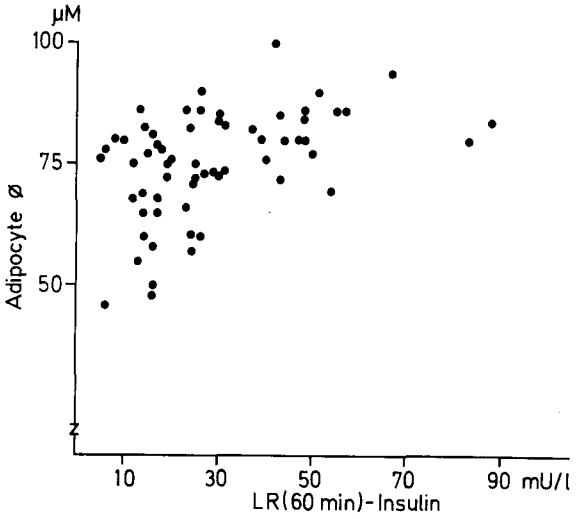

Fig. 3. Relation between adipose tissue fat cell diameter (µM) and serum insulin late response (60 min) (mU/l), in 60-year-old men (n = 67).

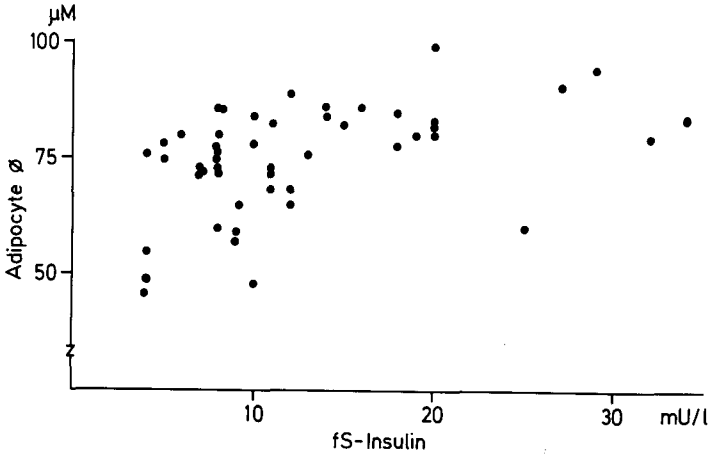

Fig. 4. Relation between adipose tissue fat cell diameter (µM) and fasting serum insulin (mU/l) in 60-year-old men.

Adipose tissue fat cell size and its relation to S-insulin

In the 60-year-old men the mean diameter of the adipocyte was 75.5 µM ± 11.1. The fat cell diameter was significantly correlated to S-insulin LR ($r = 0.45$, $p < 0.0005$) (Fig. 3) and to fS-insulin ($r = 0.39$, $p < 0.005$) (Fig. 4).

DISCUSSION

In this study comparisons were made with respect to B-glucose, S-lipids, S-insulin concentrations and intravenous glucose tolerance between two apparently healthy male groups 50 and 60 years of age. Thus, the groups studied were fairly large, the effect of disease and medication were excluded, laboratory and other investigatory routines were standardized, and body weight was taken into account.

Concerning S-lipid concentrations, most populations studied (2, 5, 16, 22, 26, 27), have shown that these values increased up to 50 years of age, after which they seem to be fairly constant. We found no appreciable differences in S-lipid concentration between the 50- and 60-year-old men studied.

Glucose tolerance has been claimed by many authors (9, 18, 29), to be generally impaired with age. Other investigators, however, consider that impaired glucose tolerance is only partially ascribable to age (13, 23). Dieterle (10) found that the glucose tolerance remained constant up to the age of 60 years in healthy subjects. Factors that might have a negative influence on glucose tolerance, are cardiovascular disease, intake of certain medicines and obesity. The latter factor was studied by Björntorp et al. (3), who found that the adipose tissue fat cell size correlated well with fasting S-insulin and with the S-insulin concentrations of glucose stimulation. In our study the k-values were significantly lower in the older than in the younger age group. This could partly be attributed to the higher body weights in the older group. The lower mean S-insulin ER value found in the older age group than in the younger men is an important factor when considering the deterioration of glucose tolerance with age. The mean fS-insulin and mean S-insulin LR concentrations did not differ between the two age groups, despite the higher relative body weight in the older men. This somewhat unexpected finding further supports the concept of diminished pancreatic beta cell function at glucose stimulation in aged subjects.

The results of studies on insulin secretion at glucose stimulation are conflicting. Thus Streeten et al. (32) and Chlouverakis et al. (7) found higher S-insulin concentrations in older subjects. According to these authors presumably due to the presence of insulin antagonists in aged persons. Duckworth et al. (11) reported increased serum concentrations of pro-insulin, possibly causing impaired glucose tolerance, in elderly subjects. Silverstone et al. (29) reported increased peripheral tissue resistance to insulin activity in elderly persons. These earlier findings might all be related to increased relative body weight in older people, which was a finding on the present study. Adlung et al. (1), however, denied the effects of insulin antagonists and peripheral tissue resistance to insulin, and ascribed the impaired glucose tolerance in elderly to defective pancreatic beta cell function, which support the present findings.

Thus, decreased glucose tolerance with age might be caused by both increased peripheral resistance to S-insulin, and to a defective release of insulin on glucose stimulation.

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