Obese Women and the Relation Between Cardiovascular Risk Profile and Hormone Therapy, Glucose Tolerance, and Psychosocial Conditions

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OBJECTIVE — To evaluate the relation between cardiovascular disease (CVD) risk factors and hormone therapy, serum hormone levels, glucose tolerance, and psychosocial and psychological conditions in subjectively healthy obese female subjects.

RESEARCH DESIGN AND METHODS — The study included 606 women, aged 50–64 years, with BMI 30–40 kg/m^2 and no history of cardiovascular or other severe diseases. One group with a CVD risk profile (n = 473) (i.e., cholesterol >7.0 mmol/l, HDL cholesterol <1.2 mmol/l, triglycerides >2.0 mmol/l, systolic or diastolic blood pressure >140/90 mmHg, or waist-to-hip ratio >0.85) was compared with women without such risk (n = 133). Steroid hormones, leptin, insulin, and oral glucose tolerance tests (OGTTs) were analyzed. A subgroup of women with baseline impaired glucose tolerance (IGT) completed a 2.5-year follow-up OGTT.

RESULTS — Fewer obese postmenopausal women with CVD risk had ever used hormone therapy (odds ratio 0.24 [95% CI 0.07–0.75]), after multivariate adjustments. Furthermore, women with CVD risk had a higher testosterone index (1.07 [1.01–1.13]) and more had insulin resistance (1.04 [1.00–1.08]) and IGT (2.92 [1.50–5.69]), while OGTT was similar at follow-up. No differences were observed regarding family history or lifestyle, except that fewer women with CVD risk consumed fruits, boiled vegetables, or whole-grain cereals. More women with CVD risk lived alone (3.26 [1.28–8.31]) and had more mental problems (1.16 [1.05–1.28]).

CONCLUSIONS — Previously healthy obese women with a CVD risk profile seemed to have a high risk of diabetes, as well as psychosocial or psychological problems. Hormone therapy was associated with reduced CVD risk. Obesity's growing burden on society makes it more important to further target individuals that are at greatest risk of future health hazards.

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Obesity, defined as BMI ≥30 kg/m^2, is affecting 30% of the U.S. population (1) and 15–20% of Scandinavian adults (2) and is becoming increasingly common in developing countries (3). The etiology involves metabolic, behavioral, and social factors (4). The genetic influence on the variability in BMI has been estimated to approximately one-third (5), but main contributors to the increasing prevalence of obesity are sedentary lifestyle and unhealthy dietary habits (3). Obesity adversely affects morbidity and life expectancy (6), mostly mediated by cardiovascular comorbidities such as hypertension, dyslipidemia, and diabetes, as well as by musculoskeletal disorders, cancer, and psychosocial and quality-of-life impairments (7,8). We have shown that obesity is associated with hypertension, type 2 diabetes, and declined psychosocial functioning in middle-aged and older women and that social isolation (i.e., living alone) increases the risk of diabetes development (9–12). The increase of cardiovascular disease (CVD) in perimenopausal women may also relate to the decrease in sex steroid hormones and redistribution of body fat from gluteo-femoral tissue to more android visceral adipose tissue (13). However, the effect of endogenous sex hormones and hormone therapy on central obesity and its complications remains unclear, and more studies with comprehensive data on women during this transition period are needed. Today, obesity is of serious economic concern, and the medical expenditures have reached dramatic proportions, having a major impact on health care resources (14). Many reasons exist to try to better identify, by a favorable selection procedure, those obese individuals who are at the highest risk of health hazards. This study of a large population of previously healthy obese women aged 50–64 years enables an evaluation of the relation between CVD risk factors and serum levels of sex hormones, insulin, and leptin, as well as oral glucose tolerance tests (OGTTs) and data on psychosocial and quality-of-life issues.

RESEARCH DESIGN AND METHODS

— A screening procedure was performed between 1995 and 2000 in 6,917 women aged 50–64 years, living in a defined area of Southern Sweden, and identified through a population register. Informed consent was obtained, and the ethics committee at Malmö/Lund approved the study.

A questionnaire was used regarding medical history; menopausal status (premenopausal, postmenopausal with or without hormone therapy); parity; pharmacological treatment; family history of diabetes or CVD; leisure-time exercise;

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Abbreviations: CVD, cardiovascular disease; HOMA-IR, homeostasis model assessment of insulin resistance; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance; SHBG, sex hormone–binding globulin; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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dietary, alcohol, and smoking habits; marital status; household; education; occupation; physical activity at work; and physical and mental health. A validated food questionnaire described types, frequencies, and estimations of amounts of various foods consumed per week during the last 3 months (15).

The baseline physical examination included body weight, height, BMI (weight in kilograms divided by the square of height in meters), minimal waist and maximal hip circumference expressed as waist-to-hip ratio (WHR), and the average of two blood pressure recordings in the seated position after a 15-min rest. Total and HDL cholesterol and triglycerides were measured on capillary whole blood (Cholestech LDX instrument; Cholestech, Hayward, CA). KRYPTOR-automated immunofluorescent hormonal assays of testosterone and estradiol were performed (B.R.A.H.M.S Ag., Hennigsdorf, Germany). Testosterone index was defined as testosterone/sex hormone–binding globulin (SHBG) × 100 and estradiol index as estradiol/SHBG × 100. These indices were used to consider free and protein-bound steroids (16). Assays of serum androstenedione, SHBG, cortisol, fasting insulin, and leptin were performed using the enzyme-linked immunosorbent assay technique (DRG, Marburg, Germany). Fasting insulin and leptin were randomly analyzed in every third women. Insulin resistance was expressed through the homeostasis assessment model of insulin resistance (HOMA-IR) (17). A fasting 75-g OGTT was performed on women with BMI ≥30 kg/m^2. Those with baseline impaired glucose tolerance (IGT) received lifestyle advice individually for 1 h regarding exercise, dietary, smoking, and alcohol habits and were invited to a new OGTT after 2.5 years. Women with isolated impaired fasting glucose or diabetes at baseline also received lifestyle advice but were not further examined.

In all, 944 women had obesity (i.e., BMI ≥30 kg/m^2), of whom 310 were excluded after adjustment for women with more than one criterion for exclusion such as previously known diabetes (n = 57), stroke (n = 10), myocardial infarction (n = 20), drug treatment of hypertension or other CVD (n = 248), drug treatment of dyslipidemia (n = 34), or other concurrent disease or handicap (n = 14). Another 28 women had severe obesity (BMI ≥40 kg/m^2) and were excluded since the vast majority (n = 27) belonged to the group with a CVD risk profile. Thus, 606 women remained and were included in the present analysis of subjects with BMI 30–40 kg/m^2 and without any previous severe medical history.

The CVD risk profile was defined according to international recommendations (18) regarding serum levels of total cholesterol, HDL cholesterol, triglycerides, blood pressure, and WHR (Table 1). The group with any such risk profile (CVD risk group) included 473 women and the group without risk profile (non-risk group) 133 women.

Table 1—*Number of women with BMI between 30 and 40 kg/m^2 according to risk profile*

	n
Nonfasting serum levels of total cholesterol >7.0 mmol/l (n = 106) or triglycerides >2.0 mmol/l (n = 254) or HDL cholesterol <1.2 mmol/l (n = 100)	328
Diastolic blood pressure >90 mmHg (n = 175) or systolic blood pressure >140 mmHg (n = 198)	103
WHR >0.85 (n = 217)	42
Without risk profile	133
Total	606

Numbers in parentheses refer to each subject that crossed the stated level.

Lifestyle, psychosocial conditions, and health-related quality of life

Self-reported dietary habits were based on four questions with three sublevels from healthy to unhealthy regarding fat, fibers, vegetables/fruits, and sweets/carbohydrates and on a food questionnaire that ensured the discrimination between a healthy and unhealthy diet. Healthy intake of fat meant low total consumption, especially of saturated fat, but relatively more vegetable oil, and healthy intake of fibers meant high total consumption of fibers, especially through whole-grain products. High total daily intake of fruits and vegetables defined healthy consumption, while a healthy pattern regarding sweets meant hardly ever using extra sugar and hardly ever eating sweets, cookies, or other bakeries. Women defined as having healthy dietary habits were those indicating a healthy pattern on at least three of four basic questions and with no indication of an unhealthy pattern. The subjects summarized leisure-time exercise during the last year into hardly any activity, <30 min/week, 30–60 min/week, >60–120 min/week, or >120 min/week of jogging and equivalent activities. Weekly consumption of wine, beer, and spirits was converted to grams alcohol. Smoking was categorized into never, past, or current smokers.

Occupational status implied having a full- or part-time occupation; being a housewife, retired, unemployed, or long-term sick listed; or having a disability pension. Subjects categorized their physical activity at work during the last year into low (sedentary), moderate (mostly walking but not lifting heavily), or high (high degree of walking and lifting). Education was categorized into comprehensive (9 years), upper secondary (12 years) school, or university degree. Marital status meant married, unmarried, divorced, or widowed. Households included women living with children, partner and children, partner or other adults only, or living alone.

Subjective well-being was measured by the validated Gothenburg Quality-of-Life instrument (19), which refers to the World Health Organization definition of health, and divides subject's perception of symptoms into mental, physical, and social well-being. Median sum score of estimations from 1 (very bad) to 7 (excellent) was calculated on 19 topics on quality of life. Also, 10 mental and 19 physical symptoms were answered with yes or no regarding whether the woman had been troubled by any symptoms during the last 3 months. The procedure has been previously described (9).

Statistics

Calculations were performed using SPSS 12.0. Values are given as means ± SD or median (interquartile range), depending on whether they showed normal or skewed distribution. Differences between groups regarding continuous variables with normal distribution were analyzed using the independent-samples t test, and the Mann-Whitney U test was applied for skewed distribution. The χ^2 test analyzed differences in categorical variables. Multivariate logistic regression analysis evaluated the risk of being associated with the CVD risk profile group. A simultaneous inclusion of all variables was performed in each model through a backward conditional procedure and with adjustment for age, BMI, parity, menopausal status, and sex hormones (androstendione, testosterone index, and estradiol). In Table 2 on

Table 2—*Descriptive anthropometric and laboratory characteristics and the multivariate-adjusted risk associated to the CVD risk profile group*

	CVD risk group	Nonrisk group	*P*	OR (95% CI)*	*P*
n	473	133			
Age (years)	57.0 ± 3.0	56.3 ± 2.7	0.017		
BMI current (kg/m^2)	32.8 ± 2.3	31.9 ± 2.0	<0.001		
BMI at 25 years of age (kg/m^2)	23.3 ± 2.9	23.3 ± 2.9	0.92		
Weight gain (>5 kg/5 years)	67	64	0.47		
Menopausal status					
Premenopausal	7	4	0.007	1.0	
Postmenopausal without hormone therapy	66	55		0.33 (0.10–1.10)	0.071
Postmenopausal with hormone therapy	27 (22% current)	41 (35% current)		0.24 (0.07–0.75)	0.014
Serum androstendione (nmol/l)	3.69 (2.91)	4.34 (2.77)	0.018	0.92 (0.85–1.00)	0.052
Serum SHBG (nmol/l)	38.5 (27.1)	50.0 (32.4)	<0.001		
Serum testosterone (nmol/l)	2.20 (1.76)	2.10 (2.13)	0.44		
Serum testosterone index	4.70 (6.23)	4.06 (4.47)	0.004	1.07 (1.01–1.13)	0.023
Serum estradiol (pmol/l)	22.7 (53.2)	30.7 (88.2)	0.006	1.00 (0.99–1.00)	0.54
Serum estradiol index	65.5 (125.1)	70.2 (184.1)	0.24		
Serum cortisol (nmol/l)	222.0 (124.4)	211.3 (109.4)	0.70		
Serum leptin (ng/ml) (*n* = 181)†	17.2 (10.6)	17.7 (10.1)	0.92		
Serum insulin (pmol/l) (*n* = 181)†	90.1 (75.6)	68.0 (49.4)	0.027	1.01 (1.00–1.01)	0.20
Serum HOMA-IR (fasting glucose × fasting insulin/22.5) (*n* = 181)†	19.8 (19.6)	14.7 (10.0)	0.010	1.04 (1.00–1.08)	0.042
OGTT at baseline (*n* = 532)					
Normal	57	68	0.055 (0.048)‡	1.0	
Isolated impaired fasting glucose	5	8		0.81 (0.31–2.11)	0.66
IGT	28	16		2.92 (1.50–5.69)	0.002
Diabetes	9	8		1.31 (0.65–2.64)	0.45
OGTT after 2.5 years (*n* = 126; baseline IGT)					
Normal	38	35	0.96		
Isolated impaired fasting glucose	1	0			
IGT	45	47			
Diabetes	16	18			

Data are means ± SD, percentage, or median (interquartile range). *Four models of logistic regression analysis were performed because of differences in numbers of subjects. Menopausal status and sex hormones (*n* = 606) were simultaneously included in one model, with adjustment for age, BMI, and parity. Data on insulin and HOMA-IR (*n* = 161) are presented from two separate models with adjustment for all other variables in the table. Data on OGTT (*n* = 532) are presented from a model including adjustment for all other variables except insulin or HOMA-IR. †Fasting serum leptin, insulin, and HOMA-IR were analyzed on a random sample of every third participant. ‡*P* = 0.048 when normal glucose tolerance was analyzed vs. glucose intolerance (I-IFG + IGT + diabetes).

laboratory data, results from four models of multivariate-adjusted analyses are presented because of differences in numbers of subjects with missing information on some variables. In the first model, on all 606 women, menopausal status and sex hormones were simultaneously analyzed, with adjustment for age, BMI, and parity. Data on insulin and HOMA-IR are presented from two separate models on 161 women, with adjustment for all other variables presented in Table 2. In the fourth model, on 532 women, data on OGTT are presented after adjustment for all other variables except insulin and HOMA-IR. Odds ratios (ORs) with 95% CIs were used to express risk estimation. The fit of the models was analyzed by Hosmer-Lemeshow goodness-of-fit statistics and statistics for the overall models by Nagelkerke R^2. *P* values <0.05 were considered statistically significant.

RESULTS

Anthropometric and biochemical characteristics

The means ± SD values in the CVD risk and nonrisk groups, respectively, were 6.23 ± 1.12 and 5.64 ± 0.75 mmol/l for total cholesterol, 1.52 ± 0.40 and 1.75 ± 0.36 mmol/l for HDL cholesterol, 2.29 ± 1.15 and 1.35 ± 0.39 mmol/l for triglycerides, 0.85 ± 0.07 and 0.79 ± 0.04 for WHR, and 90 ± 9 and 84 ± 6 mmHg for diastolic and 139 ± 17 and 126 ± 9 mmHg for systolic blood pressure (*P* < 0.001 for all).

The CVD risk group was older (*P* = 0.017) and had higher BMI (*P* < 0.001), but no differences were seen in self-reported BMI at 25 years of age or weight gain over the last 5 years (Table 2). Only eight women were obese at 25 years of age, and 68 vs. 59% (*P* = 0.055) were obese 5 years before the study. Fewer women in the CVD risk group had ever used hormone therapy (*P* = 0.007), and they had lower serum levels of androstendione (*P* = 0.018), SHBG (*P* < 0.001), and estradiol (*P* = 0.006), while the testosterone index was higher (*P* = 0.004). Corresponding differences in these hormones were seen when only women who had never used hormone therapy were studied, while no differences were seen among women who currently used hor-

mone therapy (data not shown). There was no difference in parity ($P = 0.71$).

A random subsample of 181 women was examined regarding serum insulin and HOMA-IR, which were higher in the CVD risk group ($P = 0.027$ and $P < 0.01$), while no difference was found in serum leptin (Table 2). In all, 532 women performed a baseline OGTT and more women with CVD risk had glucose intolerance ($P = 0.048$), while no difference was seen at the OGTT after 2.5 years. From the group of 153 women with IGT at baseline, 126 participated in the follow-up examination. No in-between examinations were performed. No differences were seen in other baseline biological data between the 126 participants and 27 nonparticipants or between the random group of 181 women from whom serum hormones were analyzed and the 425 remaining women.

Multivariate logistic regression analysis showed that ever use of hormone therapy was negatively associated with CVD risk (OR 0.24 [95% CI 0.07–0.75]), while testosterone index was positively associated (1.07 [1.01–1.13]). Current hormone therapy showed similar reduced risk (0.16 [0.04–0.60]; $P = 0.006$). Androstendione had a tendency for a negative association ($P = 0.052$), while HOMA-IR (1.04 [1.00–1.08]) and IGT (2.92 [1.50–5.69]) were positively associated with CVD risk. Hosmer-Lemeshow tests ranged from 0.351 to 0.873 and Nagelkerke R^2 from 0.098 to 0.251.

Family history and lifestyle

There were no differences in numbers of relatives who had diabetes, hypertension, or previous stroke or myocardial infarction ($P = 0.30–0.97$) (data not shown). Neither were there any differences between the CVD risk and nonrisk groups in leisure-time exercise ($P = 0.88$) or dietary habits ($P = 0.58$). Two-thirds of both groups never exercised or exercised <1 h per week, and four of five in each group were considered to have unhealthy dietary habits regarding intake of saturated fat ($P = 0.65$ between the two groups), carbohydrates ($P = 0.97$), fibers ($P = 0.45$), and vegetables and fruits ($P = 0.056$). However, the CVD risk group consumed less boiled vegetables ($P = 0.038$), fruits ($P = 0.001$), and wholegrain cereals ($P = 0.001$). The alcohol consumption was similar; about one-third of the women were abstainers in each group ($P = 0.39$). The smoking habits were likewise similar, with 65 and 63%, respectively, who never smoked and 14% in both groups who were current smokers ($P = 0.90$). The number of cigarettes per day was similar for current ($P = 0.28$) and past ($P = 0.18$) smokers. There was no difference in time since the latter had stopped smoking. Fully 70% of all past smokers had stopped >5 years before the examination. None of the variables on family history or lifestyle was associated with CVD risk after simultaneous inclusion in a multivariate regression analysis and with adjustment for age, BMI, parity, menopausal status, and sex hormones.

Occupation, psychosocial conditions, and quality of life

There were no differences in working hours ($P = 0.39$), physical activity at work ($P = 0.91$), or marital status ($P = 0.16$) (data not shown). More women in the CVD risk group lived alone and fewer with a partner only ($P = 0.004$), and they had more subjective mental symptoms ($P = 0.005$), particularly general fatigue, difficulty to relax, nervousness, and depression ($P = 0.004–0.049$) (Table 3). Women in the CVD risk group also had more physical symptoms ($P = 0.024$), especially breathlessness ($P = 0.031$) and joint pain ($P = 0.038$). The CVD risk group had lower mental well-being regarding the mood "energy" ($P = 0.027$) and lower physical well-being, i.e., "healthiness" ($P = 0.012$), while no difference was seen in social well-being. Multivariate regression analysis showed that living alone (OR 3.26 [1.28–8.31]) and subjective mental symptoms (1.16 [1.05–1.28]) were positively associated with CVD risk, after adjustment for age, BMI, parity, menopausal status, and sex hormones. The menopausal status variable, when used as adjusting factor, showed that hormone therapy was still associated with a persistent reduced risk throughout this model of analysis (0.19 [0.06–0.63]; $P = 0.007$). The Hosmer-Lemeshow test was 0.577 and Nagelkerke $R^2 = 0.168$.

CONCLUSIONS — Among previously healthy obese women, those with CVD risk profile regarding hypertension, dyslipidemia, or high index of abdominal fat content (WHR) also had higher risk of insulin resistance, glucose intolerance, and signs of psychosocial and mental disparities. Hormone treatment seemed to act protectively.

The economic burden of obesity on society relates to direct costs from increased morbidity and indirect costs by lost productivity, but economic calculations are quite uncertain (14) and less important than discussing solutions to the problem. Besides primary preventive efforts aiming at lifestyle changes, such as increased physical activity (20), one step would be to identify subjects who carry considerable risks of medical disorders. In this study, we used validated international guidelines (18) to ascertain that only women with values above threshold levels for high-risk markers of CVD were included and minimize the chance of arbitrary selection. However, we chose total cholesterol >7.0 mmol/l and not >5.0 mmol/l (18), since 86% of the population would have been included for the latter reason only. The inclusion of WHR added indexes of android body fat composition, which have been closely related to cardiovascular events (13). Women with severe obesity, who are at greatest risk of CVD, type 2 diabetes, and impaired quality of life, were excluded. Nearly all of these women had a CVD risk profile. By using BMI between 30 and 40 kg/m^2, we were able to study two BMI-equivalent groups and focus on the morbidity among the vast majority of today's obese population. The BMI was much lower at 25 years of age, but no difference was seen between the two groups at that time, showing that obesity in both groups was acquired later in life and not indicating any obvious discrepancy in hereditary background. This was supported by the fact that no differences were seen in cardiovascular events or diabetes among relatives. Moreover, there was no difference in weight gain over the last 5 years that explained the dissimilarities. Thus, CVD risk itself seemed to be explanatory factors for the other associated risk factors.

Most women in this study were postmenopausal, and those with current or previous hormone therapy were at a lower risk of having a CVD risk profile. However, our primary aim was not to study obese women with hormone therapy; therefore, the results cannot comprehensively describe the association between hormone therapy and different risk factors. A recent study (21) found the relation between time of hormone therapy initiation and menopause onset or age to be of importance. Women who started hormone therapy in close relation to menopause had a reduced risk of coronary heart disease. In another study (22),

Table 3—*Descriptive social and psychosocial conditions, physical and mental symptoms and health-related quality of life, and the multivariate-adjusted risk associated to the CVD risk profile group*

	CVD risk group	Nonrisk group	*P*	OR (95% CI)*	*P*
n	473	133			
Educational level					
≤9 years	32	30	0.083	1.0	
≤12 years	35	45		0.84 (0.48–1.46)	0.54
University degree	33	25		1.76 (0.92–3.34)	0.086
Household status					
With children	3	4	0.004	1.0	
Partner and children	12	14			
Partner, without children	62	74		0.99 (0.52–1.88)	0.97
Alone	23	8		3.26 (1.28–8.31)	0.013
Subjective mental symptoms					
Median sum of "yes" (maximum 10)	4.0 (4.0)	3.0 (5.0)	0.005†	1.16 (1.05–1.28)	0.004
General fatigue	63	50	0.007		
Difficulty to relax	43	34	0.049		
Nervousness	19	10	0.025		
Depression	56	42	0.004		
Subjective physical symptoms					
Median sum of "yes" (maximum 19)	5.0 (4.0)	4.0 (4.5)	0.024†	1.05 (0.96–1.14)	0.34
Breathlessness	40	29	0.031		
Joint pain	55	44	0.038		
Mental well-being					
Total median (1–7, 7 = excellent)	5.4 (1.4)	5.6 (1.6)	0.07‡	0.94 (0.62–1.43)	0.77
Energy	5.0 (2.0)	5.0 (1.0)	0.027		
Physical well-being					
Total median (1–7, 7 = excellent)	5.0 (1.4)	5.2 (1.4)	0.09‡	1.07 (0.76–1.53)	0.70
Subjective healthiness	5.0 (2.0)	6.0 (1.0)	0.012		
Fitness	4.0 (2.0)	4.0 (2.0)	0.072		
Social well-being					
Total median (1–7, 7 = excellent)	5.8 (1.4)	5.8 (1.3)	0.19‡	1.30 (0.97–1.73)	0.082
Family/housing	6.0 (2.0)	7.0 (1.0)	0.051		
Relation to partner	6.0 (2.0)	7.0 (2.0)	0.097		

Data are percentage or median (interquartile range). *One model of multiple logistic regression analysis was performed with simultaneous inclusion of all variables and with adjustment for age, BMI, parity, menopausal status, and sex hormone levels. †The 10 mental and 19 physical symptoms, except nausea and loss of weight, had a tendency for higher values in subjects with CVD risk, but only those that reached significance level are stated. ‡All 19 quality-of-life variables had a tendency for lower values in subject with CVD risk profile, but only those with significance or near-significance levels are stated.

estrogen substitution provided no overall protection against coronary heart disease or death in older postmenopausal women, while the risk seemed lower in women who had hormone therapy and were 50–59 years of age at baseline, which was similar to the age interval of the present study.

The effects of sex hormones on adipose tissue distribution are complex and partly unclear (23). Estrogen is higher and SHBG lower in obese postmenopausal women. SHBG is likewise lower in subjects with type 2 diabetes. Hormone therapy may have a positive influence on lipids and minimize the shift to central obesity and has been shown to increase SHBG and reduce levels of free testosterone. This is in line with the present results in the nonrisk group, in which more had hormone therapy and SHBG was higher and testosterone index lower. Most testosterone is bound to SHBG, and only a small percentage is free and biologically active. Testosterone binds to receptors in several organs (e.g., cardiovascular and muscle tissue) and may increase muscle mass but has possibly a negative effect on glucose metabolism (24). We adjusted serum values of sex hormones to perimenopausal status and hormone therapy, but similar findings were also encountered in women who never used hormone therapy, which verified an independent relation between sex hormones and CVD risk. Insulin and HOMA-IR are known to be high in obese women, but we found even higher levels among women with CVD risk profile, indicating that other factors involved in the metabolic syndrome contribute to insulin resistance. OGTT was performed in the majority of women at baseline, but only those with IGT were followed-up after 2.5 years. This is a limitation since the true value for diabetes development remains unknown, as we had no information regarding the incidence among women with normal glucose tolerance at baseline. Women's lifestyle seemed to be of less importance for the discrepancies between the two groups. However, physical exercise was low and dietary habits quite unhealthy in both groups. Relatively few smoked, which could be pivotal since smoking/nicotine increases insulin resistance and may possibly also moderate weight gain.

The household status of living alone seemed to be a social trait that increased the associated risk for CVD risk factor

profile. However, the interpretation is hardly that obese women living with a family are without risk compared with the general population. We have previously shown that women living alone had an increased risk to develop type 2 diabetes, and this was explained mainly by differences in lifestyle (12). There was conformity in the tendency of differences in subjective symptoms and quality-of-life variables, with a higher degree of impairments in the CVD risk group. Most abundant were the more frequent mental symptoms in this group. Health-related mental and physical quality of life was also poorer in the CVD risk group but did not remain independent as risk factors in the multivariate analysis. In contrast, other reports have described that the presence and severity of obesity mostly relate to decrements on physical functioning (7,8,25). To our knowledge, there has been no study of previously healthy obese subjects showing that impairments in mental or physical subjective health relate to CVD risk factors like dyslipidemia, hypertension, or android adiposity.

In summary, this study identified a major group of previously healthy obese women with CVD risk profile that also had high risk of diabetes and psychosocial or psychological disparities and, furthermore, another group of women that was subjectively, as well as objectively, quite healthy despite obesity. The overall objective for society must be to prevent obesity, but it may be of importance to separate those with an increased CVD risk profile from those without in order to take further preventive, or sometimes medical, interventional actions.

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