Abdominal Obesity and Breast Cancer Risk

David V. Schapira, MBChB; Nagi B. Kumar, RD, MA; Gary H. Lyman, MD, MPH; and Charles E. Cox, MD

Study Objective: To determine if body fat distribution affects breast cancer risk.

Design: Prospective case-control study.

Patients: The anthropometric measurements of 216 consecutively and newly diagnosed women with invasive carcinoma of the breast were compared with those of 432 age-matched controls. The anthropometric measurements taken were abdomen, thigh, suprailiac, biceps, triceps, subscapular, and midaxillary skinfolds; waist and hip circumference; and weight and height. Women between 25 and 83 years of age were included in the study.

Results: Patients with breast cancer had a significantly greater waist:hip circumference ratio than controls ($P < 0.001$) and a significantly greater suprailiac: thigh skinfold ratio ($P < 0.001$). The relative risk for breast cancer increased with increasing waist:hip circumference ratio ($< 0.73 = 1.00$; 0.73 to $76 = 1.90$; 0.77 to $0.80 = 2.83$; $> 0.80 = 6.46$) and with suprailiac:thigh skinfold ratio ($< 0.42 = 1.00$; 0.42 to $0.56 = 1.85$; 0.57 to $0.71 = 2.25$; $> 0.71 = 5.85$). At other sites of upper body obesity, such as the biceps and triceps, skinfolds were significantly greater in patients with breast cancer.

Conclusion: Although obese women are at slightly higher risk for developing breast cancer, women with android obesity are a segment of obese women who appear to be at a significantly higher risk for developing breast cancer.

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From H. Lee Moffitt Cancer Center and Research Institute and University of South Florida College of Medicine, Tampa, Florida. For current author addresses, see end of text.

Obesity has been correlated with the incidence of breast cancer (1-4). It has been suggested that the excess estrogen produced by obese women increases the promotional effect on mammary epithelial cells (5-7). It is now recognized that the non-protein-bound fraction of estrogen available to act on the breast is important in the promotion of breast cancer (8-11). The amount of non-protein-bound estrogen is inversely proportional to the level of sex hormone binding globulin. Patients with breast cancer have been noted to have decreased levels of sex hormone binding globulin (9, 12, 13).

Women may gain weight in areas of the upper body such as the abdomen, shoulders, and nape of the neck (android obesity) or in areas of the lower body such as the buttocks and thighs (gynoid obesity). The metabolic and hormonal abnormalities noted in obesity are more pronounced in persons with upper body fat predominance (14-23). Women with android obesity have been noted to have longer menstrual cycles and an increased incidence of hirsutism, gallbladder disease, hypertension, and diabetes than women of the same weight with a gynoid obesity (23). Women with android obesity have also been noted to have lower levels of sex hormone binding globulin and higher levels of free testosterone than women with gynoid obesity and nonobese controls (21). These hormonal abnormalities were reversed after weight loss (24). The decreased levels of sex hormone binding globulin and increased levels of non-protein-bound estrogen in women with android obesity may increase their risk for cancer. We studied whether women with breast cancer differ in body fat topography when compared with age-matched controls.

Subjects and Methods

Two hundred and sixteen consecutive, newly diagnosed women with invasive carcinoma of the breast were recruited between August 1987 and June 1988. These women were diagnosed at the H. Lee Moffitt Cancer Center at the University of South Florida. Women of all races and between 25 and 83 years of age were included in the study.

All the patients with breast cancer had been diagnosed within 3 months of entry into the study and had not been treated with adjuvant hormonal or chemotherapy. Women whose weight had deviated by more than 1.3 kg after breast surgery were excluded from the study. Other criteria for exclusion of patients and controls were pregnancy, having engaged in a dietary or therapeutic regimen for weight reduction during the year preceding the study, having reported a weight loss of over 10% of usual weight, having engaged in a cholesterol-lowering therapeutic regimen, or having a medical condition that limited or prevented the researchers from obtaining anthropometric or other measurements. Of 240 patients found eligible for the study, 216 were recruited, and 24 (10.0%) were eliminated for meeting one or more of the above criteria for exclusion.

Six of the 24 excluded subjects were eliminated from the study because of a decrease in weight of over 1.3 kg. Eleven of the subjects were eliminated because of a reported loss of over 10% of their body weight in the 3 months preceding the study, and seven were eliminated because their existing medical condition limited or prevented the researchers from obtaining anthropometric measurements. Pre-operative and postoperative weights were obtained using a Scaletronics electronic scale (Scaletronix Scale, Wheaton, Illinois).

The control population, from the Tampa Bay area, was selected from a population register of subjects recruited for various studies at the research center. The population register consisted of a random sample of 2305 healthy adults from various settings. Ten businesses were randomly selected from a list of 148 in the metropolitan area. A questionnaire including requests for demographic information was administered to all employees in these businesses with the approval of their human resources departments. Of six major retirement communities in the area, two were administered the questionnaire. Criteria for exclusion were the same as those established for the patients. The questionnaire included age, gender, height, weight, and chronic illness information.

From the eligible control population, two controls closest in age to the respective patients with breast cancer (matched to each case by year of birth) were selected from the population register. A third control was selected (control alternative) in case one of the first two controls refused to participate or met one or more of the criteria for exclusion. Of 444 eligible primary controls, 5.9% were replaced by the control alternative. Eligible participants were recruited and interviewed. Data were collected using a questionnaire that included questions on basic demographic and lifestyle data, family and medical history, and reproductive and menstrual history. The demographic characteristics of the patients with breast cancer and controls are outlined in Table 1.

Table 1. *Demographic Data for Patients with Breast Cancer and Controls*

Variable	Controls ($n = 432$)	Breast Cancer Patients ($n = 216$)
	%	
Years of Age		
< 30	1	1
30 to 40	14	14
41 to 50	24	23
51 to 60	19	20
61 to 70	25	25
71 to 80	15	15
> 80	2	2
Postmenopausal	77.8	82.4
Premenopausal	22.2	17.6
Race		
White	84.7	91.2
Black	9.0	3.7
Hispanic	5.8	3.2
Asian Pacific	0.6	1.9
Number of children		
0	20.0	20.0
1 to 3	61.4	62.8
4+	18.6	17.2
Education		
High school	56.4	55.9
College	34.3	32.4
Graduate school	9.3	11.7
Family history of breast cancer		
Present	23.0	38.0
Absent	77.0	62.0

Anthropometric Measurement

Height was measured without footwear, with feet together and heels and back against a vertical board with a steel tape attachment. Subjects were weighed in hospital gowns with no footwear, using a Scaletronics electronic scale, and weight was determined to the nearest tenth of a kilogram. The biceps, triceps, midaxillary, suprailiac, subscapular, abdomen, and thigh skinfolds were measured to the nearest 0.5 mm using a Lange skinfold caliper (Cambridge Scientific Industries, Cambridge, Maryland), with a pressure at 10 g/mm^2 of contact surface area, as recommended by the Committee on Food and Nutrition Board of the National Research Council (25). All skinfold measurements were obtained on the right side of the body, except when patients had had reconstructive surgery in the area of measurement. The location and procedures for measuring the anthropometric sites were determined as described by Behnke and Wilmore (26). The suprailiac skinfold measurements were determined according to recommendations of Jackson and Pollock (27, 28). The Durnin-Womersley equation (29) for determining total body fat using the sum of the four skinfolds (biceps, triceps, subscapular, and suprailiac) was used. Hip circumference was measured in the horizontal plane using the largest circumference around the buttocks when the subject was standing with feet together. Waist circumference was measured in the horizontal plane at the level of the umbilicus. To reduce intertester errors, all skinfold and circumference measures were taken by a single examiner, and sites for measurements were standardized.

A practice phase established reliability for both the skinfold and circumference measurements. One hundred and twenty-five subjects were tested; the examiner took three measurements per site at the established sites. Test-retest reliability was established by testing 26 subjects in the established skinfold and circumference sites before using measurements for research. The test-retest reliability for skinfold measurements ranged from 0.93889 to 0.98704 and for circumference measures, from 0.99324 to 0.99862. To reduce experimenter bias, different skinfold sites were measured in succession. The cycle was repeated at least twice and the average of the scores at each site was used as the final skinfold score (30).

Table 2. *Anthropometric Values for Patients with Breast Cancer and Controls*

Anthropometric Measurements	Means: Patients ($n = 216$)	Means: Controls ($n = 432$)	Difference in Means	Standard Error of Difference	95% CI for Difference	*P* Value
Waist circumference, *cm*	32.56	30.06	2.50	0.425	1.55 to 3.45	< 0.001
Hip circumference, *cm*	39.73	39.06	0.67	0.367	−0.15 to 1.49	NS*
Waist:hip ratio	0.82	0.77	0.05	0.014	0.02 to 0.08	< 0.001
Abdomen skinfold, *mm*	42.73	39.57	3.16	1.204	0.48 to 5.84	< 0.01
Thigh skinfold, *mm*	39.02	41.01	−1.99	1.026	−4.28 to 0.30	NS
Abdomen:thigh ratio	1.17	0.96	0.21	0.045	0.11 to 0.31	< 0.001
Suprailiac skinfold, *mm*	27.45	22.45	5.00	0.967	2.84 to 7.16	< 0.001
Biceps skinfold, *mm*	19.36	17.13	2.23	0.940	0.14 to 4.32	< 0.02
Triceps skinfold, *mm*	26.89	25.46	1.43	0.774	−0.29 to 3.15	NS
Subscapular skinfold, *mm*	24.27	21.69	2.58	0.897	0.58 to 4.58	< 0.02
Midaxillary skinfold, *mm*	24.58	22.76	1.72	0.863	−0.10 to 3.74	NS
Fat, %	40.16	38.72	1.44	0.488	0.35 to 2.53	< 0.02
Weight, *kg*	150.82	143.76	7.06	2.477	1.54 to 12.58	< 0.02
Height, *cm*	63.93	64.03	−0.10	0.200	−0.55 to 0.35	NS
Weight, (kg)/height^2(m)	25.90	24.63	1.27	0.379	0.42 to 2.12	< 0.001

* NS = not significant.

Statistical Considerations

The distribution of body measurements and derived ratios were studied in both patients and controls. The means of measured variables were compared using the Student *t*-test. Categorical variables were compared for patients and controls using the chi-square technique. Two-tailed tests of statistical significance were used throughout.

The relation between clinical variables, including body measurements and the risk for breast cancer was evaluated by logistic regression analysis (31). Modeling was done using a backward stepwise technique. Regression coefficient estimates were calculated by the method of maximum likelihood. The significance of individual covariates was assessed with the likelihood-ratio test (32).

The relative risk for breast cancer, comparing different levels of specified variables, was estimated by the odds ratio; this ratio is defined as the product of the number of cases in the high-risk group and the number of controls in the low-risk group divided by the product of the number of cases in the low-risk group and the number of the controls in the high-risk group. A relative risk of 1.0 represents the risk expected if the factor has no effect on risk. Confidence limits on odds ratio estimates were calculated using the method of Woolf (33).

Results

Factors associated with preferential abdominal and upper body fat distribution were noted more frequently in patients with breast cancer compared with controls (Table 2). The waist:hip circumference ratio was significantly greater ($P < 0.001$) in patients (mean $\pm$ SE, 0.82 ± 0.01) compared with controls (0.77 ± 0.01). The abdomen:thigh skinfold ratio was also significantly greater ($P < 0.001$) in patients (1.17 mm $\pm$ 0.04) compared with controls (0.96 mm $\pm$ 0.02). The suprailiac skinfold, a measurement of abdominal obesity, was greater ($P < 0.001$) in patients (27.45 mm $\pm$ 0.84) than in controls (22.45 mm $\pm$ 0.48). Other measurements of upper body fat distribution were significantly greater in patients compared with controls:biceps skinfold (19.36 mm $\pm$ 0.88 compared with 17.13 mm $\pm$ 0.33; $P < 0.02$). Patients with breast cancer tended to be heavier (mean weight, 68.5 kg compared with 65.4 kg; $P < 0.02$) and had a higher percentage of body fat (mean fat percentage, 40.2% compared with 38.7%; $P < 0.02$) than controls. Height did not differ significantly between the groups.

Nonanthropometric measurements that differed significantly between patients with breast cancer and controls included race ($P < 0.01$), a family history of breast cancer ($P < 0.001$), a history of another cancer ($P < 0.05$), a history of diabetes mellitus ($P < 0.05$), and previous fibrocystic disease ($P < 0.001$). These nonanthropometric measurements were included in subsequent multivariate modeling to assess for possible confounding. Other measures that did not differ significantly included age, educational level, contraceptive use, menopausal status, smoking history, and parity.

Starting with all of the factors included in Table 2, multivariate analysis (Table 3) was done using logistic regression modeling in a backward stepwise fashion. The resulting risk model is summarized in Table 4. Factors associated with predominant upper body fat deposition were significant as predictors of breast cancer. These factors were greater waist circumference, triceps, and suprailiac skinfolds and relatively smaller hip circumference and thigh skinfold. A family history of breast cancer was commoner among patients with breast cancer ($P < 0.001$).

The odds ratio for breast cancer related to abdominal obesity is shown in Table 3. The odds ratio for breast cancer rose progressively as the waist:hip circumference increased. As shown in Table 3, adjustment of the odds ratio based on consideration of the other variables in the multivariate model did not meaningfully alter the unadjusted odds ratios. At a waist:hip circumference ratio of greater than 0.80, the relative risk for breast cancer was 6.46 (95% CI, 3.76 to 11.10). The relative risk for breast cancer also increased progressively as the suprailiac:thigh skinfold increased. At a ratio of greater than 0.71, the relative risk for breast cancer was 5.83 (95% CI, 3.51 to 9.74). The risk for breast cancer also increased with increasing weight (Table 3), although the risk was not as high as that noted with upper body fat localization. At a weight of greater than 74 kg, the relative risk for breast cancer was 2.09 (95% CI, 1.30 to 3.35). When obesity was considered with other anthropometric measurements, it was not found to be a risk factor for breast cancer. The relative risk decreased to 1.12 (95% CI, 0.69 to 1.80).

Discussion

Our study showed that obesity is a risk factor for breast cancer. We found a segment of women who had

Table 3. *Significant Factors in Multivariate Analysis**

Covariate	Coefficient Estimates and Significance Tests			
	Coefficient	SD	Test Statistic	*P* Value
Intercept	1.05451	1.22059	0.864	0.3876
Family history of breast cancer	0.94691	0.21219	4.463	< 0.0001
Waist circumference	0.23782	0.04340	5.480	< 0.0001
Hip circumference	− 0.19840	0.05141	− 3.986	0.0001
Triceps skinfold	0.06263	0.01767	3.545	0.0004
Midaxillary skinfold	− 0.06196	0.01800	− 3.443	0.0006
Suprailiac skinfold	0.08071	0.01561	5.170	< 0.0001
Thigh skinfold	− 0.07379	0.01313	− 5.621	< 0.0001

* Additional variables available for entry in multivariate model: abdomen, age, triceps skinfold, diabetes, menopausal status, race, smoking history, subscapular skinfold, fibrocystic disease, height, percentage fat, Quetelet index, and weight.

Table 4. *Obesity and Fat Distribution and Relative Risk for Breast Cancer**

Variable	Controls, *n*	Patients, *n*	Unadjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Waist:hip circumference ratio						
< 0.73	120	21	1.00	NA†	1.00	NA
0.73 to 0.76	125	42	1.90	1.06 to 3.40	1.73	1.41 to 2.13
0.77 to 0.80	94	47	2.83	1.58 to 5.06	3.01	1.99 to 4.53
> 0.81	93	106	6.46	3.76 to 11.10	5.21	2.81 to 9.65
Suprailiac:thigh skinfold ratio						
< 0.42	133	27	1.00	NA	1.00	NA
0.42 to 0.56	125	48	1.85	1.09 to 3.15	1.74	1.56 to 1.93
0.57 to 0.71	94	45	2.25	1.30 to 3.89	3.02	2.45 to 3.73
> 0.71	80	96	5.85	3.51 to 9.74	5.26	3.83 to 7.21
Weight (kg)						
< 56	132	43	1.00	NA	1.00	NA
57 to 64	92	49	1.60	0.98 to 2.61	1.04	0.89 to 1.22
65 to 73	117	62	1.60	1.01 to 2.54	1.08	0.78 to 1.48
74 +	91	62	2.09	1.30 to 3.35	1.12	0.69 to 1.80

* This data represents an unmatched analysis between a single factor and breast cancer risk.
† NA = not available.

predominantly upper body obesity to be at significantly greater risk for breast cancer. Some investigators (1-4) have correlated obesity with an increased incidence of breast cancer. The hormonal perturbations that accompany android obesity (21) and that have also been noted in patients with breast cancer (9, 12, 13) may explain the even greater risk for breast cancer that android obesity confers.

Most men gain weight on the upper parts of the body such as the abdomen, shoulders, and nape of the neck (android obesity). Women may gain weight on parts of the upper body (android obesity) or on parts of the lower body, such as the buttocks and thighs (gynoid obesity). The metabolic and hormonal abnormalities noted in obese persons are more pronounced in persons with upper body fat predominance (14-23).

Obese postmenopausal women have been found to have depressed levels of sex hormone binding globulin (34-39). However, increasing upper body fat localization in women has been shown to depress levels of sex hormone binding globulin progressively and to increase levels of circulating free testosterone progressively (21). These relations were seen over a wide range of weights, from nonobese to more than double ideal body weight. The degree of obesity correlated with a reduction of sex hormone binding globulin and an increase in free testosterone, but the effect of upper body fat localization was independent of obesity. When combined, the two factors were additive.

The search among patients with breast cancer for hormonal abnormalities that may indicate possible etiologic factors has been frustrating. Although estrogens have been implicated in breast cancer (40-42), no differences have been noted among patients with breast cancer when compared with controls in cross-sectional studies (43).

Recently, the importance of unbound estrogen that is available to act on the breast has been recognized (8-11). The unbound fraction of estrogen is considered to be the biologically active component. Estrogen is bound to sex hormone binding globulin and albumin; the remaining estrogen (1% to 3% of the total circulating estrogen) is unbound. Evidence suggests that steroid hormones that bind to sex hormone binding globulin are not taken up by most target tissues, whereas the non-protein-bound fraction is (44). Thus, the level of sex hormone binding globulin will determine the amount of available estrogen that can interact with the breast. Several studies (8-11, 45, 46) with one exception (47) have shown elevated circulating non-protein-bound estradiol levels in patients with breast cancer when compared with controls. In addition, studies (9, 10, 12) have shown a decrease in sex hormone binding capacity and an increase in the non-protein-bound fraction of estrogen in patients with breast cancer. Japanese women have a lower incidence of breast cancer than British and American women. Compared with British women, Japanese women had significantly more estradiol bound to sex hormone binding globulin (48) and, conversely, less free estradiol.

Although obese women are at increased risk for breast cancer, a subpopulation of women with android obesity appears to be at significantly greater risk for breast cancer. The hormonal abnormalities associated with increased breast cancer risk, abnormalities that have been noted in women with android obesity, are reversible with weight loss. The risk for breast cancer in obese women, particularly those with android obesity, may be reduced by weight loss. Android obesity can be readily identified by measuring waist and hip circumference and determining the waist:hip circumference ratio. Because of the significantly increased risk for breast cancer conferred by android obesity, evaluation for this condition should be incorporated into breast cancer risk factor evaluation.

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Requests for Reprints: David V. Schapira, MBChB, H. Lee Moffitt Cancer Center and Research Institute, University of South Florida College of Medicine, 12902 Magnolia Drive, Tampa, FL 33612.

Current Author Addresses: Drs. Schapira, Lyman, and Cox and Ms. Kumar: H. Lee Moffitt Cancer Center and Research Institute, University of South Florida College of Medicine, 12902 Magnolia Drive, Tampa, FL 33612.

References

1. **deWaard F, Poortman J, Collette BJ.** Relationship of weight to the promotion of breast cancer after menopause. *Nutr Cancer.* 1981;**2**:237-40.
2. **Lew EA, Garfinkel L.** Variations in mortality by weight among 750,000 men and women. *J Chronic Dis.* 1979;**32**:563-76.
3. **Staszewski J.** Breast cancer and body build. *Prev Med.* 1977;**6**:410-5.
4. **Damon A.** Host factors in cancer of the breast and uterine cervix and corpus. *J Natl Cancer Inst.* 1960;**24**:483-516.
5. **Kirschner MA, Schneider G, Ertel NH, Worton E.** Obesity, androgens, estrogens and cancer risk. *Cancer Res.* 1982;**42**(Suppl):3281S-3285S.
6. **MacDonald PC, Grodin JM, Siiteri PK.** Progress in endocrinology. In: Ebling FJ, Gaul C, eds. *Proceedings of the Third International Congress of Endocrinology; Proceedings.* Amsterdam: Excerpta Medica Foundation; 1969:770.
7. **Rizkallah TH, Tovell HM, Kelly WG.** Production of estrone and fractional conversion of circulating androstendione to estrone in women with endometrial carcinoma. *J Clin Endocrinol Metab.* 1975;**40**:1045-56.
8. **Siiteri PK, Hammond GL, Nisker JA.** Increased availability of serum estrogens in breast cancer. A new hypothesis. In: Pike MG, Siiteri PK, Nelsch CW, eds. *Banbury Report.* Cold Spring Harbor, New York: Cold Spring Harbor Laboratory; 1981:87-106.
9. **Moore JW, Clark GM, Bulbrook RD, et al.** Serum concentrations of total and non-protein-bound oestradiol in patients with breast cancer and in normal controls. *Int J Cancer.* 1982;**29**:17-21.
10. **Reed MJ, Cheng RW, Noel CT, Dudley HA, James VH.** Plasma levels of estrone, estrone sulfate, and estradiol and the percentage of unbound estradiol in postmenopausal women with and without breast disease. *Cancer Res.* 1983;**43**:3940-3.
11. **Bruning PF, Bonfrer JM, Hart AA.** Non-protein bound estradiol, sex hormone binding globulin, breast cancer and breast cancer risk. *Br J Cancer.* 1985;**51**:479-84.
12. **Moore JW, Key TJ, Clark GM, et al.** Concentrations of sex-hormone-binding-globulin (SHBG) in a population of normal women: relationship to risk factors for breast cancer. *Steroids.* 1988;**52**:391-2.
13. **Siiteri PK, Hammond GL, Nisker, JA.** Increased availability of serum estrogens in breast cancer: a new hypothesis. In: Pike MC, Siiteri PK, eds. *Banbury Report. Hormones and Breast Cancer.* Cold Spring Harbor, New York: Cold Spring Harbor Laboratory; 1981:87-101.
14. **Kissebah AH, Vydelingum N, Murray R, et al.** Relation of body fat distribution to metabolic complications of obesity. *J Clin Endocrinol Metab.* 1982;**54**:254-60.
15. **Kalkhoff RK, Hartz AH, Rupley D, Kissebah AH, Kelber S.** Relationship of body fat distribution to blood pressure, carbohydrate tolerance, and plasma lipids in healthy obese women. *J Lab Clin Med.* 1983;**102**:621-7.
16. **Evans DJ, Hoffmann RG, Kalkhoff RK, Kissebah AH.** Relationship of body fat topography to insulin sensitivity and metabolic profiles in premenopausal women. *Metabolism.* 1984;**33**:68-75.
17. **Peiris AN, Meuller RA, Smith GA, Struve MF, Kissebah AH.** Splanchnic insulin metabolism in obesity. Influence of body fat distribution. *J Clin Invest.* 1986;**78**:1648-57.
18. **Smith U, Hammersten J, Bjorntorp P, Krel JG.** Regional differences and effect of weight reduction on human fat cell metabolism. *Eur J Clin Invest.* 1979;**9:327-32.**
19. **Sjostrom L, Smith U, Krotkiewski M, Bjorntorp P.** Cellularity in different regions of adipose tissue in young men and women. *Metabolism.* 1972;**21**:1143-53.
20. **Segal KR, Dunaif A, Gutin B, Albu J, Nyman A, Pi-Sunyer FX.** Body composition, not body weight, is related to cardiovascular disease risk factors and sex hormone levels in men. *J Clin Invest.* 1987;**80**:1050-5.
21. **Evans DJ, Hoffman RG, Kalkhoff RK, Kissebah AH.** Relationship of androgenic activity to body fat topography, fat cell morphology, and metabolic aberrations in premenopausal women. *J Clin Endocrinol Metab.* 1983;**57**:304-10.
22. **Hartz AJ, Rupley DC Jr, Kalkhoff RD, Rimm AA.** Relationship of obesity to diabetes: influence of obesity level and body fat distribution. *Prev Med.* 1983;**12**:351-7.
23. **Hartz AJ, Rupley DC, Rimm AA.** The association of girth measurements with disease in 32,856 women. *Am J Epidemiol.* 1984;**119**:71-80.
24. **Kopelman PG, White N, Pilkington TR, Jeffcoate SL.** The effect of weight loss on sex steroid secretion and binding in massively obese women. *Clin Endocrinol (Oxf).* 1981;**15**:113-6.
25. **Keys A.** Recommendations concerning body measurements for the characterization of nutritional status. *Human Biology.* 1956;**28**:111-23.
26. **Behnke AR, Wilmore JH.** *Evaluation and Regulation of Body Build and Composition.* Englewood Cliffs, New Jersey: Prentice-Hall; 1974.
27. **Jackson AS, Pollock ML.** Generalized equation for predicting body density of men. *Br J Nutr.* 1978;**40**:497-504.
28. **Jackson AS, Pollock ML, Ward A.** Generalized equations for predicting body density of women. *Med Sci Sports Exerc.* 1980;**12**:175-81.
29. **Durnin J, Womersley J.** Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *Br J Nutr.* 1974;**32**:77-97.
30. **Katch FI, Katch VL.** Measurement and prediction errors in body fat composition assessment: the search for perfect prediction equation. *Research Quarterly for Exercise and Sport.* 1980;**51**:249-60.
31. **Cornfield J, Gordon T, Smith WW.** Logistic regression analysis. *Bull Int Stat Inst.* 1961;**38**:97.
32. **Kleinbaum DG, Kupper LL, Morgenstern H.** *Epidemiologic Research: Principles and Quantitative Methods.* Belmont, California: Lifetime Learning Publications; 1982: 430-3.
33. **Woolf B.** On estimating the relations between blood group and disease. *Ann Hum Genet.* 1955;**10**:251.
34. **Siiteri PK.** Steroid hormones and endometrial cancers. *Cancer Res.* 1978;**38**:4360-6.
35. **Davidson BJ, Gambone JC, Lagasse LD, et al.** Free estradiol in postmenopausal women with and without endometrial cancer. *J Clin Endocrinol Metab.* 1981;**52**:404-8.
36. **Nisker JA, Hammond GL, Davidson BJ, et al.** Sex hormone-binding globulin and the percentage of free estradiol in postmenopausal women with and without endometrial carcinoma. A new biochemical basis for the association between obesity and endometrial carcinoma. *Am J Obstet Gynecol.* 1980;**138**:637-42.
37. **de Moor P, Joossens JV.** An inverse relation between body weight and the activity of the steroid binding β globulin in human plasma. *Steroidologia.* 1970;**1**:129-36.
38. **Purifoy FE, Koopmans LH, Tatum RW, Mayes DM.** Serum androgens and sex hormone binding globulin in obese Pima indian females. *Am J Phys Anthropol.* 1981;**55**:491-6.
39. **Ingram D, Nottage E, Ng S, et al.** Obesity and breast disease. The role of the female sex hormones. *Cancer.* 1989;**64**:1049-53.
40. **Rosenfield RL.** Studies of the relation of plasma androgen levels to androgen action in women. *J Steroid Biochem.* 1975;**6**:695-702.
41. **Korenman SG.** The estrogen window hypothesis of the aetiology of breast cancer. *Lancet.* 1980;**1**:700-1.
42. **Korenman SG.** The endocrinology of breast cancer. *Cancer.* 1980;**46**:874-8.
43. **Kelsey JL.** A review of the epidemiology of human breast cancer. *Epidemiol Rev.* 1979;**1**:74-109.
44. **Langley MS, Hammond GL, Bardsley A, Sellwood RA, Anderson DC.** Serum steroid binding proteins and the bioavailability of estradiol in relation to breast diseases. *J Natl Cancer Inst.* 1985;**75**:823-9.
45. **Reed MJ, Cheng RW, Noel CT, Dudley HA, James VH.** Plasma levels of estrone, estrone sulfate, and estradiol and the percentage of unbound estradiol in postmenopausal women and without breast disease. *Cancer Res.* 1983;**43**:3940-3.
46. **Ota DM, Jones LA, Jackson GL, Jackson PM, Kemp K, Bauman D.** Obesity, non-protein-bound estradiol levels, and distribution of estradiol in the sera of breast cancer patients. *Cancer.* 1986;**57**:558-62.
47. **Bruning PF, Bonfrer JM, de Jong-Bakker M, et al.** Free estradiol, sex hormone binding globulin, breast cancer and breast cancer risk [Abstract]. In: Labrie F, Proulx L, eds. *Abstracts of Satellite Symposia of the 7th International Congress of Endocrinology.* New York: Pergamon Press; 1984:424.
48. **Moore JW, Clark GM, Takatani O, Wakebayashi Y, Hayward JL, Bulbrook RD.** Distribution of 17 beta-estradiol in the sera of normal British and Japanese women. *J Natl Cancer Inst.* 1983;**71**:749-54.