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Evolutionary and medical aspects of body composition characteristics in subfertile and infertile women

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The association between body composition characteristics and female fecundity seems to be well known since a very long time. The aim of the present study was the documentation of body composition characteristics of young infertile women and interpretation of the results in an evolutionary sense. **Materials and Methods.** 43 young Austrian women aging between 18 and 29 years, suffering from infertility caused by PCOS, anorexia nervosa or primary amenorrhoea, and 19 healthy age-matched controls were enrolled in the present study. Body composition analyses and bone density analyses were performed using dual energy X-ray absorptiometry. For a better description of the sex-typical fat distribution patterns, the fat distribution index was calculated. **Results**. As could be expected, the three groups of infertile young women differed highly significantly in nearly all body composition parameters. In comparison with healthy controls, anorexia nervosa patients were characterized by a significantly reduced fat percentage, while PCOS patients were characterized by a high amount of body fat and an android fat patterning. Primary amenorrhoea was first of all related with a reduced bone mass in comparison with healthy controls. **Conclusions.** Although anorexia nervosa, PCOS and primary amenorrhoea have completely different etiologies and hormonal characteristics, the amount of body fat seems to be related with the disturbed ovarian function. Therefore the culturally independent standard of female attractiveness may be interpreted in an evolutionary sense as a visible indicator of potential female reproductive success.

Key words: infertility, body composition, weight status, fat distribution, PCOS, primary amenorrhoea, anorexia nervosa

INTRODUCTION

The association between body composition characteristics and female fecundity seems to be well known since a very long time. According to iconodiagnostic analyses, the famous upper paleolithic Venus figurines such as the Venus of Willendorf or the Venus of Lespugue are interpreted as symbols of beauty and fecundity (1). The majority of these little figurines show an extremely high amount of body fat, especially in the lower region of the body, indicating a typical gynoid kind of fat patterning. Later in our history famous painters such as Rubens presented young and attractive females as considerably fat. Even today more than 90% of cultures listed in the Human Relation area files (HRAF) prefer a slight overweight, a moderate amount of fat tissue and a gynoid kind of fat distribution as attractive, because this body type is associated with health and fecundity (2). Only in contemporary highly industrialized societies an extremely slender body is considered as attractive, while in traditional societies body fat is interpreted as an insurance of fecundity, health and high social status (2). The importance of body fat for successful reproduction is out of question today (3–5). Body fat is an essential caloric resource, especially important during phases of increased somatic stress such as pregnancy or lactation. Furthermore, body fat indicates a positive energy balance and is essential for the extraovarian estrogen synthesis. On the other hand, fat distribution patterns are also influenced by hormonal changes such as during menopausal transition (6). Thus, body composition parameters as well as fat distribution patterns may be interpreted as extragenital markers of human ovarian function. The aim of the present study was to document body composition and fat patterning of young infertile women and to test the hypothesis that body composition and fat distribution patterns are markers of potential female fertility.

MATERIALS AND METHODS

Study subjects

Forty-one young Austrian women aging 18 to 29 years (x = 23.5) suffering from infertility and 19 healthy age-matched controls (x = 23.7) were enrolled in the present study. All controls had regular menstrual cycles (26–33 day cycles) and age-typical sex hormone levels. The sample of infertile young women could be divided into three age-matched (range, 18–29 years) subgroups: 15 young women that had suffered from secondary amenorrhoea for more than nine months as a result of low body weight from anorexia nervosa. All of them were extremely underweight, but at the time of investigation their weight status was not life-threatening. Group 2 consisted of 16 young women with PCOS diagnosed by ultrasound appearance of polycystic ovaries combined with hyperandrogenemia and elevated LH levels. All of them suffered from secondary amenorrhoea or oligomenorrhoea. The third group comprised 10 young women who suffered from primary amenorrhoea. Chromosomal aberrations such as Turner syndrome were excluded from the present sample. None of the women suffering from primary amenorrhoea suffered from anatomical abnormalities; their primary amenorrhoea was classified as idiopathic. All probands stemmed from Vienna or neighboring Lower Austria and none of them had ever been pregnant. All subjects were nonsmokers and none of them were on any medication that might affect hormone metabolism or body composition.

Menstrual history

Using a structured questionnaire all probands were interviewed regarding their menstrual history. Data regarding age at menarche, minimum and maximum cycle length, duration of amenorrhoea and the use of hormonal medication were collected.

Body composition analyses

Body composition and bone density analyses were performed using dual energy X-ray absorptiometry (DEXA) (Hologic 4000) at the University Clinic for Gynecology and Obstetrics in Vienna (7). Although this method is indirect, its high reliability, relatively low costs, the relatively low radiation dose with 0.1m Sievert, a short scanning time (<7 min) and the comfort for the subjects make the dual energy X-ray absorptiometry especially suitable for such determinations. Scanning was done with a Hologic total body scanner. Absolute and relative fat mass, lean soft tissue mass and bone mineral content (BMC) of the whole body, the upper body, the head, the arms, the legs and the lower body were determined.

Fat distribution analysis

For a better description of the sex-typical fat distribution the fat distribution index (FDI) (8) was calculated: FDI = upper body fat mass (in kg) / lower body fat mass (in kg). A FDI below 0.9 indicates a gynoid fat patterning, *i.e.* the fat mass of the lower body surpasses the fat mass of the upper body. A FDI > 1.1 defines an android fat distribution. In this case the amount of upper body fat surpasses that of the lower body region. A FDI between 0.9 and 1.1. is defined as an intermediate stage of fat distribution.

Weight status

After determination of stature (in cm) and body weight (in kg) according to the methods published by Knussmann (9), the individual weight status was determined by means of body mass index (BMI) (weight in kg) / stature in m square). For weight status classification the categories published by the WHO (10) were used:

Thinness	grade 1:	BMI 17.00–18.49 (mild thinness)
	grade 2	BMI 16.00–16.99 (moderate thinness)
	grade 3	BMI < 16.00 (severe thinness)
Normal range		BMI 18.50–24.99
Overweight	grade 1	BMI 25.00–29.99 (overweight)
	grade 2	BMI 30.00–39.99 (obese 1)
	grade 3	BMI > 40.00 (obese 2)

Hormonal parameters

Blood samples for the quantitative determination of hormone levels were collected between 7.30 am and 9.30 am before the 10th day of the cycle (in menstruating women). The quantitative determination was made at the central hormone laboratory of the University Clinic for Gynecology and Obstetrics. After coagulation, the samples were centrifuged and the serum was stored at –20 °C until further processing. Assays were employed according to NCCLS guidelines as follows (intra- and interassay CV in parentheses): the following hormones were determined: 17ß-estradiol (E2), follicle-stimulating hormone (FSH), lutenizing hormone (LH), prolactin (HPRL), progesterone (P) testosterone (T), dehydroepiandrostendion-sulfate (DHEA-S) and androstendione (A).

Statistical analyses

Statistical analyses were performed with the aid of SPSS Version 10.0. After computing descriptive statistics (means, standard deviations, medians, range), Kruskal–Wallis tests were calculated in order to group differences with respect to their statistical significance. Because of the low number of probands and the results of the Kolmogorov–Smirnov test which indicated that no normal distribution of the data could be assumed, non-parametric tests were applied predominantly. Chi-squares were computed to test group differences with respect to categorical variables. Binary logistic regression analyses were performed to test the association of body composition, weight status and fat patterning with ovarian function (proband group).

RESULTS

Comparison of hormone levels

A comparison of the sex hormone levels yielded significant differences in estradiol, FSH, LH, testosterone and DHEA-S levels. As expected, PCOS patients exhibited the highest androgen levels, while women suffering from primary amenorrhoea and anorexia nervosa showed lower estrogen, gonadotropin and progesterone levels than PCOS patients and healthy controls (Table 1).

Comparison of body composition and fat distribution patterns

Regarding somatometric parameters, the three groups of infertile young women and the healthy controls differed highly significantly in weight status and all body fat and bone mineral content parameters but not in lean body mass (see Table 1). PCOS women exhibited not only an extraordinarily high amount of absolute and relative fat tissue in comparison with the young women suffering from anorexia nervosa or primary amenorrhoea and the healthy controls, but also showed a tendency towards android fat distribution patterns. The fat distribution patterns in more than 80% of PCOS women and of nearly 50% of primary amenorrhoea women were classified as intermediate or android. In contrast, about 80% of anorexia nervosa patients and controls showed a typically gynoid kind of fat patterning and none of them exhibited an android fat distribution (Fig. 1). According to the results of logistic regression analyses, anorexia nervosa patients were characterized by a significantly reduced relative fat mass, a significantly reduced total lean body mass and a significantly reduced weight status, while PCOS patients, in comparison with healthy controls, were characterized by a high fat distribution index, indicating android fat patterning and increased fat percentage. Primary amenorrhoea was above all related with a reduced bone mass and an increased weight status in comparison with healthy controls (Table 2). Since the high prevalence of android fat patterning among PCOS patients may be due to the prevalence of overweight women among this proband group, a comparison of somatometric data of 10 normal weight PCOS patients with the somatometric data of 10 age and weight matched healthy controls was performed additionally. As to be seen in Table 3, testosterone levels in PCOS patients significantly surpassed those of their healthy counterparts. Regarding body composition parameters, it turned out that even normal weight PCOS patients exhibited a significantly higher amount of absolute and re-

Table 1. **Comparison of hormonal levels and somatometric parameters in Kruskal–Wallis tests**

Hormone	P.A X (SD)	A.N. X (SD)	PCOS X (SD)	Controls X (SD)	P value
E2 pg/ml	35.9 (35.6)	16.0 (7.3)	67.3 (60.1)	78.4 (46.0)	<0.001
FSH mU/ml	2.88 (3.22)	5.65 (1.69)	5.10 (2.05)	6.80 (2.05)	<0.001
LH mU/ml	2.01 (3.70)	1.83 (2.60)	6.06 (5.01)	7.47 (4.32)	<0.001
HPRL ng/ml	13.4 (13.9)	10.5 (8.8)	22.5 (17.2)	9.8 (3.1)	n.s.
P ng/ml	0.92 (2.09)	0.40 (0.13)	1.36 (1.77)	1.23 (1.91)	<0.05
T ng/ml	0.19 (0.08)	0.36 (0.20)	0.59 (0.34)	0.32 (0.11)	<0.001
A ng/ml	1.68 (0.75)	2.44 (0.89)	2.71 (1.42)	1.99 (0.59)	n.s.
DHEA-S ug/ml	1.56 (0.90)	1.68 (0.66)	2.34 (0.88)	1.82 (0.42)	<0.05
Fat total (kg)	23.5 (11.1)	10.2 (3.2)	29.5 (12.4)	16.1 (4.8)	<0.001
Lean total (kg)	41.3 (6.7)	37.7 (2.8)	39.7 (6.6)	40.4 (4.8)	n.s.
BMC total (g)	1707.1 (200.8)	2113.9 (233.1)	2213.2 (284.2)	2223.2 (245.2)	<0.001
Fat %	33.9 (8.3)	19.9 (5.5)	39.6 (9.1)	27.1 (4.4)	<0.001
FDI	0.92 (0.27)	0.58 (0.22)	1.45 (0.23)	0.70 (0.19)	<0.001
BMI (kg/m^2)	26.12 (7.45)	17.87 (1.49)	26.08 (5.68)	20.61 (2.37)	<0.001

P.A. – primary amenorhoea, A.N. – anorexia nervosa.

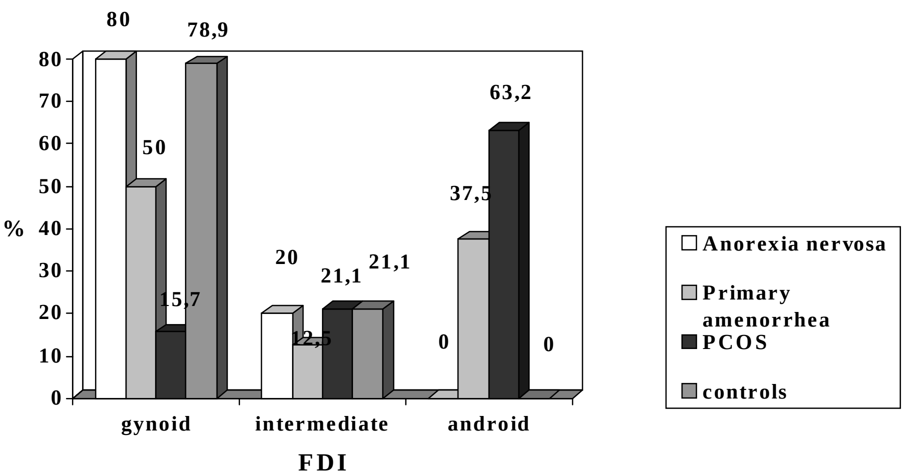

Fig. 1. Comparison of fat distribution patterns

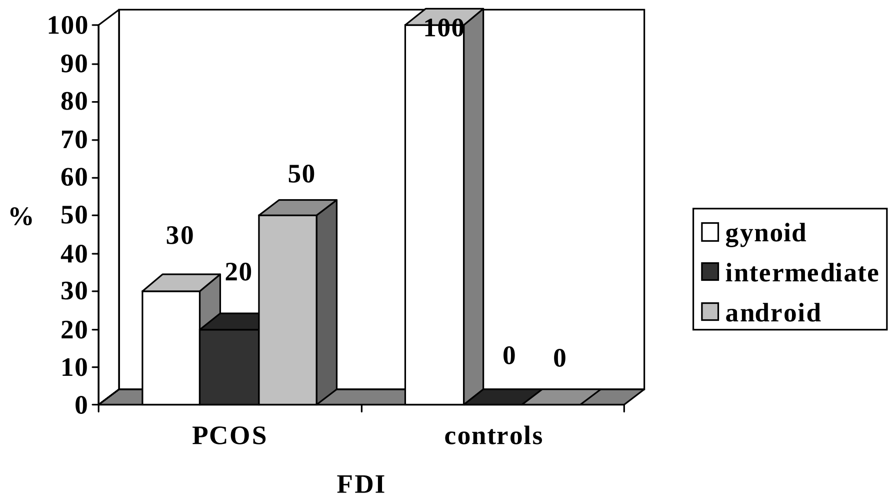

Fig. 2. Comparison of fat distribution patterns in lean PCOS patients and controls

lative body fat, but a significantly reduced amount of bone mass and lean soft tissue mass. Furthermore, a marked difference in the fat distribution patterns was observed. Even among lean PCOS women the prevalence of android or intermediate fat patterning was 70% (Fig. 2).

DISCUSSION

The results of the present study corroborate the well-documented association between female reproductive function and body composition characteristics (11–14). Young women suffering from infertility caused by PCOS, primary amenorrhoea or anorexia nervosa differed in body composition significantly from healthy age-matched controls. It is well known that female reproductive function is extremely vulnerable to energy imbalance (15–18). A reduction of metabolic fuel availability below a critical level by food re-

Table 2. **Logistic regression analysis**

Variable	Coefficient	95% confidience interval
Dependent variable: diagnosis (controls = 1, anorexia n. = 2)		
Total lean body mass	–0.44 p < 0.003	0.43–0.97
Total fat %	–0.39 p < 0.06	0.50–0.89
BMI	–0.91 p < 0.004	0.22–0.75
Dependent variable: diagnosis (controls = 1, primary amenorrhoea= 2)		
Total BMC	–0.03 p < 0.05	0.93–1.00
BMI	0.24 p < 0.04	0.99–1.65
Dependent variable: diagnosis (controls = 1, PCOS = 2)		
Total fat %	0.25 p < 0.002	1.09–1.50
FDI	0.69 p < 0.001	1.62–1.71

Table 3. **Comparison of hormone levels and somatometric parameters in lean PCOS patients and control (Kruskal–Wallis tests)**

Variable	PCOS lean X (SD)	Controls X (SD)	P value
E2 pg/ml	34.7 (15.6)	51.3 (22.2)	n.s.
FSH mU/ml	5.36 (2.81)	5.57 (1.66)	n.s.
LH mU/ml	5.41 (2.52)	4.05 (1.47)	n.s.
T ng/ml	0.73 (0.21)	0.31 (0.27)	<0.05
A ng/ml	3.39 (1.55)	1.67 (0.65)	n.s.
DHEA ng/ml	2.47 (0.67)	1.39 (0.62)	<0.05
Fat total (kg)	21.2 (5.4)	14.8 (2.5)	<0.001
Lean total (kg)	35.6 (3.9)	38.7 (3.4)	<0.05
BMC total (g)	2065.7 (276.7)	2312.7 (237.5)	<0.05
Fat %	35.7 7.6)	26.4 (3.5)	<0.001
FDI	1.01 (0.23)	0.67 (0.11)	<0.001
BMI (kg/m^2)	20.71 (1.42)	20.64 (1.63)	n.s.

striction or increased expenditure is appropriately accompanied by activation of multiple neuroendocrine changes resulting in anovulation and amenorrhoea (19). Ovarian function is especially influenced by body fat, the most important energy storage of all body composition compartments (20). On the one hand, conversion from androgens to estrogens by aromatization takes place in the adipose tissue. Nearly a third of estrogens circulating in women during the reproductive phase stem from this conversion. Furthermore, high amounts of body fat are associated with a reduced capacity to bind the sex hormone binding globulin. Therefore in obese and overweight women and girls an elevated percentage of free serum estradiol is found. On the other hand, obesity and abdominal fat patterning are associated with hyperandrogenism, mostly found in women suffering from PCOS (11,12, 21, 22). The influence of an extremely low amount of body fat on ovarian function was especially pronounced in the anorectic proband group. Anorexia nervosa is characterized by restricted food consumption and a long-time negative energy balance, which lead to a suppression of ovarian function (23–25), a condition which was not uncommon during our evolution and history when food shortages and periods of starvation were frequent experiences of our ancestors. Under these conditions it was nearly impossible for a female to maintain a sufficient amount of body fat to signal her potential reproductive capability. The typical gynoid fat patterning, however, persists even during phases of energy shortage and suppressed ovarian function and may indicate the potential possibility of reproductive success after a time of nutritional surplus (26). In contrast, the prognosis for PCOS, the most common endocrine cause of female infertility, is worse. Independently of their weight status the PCOS women exhibited an extraordinary high amount (nearly 70%) of android fat patterning. This kind of fat distribution pattern is not only in clear contradiction to female attractiveness standards in 90% of investigated cultures (2, 27), but is also strongly associated with hyperandrogenism (11, 12, 21) and markedly decreased conception rates (28–30). In human females, android fat patterning is predominantly found in the phases of life when conception is physiologically impossible, such as pregnancy, postmenopause or in severely overweight women (6). In the present sample, the android kind of fat patterning was frequent in women suffering from primary amenorhoea, too. This high prevalence of android or intermediate fat patterning among infertile young women may explain the observation that android fat patterning is considered as inattractive in so many cultures worldwide. We know that standards of female attractiveness are relatively homogeneous culturally and historically. Furthermore, it is well documented that the female reproductive potential is one of the most important criteria by which males select a mating partner. However, in the human female the ovarian function and fecundity potential are invisible signs. Therefore the morphologic features associated with potential fecundity gains in importance for sexual selection. The results of the present study indicate that fat distribution patterns are among these features.

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NEVAISINGØ IR SUSILPNËJUSIO VAISINGUMO MOTERØ KÛNO SUDËJIMO YPATUMAI EVOLIUCINIU IR MEDICININIU ASPEKTU

S a n t r a u k a

Sàsajos tarp kûno sudëjimo ypatumø ir moters vaisingumo þinomos nuo seno. Ðio darbo tikslas – nustatyti jaunø nevaisingø moterø kûno sudëjimo ypatumus ir interpretuoti juos evoliuciniu aspektu. Buvo iðtirtos 43 jaunos (nuo 18 iki 29 metø) Austrijos moterys, nevaisingos dël kiauðidþiø policistinio sindromo (PCOS), nervinës anoreksijos ar pirminës amenorëjos, taip pat 19 sveikø kontrolinës grupës moterø. Kûno sudëjimas ir kaulø tankis tirtas dvisrautës energijos rentgeno spinduliø absorbciometrijos metodu. Riebalinio audinio topografijos lytiniø skirtumø ypatumams detaliau apibûdinti apskaièiuotas riebalinio audinio pasiskirstymo indeksas. Kaip ir buvo tikëtasi, beveik visi trijø nevaisingø moterø grupiø kûno sudëjimo parametrai labai patikimai skyrësi tarpusavyje. Anoreksija serganèiø moterø riebalinis audinys buvo kur kas menkesnis nei kontrolinës grupës moterø, tuo tarpu PCOS serganèiø moterø riebalinis audinys buvo ypaè iðveðëjæs ir susikaupæs pagal androidiná tipà. Pirminës amenorëjos atveju buvo ypaè sumaþëjæs kaulø tankis palyginus su sveikø moterø. Nors nervinës anoreksijos, PCOS ir pirminës amenorëjos etiologija ir hormonø charakteristikos skiriasi, riebalinio audinio nukrypimai yra susijæ su kiauðidþiø funkcijos sutrikimu. Todël nuo kultûriniø veiksniø nepriklausantys moters kûno patrauklumo standartai gali bûti paaiðkinti evoliuciniu aspektu kaip akivaizdûs sëkmingà moters dauginimosi funkcijà sàlygojantys rodikliai.