

Research Article

The Body Composition of Women Undergoing ART, and Its Relationship with Sex Hormones and Biochemical Indicators

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***Corresponding author:** Lei Chen, Department of Obstetrics and Gynecology, Sixth Medical Center of the People's Liberation Army (PLA), General Hospital, Beijing, P.R. China**Received:** April 26, 2021; **Accepted:** May 22, 2021;**Published:** May 29, 2021**Abstract**

This study displays a retrospective cohort analysis in the Reproductive and Genetic Health Center of Peking University First Hospital. Data were collected from 411 women receiving ART. The body composition, sex hormones and biochemical indicators were assessed by Bioelectrical Impedance Analysis (BIA). Subjects were grouped by Body Mass Index (BMI) and Body Fat Percentage (BFP), and differences of body composition among groups were analyzed. Multiple linear regression analysis was used to evaluate the relationship between sex hormones, biochemical indicators and body composition. Compared with the non-overweight group (BMI <24kg/m²), the lean body mass and fat mass of the overweight group (BMI ≥24kg/m²) increased significantly (P <0.001). Notably, 43.7% of non-overweight subjects have increased body fat as distinguished by PBF. The visceral adipose tissue increased by 50.9% in subjects with more fat. Fasting Blood Glucose (FBG), triglyceride, Low Density Lipoprotein Cholesterol (LDL-C) and testosterone were positively correlated with trunk fat, while High Density Lipoprotein Cholesterol (HDL-C) and estradiol were negatively correlated with trunk fat. Moreover, total cholesterol was positively correlated with Bone Mineral Content (BMC). Therefore, this research demonstrated significant differences in body composition between overweight and non-overweight women receiving ART. Combining PBF with BMI, obesity can be identified more accurately.

Biochemical metabolism and sex hormones were related to body composition. Therefore, women receiving ART require detailed measurements of body composition, not BMI. Further studies are needed to confirm the relationship between pregnancy outcomes and body composition in women receiving ART treatment.

Keywords: Body composition; Biochemical indicators; Sex hormones; Body mass index; Body fat percentage

Introduction

The prevalence of obesity is increasing worldwide, almost tripling in the last four decades. In 2016, over 650 million adults were obese, 15% of who were women [1]. Meanwhile infertility has become a crucial health issue in recent decades. In 2010, as many as 48.5 million couples worldwide suffered from being unable to conceive [2]. More and more obese women are being evaluated for infertility [3]. It is confirmed that an increase in BMI can lead to ovulation failure [4]. Moreover, higher BMI was associated with worse ART outcomes, including lower implantation rates and increased risk of abortion [5-8]. It is assumed that the effects of obesity on sex hormones and metabolism may partly explain the differences in treatment outcomes [9]. Obesity is always characterized by a high BMI, which means not only changes in fat content, but also other physical parameters, such as Total Body Water (TBM), muscle and Bone Mineral Content (BMC). Therefore, for infertile women with the high BMI, more attention should be paid to the changes of body composition. It is necessary to explore the relationship between sexual hormones, metabolic markers and body composition.

Multi-component models give a description of body composition; two-compartment models divide total body mass into fat mass and lean body mass; three-compartment models divide total body mass into muscle, BMC and fat mass; similarly, four-compartment models further divide total body mass into TBW, protein, BMC and fat mass [10]. As a convenient, safe and portable method to estimate body composition, BIA has been used in children, cancer survivors, pregnant women, patients with chronic obstructive pulmonary disease, but it is rarely used in women receiving ART [11-13].

In the analysis of body composition, PBF seems to be a new index of obesity compared with BMI. Unlike BMI, PBF directly reflects the content and distribution of body fat. Whether BMI or PBF is more suitable for assessing obesity remains to be determined. The purpose of this study was to assess the body composition of women receiving ART with abnormal BMI, and to evaluate the effectiveness of BMI and PBF to identify fat elevation. The second goal is to determine the relationship between sex hormones, metabolic markers and body composition.

Materials and Methods

Subjects and design

From January 2017 to October 2017, 411 women who received ART treatment at the Reproductive and Genetic Health Center of Peking University First Hospital were selected. The data were collected as following: biochemical indicators (including FBG: Fasting Blood Glucose, TG: Triglyceride, TC: Total Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol and LDL-C: Low-Density Lipoprotein Cholesterol), sex hormones (including estradiol and testosterone), anthropometric data (including height, weight, BMI, WHR: Waist-Hip Ratio), and body composition (including TBW: Total Body Water, protein, BMC: Bone Mineral Content, muscle, lean body mass, FM: Total Fat Mass, TFM: Trunk Fat Mass, LAFM: Left Arm Fat Mass, LLFM: Left Leg Fat Mass, RALM: Right Arm Fat Mass, RLFM: Right Leg Fat Mass, VAT: Visceral Adipose Tissue, PBF: Percentage Body Fat and BMR: Basal Metabolic Rate). The biochemical indicators and sex hormones are considered valid within one year before or after physical measurement. All data collected as part of routine care before ART initiation; consequently no ethical permission was required for this study.

Measures and variables

Venous blood samples were collected after 10-12 hours of overnight fasting. FBG, triglyceride, total cholesterol, HDL-C, LDL-C, urea and creatinine were analyzed by automatic analyzer. Blood samples for sex hormone analysis were collected around 9:00 am on the second or third day of menstruation.

The patient's height was measured by an ultrasonic altimeter in meters with a measurement accuracy of 1cm. The nude weight was measured with an electronic scale accurate to 100 grams. The patients needed to wear underwear only, fast overnight, and empty urine and stool. BMI was calculated as weight (kg)/height (m)². According to the criteria of China, subjects were divided into overweight (BMI $\geq 24\text{kg/m}^2$, including overweight and obesity) and non-overweight (BMI $< 24\text{kg/m}^2$) [14]. Waist circumference was measured with soft elastic tape midway between the 12th rib and iliac crest. When the subjects were standing, hip circumference was determined as the widest horizontal plane of the hip. WHR was calculated as waist circumference (cm)/hip circumference (cm).

Various parameters including TBW, protein, BMC, muscle, lean body mass, FM, TFM, LAFM, LLFM, RAFM, RLFM and PBF were measured by multi-frequency bioelectrical impedance analyzer NQAPI. The characteristics of body fat elevation is PBF $> 30\%$ [15]. The bioelectrical impedance analysis device detects the human body as five cylinders (four limbs and trunk), and calculates the whole and part of the human body by using eight electrodes and multi-frequency current. 411 eligible subjects were measured. Those with metal objects such as pacemakers, defibrillators, coronary stents and artificial joints were excluded from physical analysis. Subjects were asked to have at least one diet and stress-free activity within six hours before the trial.

Statistical analysis

Statistical Package for Social Sciences (SPSS version 20) was used to analyze the data obtained. Categorical data were showed as n (%), and parametric variables were presented as mean and standard

deviation. Non-parametric variables were presented as median (interquartile range) and compared by Mann-Whitney test. The parametric bivariate analysis of variables correlation was performed using the Spearman correlation coefficient. To further identify the relationship between biochemical indicators, sex hormones and body composition, a stepwise multiple linear regression analysis was conducted. Based on collinearity and variance inflation factors, several variables strongly correlated were removed. Data of FBG, triglyceride, HDL-C, estradiol and testosterone were not normal distributed. As a result, normal scores of the data using Blom's formula were employed in multiple linear regression analysis.

Results

Demographic, sex hormonal and biochemical characteristics

In this study, the majority of women receiving ART treatment (37.7%, 155/411) were due to male factors, 34.3% (141/411), 13.6% (56/411), 10.2% (42/411), 4.1% (17/411) were due to pelvic and fallopian tube factors, unexplained infertility, ovulation problems and Diminished Ovarian Reserve (DOR), respectively.

More subjects (71.5%, 294/411) were undergoing the treatment of *In Vitro* Fertilization and Embryo Transfer (IVF-ET). The median age of the study population was 32. Median height, body weight and BMI were 162cm, 58.9kg and 22.2kg/m^2 , respectively. Because not everyone needs biochemical and testosterone tests, in addition to some missing data on estradiol, there are a number of biochemical and hormone samples less than 411. Median hormones and biochemical characteristics.

Anthropometric and physical measurement of overweight and non-overweight women

Regarding BMI, 34.3% (141/411) of women with ART treatment of this study were overweight (BMI $\geq 24\text{kg/m}^2$, including overweight and obesity). Then the body composition of overweight and non-overweight women (BMI $< 24\text{kg/m}^2$) was compared, with a median BMI of 25.9kg/m^2 and 20.9kg/m^2 , respectively. A significantly increase was observed in the total body water (TBW, 32.4 vs. 28.8kg, $P < 0.001$), protein (8.7 vs. 7.7kg, $P < 0.001$), bone mineral content (BMC, 3.2 vs. 2.8kg, $p < 0.001$), muscle (41.6 vs. 37.0kg, $p < 0.001$), lean body mass (44.3 vs. 39.3, $p < 0.001$), total fat mass (FM, 25.3 vs. 16.1kg, $p < 0.001$), trunk fat mass (TFM, 12.7 vs. 7.7kg, $p < 0.001$), left arm fat mass (LAFM, 1.9 vs. 1.1kg, $p < 0.001$), left leg fat mass (LLFM, 3.8 vs. 2.6kg, $p < 0.001$), right arm fat mass (RAFM, 1.9 vs. 1.1kg, $p < 0.001$), right leg fat mass (RLFM, 3.8 vs. 2.6kg, $p < 0.001$) and visceral adipose tissue (VAT, 122 vs. 67cm², $p < 0.001$) of the overweight women. In overweight subjects, lean body mass and fat mass increased. In addition, the basal metabolic rate (BMR) of overweight women was significantly higher than that of non-overweight women (1326 vs. 1220, $P < 0.001$).

To distinguish fat mass from total body mass in non-overweight women, PBF was combined to analyze body composition in this study. The results showed that 43.7% (118/270) non-overweight women had higher body fat levels (PBF $> 30\%$). The total fat mass (19 vs. 13.8kg, $p < 0.001$), trunk fat mass (9.2 vs. 6.3kg, $p < 0.001$), limbs fat mass (including arms and legs), visceral adipose tissue (VAT, 86 vs. 57cm², $p < 0.001$) of overweight women with PBF $> 30\%$ were higher

than those of non-overweight women with PBF $\leq 30\%$. VAT increased most (rising 50.9%), while trunk fat mass, left arm fat mass, right arm fat mass, left leg fat mass, right leg fat mass increased by 46.0%, 44.4%, 44.4%, 30.4%, 30.4%, respectively. Combined with PBF, the lean body mass (including TBW, protein, BMC and muscle) and BMR were similar of the two groups of non-overweight women.

Correlation between sex hormones, biochemical indicators and body composition FBG, triglyceride, total cholesterol and LDL-C were positively and significantly correlated with all of the body composition. Besides, testosterone, fat mass, trunk fat mass, limbs fat mass, VAT, PBF were positively correlated with body composition. On the contrary, HDL-C and estradiol were negatively correlated with body composition.

Sex hormones, biochemical indicators related to body composition the more trunk fat mass, the higher FBGn. While triglyceriden, LDL-C and testosterone were positively correlated with trunk fat mass. On the contrary, HDL-Cn and estradioln were negatively correlated with trunk fat mass. Moreover, bone mineral content can be used as a predictor of total cholesterol, and showed a positive correlation between total cholesterol and bone mineral content.

Spearman correlation analysis showed that FBG, triglyceride, HDL-C, estradiol and testosterone were correlated with FBGn ($r=1$), triglyceriden ($r=1$), HDL-Cn ($r=1$), estradioln ($r=1$) and testosterone ($r=1$), respectively (correlation coefficient was not shown in the table). Hence, in accordance with the normal scores using Blom's formula, FBG, triglyceride and testosterone positively correlated with trunk fat mass, whereas HDL-C and estradiol negatively correlated with trunk fat mass.

Discussion

In this study of women receiving ART, we found that with the elevation of BMI, the lean body mass of TBW, protein, BMC and muscle, fat mass of TFM, LAFM, LLFM, RAFM, RLFM and VAT increased. Previous studies have also shown that both lean body mass and fat mass were significantly increased in overweight or obese group

Compared to those in normal weight group [16,17]. Therefore, there are significant differences in body composition between overweight and non-overweight groups. On the other hand, it was also confirmed that BMI cannot determine the overall weight gain caused by fat or lean mass. As a result, well-muscled people with normal body fat can be misdiagnosed as overweight or obese because of their high BMI. In addition, 43.7% of subjects were considered as non-overweight, but as overweight when combined with PBF because of the increase in fat content, which indicated that BMI cannot distinguish between normal-weight people who maintained a large amount of fat and those who did not have excess fat. Therefore, a more accurate estimation of body composition can be provided when combined BMI with PBF.

In the current study, apparently normal weight subjects with elevated fat mass had a higher VAT, rather than leg fat or arm fat mass. For fat distribution, VAT plays a vital role in metabolic disorders. Previous studies have detected that VAT were closely related to cardiometabolic risk factors and remarkably influenced the

development of insulin resistance [18,19]. PBF seems to be a valid parameter reflecting total fat mass and VAT, and a larger PBF means a greater risk of metabolic diseases as a major increase in VAT.

In this study, results of multiple linear regression showed that testosterone was positively correlated with trunk fat mass, while estradiol was negatively correlated with testosterone, similar to previous studies on women [20-23]. Interestingly, there was a negative correlation between trunk fat mass and testosterone, while a positive correlation between estradiol and trunk fat mass in man [9,24-27]. This difference between sex hormones and body composition needs further study. Current study has shown that FBG was positively correlated with trunk fat mass, which can be explained by the positive correlation between fat mass, especially VAT, and insulin resistance [20,28]. Furthermore, trunk fat mass but HDL-C had a positive effect on lipid distribution. Lipid metabolism and body fat have been studied in recent years. It is concluded that lipid metabolism is disturbed by adipocytokines fat mass, leading to hypertriglyceridemia and changes in HDL-C and LDL-C [29-31].

In particular, total cholesterol was related to BMC rather than fat mass in this study. However, previous studies have shown that total cholesterol is correlated with bone mineral density, thus it is required more studies to confirm BMC as a novel predictor for total cholesterol [32-37]. Considering the effects of body composition on sex hormones and metabolism, body composition analysis is superior to BMI in assessing women receiving ART. A favorable body composition can promote hormones and metabolic status, which is beneficial to the acquisition of fertility.

There were some limitations in this study. First of all, the retrospective design cannot make cause-effect inferences. Secondly, subjects from a single reproductive center were less representative. Thirdly, we have not adjusted for recognized determinants, such as dietary habits, physical activities, socioeconomic status and history of drinking and smoking. Moreover, the data of FBG, triglyceride, HDL-C, estradiol and testosterone were not normal distributed, and were transformed to normal scores using Blom's formula when analyzing with multiple linear regression, which reduces the clinical significance of multiple linear regression.

Conclusion

In conclusion, our results showed that there are significant differences in body composition and BMI in women under ART treatment. It was noticed that non-overweight subjects may have elevated body fat mass, combining PBF can provide more accurate body composition estimation due to BMI cannot distinguish between fat and lean mass. Biochemical metabolism and sex hormones were associated with body composition. Hence measurement methods for detailed body composition analysis rather than BMI are needed to examine women receiving ART treatment, and provide a basis for a self-management. Further studies are needed to determine the relationship between pregnancy outcomes and body composition in women receiving ART.

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