

# Clitoris to Urethral Meatus Distance is Not Affected by the Obesity Compared to the Anogenital Distance

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## Research Article

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# Abstract

**Background** The distance between clitoris and urethral meatus (CUMD) for women has been considered to likely reflect the extent of prenatal androgen exposure, being similar to the anogenital distance (AGD) and the digit length ratio. But no published work has examined the association between the CUMD and the AGD or digit ratio and the effect of body weight on CUMD and AGD.

**Methods** The CUMD and AGD (including AGD-AC, from the anus to the anterior clitoris; AGD-AF, from the anus to the posterior fourchette) measurements for 117 women (18-45 years) were taken using a digital caliper, and the digit ratios were measured from photos by a digital camera. Meanwhile, data of their height, weight, and body mass index (BMI) were collected at same time.

**Results** In bivariate correlation analyses of all 117 subjects, two AGD measurements (AGD-AC and AGD-AF) were moderately correlated with one another ( $r=0.474$ ,  $p<0.001$ ), but the correlation between AGD-AC and CUMD was weak ( $r=0.172$ ,  $p=0.063$ ). Both AGD-AC and AGD-AF were notably correlated with weight ( $r=0.290$ ,  $p=0.002$  and  $r=0.189$ ,  $p=0.041$ ; respectively) and BMI ( $r=0.341$ ,  $p<0.001$  and  $r=0.204$ ,  $p=0.027$ ; respectively), whereas the CUMD was not affected by weight or BMI. Exclusion of obese individuals, the CUMD of 86 non-overweight subjects was obviously correlated with the AGD-AC ( $r=0.236$ ,  $p=0.028$ ).

**Conclusion** These results indicated that the CUMD could be a marker of prenatal androgen exposure without influence of body weight, superior to AGD-AC or AGD-AF.

## Background

Anogenital distance (AGD) is a sexually dimorphic with males' AGD measuring longer than females, and considered as a sensitive marker of in utero exposure to androgens, based on animal models and the human literature[1,2]. In the rat experiment, studies identified a fetal masculinization programming window [MPW], within which androgen action determines adult reproductive organ size and AGD [1,3]. As the critical period of fetal androgen exposure in humans is inaccessible, the AGD measurement offers the possibility of reflecting this hidden process [1,2]. Consistent with rat experimental data, the AGD measured in men was found to be associated with male reproductive health including congenital malformations, testis size, penis length, spermcount/ semen quality, testosterone levels, and prostate cancer [4-11]. In women, associations with the AGD were suggested with fertility, clitoris length, adult testosterone levels, ovarian function, endometriosis, polycystic ovary syndrome (PCOS), and pelvic organ prolapse [12-20].

It is well-established that fetal events can create predisposition to disease in adulthood. The AGD belongs to an anthropometric measurement that may be stable from childhood to adult age in healthy individuals [1,2]. Numerous studies have reported population data for AGD and utilized the methods to assess fetal androgen action across a wide range of clinical disorders and study androgen-induced individual differences and gender development [1, 2, 21, 22]. The AGD also appears to be a valid biomarker to

evaluate the effects of adverse environmental compounds on human reproductive development [2,23]. Moreover, it is worth mentioning that this measurement is non-invasive and inexpensive.

The AGD in women was usually measured in two ways [1,2]. First, AGD-AC was the distance from the anus to the anterior clitoris. Second, AGD-AF was distance from the anus to the posterior fourchette. Both AGD-AC and AGD-AF are reliable and replicable measurements among examiners using a standard way, but they are probably affected by body mass index/adiposity, particularly the AGD-AC [1,24]. Besides AGD-AC and AGD-AF, clitoris to urethral meatus distance (CUMD) has been also considered to likely reflect the extent of prenatal androgen exposure [25], but it was less studied. Women with longer CUMD measures are supposed to be exposed to higher levels of prenatal androgens than women with shorter distances, and a shorter CUMD in a woman increased her likelihood of experiencing orgasm in sexual intercourse [25].

The 2:4 digit ratio also shows sexually dimorphic with men' ratio less than women, and is a putative indication of prenatal sex hormone exposure, but inconsistently between studies [1]. Based on many researches, the AGD rather than the 2:4 digit ratio is more likely to provide an accurate biomarker of fetal androgen exposure in humans [1,21-22].

To our knowledge, to date, no published work has examined the association between the CUMD and the AGD or digit ratio in women. The aim of this study was to investigate the correlation of CUMD with the AGD or digit ratio, and the affect of body weight on the CUMD and AGD.

## Methods

### 1. Participants

The 117 subjects are women who visited the gynecological or psychosomatic clinic of hospitals and agreed on participation after listening to explanations about the study. Eligibility criteria included age 18-45, regularly menstruating, nulliparous with no pregnancy lasting more than ten weeks, not currently receiving any treatments to control the secretion of hormones (including taking birth control pills, administering gonadotropin releasing hormone, and hormone replacement therapy), no evidence of any hormonal disorder (including PCOS), no history of injury to or surgery on the genital region, no history of congenital anatomical abnormalities in genital organs including Mullerine Agenesis, and no history of an injury to the 2nd or 4th digit of both hands. The study described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and was approved by the Ethics Committee at the Pudong New Area Mental Health Center affiliated to Tongji University School of Medicine. The written informed consent was obtained from all subjects.

### 2. Anthropometric measurements

Anthropometric data were got on the same day. Height was measured by rounding off to the nearest tenth in centimeter (cm). Weight was measured by rounding off to the nearest tenth in kilogram (kg). Body mass index (BMI) was calculated as weight in kilograms divided by squared height in meters. BMI generally correlates highly with adiposity, BMI cut-offs for underweight, normal range of weight and overweight are  $\leq 18.5$ , 18.5-22.9 and  $\geq 23$ , respectively in adult Asians, according to the WHO criteria[26].

The AGD and CUMD measurements were taken using a digital caliper (Carbon Fiber Composites Digital Caliper, Wuxi Kaibaoding Tool Limited Company, Jiangsu, China), following procedures described elsewhere [18,25]. The subjects were first placed in the supine position and changed to the lithotomy position in which the legs are spread apart to be put on rests. The AGD-AC was measured as the distance from the center of the anus to the anterior clitoral surface (Fig. 1); The AGD-AF was measured as the distance from the center of the anus to the posterior fourchette. The CUMD was measured as the distance from the underside of clitoral glans to the center of the urinary meatus. In order to improve accuracy, two examiners performed each of these measurements three times, the mean value of the six measurements of each distance was used.

Measurement of Digit Ratio: A photograph of both hands was taken using a digital camera. The hands were held in supination and fingers completely extended. The lengths of index and ring fingers of both hands were measured from the bottom crease of each digit to the finger tip, using tools in Adobe Photoshop [27]. For each hand, the digit ratio (2D:4D) was subsequently calculated, namely dividing index finger (2D) length by ring finger (4D) length. Mean of right and left hand ratio was taken as mean 2D:4D ratio for each individual.

### 3. Statistical analyses

The summary statistics on subjects for the variables of interest were calculated. These included the five outcome variables CUMD, AGD-AF, AGD-AC, 2D:4D right hand, and 2D:4D left hand, as well as several potential covariates (height, weight, BMI). We used t-tests and calculated Spearman's correlations to examine relationships between these variables. All analyses were conducted in SPSS Version 23. A P value of  $<0.05$  was deemed significant.

## Results

### 1. Characteristic of the study populations

117 subjects, who met the inclusion criteria, were recruited. All subjects are Chinese women and reported being right handed. Table 1 shows the general characteristics of the study subjects. The mean age was  $28.5 \pm 6.7$  years (min-max: 18–45) and the mean BMI was  $21.5 \pm 3.4$  kg/m<sup>2</sup> (min-max: 15.4–32.0). The mean CUMD was  $23.0 \pm 4.5$  (min-max: 11.9–34.4).

Table 1  
Characteristic of the study population (n = 117)

Characteristic	Mean $\pm$ SD(min-max)
Age(years)	28.5 $\pm$ 6.7 (18–45)
Height(cm)	163.0 $\pm$ 5.7(147–175)
Weight(kg)	57.1 $\pm$ 9.4(40–86)
BMI(kg/m <sup>2</sup> )	21.5 $\pm$ 3.4(15.4–32.0)
CUMD(mm)	23.0 $\pm$ 4.5(11.9–34.4)
AGD-AC(mm)	94.9 $\pm$ 9.8(69.7-126.3)
AGD-AF(mm)	28.4 $\pm$ 6.1 (14.5–45.7)
2D:4D(left)	0.98 $\pm$ 0.04(0.88–1.07)
2D:4D(right)	0.96 $\pm$ 0.04(0.88–1.06)

## 2. The correlations between CUMD and AGD measures, digit ratios, and the influence of body weight

In bivariate correlation analyses, no statistically significant associations were observed with the CUMD and AGD measurements (Table 2). Although the two AGD measurements (AGD-AC and AGD-AF) were moderately correlated with one another ( $r = 0.474$ ,  $p < 0.001$ ), the correlation between AGD-AC and CUMD was weak ( $r = 0.172$ ,  $p = 0.063$ ). However, Table 3 showed that both AGD-AC and AGD-AF were notably correlated with weight ( $r = 0.290$ ,  $p = 0.002$  and  $r = 0.189$ ,  $p = 0.041$ ; respectively) and BMI ( $r = 0.341$ ,  $p < 0.001$  and  $r = 0.204$ ,  $p = 0.027$ ; respectively), and there was no correlation between CUMD and weight or BMI.

Table 2  
Spearman correlations between CUMD or AGD measures and height, weight, BMI [r (p-value)] with all subjects (n = 117)

	AGD-AC	AGD-AF	2D:4DLeft	2D:4DRight
CUMD	0.172 (0.063)	-0.014 (0.879)	-0.160 (0.084)	-0.060 (0.519)
AGD-AC	–	<b>0.474</b> <b>(0.000)</b>	0.074 (0.427)	0.037 (0.690)
AGD-AF	–	–	-0.056 (0.550)	0.011 (0.907)

Table 3  
Spearman correlations between CUMD or AGD measures and height, weight, BMI [r (p-value)] with all subjects (n=117)

	Height	Weight	BMI
CUMD	0.102 [0.272]	0.063 [0.500]	0.049 [0.603]
AGD-AC	-0.005 [0.956]	<b>0.290</b> [0.002]	<b>0.341</b> [0.000]
AGD-AF	-0.010 [0.911]	<b>0.189</b> [0.041]	<b>0.204</b> [0.027]

For further understanding of influences of weight / BMI on AGD-AC, AGD-AF or CUMD, we compared the general characteristics of three groups with different body weight (Table 4). The CUMD between normal range-weight group and overweight group was no different ( $23.2 \pm 4.4$  vs  $23.1 \pm 4.4$ ,  $p = 0.788$ ), but compared with normal range-weight group, the AGD-AC of the overweight group was significantly longer ( $100.3 \pm 11.3$  vs  $93.6 \pm 8.2$ ,  $p = 0.010$ ), and the AGD-AF also appeared longer in the overweight group although without significant difference ( $30.6 \pm 6.7$  vs  $27.3 \pm 5.6$ ,  $p = 0.366$ ). Meanwhile, no matter the CUMD, AGD-AC or AGD-AF, there was no significant difference between normal range-weight group and underweight group. Furthermore, the CUMD of 86 non-overweight subjects was obviously correlated with the AGD-AC ( $r = 0.236$ ,  $p = 0.028$ ) (Table 5).

Table 4  
Comparison of the general characteristics of three groups with different body weight

Variable	overweight (n=31)	p1	normal (n=67)	underweight (n=19)	p2
Age	31.1±7.0	0.620	27.6±6.5	27.5±6.3	0.873
Menarcheal Age	12.8±1.4	0.927	13.3±1.2	13.6±1.4	0.655
Height [cm]	162.0±5.9	0.962	163.0±5.5	164.7±5.8	0.359
Weight [kg]	68.4±8.5	<b>0.000</b>	54.7±4.8	47.1±4.0	0.310
BMI (kg/m <sup>2</sup> )	26.0±2.7	0.791	20.6±1.3	17.3±0.9	0.149
CUMD (mm)	23.2±4.4	0.788	23.1±4.4	21.8±4.8	0.893
AGD-AC [mm]	100.3±11.3	<b>0.010</b>	93.6±8.2	90.6±9.2	0.502
AGD-AF [mm]	30.6±6.7	0.366	27.3±5.6	28.3±6.0	0.588
Left 2D:4D Ratio	1.00±0.04	0.528	0.97±0.04	0.98±0.04	0.261
Right 2D:4D Ratio	0.97±0.04	0.985	0.96±0.04	0.96±0.03	0.737
The p1 value: overweight group compared with normal group; the p2 value: underweight group compared with normal group.					

Table 5  
Spearman correlations between CUMD and AGD measures [r (p-value)] with non-overweight subjects (n = 86)

	AGD-AC	AGD-AF
CUMD	<b>0.236</b> <b>(0.028)</b>	0.011 (0.092)
AGD-AC	--	<b>0.546</b> <b>(0.000)</b>

## Discussion

In our studies, the CUMD was measured from the underside of clitoral glans to the center of the urinary meatus, and the clitoral glans was not included. The mean CUMD (23.0 ± 4.5, min-max: 11.9–34.4 mm) in our sample was basically consistent with Bonaparte's sample (2.3 ± 0.1 cm) in an early literature [25], but was obviously shorter than ones (28.5 ± 7.1mm, min-max: 16-45mm; 3.17 ± 0.98cm, min-max: 1-6cm),

recently reported by Lloyd et al and Krissi et al respectively [27, 28]. The difference may be based on race or ethnicity.

The distance from clitoris to urethral orifice (CUMD), as one of genital dimensions of normal women, or as a possible factor associated with sexual function was studied [25, 28–30]. Moreover, the CUMD is a part of perineum. The embryogenesis and development of perineum is androgen mediated as evidenced by the larger anogenital distance (AGD) observed in men compared with women [1, 2, 13]. The CUMD is hopeful as a biomarker of prenatal androgen exposure, and probably equivalent to well-defined AGD-AC or AGD-AF. However, CUMD was weakly associated with AGD-AC in our primary analysis of all subjects, to be no statistical significance, although the correlation between AGD-AC and AGD-AF was up to medium, corresponding to the result reported elsewhere [31].

Androgen exposure during the MPW determines the maximum “potential” adult size of AGD, but secondary changes in AGD in adults may also have occurred, while the androgen-estrogen balance has been altered (eg, obesity, pregnancy, aging, and late-onset hypogonadism) [1–3, 24, 32]. Our data in further studies clearly demonstrated that the AGD-AC and AGD-AF of adult women, particularly the former, were lengthened with obesity. Meanwhile, the CUMD was not affected with increase or decrease of body weight. Exclusion of obesity, the CUMD was significantly correlated with AGD-AC, it implied that the CUMD, very likely same as AGD-AC, was affected by fetal androgen. Furthermore, the CUMD could be a marker of prenatal androgen exposure without influence of body weight. This was the advantage of CUMD indicator, compared to AGD-AC/AGD-AF indicators which were frequently used in the studies of possible role of prenatal androgen exposure. For an example, several recent studies demonstrated that AGD-AC/AGD-AF in adult patients with PCOS were longer than control, implying that extreme prenatal androgen exposure contributes to PCOS [18, 19]. Assessment of AGD-AC/AGD-AF was suggested as a diagnostic tool in PCOS [33]. But the PCOS patients usually have metabolic problems and obesity symptoms [34], therefore, eliminating the influence of obesity should be emphasized. We proposed that the CUMD measurement had better be included in the studies as a clinical or toxicological marker for fetal androgen action and risk for reproductive disorders.

The ratio between the second and fourth digit is associated with the estimated ratio of prenatal testosterone relative to prenatal estradiol, and the digits development is also androgen/estrogen mediated [35]. But the sexual dimorphic growth of digits from birth to adulthood could be due to postnatal or pubertal factors, rather than solely being the result of fetal androgen exposure [1]. Therefore, it is not surprised that the correlations between the CUMD and digit ratios in our studies were no significant meaning.

Taking into account the limitations of present study, the following points have to be pointed out. The sample is small, and the populations in our study were not healthy subjects who were randomly selected, they were patients suffered from various gynecological or psychosomatic diseases, although the admission and exclusion criteria were strictly enforced. Whereas, the body fat distribution (such as

measuring the circumference of chest, waist and hip) was not studied, the lower abdominal or gluteal-femoral obesity might have a stronger impact on the AGD-AC/AGD-AF.

## **Conclusion**

In conclusion, our results indicated that the CUMD could be a marker of prenatal androgen exposure without influence of body weight, superior to AGD-AC or AGD-AF.

## **Declarations**

## **Funding**

This study was supported by the Shanghai Pudong Municipal Health commission, China (PWZzk2017-20; PWYgy2018-10).

## **Competing interests**

The authors declare that they have no competing interests.

## **Availability of data and material**

The data and materials described in the current study are available from the corresponding author on reasonable request.

## **Authors' contributions**

BZ took part in project development, manuscript writing; ZL collected data, analyzed data and contributed to manuscript writing. MX, HX, and HL were involved in collection of data.

## **Ethics approval and consent to participate**

Ethical approval was obtained from the Ethics Committee at the Pudong New Area Mental Health Center affiliated to Tongji University School of Medicine. The written informed consent was obtained from all subjects.

## **Consent for publication**

Not applicable.

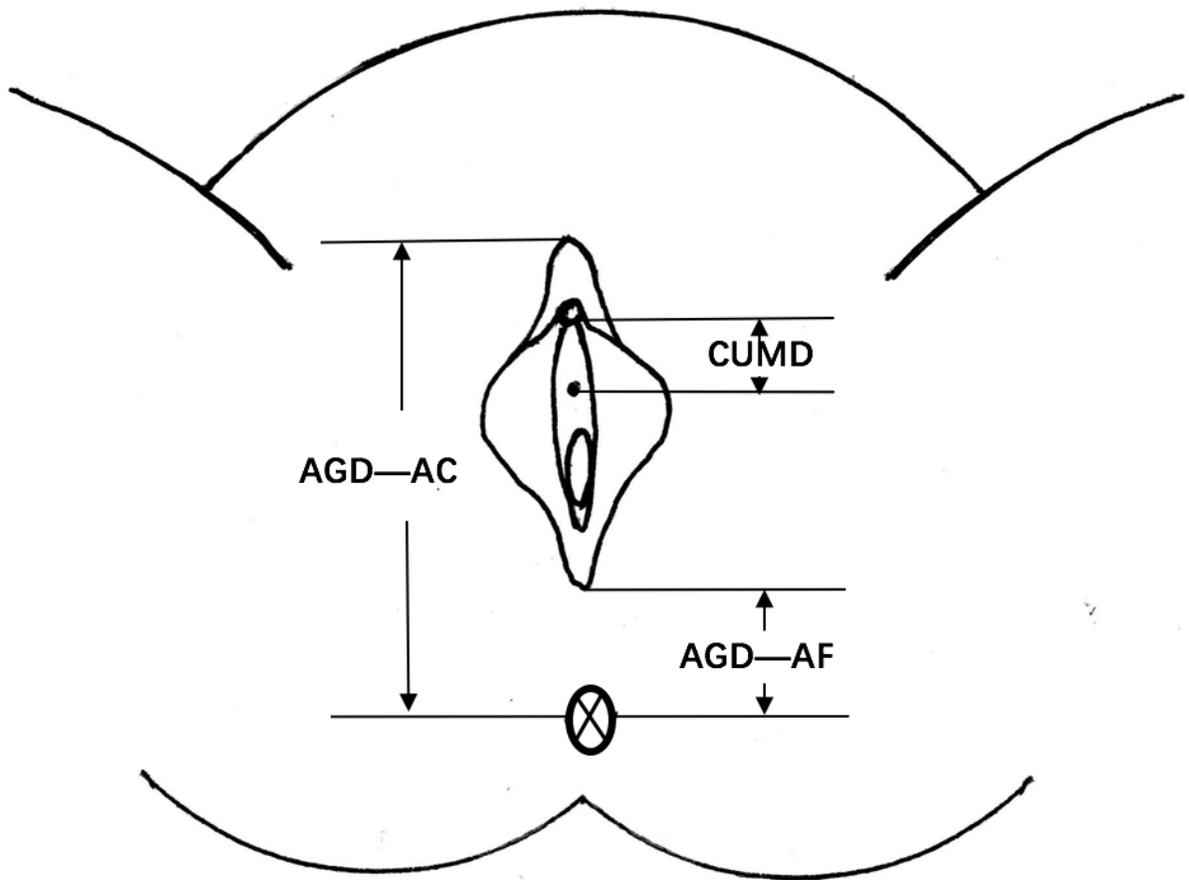
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## Figures



**Figure 1**

The graphic displayed measurements of CUMD, AGD-AC and AGD-AF. CUMD, from the underside of clitoral glans to the center of the urinary meatus; AGD-AC, from the center of the anus to the anterior clitoral surface; AGD-AF, from the center of the anus to the posterior fourchette.