Relationship Between Uterine and Ovarian Arterial Blood Flow Measured by Doppler Sonography at Different Stages of Puberty

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SUMMARY

Objective: Measuring blood flow using a special form of color Doppler ultrasonography can help radiologists to identify the stages of development of organs, such as the uterus and ovary. The aim of this study was to determine the relationship between arterial blood flow to the uterus and ovaries at different stages of puberty.

Materials and Methods: Sixty girls referred to the Children's Medical Center in Tehran for the evaluation of pubertal stages were included in the study. They were divided into three subgroups: girls without primary puberty signs ($n = 20$); girls with these puberty signs but without the beginning of menstruation ($n = 20$); and girls with signs of puberty and menstruation ($n = 20$). Uterus and ovary volumes were measured with the use of a 3.5-MHz convex transducer (Logic 500 Pro; General Electric, Milwaukee, WI, USA) and Doppler flow measurements of the uterine vessels were performed transabdominally with a 3.5-MHz color Doppler system (AU4 Idea; Esaote Biomedica, Genoa, Italy).

Results: We found no significant differences between the groups in terms of either resistance index or pulsatility index of the right ovary, left ovary or uterus. However, there were relationships between the volume of the uterus and pubertal stages, and also between the volume of the ovaries and these stages.

Conclusion: Uterine and ovarian arterial blood flow, measured by Doppler sonography, was not useful for the evaluation of pubertal stages. However, it should be investigated with a greater sample size. [*Taiwan J Obstet Gynecol* 2008;47(1):62–65]

Key Words: blood flow, Doppler sonography, ovary, puberty, uterine

Introduction

Measuring blood flow using a special form of color Doppler ultrasonography (CDS) can help radiologists to identify the stages of organ development and also life-threatening complications in serious diseases. Researchers have used CDS in preference to other ultrasound procedures, because it shows the presence or absence of blood flow in the organs, and whether or not that flow is normal, increased or absent. CDS is also noninvasive and free of ionizing radiation.

In clinical practice, assessment of reproductive organs and pubertal stages in the individual child is extremely useful [1]. This technique can present high-resolution images of these organs in the female and allow the analysis of blood flow in their vessels [2]. By this technique, the evaluation of cyclic hormonal variations and subsequent ovarian and endometrial neoangiogenesis leading to significant changes in vascular patterns can be noninvasively studied [3].

The evaluation of pubertal stages by CDS has been performed in several previous studies, but there are few studies in our country concerning the role of this technique in the evaluation of pubertal stages. The aim of this study was to determine the relationship between arterial blood flow in the uterus and ovaries at different stages of puberty in girls referred to the Children's Medical Center in Tehran.

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Materials and Methods

Study population

The study protocol was in accordance with the Helsinki II declaration and was approved by the Hospital Research Review Committee. Sixty girls referred to the Children's Medical Center in Tehran for the evaluation of pubertal stages between January 2006 and July 2006 were included. The girls participated in the study after both informed consent from parents and agreement from the minors had been obtained. Patients with chronic disease, including Cushing's syndrome, hyperprolactinemia, ovarian cysts (> 10 mm in maximum diameter) and polycystic ovaries (> five subcortical follicles 2–10 mm in maximum diameter, increased ovarian volume and increased ovarian stroma echogenicity), were excluded. Cases of GnRH-independent puberty (i.e. hypo-/hyperthyroidism, sex steroid-secreting tumors, congenital adrenal hyperplasia) were also excluded. No patients had received hormonal therapy before the study.

The pubertal development of all girls was staged by a single examiner, according to the classification of Tanner and Marshall et al [4,5]. On the basis of these stages, the girls were divided into three subgroups: girls without primary puberty signs (T_1); girls with these puberty signs but without the beginning of menstruation (T_2, T_3); and girls with the signs of puberty and menstruation (T_4, T_5). Each subgroup included 20 girls.

Ultrasound and Doppler examination

Uterine and ovarian sonographic examinations were performed with the use of a 3.5-MHz convex transducer (Logic 500 Pro; General Electric, Milwaukee, WI, USA). The ultrasound scans were performed transabdominally when the participants had a full bladder, obtained by voluntary urinary retention and oral administration of fluids. Uterine and ovarian volumes were calculated by measuring length, width and depth, assuming the forms to be ellipsoid, and using the formula based on a prolate ellipsoid:

$$\text{Volume} = \pi/6 \times D1 \times D2 \times D3$$

where D1, D2, and D3 are the maximal longitudinal, anteroposterior and transverse diameters, respectively.

Doppler flow measurements of the uterine vessels were performed transabdominally with a 3.5-MHz color Doppler system (AU4 Idea; Esaote Biomedica, Genoa, Italy). All the patients were in a recumbent position and were evaluated between 8:00 and 11:00 am to exclude the effects of circadian rhythmicity on utero-ovarian blood flow [6]. Furthermore, they rested in a waiting room for at least 15 minutes before being scanned, to minimize external effects on pelvic blood flow [7]. A 50-Hz filter was used to eliminate low frequency signals originating from vessel wall movements. Color flow images of the ascending branches of the uterine arteries were sampled lateral to the cervix in a longitudinal plane [8]. The angle of insonation was always adjusted to obtain maximum color intensity. When good signals were obtained, blood flow velocity waveforms were recorded by placing the sample volume across the vessel and activating the pulsed Doppler mode.

The blood flow velocity spectrum pattern was retrospectively analyzed at the following points: peak systolic (S); at the notch in early diastole (N); peak diastolic (D); and end-diastolic (ED) blood velocity. The time-averaged mean velocities of three even blood velocity waveforms were recorded; the pulsatility index (PI; PI = S − ED/mean velocity) was calculated according to Gosling et al [9] and the resistance index (RI; RI = (S − ED)/S) calculated according to Pourcelot [10]. Increased uterine artery vascular impedance was defined as PI of > 1.20 according to Hofstaetter et al [11].

Statistical analysis

Data are presented as mean ± standard deviation. Statistical analysis (SPSS software; SPSS Inc., Chicago, IL, USA) was performed using one-way analysis of variance. A p value of less than 0.05 was considered as statistically significant.

Results

The mean age of the girls in the three groups were 8.44 ± 1.98 years in girls with stage (T_1), 10.8 ± 1.39 years in girls with stage (T_2, T_3), and 13.5 ± 1.95 years in girls with stage (T_4, T_5). We found no significant differences in either RI or PI for the right ovary, left ovary, or uterus between the three groups (Table 1). However, there were relationships between the volume of the uterus and Tanner stages, and also between the volumes of the two ovaries and these stages (Table 2).

Discussion

There was similarity between the mean age of puberty onset in our study and other large studies [12–15]. Also, according to a similar study in Tehran by Razzaghy-Azar et al, the median age of Tanner stage 2 breast development and Tanner stage 2 pubic hair growth amongst 1,136 girls was 9.74 years and 10.49 years,

Table 1. The pulsatility index (PI) and resistance index (RI) of the left ovary, right ovary and uterine arteries in three subgroups of girls

Indices	Group 1 (T_1)	Group 2 (T_2, T_3)	Group 3 (T_4, T_5)	*p*
Right ovary RI	0.79 ± 0.05	0.79 ± 0.05	0.81 ± 0.06	0.294
Left ovary RI	0.79 ± 0.05	0.79 ± 0.04	0.80 ± 0.05	0.727
Uterine RI	0.79 ± 0.04	0.79 ± 0.04	0.80 ± 0.06	0.798
Right ovary PI	1.55 ± 0.36	1.66 ± 0.43	1.56 ± 0.25	0.777
Left ovary PI	1.51 ± 0.29	2.13 ± 1.9	1.42 ± 0.26	0.305
Uterine PI	1.65 ± 0.29	1.64 ± 0.44	1.47 ± 0.25	0.335

RI = resistance index; PI = pulsatility index.

Table 2. Uterus and ovary volumes according to pubertal stages

Indices	Group 1 (T_1)	Group 2 (T_2, T_3)	Group 3 (T_4, T_5)	*p*
Right ovary volume	279.49 ± 121.20	303.20 ± 71.06	537.60 ± 117.32	< 0.0001
Left ovary volume	225.23 ± 109.97	301.95 ± 99.99	531.36 ± 197.50	< 0.0001
Uterine volume	9,652.09 ± 6,664.84	36,792.15 ± 42,535.08	101,121.26 ± 35,259.27	< 0.0001

respectively. In their study, the median age of menarche in 399 girls was also 12.68 years [16]. Mean age at menarche was 12.91 ± 1.23 years [17], which was similar to our study results.

However, genetic factors, intrauterine growth retardation, nutritional status, adoption and its growth patterns, as well as environmental exposures and psychologic stress, have all been hypothesized to trigger the timing of puberty [18].

We also found a positive relationship between increases in uterus and ovary volumes and pubertal development. In a study by Buzi et al [19] in normal girls, uterus length increased with age, although no cut-off values could be defined between different age ranges. Also in their study, ovarian volume was significantly greater in pubertal girls with Tanner breast stage 2 than in those with only pubic and/or axillary hair [19]. Also, in a study by Griffin et al, ovarian volume increased exponentially with age, but no relationship with pubertal stage (independent of age) could be demonstrated [20]. In a study by Seth et al [21], statistically significant increases in uterine height and ovarian volume were observed with progressive pubertal stages. The maximum increase in uterine height was observed during the transition from Tanner stage 2 to stage 3. The ovarian volume, after showing an initial increase, tended to plateau, and there was no significant increase from stage 4 to stage 5 [21]; whereas in our study, the ovarian and uterine volumes increased continuously from Tanner stages 1 to 5. It has been indicated that the pelvic ultrasound parameters change progressively from birth to maturity. Pelvic ultrasound variables reach adult values during puberty, with differences in the timing that may reflect ethnic variations [19].

In our study, we found no significant relationship between increases in both RI and PI and pubertal stages. In the study by Laursen et al [22], a significant increase in uterine artery flow velocity during puberty was found, with an increase in average velocity from Tanner breast stages 1 and 2 to 5, followed by a slight decrease in adults. Also, the PI was similar in breast stage 1, stage 2, and in adults. Furthermore, a significant decline in vascular resistance, expressed by the PI, was observed in the mid-pubertal period, reflecting increasing blood flow to the rapidly growing uterus [22]. However, in a study by Ziereisen et al, a progressive modification of the Doppler signal pattern of the uterine artery during the establishment of puberty was observed [23]. Of course, several studies have demonstrated that the measures of PI and RI in the uterus and ovaries were different in the various stages of the menstrual cycle [24,25], and we did not consider this relationship in our study.

In conclusion, according to our study results, there are relationships between the volumes of both the uterus and ovaries and pubertal stages, but no relationship between either the RI or PI of these organs and pubertal stages was observed. Our study indicates that uterine and ovarian arterial blood flow, measured by Doppler sonography, is not useful for the evaluation of pubertal stages in our population. However, more studies with a greater sample size should be done in the future.

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References

1. Juul A, Teilmann G, Scheike T, et al. Pubertal development in Danish children: comparison of recent European and US data. *Int J Androl* 2006;29:247–55.
2. Zaidi J, Jacobs H, Campbell S, Tan SL. Blood flow changes in the ovarian and uterine arteries in women with polycystic ovary syndrome who respond to clomiphene citrate: correlation with serum hormone concentrations. *Ultrasound Obstet Gynecol* 1998;12:188–96.
3. Engmann L, Sladkevicius P, Agrawal R, Bekir J, Campbell S, Tan SL. The pattern of changes in ovarian stromal and uterine artery blood flow velocities during *in vitro* fertilization treatment and its relationship with outcome of the cycle. *Ultrasound Obstet Gynecol* 1999;13:26–33.
4. Tanner JM. *Growth at Adolescence*. Oxford: Blackwell & Mott, 1962.
5. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child* 1969;44:291–303.
6. Zaidi J, Jurkovic D, Campbell S, Okokon E, Tan SL. Circadian variation in uterine artery blood flow indices during the follicular phase of the menstrual cycle. *Ultrasound Obstet Gynecol* 1995;5:406–410.
7. Battaglia C, Artini PG, D'Ambrogio G, Galli PA, Genazzani AR. Uterine and ovarian blood flow measurement. Does the full bladder modify the flow resistance? *Acta Obstet Gynecol Scand* 1994;73:716–8.
8. Battaglia C, Artini PG, D'Ambrogio G, Genazzani AD, Genazzani AR. The role of color Doppler imaging in the diagnosis of polycystic ovary syndrome. *Am J Obstet Gynecol* 1995;172:108–13.
9. Gosling RG, Dunbar G, King DH, et al. The quantitative analysis of occlusive peripheral arterial disease by a non-intrusive ultrasonic technique. *Angiology* 1971;22:52–5.
10. Pourcelot L. Applications clinique de l'examen Doppler transcutane. In: Peronneau P, ed. *Velocimetric Ultrasonor Doppler*. Paris: Inserm, 1974:213–40.
11. Hofstaetter C, Dubiel M, Gudmundsson S, Marsal K. Uterine artery color Doppler assisted velocimetry and perinatal outcome. *Acta Obstet Gynecol Scand* 1996;75:612–9.
12. Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdony CJ, Bhapkar MV, Koch GG, Hasemeier CM. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network. *Pediatrics* 1997;99:505–12.
13. Harlan WR, Harlan EA, Grillo GP. Secondary sex characteristics of girls 12 to 17 years of age: the US Health Examination Survey. *J Pediatr* 1980;96:1074–8.
14. Lee PA. Normal ages of pubertal events among American males and females. *J Adolesc Health Care* 1980;1:26–9.
15. Roche AF, Wellens R, Attie KM, Siervogel RM. The timing of sexual maturation in a group of US white youths. *J Pediatr Endocrinol Metab* 1995;8:11–8.
16. Razzaghy-Azar M, Moghimi A, Sadigh N, et al. Age of puberty in Iranian girls living in Tehran. *Ann Hum Biol* 2006;33:628–33.
17. Ayatollahi SM, Dowlatabadi E, Ayatollahi SA. Age at menarche in Iran. *Ann Hum Biol* 2002;29:355–62.
18. Teilmann G, Boas M, Petersen JH, Main KM, Gormsen M, Damgaard K, Brocks V, Skakkebaek NE, Jensen TK. Early pituitary-gonadal activation before clinical signs of puberty in 5- to 8-year-old adopted girls: a study of 99 foreign adopted girls and 93 controls. *J Clin Endocrinol Metab* 2007; 92:2538–44.
19. Buzi F, Pilotta A, Dordoni D, Lombardi A, Zaglio S, Adlard P. Pelvic ultrasonography in normal girls and in girls with pubertal precocity. *Acta Paediatr* 1998;87:1138–45.
20. Griffin IJ, Cole TJ, Duncan KA, Hollman AS, Donaldson MD. Pelvic ultrasound measurements in normal girls. *Acta Paediatr* 1995;84:536–43.
21. Seth A, Aggarwal A, Sandesh K, Solanki RS, Aneja S, Kumar G. Pelvic ultrasonography in pubertal girls. *Indian J Pediatr* 2002;69:869–72.
22. Laursen EM, Holm K, Brocks V, Jarden M, Müller J. Doppler assessment of flow velocity in the uterine artery during pubertal maturation. *Ultrasound Obstet Gynecol* 1996;8:341–5.
23. Ziereisen F, Heinrichs C, Dufour D, Saerens M, Avni EF. The role of Doppler evaluation of the uterine artery in girls around puberty. *Pediatr Radiol* 2001;31:712–9.
24. Sladkevicius P, Valentin L, Marsál K. Blood flow velocity in the uterine and ovarian arteries during menstruation. *Ultrasound Obstet Gynecol* 1994;4:421–7.
25. Taylor KJ, Burns PN, Wells PN, Conway DI, Hull MG. Ultrasound Doppler flow studies of the ovarian and uterine arteries. *Br J Obstet Gynaecol* 1985;92:240–6.