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Ovarian and Uterine Findings in Pelvic Sonography

Comparison Between Prepubertal Girls, Girls With Isolated Thelarche, and Girls With Central Precocious Puberty

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Objective. To describe pelvic sonographic findings in girls as old as 7 years, to compare prepubertal girls with girls who had isolated thelarche or central precocious puberty, and to verify the accuracy of sonographic variables for distinguishing prepubertal girls from girls with central precocious puberty. ***Methods.*** Ninety-six prepubertal girls and 2 reference groups (8 girls with isolated thelarche and 8 with idiopathic central precocious puberty) were included. Ovaries were classified morphologically as homogeneous, paucicystic, macrocystic, multicystic, and having isolated cysts. Receiver operating characteristic curves were used to choose the best cutoff points. ***Results.*** Chronologic and bone age were correlated with uterine length, area, and volume and ovarian volume in prepubertal girls ($P < .0001$). Ovarian morphologic characteristics in prepubertal girls differed significantly from those of the reference groups ($P < .0001$). The best cutoff points were uterine length of 4.0 cm, uterine area of 4.5 cm^2, uterine volume of 3.0 cm^3, and ovarian volume of 1.0 cm^3. ***Conclusions.*** Uterine and ovarian growth are proportional to age in prepubertal girls. Mean ovarian volume greater than 1 cm^3 showed 100% sensitivity and specificity for discriminating between prepubertal girls and girls with central precocious puberty. Microcysts are common in prepubertal girls, but the presence of 6 or more follicles up to 10 mm in diameter may suggest central precocious puberty in girls younger than 8 years. ***Key words:*** child; ovary; puberty, precocious; sonography; uterus.

Abbreviations
CPP, central precocious puberty; GnRH, gonadotropin-releasing hormone; IT, isolated thelarche; ROC, receiver operating characteristic

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Sonography is an important imaging method for assessing pelvic disorders in children. This noninvasive, painless, and low-risk procedure is an excellent diagnostic technique in pediatric and adolescent gynecology[1–3] and has been widely used in the evaluation of children and adolescents with ambiguous genitalia, pelvic masses, pelvic pain, and late or precocious puberty.[4–6]

Sexual precocity is a common finding in pediatric gynecologic clinics and is characterized by the appearance of secondary sex characteristics before 8 years of age.[7,8]

Central precocious puberty (CPP) is a form of sexual precocity triggered by premature hypothalamic-pituitary-gonadal axis maturation and dependent on gonadotropin-releasing hormone (GnRH).[9] It may be idiopathic, familial, or secondary to a dysfunction of the central nervous system (tumor, malformation, trauma, or

infection). The development of secondary sex characteristics in CPP follows a sequence similar to that of normal puberty (thelarche, pubarche, and then menarche) but takes place at an earlier age. In this process, growth and bone maturation are accelerated, together with progressive development of sex characteristics. The speed of uterine and ovarian growth is increased. In addition, CPP may determine a decrease in final height and development of psychological problems associated with early menstruation.

Unlike CPP, isolated thelarche (IT) is not associated with maturation of the hypothalamic-pituitary-gonadal axis. These cases are usually self-limiting, although 10% may progress to CPP.[9] In IT, breast development may be unilateral or bilateral and is not associated with development of the areola.[7] It usually occurs before 2 years of age, before the gonadotropin-estradiol negative feedback mechanism becomes sensitive. No other signs of pubertal progression, such as height velocity, bone age acceleration, and progressive development or appearance of other secondary sex characteristics, are observed. In girls with IT, uterine and ovarian volumes are similar to those of prepubertal girls.[10–13] Macrocysts (follicles measuring 10–20 mm in diameter) may be found in patients with IT.[13–15]

We have recently shown that uterine and ovarian sizes are influenced by age and pubertal status.[16] However, although prepubertal girls and those with IT differ from girls with CPP in terms of uterine and ovarian dimensions,[10–13] adequate cutoff points have not yet been established to discriminate between these populations. In addition, some studies have reported overlapping values for these patients, which have made it more difficult to establish cutoff points.[10,13] The definition of morphologic standards for uterine and ovarian sizes is essential for a more effective use of pelvic sonography.[17]

Because sexual precocity begins before 8 years of age, and because age influences ovarian and uterine size, the purpose of this study was (1) to describe pelvic sonographic findings in 1- to 7-year-old prepubertal girls, (2) to compare them with findings for 2 reference groups, namely girls with IT and girls with idiopathic CPP, and (3) to verify the accuracy of sonographic variables to discriminate between prepubertal girls and girls with CPP.

Materials and Methods

This cross-sectional study was carried out at the Radiology Department, Hospital da Criança Santo Antônio, and at the Gynecological Endocrinology Unit, Hospital de Clínicas de Porto Alegre. Three groups were assessed. The prepubertal group included 96 girls between 1 and 7 years of age (mean [SD], 4.02 [1.90] years), selected consecutively and referred to the Radiology Department at Hospital da Criança Santo Antônio. Girls with any gynecologic or endocrine disease, severe or weakening conditions, urogynecologic malformations, or pelvic pain and those who had had the uterus, ovaries, or both surgically removed were excluded from the study. The 96 patients included in the study were investigated for urinary infection or abdominal discomfort between August 1998 and April 1999. None of the girls included in the study had any abdominal or pelvic abnormality shown on sonography.

This group of 96 prepubertal girls was compared with 2 age-matched reference groups from the Gynecological Endocrinology Unit at Hospital de Clínicas de Porto Alegre. These girls were consecutively assessed and had sexual precocity: IT group, n = 8; mean (SD) age, 2.75 (1.75) years; and idiopathic CPP group, n = 8; mean age, 6.13 (1.46) years.[18]

The Ethics Committee of the Hospital de Clínicas de Porto Alegre approved the research project. Informed consent was obtained from every parent or guardian. All girls with sexual precocity underwent laboratory investigation: hormone level measurements (basal luteinizing hormone and follicle-stimulating hormone, luteinizing hormone and follicle-stimulating hormone 30 and 60 minutes after intravenous GnRH, estradiol, thyroid-stimulating hormone, 17-hydroxyprogesterone, sulfate dehydroepiandrosterone, testosterone, and androstenedione), pelvic sonography, hand and wrist radiography for assessment of bone age, and brain computed tomography if CPP was confirmed.

The criteria for the diagnosis of IT were normal bone age, prepubertal height velocity (<6 cm/y), and prepubertal response to GnRH testing. The criteria for the diagnosis of CPP were accelerated bone age (SD >2), pubertal height velocity (>6 cm/y), pubertal response to GnRH testing (maximal luteinizing hormone–follicle-stimulating hormone ratio >1), and progressive development

of sex characteristics. Brain computed tomography showed no abnormalities in any patient with CPP. All other endocrinologic problems were ruled out. None of the 112 girls was or had been receiving any hormonal treatment.

Scanning was performed through a full urinary bladder with standard commercially available sonographic equipment and a 3.5-MHz probe. Images were obtained and interpreted by the same sonographer. The best images of the sagittal and axial views were recorded and used to obtain the measurements included in the study.

The uterine volume was calculated in cubic centimeters by the ellipse formula ($A \times B \times C \times 0.5233$),[17,19] where A was the largest longitudinal diameter, B was the largest anteroposterior diameter, and C was the largest transverse diameter. The uterine area was calculated in square centimeters by multiplying longitudinal and transverse diameters ($A \times C$). The ovarian volume was calculated in cubic centimeters by the same formula as for the uterine volume. There was no statistical difference between the volume of the right and left ovaries in any patient (Wilcoxon test, $P = .98$). We used the term "bilateral ovarian volume" for the average of the 2 ovarian volumes for each patient. For comparison with other methods of calculating ovarian volume, the term "individual ovarian volume" indicated the volume of right and left ovaries treated separately.

In terms of morphologic characteristics, ovaries were classified as homogeneous (absence of visible follicles or cysts),[20] paucicystic (up to 5 follicles with diameters <10 mm),[13] multicystic (≥6 follicles with diameters <10 mm),[13] macrocystic (at least 1 follicle with a diameter of 10–20 mm),[13] and isolated cysts (at least 1 cyst with a diameter >20 mm).[13] Bone age was interpreted according to the method of Greulich and Pyle[21] by the same radiologist. Pubertal development was classified according to the stages of Marshall and Tanner.[22]

Assessment of the prepubertal group (Hospital da Criança Santo Antônio) by sonography was carried out with a Sonoline 1 sonographic apparatus with 3.5- and 5-MHz transducers (Siemens AG, Munich, Germany). The same physician (E.G.) performed the sonography and reviewed the images for all patients. An Aloka SSD-500 system with 3.5- and 5-MHz transducers (Aloka Co, Ltd, Tokyo, Japan) was used for patients with sexual precocity (Gynecological Endocrinology Unit, Hospital de Clínicas de Porto Alegre). Again, the same physician (M.M.) performed the sonography and reviewed the images for all patients.

A significance level of $P = .05$ was used for statistical analysis. Results are expressed as mean and SD. The sonographic variables (uterine length, uterine area, uterine volume, and ovarian volume) did not have a normal distribution, and the following nonparametric tests were used: Wilcoxon test for related samples, Kruskal-Wallis test for comparison between continuous variables in more than 2 groups, Mann-Whitney test for comparison between continuous variables in 2 groups, Fisher exact test for comparison between categorical variables, and Spearman coefficient for correlation analysis. Receiver operating characteristic (ROC) curves were used for the choice of cutoff points for uterine volume, length, and area and ovarian volume. The positive predictive value, negative predictive value, sensitivity, and specificity of uterine and ovarian dimensions to determine the presence of CPP were calculated.

The sample size was adequate to show differences between the uterine and ovarian dimensions of the CPP group in comparison with prepubertal girls and the CPP group in comparison with girls with IT (β = 94%–100%). To assess interobserver variation, all of the reference patients (CPP and IT) were scanned by the same physician (M.M.). Fifty percent of these patients were also scanned by a second physician (E.G.). There was no difference in sonographic measurements between the 2 physicians performing sonography (Wilcoxon test, $P = .77$) in the 2 hospitals, and the correlation coefficient between observers was very good ($r = 0.84$).

Results

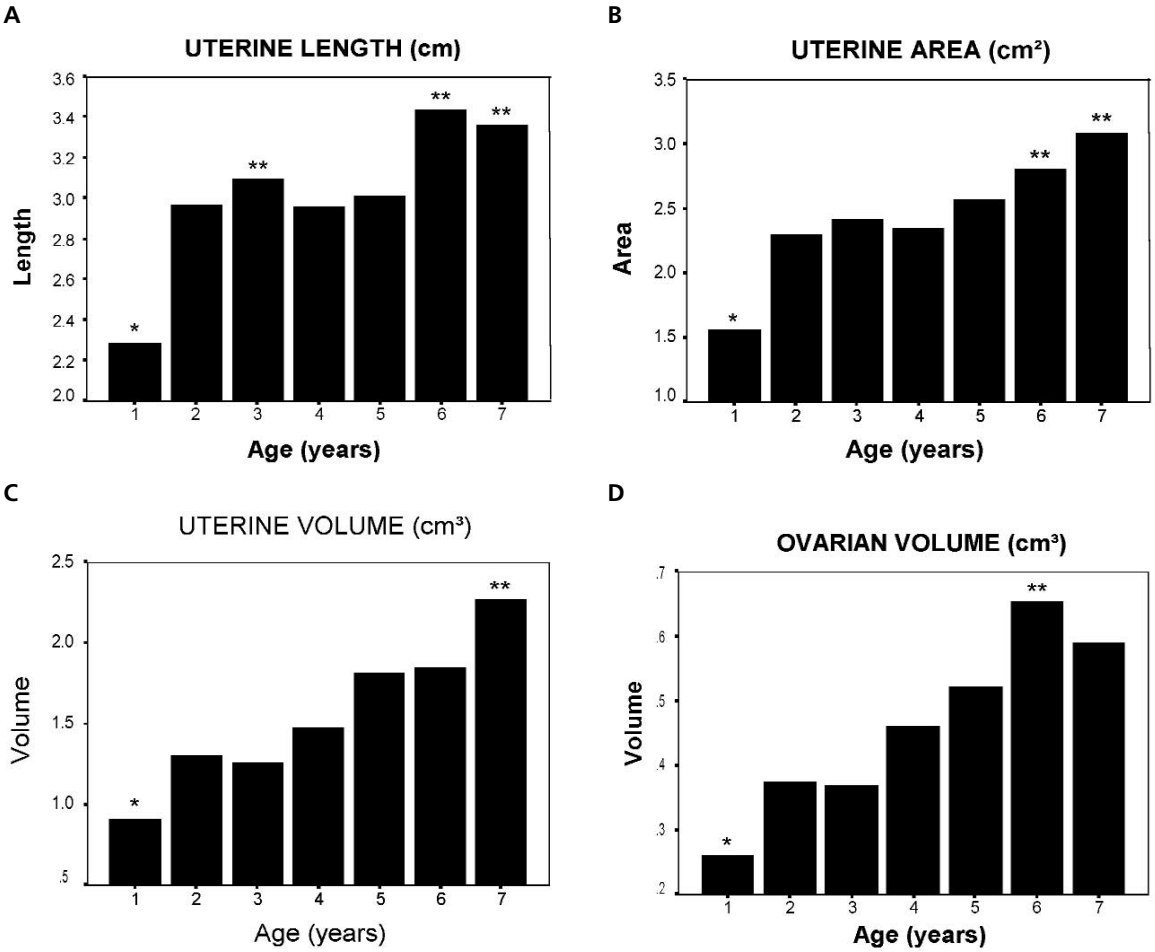
We found a positive correlation between chronologic age and uterine length ($r = 0.45$), uterine area ($r = 0.39$), uterine volume ($r = 0.44$), and ovarian volume ($r = 0.51$) in the prepubertal girls ($P < .001$), as shown in Table 1 and Figure 1. Figure 1 shows the mean values for uterine and ovarian measurements in prepubertal girls younger than 8 years.

Bone age had a good correlation with chronologic age (Spearman $r = 0.88$). Moreover, bone age had a better correlation with sonographic measurements than did chronologic age: uterine

Table 1. Comparison of Values for Uterine Length, Uterine Area, Uterine Volume, and Ovarian Volume of Healthy Prepubertal Girls According to Age

Age, y	n	Uterine Length, cm (n = 90)	Uterine Area, cm^2 (n = 90)	Uterine Volume, cm^3 (n = 90)	Ovarian Volume, cm^3 (n = 73)
r (*P* < .001)		0.45	0.39	0.44	0.51
1	9	2.29 ± 0.56	1.56 ± 0.68	0.87 ± 0.43	0.26 ± 0.12
2	14	2.96 ± 0.47	2.31 ± 0.79	1.29 ± 0.70	0.38 ± 0.11
3	21	3.09 ± 0.45	2.42 ± 0.90	1.38 ± 0.46	0.37 ± 0.11
4	14	2.96 ± 0.50	2.35 ± 0.74	1.48 ± 0.79	0.46 ± 0.14
5	11	3.01 ± 0.42	2.58 ± 0.48	1.82 ± 0.43	0.52 ± 0.22
6	14	3.44 ± 0.32	2.80 ± 0.94	1.85 ± 1.08	0.65 ± 0.23
7	13	3.36 ± 0.56	3.08 ± 1.13	2.28 ± 1.24	0.59 ± 0.25
Mean		3.06 ± 0.55	2.48 ± 0.90	1.55 ± 0.87	0.48 ± 0.20

Figure 1. Uterine and ovarian measurements in healthy prepubertal girls younger than 8 years. **A**, The uterine length of 1-year-old patients (*) was different from that of 3-, 6-, and 7-year-old patients (**) (*P* < .0001); *r* = 0.45; *P* < .001. **B**, The uterine area of 1-year-old patients (*) was different from that of 6- and 7-year-old patients (**) (*P* = .02); *r* = 0.39; *P* < .001. **C**, The uterine volume of 1-year-old patients (*) was different from that of 7-year-old patients (**) (*P* = .008); *r* = 0.44; *P* < .001. **D**, The ovarian volume of 1-year-old patients (*) was different from that of 6-year-old patients (**) (*P* = .004); *r* = 0.51; *P* < .001.



length, $r = 0.47$; $P < .001$; uterine area, $r = 0.50$; $P < .0001$; uterine volume, $r = 0.62$; $P < .0001$; and ovarian volume, $r = 0.59$; $P < .0001$.

Table 2 and Figure 2 show sonographic measurements for prepubertal girls compared with the 2 reference groups (IT and idiopathic CPP). The sonographic variables (uterine length, uterine volume, uterine area, and ovarian volume) of prepubertal girls and girls with IT were different from those of patients with CPP.

Figure 3 shows the ROC curves for each variable, and Table 3 presents the accuracy tests for sonographic measurements according to selected cutoff points. In this group of 1- to 7-year-old girls, the best cutoff points to discriminate between prepubertal girls and girls with CPP were uterine length of 4.0 cm, uterine area of 4.5 cm^2, uterine volume of 3.0 cm^3, and ovarian volume of 1.0 cm^3.

Ovarian morphologic characteristics were also different in the 3 groups ($P < .0001$): homogeneous ovaries were more frequent in the group of prepubertal girls; paucicystic and macrocystic ovaries were more frequent in patients with IT; and multicystic ovaries were more frequent in patients with CPP, as shown in Table 4.

Discussion

Pelvic sonography is an excellent diagnostic technique for gynecologic investigation in children and adolescents.[2,3] There is, however, no consensus in terms of standard values for ovarian and uterine findings, although this would be useful for discriminating between prepubertal girls and pubertal girls requiring treatment, such as in CPP.

Age showed a positive correlation with uterine length, uterine area, uterine volume, and ovarian volume in prepubertal girls younger than 8 years. Some investigators have not found an increase in uterine volume in this age group; however, most studies do not analyze girls younger than 8 years in a separate group.[4,13,19,23–26] As a result, previous reports stating that the size of the uterus and ovaries is stable between 5 and 7 years of age may be biased.[23,24]

In our study, the most prevalent morphologic finding in prepubertal girls was the homogeneous ovary, which is in agreement with other studies.[4,13,23]

Sonographic studies of patients in the reference groups revealed higher values for uterine and ovarian variables in the group with CPP, especially uterine length[10–13] and uterine area.[13]

Table 2. Comparison of Uterine Length, Uterine Volume, Uterine Area, and Ovarian Volume in the 3 Groups Younger Than 8 Years: Healthy Prepubertal Girls, Patients With IT, and Patients With CPP

Group	Age, y	Uterine Length, cm	Uterine Volume, cm^3	Uterine Area, cm^2	Ovarian Volume, cm^3
Prepubertal					
Mean	4.02*	3.06†	1.55†	2.48†	0.48†
n	96	90	90	90	73
SD	1.90	0.55	0.87	0.90	0.20
Minimum	1	1.50	0.25	0.86	0.15
Maximum	7	3.90	4.77	5.25	0.99
IT					
Mean	2.75*	2.70*	1.70*	2.82*	0.75*
n	8	8	8	8	8
SD	1.75	0.53	0.62	0.82	0.54
Minimum	1	2.20	1.00	1.54	0.17
Maximum	6	3.40	2.84	3.84	1.80
CPP					
Mean	6.13	4.47	6.76	9.44	2.03
n	8	8	8	8	8
SD	1.46	0.83	2.52	4.02	0.80
Minimum	3	2.90	3.10	4.64	1.00
Maximum	7	5.60	9.80	13.44	2.95

No significant differences were found between prepubertal girls and girls with IT.
*Different from girls with CPP ($P < .004$).
†Different from girls with CPP ($P < .0001$).

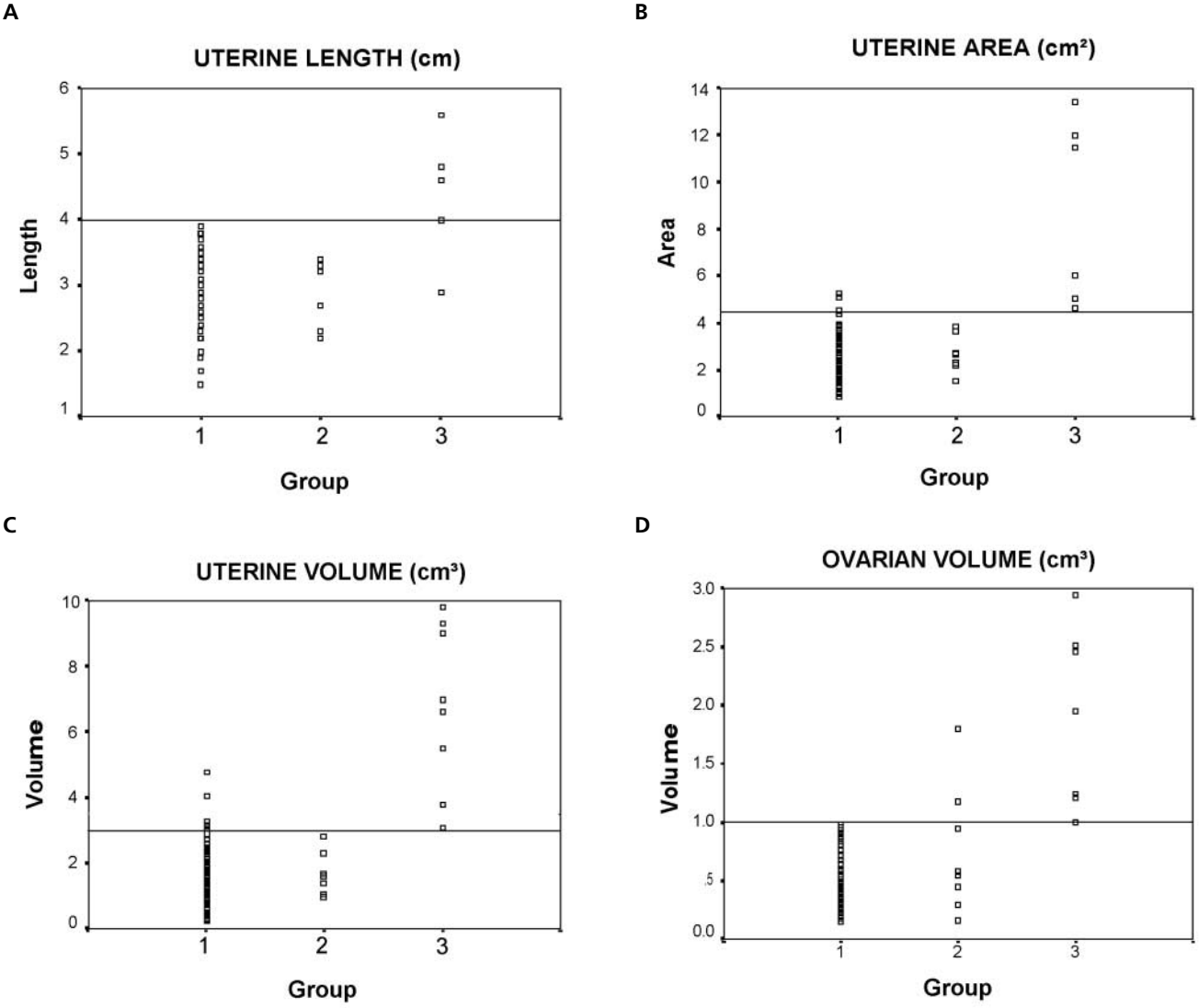
In turn, sonographic findings for the group with IT followed a pattern similar to that of prepubertal girls, in accordance with previous descriptions.[11–13]

In our study, a uterine length of 4.0 cm had sensitivity of 86% and specificity of 100% to discriminate between prepubertal girls and girls with CPP. Haber et al[11] reported sensitivity of 90% and specificity of 100% for a cutoff point of 3.6 cm. Some authors have found maximum values ranging from 3.3 to 3.5 cm,[2,27] whereas others have found values greater than 4 cm.[10–13]

Our data for uterine volume are in agreement with the results of other investigations; uterine volume was greater in patients with CPP than in prepubertal girls[4,11,12] but similar in prepubertal girls and girls with IT.[11,12] The best cutoff point we obtained for uterine volume was 3.0 cm^3 (sensitivity, 100%; specificity, 93%).

Ovarian volume can be calculated by different methods: the mean of the right ovary independent of the left,[12] the mean of the right ovary,[26] the mean of the total ovaries,[28] the mean of an average of 2 volumes for each patient,[24] and the volume of the larger ovary.[13] We chose to use the

Figure 2. Sonographic variables in prepubertal girls younger than 8 years and in 2 reference groups (patients with IT and patients with CPP). Group 1 includes prepubertal girls; group 2, girls with IT; and group 3, girls with idiopathic CPP. The horizontal line indicates the cutoff points selected by the ROC curve. **A**, Uterine length, 4 cm; **B**, uterine area, 4.5 cm^2; **C**, uterine volume, 3 cm^3; and **D**, ovarian volume, 1.0 cm^3.



average of the volumes for each patient because we found no statistical difference between the left and right sides in any patient. Moreover, we found that it was easier to interpret the sonograms with this method.

Ovarian volume was smaller in prepubertal girls than in patients with CPP, which is also in agreement with other studies.[10,11,13,15,29] In our patients, both ovaries had similar volumes. Other authors have reported the same findings.[11–13]

Our analysis of mean ovarian volume for each patient showed that the cutoff point of 1.0 cm^3 had positive and negative predictive values, sensitivity, and specificity of 100% for identifying patients with CPP. King et al[15] also concluded that bilateral ovarian growth was the best indicator of the diagnosis of CPP and that unilateral growth in association with macrocysts was indicative of precocious pseudopuberty. Haber et al[11] used a cutoff point of 1.2 cm^3 for mean ovarian volume, obtaining sensitivity of 82% and specificity of 95%. Although some authors have observed an ovarian volume greater than 1 cm^3,[13] this finding has not been unanimous; other studies have reported a maximal value of

Figure 3. Receiver operating characteristic curve: sonographic cutoff points for prepubertal girls and girls with CPP. C.P. indicates cutoff point. The most appropriate cutoff points for patients younger than 8 years for differentiating the prepubertal group from patients with CPP were as follows: **A**, uterine length, 4 cm; **B**, uterine area, 4.5 cm^2; **C**, uterine volume, 3 cm^3; and **D**, ovarian volume, 1.0 cm^3.

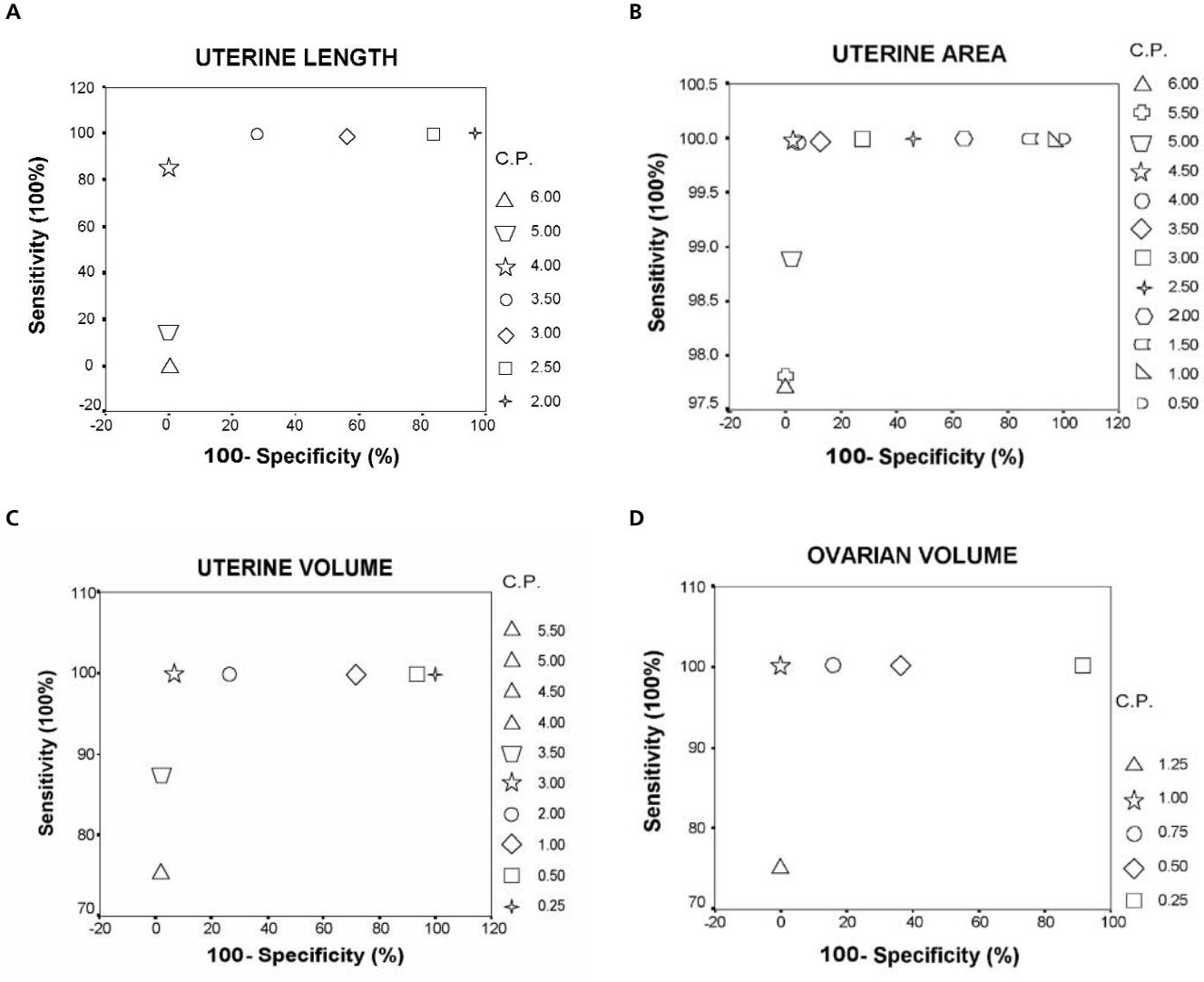


Table 3. Accuracy Tests of Sonographic Measurements in Girls Younger Than 8 Years for Identifying CPP

Cutoff Point	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
Uterine length, 4 cm	86	100	100	99
Uterine area, 4.5 cm^2	100	97	70	100
Uterine volume, 3 cm^3	100	93	57	100
Individual ovarian volume, 1.25 cm^3	81	99	93	98
Bilateral ovarian volume, 1.0 cm^3	100	100	100	100

1 cm^3.[2,15] In our study, analysis of individual ovaries (Table 3) with a cutoff point of 1.25 cm^3 had less accuracy for identifying CPP (positive predictive value, 93%; negative predictive value, 98%; sensitivity, 81%; and specificity, of 99%). Therefore, the method used to calculate ovarian volume seems to influence the selection of a cutoff point. Previous studies have also reported that ovarian volumes greater than 3 cm^3 may indicate a diagnosis of CPP.[30]

The different values reported in the literature for sonographic variables may have resulted from interobserver variation, from the resolution of the sonographic equipment, from the degree of vesical fullness, and from differences in sample size, sample population, and methods of volume calculation in the patients studied. Moreover, the cutoff points were defined by methods other than the ROC curve.

The finding of ovarian follicles in our prepubertal girls, which has also been described by others.[4,15,17,23,25,30–33] shows that follicular activity is present from an early age.[34] Ovaries are dynamic organs, which have a stromal component that increases discretely from birth to maturity and a gonadotropin-dependent follicular component.[35] Holm et al[33] observed microcysts up to 8 mm in diameter in 86% of prepubertal girls. The absence of macrocysts in our sample of prepubertal girls is also in agreement with studies that report that such structures are rare in girls younger than 10 years.[4,13,17,23,32] Macrocysts, however, can be found in patients with IT.[13–15]

Table 4. Ovarian Morphologic Characteristics in Girls Younger Than 8 Years (Prepubertal or With Sexual Precocity)

Ovarian Morphologic Characteristic	Prepubertal	IT	CPP
Homogeneous	87	2	5
Paucicystic	9	5	2
Multicystic	0	0	1
Macrocystic	0	1	0
Isolated cyst	0	0	0
Total	96	8	8

Ovarian morphologic characteristics were different in the 3 groups. Multicystic ovaries were present in 1 patient with CPP, a finding that had already been described by other authors.[13,14,30] Nonquantitative analysis is not specific. The presence of follicles smaller than 10 mm in diameter was not in itself specific for identifying patients with CPP and other forms of sexual precocity.[15] Information about the largest follicle and how many follicles exist is thus very important. Ovaries containing more than 6 follicles and described as multicystic[13] or megalocystic[30] seem to precede the occurrence of dominant follicles. Also, ovaries are GnRH dependent, and their activity may be suppressed by GnRH analogs. Therefore, the number of follicles seems to be an important element in the description of pelvic sonography in girls. The term "paucicystic," used by Buzi et al,[13] seems adequate, because it introduces an intermediate category between homogeneous and multicystic ovaries.

In conclusion, our results show that uterine and ovarian growth is proportional to age, even in prepubertal girls. A mean ovarian volume greater than 1.0 cm^3 showed 100% sensitivity and specificity for discriminating between prepubertal girls and girls with CPP girls. The presence of microcysts is common in prepubertal girls, but the presence of 6 or more follicles up to 10 mm in diameter may be indicative of CPP in girls younger than 8 years.

References

1. Comstock CH, Boal DK. Pelvic sonography of the pediatric patient. Semin Ultrasound CT MR 1984; 5: 54–67.
2. Lippe BM, Sample WF. Pelvic ultrasonography in pediatric and adolescent endocrine disorders. J Pediatr 1978; 92:897–902.
3. Cambell AB, Lastra IC, Lopez DM. Determinacion por ecotomografia del volumen ovarico y longitud uterina em ninas sanas pre y post puberales. Bol Med Del Cobre 1988; 1:3–6.
4. Salardi S, Orsini LF, Cacciari E, et al. Pelvic ultrasonography in girls with precocious puberty, congenital adrenal hyperplasia, obesity or hirsutism. J Pediatr 1988; 112:880–887.
5. Siegel MJ. Pediatric gynecologic sonography. Radiology 1991; 179:593–600.
6. Arbel-DeRowe Y, Tepper R, Rosen DJ, Beyth Y. The contribution of pelvic ultrasonography to the diagnostic process in pediatric and adolescent gynecology. J Pediatr Adolesc Gynecol 1997; 10:3–12.
7. O'Dea LSL, Siegel SF, Lee PA. Pubertal disorders: precocious and delayed puberty. In: Sanfilippo JSS, Muram D, Lee PA, Dewhurst J (eds). Pediatric and Adolescent Gynecology. Philadelphia, PA: WB Saunders Co; 1994:53–76.
8. Brook CGD. Precocious puberty. Clin Endocrinol (Oxf) 1995; 42:647–650.
9. Root AW. Precocious puberty. Pediatr Rev 2000; 21: 10–19.
10. Griffin IJ, Cole TJ, Duncan KA, Hollman AS, Donaldson MDC. Pelvic ultrasound findings in different forms of sexual precocity. Acta Paediatr 1995; 84:544–549.
11. Haber HP, Wollmann HA, Ranke MB. Pelvic ultrasonography: early differentiation between isolated premature thelarche and central precocious puberty. Eur J Pediatr 1995; 154:182–186.
12. Blogowska A. Significance of ultrasonographic examinations in diagnostics of premature and normal puberty in girls. Ann Acad Med Stetin 1997; 43:161–180.
13. 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; 87:1138–1145.
14. Stanhope R, Abdulwahid NA, Adams J, Brook CGD. Studies of gonadotrophin pulsatility and pelvic ultrasound examinations distinguish between isolated premature thelarche and central precocious puberty. Eur J Pediatr 1986; 145:190–194.
15. King LR, Siegel MJ, Solomon AL. Usefulness of ovarian volume and cysts in female isosexual precocious puberty. J Ultrasound Med 1993; 12:577–581.
16. Herter LD, Goldenziner E, Flores JA, Becker E Jr, Spritzer PM. Ovarian and uterine sonography in healthy girls between 1 and 13 years old: correlation of findings with age and pubertal status. AJR Am J Roentgenol 2002; 178:1531–1536.
17. Salardi S, Orsini LF, Cacciari E, Bovicelli L, Tassoni P, Reggiani A. Pelvic ultrasonography in premenarcheal girls: relation to puberty and sex hormone concentrations. Arch Dis Child 1985; 60:120–125.
18. Herter LD, Moretto M, Di Domenico, Spritzer PM. Sonographic size of uterus and ovaries in girls with precocious puberty. Paper presented at: 13th World Congress of Pediatric and Adolescent Gynecology, 7th Alogia Congress; April 2001; Buenos Aires, Argentina.
19. Sample WF, Lippe BM, Gyepes MT. Gray-scale ultrasonography of the normal female pelvis. Radiology 1977; 125:477–483.
20. Venturoli S, Porcu E, Fabbri R, Paradisi R, Orsini LF, Flamigni C. Ovaries and menstrual cycles in adolescence. Gynecol Obstet Invest 1984; 17:219–222.
21. Greulich WW, Pyle SI. Radiographic Atlas of Skeletal Development of the Hand and Wrist. 2nd ed. Stanford, CA: Stanford University Press; 1959.
22. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969; 44:291–303.
23. Orsini LF, Salardi S, Pilu G, Bovicelli L, Cacciari E. Pelvic organs in premenarcheal girls: real time ultrasonography. Radiology 1984; 153:113–116.
24. Haber HP, Mayer EI. Ultrasound evaluation of uterine and ovarian size from birth to puberty. Pediatr Radiol 1994; 24:11–13.
25. Griffin IJ, Cole TJ, Duncan KA, Hollman AS, Donaldson MDC. Pelvic ultrasound measurements in normal girls. Acta Paediatr 1995; 84:536–543.

26. Orbak Z, Sagsoz N, Alp H, Tan H, Yildirim H, Kaya D. Pelvic ultrasound measurements in normal girls: relation to puberty and sex hormone concentration. J Pediatr Endocrinol Metab 1998; 11:525–530.

27. Ivarsson AS, Nilsson KO, Persson P-H. Ultrasonography of the pelvic organs in prepubertal and postpubertal girls. Arch Dis Child 1983; 58:352–354.

28. Cohen HL, Tice HM, Mandel FS. Ovarian volumes measured by US: bigger than we think. Radiology 1990; 177:189–192.

29. Bridges NA, Cooke A, Healy MJR, Hindmarsh PC, Brook CGD. Ovaries in sexual precocity. Clin Endocrinol (Oxf) 1995; 42:135–140.

30. Stanhope R, Adams J, Jacobs HS, Brook CGD. Ovarian ultrasound assessment in normal children, idiopathic precocious puberty and during low dose pulsatile GnRH therapy of hypogonadotropic hypogonadism. Arch Dis Child 1985; 60:116–119.

31. Polhemus DW. Ovarian maturation and cyst formation in children. Pediatrics 1953; 11:588–594.

32. Cohen HL, Shapiro MA, Mandel FS, Shapiro ML. Normal ovaries in neonates and infants: a sonographic study of 77 patients 1 day to 24 months old. AJR Am J Roentgenol 1993; 160:583–586.

33. Holm K, Laursen EM, Brocks V, Muller J. Pubertal maturation of the internal genitalia: an ultrasound evaluation of 166 healthy girls. Ultrasound Obstet Gynecol 1995; 6:175–181.

34. Peters H, Himelstein-Braw R, Faber M. The normal development of the ovary in childhood. Acta Endocrinol (Copenh) 1976; 82:617–630.

35. Adams J. The role of pelvic ultrasound in the management of pediatric endocrine disorders. In: Brook CGD (ed). Clinical Pediatric Endocrinology. 2nd ed. Oxford, England: Blackwell Scientific Publications; 1989:675–691.