Uterine volume and endometrial thickness in healthy girls evaluated by ultrasound (3-dimensional) and magnetic resonance imaging

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Objective: To report normative data on uterine volume and endometrial thickness in girls, according to pubertal stages; to evaluate factors that affect uterine volume; and to compare transabdominal ultrasound (TAUS) and magnetic resonance imaging (MRI).
Design: Cross-sectional study of a nested cohort of girls participating in The Copenhagen Mother-Child Cohort.
Setting: General community.
Patient(s): One hundred twenty-one healthy girls, aged 9.8–14.7 years.
Intervention(s): None.
Main Outcome Measure(s): Clinical examination, including pubertal breast stage (Tanner classification: B1–B5). Uterine volume: ellipsoid TAUS (n = 112) and 3-dimensional TAUS (n = 111); ellipsoid MRI (n = 61). Endometrial thickness: TAUS (n = 110) and MRI (n = 60).
Result(s): Uterine volume and endometrial thickness were positively correlated with pubertal stages; e.g., ellipsoid TAUS: $r = 0.753$, and endometrium TAUS: 0.648. In multiple regression analyses, uterine volume was associated with the number of large follicles (TAUS >5 mm) (Beta 0.270); estradiol (E_2) (Beta 0.504); and height (Beta 0.341).

Volumes from ellipsoid vs. 3-dimensional TAUS were strongly correlated ($r = 0.931$), as were TAUS and MRI: ellipsoid volume ($r = 0.891$) and endometrial thickness ($r = 0.540$). Uterine volume was larger in TAUS compared with MRI; mean difference across the measured range: 7.7 (5.2–10.2) cm^3. Agreement was best for small uteri.
Conclusion(s): Uterine volume and endometrial thickness increased as puberty progressed. Circulating E_2 from large follicles was the main contributor to uterine and endometrial growth. The TAUS and MRI assessments of uterus and endometrium were strongly correlated. (Fertil Steril® 2015;104:452–9. ©2015 by American Society for Reproductive Medicine.)
Key Words: Uterus, endometrium, puberty, TAUS, MRI

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Imaging of internal female genitalia is important when evaluating girls and adolescents who are suspected to have reproductive endocrine pathology, such as ambiguous genitalia, pelvic pain, precocious and delayed puberty, vaginal bleeding in the prepubertal stage, and amenorrhea in adolescence (1). Visualization of internal genitalia in girls is most commonly performed as part of the evaluation of girls with precocious puberty, including biochemical assessment of the pituitary-gonadal hormone axis, evaluation of the growth pattern, bone-age assessment from a roentgenogram of the wrist, as well as signs of estrogenization, including palpation of glandular breast tissue. Uterine morphology in virgo intacta girls is

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usually assessed by transabdominal ultrasound (TAUS); however, visualization can be challenging, and magnetic resonance imaging (MRI) may be a useful alternative modality (2).

A number of studies report increasing uterine volume and endometrial thickness in prepubertal girls and as puberty progresses (3–9). The degree to which the ovarian morphology (ovarian volume and number of follicles in various sizes) and circulating levels of estradiol (E_2) affect uterine volume and endometrial thickness remains to be elucidated. Furthermore, comparative studies of uterine morphology in healthy girls assessed by TAUS and MRI have, to our knowledge, not been reported.

In this study of 121 healthy Danish girls, we report normative values of uterine size and volume, as well as endometrial thickness evaluated by TAUS and MRI. We hypothesized that uterine volume and endometrial thickness were associated with pubertal development, the number of large ovarian follicles, circulating E_2, and body size.

MATERIALS AND METHODS

Study Population

A total of 121 healthy girls participating in The Copenhagen Mother-Child Cohort were included in the study. From 1997 to 2001, a total of 2,688 Danish women were consecutively included at their first routine obstetric visit at any of 3 hospitals in Copenhagen (participation rate: 22%). The children from this cohort were examined at several time points during infancy and childhood, and 1,293 peripubertal children (584 girls) agreed to participate in an ongoing longitudinal study with annual examinations (participation rate: 43%). Detailed information has been published elsewhere (10, 11). The selection criterion for the nested cohort, for participation in the present cross-sectional study, was a high attendance rate at previous examinations (a minimum of 5 examinations: at birth, ages 3 months, 18 months, 4–9 years, and 8–13 years). Of 129 girls in the longitudinal cohort who were invited to participate in the present study, 121 consented and underwent both pelvic MRI and ultrasound examination ($n = 109$), or either ultrasound ($n = 11$) or MRI ($n = 1$).

Clinical Examination

On the day of the ultrasound and MRI evaluation, a clinical examination was performed. Height was measured using a wall-mounted stadiometer to the nearest mm (Holtain Ltd), and weight was measured to the nearest 0.1 kg, using electronic scales (Seca delta model 707, Seca; and Bisco model PERS 200, Bisco).

We evaluated the stage of pubertal development according to Marshall and Tanner (12). Girls with Tanner breast stage $\geq$B2 (evaluated by palpation) were considered to be in puberty. Three girls chose not to be examined for pubertal stages. Clinical hyperandrogenism was not systematically evaluated; however, no girls presented with severe hirsutism or acne. In a questionnaire, the girls reported whether they had experienced menarche ($n = 26$). Median (range) gynecologic age (time from menarche to examination) was 0.69 (0.03–2.30) years. Examinations were not scheduled according to their menstrual cycle. None of the girls had a history of endocrine, gynecological, or cerebral illness.

Transabdominal Ultrasound

All girls were scanned at a time when they had a full bladder. Examinations were performed by a single experienced operator (VB), using a Voluson E8 Ultrasound System (GE Medical Systems), with a multifrequency transabdominal probe (RM6C, 3–8 MHz; GE Medical Systems). Image analyses were performed concomitantly by 2 experienced operators (KS and LNJ). Uterine volume was calculated assuming an ellipsoid shape (uterus ellipsoid TAUS: $\pi/6$ x length x width x depth). The length of the uterus included both the uterine corpus and the cervix. Uterine volume was calculated in 112 girls. In the remaining girls, assessment was not possible, owing to inadequate picture quality.

The stored images were analyzed using 4DView software, version 9.1 (GE Medical Systems). Using the "Manual" option of Virtual Organ Computer-Aided Analysis, the uterus was outlined inside the volume box with a 30° rotation in plane A. From the 3-dimensional (3D) model generated by the outlined uterine capsule, uterine volume was assessed in 111 girls (uterus 3D TAUS) (Fig. 1).

Magnetic Resonance Imaging

Magnetic resonance imaging was performed with a 3-Tesla MRI (Magnetom Verio; Siemens AG). In all girls, a 3D, T2-weighted turbo spin-echo sequence (SPACE) was performed, using a 32-channel receiver array coil during free breathing with navigator respiratory triggering. The scanning parameters were: repetition time/echo time 1,600/109 ms; Turbo factor 71; echo spacing 4.34 ms; field of view 400 mm; matrix 384 x 384; and slice thickness 1.2 mm. The voxel size of the 3D sequence was 1.1 x 1.0 x 1.2 mm, and these near-isotropic voxels enabled reconstruction in all planes. The images were obtained in the coronal plane and covered the abdomen, including the pelvic region. The large field of view was necessary to provide a sufficient signal-to-noise ratio.

Uterine dimensions were measured by an experienced radiologist (EF). Uterine volume was calculated assuming an ellipsoid shape (ellipsoid MRI: $\pi/6$ x length x width x depth), and the length of the uterus included both the uterus corpus and the cervix. Uterine volume was calculated in 61 girls. In the remaining girls, assessment was not possible, owing to inadequate picture quality ($n = 28$), or the region being excluded from the scanned field ($n = 21$).

Ovarian Follicles

Methodology and results concerning the assessment of ovarian volume and follicle numbers have been published elsewhere (13). In short, follicles were measured, counted (sum of follicles from both ovaries), and grouped according to size; TAUS ($n = 94$): 1–4 mm, $\geq$5 mm; MRI ($n = 87$): 2–3 mm, 4–6 mm, $\geq$7 mm. The size categories were defined to be as detailed as possible, while still obtaining normal distribution of follicle numbers in the subgroups (after log-transformation).