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AGE AND LEAN BODY WEIGHT RELATED GROWTH CURVES OF KIDNEYS USING REAL-TIME 3-DIMENSIONAL ULTRASOUND IN PEDIATRIC UROLOGY

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ABSTRACT

Purpose: Kidney volume and growth are important parameters for evaluating and monitoring several diseases in pediatric urology. Studies have shown the significant relationship of kidney volume and function. Until now normal values of kidney size and growth have been based on 2-dimensional measurements combined with arithmetic formulas for the ellipsoid. Real-time 3-dimensional (RT3D) ultrasound is a new imaging modality. Moreover, corresponding software allows RT3D imaging within a short time exposure. We created nomograms of kidney volumes for routine diagnostics that could serve as a standard for pediatric renal growth assessment, decreasing the need for invasive tests.

Materials and Methods: RT3D volumetry of a total of 620 kidneys in 310 children with a homogeneous age distribution (range newborn to 10 years) and without any evidence of renal impairment was performed using a Voluson 730 (Kretztechnik, Ultrasound, Zipf, Austria) system. Polynomial regression analysis was applied for the prediction and estimation of growth variables of kidney volumes as a function of gender, age, body mass index or lean body weight.

Results: Stepwise multiple regression analysis incorporating the different independent variables indicated with significant correlation that age and lean body weight were the strongest predictors of kidney volumes in children.

Conclusions: This study shows that RT3D ultrasound is particularly qualified for evaluating kidney volume in pediatric urology. RT3D volumetry is suitable for monitoring renal growth, reflecting kidney function. Furthermore, this methodology is feasible in screening programs assessing congenital urogenital diseases.

KEY WORDS: kidney, growth, ultrasonography, reference values

Kidney size is an essential parameter for evaluating pediatric renal and genitourinary tract pathologies. Noninvasive imaging modalities such as ultrasound have widespread applications in pediatric urology.[1] Sonographic conventional 2-dimensional (2D) volume assessment of pediatric kidneys correlates with relative renal function from ^{99m}Tc-dimercaptosuccinic acid scintigraphy, demonstrating that ultrasound is a feasible screening technique.[2] However, using an ellipsoid model for volume calculations may not accurately evaluate renal size and mass. To our knowledge we determined kidney growth curves in children using real-time (RT) 3D ultrasound for the first time. RT3D ultrasound is a new imaging modality scanning the entire kidney in real time. Compared to conventional reconstructed 3D ultrasound this new real-time scanning technology represents an absolute advantage, particularly in neonates and small infants, in that requiring the patient to remain immobile during the scan since any movement results in significant artifacts is not necessary. This is enabled by electronically steering an ultrasound beam to interrogate a 3D volume of tissue. Furthermore, we correlated volume data with various physical specifications, such as gender, age, body mass index (BMI) and lean body weight (LBW).[3]

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MATERIALS AND METHODS

Between July 2002 and June 2003 we examined 310 children (620 renal units) ranging in age from newborn to 10 years who were referred because of enuresis, cryptorchidism and phimosis with no evidence of renal or urinary tract disease. Kidney volumes were recorded with the patient prone and plotted against height, weight, BMI and LBW with the predicted mean ± 2 SD. BMI was determined by the formula, weight in kg/height in m^2 and LBW was determined using the equations of Bunc et al based on multifrequency bioimpedance measurements in children in central Europe.[4,5]

Volumetric acquisitions were done using a Voluson 730 Expert 4D ultrasound machine combined with a 4 to 8 MHz curved array 4D probe. The system has the capability to perform volume acquisitions in real time, allowing accurate measurement even in noncompliant infants. Depending on depth we achieved frame rates of up to 8 volumes per second. We acquired at least 2 volume data sets per kidney in every child. Data were stored and later transferred to a personal computer viewing station. Using special software (3D View 2000, 2.1, GE Medical Systems, Kretztechnik) volume data files were analyzed using a volume calculation tool for volume assessment. The whole kidney was outlined. Since no dilatation was present, parenchymal area was equal to the area of the entire renal contour. With this software the surface is defined by rotation of the image plane around a fixed axis (main contour axis) and the manual definition of 2D contours in each plane. We used a 15-degree rotation angle from plane to plane, ensuring as much accuracy as possible. The organ geometry was then defined by 3D triangularization of the 2D contours, meaning that each point of the 2D contour in a plane was connected via a triangular mesh to corresponding points in the neighboring planes. As a result, kidney volume is presented in cc. Three-D kidney morphology was graphically visualized at the same time (fig. 1). System measurement accuracy had been established by acquiring images from 10 cadaver kidneys. Subsequently kidney volumes were scanned and analyzed using the RT3D ultrasound system. Mean measurement deviation was not significant (SD ± 0.956 cc, $p < 0.05$).

Statistics. Polynomial least square regression analysis was used to model growth variables of the right and left kidneys (y axis) as a function of age, BMI or LBW (x axis). Data were plotted as mean kidney volume ± 2 SD using lines determined by polynomial regression. The difference in volume between the right and left kidneys was tested by the Wilcoxon rank sum test. The Mann-Whitney U test was used to assess differences between boys and girls in left and right kidney volume. Statistical significance was considered at $p < 0.05$. SPSS for Windows 11.5 software (SPSS, Chicago, Illinois) and Matlab R12 (www.mathworks.com) were used for all analyses.

RESULTS

The polynomial regression equation to evaluate the effect of age on the volume of the left kidney was $y = 26.4328 + 0.6067x - 0.0002x^2$ ($r^2 = 0.644$) and $y = 27.7638 + 0.5816x - 0.0001x^2$ ($r^2 = 0.617$) for the volume of the right kidney (see table, figs. 2 and 3). The effect of age on kidney volume was also assessed separately in girls and boys. The polynomial regression equation for girls for the left kidney was $y = 33.6602 + 0.3956x + 0.0018x^2$ ($r^2 = 0.600$, see table, fig. 4) and for the right kidney it was $y = 33.1675 + 0.3820x + 0.0016x^2$ ($r^2 = 0.578$, see table, fig. 5). For boys the polynomial regression equation for the left kidney was $y = 23.9643 + 0.6906x - 0.0006x^2$ ($r^2 = 0.682$, see table, fig. 6) and for the right kidney it was $y = 25.5513 + 0.6840x - 0.0008x^2$ ($r^2 = 0.651$, see table, fig. 7). To review the effect of LBW on kidney volume the polynomial regression equation was $y = 5.9180 + 3.5646x - 0.0072x^2$ for the left kidney ($r^2 = 0.732$, see table, fig. 8) and $y = 10.9737 + 3.0468x - 0.0003x^2$ for the right kidney ($r^2 = 0.724$, see table, fig. 9). The polynomial regression equation to assess the effect of BMI on the left kidney was $y = 40.8640 - 1.1169x + 0.1832x^2$ ($r^2 = 0.151$) and it was $y = 35.3256 - 0.6623x + 0.1695x^2$ ($r^2 = 0.160$) for the right kidney without any statistically significant correlation ($p > 0.05$, see table). Moreover, there were no statistical differences in volume between the left and right kidneys. Gender differences were statistically significant for the right and left kidneys ($p = 0.027$ and 0.005, respectively).

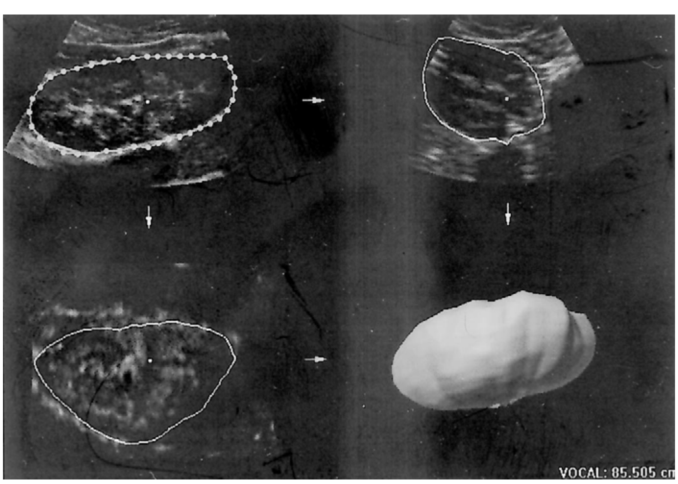

FIG. 1. Screen shot of RT3D volumetry of normal right kidney in 10-year-old girl with LBW of 28 kg.

Polynomial least square regression equation of effect of age, laterality, gender, LBW and BMI on kidney growth variables

	Lt Kidney	Rt Kidney
Age:		
Equation	$26.4328 + 0.6067x - 0.0002x^2$	$27.7638 + 0.5816x - 0.0001x^2$
r^2	0.644	0.617
Girls:		
Equation	$33.6602 + 0.3956x + 0.0018x^2$	$33.1675 + 0.3820x + 0.0016x^2$
r^2	0.600	0.578
Boys:		
Equation	$23.9643 + 0.6906x - 0.0006x^2$	$25.5513 + 0.6840x - 0.0008x^2$
r^2	0.682	0.651
LBW:		
Equation	$5.9180 + 3.5646 - 0.0072x^2$	$10.9737 + 3.0468x - 0.0003x^2$
r^2	0.732	0.724
BMI:		
Equation	$40.8640 - 1.1169x + 0.1832x^2$	$35.3256 - 0.6623x + 0.1695x^2$
r^2	0.151	0.160

$p < 0.05$.

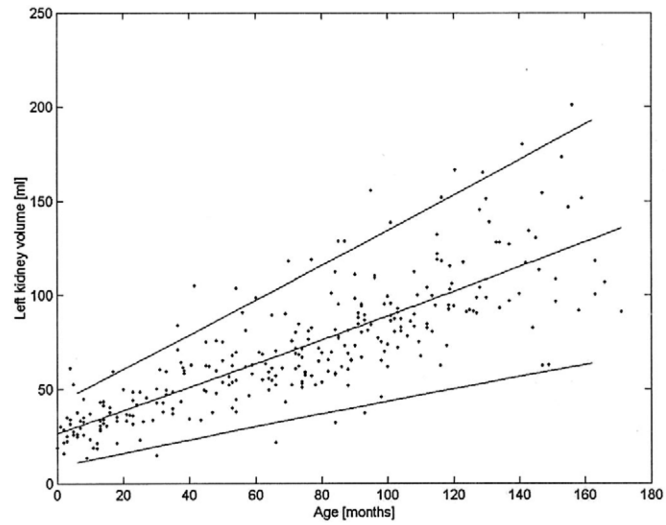

FIG. 2. Age related growth curve for left kidney volume in 291 subjects. Lines represent mean ± 2 SD ($r^2 = 0.644$).

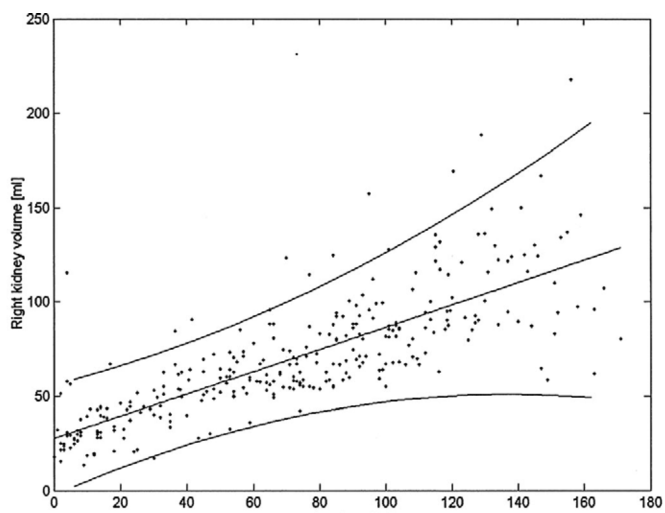

FIG. 3. Age related growth curve for right kidney volume in 302 subjects. Lines represent mean ± 2 SD ($r^2 = 0.617$).

DISCUSSION

Surveillance in pediatric urology includes the assessment kidney growth and development. Regular monitoring of kidney growth provides the clinician with one of the best indi-

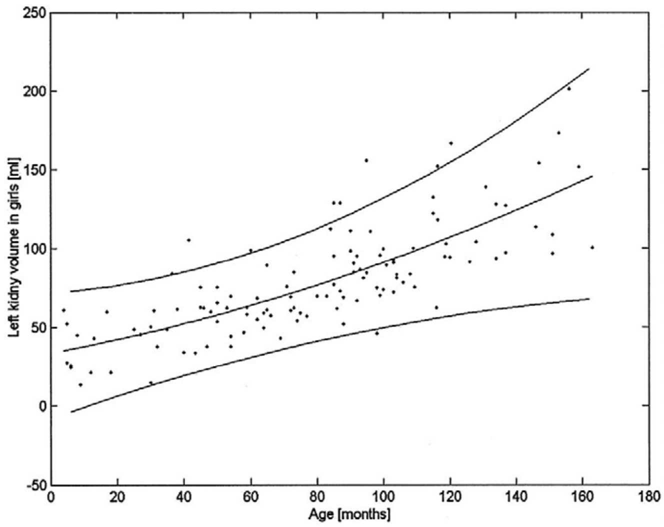

FIG. 4. Age related growth curve for left kidney volume in 120 girls. Lines represent mean ± 2 SD (r^2 = 0.600).

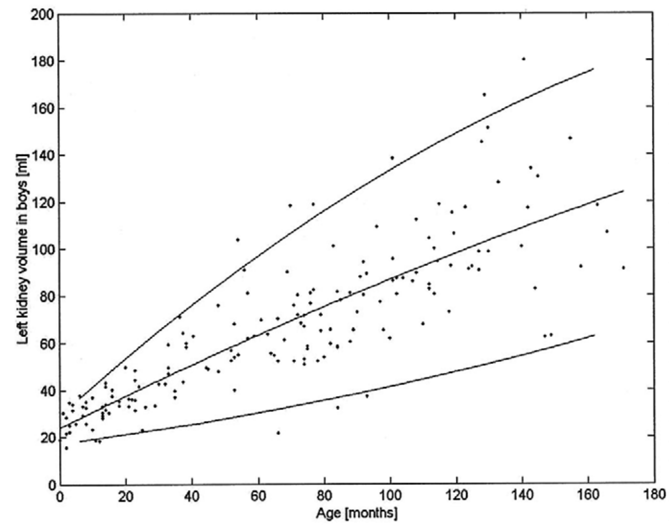

FIG. 6. Age related growth curve for left kidney volume in 171 boys. Lines represent mean ± 2 SD (r^2 = 0.682).

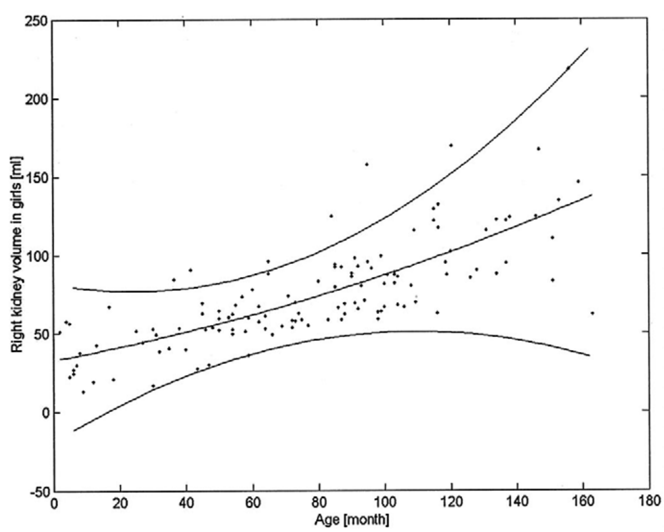

FIG. 5. Age related growth curve for right kidney volume in 125 girls. Lines represent mean ± 2 SD (r^2 = 0.578).

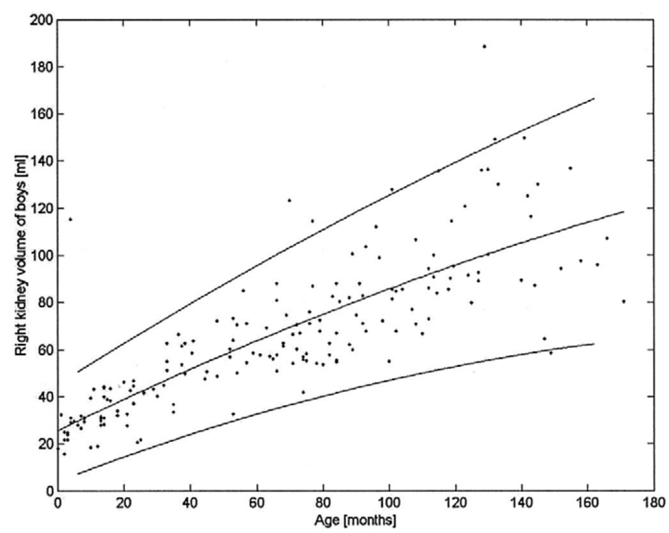

FIG. 7. Age related growth curve for right kidney volume in 177 boys. Lines represent mean ± 2 SD (r^2 = 0.651).

cators of the underlying pathological condition in genitourinary tract anomalies. For instance, children with a history of vesicoureteral reflux should be monitored during childhood. Hence, RT3D volumetry ensures that kidney growth is on target for age and size. Accurate sonographic followup ensures the early diagnosis of possible growth retardation due to parenchymal loss, particularly in children selected for conservative therapy for vesicoureteral reflux, offering different treatment options for these patients with the potential for catch-up growth.[6]

Scintigraphic followups can be decreased after surgery at the ureterovesical junction or after pyeloplasty, monitoring kidney growth potential with reference to renal function. Volumetry of the infant kidney to estimate organ growth correlates with scintigraphically determined renal function. In the case of primarily scarred kidneys, which have a significantly worse growth prognosis compared to primarily undamaged renal units, contralateral kidneys show compensatory growth when monitored accurately by kidney volume assessment.[7]

To our knowledge we describe the first application of RT3D ultrasound in pediatric kidney volume assessment. In contrast to conventional ultrasound transducers with the major disadvantage of the significant time requirement needed to create 3D data sets, RT3D ultrasound electronically interrogates a volume using a matrix array of transducers instead of the conventional linear array, resulting in continuous and rapid scanning. With real-time acquisition it is possible to acquire serial volumes of up to 8 volumes per second in which each single volume can be manipulated off line. After acquisition it is possible to select the highest quality volume for kidney assessment, whereas it is feasible to store only the selected volume or the whole volume sequence for further off line estimation.

To date most clinical measurement methods have mainly been based on 2D calculations. Length, width and parenchymal thickness are the most frequently used parameters describing kidney size. The usual model of estimating kidney volume with real-time sonography consists of the ellipsoid formula using the equation for a prolate ellipsoid. A promising technique for estimating organ volumes is the calculation of renal parenchymal area with the drawback that scans are manual rather than automatic and, therefore, operator proficiency is essential for scanning the region of interest accurately.[8] Using a multivariate regression approach and considering different demographic variables such as gender and race when creating renal length nomograms, 3D sonography provides accurate volume measurements in vitro as well as in vivo, especially for irregularly shaped organs.[9,10] When volume data are digitally stored by trained ultrasound techni-

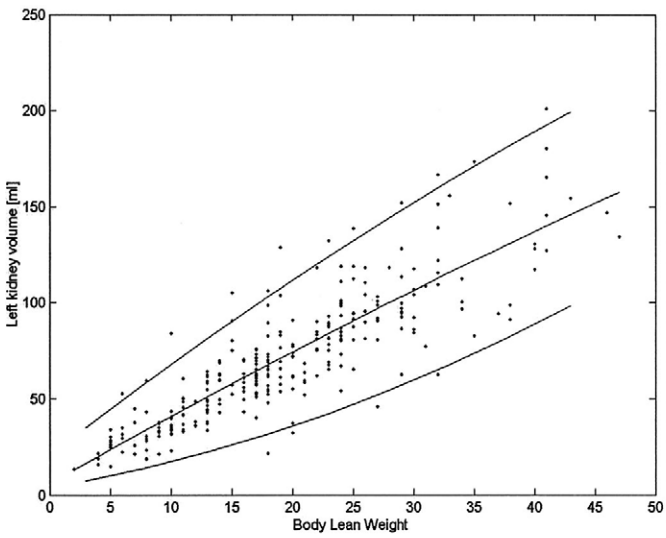

FIG. 8. Growth curve according to LBW for left kidney volume in 291 subjects. Lines represent mean ± 2 SD (r^2 = 0.732).

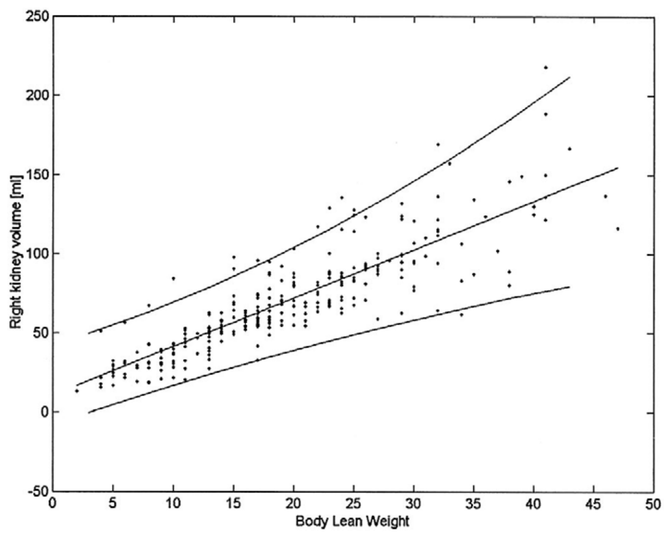

FIG. 9. Growth curve according to LBW for right kidney volume in 302 subjects. Lines represent mean ± 2 SD (r^2 = 0.724).

cians, it can be optimized easily and discussed by an expert panel thereafter. Due to the simplicity of operating and acquiring RT3D ultrasound this acquisition of data is reproducible by different observers. Consequently RT3D sonography is applicable in screening programs for the detection of congenital kidney and urinary tract abnormalities.[11] In this study by assessing cadaveric kidneys of known volume we observed that an accurate determination of organ volume is warranted under experimental conditions with a mean deviation of less than 0.5%.

Previous studies have shown that kidney volume cannot be correlated with only 1 physical parameter, such as age, sex, side, body height, weight or BMI. Increasing organ volumes can only be defined exactly by multivariate analysis including as much physical data as possible.[12] The most important single value to date has been LBW, which is with total metabolic active tissue.[13,14] LBW consists of the body cell mass, extracellular water and nonfat connective tissue, and it is essentially a fat-free mass. Our results corroborated the significant correlation between kidney volume and LBW, the strongest predictor of renal parenchymal volumes, whereas the correlation of BMI and kidney volumes was quite poor ($p > 0.05$). Boys had significantly larger kidneys than girls on the right and left sides. There was also a significant correlation between age and kidney volumes.

The long investigation time with conventional ultrasound transducers can result in significant misalignment on subsequent 3D reconstruction caused by respiration and child motion. The rapid image creation that is almost independent of child motility represents a novel technique, decreasing measurement artifacts. Although ultrasound is a noninvasive procedure, many children do not appreciate them and resist, consequently creating stressful situations with an inaccurate determination of organ dimensions. Therefore, short examination time leads to more compliant patients, ensuring proper data gathering.

CONCLUSIONS

RT3D ultrasound represents a new image modality for evaluating kidney volume and growth in infancy and childhood, decreasing the overall exposure to ionizing radiation without the necessity of sedation or general anesthesia and with a short examination time. The accuracy of a new volumetric technique could be demonstrated that may in the future provide an objective assessment of renal damage. Our nomograms depend on LBW as the most accurate biological parameter to develop a framework for pediatric renal growth charts. RT3D sonography of pediatric kidneys represents a precise qualitative and quantitative method of volume measurement, reflecting the total amount of active renal tissue.

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