Correlational Study of Endometrial Length and Thickness by 2D Ultrasound Parameter to the Endometrial Volume Obtained by 3D Ultrasound

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ABSTRACT

The study was conducted to evaluate correlation between the endometrial length and thickness on two-dimensional (2D) ultrasound to the endometrial volume calculated by three-dimensional (3D) ultrasound virtual organ computer-aided analysis (VOCAL). All patients having transvaginal scans (TVSs) at our center were included and patient having fluid in endometrium, polyp, fibroid, and pregnancy were excluded. Two-dimensional measurements of uterine length, endometrial length, effective endometrial length, endometrial thickness, and endometrial breadth in transverse section were taken. Endometrial volume was taken by 3D ultrasound software VOCAL with rotational step of 9°. A multivariate regression analysis was carried out using Excel add in stat tool software, and the 2D parameters taken were correlated with the volume obtained by VOCAL, and an equation for volume is also derived with the same multivariate regression and compared with the volume obtained by VOCAL. The analysis shows that the equation is significant as R^2 (coefficient of determination) is significant (F statistics is 39.26 whose p value is <0.0001), and almost all the regression coefficients are significant except that for endo breadth in transverse section. $R^2 = 0.5241$ indicates that almost 52% of the variation in the endometrial volume has been explained by the considered independent variables in the equation. The scatterplot graph (Fig. 1) shows a positive relationship, and no outlier is observed. Also, the residue is normally distributed which is observed in the graph. The residual graph follows normality assumption and so the equation is applicable (Fig. 2). According to these results, the most correlating 2D parameters with 3D calculated endometrial volume were endometrial length and endometrial thickness. This also conveys that when endometrium is evaluated by 2D ultrasound for its receptivity, it is essential to include endometrial length along with endometrial thickness for better prediction or evaluation of endometrial receptivity.

Keywords: 3D endometrium, Endometrial length, Endometrial thickness, Endometrial volume.

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Aim

To evaluate correlation between the endometrial length and thickness measured on two-dimensional (2D) with the endometrial volume calculated by three-dimensional (3D) ultrasound virtual organ computer-aided analysis (VOCAL).

INTRODUCTION

Endometrial assessment is a great concern in the field of infertility, whether it is timed intercourse, intrauterine insemination, *in vitro* fertilization, or intra cytoplasmic sperm injection, endometrial thickness is used as a parameter for measuring endometrium, but as is seen that some endometria are thin and long, some are thick and short, a comparison of 2D length and thickness of endometrium with the volume obtained by 3D VOCAL is done and an effort has been made to correlate 2D and 3D parameters.¹

MATERIALS AND METHODS

Scans were done with GE Voluson E10 BT 19 ultrasound machine with a transvaginal volume probe with 5–9 MHz frequency. This is a single-centered prospective correlational study conducted at our center from August 2019 to January 2020 for a duration of 6 months. All the patients undergoing TVS (transvaginal sonography) were taken for study after informed consent and TVS volumes of uterus were stored for evaluation.

After explaining the procedure and taking verbal consent, the patient is asked to empty her bladder and is taken for

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examination on a gynecology couch. Scans were done in lithotomy-like position with patients adequately covered to make her comfortable. The privacy in the room is maintained. Now transvaginal probe selection is done from the machine setting and preset for gynecology scan is selected, the transvaginal volume 5–9 MHz probe is held and ultrasound jelly is applied on its head and then it is covered with a sterile condom such that there should not be any air in-between after which again jelly is applied on the condom on probe head, the probe is now held such that the marker on the probe faces the roof and is gently slid through the introitus into the vagina. Once uterus

Fig. 1: Scatterplot of estimated volume by equation vs volume by vocal

Fig. 2: Scatterplot of estimated volume by equation vs volume by vocal

Fig. 3: B-mode image of the uterus in sagittal section with measurement of anatomical uterine length

is seen in its midsagittal plane from fundus to external os, the 2D image is optimized. On this image, the entire length of the uterus is measured from fundus to external os—*anatomical uterine length* (Fig. 3) by line trace. On the same image endometrial length is measured from the fundal end of the endometrium to the internal os—*endometrial length* (Fig. 4) as a trace. In those patients in whom the part of the endometrium is not normal due to scar or indistensibility, the length of the endometrium was measured from tip of the endometrium till the lower end of normal morphology—*effective endometrial length* (Fig. 5). Then, the fundus is brought in the center of the image and is stored on one of the two dual images. Then, the probe is rotated 90° to get the transverse section and is spanned up and down to find out the broadest diameter on the first image, the endometrial thickness (Fig. 6) is measured from the outer margin of the hyperechoic line to the hyperechoic line at the broadest distance perpendicular to the central endometrial line. On the second image, the transverse diameter of endometrium is measured from one end of the endometrium to other end, side to side—*endometrial length in transverse section* (Fig. 7).

Rotate the probe back to see the midsagittal plane of the entire uterus and switch on 3D switch. Now a box will appear, and

Fig. 4: B-mode image of the uterus in midsagittal section with measurement of endometrial length

this is the region of interest from 3D volume. The uterus should be completely in the 3D box with at least 10% of extra space all round. Having adjusted the region of interest, angle of acquisition is selected and 3D acquisition is started. The transducer is held steady, and it takes an automatic sweep, and the acquired volume is displayed on the screen as three images of three orthogonal planes (images are named as A for acquired image which is upper left, upper right is B image, and lower left is C image). Multiplanar mode is selected and a walk through is done in A and B planes to see complete endometrium is included in volume and then VOCAL is selected for volume calculation of the endometrium. After switching on VOCAL image “a” is selected which is the sagittal view to work on. When VOCAL is started, a red color dashed line perpendicular to the image A will be seen. The dashed line is kept at maximum thickness of the endometrium. The volume of endometrium is calculated by rotating the entire volume 180° with a rotation step of 9°. Click start and a circumference is drawn manually around the endometrium at every rotation step. And after every rotation, you have to click a “>>” button to proceed for next rotation and at the end of 180° that is 20 rotations, total volume of endometrium is calculated by the computer, which is displayed on the screen (Fig. 8).

Fig. 5: B-mode image of endometrium showing measurement of effective endometrial length

Fig. 6: B-mode image showing endometrial thickness measurement

Fig. 7: B-mode image showing measurement of the transverse diameter of the endometrium on transverse section of the uterus where the endometrium appears the widest

Exclusion Criteria

Patient having fluid in endometrium, polyp, fibroid, and pregnancy were excluded.

STATISTICAL ANALYSIS

A statistical analysis was carried out, to study the effect of uterine length, effective endometrial length, endometrial thickness, and endometrial transverse section measurement on endometrial volume.

The multivariate regression analysis is carried out using Excel add in stat tool software, and the results are tabulated below.

RESULTS

The equation of best fit is as follows

Volume = $-2.75312678 (0.0003)^* + 0.28297209 (0.0112)^* \text{uterine length} + 0.2995013 (0.0444)^* \text{effective endo length} + 2.92305909 (<0.0001)^*$

Endo thickness + $0.11296101 (0.3237) \text{ endo length in transverse section}.$

The analysis shows that the equation is significant as R^2 (coefficient of determination) is significant (F statistics is 39.26 whose p value is <0.0001) and almost all the regression coefficients are significant except that for endo length in transverse section (Tables 1 to 3).

$R^2 = 0.5082$ indicates that almost 50% of the variation in the endo volume has been explained by the considered independent variables in the equation.

The scatterplot of estimated volume by equation vs volume obtained by VOCAL shows one outlier, which is required to remove (Fig. 1).

Another regression is carried out after removing the outlier, and the results are shown in Tables 4 to 6.

Volume = $-2.60426033 + 0.26615925 \text{ uterine length} + 0.31943168 \text{ effective endo length} + 2.84099633 \text{ endo thickness} + 0.09538773 \text{ endo length in transverse section}$

It is observed from the output that there is no change in the number of significant parameters but R^2 increases from 50 to 52% (Fig. 2).

The scatterplot graph shows a positive relationship, and no outlier is observed. Also, the residue is normally distributed which is observed in Figure 9.

The residual graph follows normality assumption and so the equation is applicable.

Figure 10 shows the pattern of actual (observed) volume by VOCAL and estimated endometrial volume by equation is similar.

The gap between these two values may be removed by adding more variables affecting endometrial volume.

DISCUSSION

Though this study is not comparable to any as it does not correlate the 2D measurement with 3D volume measurements, any spherical/ovoid structure measured by a single diameter does not accurately judge the size of the same. Therefore, a mean of its three orthogonal dimensions is taken or volume is calculated by $x \times y \times z \times 0.523$. But to measure an irregular structure like endometrium, it is even more difficult to calculate the volumetry. With 3D ultrasound, we can now measure volume accurately and reliably for any shape.²⁻¹⁰ Raine-Fenning et al.¹¹ compared the *in vitro* validity and reliability of different 3D ultrasound methods for assessment of volumes

Fig. 8: 3D ultrasound image with VOCAL calculated endometrial volume

Table 1: Equation summary

Multiple regression for volume	Multiple R	R^2	Adjusted R^2	Standard error of estimate	Rows ignored	Outliers
Values	0.7129	0.5082	0.4953	1.185	0	1

Multiple regression obtained for volume when multivariate regression analysis is carried out using Excel add in stat tool software using uterine length, effective endometrial length, endometrial thickness, and endometrial transverse section on the volume obtained by VOCAL. $R^2 = 0.5082$ indicates that almost 50% of the variation in the endometrial volume has been explained by the considered independent variables in the equation 1. One outlier is also present in out data

Table 2: ANOVA

ANOVA	Degrees of freedom	Sum of squares	Mean of squares	F	p value
Explained	4	220.639	55.15	39.26	<0.0001
Unexplained	152	213.516	1.40		

ANOVA, analysis of variance

When ANOVA was applied during multivariate regression analysis using Excel add in stat tool software, the analysis shows that the equation is significant as R^2 (coefficient of determination) is significant (F-Statistics is: 39.26 whose p value is <0.0001).

Table 3: Regression coefficients

Regression table	Coefficient	Standard error	t value	p value	Confidence interval 95%	
					Lower	Upper
Constant	-2.753*	0.7345	-3.748	0.0003	-4.2043	-1.3019
Uterine length	0.2830*	0.1101	2.569	0.0112	0.0654	0.5005
Effective endo length	0.3*	0.1477	2.0269	0.0444	0.00757	0.5914
Endo thickness	2.923*	0.2885	10.129	<0.0001	2.3529	3.4931
Endo length in transverse section	0.1130	0.114	0.990	0.3237	-0.1124	0.3383

*Significant at 5% level of significance.

Regression coefficients obtained by multivariate regression analysis shows uterine length (p value 0.0112), effective endometrial length (p value 0.0444), endometrial thickness (p value < 0.0001) are significant (values with * indicate significant at 5% level of significance). Endometrial length in transverse section (p value 0.3237) is not significant. This shows that variation in volume mostly depends on endometrial thickness, uterine length and effective endometrial length and least depends on endometrial length in transverse section

and reported that the multiplanar and VOCAL methods with 3D ultrasound yielded similar results, although the rotational VOCAL was superior to the multiplanar method for objects with irregular shape. Although these investigators did not observe any significant differences in the measurements obtained using different steps of rotation (VOCAL, 6°, 9°, 15°, and 30°), reliability increased in direct proportion to the number of planes used, i.e., with smaller steps of rotation. In a recent publication, Rousian et al.¹² analyzed the accuracy and reproducibility of the VOCAL, inversion mode, ultrasonographic automatic volume calculation, and V-scope methods *in vitro*

(using small-volume phantoms) and *in vivo* (measuring the yolk sac). According to these authors, VOCAL (15° and 30°) had high intraobserver and interobserver reproducibility and good accuracy. Another study assessing fetal bladder volumes confirmed that VOCAL with 15° and 30° was reproducible and concordant.⁷ Barreto et al.⁹ suggested that the multiplanar (5 mm), VOCAL (30°), and XI VOCAL (5, 10, 15, and 20 planes) methods are reproducible and valid methods for estimating volumes. The XI VOCAL method tended to be superior to the others, especially in the assessment of objects with irregular shape. The measurements obtained using XI VOCAL with

Table 4: Equation summary

Multiple regression for volume	Multiple R	R^2	Adjusted R^2	Standard error of estimate	Rows ignored	Outliers
Values	0.7239	0.5241	0.5115	1.1119368	0	0

After removing the value which was shown as outlier, multiple regression obtained for volume by multivariate regression analysis using uterine length, effective endometrial length, endometrial thickness, and endometrial transverse section on the volume obtained by VOCAL. R^2 is increased from 50% to 52% after removing outlier value, showing 2% increase in R^2 (coefficient of determination). $R^2 = 0.5241$ indicates that almost 52% of the variation in the endometrial volume has been explained by the considered independent variables in the equation 2, which was 50% with equation 1

Table 5: ANOVA

ANOVA	Degrees of freedom	Sum of squares	Mean of squares	F	p value
Explained	4	208.333	52.083	41.567	<0.0001
Unexplained	151	189.201	1.253		

ANOVA, analysis of variance

Again by using ANOVA after removing the outlier, R^2 (coefficient of determination) = 0.5241 is significant (F-Statistics is: 41.567 whose p value is <0.0001). Showing that the equation 2 is significant

Table 6: Regression coefficients

Regression table	Coefficient	Standard error	t value	p value	Confidence interval 95%	
					Lower	Upper
Constant	-2.6043*	0.6946	-3.7495	0.0003	-3.976571521	-1.231949144
Uterine length	0.2662*	0.1041	2.5569	0.0115	0.06049164	0.47182685
Effective endo length	0.3194*	0.1396	2.2877	0.0235	0.043549932	0.595313428
Endo thickness	2.841*	0.2732	10.400	<0.0001	2.301272547	3.380720118
Endo length in transverse section	0.0954	0.1078	0.8847	0.3777	-0.117645568	0.308421037

Regression coefficients obtained by multivariate regression analysis shows uterine length (p value 0.0115), effective endometrial length (p value 0.0235), endometrial thickness (p value < 0.0001) are significant (values with * indicate significant at 5% level of significance). Endometrial length in transverse section (p value 0.3777) is not significant. This shows that after removing outlier also variation in volume mostly depends on endometrial thickness, uterine length and effective endometrial length and least depends on endometrial length in transverse section

Fig. 9: Histogram of residuals

10 planes was closest to the real volumes of the objects. Ruano et al. conducted a survey of fetuses with congenital diaphragmatic hernia (CDH) and demonstrated that VOCAL is more accurate compared with other methods when employed in the *in vivo* setting.¹³ Studies by Rousian et al.¹², Peixoto-Filho et al.⁷, Barreto et al.⁹ and Ruano et al.¹³ though compared 3D methods, there is no correlation between 2D and 3D data, so are not comparable with our study.

A study by Peralta et al.¹⁴ concluded that the lungs of CDH fetuses have very irregular external surfaces and this fact could justify the higher accuracy of VOCAL method in measuring these structures. One of the main advantages of this method compared with multiplanar is that the studied structure outline may be modified in each presented plan during measurement, allowing more precise assessment of irregular objects.¹⁶ These studies can to some extent

Fig. 10: Graphical presentation of actual and estimated values of endo volume

be compared with our as both relate the size assessment method for structure with irregular shape, though not completely as there is not a correlation of 2D with 3D measurements. Thus, there are several studies that have shown superiority of 3D ultrasound and VOCAL for assessment of the volume of irregular shapes. Our study is unique, to our knowledge, as there is no similar study is seen where a correlation between 2D measurement and volume calculated by 3D ultrasound is compared. Though complicated, we have been able to derive an equation by which from 2D parameters 3D volume can be calculated fairly accurately. Very interestingly, we have also been able to establish a strong parallel correlation between the volume calculated by 3D ultrasound VOCAL and the predicted volume from the equation.

CONCLUSION

The study concludes that endometrial volume calculated by 2D parameters can be 52% related to volume calculated by VOCAL; we require more 2D parameters to be included in the formula if we want to calculate volume by 2D to make it more accurate.

According to these results, the most correlating 2D parameters with 3D calculated endometrial volume were endometrial length and endometrial thickness.

This also conveys that when endometrium is evaluated by 2D ultrasound for its receptivity, it is essential to include endometrial length along with endometrial thickness for better prediction or evaluation of endometrial receptivity.

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