INTRODUCTION

Why is it important to evaluate the cervical volume and vascularization 3-dimensionally during pregnancy?

Prematurity is a major cause of perinatal morbidity and mortality despite improved postnatal care. Consequently, identification of risk factors and early cervical changes associated with preterm birth is an important area of investigation.

Sonographic evaluation of the cervix provides information which is not available by digital examination. Recent studies have shown that incompare to transabdominal ultrasound, transvaginal ultrasound provides a more reliable and objective evaluation of the uterine cervix, demonstrating that the shorter the length of the cervix the higher the risk of preterm delivery. The measurement of cervical volume could even better reflect cervical morphology. Three-dimensional (3D) imaging combined with power Doppler, theoretically provides the possibility to assess the volume and quantify the power Doppler signal in the whole target organ, whereas information from 2D ultrasound on vascularization and blood flow is restricted to a single subjectively chosen 2D plane. The measurement of cervical indices is reproducible and could be used in clinical practice and research to determine the changes of the cervical morphology and vascularization in pregnancy. Consequently, further studies of 3D ultrasound imaging of the cervix in pregnancy and clinical correlations to obstetrical events are required for better understanding the physiology and functional pathophysiology of the cervix during pregnancy.

Key Words: Three-dimensional ultrasound, VOCAL, cervical volume, power Doppler.
tissue in both tension and compression tests. Further, collagen extractability, sulfated glycosaminoglycan (GAG) content and hydration were substantially higher in the pregnant cervix. Additionally, estrogen and progesterone metabolism is regulated in cervical tissues during pregnancy.

Dynamic changes in cervical length are present at early gestation and long before delivery and can be observed either spontaneously or associated with contractions, fetal movements or peristalsis. (Fig. 3)

The recent data indicate that cervical ripening during parturition involves localized regulation of estrogen and progesterone metabolism through a complex relationship between cervical epithelium and stroma, and that steroid hormone metabolism in cervical tissues. The uterine cervix undergoes changes during pregnancy and labor that transform it from a closed, rigid, collagen dense structure to one that is distensible and dilates sufficiently to allow birth. The cervix then rapidly alters to a closed, undistensible structure after birth.

Preparturition remodeling is characterized by increased synthesis of hyaluronan, decreased expression of collagen assembly genes and increased distribution of inflammatory cells into the cervical matrix. Postpartum remodeling is characterized by decreased hyaluronan (HA) content, increased expression of genes involved in assembly of mature collagen and inflammation.

Dynamic Cervical Changes Due To Pregnancy

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DYNAMIC CERVICAL CHANGES DUE TO PREGNANCY

Three-dimensional ultrasonography has been previously shown to be accurate and highly reproducible in volume measurements of many irregularly shaped organs. The latter has also the potential to provide more accurate volume measurements than does conventional 2D ultrasound. Bega et al has also suggested that 3D ultrasound is offering a more complete assessment of the cervix than 2D ultrasound whereby multiplanar correlation showed that the standard latter procedure in the sagittal view may under- or overestimate cervical length. Farrel et al have shown that 3D volume estimation of the non-pregnant cervix is unreliable and inaccurate and therefore should not be applied in clinical practice. However, the results of their study cannot be applied to the pregnant uterus.

Hoesli et al were unable to show an additional
clinical benefit of the volume measurement of the cervix as compared to length measurement among 55 patients but demonstrated a good correlation between cervical length and cervical volume without differences between the normal cervix and the short cervix groups.\textsuperscript{13} The accuracy of 3D sonography in volume estimation of cervical carcinoma suggested that 3D measurements were more accurate than 2D assessments.\textsuperscript{14} There is evidence that angiogenic factors may play a role in cervical ripening and the birth process, therefore it would be valuable to know how cervical blood circulation changes during pregnancy.\textsuperscript{15}

The ability to save and store volumes of US data for later analysis is also of great advantage and opens up new possibilities for clinical networking and consultation.\textsuperscript{6,7,15}

WHAT IS THE POWER DOPPLER ANGIOGRAPHY AND THE VIRTUAL ORGAN COMPUTER-AIDED ANALYSIS IMAGING PROGRAM (VOCAL) FOR CERVICAL EVALUATION?

One of the latest technical achievements in the field of ultrasonography is 3D imaging combined with power Doppler, which provides the potential to quantify power Doppler signals in a whole organ.\textsuperscript{15} (Fig. 4) Few studies are available to describe the application of transvaginal 3D ultrasonography, power Doppler angiography (PD) and The Virtual Organ Computer-aided Analysis imaging program (VOCAL) for cervical evaluation.\textsuperscript{15–18}

VOCAL is a software, which is integrated into the 3D ultrasound system, which is used to calculate cervical volume (cm\textsuperscript{3}) and power Doppler flow indices from the orthogonal multiplanar views of the cervix obtained from the volume acquired. (Fig. 5 a,b).

Using the histogram facility of the VOCAL software the following Doppler indices can be calculated: Vascularization index (VI), flow index (FI) and vascularization flow index (VFI). VI is the ratio of the number of color voxels to the total number of voxels (voxel = smallest unit of volume) in the region of interest, and it reflects the density of blood vessels.

FI is calculated as the sum of weighted color voxels divided by the number of color voxels, and is related to the energy reflected from the blood corpuscles in the vessels in the region of interest, i.e. the more blood corpuscles the higher the FI values. VFI is the sum of weighted color voxels divided by the total number of voxels. It reflects both the density of blood vessels and the number of blood corpuscles flowing in the blood vessels. Normalized values for VI, FI and VFI vary between 0 and 100.\textsuperscript{15–19}

![Figure 4. 3D US combined with Power Doppler of the cervix in the 26th weeks of pregnancy using the glass body appereance mode.](image)

![Figure 5. a. 3D Ultrasound measurement of cervical volume by VOCAL. b. Multiplanar cervical images: upper left (the cervix is shown demarcated by lines), upper right and lower left quadrants show longitudinal, transverse and coronal planes of the cervix respectively. Lower right image shows the resultant 3D image of the cervix.](image)
WHAT IS THE TECHNIQUE TO CALCULATE THE CERVICAL VOLUME AND VASCULARIZATION INDICES WITH 3D US VOCAL TECHNIQUE?

The patient must be examined in the lithotomy position with an empty bladder. The ultrasound probe must be slowly introduced into the vagina and care must be taken to avoid undue pressure on the cervix. After a satisfactory gray-scale image of the cervix had been obtained, the probe can be withdrawn until the image become blurred. Then the probe can be gradually advanced again with only enough pressure to restore a satisfactory image. A sagittal view of the cervix where the internal os, the cervical canal and the external os were all seen at the same time must be obtained. (Fig. 6) The system can then be switched into the power Doppler mode and then into the 3D mode. The cervix must be centralized within the 3D sector appearing on the ultrasound screen, and data can be obtained by holding the transducer stationary while its crystals were mechanically rotated across the sector with a sweep angle of 90°. The fast volume acquisition (low resolution) setting can be preferred to minimize periodic flashing artifacts arising from pulsation of the uterine arteries and from fetal movements. The duration of the volume acquisition is usually 15–20 s depending on the dimensions of the 3D sector.15–18

Drawing must be started and continued from the same chosen section through the cervix namely “reference image”. The rotation steps can be 6°, 9°, 15°, 30°. For example, if you choose rotation steps as 30°, you need to draw the contours of the cervix six times manually using the roller ball cursor of the system or with your fingers on the digital screen.

Once the contour of the cervix is defined, the VOCAL program automatically calculates the volume and power Doppler vascularization index, flow index and vascularization-flow index.

IS THERE ANY MAJOR CHANGE IN CERVICAL VOLUME DURING THE PREGNANCY CALCULATED BY 3D US?

A recent study resulted that there is no statistically significant change in cervical volume with gestational age. However cervical volume was found to be slightly smaller at 41 weeks than it was at 17–40 weeks’ gestation. Cervical flow indices also did not change. However they noted that this does not exclude the possibility of too small vascular changes which is not detectable with the rather crude Doppler ultrasound technique.

Table 1. Reference values (minimum, percentiles and maximum) for cervical volume and blood flow indices as assessed by three-dimensional power Doppler ultrasound from 17 to 41 gestational weeks.15

<table>
<thead>
<tr>
<th></th>
<th>Min</th>
<th>10th</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
<th>90th</th>
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<tr>
<td>Volume(cm³)</td>
<td>12.5</td>
<td>22.0</td>
<td>26.0</td>
<td>32.3</td>
<td>39.7</td>
<td>51.3</td>
<td>75.6</td>
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<tr>
<td>17-40 weeks</td>
<td>13.8</td>
<td>24.8</td>
<td>31.6</td>
<td>38.4</td>
<td>47.9</td>
<td>57.5</td>
<td>81.0</td>
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<td>7.9</td>
<td>8.7</td>
<td>18.7</td>
<td>22.8</td>
<td>34.5</td>
<td>43.1</td>
<td>44.7</td>
</tr>
<tr>
<td>Para</td>
<td>14.9</td>
<td>15.0</td>
<td>22.2</td>
<td>31.5</td>
<td>41.4</td>
<td>51.1</td>
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<tr>
<td>VI (%)</td>
<td>0.2</td>
<td>1.2</td>
<td>1.7</td>
<td>3.1</td>
<td>4.9</td>
<td>8.0</td>
<td>27.8</td>
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<tr>
<td>17-30 weeks</td>
<td>0.1</td>
<td>1.6</td>
<td>2.8</td>
<td>5.3</td>
<td>9.2</td>
<td>15.4</td>
<td>24.9</td>
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<tr>
<td>Nulliparae*</td>
<td>0.1</td>
<td>1.4</td>
<td>2.5</td>
<td>4.9</td>
<td>7.7</td>
<td>12.3</td>
<td>29.1</td>
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<tr>
<td>Para</td>
<td>31-41 weeks</td>
<td>0.1</td>
<td>0.3</td>
<td>0.5</td>
<td>0.9</td>
<td>1.5</td>
<td>2.8</td>
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<tr>
<td>VFI</td>
<td>0.1</td>
<td>0.3</td>
<td>0.5</td>
<td>0.9</td>
<td>1.5</td>
<td>2.8</td>
<td>10.9</td>
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<tr>
<td>17-30 weeks</td>
<td>0.1</td>
<td>0.4</td>
<td>0.8</td>
<td>1.6</td>
<td>3.1</td>
<td>4.7</td>
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<tr>
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*The difference between nulliparous and parous women is statistically significant (P<0.0001). Fl, flow index; VFI, vascularization flow index; VI, vascularization index.
Reference values for cervical volume and blood flow indices as assessed by 3D PD US have been established for the second half of pregnancy.

A recent study including 352 nulliparous and 291 parous women who delivered at term underwent transvaginal 3D power Doppler ultrasound examination of the cervix at 17 to 41 weeks’ gestation.\textsuperscript{15} (Table 1).

Why is it difficult to measure the cervical volume?

Although volume is a common unit for classification and comparison, some authors suggest that this method seems difficult for the cervix because the sonographic demarcation between the cervix, the lower uterine segment and the surrounding vaginal tissue is not clear.\textsuperscript{13,16,17} (Fig. 7)

Figure 7. The resultant 3D volume image of the cervix by glass body appearance mode.

What kind of reasons can effect the reproducibility of the cervical volume and vascularization measurements?

Two main sources of intraobserver and interobserver variability that are related to 3D sonographic volume measurement are associated with 3D-volume acquisition and the variability associated with contour definition.\textsuperscript{19}

When the assessed volume of the region of interest (ROI) does not exactly correspond to the true volume of the organ, it affects accuracy of the volumes obtained and accuracy of color-scale or gray-scale indices calculated thereafter. That is why assessing the reliability of the volume acquisition in the cervix is important. If the assessment of ROI volume is not reproducible during repeated measurements, neither will be the calculation of these indices.\textsuperscript{15-19} Additionally, individual style of scanning may induce variation in the artifacts caused by the motion of the cervix and surrounding organs.\textsuperscript{15-19}

Are the inter- and intraobserver reproducibility of cervical volume calculations and quantification of power Doppler signals in cervical volumes proven?

3D ultrasound gray-scale and power Doppler measurement of cervical volume and vascularization have acceptable intra- and inter-observer variations and thus may be used in clinical research of cervical physiology and pathophysiology during pregnancy.\textsuperscript{16,17} That means, one can reliably acquire and calculate the cervical indices in pregnancy. However volumetric data were found to be more reliably acquirable than power Doppler measurements.\textsuperscript{16} The wide limits of agreement for cervical measurements using VOCAL was explained by the differences in the acquisition technique of the volume; however experienced observers, excellent ultrasound equipment, and standardized measurement technique may decrease these differences.\textsuperscript{16,17,19}

Does parity effects cervical volume and the vascular indices measured by 3D US?

The cervix of nulliparous and multiparous women have distinct morphological differences to the extent that clinicians are often able to differentiate the parous from the non-parous cervix. These morphological changes are accompanied by different intrapartum functional characteristics of the cervix such as rate of dilatation and effacement.\textsuperscript{3,20-22}

It was suggested that the normal cervix of parous women is modified by the content of water, elastin and collagen, and becomes longer and wider than that of nulliparous women.\textsuperscript{22} In addition, the changes from a cylindrical to a conic shape is more marked in nulliparous than in parous women. Women who underwent cesarean deliveries have cervical characteristics similar to nulliparas. It appears that mechanical, rather than hormonal, factors have a greater effect in determining the changes of cervical dimensions throughout pregnancy and postpartum.\textsuperscript{18,22}

These parity-related morphological and functional differences of the cervix might have sonographic correlations. There are only few studies comparing the cervical volumes and the blood flow regarding the parity. Recent two studies revealed no statistically significant differences between nulliparous and parous women.\textsuperscript{15,18}

Our results suggest that parity does not effect the cervical volume and flow indices in the pregnant women. Although there are individual differences, the cervix of parous women decreases in length and increases in width from midpregnancy to term.\textsuperscript{18}

However our study group was small and additional
studies on cervical volume and flow indices associated with gestational age, parity and prepregnancy BMI should be undertaken with a larger sample to determine the normal values and cut-off points for prediction of preterm delivery in pregnant women.

CONCLUSIONS

Recent studies suggest that the measurements of cervical indices are reproducible and may be used in clinical practice and research to determine the changes of the cervical morphology and vascularization in pregnancy. These changes appear to be important to understanding physiological reactions of the cervix to term labor as well as pathological processes in the cervix that preceede preterm labor. In addition, this information may clarify the sonographic counterparts of the clearly anatomical changes observed after birth and characterize the parous cervix.15–18 During the last year, our group has been carrying out a study to reveal about the full longitudinal reference data about the cervical volume and vascularization beginning from the first trimester of the pregnancy to postpartum period for the first time. At current stage of knowledge, however, volume and vascularity assessment of the cervix should be considered experimental and further studies of 3D ultrasound of the cervix in pregnancy are required to assess the potential of these sophisticated imaging methods.

REFERENCES