“Cervical Box”: a simple way to predict spontaneous delivery at term of pregnancy

Carlo Luchi, Giulia Posar, Francesca Monacci, Federica Arini, Arianna Carmignani, Tommaso Simoncini

Department of Experimental and Clinical Medicine, Division of Obstetrics and Gynecology University of Pisa - Pisa, Italy

ABSTRACT

Background and purpose: Cervical ripening is one of the most important factors involved in labor. The aim of the present study was to correlate the sonographic aspect of cervical ripening, expression of morpho-functional features and changes of cervix, with the success of spontaneous delivery.

Methods: 50 singleton pregnant women at term of their first pregnancy were enrolled and underwent to cervical assessment by transvaginal ultrasound. In all cases, cervical length was measured and the cervix has been qualitatively described as “hyperechoic” or “hypoechoic” compared to the echogenicity of fetal head bones. To quantify the echogenicity, histogram of gray scale of cervix was calculated with “ImageJ” software. Two groups were formed on the basis of the time lapse between cervical assessment and delivery: in the first one (group A), the delivery occurred within 96 hours, whereas in the second one (group B) after 96 hours. Statistical analysis has been applied for quantitative variables (mean value of echogenicity and cervical length) and qualitative variables (hyperechogenicity and hypoechogenicity).

Results: Data showed a significant higher echogenicity ($p<0.05$) in women who delivered within 96 hours from the examination, while no significant statistical difference has been seen in cervical length. Qualitative study of cervical echogenicity, as an indipendent predictive parameter of birth, provided a sensitivity of 78.3%, a specificity of 86.3%, a positive predictive value of 85.7% and a negative predictive value of 79.2%.

Conclusions: Cervical echogenicity might be a simple and useful parameter in clinical practice for the management of pregnancy at term.

KEYWORDS

Cervical length, cervical ripening, induction of labor, spontaneous delivery, transvaginal ultrasound.

Introduction

Delivery is a complex process involving changes of two different “compartments”: the maternal side (myometrium and cervix) and on the fetal side (fetus itself, fetal membranes) [1]. One of the most important events involved in labor is the “cervical ripening”. This process consists of three stages: “softening”, “effacement” and “dilatation” of cervix. Softening occurs independently from uterine contractile activity and it must be considered as an essential process for effacement and dilatation [2].

Late in pregnancy, modifications of glycosaminoglycans and water produce rearrangement and realignment of the collagen fibers in cervical structure [3]. Furthermore, the smooth muscle cells of cervix undergo apoptosis, a genetically timed event, which might explain the species-specific length of gestation [4].

There are many studies about cervical assessment techniques in pregnancy, the most used are based on ultrasound imaging [5]. In particular, cervical length is routinely measured by transvaginal ultrasound to predict preterm birth [6] and spontaneous labor at term, but the same studies defined the cervical length measurement at term only as moderate predictor of spontaneous delivery [7,8]. Furthermore, it is used in many algorithms for predicting successful labor induction [9-12].

The aim of the present study was to correlate the sonographic aspect of cervical ripening, expression of morpho-functional features and changes of cervix, with the success of spontaneous delivery, regardless of cervical length. We wanted propose a new technic for the management of pregnancies at 41-42 weeks of gestational, in particular about the time of induction of labor.

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Contact

Carlo Luchi; c.luchi@unipi.it

University of Pisa, via Roma 67, 57126, Pisa

Cell phone number: 0039 3358485247

Methods

The current study included 50 women between 40 and 41 weeks (280-287 days by last menstrual period) of pregnancy, attending our Division of Obstetrics for routine sonographic check of amniotic fluid. The including criteria for the study were first singleton pregnancy, absence of pregnancy complications, cephalic presentation, negative vaginal swab result for Group B streptococcus, intact amniotic membranes, no cervical excisional procedures and same Bishop Score. The study protocol was approved by the local Ethics Committee and all women gave their written informed consent.

Transvaginal sonography was carried by the same expert sonographer with Ultrasound Endocavity Transducer RIC6-12-D (13.0 Mhz) of GE Voluson E8. Cervical length was measured by transvaginal ultrasound according to the Fetal Medicine Foundation criteria (www.fetalmedicine.com). A sagittal view of the cervix with no compression was obtained. The image was zoomed until the cervix occupied at least two-thirds of the screen, the gain was adjusted to obtain a clear view of the cervical canal and cervical length was measured by placing the calipers on the internal and external cervical os [12]. On this image, the sonographer observed the cervical gland area (around the endocervical canal [13]) and subjectively described this region as "hyperechoic" or "hypoechoic" compared to the intensity of adjacent fetal head bones. (Figs. 1,2) To objectify the echogenicity, the images that were taken with same sonographic features, were processed on PC using "ImageJ", a Java-based image processing software developed by the National Institutes of Health. "ImageJ" is a simple software that can display, edit, analyze, process, save, and print color and grayscale images. It can calculate area and pixel value statistics of user-defined selections and it can create density histograms. In particular we used it to calculate the histogram of the gray scale in the cervical gland area, that we named "Cervical Box". The value obtained from the histogram is the mean echogenicity expressed with a number (0-255) (Fig. 3).

The 50 women were divided into two groups on the basis of the interval between the transvaginal ultrasound and the delivery. We had chosen an interval of 96 hours, because in our Hospital, the induction of labour is proposed at 41+3 (290 days) weeks; therefore 96 hours represented the interval to 42 weeks, the latest term of pregnancy. The first group consisted of women that spontaneous delivered before 96 hours from the ultrasonographic valuation while the second group consisted of women that delivered or were induced after 96 hours. Data were analyzed using the Statistical Package for Social Sciences (IBPM SPSS ver.21). Quantitative data (mean echogenicity and cervical length) were described using mean and standard deviation; comparison in two groups was conducted using independent t-test of Student. Qualitative data (hyperchogenicity and hypoechogenicity) were described using numbers and percents and were analyzed using the Chi-square test. Comparison of qualitative data with the time of delivery provided the sensitivity, the specificity, positive predictive value and negative predictive value. In this study, the true positive was the woman with hyperechoic cervix that delivered before 96 hours, while the true negative was the woman with hypoechoic cervix that delivered after 96 hours. A *P* value <0.05 was considered to be statistically significant. We considered to create a ROC Curve, but we considered no important to identify a numerical cut off of echogenicity, because in clinical practice was more useful a qualitative valuation of echogenicity.

Figure 1 "Hypoechoic" cervix. Yellow box is the region of interest, that we called "Cervical Box".

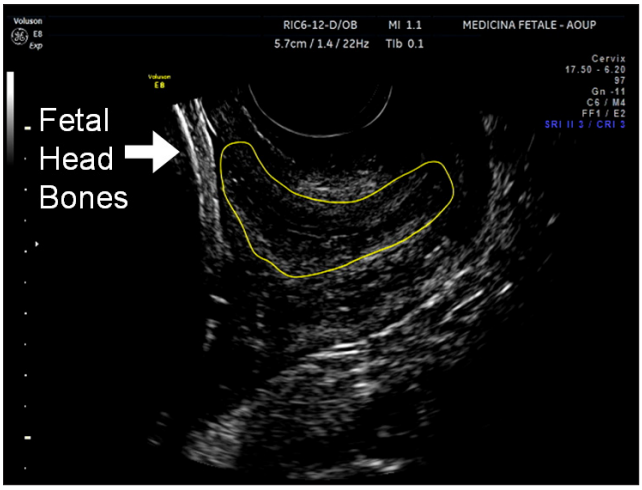


Figure 2 "Hyperchoic" cervix. Yellow box is the region of interest, that we called "Cervical Box".

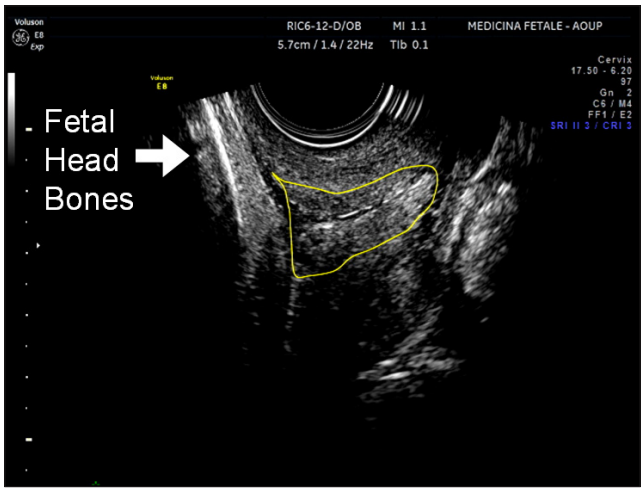
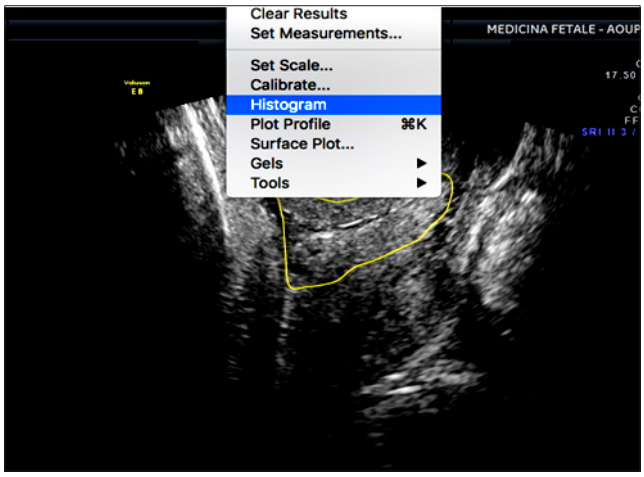


Figure 3 Calculation of "Cervical Box" echogenicity with "Image J".



Results

A total of 50 nulliparous pregnant women at term entered in the study. Among these 50 women, 5 were excluded because they delivered by cesarean section before 96 hours. For the cohort as a whole, the mean gestational age at sampling was 282 (278-287) days, and the mean gestational age at delivery was 287 (280-290) days. Delivery within 96 hours of sampling occurred in 23 (51%) cases. Demographic characteristics are showed in Table 1.

Table 1 Clinical variables of women who gave birth within or after 96 hours of enrollment.

Variables	Women delivering before 96 hours (n=23)	Women delivering after 96 hours (n=22)	Significance*
Maternal Age	30.6 ± 5.8	31.1 ± 4.3	NS
Race	100% white	100% white	NS
Parity	100% primiparous	100% primiparous	NS
Smoking	100% no	100% no	NS
GA at enrollment, day	282.4 ± 4.4	281.6 ± 1.9	NS

*Values are mean ± SD. Abbreviations: **GA**, gestational age; **NS**, not significance. *The student t-test between two groups.*

Table 2 Quantitative data in women delivering before and after 96 hours.

Variables	Women delivering before 96 hours (n=23)	Women delivering after 96 hours (n=22)	Significance*
Cervical length (mm)	22.5 ± 8.2	25.2 ± 6.1	NS
Echogenicity of Cervical Box (number 0-255)	79.1 ± 24.6	64.9 ± 15.0	P< 0.05

*Values are mean ± SD. Abbreviations: **GA**, gestational age; **NS**, not significance. *The student t-test between two groups.*

There was no difference in age, race, parity, history of smoking, or gestational age at enrollment between the two groups.

About the quantitative data, the mean of cervical length was no statistically different between the groups, instead the mean of cervical echogenicity in group of women which delivered within 96 hours was statistically higher than in group of women which delivered after 96 hours (Table 2).

The mean of cervical length in all participants was 23.8 mm and the distribution is shown in Figure 4. There was a linear trend between cervical length and interval to delivery time, but not a statistically significant difference between two groups.

The mean of "Cervical Box" echogenicity in all participants was 72.2 (number 0-255) and the distribution is shown in Figure 5. There was a statistically significant difference between two groups and also there was a linear trend between the value of echogenicity and the interval to delivery time. The qualitative data are shown in Table 3. The expert sonographer defined 21 (47%) cervix as "hyperechoic", while 24 (53%) cervix as "hypoechoic". A total of 18 women of 21 with hyperechoic cervix delivered within 96 hours while 19 women of 24 with hypoechoic cervix delivered after 96 hours.

There was an association between "hyperechoic" cervix and delivery within 96 hours according to statistically significant level (Chi-square test p<0.01; RR and 95% CI 4.11 - 1.85-9.15). Furthermore, the obtained data showed that the study of cervical echogenicity, as a diagnostic test, provided a sensitivity of 78.3%, a specificity of 86.4%, a positive predictive value of 85.7%, and a negative predictive value of 79.2%. (Table 4).

Figure 4 Association between interval to delivery time and cervical length.

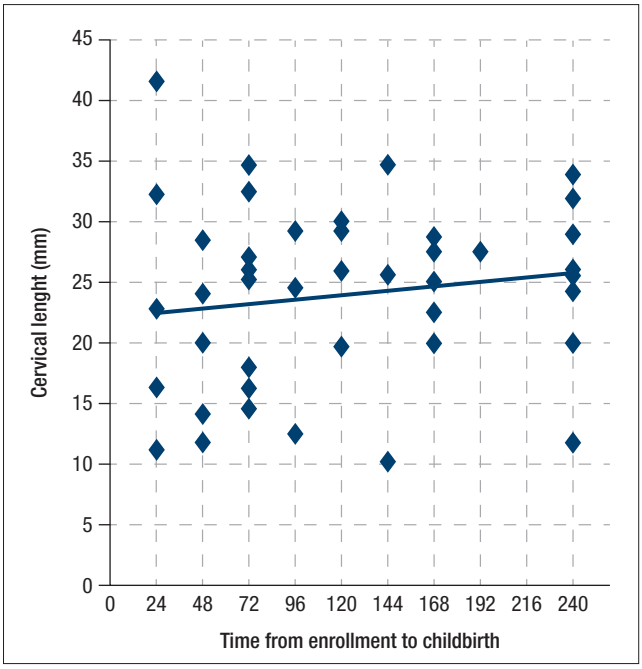


Figure 5 Association between interval to delivery time and cervical box echogenicity.

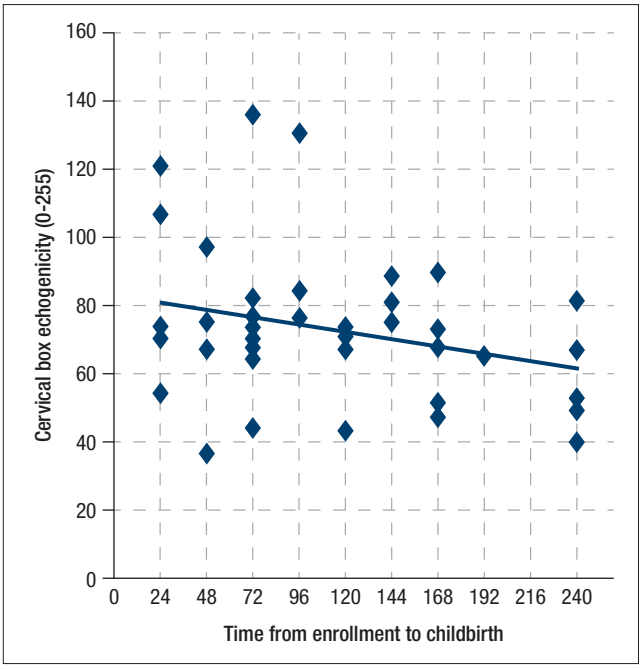


Table 3 Clinical features of women about cervical echogenicity and development time of delivery.

Variables	Women delivering before 96 hours	Women delivering after 96 hours	Tot
Hyperechoic cervix	18	3	21
Hypoechoic cervix	5	19	24
Total	23	22	45

Table 4 Probability of delivery by cervical echogenicity.

Variables	Sn	Sp	PPV	NPV	significance*	RR and 95% CI
Echogenicity	78	86	86	79	<0.01	4.11(1.85-9.11)

*Abbreviations: **Sn**, sensitivity; **Sp**, specificity; **PPV**, Positive Predictive Value, **NPV**, Negative Predictive Value; **RR**, relative risk; **CI**, confidence interval. *Chi- square test.*

Discussion

In the last few years, a consistent amount of studies regarding the use of the ultrasound technique in labor and delivery [14,15] and in the prediction of successful labor induction [9-12] has been published.

The goal of the present study was to highlight the importance of obstetric ultrasound based on cervical echogenicity for the prediction of the spontaneous delivery at term.

Our results showed a significant correlation between hyperechoic aspect of cervix and delivery within 96 hours. In particular, we found an increased echogenicity of cervical gland area, compared to the adjacent fetal head bones. These features could be associated with cervical ripening and more likely with the apoptosis of muscular cells that occurs in the softening phase of cervix. This hypothesis agrees with the high frequency ultrasound imaging study performed by Czarnota *et al*. which showed that the areas of tissue undergoing apoptosis become much brighter in comparison to surrounding viable tissues [16].

McFarlin *et al*. described the decreasing ultrasonic attenuation of cervical tissue in pregnancy. In ultrasound, attenuation of tissue has been observed to decrease significantly as water concentration increases and density decrease, so the tissue appears more echogenic: during ripening process the cervical tissue decreases in collagen concentration and increases in water. McFarlin *et al*. demonstrated that the rat cervix had a significant decreased attenuation during the pregnancy progression toward full-term and they associated it with cervical ripening, concluding that ultrasonic attenuation estimates could be an objective non-invasive method to detect interval between examination and delivery [17,18].

Kim *et al*. proposed a correlation between the days to delivery and the difference of gray scale histogram between anterior and posterior lip of cervix, related to cervical ripening process [19].

Focusing on a different gestational age, Tekensin *et al*. elaborated a quantitative assessment of cervical structure by gray-scale analysis to predict tissue changes in women with preterm labor. Their model related with the risk of preterm delivery more than cervical length, Bishop score or uterine contractions [20].

Furthermore, the present study demonstrates that cervical length measurement at term might not be considered as a predictor of spontaneous delivery. The two studied groups of women displayed no significant difference about cervical length. Interestingly, the mentioned observation is in contrast with many studies proposing cervical length as a predictor of delivery at term. However, the same studies defined the cervical length measurement at term only as moderate predictor of spontaneous delivery [7,8]. Cervical length measurement is recommended preferably to predict preterm delivery and at risk populations [21].

In conclusion, our findings demonstrate that the study of cervical echogenicity, which can be achieved easily and with minimal discomfort to the patient, is able to provide a useful prediction of the likelihood of vaginal delivery within 96 hours. This important feature can allow the obstetricians to encourage and reassure the patient in a moment extremely full of expectations for unborn [22]. Furthermore, the study wants to propose a possible use of this new ultrasound technique, that we could name "Cervicography", for the management of pregnancies at 41-42 weeks of gestational: the time of induction of labor could be delayed in order to promote spontaneous onset of labor and delivery, up to 42 weeks, decreasing the costs and the complications related to induction itself [23].

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